R-1190

原本

最　終　報　告　書

サリチル酸ベンジル：
ラットを用いた経口投与による反復投与毒性･生殖発生毒性併合試験

試験番号：R-1190

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試験施設
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1. GLP 陳述書

試験番号　　:　　R-1190

試験表題　　:　　サリチル酸ベンジル:ラットを用いた経口投与による
反復投与毒性・生殖発生毒性併合試験

本試験は以下に示す基準を遵守して実施したものです。

- 「新規化学物質等に係る試験を実施する試験施設に関する基準」
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[redacted]

試験責任者
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3. 試験実施概要

3.1 試験番号

R-1190

3.2 試験表題

サリチル酸ベンジル：ラットを用いた経口投与による反復投与毒性･生殖発生毒性併合試験

3.3 試験目的

本試験は、動物に被験物質を一定期間反復投与したときに現れる被験物質の一般毒性及び生殖発生毒性を明らかにすることを目的とした。

3.4 試験委託者

厚生労働省　医薬・生活衛生局　医薬品審査管理課　化学物質安全対策室
〒100-8916　東京都千代田区霞が関 1-2-2

3.5 試験受託者

株式会社ボゾリサーチセンター
〒151-0065　東京都渋谷区大山町 36-7

3.6 試験実施施設

3.6.1 試験施設

株式会社ボゾリサーチセンター　御殿場研究所
〒412-0039　静岡県御殿場市かまど 1284

3.6.2 試験場所（血中ホルモン測定）

株式会社ボゾリサーチセンター　つくば研究所
〒300-2611　茨城県つくば市大久保 8

3.7 被験物質

製造者	:	東京化成工業株式会社
名称	:	サリチル酸ベンジル
英語名称	:	benzyl salicylate
CAS 番号	:	118-58-1
官報公示整理番号	:	(3)-3044, (3)-1570
入手日	:	2016 年 9 月 27 日

3.8　試験日程

試験開始日　：　2016 年 10 月　4 日
被験物質出庫日　：　2016 年 10 月 18 日
動物入荷日　：　2016 年 10 月　5 日
実験開始日（投与開始日）
：　2016 年 10 月 27 日
交配開始日　：　2016 年 11 月 10 日
分娩開始日　：　2016 年 12 月　2 日
母動物剖検開始日　：　2016 年 12 月　7 日
投与終了剖検日　：　2016 年 12 月　8 日　（雄及び非交配群雌）
回復開始日　：　2016 年 12 月　8 日
回復期間終了剖検日：　2016 年 12 月 22 日
動物試験終了日　：　2016 年 12 月 22 日
実験終了日（病理組織学検査終了日）
：　2017 年　2 月 13 日
試験終了日　：　2017 年　3 月 XX 日

3.9　試験責任者

株式会社ボゾリサーチセンター　御殿場研究所　研究部門
[redacted]

3.10　試験担当者

試験主担当者　：
被験物質保存責任者：
臨床検査責任者　：
化学分析責任者　：
血中ホルモン測定責任者
：
病理検査責任者　：
[redacted]

3.11　試験成績の信頼性に影響を及ぼしたと思われる環境要因

本試験に関し､試験成績の信頼性に影響を及ぼしたと思われる環境要因はなかった。

3.12　予見することができなかった試験の信頼性に影響を及ぼす疑いのある事態及び試験計画書に従わなかったこと

病理組織学検査標本作製において、2 例（動物番号：4001、5101）で上皮小体（両側）がスライド標本から欠落した。しかし、各群 1 例のみであり、他の動物では上皮小体への被験物質の影響は評価可能であったことから、試験成績へ及ぼす影響はない

と判断した。

以上の他には本試験に関し、試験の信頼性に影響を及ぼす疑いのある事態及び試験計画書に従わなかったことはなかった。

3.13　資料保存

株式会社ボゾリサーチセンターの保存方法に従い、試験計画書（変更書を含む）原本、記録文書、生データ、報告書類（最終報告書は原本）及び標本（被験物質保存サンプルを含む）は株式会社ボゾリサーチセンター御殿場研究所の資料保存施設に最終報告書提出後 10 年間保存する。期間終了後の保存については、厚生労働省と株式会社ボゾリサーチセンター間で協議し、その処置を決定する。ただし、長期保存に耐えられない生体試料（尿、血漿）及び腟垢標本については、試験終了までに試験施設で、血中ホルモン測定終了後の残余血清については試験場所で廃棄した。また、死産児、死亡児及び生後 4 日生存児については、出生率及び生後 4 日生存率に被験物質投与の影響が認められたため保存した。

3.14　試験責任者の記名・押印

[redacted]

4. 要約

サリチル酸ベンジルをコーン油に溶解し、30、100 及び 300 mg/kg の投与量で Sprague-Dawley 系 SPF ラット（交配を行う雄及び交配群雌各 12 匹/群、交配を行わない非交配群雌として対照群及び 300 mg/kg 群に各 10 匹を追加）の雄には交配前 14 日間に加え交配期間を通して剖検前日まで（42 日間）、交配群雌には交配前 14 日間に加え交配期間及び妊娠期間を通して授乳 4 日まで（41~46 日間）、非交配群雌には 42 日間、更に 300 mg/kg 群の交配群雌で認められた妊娠期間中に全胚が死亡し吸収されたため、妊娠 25 日に未分娩であった動物（以下、妊娠期間中全胚吸収例）、分娩日（哺育 0 日）に全出産児が死亡した動物（全出産児死亡例）、哺育期間中全出生児死亡例では剖検の前日まで（38~53 日間）強制経口投与し、反復投与毒性及び生殖発生毒性を検討した。更に、0 及び 300 mg/kg 群の一部の動物（雄 5 匹と非交配群雌 5 匹）については、42 日間投与した後 14 日間の回復期間を設け、毒性変化の可逆性を検討した。なお、対照群には媒体であるコーン油を投与した。

4.1 反復投与毒性

1) 投与終了時検査

300 mg/kg 群の雌雄では詳細な一般状態の観察においてハンドリング時の発声及びハンドリングに対する反応の亢進がみられた。

摂餌量では 300 mg/kg 群の雄及び非交配群雌で投与後期に増加が認められた。

尿検査の結果、300 mg/kg 群の雄では尿量並びにナトリウム及び塩素の 1 日排泄量の高値がみられた。

血液学検査の結果、投与終了時には 300 mg/kg 群の雄及び非交配群雌で血小板数の低値及び活性化部分トロンボプラスチン時間の延長、雄及び交配群雌の妊娠期間中全胚吸収例では白血球数の低値傾向、交配群の雌で血小板数の低値傾向、雄でプロトロンビン時間の延長及びフィブリノーゲン量の高値が認められた。

血液化学検査の結果、300 mg/kg 群の雄及び非交配群雌では AST、ALT 及び ALP 並びに A/G 比の高値傾向が、雄ではアルブミンの高値及び総たん白質の低値、300 mg/kg 群の交配群雌では A/G 比の高値傾向が認められ、これらの変化は被験物質による肝臓への影響を示唆するものと考えられた。この他、雌交配群の 100 mg/kg 群で γ-GTP の高値がみられた。A/G 比の高値は、100 mg/kg 群の交配群雌においても認められた。300 mg/kg 群の非交配群の雌ではカルシウムの低下が認められたが、この変化は病理組織検査で大腿骨（骨髄）の骨梁が増加していたことに伴う変化と考えられた。300 mg/kg 群の非交配群雌ではトリグリセライドの有意な高値、交配群雌では高値傾向が認められたが、いずれも、同群で血中 T_4 濃度が低下していることから、これに伴う変化と考えられた。この他、300 mg/kg 群の雄でグルコースの低値、非交配群の雌でナトリウムの高値がそれぞれみられた。

100 mg/kg 以上の群の雄、300 mg/kg 群の非交配群雌では T_4 濃度の低値が、100 mg/kg

以上の群の交配群雌では T_4 濃度の低値傾向が認められたが、T_3 濃度には変化がみられなかった。

器官重量測定の結果、100 mg/kg 以上の群の雄、300 mg/kg 群の交配群雌及び非交配群雌で胸腺重量の低値傾向、300 mg/kg 群の雄で精巣上体重量の低値又は低値傾向、300 mg/kg 群の雄及び交配群雌で肝臓重量の高値又は高値傾向が認められたが、胸腺以外は被験物質投与によると考えられる病理組織学的変化を伴わなかった。

剖検の結果、交配群雌の 3 例で乳腺の発達不良がみられ、1 例で子宮内受胎産物の残存が認められたが、子宮内受胎産物の残存は胚が吸収されていく過程の像と考えられた。乳腺の発達不良を示した例はいずれも妊娠期間中全胚吸収例であり、出生児の哺乳による刺激をまったく受けていないことが、原因の一つであると考えられた。

病理組織学検査の結果、300 mg/kg 群の雄、交配群雌及び非交配群で、大腿骨（骨髄）の骨梁の増加、300 mg/kg 群の雄及び交配群雌で胸腺の萎縮が認められた。

2) 回復期間終了時検査

雄でカルシウム及び無機リンの高値が認められたが、この変化は投与終了時にみられた増加した大腿骨（骨髄）骨梁が、被験物質の投与を中止したことに伴い、分解され回復していく過程で起こった変化と考えられた。また、雄で A/G 比の高値及びグルコースの低値が認められたが、この変化は投与終了時に認められた変化が残留しているものと判断した。

この他、雄では平均赤血球容積、単球数、胸腺、腎臓及び精嚢の相対重量の高値並びに好酸球百分率の低値、雌では自発運動量の一過性の高値及び体重増加量、総たん白質及び脳の絶対重量の低値が認められたが､いずれも毒性学的意義は不明であった。

4.2 生殖発生毒性

性周期、交配成績、黄体数、着床痕数、着床前死亡率、着床率及び生後 0 日の性比（出産児あるいは出生児）には変化がみられなかった。しかし、300 mg/kg 群の分娩観察では 12 例中 6 例が妊娠期間中に全胚吸収しており（妊娠期間中全胚吸収例）、1 例では全出産児が死亡児であった（全出産児死亡例）。また、生存児の得られた 5 例においても哺育期間中に全出生児が死亡した（哺育期間中全出生児死亡例）。このため、300 mg/kg 群では妊娠期間の延長、出産率、分娩率、出生率、出産児数及び出生児数の低下、死産児数の増加が認められた。300 mg/kg 群では出生した全哺育児が授乳 2 日までに死亡し、生後 4 日の生存率が低下した。300 mg/kg 群の 1 腹では死産児の 5 例で神経管閉鎖障害が認められ、被験物質による催奇形作用を否定しきれなかった。また、100 mg/kg 以上の群では、雌雄の出生児の出生日体重の低値が認められ、100 mg/kg 群では生後 4 日体重の低値傾向が、更に 30 mg/kg 群では出生日体重の低値傾向及び生後 4 日体重の低値がみられた。

以上の結果から、本試験条件下でサリチル酸ベンジルを反復経口投与することにより、300 mg/kg 群の雌雄で、AST、ALT、ALP 及び A/G 比の高値と血小板数及び T_4 の低値、白血球数の低値傾向、活性化部分トロンボプラスチン時間の延長、大腿骨の骨梁の増加、胸腺の重量低下傾向及び萎縮、肝臓重量の増加又は増加傾向が、雄でフィブリノーゲン量及びアルブミン、尿検査における尿量並びにナトリウム及び塩素の 1 日排泄量の高値、精巣上体重量の低下又は低下傾向、グルコース及び総たん白質の低値及びプロトロンビン時間の延長がみられた。300 mg/kg 群の雌では更にトリグリセライド及びナトリウムの高値、カルシウムの低値が認められた。

100 mg/kg 群では、雌雄で T_4 の低値又は低値傾向、雄で胸腺重量の低値傾向、雌で A/G 比及び γ-GTP の高値がみられ、T_4 の低値及び胸腺重量の低値傾向並びに A/G 比の高値は 300 mg/kg 群でも得られた成績であり、γ-GTP の高値は他の逸脱・誘導酵素の動きと関連していると判断した。したがって、本被験物質の反復投与毒性に対する最大無毒性量（NOAEL）は雌雄いずれも 30 mg/kg であった。

生殖発生毒性に対する最大無毒性量（NOAEL）は、雄動物では 300 mg/kg、母動物では 300 mg/kg 群で分娩以降、被験物質投与の影響が認められたことから 100 mg/kg であった。一方、児動物では生後 0 日の出生児体重が 30 mg/kg 以上の群で低値あるいは低値傾向を示したことから、30 mg/kg を下回る量と推定された。

5. 緒言

厚生労働省 医薬・生活衛生局 医薬品審査管理課 化学物質安全対策室の委託により、サリチル酸ベンジルのラットを用いた経口投与による反復投与毒性･生殖発生毒性併合試験を実施したので、その成績を報告する。

なお、本試験は以下の基準を遵守し、ガイドライン等に準拠して、株式会社ボゾリサーチセンターで実施した。

5.1 GLP

- 「新規化学物質等に係る試験を実施する試験施設に関する基準」
  （平成 23 年 3 月 31 日：薬食発 0331 第 8 号、平成 23･03･29 製局第 6 号、環保企発第 110331010 号）

5.2 毒性試験ガイドライン

- 「新規化学物質等に係る試験の方法について」
  （平成 23 年 3 月 31 日：薬食発 0331 第 7 号、平成 23･03･29 製局第 5 号、環保企発第 110331009 号）
- 「新規化学物質の判定及び監視化学物質への該当性の判定等に係る試験方法及び判定基準」
  （平成 23 年 4 月 22 日:厚生労働省医薬食品局審査管理課化学物質安全対策室、経済産業省製造産業局化学物質管理課化学物質安全室、環境省総合環境政策局環境保健部企画課化学物質審査室）

5.3 動物の福祉

- 「動物の愛護及び管理に関する法律」
  （昭和 48 年 10 月 1 日法律第 105 号）
- 「実験動物の飼養及び保管並びに苦痛の軽減に関する基準」
  （平成 18 年 4 月 28 日環境省告示第 88 号）
- 「動物実験の適正な実施に向けたガイドライン」
  （日本学術会議 平成 18 年 6 月 1 日）
- 「厚生労働省の所管する実施機関における動物実験等の実施に関する基本指針の一部改正について」（平成 27 年 2 月 20 日科発 0220 第 1 号）

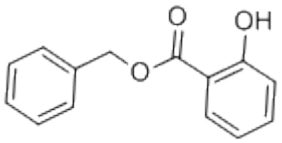
本試験は試験実施施設の動物実験委員会の承認（承認番号：G160338）を受けて実施した。

6. 試験材料及び方法

6.1 被験物質及び媒体

6.1.1 被験物質

サリチル酸ベンジルは[redacted]から購入した。また、試験開始前に赤外吸収スペクトルの測定により参照スペクトルの測定により特性が確認されている（試験番号：A-2838、Attached Data 1）。

製造者	:	[redacted]
別名*	:	salicylic acid benzyl ester; 2-hydroxybenzoic acid benzyl ester; benzyl 2-hydroxybenzoate
英語名称	:	benzyl salicylate
CAS 番号	:	118-58-1
官報公示整理番号	:	(3)-3044, (3)-1570
構造式又は示性式	:	
分子式	:	$C_{14}H_{12}O_3$
分子量	:	228.24
性状*	:	液体、透明、無色~わずかにうすい黄色
沸点/沸騰範囲*	:	194°C/1.9 kPa
融点*	:	情報なし
ロット番号	:	84OJN
濃度又は濃度範囲*	:	> 99.0%（GC）
比重（密度）*	:	1.18
保存条件*	:	密栓して冷暗所（実測値：3.5~5.0°C）
安定性	:	投与期間終了後に株式会社ボゾリサーチセンター 御殿場研究所において、残余被験物質の赤外吸収スペクトルを確認した結果、試験開始前に確認した参照スペクトルとほぼ同様であり安定性に問題はなかった（Attached Data 2）。
保存場所	:	御殿場研究所　被験物質保存室及び第 2 研究棟　被験物質調製室
取扱い上の注意*	:	作業場の換気を十分に行い、マスク、保護眼鏡、保護手袋等の適切な保護具を着用し、直接の接触を防いだ。
保存試料	:	被験物質 5 g を保存試料として御殿場研究所の資料保存施設に保存した。

残余被験物質の処置：　動物試験及び分析終了後の残余は全て廃棄処理した。
*：製造元の東京化成工業株式会社発行の製品安全データシートに基づく

6.1.2　媒体

名称　：　コーン油[注]
メーカー　：　和光純薬工業株式会社
ロット番号及び有効期限
　：　LKJ3182（2021 年 10 月）、LKN4702（2021 年 10 月）
保存方法　：　室温
保存場所　：　御殿場研究所　第 2 研究棟　被験物質調製室

注：　媒体は、本試験に先立って実施した「サリチル酸ベンジルの赤外吸収スペクトル測定法による特性試験及び安定性試験並びに HPLC 法による被験液（媒体：コーン油）中濃度測定法バリデーション及び安定性試験」（株式会社ボゾリサーチセンター、試験番号：A-2838）において、被験物質の 0.2 及び 60 mg/mL 濃度でのコーン油への溶解性及び 0.2 mg/mL 濃度でのコーン油中の安定性に良好な結果が得られていることから、コーン油を選択した。

6.2　投与液の調製及び保存方法

6.2.1　対照群投与液の採取

対照群投与液として、被験液調製当日の被験物質を取り扱う前に必要量の媒体を 1 日使用分ずつ、褐色ガラス瓶に分注した。

6.2.2　被験液の調製

濃度ごとに必要量の被験物質を秤取し、媒体にて溶解させ、規定量（6、20 又は 60 mg/mL）にメスアップした後、十分に転倒混和して被験液とした。調製は 7 日に 1 回以上の頻度で最大 7 日分を一括して行った。残液は焼却処分した。

6.2.3　投与液の保存

対照群投与液及び被験液は褐色ガラス瓶に入れ、冷所（冷蔵庫内、許容値：1~10°C、実測値：3~5°C）に保存し、安定性の確認された範囲内で投与に使用した。

6.2.4　被験液の安定性

本被験物質の 0.2 及び 100 mg/mL 濃度の被験液（媒体：コーン油）は、褐色ガラス瓶に入れ冷所（冷蔵庫内、許容値：1~10°C）で 8 日間保存後、更に非遮光室温下（許容値：1~30°C）で 24 時間保存（冷所 8 日間 + 室温 24 時間）したときに安定であることが試験施設で確認されている（試験番号：A-2838、Attached Data 3）[1]。

6.2.5 被験液の濃度確認

初回投与及び投与 6 週の投与に使用した各濃度の被験液（10 mL 採取）について、株式会社ボゾリサーチセンター御殿場研究所で HPLC 法により濃度を確認した。初回投与に使用した被験液については、投与開始前に行った確認の結果、表示値に対する測定濃度の割合は 98.0%~99.0%、6 週の投与に使用した被験液の測定値は、表示値に対して 100.0~102.5%でいずれも許容範囲内の成績を示した（Attached Data 4、5）。投与に使用した被験液の調製には問題はなかったと考えられた。なお、HPLC を用いた被験液中濃度測定法バリデーションは株式会社ボゾリサーチセンター御殿場研究所（試験番号：A-2838）[1]で実施された。分析法の概略を以下に示した。

1) 測定対象物質

サリチル酸ベンジル

2) 標準物質

被験物質の一部を標準物質として使用した。

名称 : サリチル酸ベンジル
ロット番号 : 84OJN
保存条件 : 冷暗所（冷蔵庫内、実測値：4~8°C）、密栓
保存場所 : 御殿場研究所　被験物質保存室及び分析研究部標準物質保存場所

3) 測定実測試料の調製

各測定試料を n=1 で採取し、以下の表に示すように希釈した測定実測試料を用時調製した。

被験液濃度 (mg/mL)	1 次希釈		2 次希釈		3 次希釈		希釈率
	採取量 (mL)	定容量 (mL)	1 次希釈液採取量 (mL)	定容量 (mL)	2 次希釈液採取量 (mL)	定容量 (mL)	
6	1	50	1	30	-	-	1500
20	1	100	1	50	-	-	5000
60	1	50	1	30	1	10	15000

溶媒：エタノール

4) HPLC システム

機器名及び型式		メーカー
HPLC	2690 セパレーションモジュール	Waters Corporation
検出器	2487 デュアル λUV/VIS 検出器	
データ処理ソフト	ミレニアム ^{32} クロマトグラフィーマネジャー	

5) HPLC 測定条件

カラム : Inertsil ODS-3（5 µm、4.6 mm I.D.×150 mm、ジーエルサイエンス株式会社）

カラム恒温槽設定温度 : 40°C

移動相	:	メタノール／0.1 vol%リン酸溶液（8：2）
流量	:	1 mL/min
検出	:	UV（測定波長 254 nm）
注入量	:	20 μL
オートサンプラー設定温度	:	4°C
分析時間	:	10 分間
ニードル洗浄液	:	メタノール

6.3　試験動物種及び系統の選択理由

毒性試験法ガイドラインに準じてげっ歯類であるラットを選択した。また、この試験に使用された系統のラットは一般毒性試験、生殖発生毒性試験に広く用いられ、かつ、その特性がよく知られており、背景資料が豊富であることから選択した。

6.4　試験動物

Sprague-Dawley 系 SPF ラット〔Crl:CD(SD)、日本チャールス・リバー株式会社、厚木飼育センター〕の雄 62 匹及び雌 83 匹をそれぞれ 7 週齢で入手[注)]し、入荷日を馴化 1 日と起算して、3 日間の検疫期間を含む 22 日間の馴化飼育を行った。その間、体外表、栄養状態、姿勢、行動及び排泄物などの一般状態の観察（1 回/日）、体重測定（馴化 1、3、8、15 及び 22 日の 5 回、各測定日間の体重増加量を算出した。）、詳細な一般状態の観察（群分け 5 日前の馴化 17 日に 1 回）を実施した。更に、雄について馴化終了日に陰嚢内の精巣の触診及び陰茎亀頭の観察を実施し、雌については腟垢を検疫期間終了後群分け日まで採取して性周期（検疫期間終了後 14 日間）を調べた。その結果、性周期の異常が雌 3 例（耳標番号：922、935 及び 938）及び外傷が雌 1 例（耳標番号：960）でみられた。これらの動物を除き、健康と思われる雄 62 匹中 48 匹及び雌 79 匹中 68 匹を選択し、10 週齢で投与を開始した。投与開始時の体重の変動範囲は雄で 364~420 g（平均体重：395 g）、雌で 223~275 g（平均体重：250 g）であり、雌雄ともに平均体重の±20%以内であった。

なお、動物は検疫・馴化期間中の体重推移（入荷日~群分け時）により選別後、群分け当日（投与開始の前日）の体重に基づいて、非交配群も含め各群の平均体重ができるだけ均等となるよう各群に割付けた。個体の割付けはコンピュータを用いたブロック配置法及び無作為抽出法の組み合わせ（ブロック配置法で必要な群を構成し、試験群及び群内の個体番号を無作為に割当てた）により行った。供試個体の選択条件を満たして余剰となった雌は交配予備動物（無処置動物）として継続飼育したが、使用しなかったため、全て交配期間終了後に（移管日：2016 年 11 月 29 日）試験から除外した。その他の雌雄残余動物は投与開始日（移管日：2016 年 10 月 27 日）に試験から除外した。なお、試験から除外された動物は、動物管理部門に移管した。

注）：試験計画書に従い、動物発注数は雄 60 匹及び雌 80 匹であったが、実際には雄 62 匹及

び雌 83 匹が納入された。

6.5　飼育条件

動物は温度 23±3°C（実測値：22~24°C）、相対湿度 50±20%（実測値：43~52%）、換気回数 10~15 回/h、照明 12 時間/日（07:00~19:00）の動物飼育室（飼育室番号：901 号室）に収容した。動物は床敷（ALPHA-dri、Shepherd Specialty Papers Inc.、ロット番号：05116、07116）を入れたプラスチックケージ（W440 × D275 × H180 mm：株式会社羽生精密）に、検疫・馴化期間中は同性 2 匹（入手匹数が奇数であった雌については、最後の 1 ケージは 3 匹）ずつ、群構成以降は仕切り板を入れて 2 区分とし、それぞれの区画で個別収容した。交配期間中の雄はプラスチックケージで個別に収容し、交配は雄のケージに雌を移動させて行った。交尾成立雌（妊娠 17 日以降）は床敷を入れたプラスチック製エコンケージ（W340 × D400 × H185 mm：日本クレア株式会社）に 1 腹単位で収容した。

また、エンリッチメントとして、動物試験期間中毎週 1 回、7979C.CS certified/irradiated Diamond Twists (Envigo RMS, Inc.、ロット番号：7979C-051716P、7979C-082316P)を与えた。更に、群分け後の雌雄のケージには 4 週間に 1 回程度の割合で chew toy （ステンレス棒）を設置した。

動物には CRF-1 固形飼料（放射線滅菌、オリエンタル酵母工業株式会社、ロット番号：160607、160705、160804）をステンレス製給餌器により、御殿場市営水道水を自動給水装置（プラスチックケージでの飼育時）又は給水瓶（プラスチック製エコンケージでの飼育時）により自由に摂取させた。

混入物質の分析は、使用したロットの飼料をユーロフィン・フードアンドプロダクト・テスティング株式会社で、使用したロットの床敷を N·P Analytical Laboratories で実施し、データを入手した。飲料水については、水道法に準拠した施設全体の水質の分析を定期的（年 4 回）に芝浦セムテック株式会社に依頼し、得られたデータを入手した。これらのデータにより飼料、床敷及び飲料水中の混入物質が試験成績に影響を与える可能性のないことを確認し、分析報告書の写しを保存した。

6.6　動物の識別

動物は入荷時に耳標を装着し、個体識別した。また、検疫・馴化期間中に耳標番号の若い動物の尾に油性インクによる記号を記入し、補助識別とした。群分け後は試験群、性及び群内の個体番号が区別できるよう、4 桁の数字を割り当てた（表 1-1、1-2 の群構成表参照）。各飼育ケージには投与量（群）ごとに色分けしたケージラベルをつけ、試験番号、投与経路、投与量、性、動物番号、耳標番号、剖検予定日（雄及び非交配群雌）、交尾成立日（雄及び交配群雌）及び分娩日（交配群雌）を明記した。

また、ケージラベルの裏には試験番号、性及び耳標番号のみを表示し、詳細な一般状態の観察、機能検査あるいは握力測定時にはケージラベルを裏返して観察者への投与量の情報を制限した。

6.7　投与経路、投与期間及び投与回数並びに回復期間とそれらの選択理由

投与経路は毒性試験法ガイドラインに準じ、経口投与を選択した。投与期間（投与日数）は雄及び交配群雌で交配前 14 日、更に、雄で交配開始後 28 日間（計 42 日間）、交配群雌で交配期間及び妊娠期間を通して授乳 4 日まで（計 41~46 日間）、非交配群の雌で 42 日間とした。投与回数は一般的に行われている 1 日 1 回とした。

回復動物の回復期間（回復日数）は 42 日間の投与期間が終了した後、被験物質投与に起因した変化の可逆性、持続性並びに遅発性毒性等について観察するため、14 日間を設定した。

6.8　投与方法

投与方法は、げっ歯類の経口投与に際して一般的な強制経口投与とした。投与容量は 5.0 mL/kg 体重とし、フレキシブル胃ゾンデを用いて投与液を 08:30~11:36 の間に投与した。ただし、投与時に分娩途中であった動物は分娩終了を待って、13:43~16:20 の間に投与した。対照群には媒体のみを同様に投与した。個体ごとの投与液量（表示単位：0.1 mL）は直近の体重を基準に算出した。

6.9　投与量及び群構成

投与量は 30、100 及び 300 mg/kg の 3 用量とし、これに媒体を投与する対照群を加え、計 4 群構成とした。1 群当たりの動物数は交配を行う動物として各群で雌雄各 12 匹、交配しない非交配群の対照群及び高用量群で雌各 10 匹とした。なお、対照群及び高用量群における雄の 5 匹と非交配群雌の 5 匹は、最終投与終了日以降回復動物とした。

群構成を表 1-1.及び 1-2.に示した。

表 1-1.群構成（雄）

試験群	投与量 (mg/kg)	被験液濃度 (mg/mL)	投与容量 (mL/kg)	群			
				投与終了時剖検群		回復期間終了時剖検群	
				動物数	動物番号	動物数	動物番号
対照群	0	0	5.0	7	1001-1007	5	1008-1012
低用量群	30	6	5.0	12	2001-2012		
中用量群	100	20	5.0	12	3001-3012		
高用量群	300	60	5.0	7	4001-4007	5	4008-4012

表 1-2.群構成（雌）

試験群	投与量 (mg/kg)	被験液濃度 (mg/mL)	投与容量 (mL/kg)	交配群		非交配群			
				投与終了時剖検群		投与終了時剖検群		回復期間終了時剖検群	
				動物数	動物番号	動物数	動物番号	動物数	動物番号
対照群	0	0	5.0	12	1101-1112	5	5101-5105	5	5106-5110
低用量群	30	6	5.0	12	2101-2112				
中用量群	100	20	5.0	12	3101-3112				
高用量群	300	60	5.0	12	4101-4112	5	6101-6105	5	6106-6110

6.10 投与量の設定根拠

本試験の投与量は、先に実施した「サリチル酸ベンジル: ラットを用いた 14 日間反復経口投与毒性試験（投与量設定試験）、株式会社ボゾリサーチセンター、試験番号：N-R057、投与量：250、500 及び 1000 mg/kg」[2]の結果（Attached Data 7）を参考に設定した。すなわち、500 mg/kg 以上の群では死亡が認められ、250 mg/kg 群では雄でグルコースの低値及び胸腺の絶対重量の低値が認められた以外には被験物質投与によると考えられる変化は認められず、本試験において高用量群と設定しても耐えうる量であった。以上のことから、本試験の高用量群の投与量を 250 mg/kg に近似した用量である 300 mg/kg と設定し、以下公比約 3 で除して 100 及び 30 mg/kg を中及び低用量に設定した。

6.11 観察及び検査の方法

試験日の起算は下記の通りとした。

投与開始日	：投与 1 日
投与 1 日から 7 日	：投与 1 週
回復開始日（投与 42 日の翌日）	：回復 1 日
回復 1 日から 7 日	：回復 1 週
交尾成立日	：妊娠 0 日
分娩終了日（出産日）	：授乳 0 日
出生日	：生後 0 日

6.11.1 一般状態の観察

全個体について、投与期間中は毎日 3 回（投与前、投与直後及び投与 1~3 時間後、ただし、詳細な一般状態の観察実施日は投与前と投与直後の 2 回/日）、回復期間中は毎日 2 回（午前・午後）、剖検日は 1 回（午前）、それぞれ生死、身体の外観、姿勢、行動及び排泄物（尿、糞）などの一般状態における異常の有無を観察した。なお、投与 2 日以降の動物のハンドリングを伴った定期的な観察は、詳細な一般状態の観察と兼ねて行った。

6.11.2　詳細な一般状態の観察、機能検査、握力及び自発運動量の測定

詳細な一般状態の観察は全個体について行った。

雄及び非交配群雌は投与期間中及び回復期間中毎週 1 回、交配群雌は交配前投与期間中毎週 1 回、交配期間中、妊娠期間中及び授乳期間中は指定された日（交尾動物は妊娠 1、7、14 及び 20 日、交配開始後 13 日に未交尾であった雌（動物番号：4111）は、交配開始後 6 及び 13 日（いずれも評価から除外）、分娩動物は授乳 4 日）にそれぞれ行った。このうち交配開始後 13 日に未交尾であった雌（動物番号：4111）における、交配開始後 6 及び 13 日の観察結果は、同時期の対照群の成績も存在しないことから、評価から除外した。

機能検査、握力測定及び自発運動量測定は、各群の雌雄各 5 匹（雄の群内番号 8~12 番、各群の交配群雌の分娩順で動物番号が若い順[注)]）について行った。投与期間中は交配群雌で授乳 4 日（投与 41~44 日）に、その他は投与期間終了週（投与 6 週、投与 37 日）に、回復期間中は対照群及び高用量群の雌雄について回復期間終了週（回復 2 週、回復 9 日）に行った。

上記の観察、検査及び測定は、動物をランダムにブラケット式金属製網ケージ（W254 × D350 × H170 mm：リードエンジニアリング株式会社。ただし、プラスチック製エコンケージに収容された母動物はケージのまま移動した）に配置し、観察者に対して投与量などの情報を制限（ブラインド化）した状態で行った。ただし、自発運動量測定に関しては、ブラインド化を行わなかった。なお、詳細な一般状態の観察及び機能検査の観察・検査結果については、実数データ以外はスコア化した評点法を用いて記録した。

注）　雌の高用量群は、妊娠期間中全胚吸収例、全出産児死亡例又は哺育期間中全出生児死亡例のいずれかであったため、観察対象動物が存在しなかった。交配群雌の検査対象動物を以下に示した。

試験群	動物番号
対 照 群	1101、1102、1104、1107、1110
低用量群	2101、2102、2103、2107、2112
中用量群	3102、3103、3104、3105、3108
高用量群	検査対象動物は存在しなかった。

1)　詳細な一般状態の観察

ケージ内観察は姿勢、痙攣、異常行動を、手に持っての観察はケージからの取り出し易さ、被毛・皮膚の状態、眼・鼻の分泌物、眼球突出、眼瞼閉鎖状態、可視粘膜、自律神経機能（流涙、流涎、立毛、瞳孔径、異常呼吸）、ハンドリングに対する反応、ハンドリング時の発声を、オープンフィールド内観察は覚醒状態、痙攣、異常行動、常同行動、歩行、姿勢、身繕い、立ち上がり回数、排泄物（排糞数、排尿）を調べた。

2)　機能検査

検査は聴覚反応、接近反応、接触反応、痛覚反応、瞳孔反射、空中正向反射、着地開脚幅とした。

3)　握力測定

機能検査に引き続き、CPU ゲージ MODEL-RX-5（アイコーエンジニアリング株式会社）を用いて前肢及び後肢の握力を測定した。

4)　自発運動量の測定

握力測定に引き続き、実験動物用自発運動センサーNS-AS01（株式会社ニューロサイエンス）を用いて自発運動量を測定した。測定時間は 1 時間とし、10 分間隔及び 0~60 分の測定値を集計した。

6.11.3　体重測定

雄及び非交配群雌は投与 1、8、15、22、29、36、42 日及び剖検日に、回復動物は更に回復 1、8、14 日及び剖検日に、交配群雌は投与 1、8、15 及び 22 日（投与 22 日は統計解析から除外した）、妊娠 0、7、14 及び 20 日、授乳 0 及び 4 日並びに剖検日に体重を測定した（07:46~09:46 の間（投与期間中は投与前））。

なお、投与後に分娩が終了した母動物の授乳 0 日の体重は 13:39~16:47 の間に、剖検日は前日から約 16 時間絶食させた後、相対器官重量算出用に 07:36~08:48 の間に測定した。また、妊娠期間中全胚吸収例（動物番号：4101、4103、4104、4108、4111、4112）、全出産児死亡例（動物番号：4106）及び哺育期間中全出生児死亡例（動物番号：4102、4105、4107、4109、4110）については、搬出前に体重を測定したが統計解析からは除外した。

6.11.4　摂餌量測定

雄及び非交配群雌は投与 2、8、15、30、36 及び 42 日に、回復動物は更に回復 2、8 及び 14 日に、交配群雌は投与 2、8 及び 15 日、妊娠 1、7、14 及び 20 日並びに授乳 2 及び 4 日にそれぞれ残餌量を測定し、前日の給餌量との差から 1 匹当たりの 1 日摂餌量を算出した。給餌量及び残餌量の測定は測定日の 07:54~10:18 の間に行った。

6.11.5　腟垢検査

交配群雌の全個体は投与開始日から交尾成立まで毎日（午前）腟垢を採取した。交配前投与期間中の標本は、多数の角化上皮細胞から成る腟垢像を発情の指標とし、発情回数及び発情期から次の発情期までの日数（性周期）、観察雌数に対する性周期異常を示した雌数の割合を調べた。交配期間中は腟垢内の精子の有無を調べるのに加え、腟垢像を発情前期(P)、発情期(E)、発情後期(M)及び発情休止期(D)に分類したが、データは参考成績とした。

なお、P→E→M→D（→P）の順序で周期的変化を示し、4 又は 5 日の周期を繰り返す個体を正常、それ以外を性周期異常とした。

非交配群雌は、交配群の交配成績から交尾までに要した日数あるいは交尾率に被験物質投与の影響が認められなかったことから、腟垢検査は実施しなかった。

6.11.6　交配方法

交配前投与期間終了後、同じ投与量の雄及び交配群雌を 1:1 で終夜同居させ、翌朝、腟内の腟栓形成あるいは腟垢中に精子を確認したものを交尾成立とみなした。交配開始日を 0 日と起算して交尾までに要した日数（最長 14 日間）を求めた。

6.11.7　分娩及び哺育観察

1)　母動物の観察

交尾成立雌動物は、妊娠 21 日から妊娠 25 日の午前まで 1 日 2 回（午前・午後、妊娠 25 日は午前に 1 回）、分娩の有無並びにその終了を確認するとともに分娩状態（胎盤の処理）を観察した。交尾成立から分娩終了までを妊娠期間とし、妊娠期間を 0.5 日単位で求めた。なお、分娩終了の確認は 17:00 までとした。

分娩が終了した母動物は授乳 4 日まで出生児を哺育させ、児集め、営巣及び授乳を指標として哺育状態を観察し、授乳 5 日に病理学検査に供した。

妊娠 25 日の午前までに分娩しなかった雌動物（動物番号：4101、4103、4104、4108、4111、4112）は、イソフルラン麻酔下で採血後、腹大動脈切断により放血致死させ、剖検を行った結果、全例で着床痕が認められ、妊娠したが妊娠期間中に全胚が死亡した動物（妊娠期間中全胚吸収例）であった。

分娩 0 日に全出産児が死亡した雌動物（全出産児死亡例、動物番号：4106）は、出産完了を確認後、分娩日（授乳 0 日）に、哺育期間中全出生児死亡例（動物番号：4102、4105、4107、4109、4110）ではそれぞれ全児が死亡した日に、体重測定後搬出し、採血後、放血致死させ剖検した。

2)　出生児の観察

生後 0 日に出生児数及び死産児数を数え、合わせて出産児数とした。出産児は口腔内を含む外表異常[注)]の有無を肉眼的に観察して性別を確認した。出生児（外表異常児を含む）は体重を個体別に測定した後、母動物に哺育させた。死産児はブアン液で固定して保存した。

生後 4 日まで毎日 1 回、死亡児の有無を確認した。死亡児は肉眼で外表異常の有無を観察した後、ブアン液で固定して保存した。生後 4 日に全生存児の性別を確認し、個体別に体重を測定した。外表異常の有無を肉眼的に観察した後、イソフルラン深麻酔下でブアン液に浸漬し、固定して保存した。

注）：頭部の陥没や裂、顔面の鼻吻や上下顎、口唇のゆがみや裂、口蓋の裂や口蓋縫腺の乱れ、眼瞼や耳介の大きさ、形状、左右のバランス、胸胴部のゆがみや大きさ、内部臓器の突出、尾部の長さ、形状、数、欠損、四肢部の長さ、形状、指の数、欠損及び左右のバランスに注意して観察し、正常と異なる場合を異常とした。

6.11.8　尿検査

投与期間終了週（投与 6 週、投与 40~41 日）及び回復期間終了週（回復 2 週、回復 12~13 日）に検査を行った。

投与期間中は検査当日の投与後に各群の雌雄各 5 匹（雄の群内番号 8~12 番、非交配群雌の群内番号 6~10 番）について、回復期間中は回復動物の全個体について、それぞれ採尿器をセットしたケージに収容し、絶食・自由摂水下で 4 時間尿を、次いで自由摂食・自由摂水下でその後の 20 時間尿を採取した。検査項目を表 2.に示した。採取した最初の 4 時間尿について pH 以下沈渣までの検査と尿量を、その後に得られた 20 時間尿について浸透圧、電解質（ナトリウム、カリウム及び塩素）及び尿量の測定を行った。尿量は 4 時間の尿量と 20 時間の尿量を合計して 1 日量を算出した。電解質は 20 時間尿について濃度を測定し、測定濃度と 24 時間の尿量から 1 日当たりの排泄量を算出した。なお、以下の再測定を行った。

尿検査における再測定

動物番号	項目	再測定理由	採用値
1008	Na	希釈倍率の変更	再測定値

表 2.尿検査の項目、測定法及び使用機器など

検査項目	測定方法
pH	ﾏﾙﾃｨｽﾃｨｯｸｽ試験紙 a)
たん白質	ﾏﾙﾃｨｽﾃｨｯｸｽ試験紙 a)
ケトン体	ﾏﾙﾃｨｽﾃｨｯｸｽ試験紙 a)
グルコース	ﾏﾙﾃｨｽﾃｨｯｸｽ試験紙 a)
潜血	ﾏﾙﾃｨｽﾃｨｯｸｽ試験紙 a)
ビリルビン	ﾏﾙﾃｨｽﾃｨｯｸｽ試験紙 a)
ウロビリノーゲン	ﾏﾙﾃｨｽﾃｨｯｸｽ試験紙 a)
色調	肉眼観察
沈渣	鏡検法
尿量（4 時間量）	目盛付スピッツ管を用いた容量測定（単位：mL）
浸透圧	氷点降下法 b)（単位：mOsm/kg）
ナトリウム	イオン選択電極法 c)（単位：mmol/24h）
カリウム	イオン選択電極法 c)（単位：mmol/24h）
塩素	イオン選択電極法 c)（単位：mmol/24h）
尿量（20 時間量）	容量測定（単位：mL）

使用測定機器
a)：尿自動分析装置　クリニテック 500（Siemens Healthcare Diagnostics Inc., Illinois, USA）
b)：自動浸透圧測定装置 オートアンドスタット OM-6060（アークレイ株式会社）
c)：臨床化学自動分析装置　TBA-120FR 形（東芝メディカルシステムズ株式会社）

6.11.9　血液学検査

妊娠期間中全胚吸収例、全出産児死亡例及び哺育期間中全出生児死亡例を除く全例について、剖検前日（最終投与日あるいは回復 14 日）から一夜（16~20 時間）絶食させた。そのうち、投与終了時には各群雌雄各 5 匹（動物番号が若い順、ただし交配群雌は分娩の早いものから各 5 匹[注)]、更に対照群と高用量群については非交配群雌の群内番号 1~5 の各 5 匹、回復期間終了時には回復動物について、イソフルラン麻酔下に開腹し、腹大動脈から EDTA-2K 加採血瓶（SB-41：シスメックス株式会社）に血液（約 1 mL）を採取した。得られた血液は、以下の表 3 の 1)に記載した項目及び方法により検査した。また、3.8%クエン酸ナトリウム溶液加試験管（血液 9 容に対し 1 容の割合）に採取した血液（0.9 mL）を遠心分離（3,000 rpm、約 1,600×g、10 分間）し、得られた血漿について表 3 の 2)に記載した項目及び方法により検査した。なお、採血した全例について、May-Grünwald-Giemsa 染色法による血液塗抹標本を作製したが、鏡検しなかった。

妊娠期間中全胚吸収例、全出産児死亡例及び哺育期間中全出生児死亡例についても採血し同様に検査したが、その成績は統計解析から除外した。なお、以下の再測定を行った。

血液学検査における再測定

動物番号	項目	再測定理由	採用値
2005	ADVIA 全項目	機器不良	再測定値
4003	FIB	データ取得時間の変更	再測定値
4010	PT, FIB	機器不良	再測定値

注）：交配群雌の検査対象動物を以下に示した。

試験群	動物番号
対 照 群	1101、1102、1104、1107、1110
低用量群	2101、2102、2103、2107、2112
中用量群	3102、3103、3104、3105、3108
高用量群	4101~4112

表 3.血液学検査の項目、測定法及び使用機器など

1）EDTA-2K 加血液についての検査		
検査項目	測定方法	単位
赤血球数(RBC)	2 角度レーザーフローサイトメトリー法 a)	10^4/μL
ヘモグロビン量(HGB)	シアンメトヘモグロビン変法 a)	g/dL
ヘマトクリット値(HCT)	赤血球数及び平均赤血球容積から算出 a)	%
平均赤血球容積(MCV)	2 角度レーザーフローサイトメトリー法 a)	fL
平均赤血球血色素量(MCH)	赤血球数及びヘモグロビン量から算出 a)	pg
平均赤血球血色素濃度(MCHC)	ヘモグロビン量及びヘマトクリット値から算出 a)	g/dL
網赤血球率(RETIC)	RNA 染色によるレーザーフローサイトメトリー法 a)	%
血小板数(PLT)	2 角度レーザーフローサイトメトリー法 a)	10^4/μL
白血球数(WBC)	2 角度レーザーフローサイトメトリー法 a)	10^2/μL
白血球百分率注)	ペルオキシダーゼ染色によるフローサイトメトリー法 +2 角度レーザーフローサイトメトリー法 a)	%
白血球各細胞の絶対数注)	ペルオキシダーゼ染色によるフローサイトメトリー法 +2 角度レーザーフローサイトメトリー法 a)	10^2/μL
2）クエン酸ナトリウム加血液から分離した血漿についての検査		
検査項目	測定方法	単位
プロトロンビン時間(PT)	クロット法 b)	s
活性化部分トロンボ プラスチン時間(APTT)	クロット法 b)	s
フィブリノーゲン量(FIB)	トロンボプラスチン法 b)	mg/dL
使用測定機器 a)：総合血液学検査装置　アドヴィア 120（Siemens Healthcare Diagnostics Inc., Illinois, USA） b)：血液凝固自動分析装置　ACL Elite Pro（Instrumentation Laboratory, MA, USA）		
注）：好中球(NEUT)、好酸球(EOS)、好塩基球(BASO)、リンパ球(LYMP)、単球(MONO) 及び大型非染色球(LUC)		

6.11.10　血液化学検査

血液学検査用試料と同時に、血液（約 6 mL）を凝固促進剤入り試験管（ベノジェクト II-オートセップ：テルモ株式会社）に採り、遠心分離（3,000 rpm、約 1,600×g、10 分間）し、得られた血清について表 4 の 1)に記載の項目及び方法により検査した。また、ヘパリン加試験管（血液 1 mL 当たり約 20 単位のヘパリン）に採取した血液を遠心分離（3,000 rpm、約 1,600×g、10 分間）して得られた血漿について表 4 の 2)に記載の項目及び方法により検査した。なお、妊娠期間中全胚吸収例、全出産児死亡例、哺育期間中全出生児死亡例についても同様に検査したが、その成績は統計解析から除外した。血清の一部は血中ホルモン測定のため、約 0.5 mL×3 本ずつサンプルチューブに分注し、−80°C の冷凍庫（許容範囲：−70°C 以下）に保存した後、試験場所に輸送した。

表 4.血液化学検査の項目、測定法及び使用機器など

1）分離した血清についての検査		
検査項目	測定方法	単位
ALP	Bessey-Lowry 法 [a)]	IU/L
総胆汁酸（T-BA）	3α-ヒドロキシステロイドデヒドロゲナーゼ [a)]	μmol/L
総コレステロール(T-CHO)	CEH-COD-POD 法 [a)]	mg/dL
トリグリセライド(TG)	LPL-GK-GPO-POD 法 [a)]	mg/dL
リン脂質(PL)	PLD-ChOD-POD 法 [a)]	mg/dL
総ビリルビン(T-BIL)	ビリルビンオキシダーゼ法 [a)]	mg/dL
グルコース(GLU)	グルコースデヒドロゲナーゼ法 [a)]	mg/dL
尿素窒素(BUN)	Urease-LEDH 法 [a)]	mg/dL
クレアチニン(CRNN)	Creatininase-creatinase-sarcosine oxidase-POD 法 [a)]	mg/dL
ナトリウム(Na)	イオン選択電極法 [a)]	mmol/L
カリウム(K)	イオン選択電極法 [a)]	mmol/L
塩素(Cl)	イオン選択電極法 [a)]	mmol/L
カルシウム(Ca)	OCPC 法 [a)]	mg/dL
無機リン(P)	PNP-XOD-POD 法 [a)]	mg/dL
総たん白質(TP)	Biuret 法 [a)]	g/dL
アルブミン(ALB)	BCG 法 [a)]	g/dL
A/G 比	総たん白質及びアルブミンから算出	
2）ヘパリン加血液から分離した血漿についての検査		
検査項目	測定方法	単位
AST	UV-rate 法 [a)]	IU/L
ALT	UV-rate 法 [a)]	IU/L
LDH	UV-rate 法 [a)]	IU/L
γ-GTP	L-γ-グルタミル-3-カルボキシ-4-ニトロアニリド法 [a)]	IU/L
使用測定機器 a)：臨床化学自動分析装置　TBA-120FR 形（東芝メディカルシステムズ株式会社）		

6.11.11　血中ホルモン測定

6.11.10 項で得られた血清について RIA 法により、試験場所において血中ホルモン（T_3 及び T_4）を測定した（Attached Data 6）。

6.11.12　病理学検査

1)　剖検及び器官重量測定

雄、交配群雌及び非交配群雌の投与終了時剖検群の採血対象動物は最終投与翌日に、雄及び非交配群雌の回復動物は回復期間終了日に、妊娠期間中全胚吸収例、全出産児死亡例、哺育期間中全出生児死亡例についてはそれぞれの事象が起こった日に、採血した後、採血例以外の動物はイソフルラン麻酔下で腹大動脈切断により放血致死させ、体外表並びに頭部、胸部及び腹部の器官・組織の肉眼観察を行った。なお、母動物は剖検時に黄体数及び着床痕数を数えた。

投与終了時剖検での採血

雄の採血対象動物

試験群	動物番号
対 照 群	1001~1005
低用量群	2001~2005
中用量群	3001~3005
高用量群	4001~4005

雌の採血対象動物（交配群）

試験群	動物番号
対 照 群	1101、1102、1104、1107、1110
低用量群	2101、2102、2103、2107、2112
中用量群	3102、3103、3104、3105、3108
高用量群	4101~4112

雌の採血対象動物（非交配群）

試験群	動物番号
対 照 群	5101~5105
高用量群	6101~6105

回復期間終了時剖検での採血

雄の採血対象動物

試験群	動物番号
対 照 群	1008~1012
高用量群	4008~4012

雌の採血対象動物（非交配群）

試験群	動物番号
対 照 群	5106~5110
高用量群	6106~6110

全個体について、以下に示す器官の重量を測定した。それらの器官重量（絶対重量）と剖検時の体重から体重 100 g 当たりの相対重量を算出した。なお、*印をつけた両側性の器官については左右別々に測定し、その合計値で評価した。妊娠期間中全胚吸収例、全出産児死亡例及び哺育期間中全出生児死亡例についても同様に器官重量を測定したが、剖検日の体重も含め統計解析の対象から除外した。

脳、下垂体、甲状腺*（上皮小体を含む）、副腎*、胸腺、脾臓、心臓、肝臓、腎臓*、精巣*、精巣上体*、前立腺、精嚢（凝固腺を含む）、卵巣*、子宮

2) 病理組織学検査

全個体について、以下に示す検査対象器官/組織をリン酸緩衝 10%ホルマリン液で固

定し、保存した。ただし、眼球、視神経は 3%グルタルアルデヒド・2.5%ホルマリン液で固定した後、精巣及び精巣上体はブアン液で固定した後、リン酸緩衝 10%ホルマリン液で保存した。ついで、以下に記載した動物について全ての検査対象器官/組織をパラフィン包埋した後、切片とし（検査対象器官/組織に下線を施した器官・組織は固定・保存のみとした）、ヘマトキシリン・エオジン（H･E）染色標本を作製した。両側性の器官は両側を摘出し、上皮小体、坐骨神経、眼球、視神経、顎下腺、舌下腺、腎臓、皮膚（鼠径部）、乳腺（鼠径部）、大腿骨（骨髄を含む）及び大腿部骨格筋は片側、甲状腺、副腎、精巣、卵巣、精巣上体及び精嚢（凝固腺含む）は両側、子宮は両子宮角及び頸部を鏡検した。

<H･E 染色標本作製動物>

投与終了時剖検

雄	：動物番号	1001~1005、2001~2005、3001~3005、4001~4005
非交配群雌	：動物番号	5101~5105、6101~6105
交配群雌	：動物番号	1101、1102、1104、1107、1110、2101、2102、2103、2107、2112、3102、3103、3104、3105、3108、4101~4112

回復期間終了時剖検

雄	：動物番号	1008~1012、4008~4012
非交配群雌	：動物番号	5106~5110、6106~6110

大脳、小脳（橋を含む）、坐骨神経、脊髄（胸部）、眼球、視神経、<u>ハーダー腺</u>、下垂体、甲状腺、上皮小体、副腎、胸腺、脾臓、顎下リンパ節、腸間膜リンパ節、心臓、<u>胸大動脈</u>、気管、肺（気管支を含む）、<u>舌</u>、<u>喉頭</u>、<u>食道</u>、胃、十二指腸、空腸、回腸（パイエル板を含む）、盲腸、結腸、直腸、顎下腺、舌下腺、肝臓、膵臓、腎臓、膀胱、精巣、卵巣、精巣上体、子宮、腟、前立腺、精嚢（凝固腺を含む）、皮膚（鼠径部）、乳腺（鼠径部）、<u>胸骨（骨髄を含む）</u>、大腿骨（骨髄を含む）、大腿部骨格筋、<u>個体識別部（耳標を装着した耳介）</u>

鏡検は以下の表に示すように、投与終了時又は回復期間終了時に剖検した対照群の雌雄、100 mg/kg 群の雌及び 300 mg/kg 群の雌雄の組織学検査対象動物の全検査対象器官/組織について実施した。更に、被験物質投与の影響が疑われた大腿骨（骨髄）及び胸腺については、100 mg/kg 群の雄の組織学検査対象動物、また、下垂体及び甲状腺については 30 mg/kg 群の雌雄及び 100 mg/kg 群の雄の組織学検査対象動物の鏡検を実施した。

雄					
投与終了時				回復期間終了時	
0 mg/kg	30 mg/kg	100 mg/kg	300 mg/kg	0 mg/kg	300 mg/kg
全検査対象器官/組織	下垂体 甲状腺	下垂体 甲状腺 大腿骨(骨髄) 胸腺	全検査対象器官/組織	全検査対象器官/組織	全検査対象器官/組織

交配群雌				非交配群雌			
投与終了時				投与終了時		回復期間終了時	
0 mg/kg	30 mg/kg	100 mg/kg	300 mg/kg	0 mg/kg	300 mg/kg	0 mg/kg	300 mg/kg
全検査対象器官/組織	下垂体 甲状腺	全検査対象器官/組織	全検査対象器官/組織	全検査対象器官/組織	全検査対象器官/組織	全検査対象器官/組織	全検査対象器官/組織

6.12 統計解析

6.12.1 パラメータの算出

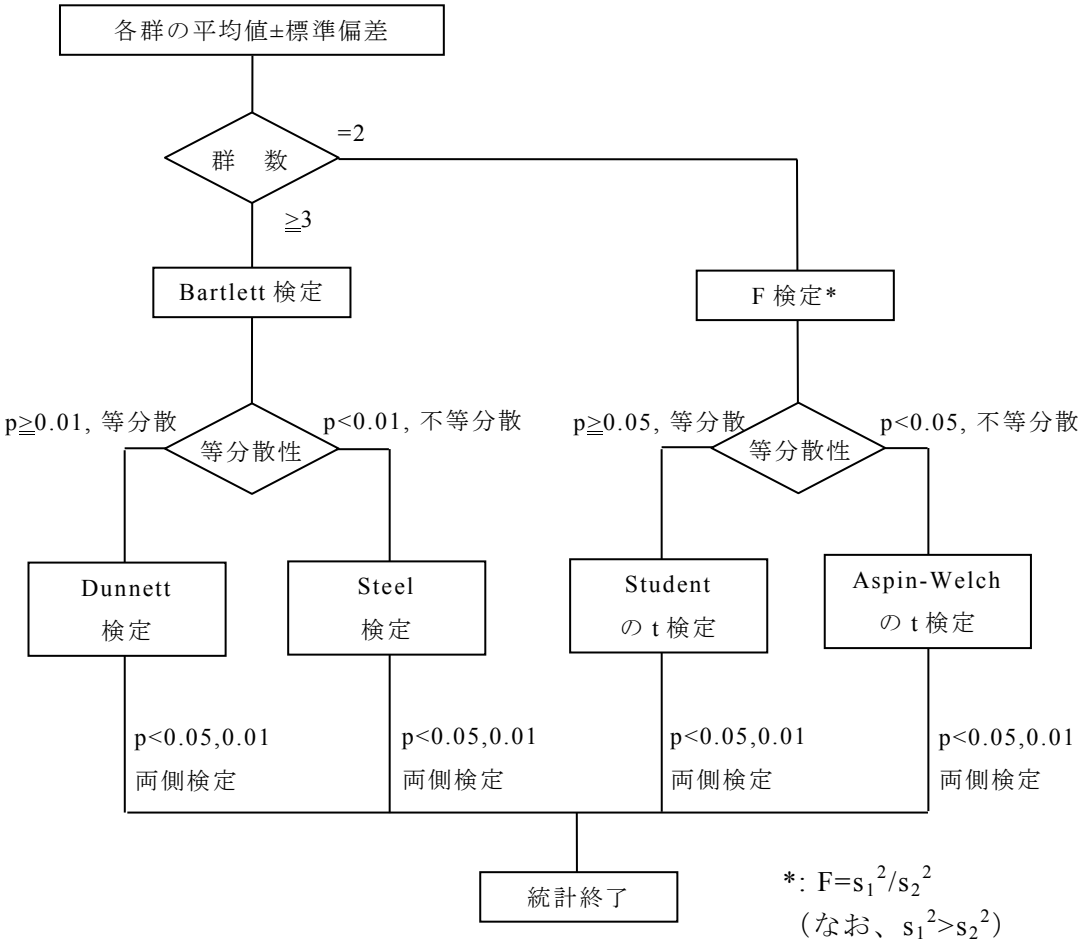
以下の式により性周期異常率、交尾率、授精率、受胎率及び出産率、生後 0 及び 4 日の性比を群ごとに、妊娠期間、着床前死亡率、着床率、分娩率、外表異常率、出生率、生後 4 日生存率を母動物（腹）ごとに算出した。なお、出生児の体重については母動物ごと雌雄別に平均値を求めた。

性周期異常率(%) =（性周期異常を示した個体数/観察雌個体数）×100
交尾率(%) =（交尾動物数/同居動物数）×100
授精率(%) =（雌を妊娠させた雄の数/交尾した雄の数）×100
受胎率(%) =（妊娠した雌の数/交尾した雌の数）×100
出産率(%) =（出生児出産雌数/妊娠雌数）×100
妊娠期間(日) = 妊娠 0 日から分娩した日までの日数
着床前死亡率(%) =〔（黄体数−着床痕数）/黄体数〕×100
着床率(%) =（着床痕数/黄体数）×100
分娩率(%) =（出産児数/着床痕数）×100
外表異常率(%) =（外表異常児数/出産児数）×100
出生率(%) =（出生児数/出産児数）×100
生後 4 日生存率(%) =（生後 4 日の生存児数/出生児数）×100
生後 0 日（死産児含む）の性比(%) =（雄出産児数/出産児数）×100
生後 0 日（出生児）の性比(%) =（雄出生児数/出生児数）×100
生後 4 日の性比(%) =（生後 4 日の雄生存児数/生後 4 日の生存児数）×100

6.12.2 検定

対照群と各用量群との差について以下の手法により統計学的有意性の検定を行った。解析には SAS Release 9.1.3（SAS Institute Inc.）を使用した。

体重、体重増加量（雄及び非交配群雌：投与 1~42 日及び回復 1~14 日、交配群雌：投与 1~15 日、妊娠 0~20 日及び授乳 0~4 日、出生児：生後 0~4 日）、摂餌量（総摂餌量含む）、発情期像発現回数、性周期（発情周期）、交尾までに要した日数、妊娠期間、黄体数、着床痕数、生存児数、オープンフィールド内観察（排糞数、立ち上がり回数）、機能検査（着地開脚幅）、握力及び自発運動量、尿検査の定量的項目、血液学検査、血液化学検査及び器官重量（含、剖検時体重）は、群ごとに平均値及び標準偏差を求め、次に示す模式図の方法に従って検定した[3] [4] [5]。



着床前死亡率、着床率、分娩率、外表異常率、出生率及び生後 4 日生存率並びに空中正向反射スコアについては、母動物ごとに率を求めた後、群ごとに平均値及び標準偏差を求め、Wilcoxon の順位和検定（有意水準 0.05 及び 0.01、両側）を行った[6]。

性周期異常率、交尾率、授精率、受胎率及び出産率、性比（生後 0 及び 4 日）並び

に聴覚反応、接近反応、接触反応、痛覚反応及び瞳孔反射の各反応・反射スコアは、各群の性周期異常を示した個体数、交尾動物数、雌を妊娠させた雄動物数、妊娠雌動物数、出生児出産雌動物数、雌雄児数、正常反応・反射のみられた動物数より算出し、Fisher の直接確率計算法により検定（有意水準 0.05 及び 0.01、両側）を行った[7]。

6.13　データ採取に使用するコンピュータシステム

- MiTOX-BOZO システム（Version 9.3.1.1、三井造船システム技研株式会社）
- Pathos5 システム（Version 5, Pathology Operating Systems Ltd.）

7. 試験結果

7.1 一般状態（Table 1-1~1-11、Appendix 1-1~1-34）

1) 投与期間

いずれの動物にも異常はみられなかった。

2) 回復期間

いずれの動物にも異常はみられなかった。

7.2 詳細な一般状態の観察、機能検査、握力測定及び自発運動量の測定（Fig. 1~4、Table 2-1~2-167、Appendix 2-1~2-328）

7.2.1 ホームケージ内観察（Table 2-1~2-23、Appendix 2-1~2-71）

1) 投与期間

いずれの動物にも異常はみられなかった。

2) 回復期間

いずれの動物にも異常はみられなかった。

7.2.2 手に持っての観察（Table 2-24~2-82、Appendix 2-72~2-142）

1) 投与期間

ハンドリング時の発声が雄では対照群で投与 5 週に 2 例、6 週に 1 例、30 mg/kg 群で投与 3 及び 4 週に各 1 例、100 mg/kg 群で投与 3 週に 1 例、300 mg/kg 群で投与 3 及び 5 週に各 2 例、4 週に 1 例、また、交配群雌では 30 mg/kg 群の妊娠 7 日に 2 例、妊娠 14 日に 1 例、100 mg/kg 群で投与 2 週に 1 例、300 mg/kg 群で投与 1 週、妊娠 7 及び 14 日に各 1 例、投与 2 週に 2 例、非交配群雌では 300 mg/kg 群の投与 3 及び 6 週に各 1 例、投与 5 週に 2 例でそれぞれ認められた。

更に、ハンドリングに対する反応の亢進が、雄では対照群で投与 5 週に 2 例、交配群雌で 300 mg/kg 群の投与 1、2 週、妊娠 7 日に各 1 例でみられた他、ケージからの取り出しやすさ観察時に抵抗を示した例が、300 mg/kg 群の交配群雌で妊娠 7 日に 1 例認められた。

2) 回復期間

いずれの動物にも被験物質投与に関連すると考えられる異常はみられなかった。

7.2.3 オープンフィールド内観察（Table 2-83~2-151、Appendix 2-143~2-284）

1) 投与期間

いずれの動物にも被験物質投与によると考えられる異常は認められなかった。

歩行観察時の歩行の減少が 100 mg/kg 群の雄で投与 3 週に 1 例で観察されたが、300 mg/kg 群には認められず、用量と関連のない変化であった。また、立ち上がり回数の有意な高値が 100 mg/kg 群の交配群雌で妊娠 7 日に認められたが、300 mg/kg 群

ではみられずこの変動も用量と関連のない変化であった。排糞回数には対照群と各被験物質投与群との間で有意差は認められなかった。

2) 回復期間

いずれの動物にも異常は認められなかった。

7.2.4 機能検査（Table 2-152~2-159、Appendix 2-285~2-306）

1) 投与期間終了週検査

いずれの動物にも聴覚反応、接近反応、接触反応、痛覚反応、瞳孔反射及び空中正向反射の成績に有意差はみられず、着地開脚幅には対照群と各被験物質投与群との間に有意差は認められなかった。

2) 回復期間終了週検査

いずれの動物にも聴覚反応、接近反応、接触反応、痛覚反応、瞳孔反射及び空中正向反射の成績に有意差はみられず、着地開脚幅には対照群と 300 mg/kg 群との間に有意差は認められなかった。

7.2.5 握力（Table 2-160~2-163、Appendix 2-307~2-317）

1) 投与期間終了週測定

対照群と各被験物質投与群との間に有意差は認められなかった。

2) 回復期間終了週測定

対照群と 300 mg/kg 群との間に有意差は認められなかった。

7.2.6 自発運動量（Fig. 1~4、Table 2-164~2-167、Appendix 2-318~2-328）

1) 投与期間終了週測定

対照群と各被験物質投与群との間に有意差は認められなかった。

2) 回復期間終了週測定

300 mg/kg 群の雌で回復 2 週の測定 30~40 分の自発運動量が有意に増加したが、一過性の変化であり、総運動量に有意差は認められなかった。

7.3 体重（Fig. 5~11、Table 3-1~3-7、Appendix 3-1~3-22）

1) 投与期間

300 mg/kg 群の交配群雌で妊娠 20 日の体重及び妊娠期間中の体重増加量に有意な低値が認められたが、これは同群の妊娠期間中全胚吸収例 6 腹で妊娠期間中に全胚が死亡し、他の 5 例も出産児数が少なかったことによる子宮内容物重量の差による有意差と考えられた。その他、交配群雌では、全群の交配前投与期間の体重及び 100 mg/kg 以下の投与群の妊娠・授乳期間中体重が対照群と同様な推移を示し、有意差は認められなかった。

各被験物質投与群の雄及び非交配群雌は、投与期間を通じて対照群と同様な体重推

移を示し有意差は認められなかった。

2)　回復期間

雌では 300 mg/kg 群で回復期間中の体重増加量が有意に低値を示した。雄では対照群との間に有意差は認められなかった。

7.4　摂餌量（Fig. 12~18、Table 4-1~4-7、Appendix 4-1~4-22）

1)　投与期間

300 mg/kg 群の雄で投与 42 日の摂餌量、非交配群雌で投与 36 及び 42 日の摂餌量並びに投与期間中の総摂餌量に有意な高値が認められた。交配群雌では対照群と各投与群との間で有意差はみられなかった。

2)　回復期間

300 mg/kg 群の雌雄いずれも対照群との間に有意差は認められなかった。

7.5　尿検査（Table 5-1~5-24、Appendix 5-1~5-30）

1)　投与期間終了週検査

定性項目について、いずれの検査項目においても各投与群と対照群との間に変化は認められなかった。

定量項目については、300 mg/kg 群の雄で尿量並びにナトリウム及び塩素の 1 日排泄量に有意な高値が認められた。

2)　回復期間終了週検査

定性項目について、いずれの検査項目においても 300 mg/kg 群と対照群との間に変化は認められなかった。

定量項目については、いずれの検査項目においても 300 mg/kg 群と対照群との間に有意差は認められなかった。

7.6　血液学検査（Table 6-1~6-7、Appendix 6-1~6-15）

1)　投与終了時検査

300 mg/kg 群の雄で血小板数の有意な低値及び白血球数の低値傾向、プロトロンビン時間及び活性化部分トロンボプラスチン時間の有意な延長及びフィブリノーゲン量の有意な高値、300 mg/kg 群の交配群雌で血小板数の低値傾向、同群の妊娠期間中全胚吸収例で白血球数の低値傾向、非交配群雌で血小板数の有意な低値及び活性化部分トロンボプラスチン時間の有意な延長が認められた。

その他、30 mg/kg 群の交配群雌でプロトロンビン時間の有意な短縮が認められたが、用量と関連のない変化であった。

2)　回復期間終了時検査

300 mg/kg 群の雄で平均赤血球容積及び単球数の高値並びに好酸球百分率の低値が認められた。

雌では全ての検査項目で対照群と各投与群の間に有意差は認められなかった。

7.7　血液化学検査（Table 7-1~7-7、Appendix 7-1~7-15）

1)　投与終了時検査

300 mg/kg 群の雄で AST、ALT、ALP 及びアルブミン、A/G 比の有意な高値、総ビリルビン、グルコース及び総たん白質の有意な低値が認められた。また、300 mg/kg 群の非交配群雌で AST、ALT、ALP、トリグリセライド、ナトリウム及び A/G 比の有意な高値、総ビリルビン及びカルシウムの有意な低値、100 mg/kg 群の交配群雌で γ-GTP 及び A/G 比の有意な高値及び総ビリルビンの有意な低値が、300 mg/kg 群の交配群雌でトリグリセライド及び A/G 比の高値傾向が認められた。

この他、100 mg/kg 群の雄で総コレステロールの有意な低値がみられたが、300 mg/kg 群では認められず用量と関連のない変化であった。

2)　回復期間終了時検査

300 mg/kg 群の雄でカルシウム及び無機リン並びに A/G 比の有意な高値及びグルコース濃度の有意な低値が、雌で総たん白質の有意な低値が認められた。

7.8　血中ホルモン濃度

1)　投与終了時検査

結果を表 5-1~5-6 に示した（Attached Data 6、作業番号：OT-160005）。

100 mg/kg 以上の投与群の雄及び 300 mg/kg 群の非交配群雌では T_4 濃度の有意な低値、100 mg/kg 群の交配群雌、300 mg/kg 群の交配群雌の妊娠期間中全胚吸収例（動物番号：4101、4103、4104、4108、4111 及び 4112）、全出産児死亡例（動物番号：4106）及び哺育期間中全出生児死亡例（動物番号：4102、4105、4107、4109、4110）では T_4 濃度の低値傾向が認められた。しかし、T_3 濃度には変化がみられなかった。

表 5-1. 投与終了時雄　血中甲状腺ホルモン濃度

Test Article Dose		T_3 (ng/mL)	T_4 (ng/mL)
サリチル酸ベンジル 0 mg/kg	Mean	0.58	33.9
	SD	0.08	3.7
	n	5	5
サリチル酸ベンジル 30 mg/kg	Mean	0.61	29.8
	SD	0.10	5.1
	n	5	5
サリチル酸ベンジル 100 mg/kg	Mean	0.52	19.2 *
	SD	0.09	2.1
	n	5	5
サリチル酸ベンジル 300 mg/kg	Mean	0.46	0.0 *
	SD	0.05	0.0
	n	5	5

*：P<0.05 （対照群との間に有意差あり）

表 5-2. 授乳 5 日交配群雌　血中甲状腺ホルモン濃度

Test Article Dose		T_3 (ng/mL)	T_4 (ng/mL)
サリチル酸ベンジル 0 mg/kg	Mean	0.60	23.9
	SD	0.07	8.8
	n	5	5
サリチル酸ベンジル 30 mg/kg	Mean	0.74	25.5
	SD	0.13	7.8
	n	5	5
サリチル酸ベンジル 100 mg/kg	Mean	0.65	18.3
	SD	0.13	1.9
	n	5	5

有意差は認められなかった。

表 5-3. 妊娠期間中全胚吸収例　血中甲状腺ホルモン濃度

Test Article Dose		T_3 (ng/mL)	T_4 (ng/mL)
サリチル酸ベンジル 300 mg/kg	Mean	0.58	15.8
	SD	0.10	2.7
	n	6	6

表 5-4. 全出産児死亡例　血中甲状腺ホルモン濃度

Test Article Dose		T_3 (ng/mL)	T_4 (ng/mL)
サリチル酸ベンジル 300 mg/kg	Value	0.80	18.4
	n	1	1

表 5-5. 哺育期間中全出生児死亡例　血中甲状腺ホルモン濃度

Test Article Dose		T_3 (ng/mL)	T_4 (ng/mL)
サリチル酸ベンジル 300 mg/kg	Mean	0.53	0.0
	SD	0.07	0.0
	N	5	5

表 5-6. 投与終了時非交配群雌　血中甲状腺ホルモン濃度

Test Article Dose		T_3 (ng/mL)	T_4 (ng/mL)
サリチル酸ベンジル 0 mg/kg	Mean	0.62	24.1
	SD	0.20	3.5
	n	5	5
サリチル酸ベンジル 300 mg/kg	Mean	0.54	2.5 **
	SD	0.12	5.6
	n	5	5

**：P<0.01 （対照群との間に有意差あり）。

2)　回復期間終了時検査

結果を表 6-1 及び 6-2 に示した（Attached Data 6、作業番号：OT-160005）。300 mg/kg 群の雌雄いずれも対照群との間に有意差は認められなかった。

表 6-1. 回復期間終了時雄　血中甲状腺ホルモン濃度

Test Article Dose		T_3 (ng/mL)	T_4 (ng/mL)
サリチル酸ベンジル 0 mg/kg	Mean	0.65	36.3
	SD	0.10	4.4
	n	5	5
サリチル酸ベンジル 300 mg/kg	Mean	0.64	35.9
	SD	0.09	5.4
	n	5	5

有意差は認められなかった。

表 6-2. 回復期間終了時雌　血中甲状腺ホルモン濃度

Test Article Dose		T_3 (ng/mL)	T_4 (ng/mL)
サリチル酸ベンジル 0 mg/kg	Mean	0.74	30.5
	SD	0.11	10.4
	n	5	5
サリチル酸ベンジル 300 mg/kg	Mean	0.72	22.3
	SD	0.08	3.8
	n	5	5

有意差は認められなかった。

7.9　器官重量（Table 8-1~8-7、Appendix 8-1~8-32）

1)　投与終了時検査

100 mg/kg 以上の群の雄では胸腺の絶対重量及び相対重量の低値傾向が認められ、300 mg/kg 群の雄では肝臓の相対重量の有意な高値並びに精巣上体の絶対重量の有意な低値及び相対重量の低値傾向が認められた。交配群雌及び非交配群雌では 300 mg/kg 群で胸腺の絶対及び相対重量の低値傾向がみられ、交配群雌ではこの他、300 mg/kg 群で肝臓の絶対及び相対重量の高値傾向が認められた。

2)　回復期間終了時検査

300 mg/kg 群の雄で腎臓及び精嚢の相対重量に有意な高値が、胸腺の相対重量に高値傾向がみられ、雌では脳の絶対重量の有意な低値がみられた。

7.10　剖検所見（Table 9-1~9-7、Appendix 9-1~9-116）

1)　投与終了時検査

300 mg/kg 群の交配群雌で乳腺の発達不良、子宮内受胎産物の残存及び肝臓の大型化がそれぞれ 3 例（動物番号：4103、4104、4111）、1 例（動物番号：4103）及び 1 例（動物番号：4102）に認められた。

この他、雄で精巣上体の黄色巣、肝臓の横隔膜ヘルニア結節、肺の暗赤色巣、腺胃の暗赤色巣が、交配群雌で肺の暗赤色巣、腺胃の暗赤色巣が認められたが、いずれも発現頻度が低く、用量依存性のみられる変化ではなかった。

2)　回復期間終了時検査

いずれの動物にも被験物質投与に起因すると考えられる変化はみられなかった。

なお、300 mg/kg 群の雌雄各 1 例の腺胃に暗赤色巣がみられたが、発現は雌雄各 1 例のみであり、試験施設においてしばしば認められる変化であることから、被験物質投与と関係しない偶発性変化と判断した。

7.11 病理組織学検査（Table 10-1~10-21、Appendix 9-1~9-116）

1) 投与終了時検査

結果を表 7-1 及び 7-2 に示した。300 mg/kg 群の雄、交配群雌及び非交配群雌で大腿骨（骨髄）の骨梁の増加、雄及び交配群雌で胸腺の萎縮がそれぞれ認められた。

表 7-1. 大腿骨（骨髄）の組織学検査結果

群	雄					
	投与終了時				回復期間終了時	
投与量 (mg/kg)	0	30	100	300	0	300
動物数	5	0	5	5	5	5
骨梁増加 軽微	0 0	― ―	0 0	5 5	0 0	0 0

群	交配群雌					非交配群雌			
	投与終了時					投与終了時		回復期間終了時	
投与量 (mg/kg)	0	30	100	300		0	300	0	300
				全胚吸収例	全児死亡				
動物数	5	0	5	6	6	5	5	5	5
骨梁増加 軽微	0 0	― ―	0 0	6 6	6 6	0 0	4 4	0 0	0 0

表 7-2. 胸腺の組織学検査結果

群	雄					
	投与終了時				回復期間終了時	
投与量 (mg/kg)	0	30	100	300	0	300
動物数	5	0	5	5	5	5
萎縮 軽微	0 0	― ―	0 0	1 1	0 0	0 0

群	交配群雌					非交配群雌			
	投与終了時					投与終了時		回復期間終了時	
投与量 (mg/kg)	0	30	100	300		0	300	0	300
				全胚吸収例	全児死亡				
動物数	5	0	5	6	6	5	5	5	5
萎縮 軽微	0 0	― ―	0 0	0 0	2 2	0 0	0 0	0 0	0 0

その他、いくつかの器官/組織に組織学的変化がみられたが、その発現状況あるいは病理学的性状から被験物質投与と関係しない偶発性変化と判断した。

2) 回復期間終了時検査

いずれの動物にも被験物質投与に起因すると考えられる変化はみられなかった。いくつかの器官/組織に組織学的変化がみられたが、その発現状況あるいは病理学的性状から被験物質投与と関係しない偶発性変化と判断した。

7.12 性周期（Table 11、Appendix 10-1~10-8）

100 mg/kg 群の 1 例（動物番号：3108）に性周期異常がみられたが、いずれの投与群も、性周期異常率、発情期像発現回数及び性周期（発情周期）には対照群と各被験物質投与群との間に有意差は認められなかった。

7.13 交配成績（Table 12-1 及び 12-2、Appendix 11-1~11-8）

全例が交尾し、妊娠した。交尾までに要した日数にも対照群と各被験物質投与群との間で有意差は認められなかった。

7.14 分娩成績（Table 13、14-1、Appendix 12-1~12-4、13-1~13-4）並びに分娩及び哺育状態（Table 1-5 及び 1-6、Appendix 1-17~1-24）

300 mg/kg 群で妊娠期間が有意に延長し、出産率、分娩率、出生率、出産児数及び出生児数の有意な低値、死産児数の有意な高値が認められた。黄体数、着床痕数、着床前死亡率、着床率及び生後 0 日の性比（出産児あるいは出生児）には対照群と各投与群との間で有意差はみられなかった。300 mg/kg 群の 6 例（動物番号：4101、4103、4104、4108、4111、4112）では妊娠 25 日になっても分娩がみられず、確認した結果、着床が確認され、妊娠期間中に全胚が死亡した状態（妊娠期間中全胚吸収例）であることが確認された。

300 mg/kg 群の他の 1 例（動物番号：4106）では着床数は 17 で正常であったが、出産したのは雌雄各 1 例の死亡児のみで生存児は認められなかった。この動物は、妊娠期間が 24 日間に遷延した。この他、妊娠期間が 23.5 日間であった動物が、100 mg/kg 群に 1 例（動物番号：3104）及び 300 mg/kg 群に 1 例（動物番号：4110）みられた。これらの例を除く妊娠動物は、妊娠 21.5 から 23 日に分娩した。分娩例では胎盤及び羊膜の処理は正常に行われた。

出産児では対照群の 1 腹（母動物番号：1105）の 1 例の出生児及び別の腹（母動物番号：1106）の 1 例の死産児で無尾、300 mg/kg 群の 1 腹（母動物番号：4107）の 5 例の死産児で外脳症又は外脳症と完全脊椎裂の合併がそれぞれ認められた。このうち、出生児及び死産児の無尾はいずれも対照群に認められた所見であり、被験物質の投与とは無関係であった。

哺育状態では、いずれの母動物にも児集め、営巣及び授乳行動に異常はみられなかった。

7.15　出生児の生存性及び性比（Table 15、Appendix 14-1~14-4）

300 mg/kg 群の生存児を出産した 5 腹では、4 腹（母動物番号：4105、4107、4109、4110）が授乳 1 日、残る 1 腹（母動物番号：4102）が授乳 2 日に全哺育児の死亡が認められ、生後 4 日の生存率が有意に低下した。性比には対照群と各被験物質投与群との間に有意差は認められなかった。

7.16　出生児の体重（Table 16-1 及び 16-2、Appendix 15-1~15-7）

100 mg/kg 以上の群の生後 0 日の出生児体重が雌雄とも有意な低値、30 mg/kg 群雌雄の出生児体重が低値傾向を示した。300 mg/kg 群の生後 4 日には生存児が存在しなかったが、100 mg/kg 群の生後 0 日から 4 日の体重増加量は対照群に比較して有意差はみられなかった。100 mg/kg 群の生後 4 日の体重は、雌雄いずれも低値傾向を示した。30 mg/kg 群の出生日（生後 0 日）の体重は、雌雄いずれも対照群に比較して有意差が認められなかったが低値傾向を示し、生後 0~4 日の増加量は雌雄とも対照群に比較して有意な低値で、生後 4 日の雌雄体重は対照群に比較して有意に低値であった。

7.17　死亡児の肉眼観察所見（Table 17、Appendix 16-1~16-4）

いずれの死亡児にも肉眼的異常はみられなかった。

7.18　出生児の生後 4 日肉眼観察所見（Table 14-2、Appendix 13-5~13-7）

対照群の 1 例（母動物番号：1105）で出生日に観察された無尾が 1 匹に認められたのみであった。

8. 考察

サリチル酸ベンジルの 0（対照群：コーン油）、30、100 及び 300 mg/kg を Sprague-Dawley 系 SPF ラットの、雄には交配前 14 日間に加え交配期間を通して剖検前日まで（42 日間）、交配群雌には交配前 14 日間に加え交配期間及び妊娠期間を通して授乳 4 日まで（41~46 日間）、非交配群雌には 42 日間、交配群雌の 300 mg/kg 群で認められた妊娠期間中全胚吸収例、全出産児死亡例、哺育期間中全出生児死亡例では剖検の前日まで（38~53 日間）、強制経口投与し、反復投与毒性及び生殖発生毒性を検討した。更に、0 及び 300 mg/kg 群の一部の動物については、雌雄ともに 42 日間投与した後 14 日間の回復期間を設け、毒性変化の可逆性及び遅発性毒性の有無を検討した。

8.1 反復投与毒性

詳細な一般状態の観察では、300 mg/kg 群で雄並びに交配群及び非交配群の雌のハンドリング時の発声及び雄並びに交配群雌のハンドリングに対する反応の亢進がみられた頻度が、若干増加していた。ただし、その程度はいずれも軽度であった。一方、100 mg/kg 以下の投与群における、これらの変化の発現頻度及び程度は、雌雄いずれも対照群に比して差はみられなかった。ハンドリング時の発声及びハンドリングに対する反応の亢進は、回復動物では認められなかった。

その他、一般状態、詳細な一般状態の観察のうちホームケージ内観察、オープンフィールド内観察、機能検査、握力及び自発運動量の測定結果には、投与終了時及び回復期間終了時のいずれも異常は認められなかった。

体重については、300 mg/kg 群の交配群雌で妊娠後期に増加抑制が認められたが、同群では胚の着床後死亡が増加していることから、変化はこれに伴うものであると判断した。雄及び非交配群雌では体重に変化はみられなかった。雌では回復期間中の体重増加量が低値を示した。

摂餌量は 300 mg/kg 群の雄及び非交配群雌で投与後期に増加が認められたが、一過性で 1 又は 2 回の測定時のみに認められた変化であり、体重には変化がみられなかった。回復期間には摂餌量の変化はみられなかった。

投与期間終了週の尿検査の結果、300 mg/kg 群の雄で尿量、ナトリウム及び塩素の排泄量が増加した。回復期間には尿検査結果に異常はみられなかった。

血液学検査の結果、投与終了時には 300 mg/kg 群の雄及び非交配群雌で血小板数の低値及び活性化部分トロンボプラスチン時間の延長が、交配群の雌では血小板数の低値傾向が、更に雄でプロトロンビン時間の延長及びフィブリノーゲン量の高値がそれぞれ認められた。病理組織学検査の結果からは肝臓には変化が認められず、全身の諸器官に出血性の変化も認められていなかったが、これらの変化は雄及び雌に共通してみられる変化であること、雄では活性化部分トロンボプラスチン時間とプロトロンビン時間の延長が共通してみられることから、被験物質の投与による変化である可能性

は高いと考えた。また、これらの変化は回復動物には認められないことから、回復性のある変化であった。この他、300 mg/kg 群の雄及び交配群雌の妊娠期間中全胚吸収例では白血球数の低値傾向が認められた。回復期間終了時には、300 mg/kg 群の雄で平均赤血球容積及び単球数の高値並びに好酸球百分率の低値が認められたが、平均赤血球容積については赤血球関係の他のパラメータに変動がないこと、単球数の高値及び好酸球百分率の低値についてはともに施設の背景値の範囲内であることから、いずれも被験物質の投与との関係は明瞭ではなかった。

血液化学検査の結果、300 mg/kg 群の雄及び非交配群雌、100 mg/kg 群の交配群雌において、総ビリルビンの低値が認められたが変化の方向性は低下であり、毒性学的意義に乏しいと判断した。300 mg/kg 群の雄及び非交配群雌では AST、ALT 及び ALP 並びに A/G 比の高値が認められた。このうち、A/G 比の高値は、100 mg/kg 群の交配群雌においてもみられ、被験物質投与による影響であると考えられた。また、300 mg/kg 群の雄ではアルブミンの高値及び総たん白質の低値、300 mg/kg 群の交配群雌では A/G 比の高値傾向も認められた。AST、ALT 及び ALP の高値はいずれも変化の程度は軽度であるものの雌雄で共通して認められた変化であり、肝臓障害の指標として互いに関連ある変化であることから、肝臓に変化があることを示唆するものと考えた。交配群雌の 100 mg/kg 群に認められた γ-GTP の高値及び 300 mg/kg 群の雄でみられた肝臓重量の高値、交配群雌でみられた肝臓重量の増加傾向もまた、肝臓になんらかの影響が及んだ変化であると考えられる。ただし、肝臓の病理組織学検査結果には雌雄いずれも被験物質投与によると考えられる変化はみられないことから、肝臓への影響は病理組織学的変化を伴わない変動であると考えられた。

300 mg/kg 群の非交配群の雌にみられたカルシウムの低下は、生体内のカルシウムバランスは主に骨によって保たれることから、大腿骨（骨髄）の骨梁が増加していたことに伴う変化と考えられる。また、300 mg/kg 群の非交配群雌にみられたトリグリセライドの有意な増加及び交配群雌に認められた増加傾向はいずれも、同群で血中 T_4 濃度が低下していることから、これに伴う変化と考えられた。

この他、投与終了時の血液化学検査では、300 mg/kg 群の雄でグルコースの低値、非交配群の雌ではナトリウムの高値がそれぞれみられた。

回復期間終了時検査の結果、雄でカルシウム及び無機リンが高値を示したが、この変化は病理組織学検査で投与終了時に認められた大腿骨（骨髄）骨梁の増加が、被験物質の投与を中止したことに伴い回復していく過程の変化と考えられた。一方、回復期間終了時検査の雄で A/G 比の高値及びグルコースの低値が残留したが、この変化は投与終了時に認められた変化が残留したものと判断した。

この他、回復期間終了時には雌では総たん白質の低値が認められた。

T_4 濃度の低値又は低値傾向が雄は 100 mg/kg 以上の群、300 mg/kg 群の非交配群雌及び 100 mg/kg 以上の群の交配群雌で共通して認められたが、いずれも T_3 濃度には変化がみられなかった。血中甲状腺ホルモンの低下の原因としては、① 甲状腺における生合成あるいは放出の抑制、② 肝臓での T_4 代謝酵素誘導による代謝の亢進、③ 血中

輸送タンパク質の量又は結合性の変化、あるいは④ 組織取り込みの増加が考えられる[8]。本試験の病理組織学検査においては、甲状腺におけるホルモンの生合成あるいは放出の抑制を伺わせる像や、肝臓における UDP-グルクロニルトランスフェラーゼ等の T_4 代謝酵素の誘導像、下垂体及び甲状腺における甲状腺ホルモンの負のフィードバックによると考えられる組織変化はいずれも認められなかった。

甲状腺ホルモンの主な輸送タンパク質はアルブミンの前駆体の 1 種であるトランスサイレチン（TTR）又はチロキシン結合グロブリン（TBG）である。本試験においては前述の通り、血清グロブリン量（総たん白質とアルブミンの差）の低値、A/G 比の高値等が、雌雄共通して認められていることから、これらの変化が甲状腺ホルモン輸送タンパク質の変化を反映しているものである可能性が考えられる。ただし、TTR 及び TBG はいずれも量的にはアルブミン量及びグロブリン量のごく一部に過ぎないことから、これらの変化がアルブミン、グロブリン量や A/G 比に直接影響を与えられるかどうかは不明である。

一方、PCB 類によるラットの甲状腺ホルモンへの影響に関する、加藤らの報告によれば[8]、PCB 類の投与によってラットにおいては T_4 の低下がみられたものの、T_3 濃度には変化がなく、甲状腺の病理組織像にも影響がみられていない。これらのホルモンの推移及び病理組織所見の発現パターンは本試験と類似している。加藤らの試験においては、PCB により Oatp2 や LAT1 など、有機アニオントランスポータの誘導が肝臓で起こり、これが T_4 の肝臓への取り込みを引き起こし、血中 T_4 濃度を低下させた可能性が考えられている。本被験物質による T_4 の低下が PCB と同じ機序で発現している証拠はないが、T_4 の生合成の抑制又は T_4 代謝の亢進がみられていない点は両者で共通しており、機序の可能性の 1 つであると考えられる。

器官重量測定の結果、投与終了時には 100 mg/kg 以上の群の雄、300 mg/kg 群の交配群雌及び非交配群雌で胸腺の絶対重量及び相対重量の低値傾向、300 mg/kg 群の雄で精巣上体の絶対重量の低値及び相対重量の低値傾向、300 mg/kg 群の雄で肝臓の相対重量の高値、300 mg/kg 群の交配群雌で肝臓の絶対及び相対重量の高値傾向が認められたが、胸腺以外は被験物質投与によると考えられる病理組織学的変化を伴わなかった。回復動物では 300 mg/kg 群の雄で胸腺、腎臓及び精嚢の相対重量の高値、雌で脳の絶対重量の低値がそれぞれ認められたが、いずれも程度は軽く、病理組織学検査結果には異常が認められなかった。

剖検の結果、交配群雌の 3 例で乳腺の発達不良がみられ、1 例で子宮内受胎産物の残存が認められたが、子宮内受胎産物の残存は妊娠期間中全胚吸収例のみでみられており、妊娠の中期~後期に全胚死亡した動物において、娩出が起こらなかった場合、胚が吸収されていく過程の像と考えられた。本試験においては妊娠期間中全胚吸収例は全部で 6 例であったが、着床痕以外の子宮内容物が確認されたのは、1 例だけであり、多くの例では全胚吸収は比較的早期に起こっていると推定されたが、この例のように妊娠の中期~比較的後期に死亡する例も存在すると考えられる。また、乳腺の発達不良を示した例はいずれも妊娠期間中全胚吸収例であり、出生児の哺乳による刺激

をまったく受けていないことが、乳腺が未発達である原因の一つであると考えられた。

病理組織学検査の結果、300 mg/kg 群の雄、交配群雌及び非交配群雌の大腿骨（骨髄）の骨梁の増加、300 mg/kg 群の雄及び交配群雌で胸腺の萎縮がそれぞれ認められた。また、重量測定の結果、胸腺の重量低下傾向が、100 mg/kg 以上の雄、300 mg/kg 群の交配群雌及び非交配群雌で認められた。被験物質であるサリチル酸ベンジルにはエストロゲン様作用があることが知られている[9]。エストロジェンは骨芽細胞あるいは破骨細胞に作用し、骨形成を促進する場合と骨吸収を抑制する場合があるが[10]、本試験では骨芽細胞の活性化はみられていないことから、骨吸収が抑制され、骨梁が増加したものと推測された。本変化は回復動物には観察されなかった。一方胸腺の萎縮は、例数も比較的少ないことから、被験物質投与に伴うストレス性の変化である可能性も考えられた。

8.2　生殖発生毒性

性周期、交配成績には被験物質投与によると考えられる異常は認められなかった。黄体数、着床痕数、着床前死亡率、着床率及び生後 0 日の性比（出産児あるいは出生児）には変化はみられなかった。一方、分娩観察において 300 mg/kg 群で妊娠期間が延長し、出産率、分娩率、出生率、出産児数及び出生児数の低下、死産児数の増加が認められたが、このうち出産率、分娩率、出生率、出産児数及び出生児数の低下、死産児数の増加は、300 mg/kg 群に 6 例みられた妊娠期間中全胚吸収例及び 1 例の全出産児死亡例に起因すると考えられ、被験物質投与による影響と考えられた。

一方、300 mg/kg 群において、妊娠期間中全胚吸収例で分娩しなかった例を除いた 6 例の妊娠期間は、23 日間であった。これは、全出産児が死亡していたため分娩刺激が弱かったと考えられる 1 例（動物番号 : 4106）における妊娠期間 24 日間の他にも、23.5 日間の妊娠期間を示した例が 1 例（動物番号 : 4110）存在したためと考えられる。妊娠期間が 23.5 日であった動物は 100 mg/kg 群にも 1 例（動物番号 : 3104）みられたが、この例については着床数が 3 と著しく少ないことに伴い、娩出作用が弱かったことに伴う変化であると推定された。一方、300 mg/kg 群の妊娠期間が 23 又は 23.5 日間であった 2 例における着床数はそれぞれ 17 又は 13 で他の例と差がないと考えられる反面、出産児数は 6 又は 3 匹、出生児数は 4 又は 1 匹で明らかに減少していることから、被験物質投与による影響で、生産児が少なくなったことによる変化と考えられた。

300 mg/kg 群の生存児を出産した 5 腹においては、全腹で授乳 2 日までに全哺育児が死亡し、生後 4 日の生存率が低下した。被験物質であるサリチル酸ベンジルは低分子量で脂溶性が高いことから乳汁中に移行することが考えられ、哺育期間中の死亡は乳汁中に移行した被験物質を摂取したことによる毒性である可能性が考えられる。ただし、後述の通り、被験物質は催奇形性（神経管閉鎖障害）を持つ可能性が考えられ、神経管閉鎖障害は外表観察では判明しない可能性もある反面、致死性であることから、胎生期に受けた催奇形作用により死に至った可能性は否定できない。

300 mg/kg 群の 1 腹（母動物番号：4107）の 5 例の死産児では外脳症又は外脳症と完全脊椎裂の合併が認められた。これらの異常は全て神経管閉鎖障害であり、神経管閉鎖障害はいずれも発生頻度がさほど高い所見ではないが、異常の認められた児はいずれも同じ腹であることから、催奇形作用があるとは断定できない。すなわち、被験物質と同じサリチル酸の化合物であるアセチルサリチル酸やサリチル酸ナトリウムでは、ラットやヒトにおいて本試験で認められたと同様な神経管閉鎖障害が起こることが報告されていることから[11]、被験物質による催奇形作用は否定しきれないと考える。ただし、300 mg/kg 群の全出生児、100 mg/kg 以下の投与群の生存児及び死亡児にはいずれも、神経管閉鎖障害は認められておらず、奇形児が出生する可能性は確認されていない。

100 mg/kg 群の出生児体重は雌雄いずれも出生日には対照群に比較して有意な低値、生後 4 日には低値傾向を示し、30 mg/kg 群の出生児体重も出生日には低値傾向、生後 4 日には有意な低値を示した。300 mg/kg 群の出生児体重も対照群に比較して低下していることから、100 mg/kg 群では母体内で児の成長阻害が起こり、出生時には低体重を引き起こしているものと考えられた。30 mg/kg 群の出生日から生後 4 日までの児の平均体重の増加量は、雌雄いずれも対照群に比較して有意な低値を示したが、100 mg/kg 群では対照群に比較して差がみられないことから被験物質投与の影響ではないと判断した。

8.3　無作用量

以上の結果から、本試験条件下でサリチル酸ベンジルを反復経口投与することにより、300 mg/kg 群の雌雄で、AST、ALT、ALP 及び A/G 比の高値と血小板数及び T_4 の低値、白血球数の低値傾向、活性化部分トロンボプラスチン時間の延長、大腿骨の骨梁の増加、胸腺の重量低下傾向及び萎縮、肝臓重量の増加又は増加傾向が、雄でフィブリノーゲン量及びアルブミン、尿検査における尿量並びにナトリウム及び塩素の 1 日排泄量の高値、精巣上体重量の低下又は低下傾向、グルコース及び総たん白質の低値及びプロトロンビン時間の延長がみられた。300 mg/kg 群の雌では更にトリグリセライド及びナトリウムの高値、カルシウムの低値が認められた。

100 mg/kg 群では、雌雄で T_4 の低値又は低値傾向、雄で胸腺重量の低値傾向、雌で A/G 比及び γ-GTP の高値がみられ、T_4 の低値及び胸腺重量の低値傾向並びに A/G 比の高値は 300 mg/kg 群でも得られた成績であり、γ-GTP の高値は他の逸脱・誘導酵素の動きと関連していると判断した。したがって、本被験物質の反復投与毒性に対する最大無毒性量（NOAEL）は雌雄いずれも 30 mg/kg であった。

生殖発生毒性に対する最大無毒性量（NOAEL）は、雄動物では 300 mg/kg、母動物では 300 mg/kg 群で分娩以降、被験物質投与の影響が認められたことから 100 mg/kg であった。一方、児動物では生後 0 日の出生児体重が 30 mg/kg 以上の群で低値又は低値傾向を示したことから、30 mg/kg を下回る量と推定された。

9. 文献

[1] [redacted]：サリチル酸ベンジルの赤外吸収スペクトル測定法による特性試験及び安定性試験並びに HPLC 法による被験液（媒体：コーン油）中濃度測定法バリデーション及び安定性試験（株式会社ボゾリサーチセンター 御殿場研究所、試験番号：A-2838、2016 年）

[2] [redacted]：サリチル酸ベンジル：ラットを用いた 14 日間反復経口投与毒性試験（投与量設定試験）（株式会社ボゾリサーチセンター、試験番号：N-R057、2016 年）

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[6] Siegel S, Castellan NJ. Jr. Nonparametric statistics for the behavioral sciences. 2nd ed. New York: McGraw-Hill; 1988.

[7] 佐久間昭（1981）：薬効評価－計画と分析–II, pp.23-27, 387-389, 東京大学出版会, 東京.

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[10] 加藤道幸、三森国敏：20 章.骨／関節　毒性病理組織学　毒性病理学会編　p506 2000

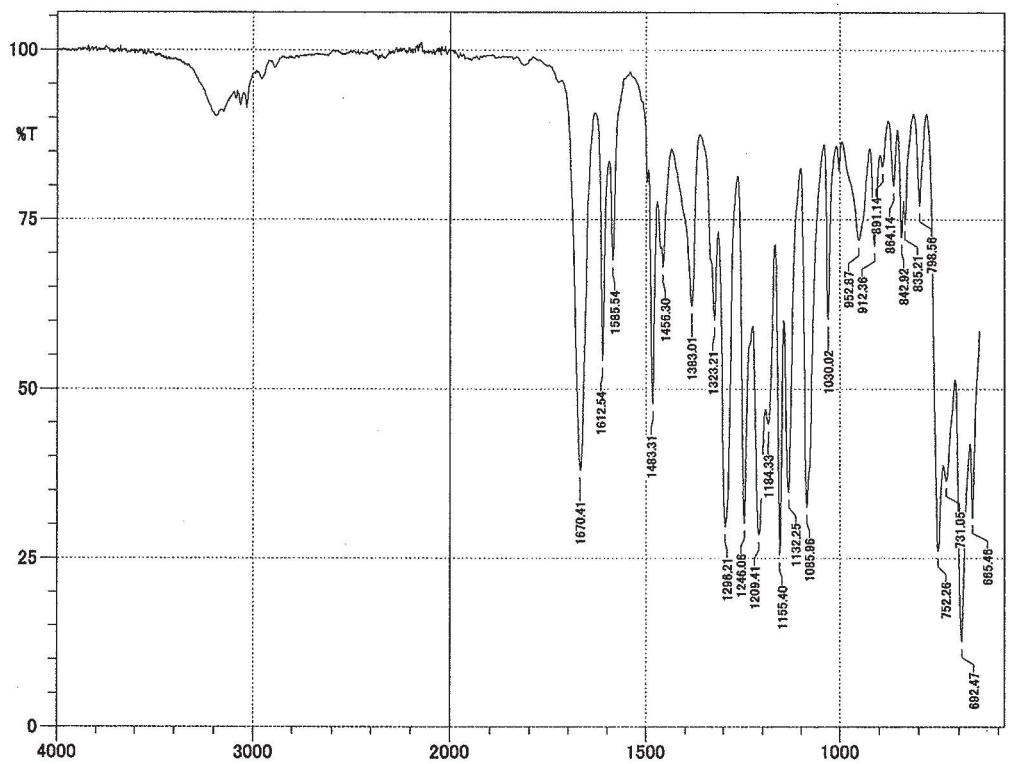
[11] Shepard Thomas H.: 2823 Salicylate-Methyl, Sodium and Acetyl Forms. Catalog of Teratogenic Agents. 13th ed. p.407 Baltimore: The Johns Hopkins University Press; 2010

R-1190
Attached Data 1

試験成績書
（サリチル酸ベンジルの特性）

試験番号　：　A-2838
ステージ　：　被験物質の使用前
測定日　：　2016 年 9 月 16 日
被験物質　：　サリチル酸ベンジル
（ロット番号：84OJN）
測定項目　：　赤外吸収スペクトル（ATR 法）

結果　：　特性のスペクトルを以下に示す。



基準　：　「新規化学物質等に係る試験を実施する試験施設に関する基準」（平成 23 年 3 月 31 日：薬食発 0331 第 8 号、平成 23･03･29 製局第 6 号、環保企発第 110331010 号）

[redacted]

試験責任者
株式会社ボゾリサーチセンター　御殿場研究所

試験番号：R-1190 (1/2)

試験成績書
（サリチル酸ベンジルの安定性）

ステージ	:	投与期間終了後
測定日	:	2016 年 12 月 26 日 2016 年 9 月 16 日（特性のスペクトル）
被験物質	:	サリチル酸ベンジル （ロット番号：84OJN）
測定項目	:	赤外吸収スペクトル（ATR 法）
判定基準	:	安定性のスペクトルを特性のスペクトル（試験番号：A-2838）と比較するとき、同一波長のところに同様の強度の吸収を認める。ただし、安定性試験において 2300 cm^{-1} 付近に吸収が観られた場合、この吸収は二酸化炭素の影響であるため評価対象としない。
結果	:	安定性のスペクトルを特性のスペクトルと比較したとき、同一波長のところに同様の強度の吸収を認めた。赤外吸収スペクトルは次のページに示す。
判定	:	適
基準	:	「新規化学物質等に係る試験を実施する試験施設に関する基準」（平成 23 年 3 月 31 日：薬食発 0331 第 8 号、平成 23･03･29 製局第 6 号、環保企発第 110331010 号）

[redacted]

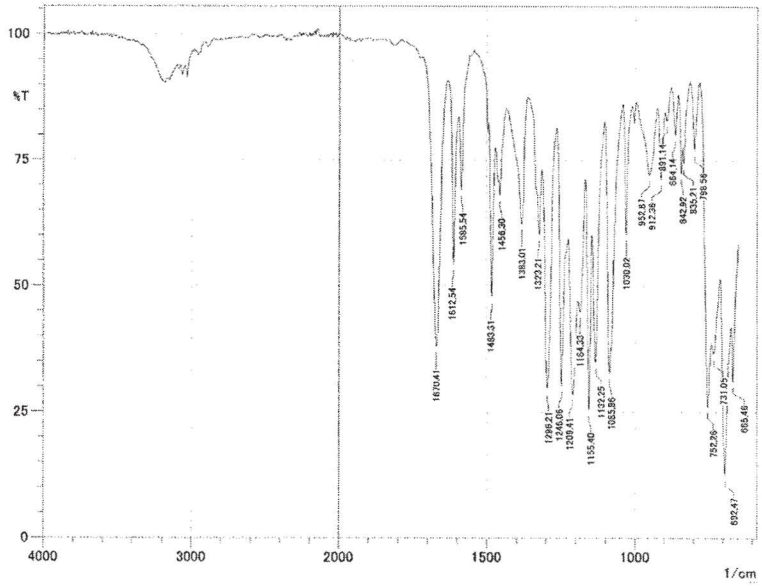
化学分析責任者
株式会社ボゾリサーチセンター　御殿場研究所

試験番号：R-1190 (2/2)

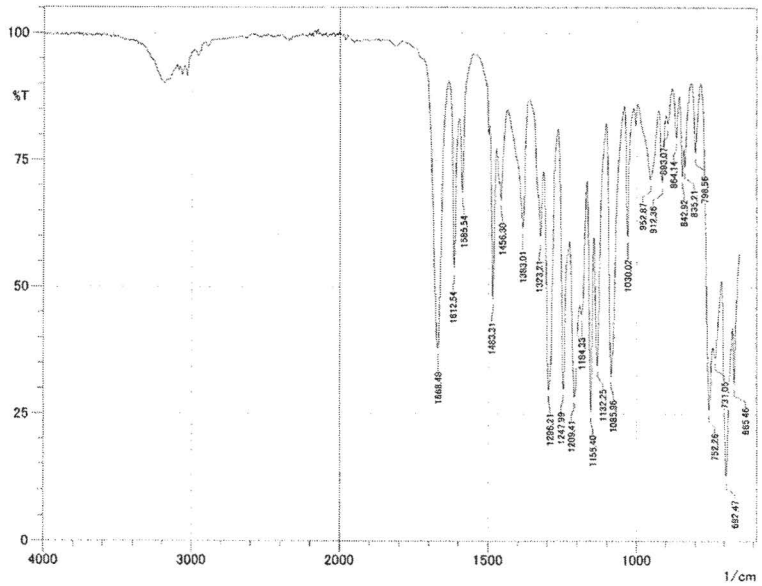
試験成績書
（サリチル酸ベンジルの安定性）

結果：

特性のスペクトル



安定性のスペクトル



試験番号：A-2838 (1/2)

試験成績書
（被験液中サリチル酸ベンジルの安定性）

被験物質	:	サリチル酸ベンジル （ロット番号：84OJN）
媒体	:	コーン油
形態	:	溶液
測定対象物質	:	サリチル酸ベンジル
保存条件	:	褐色ガラス瓶にて、冷所（冷蔵庫内、許容値：1~10°C）及び室温・非遮光保存
保存期間	:	冷所で 8 日間保存した後、室温で 24 時間保存
評価基準 安定性	:	残存率｛調製日の測定濃度の平均値（100）に対する保存後の測定濃度の平均値の割合｝が 100.0±10.0%以内。
結果	:	次ページに記載
判定	:	適
基準	:	「新規化学物質等に係る試験を実施する試験施設に関する基準」（平成 23 年 3 月 31 日：薬食発 0331 第 8 号、平成 23·03·29 製局第 6 号、環保企発第 110331010 号）

[redacted]

試験責任者
株式会社ボゾリサーチセンター　御殿場研究所

試験番号：A-2838 (2/2)

試験成績書
（被験液中サリチル酸ベンジルの安定性）

結果：

調製濃度 (mg/mL)		測定濃度 (mg/mL) 調製日	測定濃度 (mg/mL) 保存後
0.200		0.207	0.200
		0.203	0.201
		0.203	0.200
	平均値	0.204	0.201
	残存率（%）	(100)	98.5
100		102	101
		102	102
		101	101
	平均値	102	101
	残存率（%）	(100)	99.0

分析結果

試験番号 : R-1190
測定項目 : 濃度
ステージ : 初回投与
分析日 : 2016年10月24日

測定試料
被験物質 : サリチル酸ベンジル（ロット番号；84OJN）
形態 : 溶液
媒体 : コーン油
調製日 : 2016年10月24日

測定対象物質 : サリチル酸ベンジル

評価基準
濃度 : 表示値に対する割合；100.0±10.0%

結果：

表示値 (mg/mL)	測定濃度 (mg/mL)	表示値に対する割合 (%)
6	5.88	98.0
20	19.8	99.0
60	59.0	98.3

判定 : 適

分析結果

試験番号　：　R-1190
測定項目　：　濃度
ステージ　：　投与6週
分析日　：　2016年11月28日

測定試料
　被験物質　：　サリチル酸ベンジル（ロット番号；84OJN）
　形態　：　溶液
　媒体　：　コーン油
　調製日　：　2016年11月28日

測定対象物質　：　サリチル酸ベンジル

評価基準
　濃度　：　表示値に対する割合；100.0±10.0%

結果：

表示値 (mg/mL)	測定濃度 (mg/mL)	表示値に対する割合 (%)
6	6.00	100.0
20	20.5	102.5
60	60.8	101.3

判定　：　適

OT-160005

原本

作　業　報　告　書

「サリチル酸ベンジル：ラットを用いた経口投与による反復投与毒性・生殖発生毒性併合試験（試験番号：R-1190）」における
ホルモン（T_4及びT_3）測定

作業番号：OT-160005

株式会社ボゾリサーチセンター
つくば研究所

OT-160005

1. GLP 陳述書

作業番号 : OT-160005

作業表題 : 「サリチル酸ベンジル：ラットを用いた経口投与による反復投与毒性・生殖発生毒性併合試験（試験番号：R-1190）」におけるホルモン（T_4及びT_3）測定

本作業は以下の GLP 基準を遵守して実施したものです.

- 「新規化学物質等に係る試験を実施する試験施設に関する基準について」（平成 23 年 3 月 31 日：薬食発 0331 号第 8 号、平成 23・03・29 製局第 6 号、環保企発第 110331010 号）

[redacted]

試験主任者
株式会社ボゾリサーチセンター　つくば研究所

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3. ホルモン測定実施概要

3.1 作業番号

OT-160005

3.2 作業表題

「サリチル酸ベンジル：ラットを用いた経口投与による反復投与毒性・生殖発生毒性併合試験（試験番号：R-1190）」におけるホルモン（T_4及びT_3）測定

3.3 目的

「サリチル酸ベンジル：ラットを用いた経口投与による反復投与毒性・生殖発生毒性併合試験（試験番号：R-1190）」において採取された血清中のホルモン（T_4 及び T_3）濃度を測定することを目的とした。

3.4 遵守する基準

3.4.1 GLP

- 「新規化学物質等に係る試験を実施する試験施設に関する基準について」
  （平成 23 年 3 月 31 日：薬食発 0331 号第 8 号、平成 23・03・29 製局第 6 号、環保企発第 110331010 号）

3.5 試験施設

株式会社ボゾリサーチセンター　御殿場研究所
〒412-0039　静岡県御殿場市かまど 1284

3.6 試験場所

株式会社ボゾリサーチセンター　つくば研究所
〒300-2611　茨城県つくば市大久保 8 番

3.7 試験責任者

株式会社ボゾリサーチセンター　御殿場研究所　研究部門
髙　島　宏　昌
TEL：0550-82-9910　　FAX：0550-82-9911
E-mail: takashima-hiromasa@bozo.co.jp

3.8 試験主任者（ホルモン測定責任者）

株式会社ボゾリサーチセンター　つくば研究所　臨床検査部門
中　村　大　地
TEL：029-877-2770　FAX：029-865-1798

OT-160005
E-mail : [redacted]

3.9 担当者

測定主担当者 : [redacted]
統計解析担当者 :

3.10 日程

試料受領日	2016年12月28日
測定日	2017年1月6日、2017年1月10日
作業報告書作成日	2017年2月17日

3.11 予見することができなかった試験の信頼性に影響を及ぼす疑いのある事態及び試験計画書に従わなかったこと

該当事象はなかった。

3.12 資料の保存

以下のホルモン測定関係資料をファイルに綴じ込み，株式会社ボゾリサーチセンターつくば研究所の資料保存施設に保存する。その期間は作業報告書作成後5年間とする。期間終了後の取扱いについては，試験施設と株式会社ボゾリサーチセンターつくば研究所の間で協議し，その処置を決定する。

1) 作業計画書の原本
2) 試験計画書の写し
3) 試験計画書変更書の写し
4) 生データ及びその他の記録文書
5) 作業報告書の原本
6) 通信記録
7) 参考資料

3.13 試験主任者の記名・押印

[redacted]

株式会社ボゾリサーチセンター　つくば研究所

4. 要約

「サリチル酸ベンジル：ラットを用いた経口投与による反復投与毒性・生殖発生毒性併合試験（試験番号：R-1190）」において採取された血清中のホルモン（T4 及び T3）濃度を測定した。

その結果、T3 濃度では対照群と全ての投与群との間に統計的有意差は見られなかった。

一方、T4 濃度では、交配群投与終了時雄動物の中用量群及び高用量群、非交配群投与終了時雌動物の高用量群で、対照群と比べて統計的に有意な低下が見られた。なお、交配群授乳 5 日雌動物（低用量及び中用量群）では統計的有意差は認められなかった。

回復終了時剖検群では、T3、T4 濃度のいずれも統計的有意差は見られなかったことから回復性があると考えられた。

また、妊娠 25 日未分娩動物（GD25：6 例）及び授乳期間中に全哺育児が死亡した母動物（APD : 6 例）の T3 及び T4 濃度を測定した結果、GD25 の T3、T4 濃度はそれぞれ 0.40~0.66 ng/mL、11.6~18.6 ng/mL、APD の T3 濃度は 0.44~0.80 ng/mL、T4 濃度は 6 例中 1 例で 18.4 ng/mL、残り 5 例は定量下限未満（BLQ）であった。

5. 試験構成

5.1 概要

試験番号 R-1190（サリチル酸ベンジル : ラットを用いた経口投与による反復投与毒性・生殖毒性併合試験）の群構成を下表に示す。

群構成表（雄）

試験群	投与量 (mg/kg)	交配群			
		投与終了時剖検群		回復終了時剖検群	
		動物数	動物番号	動物数	動物番号
対照群	0	7	1001-1007	5	1008-1012
低用量群	30	12	2001-2012		
中用量群	100	12	3001-3012		
高用量群	300	7	4001-4007	5	4008-4012

群構成表（雌）

試験群	投与量 (mg/kg)	交配群		非交配群			
		投与終了時剖検群		投与終了時剖検群		回復終了時剖検群	
		動物数	動物番号	動物数	動物番号	動物数	動物番号
対照群	0	12	1101-1112	5	5101-5105	5	5106-5110
低用量群	30	12	2101-2112				
中用量群	100	12	3101-3112				
高用量群	300	12	4101-4112	5	6101-6105	5	6106-6110

5.2 試料

Text-Table 1

<table>
<tr><td rowspan="3">ホルモン測定試料（血清）</td><td rowspan="3">測定対象</td><td rowspan="3">試験群</td><td rowspan="3"></td><td rowspan="3">動物数</td><td colspan="4">血清試料数</td></tr>
<tr><td colspan="2">交配群</td><td colspan="2">非交配群</td></tr>
<tr><td>投与終了時剖検群</td><td>回復終了時剖検群</td><td>投与終了時剖検群</td><td>回復終了時剖検群</td></tr>
<tr><td rowspan="2"></td><td rowspan="2">対照群</td><td>雄</td><td>10</td><td>5</td><td>5</td><td>－</td><td>－</td></tr>
<tr><td>雌</td><td>15</td><td>5</td><td>－</td><td>5</td><td>5</td></tr>
<tr><td rowspan="2"></td><td rowspan="2">低用量群</td><td>雄</td><td>5</td><td>5</td><td>－</td><td>－</td><td>－</td></tr>
<tr><td>雌</td><td>5</td><td>5</td><td>－</td><td>－</td><td>－</td></tr>
<tr><td rowspan="2"></td><td rowspan="2">中用量群</td><td>雄</td><td>5</td><td>5</td><td>－</td><td>－</td><td>－</td></tr>
<tr><td>雌</td><td>5</td><td>5</td><td>－</td><td>－</td><td>－</td></tr>
<tr><td rowspan="2"></td><td rowspan="2">高用量群</td><td>雄</td><td>10</td><td>5</td><td>5</td><td>－</td><td>－</td></tr>
<tr><td>雌</td><td>10</td><td>0</td><td>－</td><td>5</td><td>5</td></tr>
<tr><td></td><td></td><td colspan="7">なお、次の動物もホルモン測定を行ったが統計解析から除外した。
妊娠 25 日未分娩動物：6 例
授乳期間中に全哺育児が死亡した母動物：6 例</td></tr>
<tr><td></td><td>血清量及び受領チューブ数</td><td colspan="7">約 0.5 mL×3 本、合計 231 本（77 検体×3 本）</td></tr>
<tr><td></td><td>試験施設での保存条件</td><td colspan="7">–80°C の冷凍庫（許容範囲：–70°C 以下）、実測値：–88~ –84°C</td></tr>
<tr><td></td><td>輸送条件</td><td colspan="7">ドライアイス同梱下で輸送された。</td></tr>
<tr><td></td><td>識別</td><td colspan="7">ラベルに明記された情報（試験番号、検査時期、検査項目、試料番号、試料名（マーカーの色分け）をもとに、試験場所で血清試料名を割り付けた。</td></tr>
<tr><td></td><td>試験場所での保存条件</td><td colspan="7">–80°C の冷凍庫（許容範囲：–70°C 以下）、実測値：–87~ –85°C</td></tr>
<tr><td></td><td>血清試料安定性（–70°C 以下）[1)-4)]</td><td colspan="7">T3、T4 保存安定性：6 週間（43 日間）、繰返し凍結融解回数：3 回まで。</td></tr>
<tr><td></td><td>残余の取扱い</td><td colspan="7">測定終了後に試験責任者からの指示に基づいて試験場所で廃棄する。</td></tr>
</table>

6. ホルモン測定

受領した試料（Text-Table 1）を用いて下記 6.1 に従い、ホルモン濃度（T3 及び T4 濃度）を測定した。

トータルカウント試料（TC）、標準試料（Cal）及び精度管理試料（QC）は duplicate、血清試料は singlicate で測定した。

Text-Table 2

項目	測定法	単位	表示桁
T3	RIA 法	ng/mL	小数第 2 位
T4	RIA 法	ng/mL	小数第 1 位

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Text-Table 3

T3 測定

キット	：RIA-gnost®- T3（Cisbio Bioassays）
保存条件	：2~8°C（実測値：3.9~5.0°C）
Lot No.	：222A
使用期限	：28-Feb-2017
表示濃度	：0.25、0.49、0.91、1.95、4.00、7.50 ng/mL（Cal-1/2、1、2、3、4、5）
定量範囲	：0.25~7.50 ng/mL（Cal-1/2~5）
測定装置	：ガンマカウンター （放射線測定装置 AccuFLEX γ7010、日立アロカメディカル）

T4 測定

キット	：RIA-gnost®- T4（Cisbio Bioassays）
保存条件	：2~8°C（実測値：3.9~5.2°C）
Lot No.	：222A
使用期限	：28-Feb-2017
表示濃度	：11.3、22.6、45.0、85.0、181.0、340.0 ng/mL（Cal-1/2、1、2、3、4、5）
定量範囲	：11.3~340.0 ng/mL（Cal-1/2~5）
測定装置	：ガンマカウンター （放射線測定装置 AccuFLEX γ7010、日立アロカメディカル）

6.1 アッセイ方法

6.1.1 T3 測定

6.1.1.1 標準試料（Cal-1/2）の調製

Cal-1 と Cal-0 を 1：1（各 70 µL：70 µL）で混合し、Cal-1/2（表示濃度：0.25 ng/mL）とした。調製当日を使用期限とした。

6.1.1.2 測定操作

1) 各試料 50 µL を Ab チューブに加えた（TC を除く）。
2) ^{125}I-T3 tracer（1 mL）をチューブに添加し、ふたをして撹拌した。TC については、tracer をプラスチックチューブ（丸底テストチューブ、WATSON）に加えた。
3) 23°C 設定のインキュベータ内で 55 分間振とうした（300rpm 設定）。
4) チューブ内の溶液をアスピレーターで除去した（TC を除く）。
5) ガンマカウンターでチューブの ^{125}I（60 秒間）の放射線計数率（cpm）を測定した。

6.1.2 T4 測定

6.1.2.1 標準試料（Cal-1/2）の調製

Cal-1 と Cal-0 を 1：1（各 30 µL：30 µL）で混合し、Cal-1/2（表示濃度：11.3 ng/mL）とした。調製当日を使用期限とした。

6.1.2.2 測定操作

1) 各試料 20 µL を Ab チューブに加えた（TC を除く）。

2) ^{125}I-T4 tracer（1 mL）をチューブに添加し、ふたをして撹拌した。TC については、tracer をプラスチックチューブ（丸底テストチューブ、WATSON）に加えた。
3) 23°C 設定のインキュベータ内で 55 分間振とうした（300rpm 設定）。
4) チューブ内の溶液をアスピレーターで除去した（TC を除く）。
5) ガンマカウンターでチューブの ^{125}I（60 秒間）の放射線計数率（cpm）を測定した。

6.2 データ解析

Magellan Tracker ver. 7.0 ソフトウェア（Magellan）を用いて、放射線計数率（cpm）から各試料の T3 及び T4 濃度を算出した。

X 軸を濃度（ng/mL、対数表示）、Y 軸を放射線計数率（cpm）の測定値とし、表示濃度のプロットから検量線を作成した。

解析法、表示桁数を下表に示した。

項目	解析法	表示桁	
		放射線計数率（cpm）	測定濃度
T3	4 パラメーター Marquardt（重みづけあり）	小数第 2 位	小数第 2 位
T4	4 パラメーター Marquardt	小数第 1 位	小数第 1 位

6.3 測定成立条件の評価

本測定は、T3、T4 ともに以下の測定成立条件を全て満たしていたことから測定成立とした。計算は Microsoft office Excel 2010（Ver.14）で実施（表示桁数で計算）した。

1) TC 及び Cal-0
- TC 及び Cal-0 の平均放射線計数率が Cal-1/2 の平均放射線計数率を超えている。
- 平均放射線計数率は以下の計算式から算出する（T3 は小数第 2 位、T4 は小数第 1 位まで表示）。

$$\text{平均放射線計数率（cpm）} = \frac{\text{個別放射線計数率（cpm）の和}}{2}$$

2) 標準試料
- 測定濃度の表示濃度に対する真度が Cal-1/2、Cal-5 で 100±25.0%以内、Cal-1~4 のうち 3 試料以上で 100±20.0%以内である。
- 真度（%）は以下の計算式から算出する（小数第 1 位まで表示）。

$$\text{真度（\%）} = \frac{\text{測定濃度}}{\text{表示濃度}} \times 100$$

3) QC
- 測定濃度が表示濃度範囲内である。

6.4 再測定

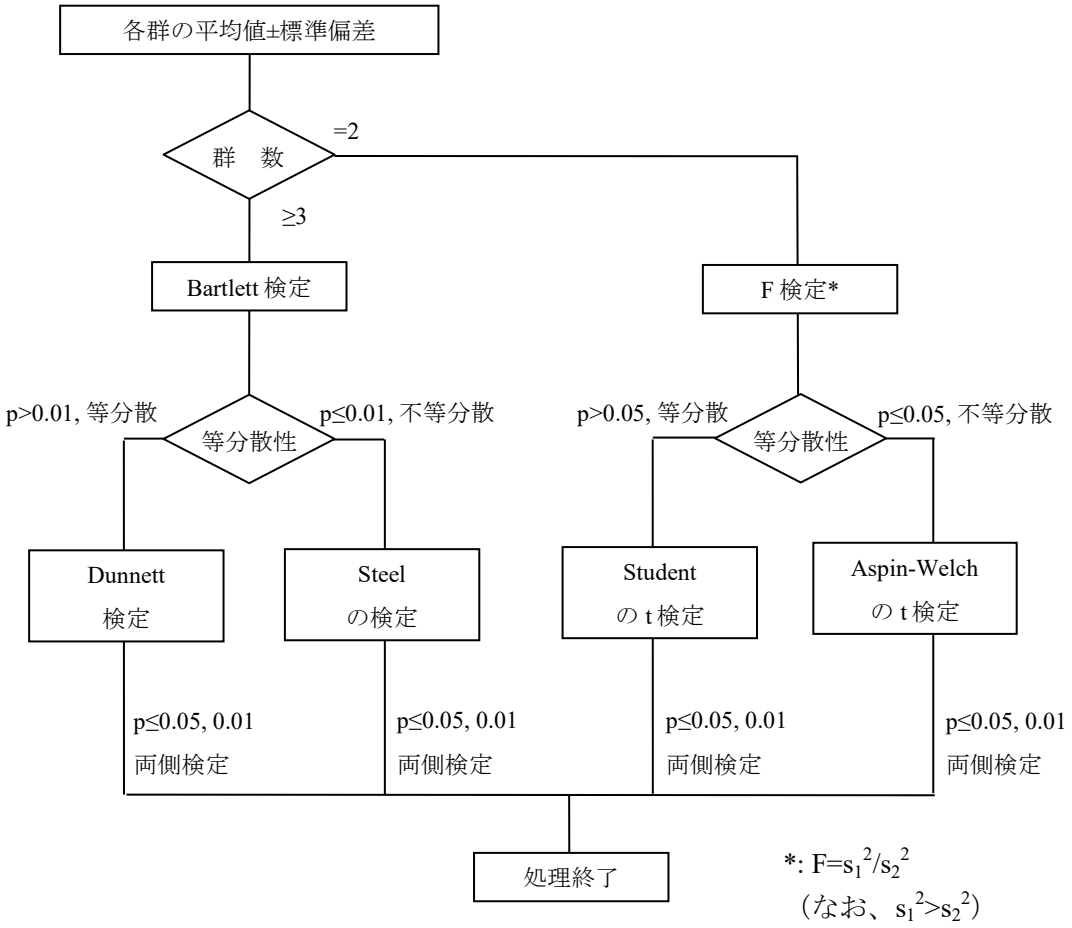
前述の測定成立条件（6.3）を満たしていたため、本測定内の測定濃度を採用した。

試料の測定濃度が定量下限を下回った場合は、「BLQ」（Below lower limit of quantification）とした。

再測定は実施しなかった。

7. 統計解析

検査項目について下記の模式図に示す方法に従って検定した。各群の平均値（Mean）及び標準偏差（SD）の算出には、それぞれ Microsoft Office Excel 2010（Ver.14）SP2 における AVERAGE 関数及び STDEV 関数を用いた。解析には SAS Release 9.1.3 を使用した。BLQ の場合は「0」を用いた。ただし、妊娠 25 日未分娩動物（GD25）及び授乳期間中に全哺育児が死亡した母動物（APD）のデータは統計解析から除外した。



8. 結果及び考察

8.1 EOA（交配群投与終了時雄動物）

T3 及び T4 濃度測定の結果を Table 1 及び Appendix 1 に示した。

T3 濃度は対照群と投与群との間に統計的有意差は認められなかったが、T4 濃度は中用量群、高用量群で有意な低下が認められた。

8.2 EOA（非交配群投与終了時雌動物）

T3 及び T4 濃度測定の結果を Table 2 及び Appendix 2 に示した。

T3 濃度は対照群と投与群との間に統計的有意差は認められなかったが、T4 濃度は高用量群で有意な低下が認められた。

8.3 LD5（交配群授乳 5 日雌動物）

T3 及び T4 濃度測定の結果を Table 3 及び Appendix 3 に示した。

T3、T4 濃度ともに、対照群と投与群との間に統計的有意差は認められなかった。

8.4 EOR（交配群回復終了時雄動物）

T3 及び T4 濃度測定の結果を Table 4 及び Appendix 4 に示した。

T3、T4 濃度ともに、対照群と投与群との間に統計的有意差は認められなかった。

8.5 EOR（非交配群回復終了時雌動物）

T3 及び T4 濃度測定の結果を Table 5 及び Appendix 5 に示した。

T3、T4 濃度ともに、対照群と投与群との間に統計的有意差は認められなかった。

8.6 GD25（妊娠 25 日未分娩動物）

T3 及び T4 濃度測定の結果を Appendix 6 に示した。

T3 濃度は 0.40~0.66 ng/mL、T4 濃度は 11.6~18.6 ng/mL であった。

8.7 APD（授乳期間中に全哺育児が死亡した母動物）

T3 及び T4 濃度測定の結果を Appendix 7 に示した。

T3 濃度は 0.44~0.80 ng/mL、T4 濃度は 6 例中 1 例で 18.4 ng/mL、残り 5 例は定量下限未満（BLQ）であった。

9. 結論

「サリチル酸ベンジル：ラットを用いた経口投与による反復投与毒性・生殖発生毒性併合試験（試験番号：R-1190）」において採取された血清中のホルモン（T4 及び T3）濃度を測定した。

その結果、T3 濃度では対照群と全ての投与群との間に統計的有意差は見られなかった。

一方、T4 濃度では、交配群投与終了時雄動物の中用量群及び高用量群、非交配群投与終了時雌動物の高用量群で、対照群と比べて統計的に有意な低下が見られた。なお、交配群授乳 5 日雌動物（低用量及び中用量群）では統計的有意差は認められなかった。

回復終了時剖検群では、T3、T4 濃度のいずれも統計的有意差は見られなかったことから回復性があると考えられた。

また、妊娠 25 日未分娩動物（GD25：6 例）及び授乳期間中に全哺育児が死亡した母動物（APD : 6 例）の T3 及び T4 濃度を測定した結果、GD25 の T3、T4 濃度はそれぞれ 0.40~0.66 ng/mL、11.6~18.6 ng/mL、APD の T3 濃度は 0.44~0.80 ng/mL、T4 濃度は 6 例中 1 例で 18.4 ng/mL、残り 5 例は定量下限未満（BLQ）であった。

10. 参考資料

1) 「ラット血清中 Triiodothyronine（T3）の RIA による測定系のバリデーション」最終報告書、株式会社ボゾリサーチセンターつくば研究所社内試験（試験番号 : N-ET114007、2014 年）

2) 「ラット血清中 Thyroxine（T4）の RIA による測定系のバリデーション」最終報告書、株式会社ボゾリサーチセンターつくば研究所社内試験（試験番号 : N-ET114008、2014 年）

3) 「ラットの血清中総 T3 長期凍結保存安定性の検討」中間報告書、株式会社ボゾリサーチセンターつくば研究所社内試験（試験番号 : N-ZT164005、2016 年）

4) 「ラットの血清中総 T4 長期凍結保存安定性の検討」中間報告書、株式会社ボゾリサーチセンターつくば研究所社内試験（試験番号 : N-ZT164006、2016 年）

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Table 1 Hormone concentrations in rat serum of EOA (Male of mating group)

Test Article Dose		T3 ng/mL	T4 ng/mL
Benzyl salicylate 0 mg/kg	Mean	0.58	33.9
	SD	0.08	3.7
	n	5	5
Benzyl salicylate 30 mg/kg	Mean	0.61	29.8
	SD	0.10	5.1
	n	5	5
Benzyl salicylate 100 mg/kg	Mean	0.52	19.2*
	SD	0.09	2.1 S2
	n	5	5
Benzyl salicylate 300 mg/kg	Mean	0.46	0.0*
	SD	0.05	0.0 S2
	n	5	5

Significantly different from control group : * P<0.05
S2: Steel Test Two-Side

Table 2 Hormone concentrations in rat serum of EOA (Female of no-mating group)

Test Article Dose		T3 ng/mL	T4 ng/mL
Benzyl salicylate 0 mg/kg	Mean	0.62	24.1
	SD	0.20	3.5
	n	5	5
Benzyl salicylate 300 mg/kg	Mean	0.54	2.5**
	SD	0.12	5.6 T2
	n	5	5

Significantly different from control group : ** P<0.01
T2: Student's t-test Two-Side

Table 3 Hormone concentrations in rat serum of LD5 (Female of mating group)

Test Article Dose		T3 ng/mL	T4 ng/mL
Benzyl salicylate 0 mg/kg	Mean	0.60	23.9
	SD	0.07	8.8
	n	5	5
Benzyl salicylate 30 mg/kg	Mean	0.74	25.5
	SD	0.13	7.8
	n	5	5
Benzyl salicylate 100 mg/kg	Mean	0.65	18.3
	SD	0.13	1.9
	n	5	5

No significant difference in any treated groups from control group

Table 4 Hormone concentrations in rat serum of EOR (Male of mating group)

Test Article Dose		T3 ng/mL	T4 ng/mL
Benzyl salicylate 0 mg/kg	Mean	0.65	36.3
	SD	0.10	4.4
	n	5	5
Benzyl salicylate 300 mg/kg	Mean	0.64	35.9
	SD	0.09	5.4
	n	5	5

No significant difference in any treated groups from control group

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Table 5 Hormone concentrations in rat serum of EOR (Female of no-mating group)

Test Article Dose		T3 ng/mL	T4 ng/mL
Benzyl salicylate 0 mg/kg	Mean	0.74	30.5
	SD	0.11	10.4
	n	5	5
Benzyl salicylate 300 mg/kg	Mean	0.72	22.3
	SD	0.08	3.8
	n	5	5

No significant difference in any treated groups from control group

Appendix 1 Hormone concentrations in rat serum of EOA (Male of mating group, individual data)

A. No.	T3 (ng/mL)	T4 (ng/mL)	A. No.	T3 (ng/mL)	T4 (ng/mL)	A. No.	T3 (ng/mL)	T4 (ng/mL)	A. No.	T3 (ng/mL)	T4 (ng/mL)
1001	0.55	28.5	2001	0.57	24.3	3001	0.62	19.5	4001	0.50	BLQ
1002	0.52	32.2	2002	0.53	37.6	3002	0.41	17.3	4002	0.38	BLQ
1003	0.58	35.5	2003	0.55	27.0	3003	0.50	18.2	4003	0.46	BLQ
1004	0.52	35.0	2004	0.65	28.3	3004	0.48	18.4	4004	0.50	BLQ
1005	0.71	38.2	2005	0.77	31.8	3005	0.60	22.6	4005	0.48	BLQ
Mean	0.58	33.9	Mean	0.61	29.8	Mean	0.52	19.2	Mean	0.46	0.0
SD	0.08	3.7	SD	0.10	5.1	SD	0.09	2.1	SD	0.05	0.0

BLQ: Below lower limit of quantification (< 11.3 ng/mL). BLQ was treated as zero for the statistical analysis.

Appendix 2 Hormone concentrations in rat serum of EOA (Female of no-mating group, individual data)

A. No.	T3 (ng/mL)	T4 (ng/mL)	A. No.	T3 (ng/mL)	T4 (ng/mL)
5101	0.69	26.3	6101	0.53	12.6
5102	0.35	19.8	6102	0.50	BLQ
5103	0.66	22.2	6103	0.68	BLQ
5104	0.51	23.5	6104	0.60	BLQ
5105	0.88	28.9	6105	0.37	BLQ
Mean	0.62	24.1	Mean	0.54	2.5
SD	0.20	3.5	SD	0.12	5.6

BLQ: Below lower limit of quantification (< 11.3 ng/mL). BLQ was treated as zero for the statistical analysis.

Appendix 3 Hormone concentrations in rat serum of LD5 (Female of mating group, individual data)

A. No.	T3 (ng/mL)	T4 (ng/mL)	A. No.	T3 (ng/mL)	T4 (ng/mL)	A. No.	T3 (ng/mL)	T4 (ng/mL)
1101	0.49	19.5	2101	0.58	13.7	3102	0.52	17.9
1102	0.61	18.2	2102	0.76	28.8	3103	0.82	19.9
1104	0.69	37.4	2103	0.70	27.1	3104	0.51	18.3
1107	0.58	16.2	2107	0.72	23.2	3105	0.65	20.0
1110	0.61	28.2	2112	0.93	34.7	3108	0.73	15.3
Mean	0.60	23.9	Mean	0.74	25.5	Mean	0.65	18.3
SD	0.07	8.8	SD	0.13	7.8	SD	0.13	1.9

Appendix 4 Hormone concentrations in rat serum of EOR (Male of mating group, individual data)

A. No.	T3 (ng/mL)	T4 (ng/mL)	A. No.	T3 (ng/mL)	T4 (ng/mL)
1008	0.59	31.6	4008	0.56	33.7
1009	0.66	36.7	4009	0.72	36.5
1010	0.69	37.5	4010	0.55	30.4
1011	0.78	42.9	4011	0.62	34.0
1012	0.53	33.0	4012	0.76	44.8
Mean	0.65	36.3	Mean	0.64	35.9
SD	0.10	4.4	SD	0.09	5.4

Appendix 5 Hormone concentrations in rat serum of EOR (Female of no-mating group, individual data)

A. No.	T3 (ng/mL)	T4 (ng/mL)	A. No.	T3 (ng/mL)	T4 (ng/mL)
5106	0.84	47.9	6106	0.59	20.2
5107	0.85	32.6	6107	0.73	18.6
5108	0.64	25.5	6108	0.79	20.3
5109	0.74	23.0	6109	0.73	24.3
5110	0.63	23.6	6110	0.75	27.9
Mean	0.74	30.5	Mean	0.72	22.3
SD	0.11	10.4	SD	0.08	3.8

Appendix 6 Hormone concentrations in rat serum of GD25 (Female of mating group, individual data)

A. No.	T3 (ng/mL)	T4 (ng/mL)
4101	0.64	18.6
4103	0.52	11.6
4104	0.61	16.3
4108	0.66	18.5
4111	0.40	13.9
4112	0.62	15.6

Appendix 7 Hormone concentrations in rat serum of APD (Female of mating group, individual data)

A. No.	T3 (ng/mL)	T4 (ng/mL)
4102	0.62	BLQ
4105	0.49	BLQ
4106	0.80	18.4
4107	0.54	BLQ
4109	0.44	BLQ
4110	0.57	BLQ

BLQ: Below lower limit of quantification (< 11.3 ng/mL)

信頼性保証書（1/2）

作業番号： OT-160005

作業表題： 「サリチル酸ベンジル：ラットを用いた経口投与による反復投与毒性・生殖発生毒性併合試験（試験番号：R-1190）」におけるホルモン（T_4 及び T_3）測定

本ホルモン測定は以下に示す基準に基づいて実施されたことを保証致します。

・「新規化学物質等に係る試験を実施する試験施設に関する基準について」
（平成 23 年 3 月 31 日：薬食発 0331 号第 8 号、平成 23・03・29 製局第 6 号、環保企発第 110331010 号）

なお、調査は下記の通り実施致しました。

2017 年 2 月 17 日
株式会社ボゾリサーチセンター
つくば研究所
試験場所信頼性保証部門責任者
石川　雅章

調査項目	調査担当者	調査日	試験主任者及び試験場所管理責任者への報告日	試験責任者，運営管理者及び主信頼性保証部門責任者への報告日
作業計画書	原田　美央子	2016 年 12 月 20 日 2016 年 12 月 27 日	2016 年 12 月 28 日	2016 年 12 月 28 日
試料受領	原田　美央子	2016 年 12 月 28 日	2016 年 12 月 28 日	2016 年 12 月 28 日
測定	原田　美央子	2017 年 1 月 6 日	2017 年 1 月 6 日	2017 年 1 月 6 日

信頼性保証書（2/2）

調 査 項 目	調査担当者	調　査　日	試験主任者 及び試験場所 管理責任者 への報告日	試験責任者， 運営管理者及び 主信頼性保証 部門責任者 への報告日
作業報告書草案、生データ	原田　美央子	2017年1月24日 2017年1月25日 2017年1月26日	2017年1月27日	2017年1月27日
改善確認	原田　美央子	2017年2月1日 2017年2月8日	2017年2月8日	2017年2月8日
作業報告書	原田　美央子	2017年2月16日	2017年2月17日	2017年2月17日

サリチル酸ベンジル: ラットを用いた 14 日間反復経口投与毒性試験（投与量設定試験）における所見

試験番号：N-R057

被験物質		媒体 a)	サリチル酸ベンジル		
投与量(mg/kg)		0	250	500	1000
投与容量(mL/kg)		5	5	5	5
使用動物数		5/5	5/5	5/5	5/5
死亡動物数		0/0	0/0	0/1	5/5
死亡発現時期		–	–	D7: 0/1	D2: 0/1 D3: 5/3 D4: –/1
一般状態	生存	–	–	–	–
	死亡			–	間代性痙攣 D3: 2/2
体重			–	D4: ↓/↓ D10: ↓/↓ D14: ↓/– 増加量: ⇓/–	
摂餌量			–	D4: ⇓/⇓ D14: –/↑	
血液学検査 HGB HCT			–	 –/↓ –/↓	
血液化学検査 AST ALT GLU TP			 –/– –/↑ ↓/– ↓/–	 ⇑/⇑ –/– ⇓/– –/–	
器官重量	絶対 胸腺 心臓 肝臓		 ↓/– – –	 ⇓/↓ ↓/– –/↑	
	相対 胸腺 肺 肝臓		–	 ↓/↓ –/↑ ⇑/⇑	
剖検	生存	腺胃暗赤色巣: 0/1	腺胃暗赤色巣: 2/3 腎臓のう胞: 1/0	前胃隆起巣: 0/1 腺胃暗赤色巣: 0/1 肺暗赤色巣: 1/0	
	死亡			前胃隆起巣: 0/1	前胃隆起巣: 3/3 前胃暗赤色巣: 0/1 腺胃暗赤色巣: 1/1 肺暗赤色化: 0/1 異常所見なし: 1/0

a) ：コーン油
– ：著変なし　　ND ：データなし又は判別不明あるいは検定不能
/ ：雄/雌
↑又は↓；$p<0.05$，⇑又は⇓；$p<0.01$，（対照群との間に有意差あり）

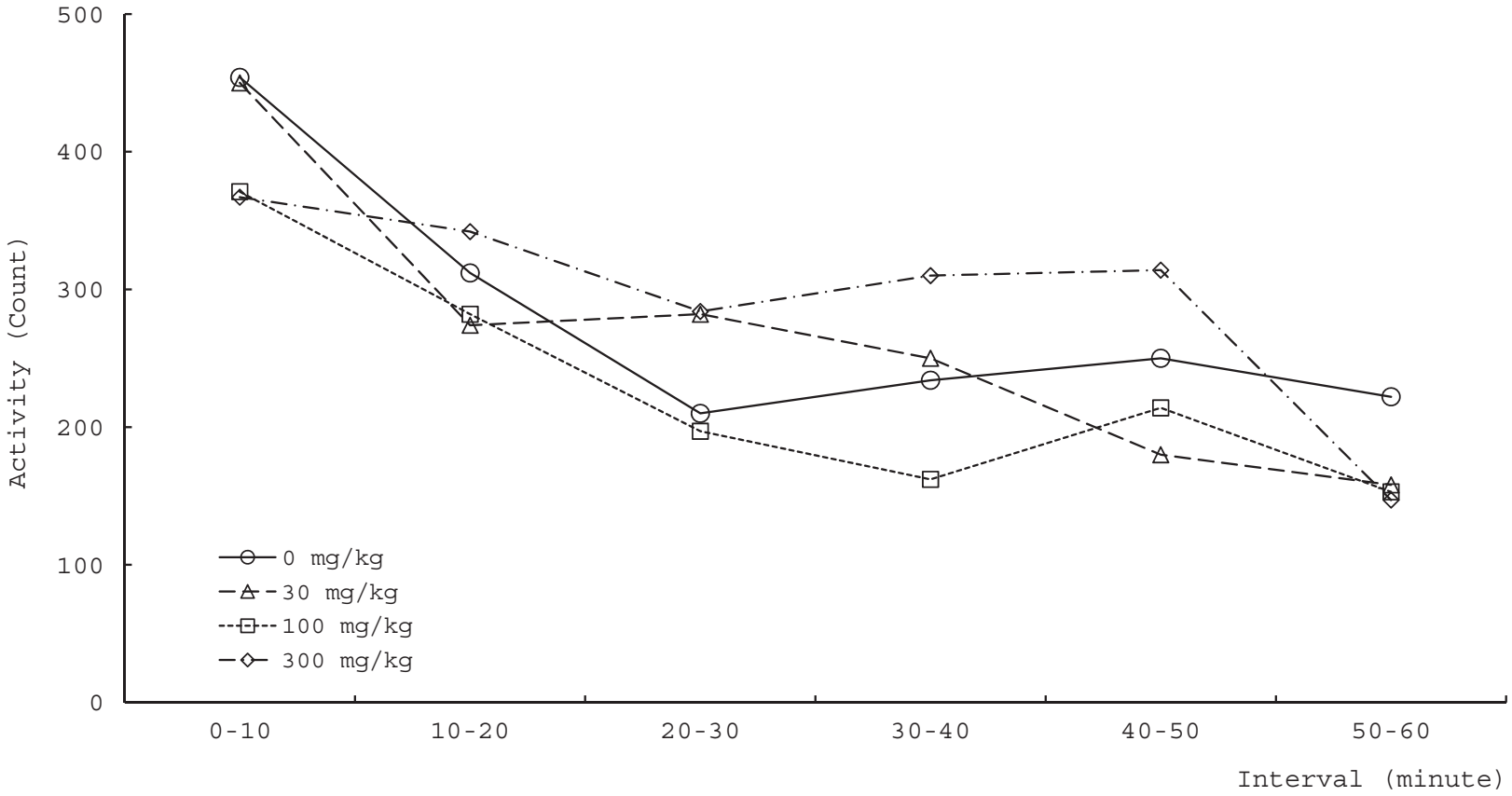

Fig.1 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Motor activity of male rats (Week 6 of administration)

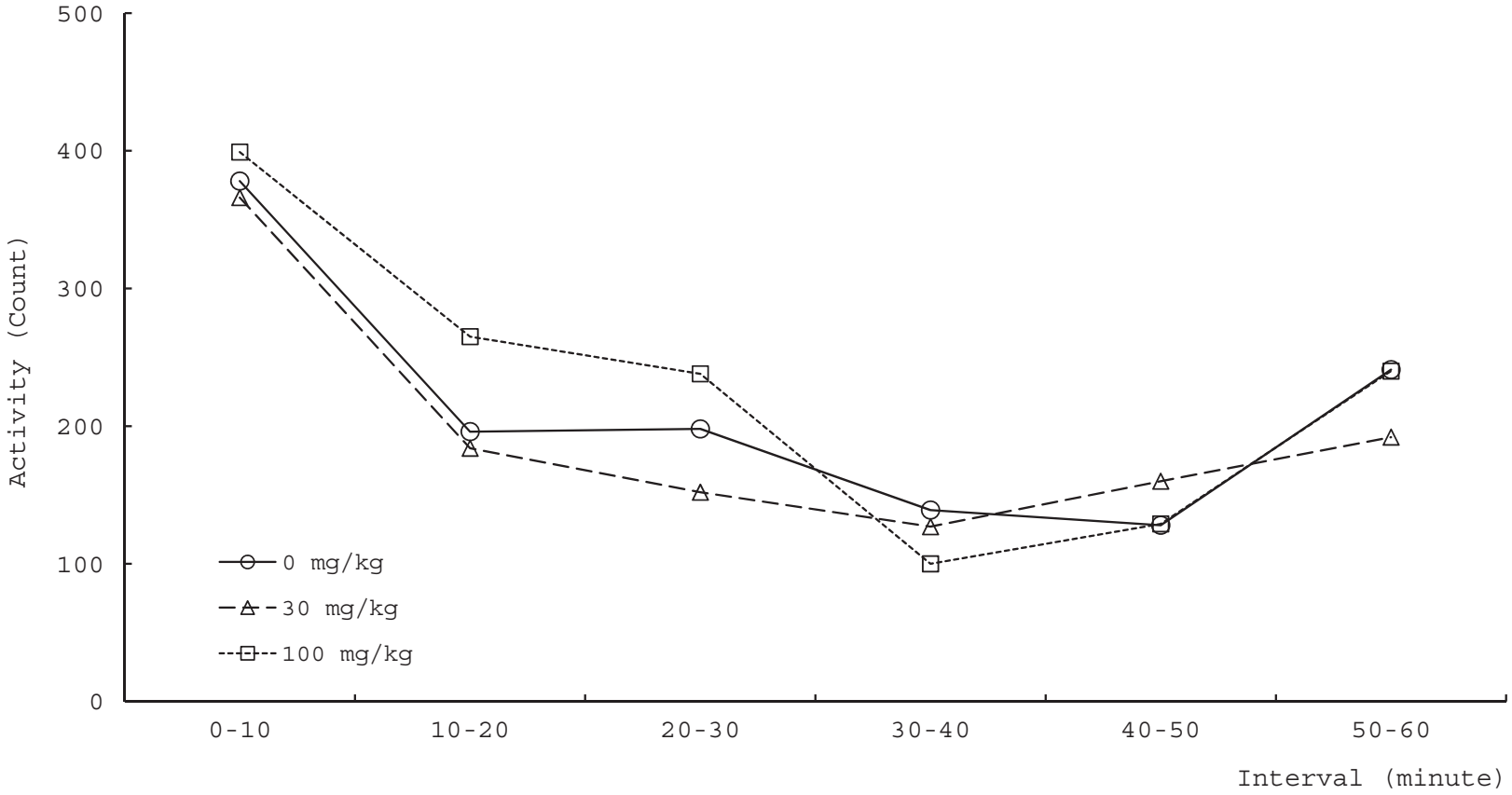

Fig.2 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Motor activity of female rats (Lactation day 4)

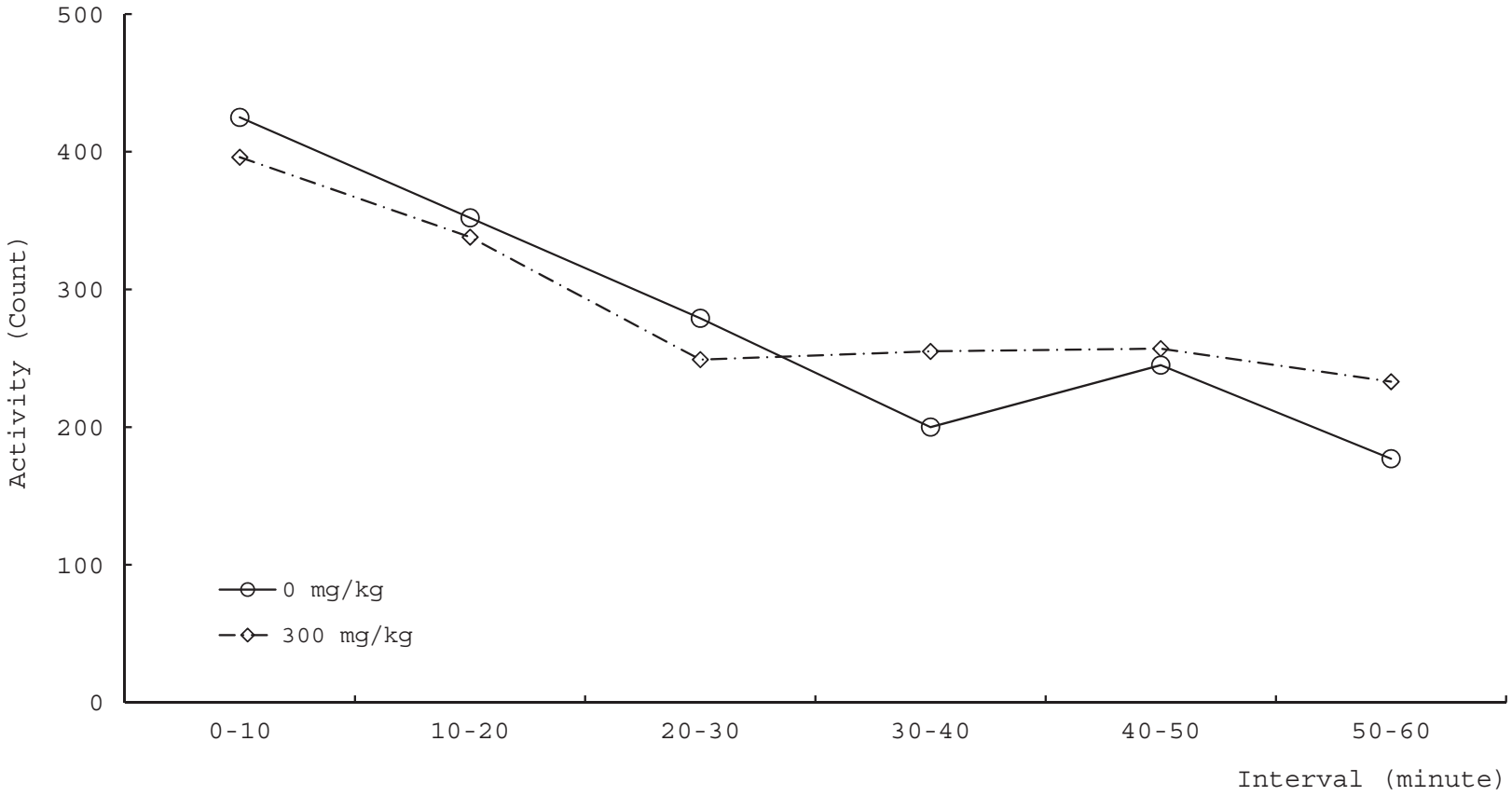

Fig.3 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Motor activity of male rats (Week 2 of recovery)

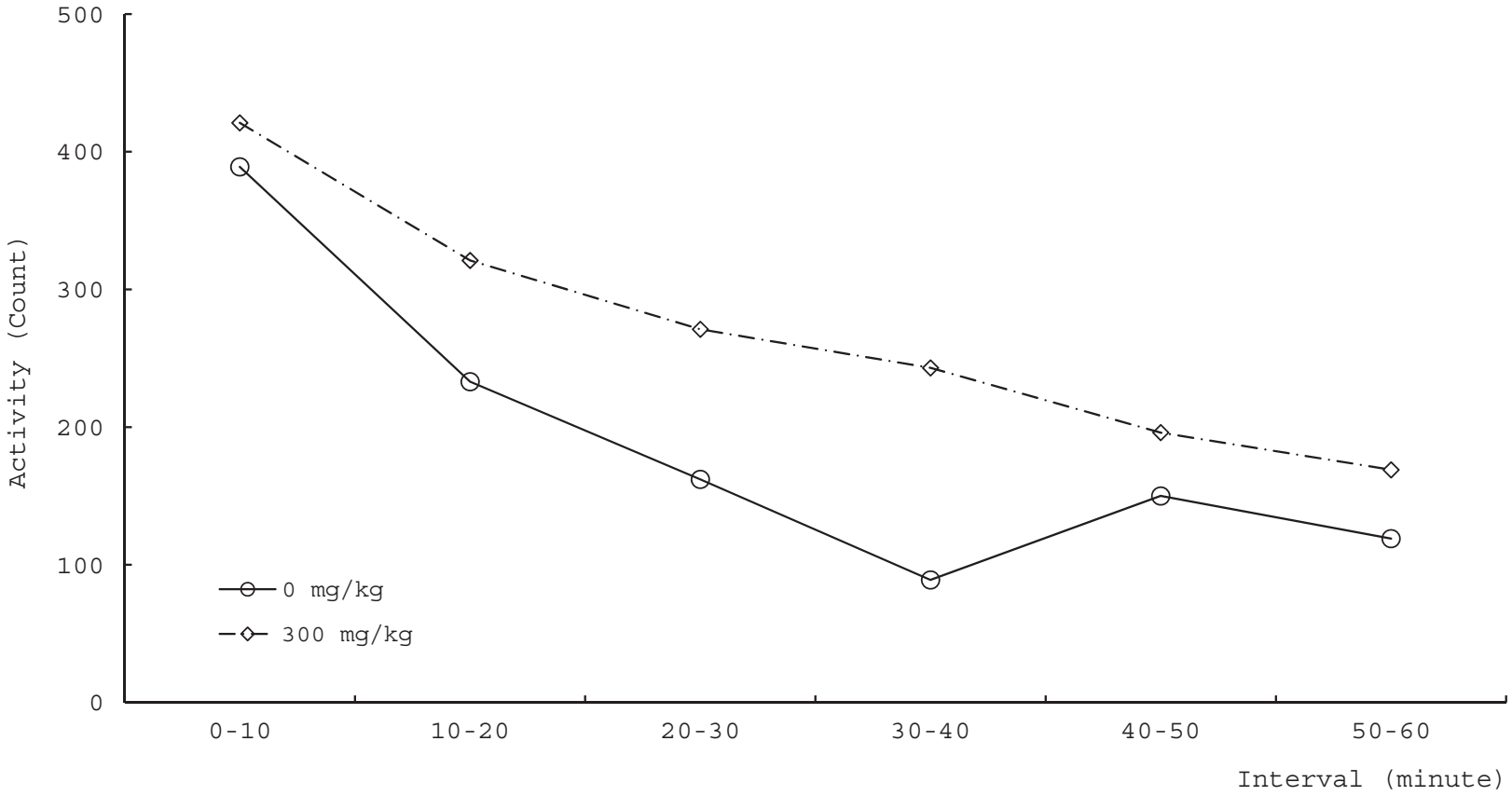

Fig.4 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Motor activity of female rats (Week 2 of recovery)

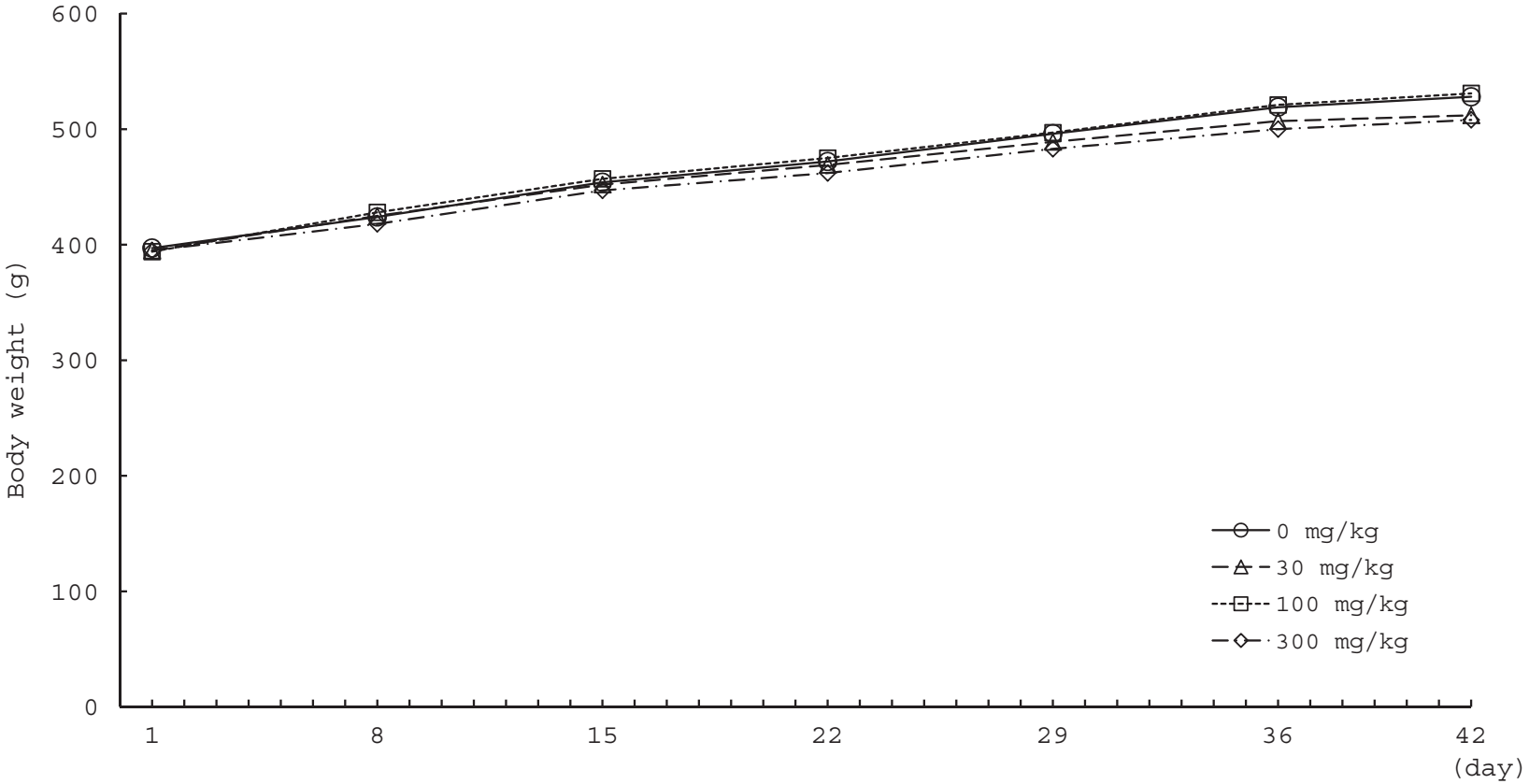

Fig.5 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Body weight of male rats (F0 before mating Day 1-15, F0 mating Day 15-43)

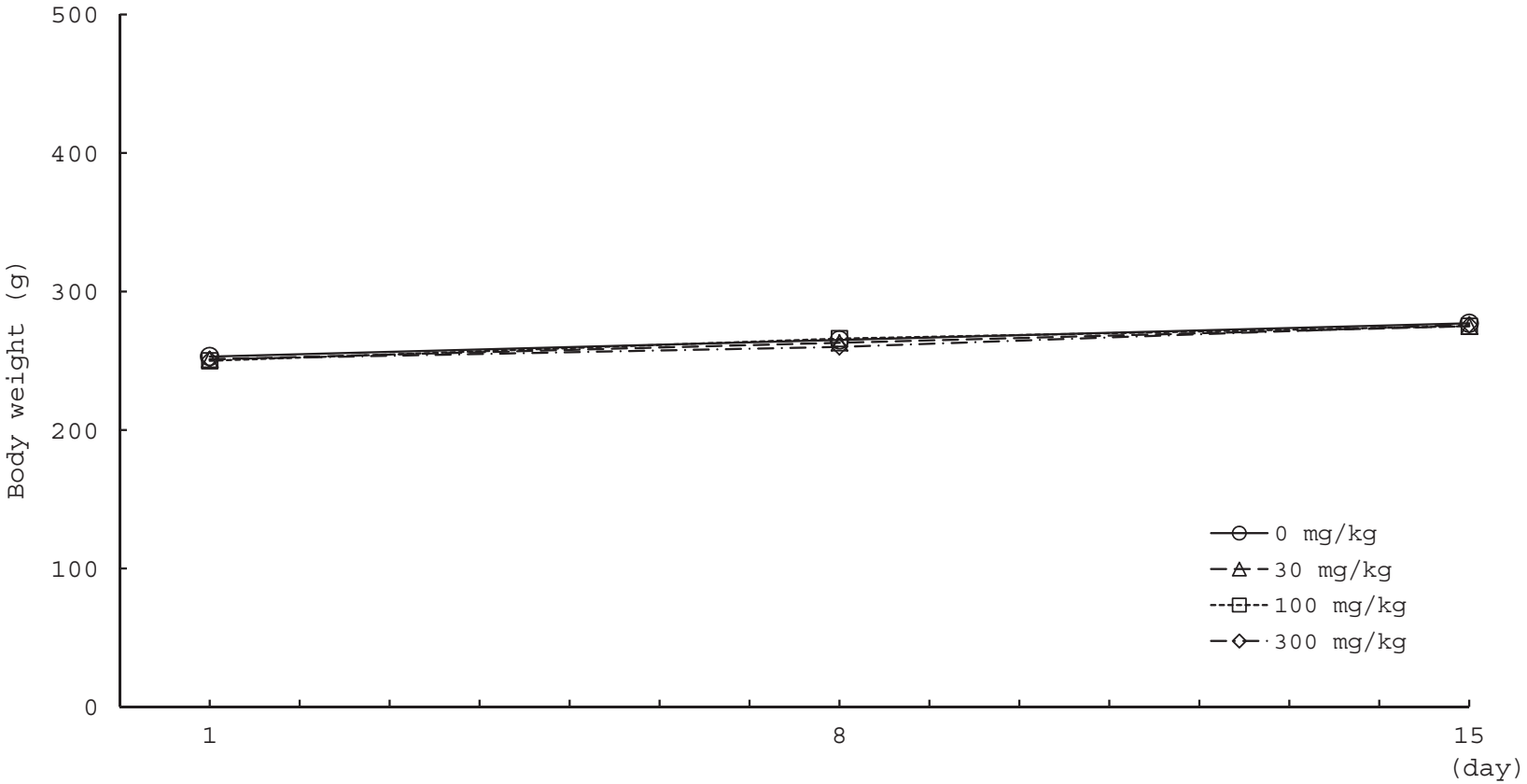

Fig.6 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Body weight of female rats (F0 before mating Day 1-15)

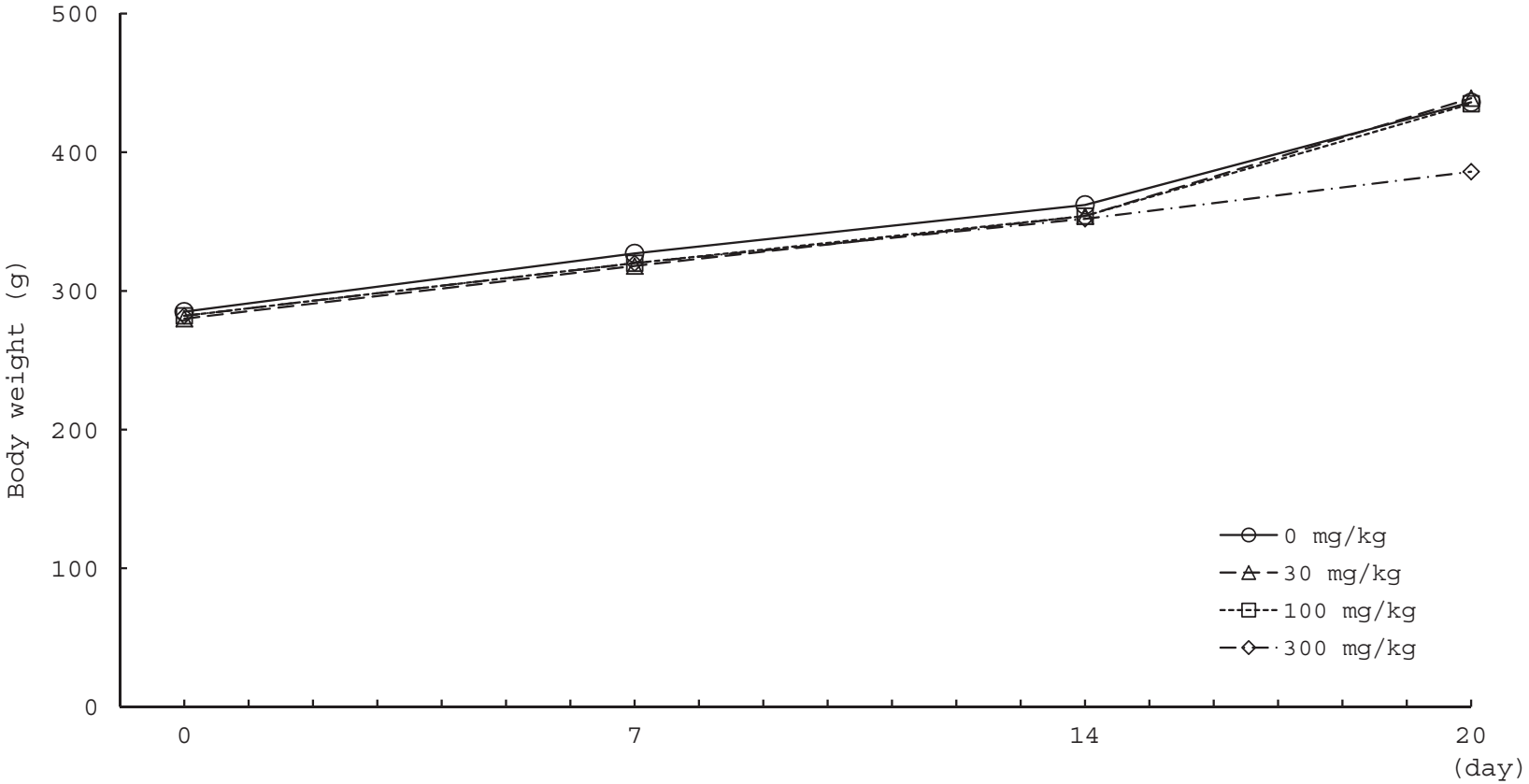

Fig.7 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Body weight of dams (F0 gestation Day 0-25)

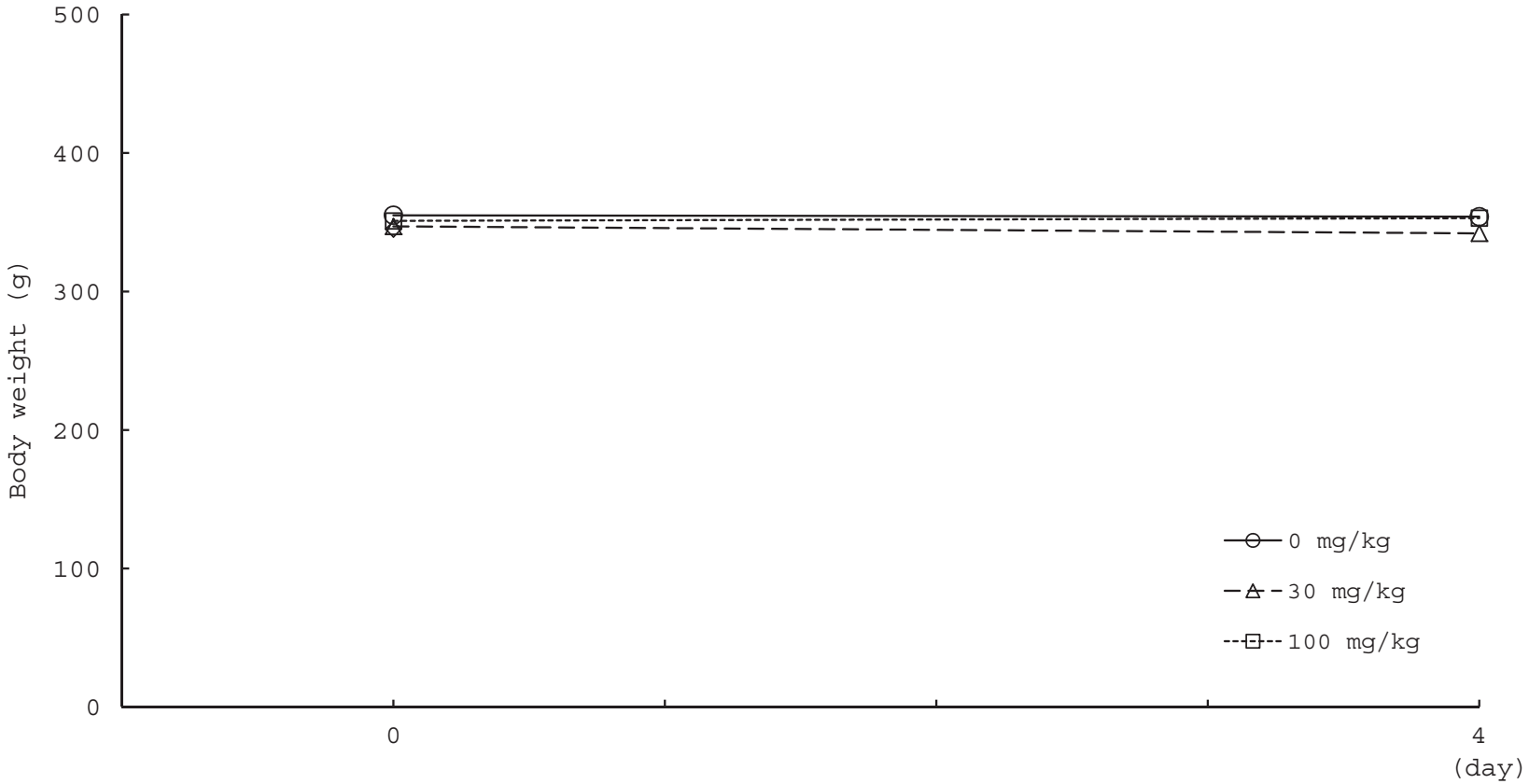

Fig.8 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Body weight of dams (F0 lactation Day 0-5)

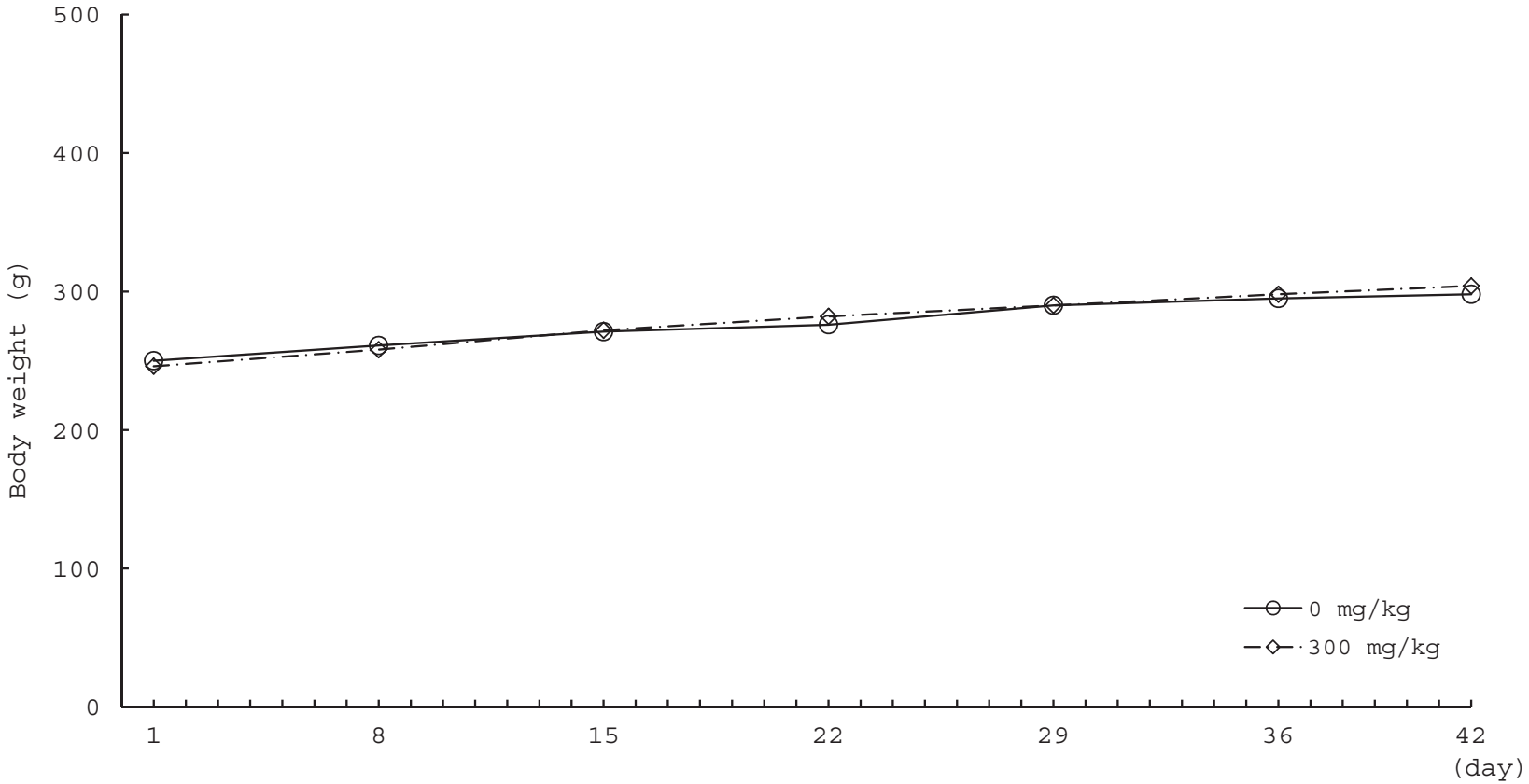

Fig.9 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Body weight of female rats (Administration period)

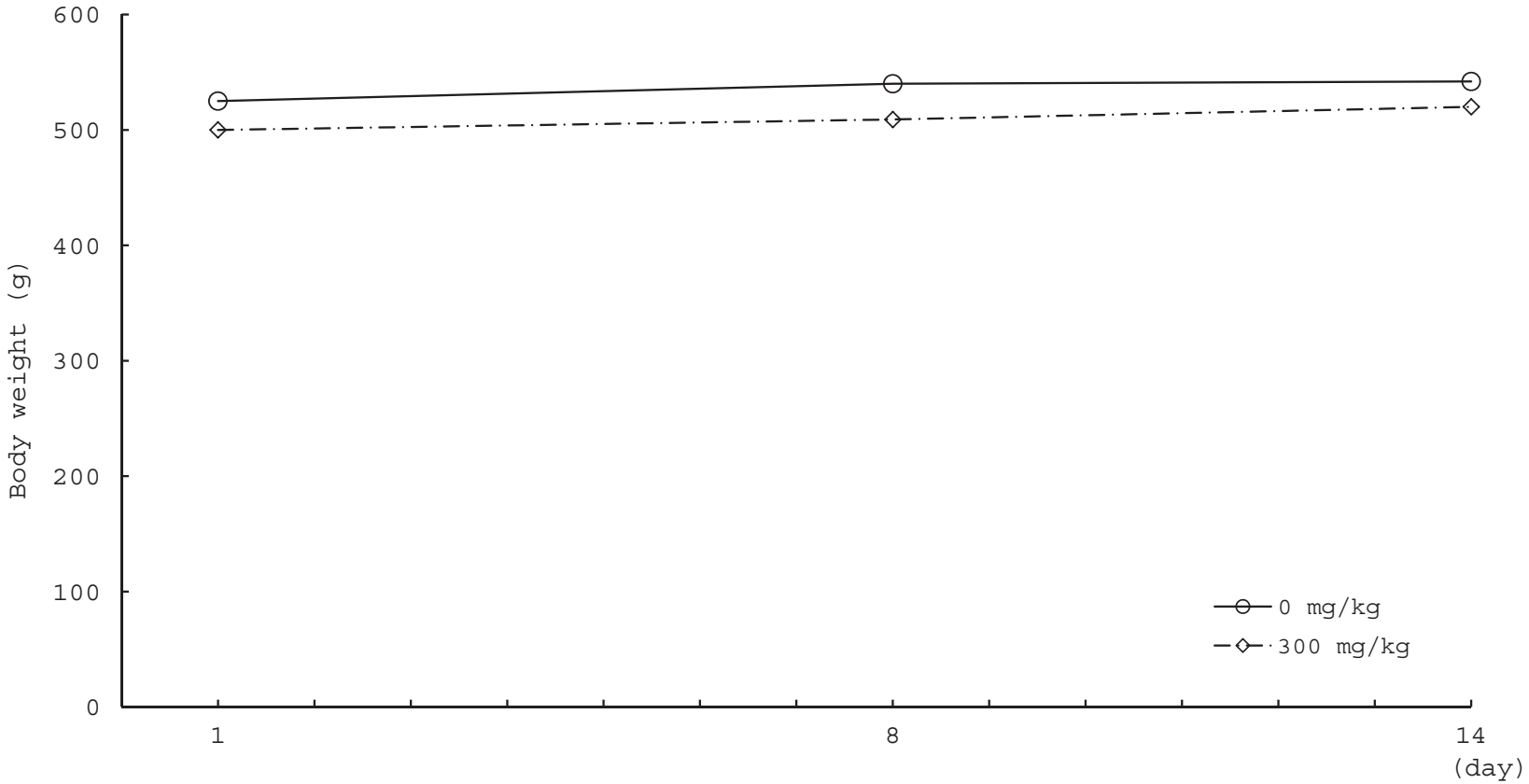

Fig.10 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Body weight of male rats (Recovery period)

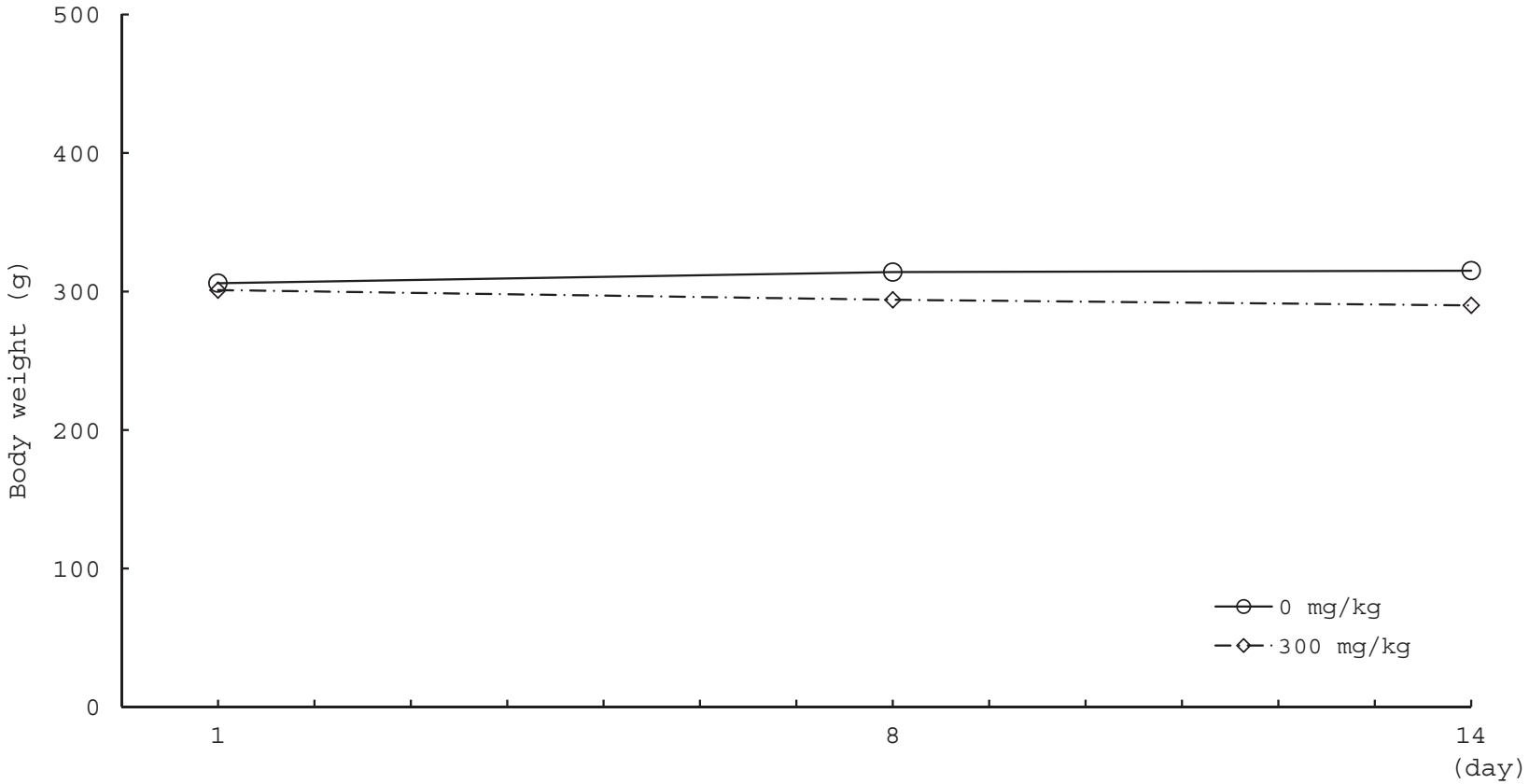

Fig.11 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Body weight of female rats (Recovery period)

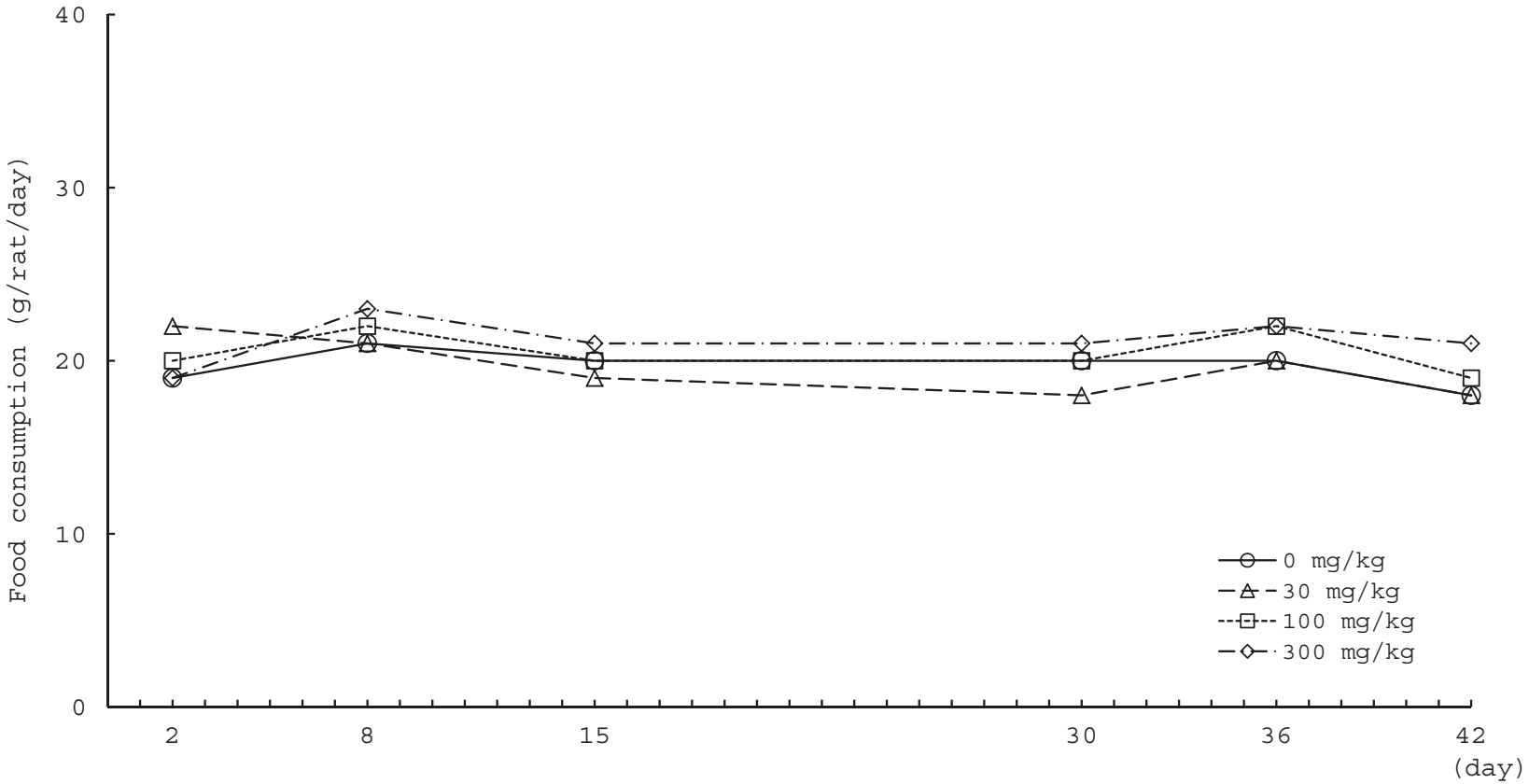

Fig.12 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Food consumption of male rats (F0 before mating Day 1-15, F0 mating Day 15-43)

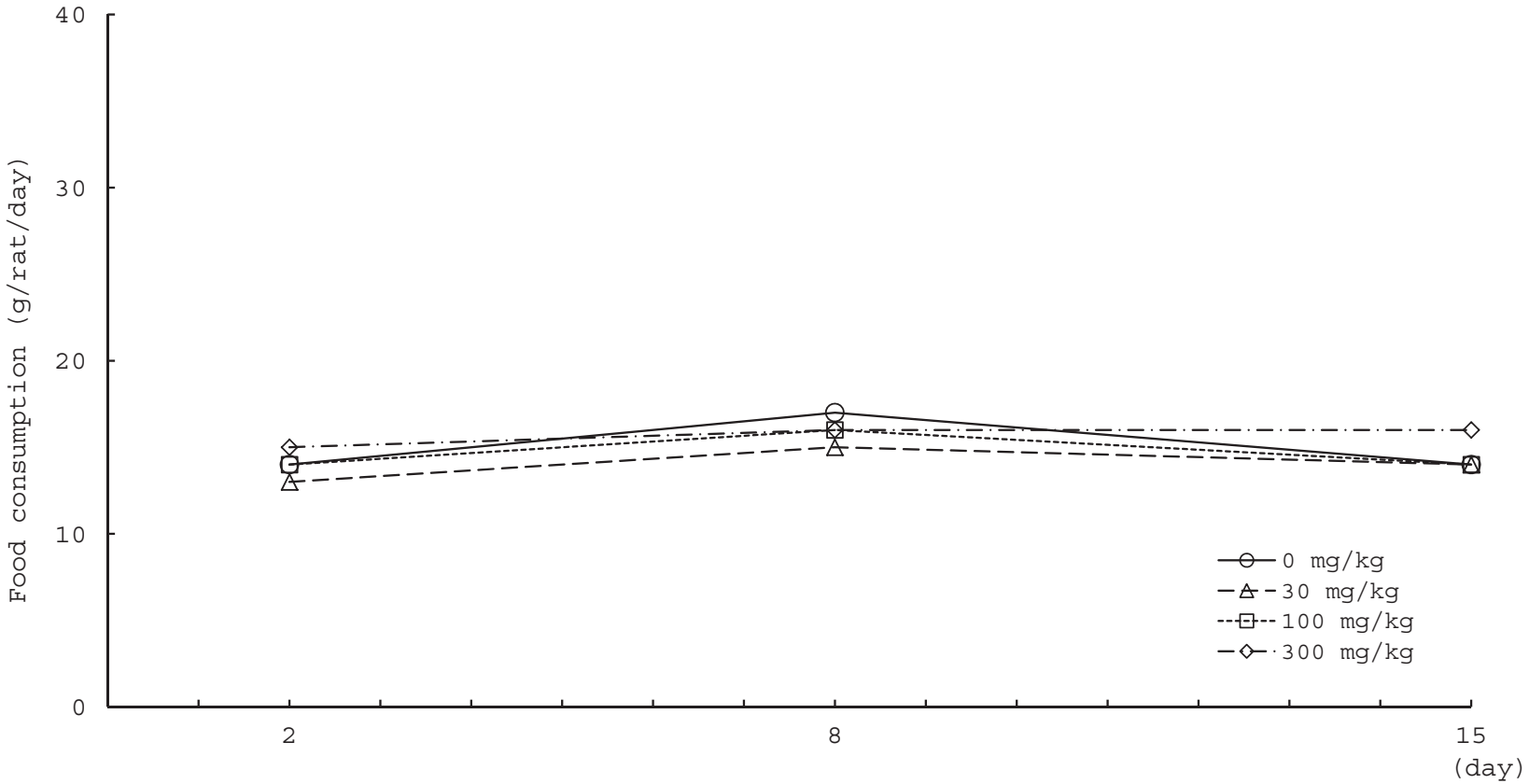

Fig.13 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Food consumption of female rats (F0 before mating Day 1-15)

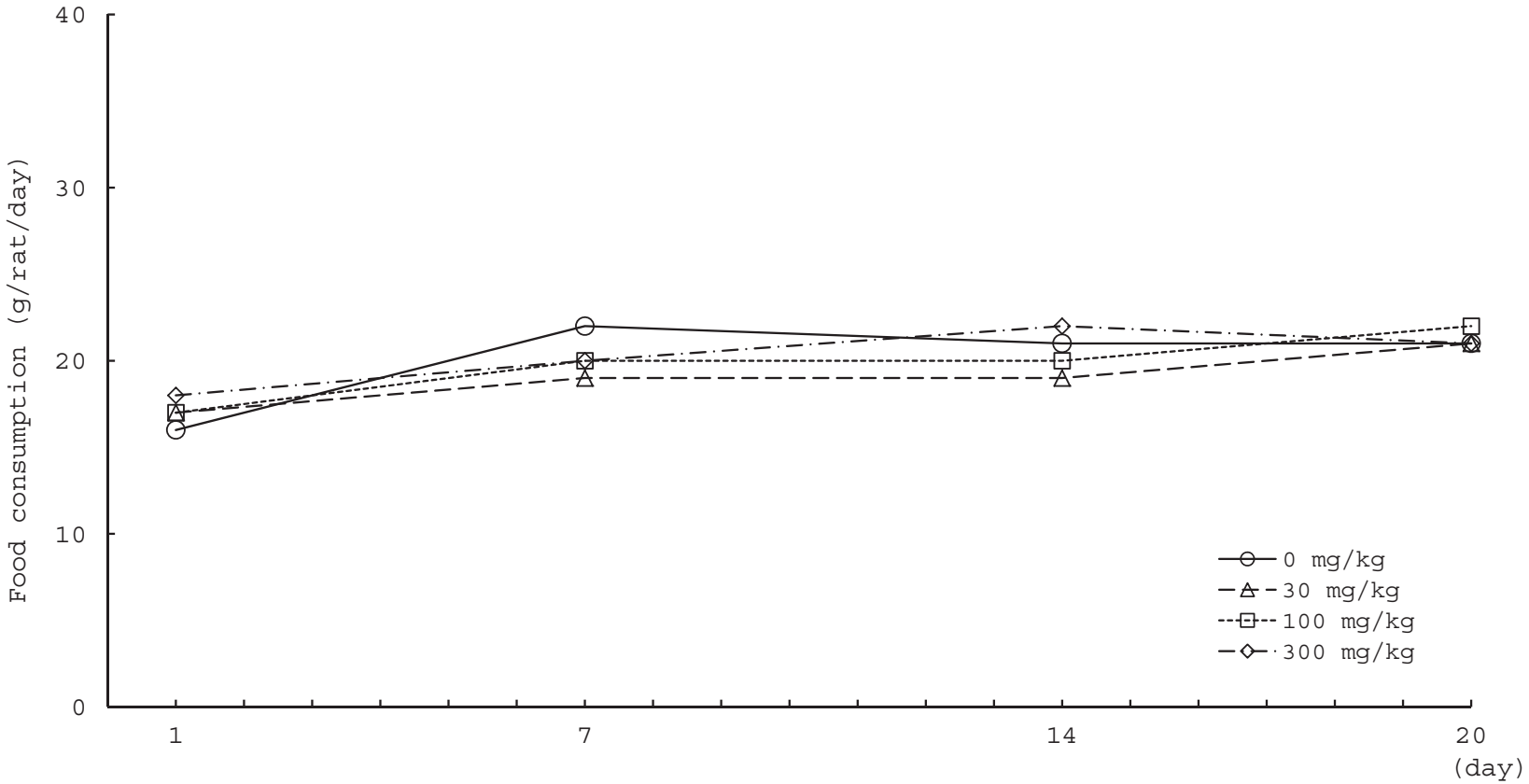

Fig.14 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Food consumption of dams (F0 gestation Day 0-25)

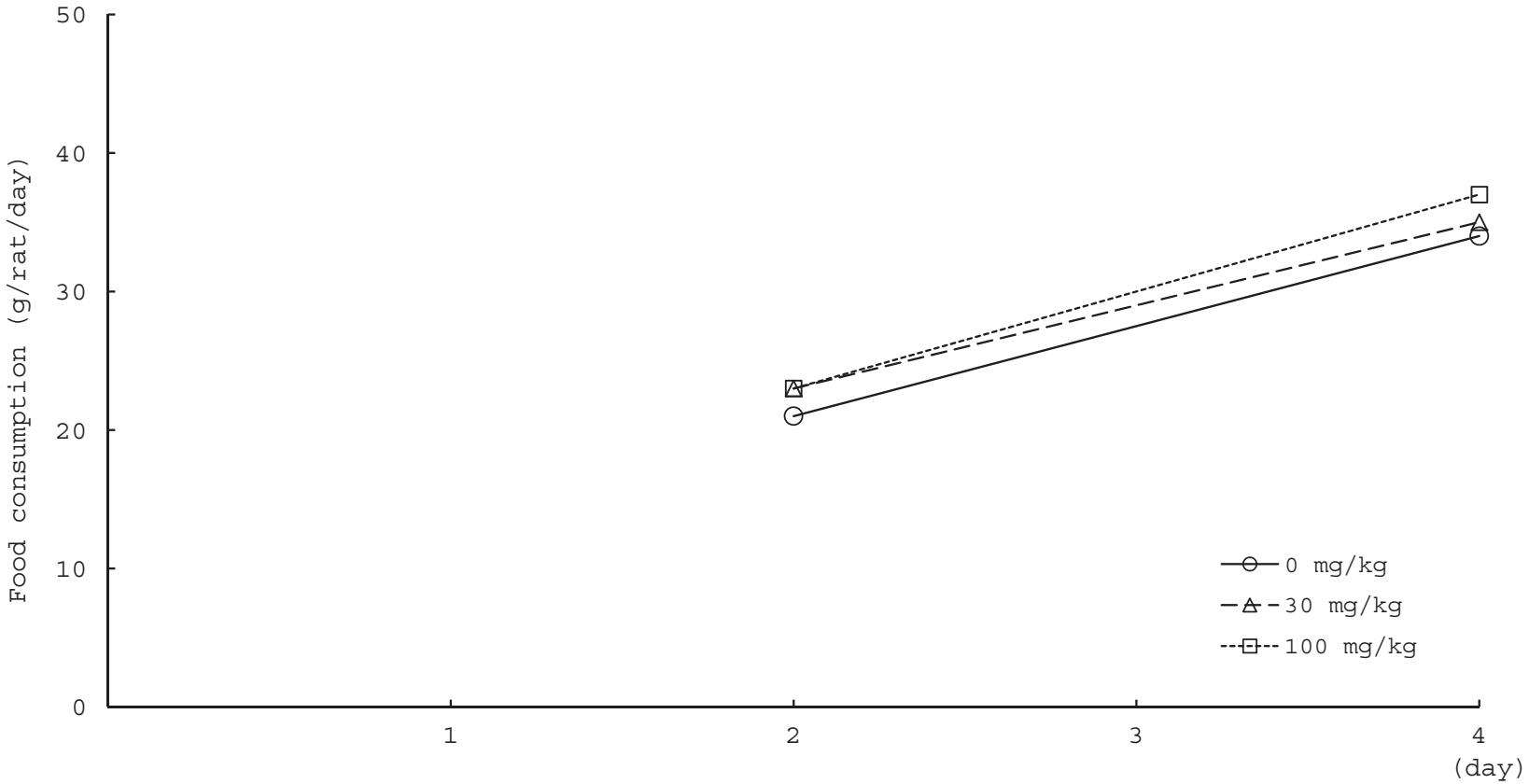

Fig.15 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Food consumption of dams (F0 lactation Day 0-5)

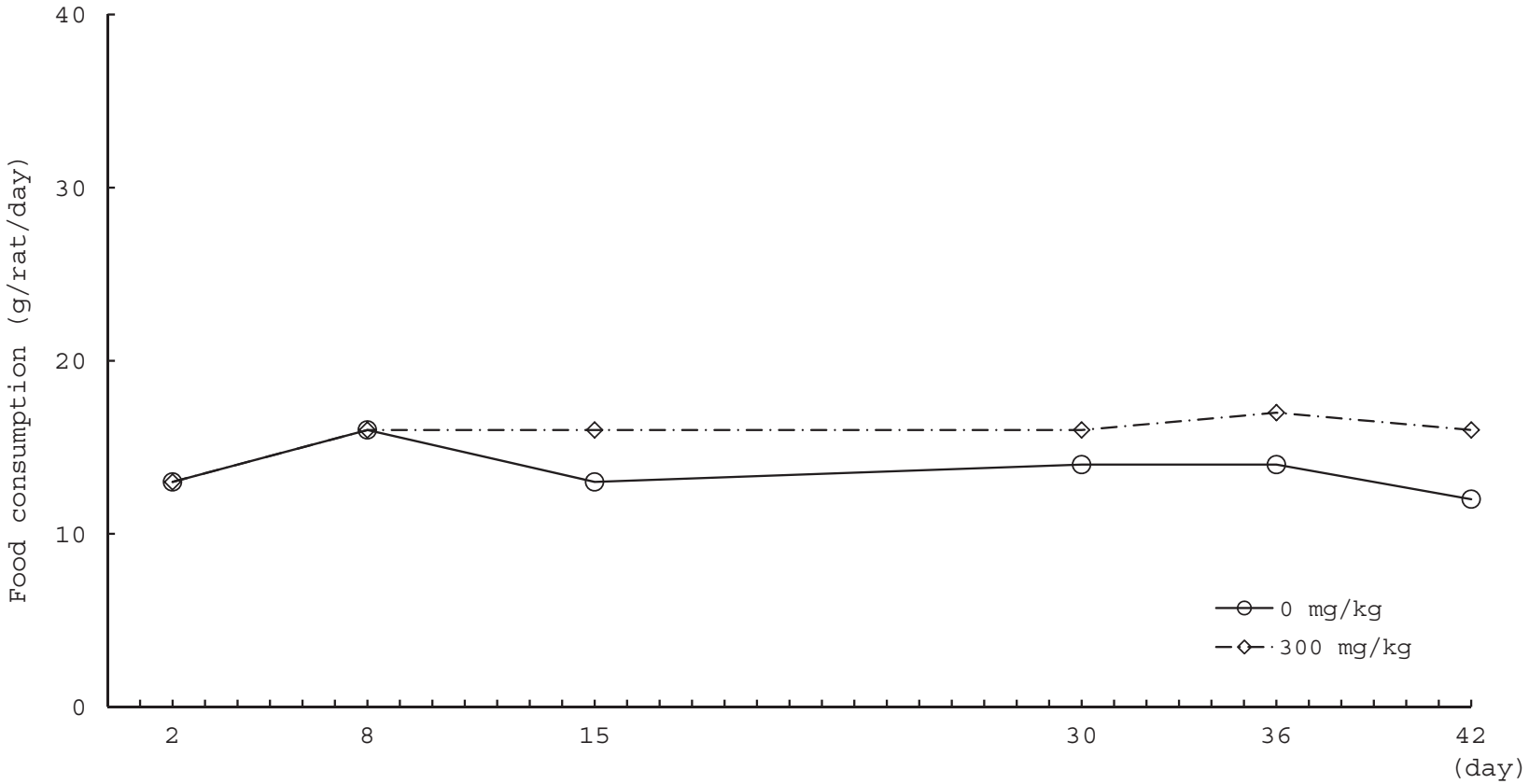

Fig.16 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Food consumption of female rats (Administration period)

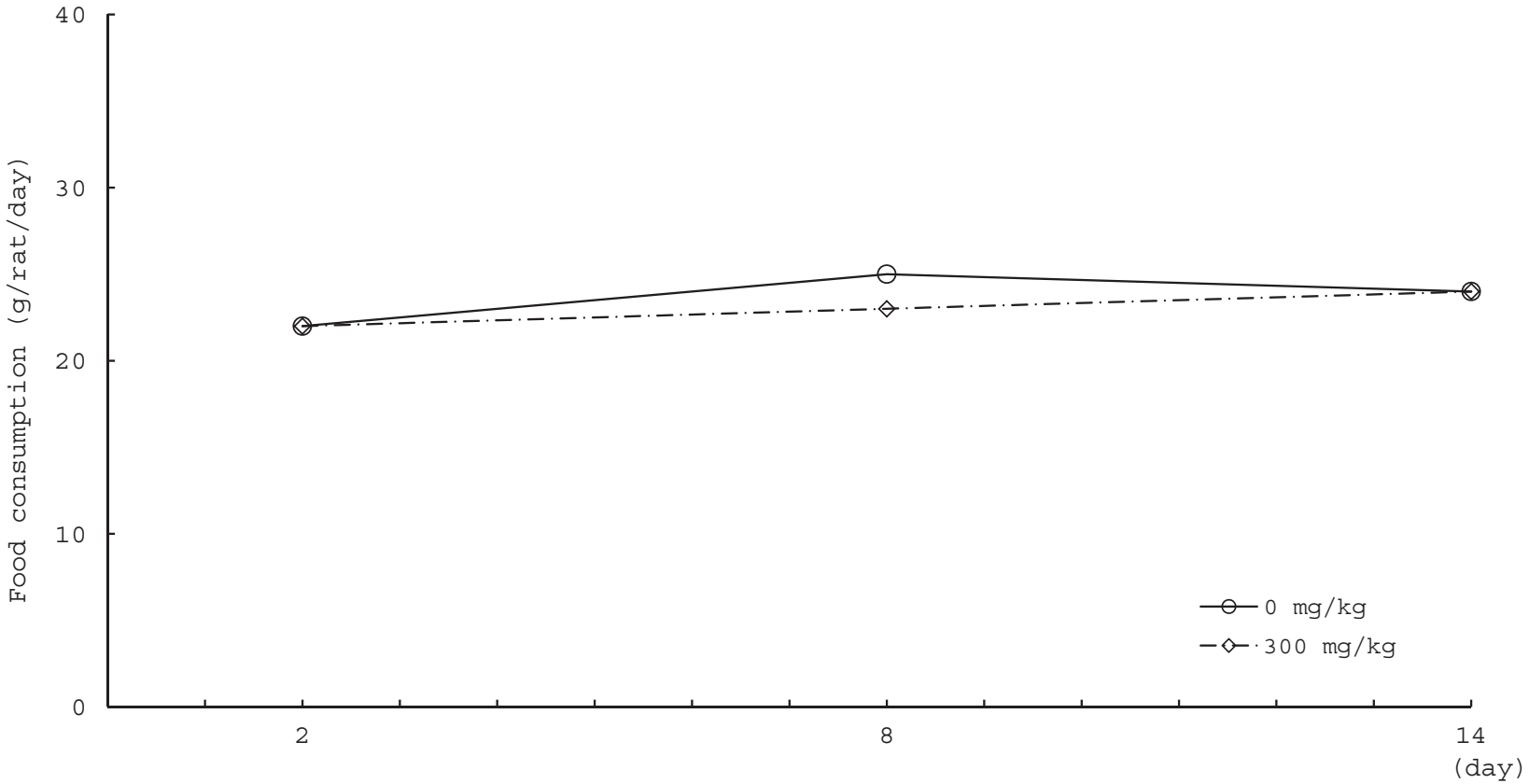

Fig.17 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Food consumption of male rats (Recovery period)

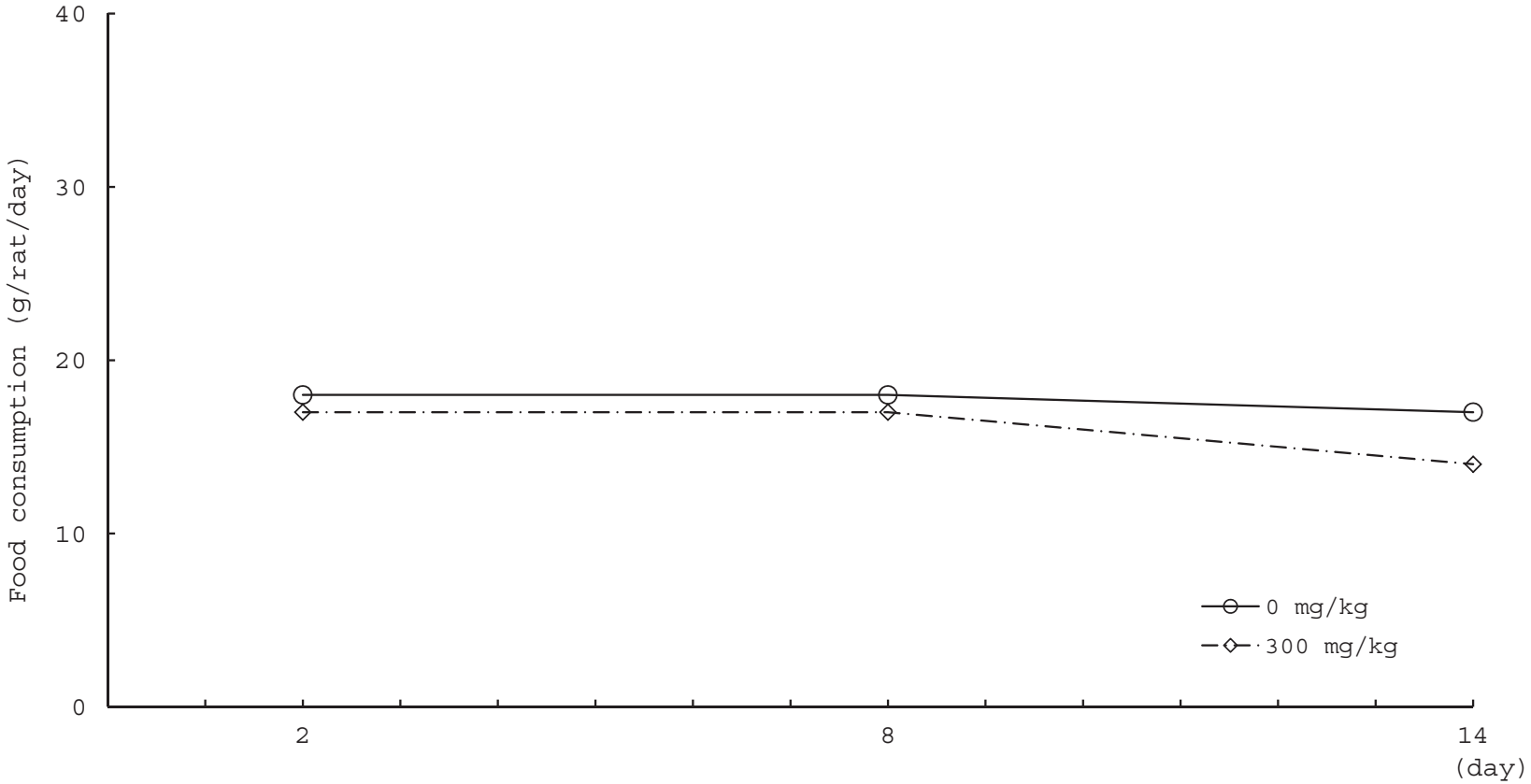

Fig.18 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Food consumption of female rats (Recovery period)

Study No.: R-1190

Table 1-1 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : F0 before mating Day 1-15, F0 mating Day 15-43

Sex : Male Species : Rat

Test article Dose	Signs	/Day 1	2	3	4	5	6	7	8	9	10	11	12	13	14
benzyl salicylate	Number of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12
0 mg/kg	Number of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0
benzyl salicylate	Number of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12
30 mg/kg	Number of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0
benzyl salicylate	Number of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12
100 mg/kg	Number of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0
benzyl salicylate	Number of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12
300 mg/kg	Number of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Study No.: R-1190

Table 1-2 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : F0 before mating Day 1-15, F0 mating Day 15-43

Sex : Male Species : Rat

Test article Dose	Signs	/Day 15	16	17	18	19	20	21	22	23	24	25	26	27	28
benzyl salicylate	Number of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12
0 mg/kg	Number of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0
benzyl salicylate	Number of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12
30 mg/kg	Number of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0
benzyl salicylate	Number of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12
100 mg/kg	Number of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0
benzyl salicylate	Number of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12
300 mg/kg	Number of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Study No.: R-1190

Table 1-3 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : F0 before mating Day 1-15, F0 mating Day 15-43

Sex : Male Species : Rat

Test article Dose	Signs	/Day 29	30	31	32	33	34	35	36	37	38	39	40	41	42	43a)
benzyl salicylate	Number of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	7
0 mg/kg	Number of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
benzyl salicylate	Number of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
30 mg/kg	Number of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
benzyl salicylate	Number of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
100 mg/kg	Number of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
benzyl salicylate	Number of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	7
300 mg/kg	Number of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

a) : Day of necropsy

Study No.: R-1190

Table 1-4 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : F0 before mating Day 1-15

Sex : Female Species : Rat

Test article Dose	Signs	/Day 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
benzyl salicylate	Number of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
0 mg/kg	Number of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
benzyl salicylate	Number of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
30 mg/kg	Number of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
benzyl salicylate	Number of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
100 mg/kg	Number of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
benzyl salicylate	Number of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
300 mg/kg	Number of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Study No.: R-1190

Table 1-5 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : F0 gestation Day 0-25

Sex : Female Species : Rat

Test article Dose	Signs	/Day 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
benzyl salicylate	Number of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	6	0		
0 mg/kg	Number of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
benzyl salicylate	Number of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	4	0		
30 mg/kg	Number of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
benzyl salicylate	Number of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	3	1	0	
100 mg/kg	Number of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
benzyl salicylate	Number of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	8	6	6a)
300 mg/kg	Number of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

a) : Not delivered

Study No.: R-1190

Table 1-6 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : F0 lactation Day 0-5

Sex : Female Species : Rat

Test article Dose	Signs	/Day 0	1	2	3	4	5a)
benzyl salicylate 0 mg/kg	Number of animals	12	12	12	12	12	12
	Number of animals with abnormal findings	0	0	0	0	0	0
benzyl salicylate 30 mg/kg	Number of animals	12	12	12	12	12	12
	Number of animals with abnormal findings	0	0	0	0	0	0
benzyl salicylate 100 mg/kg	Number of animals	12	12	12	12	12	12
	Number of animals with abnormal findings	0	0	0	0	0	0
benzyl salicylate 300 mg/kg	Number of animals	6	5b)	1c)	0d)		
	Number of animals with abnormal findings	0	0	0			

a) : Day of necropsy
b) : One dam was necropsied on lactation day 0 because all offspring were stillborn.
c) : Four dams were necropsied on lactation day 1 because all offspring died.
d) : One dam was necropsied on lactation day 2 because all offspring died.

Study No.: R-1190

Table 1-7 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : Administration Day 1-43

Sex : Female Species : Rat

Test article Dose	Signs	/Day 1	2	3	4	5	6	7	8	9	10	11	12	13	14
benzyl salicylate	Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10
0 mg/kg	Number of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0
benzyl salicylate	Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10
300 mg/kg	Number of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Study No.: R-1190

Table 1-8 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : Administration Day 1-43

Sex : Female Species : Rat

Test article Dose	Signs	/Day 15	16	17	18	19	20	21	22	23	24	25	26	27	28
benzyl salicylate	Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10
0 mg/kg	Number of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0
benzyl salicylate	Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10
300 mg/kg	Number of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Study No.: R-1190

Table 1-9 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : Administration Day 1-43

Sex : Female Species : Rat

Test article Dose	Signs	/Day 29	30	31	32	33	34	35	36	37	38	39	40	41	42	43a)
benzyl salicylate	Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5
0 mg/kg	Number of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
benzyl salicylate	Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5
300 mg/kg	Number of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

a) : Day of necropsy

Study No.: R-1190

Table 1-10 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : Recovery Day 1-15

Sex : Male Species : Rat

Test article Dose	Signs	/Day 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)
benzyl salicylate	Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Number of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
benzyl salicylate	Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
300 mg/kg	Number of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

a) : Day of necropsy

Study No.: R-1190

Table 1-11 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Clinical signs Period : Recovery Day 1-15
Sex : Female Species : Rat

Test article Dose	Signs	/Day 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)
benzyl salicylate	Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Number of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
benzyl salicylate	Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
300 mg/kg	Number of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

a) : Day of necropsy

Table 2 - 1 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 before mating

Generation : F0 Sex : Male Week : 1 Species : Rat

Test article / Dose		Posture NC			Convulsion NC			
		N	F	H	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	12	0	0	0

Test article / Dose		Abnormal NC behavior			
		0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Not calculated : NC

Table 2 - 2 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 before mating

Generation : F0 Sex : Male Week : 2 Species : Rat

Test article / Dose		Posture NC			Convulsion NC			
		N	F	H	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	12	0	0	0

Test article / Dose		Abnormal NC behavior			
		0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Not calculated : NC

Table 2 - 3 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 mating

Generation : F0 Sex : Male Week : 3 Species : Rat

Test article Dose		Posture NC N	 F	 H	Convulsion NC 0	 1	 2	 3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	12	0	0	0

Test article Dose		Abnormal NC behavior 0	 1	 2	 3
benzyl salicylate 0 mg/kg	n	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Not calculated : NC

Table 2 - 4 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 mating

Generation : F0 Sex : Male Week : 4 Species : Rat

Test article / Dose		Posture NC			Convulsion NC			
		N	F	H	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	12	0	0	0

Test article / Dose		Abnormal NC behavior			
		0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Not calculated : NC

Table 2 - 5 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 mating

Generation : F0 Sex : Male Week : 5 Species : Rat

Test article / Dose		Posture NC			Convulsion NC			
		N	F	H	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	12	0	0	0

Test article / Dose		Abnormal NC behavior			
		0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Not calculated : NC

Table 2 - 6 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 mating

Generation : F0 Sex : Male Week : 6 Species : Rat

Test article / Dose		Posture NC			Convulsion NC			
		N	F	H	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	12	0	0	0

Test article / Dose		Abnormal NC behavior			
		0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Not calculated : NC

Table 2 - 7 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 before mating

Generation : F0 Sex : Female Week : 1 Species : Rat

Test article / Dose		Posture NC			Convulsion NC			
		N	F	H	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	12	0	0	0

Test article / Dose		Abnormal NC behavior			
		0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Not calculated : NC

Table 2 - 8 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 before mating

Generation : F0 Sex : Female Week : 2 Species : Rat

Test article / Dose		Posture NC			Convulsion NC			
		N	F	H	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	12	0	0	0

Test article / Dose		Abnormal NC behavior			
		0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Not calculated : NC

Table 2 - 9 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 gestation

Generation : F0 Sex : Female Day : 1 Species : Rat

Test article / Dose		Posture NC			Convulsion NC			
		N	F	H	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	12	0	0	0

Test article / Dose		Abnormal NC behavior			
		0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Not calculated : NC

Table 2 - 10 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 gestation

Generation : F0 Sex : Female Day : 7 Species : Rat

Test article / Dose		Posture NC			Convulsion NC			
		N	F	H	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	12	0	0	0

Test article / Dose		Abnormal NC behavior			
		0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Not calculated : NC

Table 2 - 11 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 gestation

Generation : F0 Sex : Female Day : 14 Species : Rat

Test article Dose		Posture NC N	 F	 H	Convulsion NC 0	 1	 2	 3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	12	0	0	0

Test article Dose		Abnormal NC behavior 0	 1	 2	 3
benzyl salicylate 0 mg/kg	n	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Not calculated : NC

Table 2 - 12 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 gestation

Generation : F0 Sex : Female Day : 20 Species : Rat

Test article / Dose		Posture NC			Convulsion NC			
		N	F	H	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	12	0	0	0

Test article / Dose		Abnormal NC behavior			
		0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Not calculated : NC

Table 2 - 13 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 lactation

Generation : F0 Sex : Female Day : 4 Species : Rat

Test article / Dose		Posture NC			Convulsion NC			
		N	F	H	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	0

Test article / Dose		Abnormal NC behavior			
		0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Not calculated : NC

Table 2 - 14 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : Administration

Generation : F0 Sex : Female Week : 1 Species : Rat

Test article Dose		Posture NC N	 F	 H	Convulsion NC 0	 1	 2	 3
benzyl salicylate 0 mg/kg	n	10	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	10	0	0	0

Test article Dose		Abnormal NC behavior 0	 1	 2	 3
benzyl salicylate 0 mg/kg	n	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	0

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Not calculated : NC

Table 2 - 15 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : Administration

Generation : F0 Sex : Female Week : 2 Species : Rat

Test article Dose		Posture NC N	F	H	Convulsion NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	10	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	10	0	0	0

Test article Dose		Abnormal NC behavior 0	1	2	3
benzyl salicylate 0 mg/kg	n	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	0

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Not calculated : NC

Table 2 - 16 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : Administration

Generation : F0 Sex : Female Week : 3 Species : Rat

Test article Dose		Posture NC N	 F	 H	Convulsion NC 0	 1	 2	 3
benzyl salicylate 0 mg/kg	n	10	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	10	0	0	0

Test article Dose		Abnormal NC behavior 0	 1	 2	 3
benzyl salicylate 0 mg/kg	n	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	0

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Not calculated : NC

Table 2 - 17 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : Administration

Generation : F0 Sex : Female Week : 4 Species : Rat

Test article / Dose		Posture NC			Convulsion NC			
		N	F	H	0	1	2	3
benzyl salicylate 0 mg/kg	n	10	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	10	0	0	0

Test article / Dose		Abnormal NC behavior			
		0	1	2	3
benzyl salicylate 0 mg/kg	n	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	0

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Not calculated : NC

Table 2 - 18 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : Administration

Generation : F0 Sex : Female Week : 5 Species : Rat

Test article Dose		Posture NC N	F	H	Convulsion NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	10	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	10	0	0	0

Test article Dose		Abnormal NC behavior 0	1	2	3
benzyl salicylate 0 mg/kg	n	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	0

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Not calculated : NC

Table 2 - 19 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : Administration

Generation : F0 Sex : Female Week : 6 Species : Rat

Test article Dose		Posture NC N	 F	 H	Convulsion NC 0	 1	 2	 3
benzyl salicylate 0 mg/kg	n	10	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	10	0	0	0

Test article Dose		Abnormal NC behavior 0	 1	 2	 3
benzyl salicylate 0 mg/kg	n	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	0

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Not calculated : NC

Table 2 - 20 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : Recovery

Generation : F0 Sex : Male Week : 1 Species : Rat

Test article Dose		Posture NC N	F	H	Convulsion NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	5	0	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	5	0	0	0

Test article Dose		Abnormal NC behavior 0	1	2	3
benzyl salicylate 0 mg/kg	n	5	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	0

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Not calculated : NC

Table 2 - 21 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : Recovery

Generation : F0 Sex : Male Week : 2 Species : Rat

Test article Dose		Posture NC N	F	H	Convulsion NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	5	0	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	5	0	0	0

Test article Dose		Abnormal NC behavior 0	1	2	3
benzyl salicylate 0 mg/kg	n	5	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	0

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Not calculated : NC

Table 2 - 22 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : Recovery

Generation : F0 Sex : Female Week : 1 Species : Rat

Test article Dose		Posture NC N	F	H	Convulsion NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	5	0	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	5	0	0	0

Test article Dose		Abnormal NC behavior 0	1	2	3
benzyl salicylate 0 mg/kg	n	5	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	0

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Not calculated : NC

Table 2 - 23 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : Recovery

Generation : F0 Sex : Female Week : 2 Species : Rat

Test article / Dose		Posture NC			Convulsion NC			
		N	F	H	0	1	2	3
benzyl salicylate 0 mg/kg	n	5	0	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	5	0	0	0

Test article / Dose		Abnormal NC behavior			
		0	1	2	3
benzyl salicylate 0 mg/kg	n	5	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	0

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Not calculated : NC

Table 2 - 24 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 before mating

Generation : F0 Sex : Male Week : 1 Species : Rat

Test article / Dose		Ease of removal from cage NC					Fur condition NC			
		-1	0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0	12	0	0	0

Test article / Dose		Skin NC				Secretions- NC Eye, Nose		Exophthalmos NC	
		0	1	2	3	0	1	0	1
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	12	0

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Not calculated : NC

Table 2 - 25 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 before mating

Generation : F0 Sex : Male Week : 1 Species : Rat

Test article		Palpebral NC closure				Mucosal NC membranes				Lacrimation NC	
Dose		0	1	2	3	0	1	2	3	0	1
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	0	0	12	0

Test article		Piloerection NC		Pupil size NC				Salivation NC			
Dose		0	1	-1	0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	12	0	0	12	0	0	0

Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Not calculated : NC

Table 2 - 26 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 before mating

Generation : F0 Sex : Male Week : 1 Species : Rat

Test article		Abnormal NC respiration				Vocalization NC			
Dose		0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	0	0

Test article		Reactivity to NC handling				
Dose		-1	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0

Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward
Not calculated : NC

Table 2 - 27 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 before mating

Generation : F0 Sex : Male Week : 2 Species : Rat

Test article / Dose		Ease of removal from cage -1	0	1	2	3	Fur condition NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0	12	0	0	0

Test article / Dose		Skin NC 0	1	2	3	Secretions- NC Eye, Nose 0	1	Exophthalmos NC 0	1
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	12	0

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Not calculated : NC

Table 2 - 28 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 before mating

Generation : F0 Sex : Male Week : 2 Species : Rat

Test article		Palpebral NC closure				Mucosal NC membranes				Lacrimation NC	
Dose		0	1	2	3	0	1	2	3	0	1
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	0	0	12	0

Test article		Piloerection NC		Pupil size NC				Salivation NC			
Dose		0	1	-1	0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	12	0	0	12	0	0	0

Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Not calculated : NC

Table 2 - 29 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 before mating

Generation : F0 Sex : Male Week : 2 Species : Rat

Test article		Abnormal NC respiration				Vocalization NC			
Dose		0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	0	0

Test article		Reactivity to NC handling				
Dose		-1	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0

Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward
Not calculated : NC

Table 2 - 30 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 mating

Generation : F0 Sex : Male Week : 3 Species : Rat

Test article / Dose		Ease of removal from cage NC					Fur condition NC			
		-1	0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0	12	0	0	0

Test article / Dose		Skin NC				Secretions- NC Eye, Nose		Exophthalmos NC	
		0	1	2	3	0	1	0	1
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	12	0

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Not calculated : NC

Table 2 - 31 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 mating

Generation : F0 Sex : Male Week : 3 Species : Rat

Test article		Palpebral NC closure				Mucosal NC membranes				Lacrimation NC	
Dose		0	1	2	3	0	1	2	3	0	1
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	0	0	12	0

Test article		Piloerection NC		Pupil size NC				Salivation NC			
Dose		0	1	-1	0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	12	0	0	12	0	0	0

Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Not calculated : NC

Table 2 - 32 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 mating

Generation : F0 Sex : Male Week : 3 Species : Rat

Test article / Dose		Abnormal NC respiration 0	1	2	3	Vocalization NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	11	1	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	11	1	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	10	2	0	0

Test article / Dose		Reactivity to NC handling -1	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0

Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward
Not calculated : NC

Table 2 - 33 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 mating

Generation : F0 Sex : Male Week : 4 Species : Rat

Test article / Dose		Ease of removal from cage NC					Fur condition NC			
		-1	0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0	12	0	0	0

Test article / Dose		Skin NC				Secretions- NC Eye, Nose		Exophthalmos NC	
		0	1	2	3	0	1	0	1
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	12	0

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Not calculated : NC

Table 2 - 34 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 mating

Generation : F0 Sex : Male Week : 4 Species : Rat

Test article		Palpebral NC closure				Mucosal NC membranes				Lacrimation NC	
Dose		0	1	2	3	0	1	2	3	0	1
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	0	0	12	0

Test article		Piloerection NC		Pupil size NC				Salivation NC			
Dose		0	1	-1	0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	12	0	0	12	0	0	0

Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Not calculated : NC

Table 2 - 35 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 mating

Generation : F0 Sex : Male Week : 4 Species : Rat

Test article		Abnormal NC respiration				Vocalization NC			
Dose		0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	11	1	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	11	1	0	0

Test article		Reactivity to NC handling				
Dose		-1	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0

Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward
Not calculated : NC

Table 2 - 36 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 mating

Generation : F0 Sex : Male Week : 5 Species : Rat

Test article		Ease of removal from cage NC					Fur condition NC			
Dose		-1	0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0	12	0	0	0

Test article		Skin NC				Secretions- NC Eye, Nose		Exophthalmos NC	
Dose		0	1	2	3	0	1	0	1
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	12	0

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Not calculated : NC

Table 2 - 37 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 mating

Generation : F0 Sex : Male Week : 5 Species : Rat

Test article		Palpebral NC closure				Mucosal NC membranes				Lacrimation NC	
Dose		0	1	2	3	0	1	2	3	0	1
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	0	0	12	0

Test article		Piloerection NC		Pupil size NC				Salivation NC			
Dose		0	1	-1	0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	12	0	0	12	0	0	0

Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Not calculated : NC

Table 2 - 38 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 mating

Generation : F0 Sex : Male Week : 5 Species : Rat

Test article		Abnormal NC respiration				Vocalization NC			
Dose		0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0	10	2	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	10	2	0	0

Test article		Reactivity to NC handling				
Dose		-1	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	10	2	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0

Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward
Not calculated : NC

Table 2 - 39 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 mating

Generation : F0 Sex : Male Week : 6 Species : Rat

Test article		Ease of removal from cage NC					Fur condition NC			
Dose		-1	0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0	12	0	0	0

Test article		Skin NC				Secretions- NC Eye, Nose		Exophthalmos NC	
Dose		0	1	2	3	0	1	0	1
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	12	0

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Not calculated : NC

Table 2 - 40 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 mating

Generation : F0 Sex : Male Week : 6 Species : Rat

Test article		Palpebral NC closure				Mucosal NC membranes				Lacrimation NC	
Dose		0	1	2	3	0	1	2	3	0	1
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	0	0	12	0

Test article		Piloerection NC		Pupil size NC				Salivation NC			
Dose		0	1	-1	0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	12	0	0	12	0	0	0

Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Not calculated : NC

Table 2 - 41 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 mating

Generation : F0 Sex : Male Week : 6 Species : Rat

Test article		Abnormal NC respiration				Vocalization NC			
Dose		0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0	11	1	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	0	0

Test article		Reactivity to NC handling				
Dose		-1	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0

Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward
Not calculated : NC

Table 2 - 42 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 before mating

Generation : F0 Sex : Female Week : 1 Species : Rat

Test article / Dose		Ease of removal from cage NC					Fur condition NC			
		-1	0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0	12	0	0	0

Test article / Dose		Skin NC				Secretions- NC Eye, Nose		Exophthalmos NC	
		0	1	2	3	0	1	0	1
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	12	0

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Not calculated : NC

Table 2 - 43 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 before mating

Generation : F0 Sex : Female Week : 1 Species : Rat

Test article		Palpebral NC closure				Mucosal NC membranes				Lacrimation NC	
Dose		0	1	2	3	0	1	2	3	0	1
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	0	0	12	0

Test article		Piloerection NC		Pupil size NC				Salivation NC			
Dose		0	1	-1	0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	12	0	0	12	0	0	0

Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Not calculated : NC

Table 2 - 44 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 before mating

Generation : F0 Sex : Female Week : 1 Species : Rat

Test article		Abnormal NC respiration				Vocalization NC			
Dose		0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	11	1	0	0

Test article		Reactivity to NC handling				
Dose		-1	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	11	1	0	0

Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward
Not calculated : NC

Table 2 - 45 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 before mating

Generation : F0 Sex : Female Week : 2 Species : Rat

Test article / Dose		Ease of removal from cage -1	0	1	2	3	Fur condition NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0	12	0	0	0

Test article / Dose		Skin NC 0	1	2	3	Secretions- NC Eye, Nose 0	1	Exophthalmos NC 0	1
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	12	0

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Not calculated : NC

Table 2 - 46 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 before mating

Generation : F0 Sex : Female Week : 2 Species : Rat

Test article		Palpebral NC closure				Mucosal NC membranes				Lacrimation NC	
Dose		0	1	2	3	0	1	2	3	0	1
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	0	0	12	0

Test article		Piloerection NC		Pupil size NC				Salivation NC			
Dose		0	1	-1	0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	12	0	0	12	0	0	0

Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Not calculated : NC

Table 2 - 47 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 before mating

Generation : F0 Sex : Female Week : 2 Species : Rat

Test article		Abnormal NC respiration				Vocalization NC			
Dose		0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	11	1	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	10	2	0	0

Test article		Reactivity to NC handling				
Dose		-1	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	11	1	0	0

Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward
Not calculated : NC

Table 2 - 48 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 gestation

Generation : F0 Sex : Female Day : 1 Species : Rat

Test article		Ease of removal from cage NC					Fur condition NC			
Dose		-1	0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0	12	0	0	0

Test article		Skin NC				Secretions- NC Eye, Nose		Exophthalmos NC	
Dose		0	1	2	3	0	1	0	1
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	12	0

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Not calculated : NC

Table 2 - 49 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 gestation

Generation : F0 Sex : Female Day : 1 Species : Rat

Test article		Palpebral NC closure				Mucosal NC membranes				Lacrimation NC	
Dose		0	1	2	3	0	1	2	3	0	1
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	0	0	12	0

Test article		Piloerection NC		Pupil size NC				Salivation NC			
Dose		0	1	-1	0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	12	0	0	12	0	0	0

Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Not calculated : NC

Table 2 - 50 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 gestation

Generation : F0 Sex : Female Day : 1 Species : Rat

Test article		Abnormal NC respiration				Vocalization NC			
Dose		0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	0	0

Test article		Reactivity to NC handling				
Dose		-1	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0

Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward
Not calculated : NC

Table 2 - 51 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 gestation

Generation : F0 Sex : Female Day : 7 Species : Rat

Test article		Ease of removal from cage NC					Fur condition NC			
Dose		-1	0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	11	1	0	0	12	0	0	0

Test article		Skin NC				Secretions- NC Eye, Nose		Exophthalmos NC	
Dose		0	1	2	3	0	1	0	1
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	12	0

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Not calculated : NC

Table 2 - 52 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 gestation

Generation : F0 Sex : Female Day : 7 Species : Rat

Test article		Palpebral NC closure				Mucosal NC membranes				Lacrimation NC	
Dose		0	1	2	3	0	1	2	3	0	1
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	0	0	12	0

Test article		Piloerection NC		Pupil size NC				Salivation NC			
Dose		0	1	-1	0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	12	0	0	12	0	0	0

Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Not calculated : NC

Table 2 - 53 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 gestation

Generation : F0 Sex : Female Day : 7 Species : Rat

Test article		Abnormal NC respiration				Vocalization NC			
Dose		0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	10	2	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	11	1	0	0

Test article		Reactivity to NC handling				
Dose		-1	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	11	1	0	0

Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward
Not calculated : NC

Table 2 - 54 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 gestation

Generation : F0 Sex : Female Day : 14 Species : Rat

Test article		Ease of removal from cage NC					Fur condition NC			
Dose		-1	0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0	12	0	0	0

Test article		Skin NC				Secretions- NC Eye, Nose		Exophthalmos NC	
Dose		0	1	2	3	0	1	0	1
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	12	0

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Not calculated : NC

Table 2 - 55 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 gestation

Generation : F0 Sex : Female Day : 14 Species : Rat

Test article		Palpebral NC closure				Mucosal NC membranes				Lacrimation NC	
Dose		0	1	2	3	0	1	2	3	0	1
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	0	0	12	0

Test article		Piloerection NC		Pupil size NC				Salivation NC			
Dose		0	1	-1	0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	12	0	0	12	0	0	0

Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Not calculated : NC

Table 2 - 56 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 gestation

Generation : F0 Sex : Female Day : 14 Species : Rat

Test article		Abnormal NC respiration				Vocalization NC			
Dose		0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	11	1	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	11	1	0	0

Test article		Reactivity to NC handling				
Dose		-1	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0

Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward
Not calculated : NC

Table 2 - 57 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 gestation

Generation : F0 Sex : Female Day : 20 Species : Rat

Test article		Ease of removal from cage NC					Fur condition NC			
Dose		-1	0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0	12	0	0	0

Test article		Skin NC				Secretions- NC Eye, Nose		Exophthalmos NC	
Dose		0	1	2	3	0	1	0	1
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	12	0

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Not calculated : NC

Table 2 - 58 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 gestation

Generation : F0 Sex : Female Day : 20 Species : Rat

Test article		Palpebral NC closure				Mucosal NC membranes				Lacrimation NC	
Dose		0	1	2	3	0	1	2	3	0	1
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	0	0	12	0

Test article		Piloerection NC		Pupil size NC				Salivation NC			
Dose		0	1	-1	0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	12	0	0	12	0	0	0

Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Not calculated : NC

Table 2 - 59 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 gestation

Generation : F0 Sex : Female Day : 20 Species : Rat

Test article		Abnormal NC respiration				Vocalization NC			
Dose		0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	0	0

Test article		Reactivity to NC handling				
Dose		-1	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0

Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward
Not calculated : NC

Table 2 - 60 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 lactation

Generation : F0 Sex : Female Day : 4 Species : Rat

Test article / Dose		Ease of removal from cage NC -1	0	1	2	3	Fur condition NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0	12	0	0	0

Test article / Dose		Skin NC 0	1	2	3	Secretions-Eye, Nose NC 0	1	Exophthalmos NC 0	1
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	12	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	12	0

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Not calculated : NC

Table 2 - 61 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 lactation

Generation : F0 Sex : Female Day : 4 Species : Rat

Test article		Palpebral NC closure				Mucosal NC membranes				Lacrimation NC	
Dose		0	1	2	3	0	1	2	3	0	1
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0	12	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0	12	0

Test article		Piloerection NC		Pupil size NC				Salivation NC			
Dose		0	1	-1	0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	12	0	0	0

Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Not calculated : NC

Table 2 - 62 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : F0 lactation

Generation : F0 Sex : Female Day : 4 Species : Rat

Test article / Dose		Abnormal NC respiration 0	1	2	3	Vocalization NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0

Test article / Dose		Reactivity to NC handling -1	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0

Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward
Not calculated : NC

Table 2 - 63 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : Administration

Generation : F0 Sex : Female Week : 1 Species : Rat

Test article / Dose		Ease of removal from cage NC -1	0	1	2	3	Fur condition NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	0	10	0	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	0	10	0	0	0	10	0	0	0

Test article / Dose		Skin NC 0	1	2	3	Secretions- NC Eye, Nose 0	1	Exophthalmos NC 0	1
benzyl salicylate 0 mg/kg	n	10	0	0	0	10	0	10	0
benzyl salicylate 300 mg/kg	n	10	0	0	0	10	0	10	0

Test article / Dose		Palpebral NC closure 0	1	2	3	Mucosal NC membranes 0	1	2	3	Lacrimation NC 0	1
benzyl salicylate 0 mg/kg	n	10	0	0	0	10	0	0	0	10	0
benzyl salicylate 300 mg/kg	n	10	0	0	0	10	0	0	0	10	0

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Not calculated : NC

Table 2 - 64 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : Administration

Generation : F0 Sex : Female Week : 1 Species : Rat

Test article		Piloerection NC		Pupil size NC			Salivation NC			
Dose		0	1	-1	0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	10	0	0	10	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	10	0	0	10	0	0	0

Test article		Abnormal NC respiration				Vocalization NC			
Dose		0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	10	0	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	0	10	0	0	0

Test article		Reactivity to NC handling				
Dose		-1	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	0	10	0	0	0

Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward
Not calculated : NC

Table 2 - 65 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : Administration

Generation : F0 Sex : Female Week : 2 Species : Rat

Test article		Ease of removal from cage NC					Fur condition NC			
Dose		-1	0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	10	0	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	0	10	0	0	0	10	0	0	0

Test article		Skin NC				Secretions- NC Eye, Nose		Exophthalmos NC	
Dose		0	1	2	3	0	1	0	1
benzyl salicylate 0 mg/kg	n	10	0	0	0	10	0	10	0
benzyl salicylate 300 mg/kg	n	10	0	0	0	10	0	10	0

Test article		Palpebral NC closure				Mucosal NC membranes				Lacrimation NC	
Dose		0	1	2	3	0	1	2	3	0	1
benzyl salicylate 0 mg/kg	n	10	0	0	0	10	0	0	0	10	0
benzyl salicylate 300 mg/kg	n	10	0	0	0	10	0	0	0	10	0

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Not calculated : NC

Table 2 - 66 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : Administration

Generation : F0 Sex : Female Week : 2 Species : Rat

Test article		Piloerection NC		Pupil size NC			Salivation NC			
Dose		0	1	-1	0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	10	0	0	10	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	10	0	0	10	0	0	0

Test article		Abnormal NC respiration				Vocalization NC			
Dose		0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	10	0	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	0	10	0	0	0

Test article		Reactivity to NC handling				
Dose		-1	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	0	10	0	0	0

Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward
Not calculated : NC

Table 2 - 67 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : Administration

Generation : F0 Sex : Female Week : 3 Species : Rat

Test article		Ease of removal from cage NC					Fur condition NC			
Dose		-1	0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	10	0	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	0	10	0	0	0	10	0	0	0

Test article		Skin NC				Secretions- NC Eye, Nose		Exophthalmos NC	
Dose		0	1	2	3	0	1	0	1
benzyl salicylate 0 mg/kg	n	10	0	0	0	10	0	10	0
benzyl salicylate 300 mg/kg	n	10	0	0	0	10	0	10	0

Test article		Palpebral NC closure				Mucosal NC membranes				Lacrimation NC	
Dose		0	1	2	3	0	1	2	3	0	1
benzyl salicylate 0 mg/kg	n	10	0	0	0	10	0	0	0	10	0
benzyl salicylate 300 mg/kg	n	10	0	0	0	10	0	0	0	10	0

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Not calculated : NC

Table 2 - 68 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : Administration

Generation : F0 Sex : Female Week : 3 Species : Rat

Test article		Piloerection NC		Pupil size NC			Salivation NC			
Dose		0	1	-1	0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	10	0	0	10	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	10	0	0	10	0	0	0

Test article		Abnormal NC respiration				Vocalization NC			
Dose		0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	10	0	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	0	9	1	0	0

Test article		Reactivity to NC handling				
Dose		-1	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	0	10	0	0	0

Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward
Not calculated : NC

Table 2 - 69 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : Administration

Generation : F0 Sex : Female Week : 4 Species : Rat

Test article		Ease of removal from cage NC					Fur condition NC			
Dose		-1	0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	10	0	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	0	10	0	0	0	10	0	0	0

Test article		Skin NC				Secretions- NC Eye, Nose		Exophthalmos NC	
Dose		0	1	2	3	0	1	0	1
benzyl salicylate 0 mg/kg	n	10	0	0	0	10	0	10	0
benzyl salicylate 300 mg/kg	n	10	0	0	0	10	0	10	0

Test article		Palpebral NC closure				Mucosal NC membranes				Lacrimation NC	
Dose		0	1	2	3	0	1	2	3	0	1
benzyl salicylate 0 mg/kg	n	10	0	0	0	10	0	0	0	10	0
benzyl salicylate 300 mg/kg	n	10	0	0	0	10	0	0	0	10	0

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Not calculated : NC

Table 2 - 70 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : Administration

Generation : F0 Sex : Female Week : 4 Species : Rat

Test article		Piloerection NC		Pupil size NC			Salivation NC			
Dose		0	1	-1	0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	10	0	0	10	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	10	0	0	10	0	0	0

Test article		Abnormal NC respiration				Vocalization NC			
Dose		0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	10	0	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	0	10	0	0	0

Test article		Reactivity to NC handling				
Dose		-1	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	0	10	0	0	0

Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward
Not calculated : NC

Table 2 - 71 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : Administration

Generation : F0 Sex : Female Week : 5 Species : Rat

Test article		Ease of removal from cage NC					Fur condition NC			
Dose		-1	0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	10	0	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	0	10	0	0	0	10	0	0	0

Test article		Skin NC				Secretions- NC Eye, Nose		Exophthalmos NC	
Dose		0	1	2	3	0	1	0	1
benzyl salicylate 0 mg/kg	n	10	0	0	0	10	0	10	0
benzyl salicylate 300 mg/kg	n	10	0	0	0	10	0	10	0

Test article		Palpebral NC closure				Mucosal NC membranes				Lacrimation NC	
Dose		0	1	2	3	0	1	2	3	0	1
benzyl salicylate 0 mg/kg	n	10	0	0	0	10	0	0	0	10	0
benzyl salicylate 300 mg/kg	n	10	0	0	0	10	0	0	0	10	0

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Not calculated : NC

Table 2 - 72 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : Administration

Generation : F0 Sex : Female Week : 5 Species : Rat

Test article		Piloerection NC		Pupil size NC			Salivation NC			
Dose		0	1	-1	0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	10	0	0	10	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	10	0	0	10	0	0	0

Test article		Abnormal NC respiration				Vocalization NC			
Dose		0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	10	0	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	0	8	2	0	0

Test article		Reactivity to NC handling				
Dose		-1	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	0	10	0	0	0

Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward
Not calculated : NC

Table 2 - 73 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : Administration

Generation : F0 Sex : Female Week : 6 Species : Rat

Test article / Dose		Ease of removal from cage NC -1	0	1	2	3	Fur condition NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	0	10	0	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	0	10	0	0	0	10	0	0	0

Test article / Dose		Skin NC 0	1	2	3	Secretions- NC Eye, Nose 0	1	Exophthalmos NC 0	1
benzyl salicylate 0 mg/kg	n	10	0	0	0	10	0	10	0
benzyl salicylate 300 mg/kg	n	10	0	0	0	10	0	10	0

Test article / Dose		Palpebral NC closure 0	1	2	3	Mucosal NC membranes 0	1	2	3	Lacrimation NC 0	1
benzyl salicylate 0 mg/kg	n	10	0	0	0	10	0	0	0	10	0
benzyl salicylate 300 mg/kg	n	10	0	0	0	10	0	0	0	10	0

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Not calculated : NC

Table 2 - 74 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : Administration

Generation : F0 Sex : Female Week : 6 Species : Rat

Test article		Piloerection NC		Pupil size NC			Salivation NC			
Dose		0	1	-1	0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	10	0	0	10	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	10	0	0	10	0	0	0

Test article		Abnormal NC respiration				Vocalization NC			
Dose		0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	10	0	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	0	9	1	0	0

Test article		Reactivity to NC handling				
Dose		-1	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	0	10	0	0	0

Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward
Not calculated : NC

Table 2 - 75 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : Recovery

Generation : F0 Sex : Male Week : 1 Species : Rat

Test article		Ease of removal from cage NC					Fur condition NC			
Dose		-1	0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	5	0	0	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	0	5	0	0	0	5	0	0	0

Test article		Skin NC				Secretions- NC Eye, Nose		Exophthalmos NC	
Dose		0	1	2	3	0	1	0	1
benzyl salicylate 0 mg/kg	n	5	0	0	0	5	0	5	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	5	0	5	0

Test article		Palpebral NC closure				Mucosal NC membranes				Lacrimation NC	
Dose		0	1	2	3	0	1	2	3	0	1
benzyl salicylate 0 mg/kg	n	5	0	0	0	5	0	0	0	5	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	5	0	0	0	5	0

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Not calculated : NC

Table 2 - 76 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : Recovery

Generation : F0 Sex : Male Week : 1 Species : Rat

Test article		Piloerection NC		Pupil size NC			Salivation NC			
Dose		0	1	-1	0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	5	0	0	5	0	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	5	0	0	5	0	0	0

Test article		Abnormal NC respiration				Vocalization NC			
Dose		0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	5	0	0	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	5	0	0	0

Test article		Reactivity to NC handling				
Dose		-1	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	0	5	0	0	0

Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward
Not calculated : NC

Table 2 - 77 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : Recovery

Generation : F0 Sex : Male Week : 2 Species : Rat

Test article / Dose		Ease of removal from cage NC -1	0	1	2	3	Fur condition NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	0	5	0	0	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	0	5	0	0	0	5	0	0	0

Test article / Dose		Skin NC 0	1	2	3	Secretions- NC Eye, Nose 0	1	Exophthalmos NC 0	1
benzyl salicylate 0 mg/kg	n	5	0	0	0	5	0	5	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	5	0	5	0

Test article / Dose		Palpebral NC closure 0	1	2	3	Mucosal NC membranes 0	1	2	3	Lacrimation NC 0	1
benzyl salicylate 0 mg/kg	n	5	0	0	0	5	0	0	0	5	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	5	0	0	0	5	0

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Not calculated : NC

Table 2 - 78 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : Recovery

Generation : F0 Sex : Male Week : 2 Species : Rat

Test article		Piloerection NC		Pupil size NC			Salivation NC			
Dose		0	1	-1	0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	5	0	0	5	0	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	5	0	0	5	0	0	0

Test article		Abnormal NC respiration				Vocalization NC			
Dose		0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	5	0	0	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	5	0	0	0

Test article		Reactivity to NC handling				
Dose		-1	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	0	5	0	0	0

Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward
Not calculated : NC

Table 2 - 79 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : Recovery

Generation : F0 Sex : Female Week : 1 Species : Rat

Test article		Ease of removal from cage NC					Fur condition NC			
Dose		-1	0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	5	0	0	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	0	5	0	0	0	5	0	0	0

Test article		Skin NC				Secretions- NC Eye, Nose		Exophthalmos NC	
Dose		0	1	2	3	0	1	0	1
benzyl salicylate 0 mg/kg	n	5	0	0	0	5	0	5	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	5	0	5	0

Test article		Palpebral closure NC				Mucosal membranes NC				Lacrimation NC	
Dose		0	1	2	3	0	1	2	3	0	1
benzyl salicylate 0 mg/kg	n	5	0	0	0	5	0	0	0	5	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	5	0	0	0	5	0

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Not calculated : NC

Table 2 - 80 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : Recovery

Generation : F0 Sex : Female Week : 1 Species : Rat

Test article		Piloerection NC		Pupil size NC			Salivation NC			
Dose		0	1	-1	0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	5	0	0	5	0	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	5	0	0	5	0	0	0

Test article		Abnormal NC respiration				Vocalization NC			
Dose		0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	5	0	0	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	5	0	0	0

Test article		Reactivity to NC handling				
Dose		-1	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	0	5	0	0	0

Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward
Not calculated : NC

Table 2 - 81 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : Recovery

Generation : F0 Sex : Female Week : 2 Species : Rat

Test article / Dose		Ease of removal from cage NC -1	0	1	2	3	Fur condition NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	0	5	0	0	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	0	5	0	0	0	5	0	0	0

Test article / Dose		Skin NC 0	1	2	3	Secretions- NC Eye, Nose 0	1	Exophthalmos NC 0	1
benzyl salicylate 0 mg/kg	n	5	0	0	0	5	0	5	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	5	0	5	0

Test article / Dose		Palpebral NC closure 0	1	2	3	Mucosal NC membranes 0	1	2	3	Lacrimation NC 0	1
benzyl salicylate 0 mg/kg	n	5	0	0	0	5	0	0	0	5	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	5	0	0	0	5	0

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Not calculated : NC

Table 2 - 82 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

In-the-hand observation Period : Recovery

Generation : F0 Sex : Female Week : 2 Species : Rat

Test article		Piloerection NC		Pupil size NC			Salivation NC			
Dose		0	1	-1	0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	5	0	0	5	0	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	5	0	0	5	0	0	0

Test article		Abnormal NC respiration				Vocalization NC			
Dose		0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	5	0	0	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	5	0	0	0

Test article		Reactivity to NC handling				
Dose		-1	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	0	5	0	0	0

Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward
Not calculated : NC

Table 2 - 83 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 before mating

Generation : F0 Sex : Male Week : 1 Species : Rat

Test article		Arousal NC					Convulsion NC			
Dose		-2	-1	0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	0	12	0	0	12	0	0	0

Test article		Abnormal NC behavior				Stereotypy NC			
Dose		0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	0	0

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Not calculated : NC

Table 2 - 84 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 before mating

Generation : F0 Sex : Male Week : 1 Species : Rat

Test article Dose		Gait NC U	0	1	2	3	Posture NC N	F	H
benzyl salicylate 0 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0	12	0	0

Test article Dose		Grooming NC 0	1	2	Urination NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	11	1	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	11	1	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	12	0	0	0

Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
Not calculated : NC

Table 2 - 85 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 before mating

Generation : F0 Sex : Male Week : 1 Species : Rat

Test article Dose		Rearing	Defecation count
benzyl salicylate 0 mg/kg	n	12	12
	Mean	4	1
	S.D.	2	1
benzyl salicylate 30 mg/kg	n	12	12
	Mean	4	1
	S.D.	2	1
benzyl salicylate 100 mg/kg	n	12	12
	Mean	5	0
	S.D.	3	1
benzyl salicylate 300 mg/kg	n	12	12
	Mean	5	1
	S.D.	3	2

Not significantly different from benzyl salicylate 0 mg/kg

Table 2 - 86 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 before mating

Generation : F0 Sex : Male Week : 2 Species : Rat

Test article / Dose		Arousal NC -2	-1	0	1	2	Convulsion NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	0	12	0	0	12	0	0	0

Test article / Dose		Abnormal NC behavior 0	1	2	3	Stereotypy NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	0	0

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Not calculated : NC

Table 2 - 87 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 before mating

Generation : F0 Sex : Male Week : 2 Species : Rat

Test article Dose		Gait NC U	0	1	2	3	Posture NC N	F	H
benzyl salicylate 0 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0	12	0	0

Test article Dose		Grooming NC 0	1	2	Urination NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	10	2	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	9	3	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	10	2	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	12	0	0	0

Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
Not calculated : NC

Table 2 - 88 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 before mating

Generation : F0 Sex : Male Week : 2 Species : Rat

Test article Dose		Rearing	Defecation count
benzyl salicylate 0 mg/kg	n	12	12
	Mean	5	0
	S.D.	2	1
benzyl salicylate 30 mg/kg	n	12	12
	Mean	4	0
	S.D.	2	1
benzyl salicylate 100 mg/kg	n	12	12
	Mean	4	1
	S.D.	2	1
benzyl salicylate 300 mg/kg	n	12	12
	Mean	5	0
	S.D.	2	1

Not significantly different from benzyl salicylate 0 mg/kg

Table 2 - 89 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 mating

Generation : F0 Sex : Male Week : 3 Species : Rat

Test article / Dose		Arousal NC -2	-1	0	1	2	Convulsion NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	0	12	0	0	12	0	0	0

Test article / Dose		Abnormal NC behavior 0	1	2	3	Stereotypy NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	0	0

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Not calculated : NC

Table 2 - 90 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 mating

Generation : F0 Sex : Male Week : 3 Species : Rat

Test article / Dose		Gait NC					Posture NC		
		U	0	1	2	3	N	F	H
benzyl salicylate 0 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 100 mg/kg	n	1	11	0	0	0	12	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0	12	0	0

Test article / Dose		Grooming NC			Urination NC			
		0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	11	1	0	0

Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
Not calculated : NC

Table 2 - 91 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 mating

Generation : F0 Sex : Male Week : 3 Species : Rat

Test article Dose		Rearing	Defecation count
benzyl salicylate 0 mg/kg	n	12	12
	Mean	4	0
	S.D.	2	1
benzyl salicylate 30 mg/kg	n	12	12
	Mean	5	0
	S.D.	2	1
benzyl salicylate 100 mg/kg	n	12	12
	Mean	4	0
	S.D.	2	0
benzyl salicylate 300 mg/kg	n	12	12
	Mean	4	0
	S.D.	1	0

Not significantly different from benzyl salicylate 0 mg/kg

Table 2 - 92 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 mating

Generation : F0 Sex : Male Week : 4 Species : Rat

Test article / Dose		Arousal NC -2	-1	0	1	2	Convulsion NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	0	12	0	0	12	0	0	0

Test article / Dose		Abnormal NC behavior 0	1	2	3	Stereotypy NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	0	0

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Not calculated : NC

Table 2 - 93 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 mating

Generation : F0 Sex : Male Week : 4 Species : Rat

Test article Dose		Gait NC U	0	1	2	3	Posture NC N	F	H
benzyl salicylate 0 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0	12	0	0

Test article Dose		Grooming NC 0	1	2	Urination NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	11	1	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	10	2	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	8	4	0	0

Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
Not calculated : NC

Table 2 - 94 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 mating

Generation : F0 Sex : Male Week : 4 Species : Rat

Test article Dose		Rearing	Defecation count
benzyl salicylate 0 mg/kg	n	12	12
	Mean	5	0
	S.D.	2	0
benzyl salicylate 30 mg/kg	n	12	12
	Mean	4	0
	S.D.	1	1
benzyl salicylate 100 mg/kg	n	12	12
	Mean	4	0
	S.D.	3	0
benzyl salicylate 300 mg/kg	n	12	12
	Mean	5	0
	S.D.	1	0

Not significantly different from benzyl salicylate 0 mg/kg

Table 2 - 95 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 mating

Generation : F0 Sex : Male Week : 5 Species : Rat

Test article / Dose		Arousal NC -2	-1	0	1	2	Convulsion NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	0	12	0	0	12	0	0	0

Test article / Dose		Abnormal NC behavior 0	1	2	3	Stereotypy NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	0	0

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Not calculated : NC

Table 2 - 96 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 mating

Generation : F0 Sex : Male Week : 5 Species : Rat

Test article Dose		Gait NC U	0	1	2	3	Posture NC N	F	H
benzyl salicylate 0 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0	12	0	0

Test article Dose		Grooming NC 0	1	2	Urination NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	11	1	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	10	2	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	11	1	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	10	2	0	0

Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
Not calculated : NC

Table 2 - 97 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 mating

Generation : F0 Sex : Male Week : 5 Species : Rat

Test article Dose		Rearing	Defecation count
benzyl salicylate 0 mg/kg	n	12	12
	Mean	5	0
	S.D.	1	0
benzyl salicylate 30 mg/kg	n	12	12
	Mean	5	0
	S.D.	2	0
benzyl salicylate 100 mg/kg	n	12	12
	Mean	5	0
	S.D.	2	0
benzyl salicylate 300 mg/kg	n	12	12
	Mean	5	0
	S.D.	2	0

Not significantly different from benzyl salicylate 0 mg/kg

Table 2 - 98 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 mating

Generation : F0 Sex : Male Week : 6 Species : Rat

Test article / Dose		Arousal NC -2	-1	0	1	2	Convulsion NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	0	12	0	0	12	0	0	0

Test article / Dose		Abnormal NC behavior 0	1	2	3	Stereotypy NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	0	0

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Not calculated : NC

Table 2 - 99 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 mating

Generation : F0 Sex : Male Week : 6 Species : Rat

Test article Dose		Gait NC U	0	1	2	3	Posture NC N	F	H
benzyl salicylate 0 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0	12	0	0

Test article Dose		Grooming NC 0	1	2	Urination NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	11	1	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	10	2	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	11	1	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	8	4	0	0

Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
Not calculated : NC

Table 2 - 100 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 mating

Generation : F0 Sex : Male Week : 6 Species : Rat

Test article Dose		Rearing	Defecation count
benzyl salicylate 0 mg/kg	n	12	12
	Mean	6	0
	S.D.	2	0
benzyl salicylate 30 mg/kg	n	12	12
	Mean	5	0
	S.D.	2	1
benzyl salicylate 100 mg/kg	n	12	12
	Mean	5	0
	S.D.	2	0
benzyl salicylate 300 mg/kg	n	12	12
	Mean	4	0
	S.D.	1	0

Not significantly different from benzyl salicylate 0 mg/kg

Table 2 - 101 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 before mating

Generation : F0 Sex : Female Week : 1 Species : Rat

Test article		Arousal NC					Convulsion NC			
Dose		-2	-1	0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	0	12	0	0	12	0	0	0

Test article		Abnormal NC behavior				Stereotypy NC			
Dose		0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	0	0

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Not calculated : NC

Table 2 - 102 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 before mating

Generation : F0 Sex : Female Week : 1 Species : Rat

Test article / Dose		Gait NC					Posture NC		
		U	0	1	2	3	N	F	H
benzyl salicylate 0 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0	12	0	0

Test article / Dose		Grooming NC			Urination NC			
		0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	12	0	0	0

Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
Not calculated : NC

Table 2 - 103 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 before mating

Generation : F0 Sex : Female Week : 1 Species : Rat

Test article Dose		Rearing	Defecation count
benzyl salicylate 0 mg/kg	n	12	12
	Mean	7	0
	S.D.	2	0
benzyl salicylate 30 mg/kg	n	12	12
	Mean	7	0
	S.D.	1	0
			EF
benzyl salicylate 100 mg/kg	n	12	12
	Mean	8	0
	S.D.	2	0
			EF
benzyl salicylate 300 mg/kg	n	12	12
	Mean	7	0
	S.D.	2	0
			EF

Not significantly different from benzyl salicylate 0 mg/kg

EF : The group mean is the same and unbiased variance 0 for all groups. All data of all groups are same.

Table 2 - 104 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 before mating

Generation : F0 Sex : Female Week : 2 Species : Rat

Test article		Arousal NC					Convulsion NC			
Dose		-2	-1	0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	0	12	0	0	12	0	0	0

Test article		Abnormal NC behavior				Stereotypy NC			
Dose		0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	0	0

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Not calculated : NC

Table 2 - 105 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 before mating

Generation : F0 Sex : Female Week : 2 Species : Rat

Test article Dose		Gait NC U	0	1	2	3	Posture NC N	F	H
benzyl salicylate 0 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0	12	0	0

Test article Dose		Grooming NC 0	1	2	Urination NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	12	0	0	0

Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
Not calculated : NC

Table 2 - 106 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 before mating

Generation : F0 Sex : Female Week : 2 Species : Rat

Test article Dose		Rearing	Defecation count
benzyl salicylate 0 mg/kg	n	12	12
	Mean	7	0
	S.D.	2	0
benzyl salicylate 30 mg/kg	n	12	12
	Mean	8	0
	S.D.	3	0
			EF
benzyl salicylate 100 mg/kg	n	12	12
	Mean	8	0
	S.D.	1	0
			EF
benzyl salicylate 300 mg/kg	n	12	12
	Mean	8	0
	S.D.	2	0
			EF

Not significantly different from benzyl salicylate 0 mg/kg

EF : The group mean is the same and unbiased variance 0 for all groups. All data of all groups are same.

Table 2 - 107 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 gestation

Generation : F0 Sex : Female Day : 1 Species : Rat

Test article		Arousal NC					Convulsion NC			
Dose		-2	-1	0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	0	12	0	0	12	0	0	0

Test article		Abnormal NC behavior				Stereotypy NC			
Dose		0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	0	0

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Not calculated : NC

Table 2 - 108 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 gestation

Generation : F0 Sex : Female Day : 1 Species : Rat

Test article Dose		Gait NC U	0	1	2	3	Posture NC N	F	H
benzyl salicylate 0 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0	12	0	0

Test article Dose		Grooming NC 0	1	2	Urination NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	12	0	0	0

Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
Not calculated : NC

Table 2 - 109 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 gestation

Generation : F0 Sex : Female Day : 1 Species : Rat

Test article Dose		Rearing	Defecation count
benzyl salicylate 0 mg/kg	n	12	12
	Mean	6	0
	S.D.	2	0
benzyl salicylate 30 mg/kg	n	12	12
	Mean	6	0
	S.D.	1	0
			EF
benzyl salicylate 100 mg/kg	n	12	12
	Mean	8	0
	S.D.	3	0
			EF
benzyl salicylate 300 mg/kg	n	12	12
	Mean	6	0
	S.D.	2	0
			EF

Not significantly different from benzyl salicylate 0 mg/kg

EF : The group mean is the same and unbiased variance 0 for all groups. All data of all groups are same.

Table 2 - 110 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 gestation

Generation : F0 Sex : Female Day : 7 Species : Rat

Test article		Arousal NC					Convulsion NC			
Dose		-2	-1	0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	0	12	0	0	12	0	0	0

Test article		Abnormal NC behavior				Stereotypy NC			
Dose		0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	0	0

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Not calculated : NC

Table 2 - 111 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 gestation

Generation : F0 Sex : Female Day : 7 Species : Rat

Test article Dose		Gait NC U	0	1	2	3	Posture NC N	F	H
benzyl salicylate 0 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0	12	0	0

Test article Dose		Grooming NC 0	1	2	Urination NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	12	0	0	0

Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
Not calculated : NC

Table 2 - 112 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 gestation

Generation : F0 Sex : Female Day : 7 Species : Rat

Test article Dose		Rearing	Defecation count
benzyl salicylate 0 mg/kg	n	12	12
	Mean	5	0
	S.D.	1	0
benzyl salicylate 30 mg/kg	n	12	12
	Mean	6	0
	S.D.	2	0
			EF
benzyl salicylate 100 mg/kg	n	12	12
	Mean	7	0
	S.D.	2	0
		DT *	EF
benzyl salicylate 300 mg/kg	n	12	12
	Mean	6	0
	S.D.	2	0
			EF

Significantly different from benzyl salicylate 0 mg/kg : * P<0.05
DT : Dunnett test (two-side)
EF : The group mean is the same and unbiased variance 0 for all groups. All data of all groups are same.

Table 2 - 113 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 gestation

Generation : F0 Sex : Female Day : 14 Species : Rat

Test article / Dose		Arousal NC -2	-1	0	1	2	Convulsion NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	0	12	0	0	12	0	0	0

Test article / Dose		Abnormal NC behavior 0	1	2	3	Stereotypy NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	0	0

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Not calculated : NC

Table 2 - 114 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 gestation

Generation : F0 Sex : Female Day : 14 Species : Rat

Test article Dose		Gait NC U	0	1	2	3	Posture NC N	F	H
benzyl salicylate 0 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0	12	0	0

Test article Dose		Grooming NC 0	1	2	Urination NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	11	1	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	12	0	0	0

Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
Not calculated : NC

Table 2 - 115 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 gestation

Generation : F0 Sex : Female Day : 14 Species : Rat

Test article Dose		Rearing	Defecation count
benzyl salicylate 0 mg/kg	n	12	12
	Mean	4	0
	S.D.	2	0
benzyl salicylate 30 mg/kg	n	12	12
	Mean	5	0
	S.D.	2	0
			EF
benzyl salicylate 100 mg/kg	n	12	12
	Mean	6	0
	S.D.	2	0
			EF
benzyl salicylate 300 mg/kg	n	12	12
	Mean	4	0
	S.D.	2	0
			EF

Not significantly different from benzyl salicylate 0 mg/kg

EF : The group mean is the same and unbiased variance 0 for all groups. All data of all groups are same.

Table 2 - 116 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 gestation

Generation : F0 Sex : Female Day : 20 Species : Rat

Test article		Arousal NC					Convulsion NC			
Dose		-2	-1	0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	0	0	12	0	0	12	0	0	0

Test article		Abnormal NC behavior				Stereotypy NC			
Dose		0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	0	12	0	0	0

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Not calculated : NC

Table 2 - 117 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 gestation

Generation : F0 Sex : Female Day : 20 Species : Rat

Test article Dose		Gait NC U	0	1	2	3	Posture NC N	F	H
benzyl salicylate 0 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 300 mg/kg	n	0	12	0	0	0	12	0	0

Test article Dose		Grooming NC 0	1	2	Urination NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	11	1	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 300 mg/kg	n	12	0	0	11	1	0	0

Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
Not calculated : NC

Table 2 - 118 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 gestation

Generation : F0 Sex : Female Day : 20 Species : Rat

Test article Dose		Rearing	Defecation count
benzyl salicylate 0 mg/kg	n	12	12
	Mean	4	0
	S.D.	2	0
benzyl salicylate 30 mg/kg	n	12	12
	Mean	4	0
	S.D.	1	0
			EF
benzyl salicylate 100 mg/kg	n	12	12
	Mean	6	0
	S.D.	2	0
			EF
benzyl salicylate 300 mg/kg	n	12	12
	Mean	5	0
	S.D.	2	0
			EF

Not significantly different from benzyl salicylate 0 mg/kg

EF : The group mean is the same and unbiased variance 0 for all groups. All data of all groups are same.

Table 2 - 119 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 lactation

Generation : F0 Sex : Female Day : 4 Species : Rat

Test article / Dose		Arousal NC -2	-1	0	1	2	Convulsion NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	0	0	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	0	0	12	0	0	12	0	0	0

Test article / Dose		Abnormal NC behavior 0	1	2	3	Stereotypy NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	0	12	0	0	0

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Not calculated : NC

Table 2 - 120 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 lactation

Generation : F0 Sex : Female Day : 4 Species : Rat

Test article / Dose		Gait NC					Posture NC		
		U	0	1	2	3	N	F	H
benzyl salicylate 0 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 30 mg/kg	n	0	12	0	0	0	12	0	0
benzyl salicylate 100 mg/kg	n	0	12	0	0	0	12	0	0

Test article / Dose		Grooming NC			Urination NC			
		0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 30 mg/kg	n	12	0	0	12	0	0	0
benzyl salicylate 100 mg/kg	n	12	0	0	12	0	0	0

Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
Not calculated : NC

Table 2 - 121 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 lactation

Generation : F0 Sex : Female Day : 4 Species : Rat

Test article Dose		Rearing	Defecation count
benzyl salicylate 0 mg/kg	n	12	12
	Mean	5	0
	S.D.	2	0
benzyl salicylate 30 mg/kg	n	12	12
	Mean	5	0
	S.D.	1	0
			EF
benzyl salicylate 100 mg/kg	n	12	12
	Mean	6	0
	S.D.	2	0
			EF

Not significantly different from benzyl salicylate 0 mg/kg

EF : The group mean is the same and unbiased variance 0 for all groups. All data of all groups are same.

Table 2 - 122 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Administration

Generation : F0 Sex : Female Week : 1 Species : Rat

Test article / Dose		Arousal NC -2	-1	0	1	2	Convulsion NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	0	0	10	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	0	0	10	0	0	10	0	0	0

Test article / Dose		Abnormal NC behavior 0	1	2	3	Stereotypy NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	10	0	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	0	10	0	0	0

Test article / Dose		Gait NC U	0	1	2	3	Posture NC N	F	H
benzyl salicylate 0 mg/kg	n	0	10	0	0	0	10	0	0
benzyl salicylate 300 mg/kg	n	0	10	0	0	0	10	0	0

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Not calculated : NC

Table 2 - 123 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Administration

Generation : F0 Sex : Female Week : 1 Species : Rat

Test article		Grooming NC			Urination NC			
Dose		0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	10	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	10	0	0	0

Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
Not calculated : NC

Table 2 - 124 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Administration

Generation : F0 Sex : Female Week : 1 Species : Rat

Test article Dose		Rearing	Defecation count
benzyl salicylate	n	10	10
0 mg/kg	Mean	8	0
	S.D.	2	0
benzyl salicylate	n	10	10
300 mg/kg	Mean	6	0
	S.D.	2	0
			EF

Not significantly different from benzyl salicylate 0 mg/kg

EF : The group mean is the same and unbiased variance 0 for all groups. All data of all groups are same.

Table 2 - 125 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Administration

Generation : F0 Sex : Female Week : 2 Species : Rat

Test article / Dose		Arousal NC -2	-1	0	1	2	Convulsion NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	0	0	10	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	0	0	10	0	0	10	0	0	0

Test article / Dose		Abnormal NC behavior 0	1	2	3	Stereotypy NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	10	0	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	0	10	0	0	0

Test article / Dose		Gait NC U	0	1	2	3	Posture NC N	F	H
benzyl salicylate 0 mg/kg	n	0	10	0	0	0	10	0	0
benzyl salicylate 300 mg/kg	n	0	10	0	0	0	10	0	0

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Not calculated : NC

Table 2 - 126 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Administration

Generation : F0 Sex : Female Week : 2 Species : Rat

Test article		Grooming NC			Urination NC			
Dose		0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	10	0	0	9	1	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	9	1	0	0

Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
Not calculated : NC

Table 2 - 127 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Administration

Generation : F0 Sex : Female Week : 2 Species : Rat

Test article Dose		Rearing	Defecation count
benzyl salicylate	n	10	10
0 mg/kg	Mean	9	0
	S.D.	2	0
benzyl salicylate	n	10	10
300 mg/kg	Mean	8	0
	S.D.	2	0
			EF

Not significantly different from benzyl salicylate 0 mg/kg

EF : The group mean is the same and unbiased variance 0 for all groups. All data of all groups are same.

Table 2 - 128 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Administration

Generation : F0 Sex : Female Week : 3 Species : Rat

Test article / Dose		Arousal NC -2	-1	0	1	2	Convulsion NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	0	0	10	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	0	0	10	0	0	10	0	0	0

Test article / Dose		Abnormal NC behavior 0	1	2	3	Stereotypy NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	10	0	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	0	10	0	0	0

Test article / Dose		Gait NC U	0	1	2	3	Posture NC N	F	H
benzyl salicylate 0 mg/kg	n	0	10	0	0	0	10	0	0
benzyl salicylate 300 mg/kg	n	0	10	0	0	0	10	0	0

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Not calculated : NC

Table 2 - 129 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Administration

Generation : F0 Sex : Female Week : 3 Species : Rat

Test article		Grooming NC			Urination NC			
Dose		0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	10	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	10	0	0	0

Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
Not calculated : NC

Table 2 - 130 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Administration

Generation : F0 Sex : Female Week : 3 Species : Rat

Test article Dose		Rearing	Defecation count
benzyl salicylate 0 mg/kg	n	10	10
	Mean	9	0
	S.D.	2	0
benzyl salicylate 300 mg/kg	n	10	10
	Mean	9	0
	S.D.	3	0
			EF

Not significantly different from benzyl salicylate 0 mg/kg

EF : The group mean is the same and unbiased variance 0 for all groups. All data of all groups are same.

Table 2 - 131 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Administration

Generation : F0 Sex : Female Week : 4 Species : Rat

Test article / Dose		Arousal NC -2	-1	0	1	2	Convulsion NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	0	0	10	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	0	0	10	0	0	10	0	0	0

Test article / Dose		Abnormal NC behavior 0	1	2	3	Stereotypy NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	10	0	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	0	10	0	0	0

Test article / Dose		Gait NC U	0	1	2	3	Posture NC N	F	H
benzyl salicylate 0 mg/kg	n	0	10	0	0	0	10	0	0
benzyl salicylate 300 mg/kg	n	0	10	0	0	0	10	0	0

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Not calculated : NC

Table 2 - 132 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Administration

Generation : F0 Sex : Female Week : 4 Species : Rat

Test article		Grooming NC			Urination NC			
Dose		0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	10	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	9	1	0	0

Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
Not calculated : NC

Table 2 - 133 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Administration

Generation : F0 Sex : Female Week : 4 Species : Rat

Test article Dose		Rearing	Defecation count
benzyl salicylate	n	10	10
0 mg/kg	Mean	9	0
	S.D.	3	0
benzyl salicylate	n	10	10
300 mg/kg	Mean	8	0
	S.D.	2	0
			EF

Not significantly different from benzyl salicylate 0 mg/kg

EF : The group mean is the same and unbiased variance 0 for all groups. All data of all groups are same.

Table 2 - 134 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Administration

Generation : F0 Sex : Female Week : 5 Species : Rat

Test article / Dose		Arousal NC -2	-1	0	1	2	Convulsion NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	0	0	10	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	0	0	10	0	0	10	0	0	0

Test article / Dose		Abnormal NC behavior 0	1	2	3	Stereotypy NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	10	0	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	0	10	0	0	0

Test article / Dose		Gait NC U	0	1	2	3	Posture NC N	F	H
benzyl salicylate 0 mg/kg	n	0	10	0	0	0	10	0	0
benzyl salicylate 300 mg/kg	n	0	10	0	0	0	10	0	0

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Not calculated : NC

Table 2 - 135 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Administration

Generation : F0 Sex : Female Week : 5 Species : Rat

Test article		Grooming NC			Urination NC			
Dose		0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	10	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	8	2	0	0

Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
Not calculated : NC

Table 2 - 136 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Administration

Generation : F0 Sex : Female Week : 5 Species : Rat

Test article Dose		Rearing	Defecation count
benzyl salicylate	n	10	10
0 mg/kg	Mean	8	0
	S.D.	2	0
benzyl salicylate	n	10	10
300 mg/kg	Mean	6	0
	S.D.	2	0
			EF

Not significantly different from benzyl salicylate 0 mg/kg

EF : The group mean is the same and unbiased variance 0 for all groups. All data of all groups are same.

Table 2 - 137 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Administration

Generation : F0 Sex : Female Week : 6 Species : Rat

Test article / Dose		Arousal NC -2	-1	0	1	2	Convulsion NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	0	0	10	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	0	0	10	0	0	10	0	0	0

Test article / Dose		Abnormal NC behavior 0	1	2	3	Stereotypy NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	10	0	0	0	10	0	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	0	10	0	0	0

Test article / Dose		Gait NC U	0	1	2	3	Posture NC N	F	H
benzyl salicylate 0 mg/kg	n	0	10	0	0	0	10	0	0
benzyl salicylate 300 mg/kg	n	0	10	0	0	0	10	0	0

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Not calculated : NC

Table 2 - 138 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Administration

Generation : F0 Sex : Female Week : 6 Species : Rat

Test article		Grooming NC			Urination NC			
Dose		0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	10	0	0	9	1	0	0
benzyl salicylate 300 mg/kg	n	10	0	0	8	2	0	0

Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
Not calculated : NC

Table 2 - 139 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Administration

Generation : F0 Sex : Female Week : 6 Species : Rat

Test article Dose		Rearing	Defecation count
benzyl salicylate	n	10	10
0 mg/kg	Mean	7	0
	S.D.	1	0
benzyl salicylate	n	10	10
300 mg/kg	Mean	7	0
	S.D.	2	0
			EF

Not significantly different from benzyl salicylate 0 mg/kg

EF : The group mean is the same and unbiased variance 0 for all groups. All data of all groups are same.

Table 2 - 140 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Recovery

Generation : F0 Sex : Male Week : 1 Species : Rat

Test article / Dose		Arousal NC -2	-1	0	1	2	Convulsion NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	0	0	5	0	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	0	0	5	0	0	5	0	0	0

Test article / Dose		Abnormal NC behavior 0	1	2	3	Stereotypy NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	5	0	0	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	5	0	0	0

Test article / Dose		Gait NC U	0	1	2	3	Posture NC N	F	H
benzyl salicylate 0 mg/kg	n	0	5	0	0	0	5	0	0
benzyl salicylate 300 mg/kg	n	0	5	0	0	0	5	0	0

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Not calculated : NC

Table 2 - 141 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Recovery

Generation : F0 Sex : Male Week : 1 Species : Rat

Test article		Grooming NC			Urination NC			
Dose		0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	5	0	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	4	1	0	0

Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
Not calculated : NC

Table 2 - 142 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Recovery

Generation : F0 Sex : Male Week : 1 Species : Rat

Test article Dose		Rearing	Defecation count
benzyl salicylate	n	5	5
0 mg/kg	Mean	3	1
	S.D.	2	1
benzyl salicylate	n	5	5
300 mg/kg	Mean	4	0
	S.D.	2	0

Not significantly different from benzyl salicylate 0 mg/kg

Table 2 - 143 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Recovery

Generation : F0 Sex : Male Week : 2 Species : Rat

Test article		Arousal NC					Convulsion NC			
Dose		-2	-1	0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	0	0	5	0	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	0	0	5	0	0	5	0	0	0

Test article		Abnormal NC behavior				Stereotypy NC			
Dose		0	1	2	3	0	1	2	3
benzyl salicylate 0 mg/kg	n	5	0	0	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	5	0	0	0

Test article		Gait NC					Posture NC		
Dose		U	0	1	2	3	N	F	H
benzyl salicylate 0 mg/kg	n	0	5	0	0	0	5	0	0
benzyl salicylate 300 mg/kg	n	0	5	0	0	0	5	0	0

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Not calculated : NC

Table 2 - 144 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Recovery

Generation : F0 Sex : Male Week : 2 Species : Rat

Test article		Grooming NC			Urination NC			
Dose		0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	5	0	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	3	2	0	0

Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
Not calculated : NC

Table 2 - 145 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Recovery

Generation : F0 Sex : Male Week : 2 Species : Rat

Test article Dose		Rearing	Defecation count
benzyl salicylate	n	5	5
0 mg/kg	Mean	5	0
	S.D.	1	0
benzyl salicylate	n	5	5
300 mg/kg	Mean	5	0
	S.D.	2	0
			EF

Not significantly different from benzyl salicylate 0 mg/kg

EF : The group mean is the same and unbiased variance 0 for all groups. All data of all groups are same.

Table 2 - 146 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Recovery

Generation : F0 Sex : Female Week : 1 Species : Rat

Test article / Dose		Arousal NC -2	-1	0	1	2	Convulsion NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	0	0	5	0	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	0	0	5	0	0	5	0	0	0

Test article / Dose		Abnormal NC behavior 0	1	2	3	Stereotypy NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	5	0	0	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	5	0	0	0

Test article / Dose		Gait NC U	0	1	2	3	Posture NC N	F	H
benzyl salicylate 0 mg/kg	n	0	5	0	0	0	5	0	0
benzyl salicylate 300 mg/kg	n	0	5	0	0	0	5	0	0

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Not calculated : NC

Table 2 - 147 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Recovery

Generation : F0 Sex : Female Week : 1 Species : Rat

Test article		Grooming NC			Urination NC			
Dose		0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	5	0	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	5	0	0	0

Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
Not calculated : NC

Table 2 - 148 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Recovery

Generation : F0 Sex : Female Week : 1 Species : Rat

Test article Dose		Rearing	Defecation count
benzyl salicylate 0 mg/kg	n	5	5
	Mean	7	0
	S.D.	2	0
benzyl salicylate 300 mg/kg	n	5	5
	Mean	7	0
	S.D.	2	0
			EF

Not significantly different from benzyl salicylate 0 mg/kg

EF : The group mean is the same and unbiased variance 0 for all groups. All data of all groups are same.

Table 2 - 149 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Recovery

Generation : F0 Sex : Female Week : 2 Species : Rat

Test article / Dose		Arousal NC -2	-1	0	1	2	Convulsion NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	0	0	5	0	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	0	0	5	0	0	5	0	0	0

Test article / Dose		Abnormal NC behavior 0	1	2	3	Stereotypy NC 0	1	2	3
benzyl salicylate 0 mg/kg	n	5	0	0	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	5	0	0	0

Test article / Dose		Gait NC U	0	1	2	3	Posture NC N	F	H
benzyl salicylate 0 mg/kg	n	0	5	0	0	0	5	0	0
benzyl salicylate 300 mg/kg	n	0	5	0	0	0	5	0	0

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Not calculated : NC

Table 2 - 150 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Recovery

Generation : F0 Sex : Female Week : 2 Species : Rat

Test article		Grooming NC			Urination NC			
Dose		0	1	2	0	1	2	3
benzyl salicylate 0 mg/kg	n	5	0	0	4	1	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	5	0	0	0

Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
Not calculated : NC

Table 2 - 151 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Recovery

Generation : F0 Sex : Female Week : 2 Species : Rat

Test article Dose		Rearing	Defecation count
benzyl salicylate	n	5	5
0 mg/kg	Mean	7	0
	S.D.	1	0
benzyl salicylate	n	5	5
300 mg/kg	Mean	8	0
	S.D.	2	0
			EF

Not significantly different from benzyl salicylate 0 mg/kg

EF : The group mean is the same and unbiased variance 0 for all groups. All data of all groups are same.

Table 2 - 152 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Manipulative test Period : F0 mating

Generation : F0 Sex : Male Week : 6 Species : Rat

Test article		Auditory response				Approach response			Touch response		
Dose		-2	-1	0	1	-1	0	1	-1	0	1
benzyl salicylate 0 mg/kg	n	0	0	5	0	0	5	0	0	5	0
benzyl salicylate 30 mg/kg	n	0	0	5	0	0	5	0	0	5	0
		EF	EF	EF	EF	EF	EF	EF	EF	EF	EF
benzyl salicylate 100 mg/kg	n	0	0	5	0	0	5	0	0	5	0
		EF	EF	EF	EF	EF	EF	EF	EF	EF	EF
benzyl salicylate 300 mg/kg	n	0	0	5	0	0	5	0	0	5	0
		EF	EF	EF	EF	EF	EF	EF	EF	EF	EF

Test article		Tail pinch response				Pupillary reflex			
Dose		-2	-1	0	1	P	F	L	R
benzyl salicylate 0 mg/kg	n	0	0	5	0	5	0	0	0
benzyl salicylate 30 mg/kg	n	0	0	5	0	5	0	0	0
		EF	EF	EF	EF	EF	EF	EF	EF
benzyl salicylate 100 mg/kg	n	0	0	5	0	5	0	0	0
		EF	EF	EF	EF	EF	EF	EF	EF
benzyl salicylate 300 mg/kg	n	0	0	5	0	5	0	0	0
		EF	EF	EF	EF	EF	EF	EF	EF

Auditory response) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
Approach response) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
Touch response) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
Tail pinch response) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
Pupillary reflex) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds
Not significantly different from benzyl salicylate 0 mg/kg
EF : The group mean is the same and unbiased variance 0 for all groups. All data of all groups are same.

Table 2 - 153 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Manipulative test Period : F0 mating

Generation : F0 Sex : Male Week : 6 Species : Rat

Test article Dose		Aerial righting reflex	Landing foot splay mm
benzyl salicylate 0 mg/kg	n	5	5
	Mean	0	83
	S.D.	0	21
benzyl salicylate 30 mg/kg	n	5	5
	Mean	0	71
	S.D.	0	17
		EF	
benzyl salicylate 100 mg/kg	n	5	5
	Mean	0	77
	S.D.	0	20
		EF	
benzyl salicylate 300 mg/kg	n	5	5
	Mean	0	93
	S.D.	0	18
		EF	

Aerial righting reflex) Total score

Not significantly different from benzyl salicylate 0 mg/kg

EF : The group mean is the same and unbiased variance 0 for all groups. All data of all groups are same.

Table 2 - 154 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Manipulative test Period : F0 lactation

Generation : F0 Sex : Female Day : 4 Species : Rat

Test article		Auditory response				Approach response			Touch response		
Dose		-2	-1	0	1	-1	0	1	-1	0	1
benzyl salicylate 0 mg/kg	n	0	0	5	0	0	5	0	0	5	0
benzyl salicylate 30 mg/kg	n	0	0	5	0	0	5	0	0	5	0
		EF	EF	EF	EF	EF	EF	EF	EF	EF	EF
benzyl salicylate 100 mg/kg	n	0	0	5	0	0	5	0	0	5	0
		EF	EF	EF	EF	EF	EF	EF	EF	EF	EF

Test article		Tail pinch response				Pupillary reflex			
Dose		-2	-1	0	1	P	F	L	R
benzyl salicylate 0 mg/kg	n	0	0	5	0	5	0	0	0
benzyl salicylate 30 mg/kg	n	0	0	5	0	5	0	0	0
		EF	EF	EF	EF	EF	EF	EF	EF
benzyl salicylate 100 mg/kg	n	0	0	5	0	5	0	0	0
		EF	EF	EF	EF	EF	EF	EF	EF

Auditory response) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
Approach response) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
Touch response) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
Tail pinch response) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
Pupillary reflex) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds
Not significantly different from benzyl salicylate 0 mg/kg
EF : The group mean is the same and unbiased variance 0 for all groups. All data of all groups are same.

Table 2 - 155 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Manipulative test Period : F0 lactation

Generation : F0 Sex : Female Day : 4 Species : Rat

Test article Dose		Aerial righting reflex	Landing foot splay mm
benzyl salicylate 0 mg/kg	n	5	5
	Mean	0	55
	S.D.	0	9
benzyl salicylate 30 mg/kg	n	5	5
	Mean	0	60
	S.D.	0	13
		EF	
benzyl salicylate 100 mg/kg	n	5	5
	Mean	0	56
	S.D.	0	20
		EF	

Aerial righting reflex) Total score

Not significantly different from benzyl salicylate 0 mg/kg

EF : The group mean is the same and unbiased variance 0 for all groups. All data of all groups are same.

Table 2 - 156 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Manipulative test Period : Recovery

Generation : F0 Sex : Male Week : 2 Species : Rat

Test article		Auditory response				Approach response			Touch response		
Dose		-2	-1	0	1	-1	0	1	-1	0	1
benzyl salicylate 0 mg/kg	n	0	0	5	0	0	5	0	0	5	0
benzyl salicylate 300 mg/kg	n	0	0	5	0	0	5	0	0	5	0
		EF	EF	EF	EF	EF	EF	EF	EF	EF	EF

Test article		Tail pinch response				Pupillary reflex			
Dose		-2	-1	0	1	P	F	L	R
benzyl salicylate 0 mg/kg	n	0	0	5	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	0	0	5	0	5	0	0	0
		EF	EF	EF	EF	EF	EF	EF	EF

Auditory response) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
Approach response) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
Touch response) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
Tail pinch response) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
Pupillary reflex) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds
Not significantly different from benzyl salicylate 0 mg/kg
EF : The group mean is the same and unbiased variance 0 for all groups. All data of all groups are same.

Table 2 - 157 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Manipulative test Period : Recovery

Generation : F0 Sex : Male Week : 2 Species : Rat

Test article Dose		Aerial righting reflex	Landing foot splay mm
benzyl salicylate	n	5	5
0 mg/kg	Mean	0	87
	S.D.	0	14
benzyl salicylate	n	5	5
300 mg/kg	Mean	0	87
	S.D.	0	22
		EF	

Aerial righting reflex) Total score

Not significantly different from benzyl salicylate 0 mg/kg

EF : The group mean is the same and unbiased variance 0 for all groups. All data of all groups are same.

Table 2 - 158 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Manipulative test Period : Recovery

Generation : F0 Sex : Female Week : 2 Species : Rat

Test article		Auditory response				Approach response			Touch response		
Dose		-2	-1	0	1	-1	0	1	-1	0	1
benzyl salicylate 0 mg/kg	n	0	0	5	0	0	5	0	0	5	0
benzyl salicylate 300 mg/kg	n	0	0	5	0	0	5	0	0	5	0
		EF	EF	EF	EF	EF	EF	EF	EF	EF	EF

Test article		Tail pinch response				Pupillary reflex			
Dose		-2	-1	0	1	P	F	L	R
benzyl salicylate 0 mg/kg	n	0	0	5	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	0	0	5	0	5	0	0	0
		EF	EF	EF	EF	EF	EF	EF	EF

Auditory response) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
Approach response) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
Touch response) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
Tail pinch response) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
Pupillary reflex) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds
Not significantly different from benzyl salicylate 0 mg/kg
EF : The group mean is the same and unbiased variance 0 for all groups. All data of all groups are same.

Table 2 - 159 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Manipulative test Period : Recovery

Generation : F0 Sex : Female Week : 2 Species : Rat

Test article Dose		Aerial righting reflex	Landing foot splay mm
benzyl salicylate	n	5	5
0 mg/kg	Mean	0	62
	S.D.	0	17
benzyl salicylate	n	5	5
300 mg/kg	Mean	0	55
	S.D.	0	30
		EF	

Aerial righting reflex) Total score

Not significantly different from benzyl salicylate 0 mg/kg

EF : The group mean is the same and unbiased variance 0 for all groups. All data of all groups are same.

Table 2 - 160 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Grip strength Period : F0 mating

Generation : F0 Sex : Male Week : 6 Species : Rat

Test article Dose		Grip strength of fore limb g	Grip strength of hind limb g
benzyl salicylate 0 mg/kg	n	5	5
	Mean	1708	1046
	S.D.	108	35
benzyl salicylate 30 mg/kg	n	5	5
	Mean	1645	998
	S.D.	197	146
benzyl salicylate 100 mg/kg	n	5	5
	Mean	1675	1054
	S.D.	205	157
benzyl salicylate 300 mg/kg	n	5	5
	Mean	1685	1214
	S.D.	208	150

Not significantly different from benzyl salicylate 0 mg/kg

Table 2 - 161 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Grip strength Period : F0 lactation

Generation : F0 Sex : Female Day : 4 Species : Rat

Test article Dose		Grip strength of fore limb g	Grip strength of hind limb g
benzyl salicylate 0 mg/kg	n	5	5
	Mean	1248	854
	S.D.	194	204
benzyl salicylate 30 mg/kg	n	5	5
	Mean	1100	907
	S.D.	213	143
benzyl salicylate 100 mg/kg	n	5	5
	Mean	1241	969
	S.D.	214	163

Not significantly different from benzyl salicylate 0 mg/kg

Table 2 - 162 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Grip strength Period : Recovery

Generation : F0 Sex : Male Week : 2 Species : Rat

Test article Dose		Grip strength of fore limb g	Grip strength of hind limb g
benzyl salicylate	n	5	5
0 mg/kg	Mean	1931	1116
	S.D.	340	218
benzyl salicylate	n	5	5
300 mg/kg	Mean	1784	1181
	S.D.	227	202

Not significantly different from benzyl salicylate 0 mg/kg

Table 2 - 163 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Grip strength Period : Recovery

Generation : F0 Sex : Female Week : 2 Species : Rat

Test article Dose		Grip strength of fore limb g	Grip strength of hind limb g
benzyl salicylate	n	5	5
0 mg/kg	Mean	1261	744
	S.D.	158	162
benzyl salicylate	n	5	5
300 mg/kg	Mean	1190	795
	S.D.	41	102

Not significantly different from benzyl salicylate 0 mg/kg

Table 2 - 164 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Motor activity Period : F0 mating

Generation : F0 Sex : Male Week : 6 Species : Rat

Test article Dose		0'-10' Count	10'-20' Count	20'-30' Count	30'-40' Count	40'-50' Count	50'-60' Count	Total(0'-60') Count
benzyl salicylate	n	5	5	5	5	5	5	5
0 mg/kg	Mean	454	312	210	234	250	222	1682
	S.D.	41	83	104	134	72	109	416
benzyl salicylate	n	5	5	5	5	5	5	5
30 mg/kg	Mean	450	274	282	250	180	158	1594
	S.D.	57	97	98	68	113	104	398
benzyl salicylate	n	5	5	5	5	5	5	5
100 mg/kg	Mean	371	282	197	162	214	153	1379
	S.D.	96	143	157	111	173	132	338
benzyl salicylate	n	5	5	5	5	5	5	5
300 mg/kg	Mean	367	342	284	310	314	147	1763
	S.D.	105	50	101	46	43	143	359

Not significantly different from benzyl salicylate 0 mg/kg

Table 2 - 165 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Motor activity Period : F0 lactation

Generation : F0 Sex : Female Day : 4 Species : Rat

Test article Dose		0'-10' Count	10'-20' Count	20'-30' Count	30'-40' Count	40'-50' Count	50'-60' Count	Total(0'-60') Count
benzyl salicylate	n	5	5	5	5	5	5	5
0 mg/kg	Mean	378	196	198	139	128	241	1279
	S.D.	55	102	135	120	118	93	377
benzyl salicylate	n	5	5	5	5	5	5	5
30 mg/kg	Mean	366	184	152	127	160	192	1181
	S.D.	55	55	116	142	145	124	537
benzyl salicylate	n	5	5	5	5	5	5	5
100 mg/kg	Mean	399	265	238	100	129	240	1371
	S.D.	56	91	134	128	118	116	454

Not significantly different from benzyl salicylate 0 mg/kg

Table 2 - 166 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Motor activity Period : Recovery

Generation : F0 Sex : Male Week : 2 Species : Rat

Test article Dose		0'-10' Count	10'-20' Count	20'-30' Count	30'-40' Count	40'-50' Count	50'-60' Count	Total(0'-60') Count
benzyl salicylate	n	5	5	5	5	5	5	5
0 mg/kg	Mean	425	352	279	200	245	177	1679
	S.D.	27	76	66	114	152	142	513
benzyl salicylate	n	5	5	5	5	5	5	5
300 mg/kg	Mean	396	338	249	255	257	233	1729
	S.D.	43	116	128	156	67	142	433

Not significantly different from benzyl salicylate 0 mg/kg

Table 2 - 167 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Motor activity Period : Recovery

Generation : F0 Sex : Female Week : 2 Species : Rat

Test article Dose		0'-10' Count	10'-20' Count	20'-30' Count	30'-40' Count	40'-50' Count	50'-60' Count	Total(0'-60') Count
benzyl salicylate	n	5	5	5	5	5	5	5
0 mg/kg	Mean	389	233	162	89	150	119	1142
	S.D.	47	96	55	74	58	98	130
benzyl salicylate	n	5	5	5	5	5	5	5
300 mg/kg	Mean	421	321	271	243	196	169	1621
	S.D.	26	46	104	116	139	162	476
					T2 *			

Significantly different from benzyl salicylate 0 mg/kg : * P<0.05

T2 : Student t-test (two-side)

Table 3 - 1 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight Period : F0 before mating Day 1-15, F0 mating Day 15-43

Sex : Male Unit : g Species : Rat

Test article	/Day	1	8	15	22	29	36	42	Body weight gain
Dose									
benzyl salicylate	n	12	12	12	12	12	12	12	12
0 mg/kg	Mean	397	424	454	472	496	519	528	131
	S.D.	14	18	23	27	32	35	37	27
benzyl salicylate	n	12	12	12	12	12	12	12	12
30 mg/kg	Mean	395	425	452	469	489	507	512	117
	S.D.	16	18	20	22	24	29	29	18
benzyl salicylate	n	12	12	12	12	12	12	12	12
100 mg/kg	Mean	394	428	457	475	497	521	531	137
	S.D.	15	15	21	22	26	31	35	23
benzyl salicylate	n	12	12	12	12	12	12	12	12
300 mg/kg	Mean	395	418	447	462	483	500	508	113
	S.D.	15	19	22	20	20	20	23	21

Not significantly different from benzyl salicylate 0 mg/kg

Table 3 - 2 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight Period : F0 before mating Day 1-15

Sex : Female Unit : g Species : Rat

Test article		/Day			Body weight
Dose		1	8	15	gain
benzyl salicylate	n	12	12	12	12
0 mg/kg	Mean	253	265	277	24
	S.D.	12	14	15	9
benzyl salicylate	n	12	12	12	12
30 mg/kg	Mean	251	263	275	24
	S.D.	14	15	18	10
benzyl salicylate	n	12	12	12	12
100 mg/kg	Mean	250	266	275	25
	S.D.	10	17	22	15
benzyl salicylate	n	12	12	12	12
300 mg/kg	Mean	251	260	276	25
	S.D.	11	13	12	9

Not significantly different from benzyl salicylate 0 mg/kg

Table 3 - 3 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight Period : F0 gestation Day 0-25

Sex : Female Unit : g Species : Rat

Test article		/Day				Body weight
Dose		0	7	14	20	gain
benzyl salicylate	n	12	12	12	12	12
0 mg/kg	Mean	285	327	362	436	151
	S.D.	17	22	25	29	20
benzyl salicylate	n	12	12	12	12	12
30 mg/kg	Mean	280	318	354	439	159
	S.D.	17	19	21	21	10
benzyl salicylate	n	12	12	12	12	12
100 mg/kg	Mean	282	320	354	435	153
	S.D.	17	20	23	36	29
benzyl salicylate	n	12	12	12	12	12
300 mg/kg	Mean	282	320	352	386	104
	S.D.	23	20	22	21	24
					DT **	DT **

Significantly different from benzyl salicylate 0 mg/kg : ** P<0.01

DT : Dunnett test (two-side)

Table 3 - 4 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight Period : F0 lactation Day 0-5

Sex : Female Unit : g Species : Rat

Test article		/Day		Body weight
Dose		0	4	gain
benzyl salicylate	n	12	12	12
0 mg/kg	Mean	355	354	-1
	S.D.	23	21	12
benzyl salicylate	n	12	12	12
30 mg/kg	Mean	347	342	-5
	S.D.	20	19	9
benzyl salicylate	n	12	12	12
100 mg/kg	Mean	351	353	2
	S.D.	23	28	12
benzyl salicylate	n	5 a)	0 b)	
300 mg/kg	Mean	345		
	S.D.	16		

Not significantly different from benzyl salicylate 0 mg/kg

a): Six dams were not delivered and one dam was necropsied on lactation day 0 because all offspring were stillborn.

b): Five dams were necropsied on lactation days 1 and 2 because all offspring died.

Table 3 - 5 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight Period : Administration

Sex : Female Unit : g Species : Rat

Test article		/Day							Body weight
Dose		1	8	15	22	29	36	42	gain
benzyl salicylate	n	10	10	10	10	10	10	10	10
0 mg/kg	Mean	250	261	271	276	290	295	298	49
	S.D.	7	10	13	12	13	14	14	14
benzyl salicylate	n	10	10	10	10	10	10	10	10
300 mg/kg	Mean	246	258	272	282	290	298	304	58
	S.D.	11	10	13	13	16	15	17	15

Not significantly different from benzyl salicylate 0 mg/kg

Table 3 - 6 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight Period : Recovery Day 1-15

Sex : Male Unit : g Species : Rat

Test article		/Day			Body weight
Dose		1	8	14	gain
benzyl salicylate	n	5	5	5	5
0 mg/kg	Mean	525	540	542	17
	S.D.	36	40	44	10
benzyl salicylate	n	5	5	5	5
300 mg/kg	Mean	500	509	520	20
	S.D.	9	13	15	7

Not significantly different from benzyl salicylate 0 mg/kg

Table 3 - 7 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight Period : Recovery Day 1-15

Sex : Female Unit : g Species : Rat

Test article		/Day			Body weight
Dose		1	8	14	gain
benzyl salicylate	n	5	5	5	5
0 mg/kg	Mean	306	314	315	9
	S.D.	11	16	17	6
benzyl salicylate	n	5	5	5	5
300 mg/kg	Mean	301	294	290	-11
	S.D.	17	20	23	14
					T2 *

Significantly different from benzyl salicylate 0 mg/kg : * P<0.05

T2 : Student t-test (two-side)

Table 4 - 1 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Food consumption Period : F0 before mating Day 1-15, F0 mating Day 15-43

Sex : Male Unit : g Species : Rat

Test article		/Day						Total food
Dose		2	8	15	30	36	42	consumption
benzyl salicylate	n	12	12	12	12	12	12	12
0 mg/kg	Mean	19	21	20	20	20	18	117
	S.D.	3	3	3	2	3	3	14
benzyl salicylate	n	12	12	12	12	12	12	12
30 mg/kg	Mean	22	21	19	18	20	18	119
	S.D.	3	2	2	2	2	2	9
benzyl salicylate	n	12	12	12	12	12	12	12
100 mg/kg	Mean	20	22	20	20	22	19	122
	S.D.	5	2	2	3	2	4	14
benzyl salicylate	n	12	12	12	12	12	12	12
300 mg/kg	Mean	19	23	21	21	22	21	127
	S.D.	3	1	2	1	2	2	8
							DT *	

Significantly different from benzyl salicylate 0 mg/kg : * P<0.05

DT : Dunnett test (two-side)

Table 4 - 2 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Food consumption Period : F0 before mating Day 1-15

Sex : Female Unit : g Species : Rat

Test article Dose		/Day 2	8	15	Total food consumption
benzyl salicylate 0 mg/kg	n	12	12	12	12
	Mean	14	17	14	45
	S.D.	2	2	2	4
benzyl salicylate 30 mg/kg	n	12	12	12	12
	Mean	13	15	14	42
	S.D.	2	2	2	3
benzyl salicylate 100 mg/kg	n	12	12	12	12
	Mean	14	16	14	45
	S.D.	3	2	3	7
benzyl salicylate 300 mg/kg	n	12	12	12	12
	Mean	15	16	16	47
	S.D.	3	3	2	5

Not significantly different from benzyl salicylate 0 mg/kg

Table 4 - 3 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Food consumption Period : F0 gestation Day 0-25

Sex : Female Unit : g Species : Rat

Test article		/Day				Total food
Dose		1	7	14	20	consumption
benzyl salicylate	n	12	12	12	12	12
0 mg/kg	Mean	16	22	21	21	80
	S.D.	4	4	4	3	10
benzyl salicylate	n	12	12	12	12	12
30 mg/kg	Mean	17	19	19	21	76
	S.D.	2	2	3	2	7
benzyl salicylate	n	12	12	12	12	12
100 mg/kg	Mean	17	20	20	22	79
	S.D.	2	3	3	3	8
benzyl salicylate	n	12	12	12	12	12
300 mg/kg	Mean	18	20	22	21	81
	S.D.	2	3	3	3	8

Not significantly different from benzyl salicylate 0 mg/kg

Table 4 - 4 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Food consumption Period : F0 lactation Day 0-5

Sex : Female Unit : g Species : Rat

Test article Dose		/Day 2	4	Total food consumption
benzyl salicylate 0 mg/kg	n	12	12	12
	Mean	21	34	55
	S.D.	7	7	12
benzyl salicylate 30 mg/kg	n	12	12	12
	Mean	23	35	58
	S.D.	4	5	7
benzyl salicylate 100 mg/kg	n	12	12	12
	Mean	23	37	59
	S.D.	4	7	11
benzyl salicylate 300 mg/kg	n	0 a)		
	Mean			
	S.D.			

Not significantly different from benzyl salicylate 0 mg/kg

a): Six dams were not delivered, one dam was necropsied on lactation day 0 because all offspring were stillborn and five dams were necropsied on lactation days 1 and 2 because all offspring died.

Table 4 - 5 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Food consumption Period : Administration

Sex : Female Unit : g Species : Rat

Test article		/Day						Total food
Dose		2	8	15	30	36	42	consumption
benzyl salicylate	n	10	10	10	10	10	10	10
0 mg/kg	Mean	13	16	13	14	14	12	83
	S.D.	2	1	2	2	2	3	6
benzyl salicylate	n	10	10	10	10	10	10	10
300 mg/kg	Mean	13	16	16	16	17	16	94
	S.D.	2	2	3	2	2	3	8
						T2 **	T2 **	T2 **

Significantly different from benzyl salicylate 0 mg/kg : ** P<0.01

T2 : Student t-test (two-side)

Table 4 - 6 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Food consumption Period : Recovery Day 1-15

Sex : Male Unit : g Species : Rat

Test article		/Day			Total food
Dose		2	8	14	consumption
benzyl salicylate	n	5	5	5	5
0 mg/kg	Mean	22	25	24	71
	S.D.	3	2	3	7
benzyl salicylate	n	5	5	5	5
300 mg/kg	Mean	22	23	24	69
	S.D.	1	3	2	4

Not significantly different from benzyl salicylate 0 mg/kg

Table 4 - 7 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Food consumption Period : Recovery Day 1-15

Sex : Female Unit : g Species : Rat

Test article		/Day			Total food
Dose		2	8	14	consumption
benzyl salicylate	n	5	5	5	5
0 mg/kg	Mean	18	18	17	54
	S.D.	2	4	2	5
benzyl salicylate	n	5	5	5	5
300 mg/kg	Mean	17	17	14	49
	S.D.	1	1	2	3

Not significantly different from benzyl salicylate 0 mg/kg

Table 5 - 1 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 6 of administration

Sex : Male Species : Rat

Test article / Dose		pH								
		5.0	5.5	6.0	6.5	7.0	7.5	8.0	8.5	>=9.0
benzyl salicylate 0 mg/kg	n	0	0	1	0	1	0	1	1	1
benzyl salicylate 30 mg/kg	n	0	0	0	0	0	0	0	3	2
benzyl salicylate 100 mg/kg	n	0	0	0	0	1	1	0	1	2
benzyl salicylate 300 mg/kg	n	0	0	0	0	0	2	0	3	0

Test article / Dose		Protein					Ketones				
		-	+/-	1+	2+	3+	-	+/-	1+	2+	3+
benzyl salicylate 0 mg/kg	n	0	2	1	2	0	1	1	1	2	0
benzyl salicylate 30 mg/kg	n	0	3	1	1	0	1	2	2	0	0
benzyl salicylate 100 mg/kg	n	0	4	0	1	0	1	2	1	1	0
benzyl salicylate 300 mg/kg	n	0	2	3	0	0	1	2	2	0	0

Protein) -:Negative , +/-:15 , 1+:30 , 2+:100 , 3+:≥300 mg/dL
Ketones) -:Negative , +/-:5 , 1+:15 , 2+:40 , 3+:80 mg/dL

Table 5 - 2 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 6 of administration

Sex : Male Species : Rat

Test article		Glucose					Occult Blood				
Dose		-	1+	2+	3+	4+	-	+/-	1+	2+	3+
benzyl salicylate 0 mg/kg	n	4	1	0	0	0	1	1	3	0	0
benzyl salicylate 30 mg/kg	n	5	0	0	0	0	2	3	0	0	0
benzyl salicylate 100 mg/kg	n	5	0	0	0	0	2	3	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	0	4	1	0	0	0

Test article		Bilirubin				Urobilinogen			
Dose		-	1+	2+	3+	+/-	1+	2+	3+
benzyl salicylate 0 mg/kg	n	3	2	0	0	5	0	0	0
benzyl salicylate 30 mg/kg	n	5	0	0	0	5	0	0	0
benzyl salicylate 100 mg/kg	n	4	1	0	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	5	0	0	0

Glucose) -:Negative , 1+:100 , 2+:250 , 3+:500 , 4+:≥1000 mg/dL
Occult Blood) -:Negative , +/-:0.015 , 1+:0.062 , 2+:0.135 , 3+: 0.405 mg/dL
Bilirubin) -:Negative , 1+:0.8 , 2+:1.6 , 3+:3.2 mg/dL
Urobilinogen) +/-:0.1 - 1.0 , 1+:2.0 , 2+:4.0 , 3+:≥8.0 Ehrlich U/dL

Table 5 - 3 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 6 of administration

Sex : Male Species : Rat

Test article Dose		Color									
		LY	Y	DY	BR	RE	RB	WH	BL	CL	OT
benzyl salicylate 0 mg/kg	n	0	5	0	0	0	0	0	0	0	0
benzyl salicylate 30 mg/kg	n	0	5	0	0	0	0	0	0	0	0
benzyl salicylate 100 mg/kg	n	0	5	0	0	0	0	0	0	0	0
benzyl salicylate 300 mg/kg	n	0	5	0	0	0	0	0	0	0	0

Color LY: Light Yellow Y: Yellow DY: Dark Yellow BR: Brown RE: Red RB: Reddish brown WH: White BL: Blue CL: Colorless OT: Other

Table 5 - 4 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 6 of administration

Sex : Male Species : Rat

Test article Dose		RBC -	RBC +/-	RBC 1+	RBC 2+	RBC 3+	WBC -	WBC +/-	WBC 1+	WBC 2+	WBC 3+
benzyl salicylate 0 mg/kg	n	5	0	0	0	0	5	0	0	0	0
benzyl salicylate 30 mg/kg	n	5	0	0	0	0	5	0	0	0	0
benzyl salicylate 100 mg/kg	n	5	0	0	0	0	5	0	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	0	5	0	0	0	0

Test article Dose		Squamous epithelial cells -	Squamous epithelial cells +/-	Squamous epithelial cells 1+	Squamous epithelial cells 2+	Squamous epithelial cells 3+	Small round epithelial cells -	Small round epithelial cells +/-	Small round epithelial cells 1+	Small round epithelial cells 2+	Small round epithelial cells 3+
benzyl salicylate 0 mg/kg	n	0	5	0	0	0	5	0	0	0	0
benzyl salicylate 30 mg/kg	n	0	5	0	0	0	5	0	0	0	0
benzyl salicylate 100 mg/kg	n	0	5	0	0	0	5	0	0	0	0
benzyl salicylate 300 mg/kg	n	0	5	0	0	0	5	0	0	0	0

RBC) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
WBC) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Squamous epithelial cells) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Small round epithelial cells) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe

Table 5 - 5 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 6 of administration

Sex : Male Species : Rat

Test article / Dose		Cast -	Cast +/-	Cast 1+	Cast 2+	Cast 3+	Crystal phosphate salts -	Crystal phosphate salts +/-	Crystal phosphate salts 1+	Crystal phosphate salts 2+	Crystal phosphate salts 3+
benzyl salicylate 0 mg/kg	n	5	0	0	0	0	4	1	0	0	0
benzyl salicylate 30 mg/kg	n	5	0	0	0	0	4	1	0	0	0
benzyl salicylate 100 mg/kg	n	5	0	0	0	0	5	0	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	0	5	0	0	0	0

Test article / Dose		Crystal calcium oxalate -	Crystal calcium oxalate +/-	Crystal calcium oxalate 1+	Crystal calcium oxalate 2+	Crystal calcium oxalate 3+
benzyl salicylate 0 mg/kg	n	5	0	0	0	0
benzyl salicylate 30 mg/kg	n	5	0	0	0	0
benzyl salicylate 100 mg/kg	n	5	0	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	0

Cast) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Crystal phosphate salts) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Crystal calcium oxalate) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe

Table 5 - 6 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 6 of administration

Sex : Male Species : Rat

Test article Dose		Urine volume mL/24h	Osmotic pressure mOsm/kg	U-Na mmol/24h	U-K mmol/24h	U-Cl mmol/24h
benzyl salicylate	n	5	5	5	5	5
0 mg/kg	Mean	8.1	1578	0.8	1.9	1.3
	S.D.	2.6	787	0.6	0.9	0.7
benzyl salicylate	n	5	5	5	5	5
30 mg/kg	Mean	8.4	1860	1.1	2.2	1.6
	S.D.	3.7	531	0.2	0.4	0.3
benzyl salicylate	n	5	5	5	5	5
100 mg/kg	Mean	12.3	1508	1.3	2.7	1.8
	S.D.	5.3	437	0.5	0.7	0.6
benzyl salicylate	n	5	5	5	5	5
300 mg/kg	Mean	17.4	1410	1.8	3.0	2.5
	S.D.	8.2	472	0.6	0.6	0.7
		DT *		DT *		DT *

Significantly different from benzyl salicylate 0 mg/kg : * P<0.05

DT : Dunnett test (two-side)

Table 5 - 7 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 6 of administration

Sex : Female Species : Rat

Test article / Dose		pH 5.0	5.5	6.0	6.5	7.0	7.5	8.0	8.5	>=9.0
benzyl salicylate 0 mg/kg	n	0	0	0	0	2	0	0	1	2
benzyl salicylate 300 mg/kg	n	0	1	1	0	0	1	0	1	1

Test article / Dose		Protein -	+/-	1+	2+	3+	Ketones -	+/-	1+	2+	3+
benzyl salicylate 0 mg/kg	n	3	1	1	0	0	2	3	0	0	0
benzyl salicylate 300 mg/kg	n	3	1	1	0	0	3	2	0	0	0

Protein) -:Negative , +/-:15 , 1+:30 , 2+:100 , 3+:≥300 mg/dL
Ketones) -:Negative , +/-:5 , 1+:15 , 2+:40 , 3+:80 mg/dL

Table 5 - 8 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 6 of administration

Sex : Female Species : Rat

Test article		Glucose					Occult Blood				
Dose		-	1+	2+	3+	4+	-	+/-	1+	2+	3+
benzyl salicylate 0 mg/kg	n	5	0	0	0	0	5	0	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	0	5	0	0	0	0

Test article		Bilirubin				Urobilinogen			
Dose		-	1+	2+	3+	+/-	1+	2+	3+
benzyl salicylate 0 mg/kg	n	4	1	0	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	4	1	0	0	5	0	0	0

Glucose) -:Negative , 1+:100 , 2+:250 , 3+:500 , 4+:≥1000 mg/dL
Occult Blood) -:Negative , +/-:0.015 , 1+:0.062 , 2+:0.135 , 3+: 0.405 mg/dL
Bilirubin) -:Negative , 1+:0.8 , 2+:1.6 , 3+:3.2 mg/dL
Urobilinogen) +/-:0.1 - 1.0 , 1+:2.0 , 2+:4.0 , 3+: ≥8.0 Ehrlich U/dL

Table 5 - 9 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 6 of administration

Sex : Female Species : Rat

Test article Dose		Color									
		LY	Y	DY	BR	RE	RB	WH	BL	CL	OT
benzyl salicylate 0 mg/kg	n	0	5	0	0	0	0	0	0	0	0
benzyl salicylate 300 mg/kg	n	0	5	0	0	0	0	0	0	0	0

Color LY: Light Yellow Y: Yellow DY: Dark Yellow BR: Brown RE: Red RB: Reddish brown WH: White BL: Blue CL: Colorless OT: Other

Table 5 - 10 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 6 of administration

Sex : Female Species : Rat

Test article Dose		RBC -	+/-	1+	2+	3+	WBC -	+/-	1+	2+	3+
benzyl salicylate 0 mg/kg	n	5	0	0	0	0	5	0	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	0	5	0	0	0	0

Test article Dose		Squamous epithelial cells -	+/-	1+	2+	3+	Small round epithelial cells -	+/-	1+	2+	3+
benzyl salicylate 0 mg/kg	n	0	5	0	0	0	5	0	0	0	0
benzyl salicylate 300 mg/kg	n	0	5	0	0	0	5	0	0	0	0

RBC) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
WBC) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Squamous epithelial cells) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Small round epithelial cells) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe

Table 5 - 11 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 6 of administration

Sex : Female Species : Rat

Test article		Cast					Crystal phosphate salts				
Dose		-	+/-	1+	2+	3+	-	+/-	1+	2+	3+
benzyl salicylate 0 mg/kg	n	5	0	0	0	0	4	1	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	0	5	0	0	0	0

Test article		Crystal calcium oxalate				
Dose		-	+/-	1+	2+	3+
benzyl salicylate 0 mg/kg	n	5	0	0	0	0
benzyl salicylate 300 mg/kg	n	4	1	0	0	0

Cast) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Crystal phosphate salts) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Crystal calcium oxalate) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe

Table 5 - 12 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 6 of administration

Sex : Female Species : Rat

Test article Dose		Urine volume mL/24h	Osmotic pressure mOsm/kg	U-Na mmol/24h	U-K mmol/24h	U-Cl mmol/24h
benzyl salicylate	n	5	5	5	5	5
0 mg/kg	Mean	8.4	1772	1.1	2.0	1.5
	S.D.	3.6	561	0.3	0.4	0.3
benzyl salicylate	n	5	5	5	5	5
300 mg/kg	Mean	10.7	1324	1.1	1.7	1.3
	S.D.	3.8	286	0.2	0.1	0.2

Not significantly different from benzyl salicylate 0 mg/kg

Table 5 - 13 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 2 of recovery

Sex : Male Species : Rat

Test article		pH								
Dose		5.0	5.5	6.0	6.5	7.0	7.5	8.0	8.5	>=9.0
benzyl salicylate 0 mg/kg	n	0	0	0	0	0	0	0	4	1
benzyl salicylate 300 mg/kg	n	0	0	0	0	0	0	1	3	1

Test article		Protein					Ketones				
Dose		-	+/-	1+	2+	3+	-	+/-	1+	2+	3+
benzyl salicylate 0 mg/kg	n	0	2	3	0	0	2	0	3	0	0
benzyl salicylate 300 mg/kg	n	1	2	2	0	0	0	2	3	0	0

Protein) -:Negative , +/-:15 , 1+:30 , 2+:100 , 3+:≥300 mg/dL
Ketones) -:Negative , +/-:5 , 1+:15 , 2+:40 , 3+:80 mg/dL

Table 5 - 14 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 2 of recovery

Sex : Male Species : Rat

Test article		Glucose					Occult Blood				
Dose		-	1+	2+	3+	4+	-	+/-	1+	2+	3+
benzyl salicylate 0 mg/kg	n	5	0	0	0	0	2	3	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	0	0	5	0	0	0

Test article		Bilirubin				Urobilinogen			
Dose		-	1+	2+	3+	+/-	1+	2+	3+
benzyl salicylate 0 mg/kg	n	4	1	0	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	5	0	0	0

Glucose) -:Negative , 1+:100 , 2+:250 , 3+:500 , 4+:≥1000 mg/dL
Occult Blood) -:Negative , +/-:0.015 , 1+:0.062 , 2+:0.135 , 3+: 0.405 mg/dL
Bilirubin) -:Negative , 1+:0.8 , 2+:1.6 , 3+:3.2 mg/dL
Urobilinogen) +/-:0.1 - 1.0 , 1+:2.0 , 2+:4.0 , 3+: ≥8.0 Ehrlich U/dL

Table 5 - 15 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 2 of recovery

Sex : Male Species : Rat

Test article Dose		Color									
		LY	Y	DY	BR	RE	RB	WH	BL	CL	OT
benzyl salicylate 0 mg/kg	n	0	5	0	0	0	0	0	0	0	0
benzyl salicylate 300 mg/kg	n	0	5	0	0	0	0	0	0	0	0

Color LY: Light Yellow Y: Yellow DY: Dark Yellow BR: Brown RE: Red RB: Reddish brown WH: White BL: Blue CL: Colorless OT: Other

Table 5 - 16 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 2 of recovery

Sex : Male Species : Rat

Test article / Dose		RBC -	RBC +/-	RBC 1+	RBC 2+	RBC 3+	WBC -	WBC +/-	WBC 1+	WBC 2+	WBC 3+
benzyl salicylate 0 mg/kg	n	5	0	0	0	0	5	0	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	0	5	0	0	0	0

Test article / Dose		Squamous epithelial cells -	Squamous epithelial cells +/-	Squamous epithelial cells 1+	Squamous epithelial cells 2+	Squamous epithelial cells 3+	Small round epithelial cells -	Small round epithelial cells +/-	Small round epithelial cells 1+	Small round epithelial cells 2+	Small round epithelial cells 3+
benzyl salicylate 0 mg/kg	n	0	5	0	0	0	5	0	0	0	0
benzyl salicylate 300 mg/kg	n	0	5	0	0	0	5	0	0	0	0

RBC) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
WBC) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Squamous epithelial cells) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Small round epithelial cells) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe

Table 5 - 17 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 2 of recovery

Sex : Male Species : Rat

Test article		Cast					Crystal phosphate salts				
Dose		-	+/-	1+	2+	3+	-	+/-	1+	2+	3+
benzyl salicylate 0 mg/kg	n	5	0	0	0	0	5	0	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	0	5	0	0	0	0

Test article		Crystal calcium oxalate				
Dose		-	+/-	1+	2+	3+
benzyl salicylate 0 mg/kg	n	5	0	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	0

Cast) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Crystal phosphate salts) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Crystal calcium oxalate) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe

Table 5 - 18 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 2 of recovery

Sex : Male Species : Rat

Test article Dose		Urine volume mL/24h	Osmotic pressure mOsm/kg	U-Na mmol/24h	U-K mmol/24h	U-Cl mmol/24h
benzyl salicylate	n	5	5	5	5	5
0 mg/kg	Mean	12.9	2204	1.9	4.1	2.8
	S.D.	3.3	397	0.4	1.2	0.7
benzyl salicylate	n	5	5	5	5	5
300 mg/kg	Mean	13.8	1970	1.6	4.2	2.6
	S.D.	3.5	444	0.1	0.9	0.4

Not significantly different from benzyl salicylate 0 mg/kg

Table 5 - 19 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 2 of recovery

Sex : Female Species : Rat

Test article / Dose		pH								
		5.0	5.5	6.0	6.5	7.0	7.5	8.0	8.5	>=9.0
benzyl salicylate 0 mg/kg	n	0	0	0	1	1	0	0	1	2
benzyl salicylate 300 mg/kg	n	0	0	0	0	2	0	1	1	1

Test article / Dose		Protein					Ketones				
		-	+/-	1+	2+	3+	-	+/-	1+	2+	3+
benzyl salicylate 0 mg/kg	n	2	2	1	0	0	3	2	0	0	0
benzyl salicylate 300 mg/kg	n	3	1	1	0	0	3	2	0	0	0

Protein) -:Negative , +/-:15 , 1+:30 , 2+:100 , 3+:≥300 mg/dL
Ketones) -:Negative , +/-:5 , 1+:15 , 2+:40 , 3+:80 mg/dL

Table 5 - 20 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 2 of recovery

Sex : Female Species : Rat

Test article		Glucose					Occult Blood				
Dose		-	1+	2+	3+	4+	-	+/-	1+	2+	3+
benzyl salicylate 0 mg/kg	n	5	0	0	0	0	5	0	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	0	5	0	0	0	0

Test article		Bilirubin				Urobilinogen			
Dose		-	1+	2+	3+	+/-	1+	2+	3+
benzyl salicylate 0 mg/kg	n	4	1	0	0	5	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	5	0	0	0

Glucose) -:Negative , 1+:100 , 2+:250 , 3+:500 , 4+:≥1000 mg/dL
Occult Blood) -:Negative , +/-:0.015 , 1+:0.062 , 2+:0.135 , 3+: 0.405 mg/dL
Bilirubin) -:Negative , 1+:0.8 , 2+:1.6 , 3+:3.2 mg/dL
Urobilinogen) +/-:0.1 - 1.0 , 1+:2.0 , 2+:4.0 , 3+: ≥8.0 Ehrlich U/dL

Table 5 - 21 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 2 of recovery

Sex : Female Species : Rat

Test article Dose		Color									
		LY	Y	DY	BR	RE	RB	WH	BL	CL	OT
benzyl salicylate 0 mg/kg	n	0	5	0	0	0	0	0	0	0	0
benzyl salicylate 300 mg/kg	n	0	5	0	0	0	0	0	0	0	0

Color LY: Light Yellow Y: Yellow DY: Dark Yellow BR: Brown RE: Red RB: Reddish brown WH: White BL: Blue CL: Colorless OT: Other

Table 5 - 22 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 2 of recovery

Sex : Female Species : Rat

Test article / Dose		RBC -	RBC +/-	RBC 1+	RBC 2+	RBC 3+	WBC -	WBC +/-	WBC 1+	WBC 2+	WBC 3+
benzyl salicylate 0 mg/kg	n	5	0	0	0	0	5	0	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	0	5	0	0	0	0

Test article / Dose		Squamous epithelial cells -	Squamous epithelial cells +/-	Squamous epithelial cells 1+	Squamous epithelial cells 2+	Squamous epithelial cells 3+	Small round epithelial cells -	Small round epithelial cells +/-	Small round epithelial cells 1+	Small round epithelial cells 2+	Small round epithelial cells 3+
benzyl salicylate 0 mg/kg	n	0	5	0	0	0	5	0	0	0	0
benzyl salicylate 300 mg/kg	n	0	5	0	0	0	5	0	0	0	0

RBC) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
WBC) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Squamous epithelial cells) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Small round epithelial cells) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe

Table 5 - 23 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 2 of recovery

Sex : Female Species : Rat

Test article		Cast					Crystal phosphate salts				
Dose		-	+/-	1+	2+	3+	-	+/-	1+	2+	3+
benzyl salicylate 0 mg/kg	n	5	0	0	0	0	5	0	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	0	4	1	0	0	0

Test article		Crystal calcium oxalate				
Dose		-	+/-	1+	2+	3+
benzyl salicylate 0 mg/kg	n	5	0	0	0	0
benzyl salicylate 300 mg/kg	n	5	0	0	0	0

Cast) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Crystal phosphate salts) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Crystal calcium oxalate) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe

Table 5 - 24 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 2 of recovery

Sex : Female Species : Rat

Test article Dose		Urine volume mL/24h	Osmotic pressure mOsm/kg	U-Na mmol/24h	U-K mmol/24h	U-Cl mmol/24h
benzyl salicylate	n	5	5	5	5	5
0 mg/kg	Mean	10.2	2085	1.4	2.5	1.9
	S.D.	5.9	860	0.5	0.9	0.7
benzyl salicylate	n	5	5	5	5	5
300 mg/kg	Mean	8.5	2100	1.1	2.3	1.5
	S.D.	4.4	642	0.3	0.5	0.4

Not significantly different from benzyl salicylate 0 mg/kg

Table 6 - 1 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Hematology Stage : End of administration

Sex : Male Species : Rat

Test article / Dose		RBC	HGB	HCT	MCV	MCH	MCHC	RETIC	PLT	WBC	LYMP
		10^4/μL	g/dL	%	fL	pg	g/dL	%	10^4/μL	10^2/μL	%
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	827	15.4	44.7	54.0	18.6	34.5	2.3	97.5	83.9	74.7
	S.D.	33	0.4	1.3	1.4	0.4	0.7	0.3	10.5	15.6	8.1
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
30 mg/kg	Mean	853	15.4	45.2	53.0	18.1	34.2	2.1	92.4	78.1	75.7
	S.D.	16	0.5	1.0	1.1	0.5	0.5	0.4	11.3	14.5	10.3
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
100 mg/kg	Mean	838	15.7	45.5	54.3	18.7	34.5	2.2	93.5	75.1	71.0
	S.D.	23	0.3	1.0	1.1	0.4	0.4	0.3	11.0	23.8	3.3
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
300 mg/kg	Mean	829	15.2	45.0	54.2	18.3	33.8	2.6	76.4	69.4	62.7
	S.D.	19	0.4	1.8	1.1	0.1	0.5	0.2	6.2	15.5	9.1
									DT *		

Test article / Dose		NEUT	EOS	BASO	MONO	LUC	#LYMP	#NEUT	#EOS	#BASO	#MONO
		%	%	%	%	%	10^2/μL	10^2/μL	10^2/μL	10^2/μL	10^2/μL
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	20.9	1.3	0.2	2.4	0.6	62.1	18.0	1.1	0.2	2.0
	S.D.	8.0	0.4	0.1	0.2	0.1	10.4	8.9	0.5	0.1	0.5
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
30 mg/kg	Mean	19.4	1.0	0.2	3.2	0.6	58.9	15.3	0.8	0.2	2.5
	S.D.	9.1	0.4	0.0	1.1	0.1	12.9	8.0	0.3	0.1	0.9
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
100 mg/kg	Mean	24.8	0.8	0.3	2.7	0.4	53.7	18.3	0.6	0.2	2.0
	S.D.	3.5	0.3	0.1	1.0	0.3	18.6	4.8	0.3	0.1	0.9
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
300 mg/kg	Mean	33.4	0.8	0.2	2.6	0.4	43.5	23.0	0.6	0.1	1.9
	S.D.	9.0	0.2	0.1	0.8	0.1	12.2	7.6	0.2	0.0	0.8

Significantly different from benzyl salicylate 0 mg/kg : * $P<0.05$

DT : Dunnett test (two-side)

Table 6 - 2 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Hematology Stage : End of administration

Sex : Male Species : Rat

Test article Dose		#LUC 10^2/μL	PT s	APTT s	FIB mg/dL
benzyl salicylate	n	5	5	5	5
0 mg/kg	Mean	0.5	12.8	16.9	265
	S.D.	0.1	1.7	2.7	6
benzyl salicylate	n	5	5	5	5
30 mg/kg	Mean	0.5	13.1	17.3	257
	S.D.	0.1	0.9	0.7	10
benzyl salicylate	n	5	5	5	5
100 mg/kg	Mean	0.3	15.4	18.9	276
	S.D.	0.2	2.6	2.4	19
benzyl salicylate	n	5	5	5	5
300 mg/kg	Mean	0.3	27.7	29.6	363
	S.D.	0.1	8.8	6.7	45
			ST *	ST *	ST *

Significantly different from benzyl salicylate 0 mg/kg : * P<0.05

ST : Steel test (two-side)

Table 6 - 3 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Hematology Stage : Lactation day 5

Sex : Female Species : Rat

Test article / Dose		RBC	HGB	HCT	MCV	MCH	MCHC	RETIC	PLT	WBC	LYMP
		10^4/μL	g/dL	%	fL	pg	g/dL	%	10^4/μL	10^2/μL	%
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	688	13.3	39.1	56.9	19.4	34.1	5.3	128.9	107.4	56.3
	S.D.	51	0.9	2.2	1.3	0.4	0.5	1.5	13.6	6.5	8.4
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
30 mg/kg	Mean	688	13.1	38.4	55.8	19.0	34.1	6.1	145.7	115.6	62.2
	S.D.	44	0.7	1.8	1.3	0.4	0.3	2.5	16.3	32.7	8.8
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
100 mg/kg	Mean	658	12.9	37.6	57.2	19.6	34.3	7.0	142.2	104.5	62.3
	S.D.	17	0.4	1.2	2.0	0.7	0.4	1.5	14.4	18.1	13.0

Test article / Dose		NEUT	EOS	BASO	MONO	LUC	#LYMP	#NEUT	#EOS	#BASO	#MONO
		%	%	%	%	%	10^2/μL	10^2/μL	10^2/μL	10^2/μL	10^2/μL
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	38.3	0.8	0.2	3.7	0.7	60.5	41.2	0.8	0.2	4.0
	S.D.	8.2	0.2	0.1	1.4	0.3	9.6	9.0	0.2	0.1	1.4
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
30 mg/kg	Mean	32.0	0.8	0.3	3.9	0.8	73.4	35.9	0.9	0.4	4.3
	S.D.	8.3	0.5	0.1	1.2	0.4	28.4	10.4	0.4	0.2	0.8
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
100 mg/kg	Mean	32.3	0.8	0.3	3.6	0.7	63.8	35.1	0.8	0.2	3.8
	S.D.	12.7	0.4	0.1	0.8	0.4	10.9	15.7	0.4	0.1	1.0

Not significantly different from benzyl salicylate 0 mg/kg

Table 6 - 4 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Hematology Stage : Lactation day 5

Sex : Female Species : Rat

Test article Dose		#LUC 10^2/μL	PT s	APTT s	FIB mg/dL
benzyl salicylate	n	5	5	5	5
0 mg/kg	Mean	0.7	13.8	15.9	324
	S.D.	0.3	1.4	3.2	58
benzyl salicylate	n	5	5	5	5
30 mg/kg	Mean	0.9	11.6	13.4	312
	S.D.	0.4	0.8	0.9	52
			DT *		
benzyl salicylate	n	5	5	5	5
100 mg/kg	Mean	0.7	12.3	13.9	305
	S.D.	0.4	1.2	1.4	37

Significantly different from benzyl salicylate 0 mg/kg : * P<0.05

DT : Dunnett test (two-side)

Table 6 - 5 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Hematology Stage : End of administration

Sex : Female Species : Rat

Test article / Dose		RBC	HGB	HCT	MCV	MCH	MCHC	RETIC	PLT	WBC	LYMP
		10^4/μL	g/dL	%	fL	pg	g/dL	%	10^4/μL	10^2/μL	%
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	761	14.3	41.8	54.9	18.8	34.2	2.4	107.1	71.7	73.4
	S.D.	21	0.4	1.3	1.3	0.4	0.3	0.4	20.6	45.0	15.5
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
300 mg/kg	Mean	747	14.4	41.9	56.1	19.3	34.4	2.6	82.3	63.0	77.3
	S.D.	49	0.8	2.0	1.2	0.6	0.6	0.5	10.1	14.1	7.0
									T2 *		

Test article / Dose		NEUT	EOS	BASO	MONO	LUC	#LYMP	#NEUT	#EOS	#BASO	#MONO
		%	%	%	%	%	10^2/μL	10^2/μL	10^2/μL	10^2/μL	10^2/μL
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	22.0	1.0	0.2	2.7	0.7	48.6	19.2	0.6	0.2	2.5
	S.D.	14.4	0.3	0.1	1.7	0.2	18.9	25.5	0.2	0.2	3.4
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
300 mg/kg	Mean	18.8	0.8	0.1	2.4	0.6	49.2	11.4	0.5	0.1	1.4
	S.D.	5.9	0.5	0.0	1.2	0.1	14.5	3.0	0.2	0.0	0.4

Test article / Dose		#LUC	PT	APTT	FIB
		10^2/μL	s	s	mg/dL
benzyl salicylate	n	5	5	5	5
0 mg/kg	Mean	0.5	12.7	13.6	239
	S.D.	0.3	0.7	1.1	89
benzyl salicylate	n	5	5	5	5
300 mg/kg	Mean	0.4	12.3	16.5	250
	S.D.	0.1	1.1	1.8	18
				T2 *	

Significantly different from benzyl salicylate 0 mg/kg : * P<0.05

T2 : Student t-test (two-side)

Table 6 - 6 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Hematology Stage : End of recovery

Sex : Male Species : Rat

Test article Dose		RBC 10^4/μL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RETIC %	PLT 10^4/μL	WBC 10^2/μL	LYMP %
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	853	15.3	44.7	52.5	18.0	34.3	1.9	96.1	76.7	73.9
	S.D.	47	0.4	1.4	1.3	0.6	0.5	0.3	10.3	28.0	5.6
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
300 mg/kg	Mean	850	15.8	46.8	55.1	18.7	33.9	2.2	98.1	90.2	70.7
	S.D.	34	0.6	1.8	1.7	0.5	0.2	0.3	16.0	18.7	12.7
					T2 *						

Test article Dose		NEUT %	EOS %	BASO %	MONO %	LUC %	#LYMP 10^2/μL	#NEUT 10^2/μL	#EOS 10^2/μL	#BASO 10^2/μL	#MONO 10^2/μL
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	21.5	1.9	0.3	1.9	0.5	57.1	16.2	1.4	0.2	1.5
	S.D.	5.3	0.5	0.1	0.4	0.2	22.6	5.8	0.2	0.1	0.6
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
300 mg/kg	Mean	24.5	1.1	0.2	2.8	0.6	65.2	20.7	1.0	0.2	2.4
	S.D.	12.6	0.4	0.1	0.8	0.1	23.8	8.8	0.5	0.1	0.4
			T2 *								T2 *

Test article Dose		#LUC 10^2/μL	PT s	APTT s	FIB mg/dL
benzyl salicylate	n	5	5	5	5
0 mg/kg	Mean	0.4	15.3	18.8	299
	S.D.	0.3	2.1	1.8	38
benzyl salicylate	n	5	5	5	5
300 mg/kg	Mean	0.5	13.6	17.9	261
	S.D.	0.2	1.3	1.6	38

Significantly different from benzyl salicylate 0 mg/kg : * P<0.05

T2 : Student t-test (two-side)

Table 6 - 7 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Hematology Stage : End of recovery

Sex : Female Species : Rat

Test article Dose		RBC 10^4/μL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RETIC %	PLT 10^4/μL	WBC 10^2/μL	LYMP %
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	774	14.8	42.2	54.6	19.1	35.1	1.7	116.8	51.0	78.3
	S.D.	47	0.3	1.5	1.7	0.9	0.6	0.2	23.7	13.0	5.5
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
300 mg/kg	Mean	774	14.6	42.0	54.3	18.8	34.7	1.7	106.1	57.5	71.8
	S.D.	23	0.5	1.3	0.3	0.2	0.3	0.5	8.7	18.8	15.0

Test article Dose		NEUT %	EOS %	BASO %	MONO %	LUC %	#LYMP 10^2/μL	#NEUT 10^2/μL	#EOS 10^2/μL	#BASO 10^2/μL	#MONO 10^2/μL
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	16.3	2.0	0.2	2.8	0.5	39.5	8.7	1.0	0.1	1.5
	S.D.	4.8	0.8	0.1	0.8	0.2	8.3	4.6	0.4	0.0	0.7
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
300 mg/kg	Mean	22.4	1.4	0.2	3.5	0.7	41.3	12.9	0.8	0.1	2.0
	S.D.	14.4	0.2	0.1	0.8	0.3	17.5	10.1	0.3	0.1	0.6

Test article Dose		#LUC 10^2/μL	PT s	APTT s	FIB mg/dL
benzyl salicylate	n	5	5	5	5
0 mg/kg	Mean	0.2	10.9	14.4	188
	S.D.	0.1	0.5	1.9	15
benzyl salicylate	n	5	5	5	5
300 mg/kg	Mean	0.3	10.9	14.4	211
	S.D.	0.2	1.0	2.0	41

Not significantly different from benzyl salicylate 0 mg/kg

Table 7 - 1 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Blood chemistry Stage : End of administration

Sex : Male Species : Rat

Test article Dose		AST IU/L	ALT IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	T-BA μmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	63	38	58	1	429	37.9	59	33	93	0.1
	S.D.	9	5	27	1	93	43.2	9	9	10	0.0
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
30 mg/kg	Mean	61	34	42	0	390	9.0	49	30	80	0.1
	S.D.	6	6	11	0	30	3.5	5	13	5	0.0
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
100 mg/kg	Mean	64	36	45	0	458	23.4	47	45	83	0.0
	S.D.	9	10	8	0	183	17.9	8	21	11	0.1
								DT *			
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
300 mg/kg	Mean	100	67	57	0	720	26.7	54	55	100	0.0
	S.D.	34	19	25	1	154	22.3	5	18	10	0.0
		ST *	DT **			DT **					ST **

Test article Dose		GLU mg/dL	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	135	13	0.24	143	4.3	106	9.9	5.7	5.8	3.1
	S.D.	5	2	0.02	1	0.2	0	0.2	0.7	0.3	0.1
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
30 mg/kg	Mean	138	12	0.24	144	4.3	107	9.8	5.6	5.6	3.0
	S.D.	4	1	0.04	1	0.3	1	0.2	0.5	0.1	0.1
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
100 mg/kg	Mean	133	14	0.25	143	4.5	106	9.9	6.4	5.6	3.1
	S.D.	10	4	0.05	1	0.4	2	0.2	1.0	0.1	0.1
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
300 mg/kg	Mean	121	15	0.30	144	4.0	107	9.9	6.2	5.4	3.2
	S.D.	11	3	0.02	2	0.3	3	0.2	0.7	0.2	0.1
		DT *								DT *	DT *

Significantly different from benzyl salicylate 0 mg/kg : * P<0.05, ** P<0.01

DT : Dunnett test (two-side), ST : Steel test (two-side)

Table 7 - 2 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Blood chemistry Stage : End of administration

Sex : Male Species : Rat

Test article Dose		A/G
benzyl salicylate 0 mg/kg	n	5
	Mean	1.1
	S.D.	0.1
benzyl salicylate 30 mg/kg	n	5
	Mean	1.2
	S.D.	0.1
benzyl salicylate 100 mg/kg	n	5
	Mean	1.3
	S.D.	0.1
benzyl salicylate 300 mg/kg	n	5
	Mean	1.5
	S.D.	0.1
		DT **

Significantly different from benzyl salicylate 0 mg/kg : ** P<0.01

DT : Dunnett test (two-side)

Table 7 - 3 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Blood chemistry Stage : Lactation day 5

Sex : Female Species : Rat

Test article Dose		AST IU/L	ALT IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	T-BA μmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	72	57	45	0	332	21.2	61	54	112	0.1
	S.D.	5	14	10	0	83	9.4	15	24	19	0.0
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
30 mg/kg	Mean	66	50	52	1	291	53.2	64	93	131	0.1
	S.D.	5	12	11	1	111	65.4	10	45	24	0.0
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
100 mg/kg	Mean	71	51	53	1	220	27.5	68	104	132	0.0
	S.D.	10	12	20	0	52	9.0	13	49	23	0.0
					ST *						ST *

Test article Dose		GLU mg/dL	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	127	19	0.31	141	3.9	106	10.6	7.4	5.8	3.2
	S.D.	10	5	0.06	1	0.4	1	0.2	0.7	0.2	0.1
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
30 mg/kg	Mean	116	20	0.29	141	4.2	105	10.9	7.9	6.0	3.4
	S.D.	12	8	0.05	1	0.3	1	0.2	0.9	0.3	0.2
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
100 mg/kg	Mean	113	19	0.33	141	4.1	104	10.8	7.4	5.9	3.3
	S.D.	12	3	0.03	1	0.3	1	0.2	1.7	0.2	0.1

Significantly different from benzyl salicylate 0 mg/kg : * P<0.05

ST : Steel test (two-side)

Table 7 - 4 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Blood chemistry Stage : Lactation day 5

Sex : Female Species : Rat

Test article Dose		A/G
benzyl salicylate 0 mg/kg	n	5
	Mean	1.2
	S.D.	0.1
benzyl salicylate 30 mg/kg	n	5
	Mean	1.3
	S.D.	0.0
benzyl salicylate 100 mg/kg	n	5
	Mean	1.3
	S.D.	0.0
		DT *

Significantly different from benzyl salicylate 0 mg/kg : * P<0.05

DT : Dunnett test (two-side)

Table 7 - 5 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Blood chemistry Stage : End of administration

Sex : Female Species : Rat

Test article Dose		AST IU/L	ALT IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	T-BA μmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	52	28	42	1	205	21.4	63	19	121	0.1
	S.D.	4	7	4	1	61	8.6	22	4	37	0.0
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
300 mg/kg	Mean	83	63	37	1	337	28.4	62	54	128	0.0
	S.D.	18	22	4	0	51	3.6	11	28	19	0.0
		A2 *	A2 *			T2 **			A2 *		T2 **

Test article Dose		GLU mg/dL	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	126	14	0.30	140	4.1	107	10.2	4.1	6.3	3.5
	S.D.	15	3	0.03	1	0.2	1	0.5	0.3	0.6	0.7
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
300 mg/kg	Mean	116	14	0.32	142	4.1	108	9.6	4.6	5.7	3.5
	S.D.	19	5	0.06	0	0.3	2	0.3	0.3	0.2	0.2
					A2 *			T2 *			

Test article Dose		A/G
benzyl salicylate	n	5
0 mg/kg	Mean	1.3
	S.D.	0.3
benzyl salicylate	n	5
300 mg/kg	Mean	1.6
	S.D.	0.2
		T2 *

Significantly different from benzyl salicylate 0 mg/kg : * P<0.05, ** P<0.01

A2 : Welch test (two-side), T2 : Student t-test (two-side)

Table 7 - 6 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Blood chemistry Stage : End of recovery

Sex : Male Species : Rat

Test article Dose		AST IU/L	ALT IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	T-BA μmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	69	33	40	0	328	7.2	64	43	95	0.1
	S.D.	13	2	5	0	111	2.4	6	15	7	0.0
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
300 mg/kg	Mean	59	35	37	0	336	9.6	61	54	95	0.1
	S.D.	1	6	5	1	54	2.2	11	31	16	0.0
											EF

Test article Dose		GLU mg/dL	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	139	17	0.23	144	4.4	108	9.8	5.9	6.0	3.1
	S.D.	11	1	0.03	1	0.2	1	0.3	0.5	0.3	0.0
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
300 mg/kg	Mean	124	15	0.20	144	4.4	108	10.2	6.9	5.8	3.1
	S.D.	8	2	0.02	1	0.1	1	0.3	0.6	0.1	0.1
		T2 *						T2 *	T2 *		

Test article Dose		A/G
benzyl salicylate	n	5
0 mg/kg	Mean	1.1
	S.D.	0.1
benzyl salicylate	n	5
300 mg/kg	Mean	1.2
	S.D.	0.1
		T2 *

Significantly different from benzyl salicylate 0 mg/kg : * P<0.05

T2 : Student t-test (two-side)

EF : The group mean is the same and unbiased variance 0 for all groups. All data of all groups are same.

Table 7 - 7 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Blood chemistry Stage : End of recovery

Sex : Female Species : Rat

Test article Dose		AST IU/L	ALT IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	T-BA μmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	58	31	41	0	132	16.0	80	34	146	0.1
	S.D.	7	4	5	0	24	8.5	8	25	15	0.0
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
300 mg/kg	Mean	73	28	55	0	149	10.9	78	18	136	0.1
	S.D.	25	8	23	1	38	1.0	20	6	23	0.0
											EF

Test article Dose		GLU mg/dL	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	126	19	0.30	142	4.2	108	10.2	4.0	6.7	3.7
	S.D.	14	4	0.04	1	0.1	2	0.3	0.6	0.4	0.3
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
300 mg/kg	Mean	127	18	0.30	142	4.0	108	10.2	5.0	6.2	3.5
	S.D.	12	5	0.06	1	0.3	1	0.1	0.7	0.3	0.2
										T2 *	

Test article Dose		A/G
benzyl salicylate	n	5
0 mg/kg	Mean	1.2
	S.D.	0.1
benzyl salicylate	n	5
300 mg/kg	Mean	1.3
	S.D.	0.1

Significantly different from benzyl salicylate 0 mg/kg : * P<0.05

T2 : Student t-test (two-side)

EF : The group mean is the same and unbiased variance 0 for all groups. All data of all groups are same.

Table 8 - 1 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Organ weight Stage : End of administration

Sex : Male Species : Rat

Test article		Body weight	Brain		Pituitary		Thyroid-RL		Thymus	
			AB	RE	AB	RE	AB	RE	AB	RE
Dose		g	g	g/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g
benzyl salicylate	n	7	7	7	7	7	7	7	7	7
0 mg/kg	Mean	517	2.16	0.42	13.0	2.5	18.4	3.5	343	66
	S.D.	39	0.08	0.03	1.1	0.2	6.5	1.1	59	11
benzyl salicylate	n	12	12	12	12	12	12	12	12	12
30 mg/kg	Mean	497	2.14	0.43	12.8	2.6	22.0	4.4	324	65
	S.D.	27	0.06	0.02	1.3	0.3	6.4	1.3	102	21
benzyl salicylate	n	12	12	12	12	12	12	12	12	12
100 mg/kg	Mean	515	2.13	0.42	12.6	2.4	20.6	4.0	268	52
	S.D.	32	0.04	0.03	1.2	0.2	2.5	0.4	68	11
benzyl salicylate	n	7	7	7	7	7	7	7	7	7
300 mg/kg	Mean	492	2.17	0.44	12.5	2.5	21.9	4.5	244	50
	S.D.	26	0.06	0.03	0.9	0.2	3.2	0.6	95	19

Test article		Heart		Liver		Spleen		Kidney-RL		Adrenal-RL	
		AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Dose		g	g/100g	g	g/100g	g	g/100g	g	g/100g	mg	mg/100g
benzyl salicylate	n	7	7	7	7	7	7	7	7	7	7
0 mg/kg	Mean	1.45	0.28	13.42	2.59	0.77	0.15	3.38	0.65	60	12
	S.D.	0.14	0.02	1.44	0.13	0.11	0.02	0.24	0.03	8	1
benzyl salicylate	n	12	12	12	12	12	12	12	12	12	12
30 mg/kg	Mean	1.44	0.29	12.23	2.46	0.71	0.14	3.28	0.66	61	12
	S.D.	0.13	0.03	1.10	0.19	0.09	0.02	0.21	0.04	9	2
benzyl salicylate	n	12	12	12	12	12	12	12	12	12	12
100 mg/kg	Mean	1.45	0.28	12.78	2.48	0.74	0.14	3.38	0.66	65	13
	S.D.	0.13	0.03	0.86	0.12	0.08	0.02	0.23	0.06	8	2
benzyl salicylate	n	7	7	7	7	7	7	7	7	7	7
300 mg/kg	Mean	1.38	0.28	13.72	2.78	0.70	0.14	3.38	0.69	60	12
	S.D.	0.06	0.02	1.35	0.14	0.07	0.02	0.27	0.04	6	2
					DT *						

AB : Absolute weight, RE : Relative weight by body weight

Significantly different from benzyl salicylate 0 mg/kg : * P<0.05

DT : Dunnett test (two-side)

Table 8 - 2 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Organ weight Stage : End of administration

Sex : Male Species : Rat

Test article		Testis-RL		Epididymis-RL		Prostate		Seminal vesicle	
		AB	RE	AB	RE	AB	RE	AB	RE
Dose		g	g/100g	mg	mg/100g	g	g/100g	g	g/100g
benzyl salicylate	n	7	7	7	7	7	7	7	7
0 mg/kg	Mean	3.37	0.65	1370	266	1.41	0.27	1.92	0.37
	S.D.	0.17	0.06	81	21	0.24	0.04	0.18	0.03
benzyl salicylate	n	12	12	12	12	12	12	12	12
30 mg/kg	Mean	3.34	0.67	1312	265	1.32	0.27	1.79	0.36
	S.D.	0.19	0.05	68	19	0.22	0.05	0.37	0.07
benzyl salicylate	n	12	12	12	12	12	12	12	12
100 mg/kg	Mean	3.29	0.64	1268	248	1.25	0.24	1.65	0.32
	S.D.	0.36	0.09	141	38	0.15	0.03	0.25	0.06
benzyl salicylate	n	7	7	7	7	7	7	7	7
300 mg/kg	Mean	3.33	0.68	1234	251	1.19	0.24	1.92	0.39
	S.D.	0.27	0.08	48	15	0.11	0.03	0.29	0.07
				DT *					

AB : Absolute weight, RE : Relative weight by body weight

Significantly different from benzyl salicylate 0 mg/kg : * P<0.05

DT : Dunnett test (two-side)

Table 8 - 3 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Organ weight Stage : Lactation day 5

Sex : Female Species : Rat

Test article		Body weight	Brain		Pituitary		Thyroid-RL		Thymus	
			AB	RE	AB	RE	AB	RE	AB	RE
Dose		g	g	g/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g
benzyl salicylate	n	12	12	12	12	12	12	12	12	12
0 mg/kg	Mean	338	2.03	0.60	17.2	5.1	18.1	5.4	221	65
	S.D.	18	0.08	0.03	1.9	0.6	4.3	1.4	59	16
benzyl salicylate	n	12	12	12	12	12	12	12	12	12
30 mg/kg	Mean	331	2.02	0.61	18.0	5.4	17.7	5.4	212	64
	S.D.	18	0.12	0.05	2.6	0.8	1.9	0.6	44	12
benzyl salicylate	n	12	12	12	12	12	12	12	12	12
100 mg/kg	Mean	334	2.01	0.61	18.6	5.6	18.2	5.4	218	65
	S.D.	21	0.06	0.03	2.6	0.8	2.6	0.7	48	13

Test article		Heart		Liver		Spleen		Kidney-RL		Adrenal-RL	
		AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Dose		g	g/100g	g	g/100g	g	g/100g	g	g/100g	mg	mg/100g
benzyl salicylate	n	12	12	12	12	12	12	12	12	12	12
0 mg/kg	Mean	1.10	0.32	10.64	3.15	0.67	0.20	2.14	0.63	77	23
	S.D.	0.11	0.02	0.92	0.20	0.12	0.03	0.13	0.04	10	3
benzyl salicylate	n	12	12	12	12	12	12	12	12	12	12
30 mg/kg	Mean	1.08	0.33	10.51	3.18	0.68	0.21	2.15	0.65	74	23
	S.D.	0.12	0.03	0.81	0.24	0.14	0.03	0.20	0.06	9	2
benzyl salicylate	n	12	12	12	12	12	12	12	12	12	12
100 mg/kg	Mean	1.09	0.33	10.52	3.16	0.68	0.20	2.17	0.65	68	20
	S.D.	0.11	0.04	0.83	0.19	0.09	0.03	0.17	0.05	12	3

AB : Absolute weight, RE : Relative weight by body weight

Not significantly different from benzyl salicylate 0 mg/kg

Table 8 - 4 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Organ weight Stage : Lactation day 5

Sex : Female Species : Rat

Test article		Ovary-RL		Uterus	
		AB	RE	AB	RE
Dose		mg	mg/100g	mg	mg/100g
benzyl salicylate	n	12	12	12	12
0 mg/kg	Mean	106.7	31.4	720	213
	S.D.	20.8	5.1	101	28
benzyl salicylate	n	12	12	12	12
30 mg/kg	Mean	105.2	31.8	771	234
	S.D.	7.8	2.7	99	35
benzyl salicylate	n	12	12	12	12
100 mg/kg	Mean	106.9	32.1	667	201
	S.D.	18.4	5.2	67	23

AB : Absolute weight, RE : Relative weight by body weight

Not significantly different from benzyl salicylate 0 mg/kg

Table 8 - 5 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Organ weight Stage : End of administration

Sex : Female Species : Rat

Test article		Body weight	Brain		Pituitary		Thyroid-RL		Thymus	
			AB	RE	AB	RE	AB	RE	AB	RE
Dose		g	g	g/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g
benzyl salicylate	n	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	285	1.93	0.68	16.3	5.7	13.8	4.9	240	84
	S.D.	16	0.11	0.08	2.8	0.7	2.5	1.0	66	22
benzyl salicylate	n	5	5	5	5	5	5	5	5	5
300 mg/kg	Mean	291	2.00	0.69	16.7	5.8	16.3	5.6	185	63
	S.D.	11	0.08	0.02	2.0	0.8	2.7	0.8	31	10

Test article		Heart		Liver		Spleen		Kidney-RL		Adrenal-RL	
		AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Dose		g	g/100g	g	g/100g	g	g/100g	g	g/100g	mg	mg/100g
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	0.97	0.34	7.24	2.55	0.61	0.22	1.87	0.66	65	23
	S.D.	0.18	0.08	0.67	0.28	0.25	0.10	0.11	0.04	14	6
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
300 mg/kg	Mean	0.95	0.33	7.86	2.70	0.55	0.19	2.02	0.70	58	20
	S.D.	0.04	0.02	0.43	0.08	0.04	0.01	0.25	0.07	7	2

Test article		Ovary-RL		Uterus	
		AB	RE	AB	RE
Dose		mg	mg/100g	mg	mg/100g
benzyl salicylate	n	5	5	5	5
0 mg/kg	Mean	77.5	27.3	558	197
	S.D.	9.6	3.9	140	55
benzyl salicylate	n	5	5	5	5
300 mg/kg	Mean	71.6	24.6	561	193
	S.D.	8.1	2.7	117	40

AB : Absolute weight, RE : Relative weight by body weight

Not significantly different from benzyl salicylate 0 mg/kg

Table 8 - 6 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Organ weight Stage : End of recovery

Sex : Male Species : Rat

Test article		Body weight	Brain		Pituitary		Thyroid-RL		Thymus	
			AB	RE	AB	RE	AB	RE	AB	RE
Dose		g	g	g/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g
benzyl salicylate	n	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	525	2.16	0.41	12.3	2.4	23.6	4.5	316	60
	S.D.	45	0.06	0.04	0.8	0.3	4.3	0.8	31	7
benzyl salicylate	n	5	5	5	5	5	5	5	5	5
300 mg/kg	Mean	504	2.13	0.42	12.8	2.5	23.3	4.6	339	67
	S.D.	15	0.07	0.03	1.1	0.2	3.7	0.6	42	8

Test article		Heart		Liver		Spleen		Kidney-RL		Adrenal-RL	
		AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Dose		g	g/100g	g	g/100g	g	g/100g	g	g/100g	mg	mg/100g
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	1.42	0.27	12.82	2.42	0.64	0.12	3.28	0.63	63	12
	S.D.	0.04	0.02	2.52	0.26	0.07	0.01	0.26	0.03	9	2
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
300 mg/kg	Mean	1.53	0.30	12.45	2.47	0.73	0.14	3.42	0.68	57	11
	S.D.	0.17	0.04	0.65	0.13	0.13	0.03	0.18	0.04	5	1
									T2 *		

Test article		Testis-RL		Epididymis-RL		Prostate		Seminal vesicle	
		AB	RE	AB	RE	AB	RE	AB	RE
Dose		g	g/100g	mg	mg/100g	g	g/100g	g	g/100g
benzyl salicylate	n	5	5	5	5	5	5	5	5
0 mg/kg	Mean	3.24	0.62	1221	234	1.19	0.23	1.71	0.33
	S.D.	0.23	0.06	102	25	0.11	0.01	0.11	0.04
benzyl salicylate	n	5	5	5	5	5	5	5	5
300 mg/kg	Mean	3.12	0.62	1269	252	1.41	0.28	2.05	0.41
	S.D.	0.14	0.04	54	17	0.19	0.04	0.31	0.06
									T2 *

AB : Absolute weight, RE : Relative weight by body weight

Significantly different from benzyl salicylate 0 mg/kg : * P<0.05

T2 : Student t-test (two-side)

Table 8 - 7 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Organ weight Stage : End of recovery

Sex : Female Species : Rat

Test article		Body weight	Brain		Pituitary		Thyroid-RL		Thymus	
			AB	RE	AB	RE	AB	RE	AB	RE
Dose		g	g	g/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g
benzyl salicylate	n	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	305	2.00	0.66	15.7	5.1	15.5	5.1	277	91
	S.D.	16	0.03	0.04	0.7	0.4	1.2	0.5	65	20
benzyl salicylate	n	5	5	5	5	5	5	5	5	5
300 mg/kg	Mean	279	1.92	0.69	16.2	5.8	14.5	5.2	275	98
	S.D.	20	0.06	0.05	0.9	0.7	1.3	0.6	78	25
			T2 *							

Test article		Heart		Liver		Spleen		Kidney-RL		Adrenal-RL	
		AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Dose		g	g/100g	g	g/100g	g	g/100g	g	g/100g	mg	mg/100g
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	1.04	0.34	7.48	2.45	0.49	0.16	2.02	0.66	67	22
	S.D.	0.13	0.04	0.70	0.18	0.06	0.02	0.20	0.06	11	3
benzyl salicylate	n	5	5	5	5	5	5	5	5	5	5
300 mg/kg	Mean	0.92	0.33	7.06	2.54	0.49	0.18	1.97	0.71	65	24
	S.D.	0.08	0.04	0.34	0.19	0.05	0.01	0.21	0.07	8	4

Test article		Ovary-RL		Uterus	
		AB	RE	AB	RE
Dose		mg	mg/100g	mg	mg/100g
benzyl salicylate	n	5	5	5	5
0 mg/kg	Mean	88.7	29.0	586	194
	S.D.	20.4	5.5	85	37
benzyl salicylate	n	5	5	5	5
300 mg/kg	Mean	77.3	27.8	565	205
	S.D.	4.4	1.7	117	55

AB : Absolute weight, RE : Relative weight by body weight

Significantly different from benzyl salicylate 0 mg/kg : * P<0.05

T2 : Student t-test (two-side)

Study No. : R-1190

Table 9-1 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Gross pathological findings (End of administration period (D42))

Species : Rat

Organs	Sex:	M	M	M	M
	Dose(mg/kg):	0	30	100	300
Findings	Number:	7	12	12	7
Epididymis					
Focus,yellow		0	0	1	0
Liver					
Hepatodiaphragmatic nodule		0	0	1	0
Lung(bronchus)					
Focus,dark red		0	1	1	1
Stomach					
Focus,dark red,glandular stomach		0	2	1	1

M : Male

Study No. : R-1190

Table 9-2 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Gross pathological findings (End of administration period (D42))

Species : Rat

Organs	Sex:	F	F
	Dose(mg/kg):	0	300
Findings	Number:	5	5
All tissues			
Not remarkable		5	5

F : Female

Study No. : R-1190

Table 9-3 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Gross pathological findings (End of administration period (L4))

Species : Rat

Organs	Sex:	F	F	F
	Dose(mg/kg):	0	30	100
Findings	Number:	12	12	12
Lung(bronchus)				
Focus,dark red		0	1	0
Stomach				
Focus,dark red,glandular stomach		2	1	0

F : Female

Study No. : R-1190

Table 9-4 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Gross pathological findings (End of recovery period)

Species : Rat

Organs	Sex:	M	M
	Dose(mg/kg):	0	300
Findings	Number:	5	5
Stomach			
Focus,dark red,glandular stomach		0	1

M : Male

Study No. : R-1190

Table 9-5 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Gross pathological findings (End of recovery period)

Species : Rat

Organs	Sex:	F	F
	Dose(mg/kg):	0	300
Findings	Number:	5	5
Stomach			
Focus,dark red,glandular stomach		0	1

F : Female

Study No. : R-1190

Table 9-6 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Gross pathological findings (Undelivered)

Species : Rat

Organs	Sex:	F
	Dose(mg/kg):	300
Findings	Number:	6
Mammary gland,inguinal		
Poor development		3
Uterus		
Retention,conceptus		1

F : Female

Study No. : R-1190

Table 9-7 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Gross pathological findings (All littermates died)

Species : Rat

Organs	Sex:	F
	Dose(mg/kg):	300
Findings	Number:	6
Liver		
Large		1

F : Female

Study No. : R-1190

Table 10-1 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Histopathological findings (End of administration period (D42))

Species : Rat

Organs / Findings	Sex:	M	M	M	M
	Dose(mg/kg):	0	30	100	300
	Number:	7	12	12	7
Adrenal					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Bone+Bone marrow,femoral					
Number examined		5	0	5	5
Not remarkable		5	0	5	0
Increased trabecular bone		0	0	0	5
minimal		0	0	0	5
Cerebellum(pons)					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Cerebrum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Epididymis					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Eye					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Heart					
Number examined		5	0	0	5
Not remarkable		4	0	0	2
Cell infiltration,focal		1	0	0	3
minimal		1	0	0	3
Intestine,duodenum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,jejunum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,ileum(Peyer's patch)					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,cecum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,colon					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,rectum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Kidney					
Number examined		5	0	0	5
Not remarkable		4	0	0	4
Basophilia,tubular		1	0	0	1
minimal		1	0	0	1

M : Male

Study No. : R-1190

Table 10-2 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Histopathological findings (End of administration period (D42))

Species : Rat

Organs / Findings	Sex:	M	M	M	M
	Dose(mg/kg):	0	30	100	300
	Number:	7	12	12	7
Liver					
Number examined		5	0	0	5
Not remarkable		3	0	0	5
Necrosis,focal		1	0	0	0
minimal		1	0	0	0
Microgranuloma		1	0	0	0
minimal		1	0	0	0
Lung(bronchus)					
Number examined		5	0	0	5
Not remarkable		5	0	0	4
Hemorrhage,focal		0	0	0	1
minimal		0	0	0	1
Lymph node,mesenteric					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Lymph node,submandibular					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Mammary gland,inguinal					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Optic nerve					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Pancreas					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Parathyroid					
Number examined		5	0	0	4
Not remarkable		5	0	0	4
No sample		0	0	0	1
Pituitary					
Number examined		5	5	5	5
Not remarkable		5	4	5	4
Cyst,pars distalis		0	1	0	1
minimal		0	1	0	1
Prostate					
Number examined		5	0	0	5
Not remarkable		3	0	0	4
Cell infiltration		2	0	0	1
minimal		1	0	0	1
mild		1	0	0	0
Salivary gland,sublingual					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Salivary gland,submandibular					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Sciatic nerve					
Number examined		5	0	0	5
Not remarkable		5	0	0	5

M : Male

Study No. : R-1190

Table 10-3 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Histopathological findings (End of administration period (D42))

Species : Rat

Organs / Sex:	M	M	M	M
Dose(mg/kg):	0	30	100	300
Findings / Number:	7	12	12	7
Seminal vesicle(coagulating gland)				
Number examined	5	0	0	5
Not remarkable	5	0	0	5
Skeletal muscle,femoral				
Number examined	5	0	0	5
Not remarkable	5	0	0	5
Skin,inguinal				
Number examined	5	0	0	5
Not remarkable	5	0	0	5
Spinal cord,thoracic				
Number examined	5	0	0	5
Not remarkable	5	0	0	5
Spleen				
Number examined	5	0	0	5
Not remarkable	5	0	0	5
Stomach				
Number examined	5	0	0	5
Not remarkable	5	0	0	5
Testis				
Number examined	5	0	0	5
Not remarkable	4	0	0	4
Atrophy,seminiferous tubular	1	0	0	1
minimal	1	0	0	1
Thymus				
Number examined	5	0	5	5
Not remarkable	5	0	5	4
Atrophy	0	0	0	1
minimal	0	0	0	1
Thyroid				
Number examined	5	5	5	5
Not remarkable	5	5	5	5
Trachea				
Number examined	5	0	0	5
Not remarkable	5	0	0	5
Urinary bladder				
Number examined	5	0	0	5
Not remarkable	5	0	0	5

M : Male

Study No. : R-1190

Table 10-4 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Histopathological findings (End of administration period (D42))

Species : Rat

Organs / Findings	Sex:	F	F
	Dose(mg/kg):	0	300
	Number:	5	5
Adrenal			
Number examined		5	5
Not remarkable		5	5
Bone+Bone marrow,femoral			
Number examined		5	5
Not remarkable		5	1
Increased trabecular bone		0	4
minimal		0	4
Cerebellum(pons)			
Number examined		5	5
Not remarkable		5	5
Cerebrum			
Number examined		5	5
Not remarkable		5	5
Eye			
Number examined		5	5
Not remarkable		4	5
Dysplasia,retinal		1	0
minimal		1	0
Heart			
Number examined		5	5
Not remarkable		4	5
Cell infiltration,focal		1	0
minimal		1	0
Intestine,duodenum			
Number examined		5	5
Not remarkable		5	4
Erosion/ulcer		0	1
minimal		0	1
Intestine,jejunum			
Number examined		5	5
Not remarkable		5	5
Intestine,ileum(Peyer's patch)			
Number examined		5	5
Not remarkable		5	5
Intestine,cecum			
Number examined		5	5
Not remarkable		5	5
Intestine,colon			
Number examined		5	5
Not remarkable		4	5
Arteritis		1	0
mild		1	0
Intestine,rectum			
Number examined		5	5
Not remarkable		4	5
Arteritis		1	0
mild		1	0
Kidney			
Number examined		5	5
Not remarkable		4	5
Pyelitis		1	0
minimal		1	0

F : Female

Study No. : R-1190

Table 10-5 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Histopathological findings (End of administration period (D42))

Species : Rat

Organs / Findings	Sex:	F	F
	Dose(mg/kg):	0	300
	Number:	5	5
Liver			
Number examined		5	5
Not remarkable		5	5
Lung(bronchus)			
Number examined		5	5
Not remarkable		4	5
Aggregation,alveolar macrophage		1	0
minimal		1	0
Lymph node,mesenteric			
Number examined		5	5
Not remarkable		5	5
Lymph node,submandibular			
Number examined		5	5
Not remarkable		5	5
Mammary gland,inguinal			
Number examined		5	5
Not remarkable		5	5
Optic nerve			
Number examined		5	5
Not remarkable		5	5
Ovary			
Number examined		5	5
Not remarkable		4	5
Atrophy		1	0
minimal		1	0
Pancreas			
Number examined		5	5
Not remarkable		4	5
Arteritis		1	0
mild		1	0
Parathyroid			
Number examined		4	5
Not remarkable		4	5
No sample		1	0
Pituitary			
Number examined		5	5
Not remarkable		5	5
Salivary gland,sublingual			
Number examined		5	5
Not remarkable		5	5
Salivary gland,submandibular			
Number examined		5	5
Not remarkable		5	5
Sciatic nerve			
Number examined		5	5
Not remarkable		5	5

F : Female

Study No. : R-1190

Table 10-6 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Histopathological findings (End of administration period (D42))

Species : Rat

Organs / Findings	Sex:	F	F
	Dose(mg/kg):	0	300
	Number:	5	5
Skeletal muscle,femoral			
Number examined		5	5
Not remarkable		5	5
Skin,inguinal			
Number examined		5	5
Not remarkable		5	5
Spinal cord,thoracic			
Number examined		5	5
Not remarkable		5	5
Spleen			
Number examined		5	5
Not remarkable		5	5
Stomach			
Number examined		5	5
Not remarkable		4	5
Arteritis		1	0
mild		1	0
Thymus			
Number examined		5	5
Not remarkable		5	5
Thyroid			
Number examined		5	5
Not remarkable		5	5
Trachea			
Number examined		5	5
Not remarkable		5	5
Urinary bladder			
Number examined		5	5
Not remarkable		5	5
Uterus			
Number examined		5	5
Not remarkable		4	5
Arteritis		1	0
mild		1	0
Vagina			
Number examined		5	5
Not remarkable		3	5
Thickening,mucus cell layer		1	0
minimal		1	0
Thickening,squamous cell layer		1	0
minimal		1	0

F : Female

Study No. : R-1190

Table 10-7 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Histopathological findings (End of administration period (L4))

Species : Rat

Organs / Findings	Sex:	F	F	F
	Dose(mg/kg):	0	30	100
	Number:	12	12	12
Adrenal				
Number examined		5	0	5
Not remarkable		5	0	5
Bone+Bone marrow,femoral				
Number examined		5	0	5
Not remarkable		5	0	5
Cerebellum(pons)				
Number examined		5	0	5
Not remarkable		5	0	5
Cerebrum				
Number examined		5	0	5
Not remarkable		5	0	5
Eye				
Number examined		5	0	5
Not remarkable		5	0	5
Heart				
Number examined		5	0	5
Not remarkable		5	0	5
Intestine,duodenum				
Number examined		5	0	5
Not remarkable		5	0	5
Intestine,jejunum				
Number examined		5	0	5
Not remarkable		5	0	5
Intestine,ileum(Peyer's patch)				
Number examined		5	0	5
Not remarkable		5	0	5
Intestine,cecum				
Number examined		5	0	5
Not remarkable		5	0	5
Intestine,colon				
Number examined		5	0	5
Not remarkable		5	0	5
Intestine,rectum				
Number examined		5	0	5
Not remarkable		5	0	5
Kidney				
Number examined		5	0	5
Not remarkable		5	0	4
Cyst		0	0	1
minimal		0	0	1
Liver				
Number examined		5	0	5
Not remarkable		5	0	5
Lung(bronchus)				
Number examined		5	0	5
Not remarkable		4	0	5
Aggregation,alveolar macrophage		1	0	0
minimal		1	0	0

F : Female

Study No. : R-1190

Table 10-8 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Histopathological findings (End of administration period (L4))

Species : Rat

Organs / Findings	Sex:	F	F	F
	Dose(mg/kg):	0	30	100
	Number:	12	12	12
Lymph node,mesenteric				
Number examined		5	0	5
Not remarkable		5	0	5
Lymph node,submandibular				
Number examined		5	0	5
Not remarkable		5	0	5
Mammary gland,inguinal				
Number examined		5	0	5
Not remarkable		5	0	5
Optic nerve				
Number examined		5	0	5
Not remarkable		5	0	5
Ovary				
Number examined		5	0	5
Not remarkable		5	0	5
Pancreas				
Number examined		5	0	5
Not remarkable		5	0	5
Parathyroid				
Number examined		5	0	5
Not remarkable		5	0	5
Pituitary				
Number examined		5	5	5
Not remarkable		5	4	5
Cyst,pars intermedia		0	1	0
mild		0	1	0
Salivary gland,sublingual				
Number examined		5	0	5
Not remarkable		5	0	5
Salivary gland,submandibular				
Number examined		5	0	5
Not remarkable		5	0	5
Sciatic nerve				
Number examined		5	0	5
Not remarkable		5	0	5
Skeletal muscle,femoral				
Number examined		5	0	5
Not remarkable		5	0	5
Skin,inguinal				
Number examined		5	0	5
Not remarkable		5	0	5
Spinal cord,thoracic				
Number examined		5	0	5
Not remarkable		5	0	5
Spleen				
Number examined		5	0	5
Not remarkable		5	0	5

F : Female

Study No. : R-1190

Table 10-9 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Histopathological findings (End of administration period (L4))

Species : Rat

Organs / Findings	Sex:	F	F	F
	Dose(mg/kg):	0	30	100
	Number:	12	12	12
Stomach				
Number examined		5	0	5
Not remarkable		4	0	5
Erosion/Ulcer,glandular stomach		1	0	0
minimal		1	0	0
Thymus				
Number examined		5	0	5
Not remarkable		5	0	5
Thyroid				
Number examined		5	5	5
Not remarkable		5	5	5
Trachea				
Number examined		5	0	5
Not remarkable		5	0	5
Urinary bladder				
Number examined		5	0	5
Not remarkable		5	0	5
Uterus				
Number examined		5	0	5
Not remarkable		5	0	5
Vagina				
Number examined		5	0	5
Not remarkable		5	0	5

F : Female

Study No. : R-1190

Table 10-10 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Histopathological findings (End of recovery)

Species : Rat

Organs / Findings	Sex:	M	M
	Dose(mg/kg):	0	300
	Number:	5	5
Adrenal			
Number examined		5	5
Not remarkable		5	5
Bone+Bone marrow,femoral			
Number examined		5	5
Not remarkable		5	5
Cerebellum(pons)			
Number examined		5	5
Not remarkable		5	5
Cerebrum			
Number examined		5	5
Not remarkable		5	5
Epididymis			
Number examined		5	5
Not remarkable		4	5
Hypospermia		1	0
mild		1	0
Eye			
Number examined		5	5
Not remarkable		5	5
Heart			
Number examined		5	5
Not remarkable		5	4
Cell infiltration,focal		0	1
minimal		0	1
Intestine,duodenum			
Number examined		5	5
Not remarkable		5	5
Intestine,jejunum			
Number examined		5	5
Not remarkable		5	5
Intestine,ileum(Peyer's patch)			
Number examined		5	5
Not remarkable		5	5
Intestine,cecum			
Number examined		5	5
Not remarkable		5	5
Intestine,colon			
Number examined		5	5
Not remarkable		5	5
Intestine,rectum			
Number examined		5	5
Not remarkable		5	5
Kidney			
Number examined		5	5
Not remarkable		5	3
Basophilia,tubular		0	2
minimal		0	2

M : Male

Study No. : R-1190

Table 10-11 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Histopathological findings (End of recovery)

Species : Rat

Organs / Findings	Sex:	M	M
	Dose(mg/kg):	0	300
	Number:	5	5
Liver			
Number examined		5	5
Not remarkable		5	5
Lung(bronchus)			
Number examined		5	5
Not remarkable		5	5
Lymph node,mesenteric			
Number examined		5	5
Not remarkable		5	5
Lymph node,submandibular			
Number examined		5	5
Not remarkable		5	5
Mammary gland,inguinal			
Number examined		5	5
Not remarkable		5	5
Optic nerve			
Number examined		5	5
Not remarkable		5	5
Pancreas			
Number examined		5	5
Not remarkable		5	5
Parathyroid			
Number examined		5	5
Not remarkable		5	5
Pituitary			
Number examined		5	5
Not remarkable		5	4
Cyst,pars intermedia		0	1
mild		0	1
Prostate			
Number examined		5	5
Not remarkable		3	5
Cell infiltration		2	0
minimal		2	0
Salivary gland,sublingual			
Number examined		5	5
Not remarkable		5	5
Salivary gland,submandibular			
Number examined		5	5
Not remarkable		5	5
Sciatic nerve			
Number examined		5	5
Not remarkable		5	5
Seminal vesicle(coagulating gland)			
Number examined		5	5
Not remarkable		5	5
Skeletal muscle,femoral			
Number examined		5	5
Not remarkable		5	5

M : Male

Study No. : R-1190

Table 10-12 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Histopathological findings (End of recovery)

Species : Rat

Organs	Sex:	M	M
	Dose(mg/kg):	0	300
Findings	Number:	5	5
Skin,inguinal			
Number examined		5	5
Not remarkable		5	5
Spinal cord,thoracic			
Number examined		5	5
Not remarkable		5	5
Spleen			
Number examined		5	5
Not remarkable		5	5
Stomach			
Number examined		5	5
Not remarkable		5	4
Erosion/Ulcer,glandular stomach		0	1
minimal		0	1
Testis			
Number examined		5	5
Not remarkable		4	5
Atrophy,seminiferous tubular		1	0
moderate		1	0
Granuloma,spermatic		1	0
mild		1	0
Thymus			
Number examined		5	5
Not remarkable		5	5
Thyroid			
Number examined		5	5
Not remarkable		5	5
Trachea			
Number examined		5	5
Not remarkable		5	5
Urinary bladder			
Number examined		5	5
Not remarkable		5	5

M : Male

Study No. : R-1190

Table 10-13 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Histopathological findings (End of recovery)

Species : Rat

Organs / Findings	Sex:	F	F
	Dose(mg/kg):	0	300
	Number:	5	5
Adrenal			
Number examined		5	5
Not remarkable		5	5
Bone+Bone marrow,femoral			
Number examined		5	5
Not remarkable		5	5
Cerebellum(pons)			
Number examined		5	5
Not remarkable		5	5
Cerebrum			
Number examined		5	5
Not remarkable		5	5
Eye			
Number examined		5	5
Not remarkable		5	4
Dysplasia,retinal		0	1
minimal		0	1
Heart			
Number examined		5	5
Not remarkable		5	5
Intestine,duodenum			
Number examined		5	5
Not remarkable		5	5
Intestine,jejunum			
Number examined		5	5
Not remarkable		5	5
Intestine,ileum(Peyer's patch)			
Number examined		5	5
Not remarkable		5	5
Intestine,cecum			
Number examined		5	5
Not remarkable		5	5
Intestine,colon			
Number examined		5	5
Not remarkable		5	5
Intestine,rectum			
Number examined		5	5
Not remarkable		5	5
Kidney			
Number examined		5	5
Not remarkable		4	5
Urinary cast,hyaline		1	0
minimal		1	0
Liver			
Number examined		5	5
Not remarkable		5	5
Lung(bronchus)			
Number examined		5	5
Not remarkable		5	5

F : Female

Study No. : R-1190

Table 10-14 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Histopathological findings (End of recovery)

Species : Rat

Organs / Sex:	F	F
Dose(mg/kg):	0	300
Findings / Number:	5	5
Lymph node,mesenteric		
Number examined	5	5
Not remarkable	5	5
Lymph node,submandibular		
Number examined	5	5
Not remarkable	5	5
Mammary gland,inguinal		
Number examined	5	5
Not remarkable	5	5
Optic nerve		
Number examined	5	5
Not remarkable	5	5
Ovary		
Number examined	5	5
Not remarkable	5	5
Pancreas		
Number examined	5	5
Not remarkable	5	5
Parathyroid		
Number examined	5	5
Not remarkable	5	5
Pituitary		
Number examined	5	5
Not remarkable	5	5
Salivary gland,sublingual		
Number examined	5	5
Not remarkable	5	5
Salivary gland,submandibular		
Number examined	5	5
Not remarkable	5	5
Sciatic nerve		
Number examined	5	5
Not remarkable	5	5
Skeletal muscle,femoral		
Number examined	5	5
Not remarkable	5	5
Skin,inguinal		
Number examined	5	5
Not remarkable	5	5
Spinal cord,thoracic		
Number examined	5	5
Not remarkable	5	5
Spleen		
Number examined	5	5
Not remarkable	5	5
Stomach		
Number examined	5	5
Not remarkable	5	4
Erosion/Ulcer,glandular stomach	0	1
minimal	0	1

F : Female

Study No. : R-1190

Table 10-15 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Histopathological findings (End of recovery)

Species : Rat

Organs	Sex:	F	F
	Dose(mg/kg):	0	300
Findings	Number:	5	5
Thymus			
Number examined		5	5
Not remarkable		5	5
Thyroid			
Number examined		5	5
Not remarkable		5	5
Trachea			
Number examined		5	5
Not remarkable		5	5
Urinary bladder			
Number examined		5	5
Not remarkable		5	5
Uterus			
Number examined		5	5
Not remarkable		5	5
Vagina			
Number examined		5	5
Not remarkable		5	5

F : Female

Study No. : R-1190

Table 10-16 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Histopathological findings (Undelivered)

Species : Rat

Organs	Sex:	F
	Dose(mg/kg):	300
Findings	Number:	6
Adrenal		
Number examined		6
Not remarkable		6
Bone+Bone marrow,femoral		
Number examined		6
Increased trabecular bone		6
minimal		6
Cerebellum(pons)		
Number examined		6
Not remarkable		6
Cerebrum		
Number examined		6
Not remarkable		6
Eye		
Number examined		6
Not remarkable		6
Heart		
Number examined		6
Not remarkable		5
Cell infiltration,focal		1
minimal		1
Intestine,duodenum		
Number examined		6
Not remarkable		6
Intestine,jejunum		
Number examined		6
Not remarkable		6
Intestine,ileum(Peyer's patch)		
Number examined		6
Not remarkable		6
Intestine,cecum		
Number examined		6
Not remarkable		6
Intestine,colon		
Number examined		6
Not remarkable		6
Intestine,rectum		
Number examined		6
Not remarkable		6
Kidney		
Number examined		6
Not remarkable		6
Liver		
Number examined		6
Not remarkable		6
Lung(bronchus)		
Number examined		6
Not remarkable		6

F : Female

Study No. : R-1190

Table 10-17 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Histopathological findings (Undelivered)

Species : Rat

Organs	Sex:	F
	Dose(mg/kg):	300
Findings	Number:	6
Lymph node,mesenteric		
Number examined		6
Not remarkable		6
Lymph node,submandibular		
Number examined		6
Not remarkable		6
Mammary gland,inguinal		
Number examined		6
Not remarkable		6
Optic nerve		
Number examined		6
Not remarkable		6
Ovary		
Number examined		6
Not remarkable		6
Pancreas		
Number examined		6
Not remarkable		6
Parathyroid		
Number examined		6
Not remarkable		6
Pituitary		
Number examined		6
Not remarkable		6
Salivary gland,sublingual		
Number examined		6
Not remarkable		6
Salivary gland,submandibular		
Number examined		6
Not remarkable		6
Sciatic nerve		
Number examined		6
Not remarkable		6
Skeletal muscle,femoral		
Number examined		6
Not remarkable		6
Skin,inguinal		
Number examined		6
Not remarkable		6
Spinal cord,thoracic		
Number examined		6
Not remarkable		6
Spleen		
Number examined		6
Not remarkable		6
Stomach		
Number examined		6
Not remarkable		6

F : Female

Study No. : R-1190

Table 10-18 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Histopathological findings (Undelivered)

Species : Rat

Organs	Sex:	F
	Dose(mg/kg):	300
Findings	Number:	6
Thymus		
Number examined		6
Not remarkable		6
Thyroid		
Number examined		6
Not remarkable		6
Trachea		
Number examined		6
Not remarkable		6
Urinary bladder		
Number examined		6
Not remarkable		6
Uterus		
Number examined		6
Not remarkable		5
Retention,conceptus		1
Present		1
Vagina		
Number examined		6
Not remarkable		6

F : Female

Study No. : R-1190

Table 10-19 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Histopathological findings (All littermates died)

Species : Rat

Organs	Sex:	F
	Dose(mg/kg):	300
Findings	Number:	6
Adrenal		
Number examined		6
Not remarkable		6
Bone+Bone marrow,femoral		
Number examined		6
Increased trabecular bone		6
minimal		6
Cerebellum(pons)		
Number examined		6
Not remarkable		6
Cerebrum		
Number examined		6
Not remarkable		6
Eye		
Number examined		6
Not remarkable		6
Heart		
Number examined		6
Not remarkable		6
Intestine,duodenum		
Number examined		6
Not remarkable		6
Intestine,jejunum		
Number examined		6
Not remarkable		6
Intestine,ileum(Peyer's patch)		
Number examined		6
Not remarkable		6
Intestine,cecum		
Number examined		6
Not remarkable		6
Intestine,colon		
Number examined		6
Not remarkable		6
Intestine,rectum		
Number examined		6
Not remarkable		6
Kidney		
Number examined		6
Not remarkable		5
Urinary cast,hyaline		1
minimal		1
Liver		
Number examined		6
Not remarkable		6
Lung(bronchus)		
Number examined		6
Not remarkable		6

F : Female

Study No. : R-1190

Table 10-20 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Histopathological findings (All littermates died)

Species : Rat

Organs	Sex:	F
	Dose(mg/kg):	300
Findings	Number:	6
Lymph node,mesenteric		
Number examined		6
Not remarkable		6
Lymph node,submandibular		
Number examined		6
Not remarkable		6
Mammary gland,inguinal		
Number examined		6
Not remarkable		6
Optic nerve		
Number examined		6
Not remarkable		6
Ovary		
Number examined		6
Not remarkable		6
Pancreas		
Number examined		6
Not remarkable		6
Parathyroid		
Number examined		6
Not remarkable		6
Pituitary		
Number examined		6
Not remarkable		5
Cyst,pars distalis		1
minimal		1
Salivary gland,sublingual		
Number examined		6
Not remarkable		6
Salivary gland,submandibular		
Number examined		6
Not remarkable		6
Sciatic nerve		
Number examined		6
Not remarkable		6
Skeletal muscle,femoral		
Number examined		6
Not remarkable		6
Skin,inguinal		
Number examined		6
Not remarkable		6
Spinal cord,thoracic		
Number examined		6
Not remarkable		6
Spleen		
Number examined		6
Not remarkable		6

F : Female

Study No. : R-1190

Table 10-21 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Histopathological findings (All littermates died)

Species : Rat

Organs	Sex:	F
	Dose(mg/kg):	300
Findings	Number:	6
Stomach		
Number examined		6
Not remarkable		6
Thymus		
Number examined		6
Not remarkable		4
Atrophy		2
minimal		2
Thyroid		
Number examined		6
Not remarkable		6
Trachea		
Number examined		6
Not remarkable		6
Urinary bladder		
Number examined		6
Not remarkable		6
Uterus		
Number examined		6
Not remarkable		6
Vagina		
Number examined		6
Not remarkable		6

F : Female

Table 11 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Estrus cycles

Generation : F0

Study No. : R-1190

Species : Rat

Test article Dose		/Before mating Mean estrous cycle (Days)	Number of estrus	Number of animals with abnormal estrous cycle	Abnormal estrous cycle index (%)
benzyl salicylate 0 mg/kg	n	12	12	12 (0)	0.0
	Mean	4.2	3.6		
	S.D.	0.4	0.5		
benzyl salicylate 30 mg/kg	n	12	12	12 (0)	0.0
	Mean	4.0	3.8		
	S.D.	0.0	0.5		
benzyl salicylate 100 mg/kg	n	11	12	12 (1)	8.3
	Mean	4.1	3.5		
	S.D.	0.3	1.2		
benzyl salicylate 300 mg/kg	n	12	12	12 (0)	0.0
	Mean	4.0	3.6		
	S.D.	0.1	0.5		

() : Values in brackets represent number of animals with abnormal estrous cycle.

Abnormal estrous cycle index = (Number of animals with abnormal estrous cycle / Number of animals examined)×100

Not significantly different from benzyl salicylate 0 mg/kg

Table 12 - 1

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Reproductive performance

Generation : F0 Sex : Male

Study No. : R-1190

Species : Rat

Test article Dose		Number of pairs	Elapsed day of conceiving	1st mating Copulation index (%) a)	1st mating Fertility index (%) b)
benzyl salicylate	n	12	12	(12/12)	(12/12)
0 mg/kg	Mean		3.1	100.0	100.0
	S.D.		1.2		
benzyl salicylate	n	12	12	(12/12)	(12/12)
30 mg/kg	Mean		2.3	100.0	100.0
	S.D.		1.0		
benzyl salicylate	n	12	12	(12/12)	(12/12)
100 mg/kg	Mean		2.7	100.0	100.0
	S.D.		1.3		
benzyl salicylate	n	12	12	(12/12)	(12/12)
300 mg/kg	Mean		3.0	100.0	100.0
	S.D.		3.6		

Not significantly different from benzyl salicylate 0 mg/kg

a): (Number of copulated animals / Number of mated animals)×100

b): (Number of males which impregnated females / Number of copulated males)×100

Table 12 - 2 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Reproductive performance

Generation : F0 Sex : Female Species : Rat

Test article Dose		Number of pairs	Elapsed day of conceiving	1st mating Copulation index (%) a)	1st mating Fertility index (%) b)
benzyl salicylate	n	12	12	(12/12)	(12/12)
0 mg/kg	Mean		3.1	100.0	100.0
	S.D.		1.2		
benzyl salicylate	n	12	12	(12/12)	(12/12)
30 mg/kg	Mean		2.3	100.0	100.0
	S.D.		1.0		
benzyl salicylate	n	12	12	(12/12)	(12/12)
100 mg/kg	Mean		2.7	100.0	100.0
	S.D.		1.3		
benzyl salicylate	n	12	12	(12/12)	(12/12)
300 mg/kg	Mean		3.0	100.0	100.0
	S.D.		3.6		

Not significantly different from benzyl salicylate 0 mg/kg

a): (Number of copulated animals / Number of mated animals)×100

b): (Number of pregnant females / Number of copulated females)×100

Table 13 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Delivery data

Generation : F0 Species : Rat

Test article Dose		Gestation period (day)	Gestation index (%) a)	Number of corpora lutea	Number of implan-tation	Preimplan-tation loss (%) b)	Implantation index (%) c)	Delivery index (%) d)	Live birth index (%) e)	Number of offspring	Number of live newborns M	F	Total	Sex ratio (%) live-borns f)	delivered pups g)	Number of dead newborns
benzyl salicylate	n	12	12/12	12	12	12	12	12	12	12	12	12	12	77/145	78/149	12
0 mg/kg	Mean	22.3	100.0	13.8	13.6	2.0	98.0	92.9	97.0	12.4	6.4	5.7	12.1	53.1	52.3	0.3
	S.D.	0.4		4.0	4.1	3.8	3.8	10.3	5.7	3.3	2.6	2.5	3.3			0.7
benzyl salicylate	n	12	12/12	12	12	12	12	12	12	12	12	12	12	86/178	87/179	12
30 mg/kg	Mean	22.1	100.0	16.2	16.2	0.0	100.0	92.2	99.4	14.9	7.2	7.7	14.8	48.3	48.6	0.1
	S.D.	0.4		1.3	1.3	0.0	0.0	8.6	1.9	2.0	1.3	1.5	2.0			0.3
benzyl salicylate	n	12	12/12	12	12	12	12	12	12	12	12	12	12	83/160	83/161	12
100 mg/kg	Mean	22.3	100.0	15.8	14.5	8.3	91.7	93.3	99.4	13.4	6.9	6.4	13.3	51.9	51.6	0.1
	S.D.	0.5		0.7	3.7	23.3	23.3	9.9	2.0	3.6	2.4	2.3	3.6			0.3
benzyl salicylate	n	6	5/12	6	6	6	6	6	6	6	6	6	6	10/17	23/40	6
300 mg/kg	Mean	23.0	41.7	15.7	15.5	0.9	99.1	43.3	37.7	6.7	1.7	1.2	2.8	58.8	57.5	3.8
	S.D.	0.6		2.0	1.8	2.3	2.3	26.4	25.5	4.0	1.4	1.6	2.2			2.8
		DT **	FT **					W2 **	W2 **	DT **	DT **	DT **	DT **			ST **

M : Male, F : Female

Significantly different from benzyl salicylate 0 mg/kg : ** P<0.01

a): (Number of females which delivered liveborns / Number of pregnant females)×100

b): [(Number of corpora lutea - Number of implantation) / Number of corpora lutea]×100

c): (Number of implantation / Number of corpora lutea)×100

d): (Number of delivered pups / Number of implantation)×100

e): (Number of liveborns / Number of delivered pups)×100

f): (Number of liveborn males / Number of liveborns)×100

g): (Number of delivered males / Number of delivered pups)×100

DT : Dunnett test (two-side), FT : Fisher's exact test (two-side), ST : Steel test (two-side), W2 : Wilcoxon rank sum test (two-side)

Table 14 - 1 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

External examination of offspring

Generation : F0

Study No. : R-1190

Days after birth : 0

Species : Rat

Test article		benzyl salicylate	benzyl salicylate	benzyl salicylate	benzyl salicylate
Dose		0 mg/kg	30 mg/kg	100 mg/kg	300 mg/kg
Number of dams		12	12	12	6
Number of offspring		149	179	161	40
Number of offspring with any anomaly	n	2a)	0	0	5b)
	Mean	1.9	0.0	0.0	11.9
	S.D.	5.0	0.0	0.0	29.1

n : Number of anomalous offspring

Mean : Number of anomalous offspring / Number of offspring examined x 100(%), on litter basis

a) : Acaudia

b) : Exencephaly (n: 3), Exencephaly and Holorachischisis (n: 2)

Not significantly different from benzyl salicylate 0 mg/kg

Table 14 - 2 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
External examination of offspring
Generation : F0

Study No. : R-1190
Days after birth : 4
Species : Rat

Test article	benzyl salicylate	benzyl salicylate	benzyl salicylate
Dose	0 mg/kg	30 mg/kg	100 mg/kg
Number of dams	12	12	12
Number of offspring	144	176	158
Number of offspring with any anomaly	1a)	0	0

a) : Acaudia

Table 15 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Viability index and sex ratio of offspring on day 4 after birth

Generation : F0

Study No. : R-1190

Species : Rat

Test article Dose		Number of live offspring Day 0	Day 4	Viability index (%)a)	Sex ratio (%)b)
benzyl salicylate	n	12	12	12	77/144
0 mg/kg	Mean	12.1	12.0	99.4	53.5
	S.D.	3.3	3.2	1.9	
benzyl salicylate	n	12	12	12	85/176
30 mg/kg	Mean	14.8	14.7	99.0	48.3
	S.D.	2.0	2.0	3.6	
benzyl salicylate	n	12	12	12	81/158
100 mg/kg	Mean	13.3	13.2	98.8	51.3
	S.D.	3.6	3.6	2.9	
benzyl salicylate	n	6	5	5	
300 mg/kg	Mean	2.8	0.0	0.0 W2**	
	S.D.	2.2	0.0	0.0	

a) : (Number of live offspring on day 4 after birth / Number of live newborns) × 100

b) : (Number of live males on day 4 after birth / Number of live offspring on day 4 after birth) × 100

Significantly different from benzyl salicylate 0 mg/kg : ** P<0.01

W2 : Wilcoxon rank sum test (two-side)

Table 16 - 1

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Body weight of offspring

Generation : F0

Unit : g

Species : Rat

Test article Dose			/Days after birth 0	 4/Pre-culled
benzyl salicylate 0 mg/kg	Male	n	12	12
		Mean	7.1	11.5
		S.D.	0.5	1.2
	Female	n	12	12
		Mean	6.7	11.0
		S.D.	0.7	1.7
benzyl salicylate 30 mg/kg	Male	n	12	12
		Mean	6.6	10.4
		S.D.	0.6	1.1
				DT *
	Female	n	12	12
		Mean	6.2	9.8
		S.D.	0.6	1.1
				DT *
benzyl salicylate 100 mg/kg	Male	n	12	12
		Mean	6.5	10.7
		S.D.	0.5	0.8
			DT *	
	Female	n	11	11
		Mean	6.0	10.1
		S.D.	0.4	0.8
			DT *	
benzyl salicylate 300 mg/kg	Male	n	5	
		Mean	4.9	
		S.D.	0.6	
			DT **	
	Female	n	3	
		Mean	4.3	
		S.D.	0.7	
			DT **	

Significantly different from benzyl salicylate 0 mg/kg : * P<0.05, ** P<0.01

DT : Dunnett test (two-side)

Table 16 - 2

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Body weight gain of offspring

Base : Day 4 after birth

Generation : F0

Unit : g

Species : Rat

Test article Dose			/Days after birth /Before culling 0-4
benzyl salicylate 0 mg/kg	Male	n	12
		Mean	4.4
		S.D.	0.8
	Female	n	12
		Mean	4.3
		S.D.	1.0
benzyl salicylate 30 mg/kg	Male	n	12
		Mean	3.8
		S.D.	0.6
			DT *
	Female	n	12
		Mean	3.5
		S.D.	0.6
			DT *
benzyl salicylate 100 mg/kg	Male	n	12
		Mean	4.2
		S.D.	0.5
	Female	n	11
		Mean	4.1
		S.D.	0.5

Significantly different from benzyl salicylate 0 mg/kg : * P<0.05

DT : Dunnett test (two-side)

Table 17 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
External examination of dead offspring
Generation : F0

Study No. : R-1190

Species : Rat

Test article	benzyl salicylate	benzyl salicylate	benzyl salicylate	benzyl salicylate
Dose	0 mg/kg	30 mg/kg	100 mg/kg	300 mg/kg
Number of dams	12	12	12	5
Number of offspring	1	2	0	3
Number of offspring with any anomaly	0	0	0	0

Study No.: R-1190

Appendix 1-1 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : F0 before mating Day 1-15, F0 mating Day 15-43

Sex : Male Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	/Day 1	2	3	4	5	6	7	8	9	10	11	12	13	14
1001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1010	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1011	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1012	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- : No abnormal findings

Study No.: R-1190

Appendix 1-2 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : F0 before mating Day 1-15, F0 mating Day 15-43

Sex : Male Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	/Day 15	16	17	18	19	20	21	22	23	24	25	26	27	28
1001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1010	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1011	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1012	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- : No abnormal findings

Study No.: R-1190

Appendix 1-3 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : F0 before mating Day 1-15, F0 mating Day 15-43

Sex : Male Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	/Day 29	30	31	32	33	34	35	36	37	38	39	40	41	42	43a)
1001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1002	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1003	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1004	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1005	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1006	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1007	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1008	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
1009	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
1010	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
1011	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
1012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	

a) : Day of necropsy
- : No abnormal findings

Study No.: R-1190

Appendix 1-4 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : F0 before mating Day 1-15, F0 mating Day 15-43

Sex : Male Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	/Day 1	2	3	4	5	6	7	8	9	10	11	12	13	14
2001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2010	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2011	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2012	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- : No abnormal findings

Study No.: R-1190

Appendix 1-5 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : F0 before mating Day 1-15, F0 mating Day 15-43

Sex : Male Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	/Day 15	16	17	18	19	20	21	22	23	24	25	26	27	28
2001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2010	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2011	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2012	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- : No abnormal findings

Study No.: R-1190

Appendix 1-6 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : F0 before mating Day 1-15, F0 mating Day 15-43

Sex : Male Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	/Day 29	30	31	32	33	34	35	36	37	38	39	40	41	42	43a)
2001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2002	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2003	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2004	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2005	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2006	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2007	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2008	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2009	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2010	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2011	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

a) : Day of necropsy
- : No abnormal findings

Study No.: R-1190

Appendix 1-7 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : F0 before mating Day 1-15, F0 mating Day 15-43

Sex : Male Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	/Day 1	2	3	4	5	6	7	8	9	10	11	12	13	14
3001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3010	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3011	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3012	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- : No abnormal findings

Study No.: R-1190

Appendix 1-8 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : F0 before mating Day 1-15, F0 mating Day 15-43

Sex : Male Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	/Day 15	16	17	18	19	20	21	22	23	24	25	26	27	28
3001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3010	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3011	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3012	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- : No abnormal findings

Study No.: R-1190

Appendix 1-9 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : F0 before mating Day 1-15, F0 mating Day 15-43

Sex : Male Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	/Day 29	30	31	32	33	34	35	36	37	38	39	40	41	42	43a)
3001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3002	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3003	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3004	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3005	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3006	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3007	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3008	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3009	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3010	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3011	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

a) : Day of necropsy
- : No abnormal findings

Study No.: R-1190

Appendix 1-10 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : F0 before mating Day 1-15, F0 mating Day 15-43

Sex : Male Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	/Day 1	2	3	4	5	6	7	8	9	10	11	12	13	14
4001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4010	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4011	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4012	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- : No abnormal findings

Study No.: R-1190

Appendix 1-11 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : F0 before mating Day 1-15, F0 mating Day 15-43

Sex : Male Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	/Day 15	16	17	18	19	20	21	22	23	24	25	26	27	28
4001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4010	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4011	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4012	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- : No abnormal findings

Study No.: R-1190

Appendix 1-12 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : F0 before mating Day 1-15, F0 mating Day 15-43

Sex : Male Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	/Day 29	30	31	32	33	34	35	36	37	38	39	40	41	42	43a)
4001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4002	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4003	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4004	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4005	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4006	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4007	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4008	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
4009	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
4010	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
4011	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
4012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	

a) : Day of necropsy

- : No abnormal findings

Study No.: R-1190

Appendix 1-13 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : F0 before mating Day 1-15

Sex : Female Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	/Day 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1111	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1112	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- : No abnormal findings

Study No.: R-1190

Appendix 1-14 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : F0 before mating Day 1-15

Sex : Female Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	/Day 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
2101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2111	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2112	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- : No abnormal findings

Study No.: R-1190

Appendix 1-15 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : F0 before mating Day 1-15

Sex : Female Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	/Day 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
3101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3111	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3112	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- : No abnormal findings

Study No.: R-1190

Appendix 1-16 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : F0 before mating Day 1-15

Sex : Female Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	/Day 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
4101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4111	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4112	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- : No abnormal findings

Study No.: R-1190

Appendix 1-17 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : F0 gestation Day 0-25

Sex : Female Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	/Day 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
1101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d			
1102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d			
1103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d			
1104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d				
1105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d			
1106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d			
1107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d			
1108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d			
1109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d	d		
1110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d			
1111	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d			
1112	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d			

- : No abnormal findings
d : Delivery
/d : Found delivery after the observation of general conditions.

Study No.: R-1190

Appendix 1-18 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : F0 gestation Day 0-25

Sex : Female Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	/Day 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
2101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d				
2102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d			
2103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d			
2104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d			
2105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d			
2106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d			
2107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d				
2108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d			
2109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d			
2110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d				
2111	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d			
2112	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d			

- : No abnormal findings
d : Delivery
/d : Found delivery after the observation of general conditions.

Study No.: R-1190

Appendix 1-19 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : F0 gestation Day 0-25

Sex : Female Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	/Day 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
3101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d			
3102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d			
3103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d			
3104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d		
3105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d			
3106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d			
3107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d			
3108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d			
3109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d			
3110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d			
3111	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d			
3112	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d			

- : No abnormal findings
d : Delivery
/d : Found delivery after the observation of general conditions.

Study No.: R-1190

Appendix 1-20 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : F0 gestation Day 0-25

Sex : Female Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	/Day 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
4101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d			
4103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d			
4106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
4107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d			
4108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d		
4110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d		
4111	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4112	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- : No abnormal findings
d : Delivery
/d : Found delivery after the observation of general conditions.

Study No.: R-1190

Appendix 1-21 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : F0 lactation Day 0-5

Sex : Female Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	/Day 0	1	2	3	4	5a)
1101	-	-	-	-	-	-
1102	-	-	-	-	-	-
1103	-	-	-	-	-	-
1104	-	-	-	-	-	-
1105	-	-	-	-	-	-
1106	-	-	-	-	-	-
1107	-	-	-	-	-	-
1108	-	-	-	-	-	-
1109	-	-	-	-	-	-
1110	-	-	-	-	-	-
1111	-	-	-	-	-	-
1112	-	-	-	-	-	-

a) : Day of necropsy
- : No abnormal findings

Study No.: R-1190

Appendix 1-22 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : F0 lactation Day 0-5

Sex : Female Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	/Day 0	1	2	3	4	5a)
2101	-	-	-	-	-	-
2102	-	-	-	-	-	-
2103	-	-	-	-	-	-
2104	-	-	-	-	-	-
2105	-	-	-	-	-	-
2106	-	-	-	-	-	-
2107	-	-	-	-	-	-
2108	-	-	-	-	-	-
2109	-	-	-	-	-	-
2110	-	-	-	-	-	-
2111	-	-	-	-	-	-
2112	-	-	-	-	-	-

a) : Day of necropsy
- : No abnormal findings

Study No.: R-1190

Appendix 1-23 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : F0 lactation Day 0-5

Sex : Female Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	/Day 0	1	2	3	4	5a)
3101	-	-	-	-	-	-
3102	-	-	-	-	-	-
3103	-	-	-	-	-	-
3104	-	-	-	-	-	-
3105	-	-	-	-	-	-
3106	-	-	-	-	-	-
3107	-	-	-	-	-	-
3108	-	-	-	-	-	-
3109	-	-	-	-	-	-
3110	-	-	-	-	-	-
3111	-	-	-	-	-	-
3112	-	-	-	-	-	-

a) : Day of necropsy
- : No abnormal findings

Study No.: R-1190

Appendix 1-24 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : F0 lactation Day 0-5

Sex : Female Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	/Day 0	1	2	3	4	5a)
4102	-	-	-			
4105	-	-				
4106	-					
4107	-	-				
4109	-	-				
4110	-	-				

a) : Day of necropsy
- : No abnormal findings
Animal No. 4101, 4103, 4104, 4108, 4111, 4112 : Not delivered
Animal No. 4106 : Necropsied on lactation day 0 because all offspring were stillborn
Animal No. 4105, 4107, 4109, 4110 : Necropsied on lactation day 1 because all offspring died
Animal No. 4102 : Necropsied on lactation day 2 because all offspring died

Study No.: R-1190

Appendix 1-25 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : Administration Day 1-43

Sex : Female Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	/Day 1	2	3	4	5	6	7	8	9	10	11	12	13	14
5101	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5102	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5103	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5104	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5106	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5107	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5108	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5109	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5110	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- : No abnormal findings

Study No.: R-1190

Appendix 1-26 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : Administration Day 1-43

Sex : Female Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	/Day 15	16	17	18	19	20	21	22	23	24	25	26	27	28
5101	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5102	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5103	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5104	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5106	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5107	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5108	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5109	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5110	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- : No abnormal findings

Study No.: R-1190

Appendix 1-27 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : Administration Day 1-43

Sex : Female Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	/Day 29	30	31	32	33	34	35	36	37	38	39	40	41	42	43a)
5101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
5107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
5108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
5109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
5110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	

a) : Day of necropsy
- : No abnormal findings

Study No.: R-1190

Appendix 1-28 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : Administration Day 1-43

Sex : Female Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	/Day 1	2	3	4	5	6	7	8	9	10	11	12	13	14
6101	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6102	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6103	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6104	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6106	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6107	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6108	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6109	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6110	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- : No abnormal findings

Study No.: R-1190

Appendix 1-29 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : Administration Day 1-43

Sex : Female Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	/Day 15	16	17	18	19	20	21	22	23	24	25	26	27	28
6101	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6102	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6103	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6104	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6106	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6107	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6108	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6109	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6110	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- : No abnormal findings

Study No.: R-1190

Appendix 1-30 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : Administration Day 1-43

Sex : Female Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	/Day 29	30	31	32	33	34	35	36	37	38	39	40	41	42	43a)
6101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
6107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
6108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
6109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
6110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	

a) : Day of necropsy
- : No abnormal findings

Study No.: R-1190

Appendix 1-31 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : Recovery Day 1-15

Sex : Male Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	/Day 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)
1008	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1009	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1010	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1011	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

a) : Day of necropsy
- : No abnormal findings

Study No.: R-1190

Appendix 1-32 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : Recovery Day 1-15

Sex : Male Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	/Day 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)
4008	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4009	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4010	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4011	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

a) : Day of necropsy
- : No abnormal findings

Study No.: R-1190

Appendix 1-33 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : Recovery Day 1-15

Sex : Female Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	/Day 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)
5106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

a) : Day of necropsy
- : No abnormal findings

Study No.: R-1190

Appendix 1-34 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Clinical signs Period : Recovery Day 1-15

Sex : Female Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	/Day 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)
6106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

a) : Day of necropsy

- : No abnormal findings

Appendix 2 - 1 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 before mating

Generation : F0 Sex : Male Week : 1 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
1001	N	0	0
1002	N	0	0
1003	N	0	0
1004	N	0	0
1005	N	0	0
1006	N	0	0
1007	N	0	0
1008	N	0	0
1009	N	0	0
1010	N	0	0
1011	N	0	0
1012	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 2 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 before mating

Generation : F0 Sex : Male Week : 1 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
2001	N	0	0
2002	N	0	0
2003	N	0	0
2004	N	0	0
2005	N	0	0
2006	N	0	0
2007	N	0	0
2008	N	0	0
2009	N	0	0
2010	N	0	0
2011	N	0	0
2012	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 3 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 before mating

Generation : F0 Sex : Male Week : 1 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
3001	N	0	0
3002	N	0	0
3003	N	0	0
3004	N	0	0
3005	N	0	0
3006	N	0	0
3007	N	0	0
3008	N	0	0
3009	N	0	0
3010	N	0	0
3011	N	0	0
3012	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 4 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 before mating

Generation : F0 Sex : Male Week : 1 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
4001	N	0	0
4002	N	0	0
4003	N	0	0
4004	N	0	0
4005	N	0	0
4006	N	0	0
4007	N	0	0
4008	N	0	0
4009	N	0	0
4010	N	0	0
4011	N	0	0
4012	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 5 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 before mating

Generation : F0 Sex : Male Week : 2 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
1001	N	0	0
1002	N	0	0
1003	N	0	0
1004	N	0	0
1005	N	0	0
1006	N	0	0
1007	N	0	0
1008	N	0	0
1009	N	0	0
1010	N	0	0
1011	N	0	0
1012	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 6 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 before mating

Generation : F0 Sex : Male Week : 2 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
2001	N	0	0
2002	N	0	0
2003	N	0	0
2004	N	0	0
2005	N	0	0
2006	N	0	0
2007	N	0	0
2008	N	0	0
2009	N	0	0
2010	N	0	0
2011	N	0	0
2012	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 7 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 before mating

Generation : F0 Sex : Male Week : 2 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
3001	N	0	0
3002	N	0	0
3003	N	0	0
3004	N	0	0
3005	N	0	0
3006	N	0	0
3007	N	0	0
3008	N	0	0
3009	N	0	0
3010	N	0	0
3011	N	0	0
3012	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 8 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 before mating

Generation : F0 Sex : Male Week : 2 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
4001	N	0	0
4002	N	0	0
4003	N	0	0
4004	N	0	0
4005	N	0	0
4006	N	0	0
4007	N	0	0
4008	N	0	0
4009	N	0	0
4010	N	0	0
4011	N	0	0
4012	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 9 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 mating

Generation : F0 Sex : Male Week : 3 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
1001	N	0	0
1002	N	0	0
1003	N	0	0
1004	N	0	0
1005	N	0	0
1006	N	0	0
1007	N	0	0
1008	N	0	0
1009	N	0	0
1010	N	0	0
1011	N	0	0
1012	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 10 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 mating

Generation : F0 Sex : Male Week : 3 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
2001	N	0	0
2002	N	0	0
2003	N	0	0
2004	N	0	0
2005	N	0	0
2006	N	0	0
2007	N	0	0
2008	N	0	0
2009	N	0	0
2010	N	0	0
2011	N	0	0
2012	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 11 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 mating

Generation : F0 Sex : Male Week : 3 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
3001	N	0	0
3002	N	0	0
3003	N	0	0
3004	N	0	0
3005	N	0	0
3006	N	0	0
3007	N	0	0
3008	N	0	0
3009	N	0	0
3010	N	0	0
3011	N	0	0
3012	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 12 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 mating

Generation : F0 Sex : Male Week : 3 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
4001	N	0	0
4002	N	0	0
4003	N	0	0
4004	N	0	0
4005	N	0	0
4006	N	0	0
4007	N	0	0
4008	N	0	0
4009	N	0	0
4010	N	0	0
4011	N	0	0
4012	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 13 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 mating

Generation : F0 Sex : Male Week : 4 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
1001	N	0	0
1002	N	0	0
1003	N	0	0
1004	N	0	0
1005	N	0	0
1006	N	0	0
1007	N	0	0
1008	N	0	0
1009	N	0	0
1010	N	0	0
1011	N	0	0
1012	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 14 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 mating

Generation : F0 Sex : Male Week : 4 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
2001	N	0	0
2002	N	0	0
2003	N	0	0
2004	N	0	0
2005	N	0	0
2006	N	0	0
2007	N	0	0
2008	N	0	0
2009	N	0	0
2010	N	0	0
2011	N	0	0
2012	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 15 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 mating

Generation : F0 Sex : Male Week : 4 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
3001	N	0	0
3002	N	0	0
3003	N	0	0
3004	N	0	0
3005	N	0	0
3006	N	0	0
3007	N	0	0
3008	N	0	0
3009	N	0	0
3010	N	0	0
3011	N	0	0
3012	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 16 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 mating

Generation : F0 Sex : Male Week : 4 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
4001	N	0	0
4002	N	0	0
4003	N	0	0
4004	N	0	0
4005	N	0	0
4006	N	0	0
4007	N	0	0
4008	N	0	0
4009	N	0	0
4010	N	0	0
4011	N	0	0
4012	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 17 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 mating

Generation : F0 Sex : Male Week : 5 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
1001	N	0	0
1002	N	0	0
1003	N	0	0
1004	N	0	0
1005	N	0	0
1006	N	0	0
1007	N	0	0
1008	N	0	0
1009	N	0	0
1010	N	0	0
1011	N	0	0
1012	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 18 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 mating

Generation : F0 Sex : Male Week : 5 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
2001	N	0	0
2002	N	0	0
2003	N	0	0
2004	N	0	0
2005	N	0	0
2006	N	0	0
2007	N	0	0
2008	N	0	0
2009	N	0	0
2010	N	0	0
2011	N	0	0
2012	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 19 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 mating

Generation : F0 Sex : Male Week : 5 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
3001	N	0	0
3002	N	0	0
3003	N	0	0
3004	N	0	0
3005	N	0	0
3006	N	0	0
3007	N	0	0
3008	N	0	0
3009	N	0	0
3010	N	0	0
3011	N	0	0
3012	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 20 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 mating

Generation : F0 Sex : Male Week : 5 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
4001	N	0	0
4002	N	0	0
4003	N	0	0
4004	N	0	0
4005	N	0	0
4006	N	0	0
4007	N	0	0
4008	N	0	0
4009	N	0	0
4010	N	0	0
4011	N	0	0
4012	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 21 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 mating

Generation : F0 Sex : Male Week : 6 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
1001	N	0	0
1002	N	0	0
1003	N	0	0
1004	N	0	0
1005	N	0	0
1006	N	0	0
1007	N	0	0
1008	N	0	0
1009	N	0	0
1010	N	0	0
1011	N	0	0
1012	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 22 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 mating

Generation : F0 Sex : Male Week : 6 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
2001	N	0	0
2002	N	0	0
2003	N	0	0
2004	N	0	0
2005	N	0	0
2006	N	0	0
2007	N	0	0
2008	N	0	0
2009	N	0	0
2010	N	0	0
2011	N	0	0
2012	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 23 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 mating

Generation : F0 Sex : Male Week : 6 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
3001	N	0	0
3002	N	0	0
3003	N	0	0
3004	N	0	0
3005	N	0	0
3006	N	0	0
3007	N	0	0
3008	N	0	0
3009	N	0	0
3010	N	0	0
3011	N	0	0
3012	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 24 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 mating

Generation : F0 Sex : Male Week : 6 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
4001	N	0	0
4002	N	0	0
4003	N	0	0
4004	N	0	0
4005	N	0	0
4006	N	0	0
4007	N	0	0
4008	N	0	0
4009	N	0	0
4010	N	0	0
4011	N	0	0
4012	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 25 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 before mating

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
1101	N	0	0
1102	N	0	0
1103	N	0	0
1104	N	0	0
1105	N	0	0
1106	N	0	0
1107	N	0	0
1108	N	0	0
1109	N	0	0
1110	N	0	0
1111	N	0	0
1112	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 26 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 before mating

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
2101	N	0	0
2102	N	0	0
2103	N	0	0
2104	N	0	0
2105	N	0	0
2106	N	0	0
2107	N	0	0
2108	N	0	0
2109	N	0	0
2110	N	0	0
2111	N	0	0
2112	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 27 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 before mating

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
3101	N	0	0
3102	N	0	0
3103	N	0	0
3104	N	0	0
3105	N	0	0
3106	N	0	0
3107	N	0	0
3108	N	0	0
3109	N	0	0
3110	N	0	0
3111	N	0	0
3112	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 28 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 before mating

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
4101	N	0	0
4102	N	0	0
4103	N	0	0
4104	N	0	0
4105	N	0	0
4106	N	0	0
4107	N	0	0
4108	N	0	0
4109	N	0	0
4110	N	0	0
4111	N	0	0
4112	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 29 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 before mating

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
1101	N	0	0
1102	N	0	0
1103	N	0	0
1104	N	0	0
1105	N	0	0
1106	N	0	0
1107	N	0	0
1108	N	0	0
1109	N	0	0
1110	N	0	0
1111	N	0	0
1112	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Home cage observation

Period : F0 before mating

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
2101	N	0	0
2102	N	0	0
2103	N	0	0
2104	N	0	0
2105	N	0	0
2106	N	0	0
2107	N	0	0
2108	N	0	0
2109	N	0	0
2110	N	0	0
2111	N	0	0
2112	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 31 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 before mating

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
3101	N	0	0
3102	N	0	0
3103	N	0	0
3104	N	0	0
3105	N	0	0
3106	N	0	0
3107	N	0	0
3108	N	0	0
3109	N	0	0
3110	N	0	0
3111	N	0	0
3112	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 32 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 before mating

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
4101	N	0	0
4102	N	0	0
4103	N	0	0
4104	N	0	0
4105	N	0	0
4106	N	0	0
4107	N	0	0
4108	N	0	0
4109	N	0	0
4110	N	0	0
4111	N	0	0
4112	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 33 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 gestation

Generation : F0 Sex : Female Day : 1 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
1101	N	0	0
1102	N	0	0
1103	N	0	0
1104	N	0	0
1105	N	0	0
1106	N	0	0
1107	N	0	0
1108	N	0	0
1109	N	0	0
1110	N	0	0
1111	N	0	0
1112	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 34 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 gestation

Generation : F0 Sex : Female Day : 1 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
2101	N	0	0
2102	N	0	0
2103	N	0	0
2104	N	0	0
2105	N	0	0
2106	N	0	0
2107	N	0	0
2108	N	0	0
2109	N	0	0
2110	N	0	0
2111	N	0	0
2112	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 35 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 gestation

Generation : F0 Sex : Female Day : 1 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
3101	N	0	0
3102	N	0	0
3103	N	0	0
3104	N	0	0
3105	N	0	0
3106	N	0	0
3107	N	0	0
3108	N	0	0
3109	N	0	0
3110	N	0	0
3111	N	0	0
3112	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 36 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 gestation

Generation : F0 Sex : Female Day : 1 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
4101	N	0	0
4102	N	0	0
4103	N	0	0
4104	N	0	0
4105	N	0	0
4106	N	0	0
4107	N	0	0
4108	N	0	0
4109	N	0	0
4110	N	0	0
4111	N	0	0
4112	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Home cage observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 7 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
1101	N	0	0
1102	N	0	0
1103	N	0	0
1104	N	0	0
1105	N	0	0
1106	N	0	0
1107	N	0	0
1108	N	0	0
1109	N	0	0
1110	N	0	0
1111	N	0	0
1112	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 38 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 gestation

Generation : F0 Sex : Female Day : 7 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
2101	N	0	0
2102	N	0	0
2103	N	0	0
2104	N	0	0
2105	N	0	0
2106	N	0	0
2107	N	0	0
2108	N	0	0
2109	N	0	0
2110	N	0	0
2111	N	0	0
2112	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 39 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 gestation

Generation : F0 Sex : Female Day : 7 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
3101	N	0	0
3102	N	0	0
3103	N	0	0
3104	N	0	0
3105	N	0	0
3106	N	0	0
3107	N	0	0
3108	N	0	0
3109	N	0	0
3110	N	0	0
3111	N	0	0
3112	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 40 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 gestation

Generation : F0 Sex : Female Day : 7 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
4101	N	0	0
4102	N	0	0
4103	N	0	0
4104	N	0	0
4105	N	0	0
4106	N	0	0
4107	N	0	0
4108	N	0	0
4109	N	0	0
4110	N	0	0
4111	N	0	0
4112	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 41 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 gestation

Generation : F0 Sex : Female Day : 14 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
1101	N	0	0
1102	N	0	0
1103	N	0	0
1104	N	0	0
1105	N	0	0
1106	N	0	0
1107	N	0	0
1108	N	0	0
1109	N	0	0
1110	N	0	0
1111	N	0	0
1112	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 42 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 gestation

Generation : F0 Sex : Female Day : 14 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
2101	N	0	0
2102	N	0	0
2103	N	0	0
2104	N	0	0
2105	N	0	0
2106	N	0	0
2107	N	0	0
2108	N	0	0
2109	N	0	0
2110	N	0	0
2111	N	0	0
2112	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 43 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 gestation

Generation : F0 Sex : Female Day : 14 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
3101	N	0	0
3102	N	0	0
3103	N	0	0
3104	N	0	0
3105	N	0	0
3106	N	0	0
3107	N	0	0
3108	N	0	0
3109	N	0	0
3110	N	0	0
3111	N	0	0
3112	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 44 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 gestation

Generation : F0 Sex : Female Day : 14 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
4101	N	0	0
4102	N	0	0
4103	N	0	0
4104	N	0	0
4105	N	0	0
4106	N	0	0
4107	N	0	0
4108	N	0	0
4109	N	0	0
4110	N	0	0
4111	N	0	0
4112	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 45 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 gestation

Generation : F0 Sex : Female Day : 20 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
1101	N	0	0
1102	N	0	0
1103	N	0	0
1104	N	0	0
1105	N	0	0
1106	N	0	0
1107	N	0	0
1108	N	0	0
1109	N	0	0
1110	N	0	0
1111	N	0	0
1112	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Home cage observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 20 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
2101	N	0	0
2102	N	0	0
2103	N	0	0
2104	N	0	0
2105	N	0	0
2106	N	0	0
2107	N	0	0
2108	N	0	0
2109	N	0	0
2110	N	0	0
2111	N	0	0
2112	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Home cage observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 20 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
3101	N	0	0
3102	N	0	0
3103	N	0	0
3104	N	0	0
3105	N	0	0
3106	N	0	0
3107	N	0	0
3108	N	0	0
3109	N	0	0
3110	N	0	0
3111	N	0	0
3112	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 48 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 gestation

Generation : F0 Sex : Female Day : 20 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
4101	N	0	0
4102	N	0	0
4103	N	0	0
4104	N	0	0
4105	N	0	0
4106	N	0	0
4107	N	0	0
4108	N	0	0
4109	N	0	0
4110	N	0	0
4111	N	0	0
4112	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 49 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 lactation

Generation : F0 Sex : Female Day : 4 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
1101	N	0	0
1102	N	0	0
1103	N	0	0
1104	N	0	0
1105	N	0	0
1106	N	0	0
1107	N	0	0
1108	N	0	0
1109	N	0	0
1110	N	0	0
1111	N	0	0
1112	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 50 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 lactation

Generation : F0 Sex : Female Day : 4 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
2101	N	0	0
2102	N	0	0
2103	N	0	0
2104	N	0	0
2105	N	0	0
2106	N	0	0
2107	N	0	0
2108	N	0	0
2109	N	0	0
2110	N	0	0
2111	N	0	0
2112	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 51 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : F0 lactation

Generation : F0 Sex : Female Day : 4 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
3101	N	0	0
3102	N	0	0
3103	N	0	0
3104	N	0	0
3105	N	0	0
3106	N	0	0
3107	N	0	0
3108	N	0	0
3109	N	0	0
3110	N	0	0
3111	N	0	0
3112	N	0	0
n	12	12	12

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Home cage observation

Period : Administration

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
5101	N	0	0
5102	N	0	0
5103	N	0	0
5104	N	0	0
5105	N	0	0
5106	N	0	0
5107	N	0	0
5108	N	0	0
5109	N	0	0
5110	N	0	0
n	10	10	10

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Home cage observation

Period : Administration

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
6101	N	0	0
6102	N	0	0
6103	N	0	0
6104	N	0	0
6105	N	0	0
6106	N	0	0
6107	N	0	0
6108	N	0	0
6109	N	0	0
6110	N	0	0
n	10	10	10

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 54 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : Administration

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
5101	N	0	0
5102	N	0	0
5103	N	0	0
5104	N	0	0
5105	N	0	0
5106	N	0	0
5107	N	0	0
5108	N	0	0
5109	N	0	0
5110	N	0	0
n	10	10	10

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 55 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : Administration

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
6101	N	0	0
6102	N	0	0
6103	N	0	0
6104	N	0	0
6105	N	0	0
6106	N	0	0
6107	N	0	0
6108	N	0	0
6109	N	0	0
6110	N	0	0
n	10	10	10

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Home cage observation

Period : Administration

Generation : F0 Sex : Female Week : 3 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
5101	N	0	0
5102	N	0	0
5103	N	0	0
5104	N	0	0
5105	N	0	0
5106	N	0	0
5107	N	0	0
5108	N	0	0
5109	N	0	0
5110	N	0	0
n	10	10	10

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Home cage observation

Period : Administration

Generation : F0 Sex : Female Week : 3 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
6101	N	0	0
6102	N	0	0
6103	N	0	0
6104	N	0	0
6105	N	0	0
6106	N	0	0
6107	N	0	0
6108	N	0	0
6109	N	0	0
6110	N	0	0
n	10	10	10

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Home cage observation

Period : Administration

Generation : F0 Sex : Female Week : 4 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
5101	N	0	0
5102	N	0	0
5103	N	0	0
5104	N	0	0
5105	N	0	0
5106	N	0	0
5107	N	0	0
5108	N	0	0
5109	N	0	0
5110	N	0	0
n	10	10	10

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Home cage observation

Period : Administration

Generation : F0 Sex : Female Week : 4 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
6101	N	0	0
6102	N	0	0
6103	N	0	0
6104	N	0	0
6105	N	0	0
6106	N	0	0
6107	N	0	0
6108	N	0	0
6109	N	0	0
6110	N	0	0
n	10	10	10

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Home cage observation

Period : Administration

Generation : F0 Sex : Female Week : 5 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
5101	N	0	0
5102	N	0	0
5103	N	0	0
5104	N	0	0
5105	N	0	0
5106	N	0	0
5107	N	0	0
5108	N	0	0
5109	N	0	0
5110	N	0	0
n	10	10	10

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 61 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : Administration

Generation : F0 Sex : Female Week : 5 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
6101	N	0	0
6102	N	0	0
6103	N	0	0
6104	N	0	0
6105	N	0	0
6106	N	0	0
6107	N	0	0
6108	N	0	0
6109	N	0	0
6110	N	0	0
n	10	10	10

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Home cage observation

Period : Administration

Generation : F0 Sex : Female Week : 6 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
5101	N	0	0
5102	N	0	0
5103	N	0	0
5104	N	0	0
5105	N	0	0
5106	N	0	0
5107	N	0	0
5108	N	0	0
5109	N	0	0
5110	N	0	0
n	10	10	10

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Home cage observation

Period : Administration

Generation : F0 Sex : Female Week : 6 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
6101	N	0	0
6102	N	0	0
6103	N	0	0
6104	N	0	0
6105	N	0	0
6106	N	0	0
6107	N	0	0
6108	N	0	0
6109	N	0	0
6110	N	0	0
n	10	10	10

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Home cage observation

Period : Recovery

Generation : F0 Sex : Male Week : 1 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
1008	N	0	0
1009	N	0	0
1010	N	0	0
1011	N	0	0
1012	N	0	0
n	5	5	5

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 65 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : Recovery

Generation : F0 Sex : Male Week : 1 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
4008	N	0	0
4009	N	0	0
4010	N	0	0
4011	N	0	0
4012	N	0	0
n	5	5	5

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Home cage observation

Period : Recovery

Generation : F0 Sex : Male Week : 2 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
1008	N	0	0
1009	N	0	0
1010	N	0	0
1011	N	0	0
1012	N	0	0
n	5	5	5

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 67 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : Recovery

Generation : F0 Sex : Male Week : 2 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
4008	N	0	0
4009	N	0	0
4010	N	0	0
4011	N	0	0
4012	N	0	0
n	5	5	5

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 68 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : Recovery

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
5106	N	0	0
5107	N	0	0
5108	N	0	0
5109	N	0	0
5110	N	0	0
n	5	5	5

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 69 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : Recovery

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
6106	N	0	0
6107	N	0	0
6108	N	0	0
6109	N	0	0
6110	N	0	0
n	5	5	5

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 70 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : Recovery

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
5106	N	0	0
5107	N	0	0
5108	N	0	0
5109	N	0	0
5110	N	0	0
n	5	5	5

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2 - 71 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Home cage observation Period : Recovery

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Posture	Convulsion	Abnormal behavior
6106	N	0	0
6107	N	0	0
6108	N	0	0
6109	N	0	0
6110	N	0	0
n	5	5	5

Posture) N: Normal, F: Flattened, H: Hunched
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 before mating

Generation : F0 Sex : Male Week : 1 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
1001	0	0	0	0	0	0	0	0
1002	0	0	0	0	0	0	0	0
1003	0	0	0	0	0	0	0	0
1004	0	0	0	0	0	0	0	0
1005	0	0	0	0	0	0	0	0
1006	0	0	0	0	0	0	0	0
1007	0	0	0	0	0	0	0	0
1008	0	0	0	0	0	0	0	0
1009	0	0	0	0	0	0	0	0
1010	0	0	0	0	0	0	0	0
1011	0	0	0	0	0	0	0	0
1012	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
1001	0	0	0	0	0	0
1002	0	0	0	0	0	0
1003	0	0	0	0	0	0
1004	0	0	0	0	0	0
1005	0	0	0	0	0	0
1006	0	0	0	0	0	0
1007	0	0	0	0	0	0
1008	0	0	0	0	0	0
1009	0	0	0	0	0	0
1010	0	0	0	0	0	0
1011	0	0	0	0	0	0
1012	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

In-the-hand observation

Period : F0 before mating

Generation : F0 Sex : Male Week : 1 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
2001	0	0	0	0	0	0	0	0
2002	0	0	0	0	0	0	0	0
2003	0	0	0	0	0	0	0	0
2004	0	0	0	0	0	0	0	0
2005	0	0	0	0	0	0	0	0
2006	0	0	0	0	0	0	0	0
2007	0	0	0	0	0	0	0	0
2008	0	0	0	0	0	0	0	0
2009	0	0	0	0	0	0	0	0
2010	0	0	0	0	0	0	0	0
2011	0	0	0	0	0	0	0	0
2012	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
2001	0	0	0	0	0	0
2002	0	0	0	0	0	0
2003	0	0	0	0	0	0
2004	0	0	0	0	0	0
2005	0	0	0	0	0	0
2006	0	0	0	0	0	0
2007	0	0	0	0	0	0
2008	0	0	0	0	0	0
2009	0	0	0	0	0	0
2010	0	0	0	0	0	0
2011	0	0	0	0	0	0
2012	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 before mating

Generation : F0 Sex : Male Week : 1 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
3001	0	0	0	0	0	0	0	0
3002	0	0	0	0	0	0	0	0
3003	0	0	0	0	0	0	0	0
3004	0	0	0	0	0	0	0	0
3005	0	0	0	0	0	0	0	0
3006	0	0	0	0	0	0	0	0
3007	0	0	0	0	0	0	0	0
3008	0	0	0	0	0	0	0	0
3009	0	0	0	0	0	0	0	0
3010	0	0	0	0	0	0	0	0
3011	0	0	0	0	0	0	0	0
3012	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
3001	0	0	0	0	0	0
3002	0	0	0	0	0	0
3003	0	0	0	0	0	0
3004	0	0	0	0	0	0
3005	0	0	0	0	0	0
3006	0	0	0	0	0	0
3007	0	0	0	0	0	0
3008	0	0	0	0	0	0
3009	0	0	0	0	0	0
3010	0	0	0	0	0	0
3011	0	0	0	0	0	0
3012	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 before mating

Generation : F0 Sex : Male Week : 1 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
4001	0	0	0	0	0	0	0	0
4002	0	0	0	0	0	0	0	0
4003	0	0	0	0	0	0	0	0
4004	0	0	0	0	0	0	0	0
4005	0	0	0	0	0	0	0	0
4006	0	0	0	0	0	0	0	0
4007	0	0	0	0	0	0	0	0
4008	0	0	0	0	0	0	0	0
4009	0	0	0	0	0	0	0	0
4010	0	0	0	0	0	0	0	0
4011	0	0	0	0	0	0	0	0
4012	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
4001	0	0	0	0	0	0
4002	0	0	0	0	0	0
4003	0	0	0	0	0	0
4004	0	0	0	0	0	0
4005	0	0	0	0	0	0
4006	0	0	0	0	0	0
4007	0	0	0	0	0	0
4008	0	0	0	0	0	0
4009	0	0	0	0	0	0
4010	0	0	0	0	0	0
4011	0	0	0	0	0	0
4012	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 before mating

Generation : F0 Sex : Male Week : 2 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
1001	0	0	0	0	0	0	0	0
1002	0	0	0	0	0	0	0	0
1003	0	0	0	0	0	0	0	0
1004	0	0	0	0	0	0	0	0
1005	0	0	0	0	0	0	0	0
1006	0	0	0	0	0	0	0	0
1007	0	0	0	0	0	0	0	0
1008	0	0	0	0	0	0	0	0
1009	0	0	0	0	0	0	0	0
1010	0	0	0	0	0	0	0	0
1011	0	0	0	0	0	0	0	0
1012	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
1001	0	0	0	0	0	0
1002	0	0	0	0	0	0
1003	0	0	0	0	0	0
1004	0	0	0	0	0	0
1005	0	0	0	0	0	0
1006	0	0	0	0	0	0
1007	0	0	0	0	0	0
1008	0	0	0	0	0	0
1009	0	0	0	0	0	0
1010	0	0	0	0	0	0
1011	0	0	0	0	0	0
1012	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

In-the-hand observation

Period : F0 before mating

Generation : F0 Sex : Male Week : 2 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
2001	0	0	0	0	0	0	0	0
2002	0	0	0	0	0	0	0	0
2003	0	0	0	0	0	0	0	0
2004	0	0	0	0	0	0	0	0
2005	0	0	0	0	0	0	0	0
2006	0	0	0	0	0	0	0	0
2007	0	0	0	0	0	0	0	0
2008	0	0	0	0	0	0	0	0
2009	0	0	0	0	0	0	0	0
2010	0	0	0	0	0	0	0	0
2011	0	0	0	0	0	0	0	0
2012	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
2001	0	0	0	0	0	0
2002	0	0	0	0	0	0
2003	0	0	0	0	0	0
2004	0	0	0	0	0	0
2005	0	0	0	0	0	0
2006	0	0	0	0	0	0
2007	0	0	0	0	0	0
2008	0	0	0	0	0	0
2009	0	0	0	0	0	0
2010	0	0	0	0	0	0
2011	0	0	0	0	0	0
2012	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 before mating

Generation : F0 Sex : Male Week : 2 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
3001	0	0	0	0	0	0	0	0
3002	0	0	0	0	0	0	0	0
3003	0	0	0	0	0	0	0	0
3004	0	0	0	0	0	0	0	0
3005	0	0	0	0	0	0	0	0
3006	0	0	0	0	0	0	0	0
3007	0	0	0	0	0	0	0	0
3008	0	0	0	0	0	0	0	0
3009	0	0	0	0	0	0	0	0
3010	0	0	0	0	0	0	0	0
3011	0	0	0	0	0	0	0	0
3012	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
3001	0	0	0	0	0	0
3002	0	0	0	0	0	0
3003	0	0	0	0	0	0
3004	0	0	0	0	0	0
3005	0	0	0	0	0	0
3006	0	0	0	0	0	0
3007	0	0	0	0	0	0
3008	0	0	0	0	0	0
3009	0	0	0	0	0	0
3010	0	0	0	0	0	0
3011	0	0	0	0	0	0
3012	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

In-the-hand observation

Period : F0 before mating

Generation : F0 Sex : Male Week : 2 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
4001	0	0	0	0	0	0	0	0
4002	0	0	0	0	0	0	0	0
4003	0	0	0	0	0	0	0	0
4004	0	0	0	0	0	0	0	0
4005	0	0	0	0	0	0	0	0
4006	0	0	0	0	0	0	0	0
4007	0	0	0	0	0	0	0	0
4008	0	0	0	0	0	0	0	0
4009	0	0	0	0	0	0	0	0
4010	0	0	0	0	0	0	0	0
4011	0	0	0	0	0	0	0	0
4012	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
4001	0	0	0	0	0	0
4002	0	0	0	0	0	0
4003	0	0	0	0	0	0
4004	0	0	0	0	0	0
4005	0	0	0	0	0	0
4006	0	0	0	0	0	0
4007	0	0	0	0	0	0
4008	0	0	0	0	0	0
4009	0	0	0	0	0	0
4010	0	0	0	0	0	0
4011	0	0	0	0	0	0
4012	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

In-the-hand observation

Period : F0 mating

Generation : F0 Sex : Male Week : 3 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
1001	0	0	0	0	0	0	0	0
1002	0	0	0	0	0	0	0	0
1003	0	0	0	0	0	0	0	0
1004	0	0	0	0	0	0	0	0
1005	0	0	0	0	0	0	0	0
1006	0	0	0	0	0	0	0	0
1007	0	0	0	0	0	0	0	0
1008	0	0	0	0	0	0	0	0
1009	0	0	0	0	0	0	0	0
1010	0	0	0	0	0	0	0	0
1011	0	0	0	0	0	0	0	0
1012	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
1001	0	0	0	0	0	0
1002	0	0	0	0	0	0
1003	0	0	0	0	0	0
1004	0	0	0	0	0	0
1005	0	0	0	0	0	0
1006	0	0	0	0	0	0
1007	0	0	0	0	0	0
1008	0	0	0	0	0	0
1009	0	0	0	0	0	0
1010	0	0	0	0	0	0
1011	0	0	0	0	0	0
1012	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 mating

Generation : F0 Sex : Male Week : 3 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
2001	0	0	0	0	0	0	0	0
2002	0	0	0	0	0	0	0	0
2003	0	0	0	0	0	0	0	0
2004	0	0	0	0	0	0	0	0
2005	0	0	0	0	0	0	0	0
2006	0	0	0	0	0	0	0	0
2007	0	0	0	0	0	0	0	0
2008	0	0	0	0	0	0	0	0
2009	0	0	0	0	0	0	0	0
2010	0	0	0	0	0	0	0	0
2011	0	0	0	0	0	0	0	0
2012	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
2001	0	0	0	0	0	0
2002	0	0	0	0	0	0
2003	0	0	0	0	0	0
2004	0	0	0	0	0	0
2005	0	0	0	0	0	0
2006	0	0	0	0	0	0
2007	0	0	0	0	1	0
2008	0	0	0	0	0	0
2009	0	0	0	0	0	0
2010	0	0	0	0	0	0
2011	0	0	0	0	0	0
2012	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 mating

Generation : F0 Sex : Male Week : 3 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
3001	0	0	0	0	0	0	0	0
3002	0	0	0	0	0	0	0	0
3003	0	0	0	0	0	0	0	0
3004	0	0	0	0	0	0	0	0
3005	0	0	0	0	0	0	0	0
3006	0	0	0	0	0	0	0	0
3007	0	0	0	0	0	0	0	0
3008	0	0	0	0	0	0	0	0
3009	0	0	0	0	0	0	0	0
3010	0	0	0	0	0	0	0	0
3011	0	0	0	0	0	0	0	0
3012	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
3001	0	0	0	0	0	0
3002	0	0	0	0	0	0
3003	0	0	0	0	0	0
3004	0	0	0	0	0	0
3005	0	0	0	0	0	0
3006	0	0	0	0	0	0
3007	0	0	0	0	0	0
3008	0	0	0	0	0	0
3009	0	0	0	0	1	0
3010	0	0	0	0	0	0
3011	0	0	0	0	0	0
3012	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 mating

Generation : F0 Sex : Male Week : 3 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
4001	0	0	0	0	0	0	0	0
4002	0	0	0	0	0	0	0	0
4003	0	0	0	0	0	0	0	0
4004	0	0	0	0	0	0	0	0
4005	0	0	0	0	0	0	0	0
4006	0	0	0	0	0	0	0	0
4007	0	0	0	0	0	0	0	0
4008	0	0	0	0	0	0	0	0
4009	0	0	0	0	0	0	0	0
4010	0	0	0	0	0	0	0	0
4011	0	0	0	0	0	0	0	0
4012	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
4001	0	0	0	0	0	0
4002	0	0	0	0	0	0
4003	0	0	0	0	1	0
4004	0	0	0	0	0	0
4005	0	0	0	0	1	0
4006	0	0	0	0	0	0
4007	0	0	0	0	0	0
4008	0	0	0	0	0	0
4009	0	0	0	0	0	0
4010	0	0	0	0	0	0
4011	0	0	0	0	0	0
4012	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 mating

Generation : F0 Sex : Male Week : 4 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
1001	0	0	0	0	0	0	0	0
1002	0	0	0	0	0	0	0	0
1003	0	0	0	0	0	0	0	0
1004	0	0	0	0	0	0	0	0
1005	0	0	0	0	0	0	0	0
1006	0	0	0	0	0	0	0	0
1007	0	0	0	0	0	0	0	0
1008	0	0	0	0	0	0	0	0
1009	0	0	0	0	0	0	0	0
1010	0	0	0	0	0	0	0	0
1011	0	0	0	0	0	0	0	0
1012	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
1001	0	0	0	0	0	0
1002	0	0	0	0	0	0
1003	0	0	0	0	0	0
1004	0	0	0	0	0	0
1005	0	0	0	0	0	0
1006	0	0	0	0	0	0
1007	0	0	0	0	0	0
1008	0	0	0	0	0	0
1009	0	0	0	0	0	0
1010	0	0	0	0	0	0
1011	0	0	0	0	0	0
1012	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 mating

Generation : F0 Sex : Male Week : 4 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
2001	0	0	0	0	0	0	0	0
2002	0	0	0	0	0	0	0	0
2003	0	0	0	0	0	0	0	0
2004	0	0	0	0	0	0	0	0
2005	0	0	0	0	0	0	0	0
2006	0	0	0	0	0	0	0	0
2007	0	0	0	0	0	0	0	0
2008	0	0	0	0	0	0	0	0
2009	0	0	0	0	0	0	0	0
2010	0	0	0	0	0	0	0	0
2011	0	0	0	0	0	0	0	0
2012	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
2001	0	0	0	0	0	0
2002	0	0	0	0	0	0
2003	0	0	0	0	0	0
2004	0	0	0	0	0	0
2005	0	0	0	0	0	0
2006	0	0	0	0	0	0
2007	0	0	0	0	1	0
2008	0	0	0	0	0	0
2009	0	0	0	0	0	0
2010	0	0	0	0	0	0
2011	0	0	0	0	0	0
2012	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 mating

Generation : F0 Sex : Male Week : 4 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
3001	0	0	0	0	0	0	0	0
3002	0	0	0	0	0	0	0	0
3003	0	0	0	0	0	0	0	0
3004	0	0	0	0	0	0	0	0
3005	0	0	0	0	0	0	0	0
3006	0	0	0	0	0	0	0	0
3007	0	0	0	0	0	0	0	0
3008	0	0	0	0	0	0	0	0
3009	0	0	0	0	0	0	0	0
3010	0	0	0	0	0	0	0	0
3011	0	0	0	0	0	0	0	0
3012	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
3001	0	0	0	0	0	0
3002	0	0	0	0	0	0
3003	0	0	0	0	0	0
3004	0	0	0	0	0	0
3005	0	0	0	0	0	0
3006	0	0	0	0	0	0
3007	0	0	0	0	0	0
3008	0	0	0	0	0	0
3009	0	0	0	0	0	0
3010	0	0	0	0	0	0
3011	0	0	0	0	0	0
3012	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 mating

Generation : F0 Sex : Male Week : 4 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
4001	0	0	0	0	0	0	0	0
4002	0	0	0	0	0	0	0	0
4003	0	0	0	0	0	0	0	0
4004	0	0	0	0	0	0	0	0
4005	0	0	0	0	0	0	0	0
4006	0	0	0	0	0	0	0	0
4007	0	0	0	0	0	0	0	0
4008	0	0	0	0	0	0	0	0
4009	0	0	0	0	0	0	0	0
4010	0	0	0	0	0	0	0	0
4011	0	0	0	0	0	0	0	0
4012	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
4001	0	0	0	0	0	0
4002	0	0	0	0	0	0
4003	0	0	0	0	1	0
4004	0	0	0	0	0	0
4005	0	0	0	0	0	0
4006	0	0	0	0	0	0
4007	0	0	0	0	0	0
4008	0	0	0	0	0	0
4009	0	0	0	0	0	0
4010	0	0	0	0	0	0
4011	0	0	0	0	0	0
4012	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 mating

Generation : F0 Sex : Male Week : 5 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
1001	0	0	0	0	0	0	0	0
1002	0	0	0	0	0	0	0	0
1003	0	0	0	0	0	0	0	0
1004	0	0	0	0	0	0	0	0
1005	0	0	0	0	0	0	0	0
1006	0	0	0	0	0	0	0	0
1007	0	0	0	0	0	0	0	0
1008	0	0	0	0	0	0	0	0
1009	0	0	0	0	0	0	0	0
1010	0	0	0	0	0	0	0	0
1011	0	0	0	0	0	0	0	0
1012	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
1001	0	0	0	0	0	0
1002	0	0	0	0	0	0
1003	0	0	0	0	0	0
1004	0	0	0	0	0	0
1005	0	0	0	0	1	1
1006	0	0	0	0	0	0
1007	0	0	0	0	0	0
1008	0	0	0	0	0	0
1009	0	0	0	0	0	0
1010	0	0	0	0	1	1
1011	0	0	0	0	0	0
1012	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 mating

Generation : F0 Sex : Male Week : 5 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
2001	0	0	0	0	0	0	0	0
2002	0	0	0	0	0	0	0	0
2003	0	0	0	0	0	0	0	0
2004	0	0	0	0	0	0	0	0
2005	0	0	0	0	0	0	0	0
2006	0	0	0	0	0	0	0	0
2007	0	0	0	0	0	0	0	0
2008	0	0	0	0	0	0	0	0
2009	0	0	0	0	0	0	0	0
2010	0	0	0	0	0	0	0	0
2011	0	0	0	0	0	0	0	0
2012	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
2001	0	0	0	0	0	0
2002	0	0	0	0	0	0
2003	0	0	0	0	0	0
2004	0	0	0	0	0	0
2005	0	0	0	0	0	0
2006	0	0	0	0	0	0
2007	0	0	0	0	0	0
2008	0	0	0	0	0	0
2009	0	0	0	0	0	0
2010	0	0	0	0	0	0
2011	0	0	0	0	0	0
2012	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 mating

Generation : F0 Sex : Male Week : 5 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
3001	0	0	0	0	0	0	0	0
3002	0	0	0	0	0	0	0	0
3003	0	0	0	0	0	0	0	0
3004	0	0	0	0	0	0	0	0
3005	0	0	0	0	0	0	0	0
3006	0	0	0	0	0	0	0	0
3007	0	0	0	0	0	0	0	0
3008	0	0	0	0	0	0	0	0
3009	0	0	0	0	0	0	0	0
3010	0	0	0	0	0	0	0	0
3011	0	0	0	0	0	0	0	0
3012	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
3001	0	0	0	0	0	0
3002	0	0	0	0	0	0
3003	0	0	0	0	0	0
3004	0	0	0	0	0	0
3005	0	0	0	0	0	0
3006	0	0	0	0	0	0
3007	0	0	0	0	0	0
3008	0	0	0	0	0	0
3009	0	0	0	0	0	0
3010	0	0	0	0	0	0
3011	0	0	0	0	0	0
3012	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 mating

Generation : F0 Sex : Male Week : 5 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
4001	0	0	0	0	0	0	0	0
4002	0	0	0	0	0	0	0	0
4003	0	0	0	0	0	0	0	0
4004	0	0	0	0	0	0	0	0
4005	0	0	0	0	0	0	0	0
4006	0	0	0	0	0	0	0	0
4007	0	0	0	0	0	0	0	0
4008	0	0	0	0	0	0	0	0
4009	0	0	0	0	0	0	0	0
4010	0	0	0	0	0	0	0	0
4011	0	0	0	0	0	0	0	0
4012	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
4001	0	0	0	0	0	0
4002	0	0	0	0	0	0
4003	0	0	0	0	0	0
4004	0	0	0	0	0	0
4005	0	0	0	0	0	0
4006	0	0	0	0	0	0
4007	0	0	0	0	0	0
4008	0	0	0	0	1	0
4009	0	0	0	0	0	0
4010	0	0	0	0	0	0
4011	0	0	0	0	0	0
4012	0	0	0	0	1	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 mating

Generation : F0 Sex : Male Week : 6 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
1001	0	0	0	0	0	0	0	0
1002	0	0	0	0	0	0	0	0
1003	0	0	0	0	0	0	0	0
1004	0	0	0	0	0	0	0	0
1005	0	0	0	0	0	0	0	0
1006	0	0	0	0	0	0	0	0
1007	0	0	0	0	0	0	0	0
1008	0	0	0	0	0	0	0	0
1009	0	0	0	0	0	0	0	0
1010	0	0	0	0	0	0	0	0
1011	0	0	0	0	0	0	0	0
1012	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
1001	0	0	0	0	0	0
1002	0	0	0	0	0	0
1003	0	0	0	0	0	0
1004	0	0	0	0	0	0
1005	0	0	0	0	0	0
1006	0	0	0	0	0	0
1007	0	0	0	0	0	0
1008	0	0	0	0	0	0
1009	0	0	0	0	0	0
1010	0	0	0	0	0	0
1011	0	0	0	0	0	0
1012	0	0	0	0	1	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 mating

Generation : F0 Sex : Male Week : 6 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
2001	0	0	0	0	0	0	0	0
2002	0	0	0	0	0	0	0	0
2003	0	0	0	0	0	0	0	0
2004	0	0	0	0	0	0	0	0
2005	0	0	0	0	0	0	0	0
2006	0	0	0	0	0	0	0	0
2007	0	0	0	0	0	0	0	0
2008	0	0	0	0	0	0	0	0
2009	0	0	0	0	0	0	0	0
2010	0	0	0	0	0	0	0	0
2011	0	0	0	0	0	0	0	0
2012	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
2001	0	0	0	0	0	0
2002	0	0	0	0	0	0
2003	0	0	0	0	0	0
2004	0	0	0	0	0	0
2005	0	0	0	0	0	0
2006	0	0	0	0	0	0
2007	0	0	0	0	0	0
2008	0	0	0	0	0	0
2009	0	0	0	0	0	0
2010	0	0	0	0	0	0
2011	0	0	0	0	0	0
2012	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 mating

Generation : F0 Sex : Male Week : 6 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
3001	0	0	0	0	0	0	0	0
3002	0	0	0	0	0	0	0	0
3003	0	0	0	0	0	0	0	0
3004	0	0	0	0	0	0	0	0
3005	0	0	0	0	0	0	0	0
3006	0	0	0	0	0	0	0	0
3007	0	0	0	0	0	0	0	0
3008	0	0	0	0	0	0	0	0
3009	0	0	0	0	0	0	0	0
3010	0	0	0	0	0	0	0	0
3011	0	0	0	0	0	0	0	0
3012	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
3001	0	0	0	0	0	0
3002	0	0	0	0	0	0
3003	0	0	0	0	0	0
3004	0	0	0	0	0	0
3005	0	0	0	0	0	0
3006	0	0	0	0	0	0
3007	0	0	0	0	0	0
3008	0	0	0	0	0	0
3009	0	0	0	0	0	0
3010	0	0	0	0	0	0
3011	0	0	0	0	0	0
3012	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 mating

Generation : F0 Sex : Male Week : 6 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
4001	0	0	0	0	0	0	0	0
4002	0	0	0	0	0	0	0	0
4003	0	0	0	0	0	0	0	0
4004	0	0	0	0	0	0	0	0
4005	0	0	0	0	0	0	0	0
4006	0	0	0	0	0	0	0	0
4007	0	0	0	0	0	0	0	0
4008	0	0	0	0	0	0	0	0
4009	0	0	0	0	0	0	0	0
4010	0	0	0	0	0	0	0	0
4011	0	0	0	0	0	0	0	0
4012	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
4001	0	0	0	0	0	0
4002	0	0	0	0	0	0
4003	0	0	0	0	0	0
4004	0	0	0	0	0	0
4005	0	0	0	0	0	0
4006	0	0	0	0	0	0
4007	0	0	0	0	0	0
4008	0	0	0	0	0	0
4009	0	0	0	0	0	0
4010	0	0	0	0	0	0
4011	0	0	0	0	0	0
4012	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 before mating

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
1101	0	0	0	0	0	0	0	0
1102	0	0	0	0	0	0	0	0
1103	0	0	0	0	0	0	0	0
1104	0	0	0	0	0	0	0	0
1105	0	0	0	0	0	0	0	0
1106	0	0	0	0	0	0	0	0
1107	0	0	0	0	0	0	0	0
1108	0	0	0	0	0	0	0	0
1109	0	0	0	0	0	0	0	0
1110	0	0	0	0	0	0	0	0
1111	0	0	0	0	0	0	0	0
1112	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
1101	0	0	0	0	0	0
1102	0	0	0	0	0	0
1103	0	0	0	0	0	0
1104	0	0	0	0	0	0
1105	0	0	0	0	0	0
1106	0	0	0	0	0	0
1107	0	0	0	0	0	0
1108	0	0	0	0	0	0
1109	0	0	0	0	0	0
1110	0	0	0	0	0	0
1111	0	0	0	0	0	0
1112	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

In-the-hand observation

Period : F0 before mating

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
2101	0	0	0	0	0	0	0	0
2102	0	0	0	0	0	0	0	0
2103	0	0	0	0	0	0	0	0
2104	0	0	0	0	0	0	0	0
2105	0	0	0	0	0	0	0	0
2106	0	0	0	0	0	0	0	0
2107	0	0	0	0	0	0	0	0
2108	0	0	0	0	0	0	0	0
2109	0	0	0	0	0	0	0	0
2110	0	0	0	0	0	0	0	0
2111	0	0	0	0	0	0	0	0
2112	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
2101	0	0	0	0	0	0
2102	0	0	0	0	0	0
2103	0	0	0	0	0	0
2104	0	0	0	0	0	0
2105	0	0	0	0	0	0
2106	0	0	0	0	0	0
2107	0	0	0	0	0	0
2108	0	0	0	0	0	0
2109	0	0	0	0	0	0
2110	0	0	0	0	0	0
2111	0	0	0	0	0	0
2112	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 before mating

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
3101	0	0	0	0	0	0	0	0
3102	0	0	0	0	0	0	0	0
3103	0	0	0	0	0	0	0	0
3104	0	0	0	0	0	0	0	0
3105	0	0	0	0	0	0	0	0
3106	0	0	0	0	0	0	0	0
3107	0	0	0	0	0	0	0	0
3108	0	0	0	0	0	0	0	0
3109	0	0	0	0	0	0	0	0
3110	0	0	0	0	0	0	0	0
3111	0	0	0	0	0	0	0	0
3112	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
3101	0	0	0	0	0	0
3102	0	0	0	0	0	0
3103	0	0	0	0	0	0
3104	0	0	0	0	0	0
3105	0	0	0	0	0	0
3106	0	0	0	0	0	0
3107	0	0	0	0	0	0
3108	0	0	0	0	0	0
3109	0	0	0	0	0	0
3110	0	0	0	0	0	0
3111	0	0	0	0	0	0
3112	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 before mating

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
4101	0	0	0	0	0	0	0	0
4102	0	0	0	0	0	0	0	0
4103	0	0	0	0	0	0	0	0
4104	0	0	0	0	0	0	0	0
4105	0	0	0	0	0	0	0	0
4106	0	0	0	0	0	0	0	0
4107	0	0	0	0	0	0	0	0
4108	0	0	0	0	0	0	0	0
4109	0	0	0	0	0	0	0	0
4110	0	0	0	0	0	0	0	0
4111	0	0	0	0	0	0	0	0
4112	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
4101	0	0	0	0	0	0
4102	0	0	0	0	0	0
4103	0	0	0	0	0	0
4104	0	0	0	0	0	0
4105	0	0	0	0	0	0
4106	0	0	0	0	0	0
4107	0	0	0	0	0	0
4108	0	0	0	0	0	0
4109	0	0	0	0	0	0
4110	0	0	0	0	1	1
4111	0	0	0	0	0	0
4112	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 before mating

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
1101	0	0	0	0	0	0	0	0
1102	0	0	0	0	0	0	0	0
1103	0	0	0	0	0	0	0	0
1104	0	0	0	0	0	0	0	0
1105	0	0	0	0	0	0	0	0
1106	0	0	0	0	0	0	0	0
1107	0	0	0	0	0	0	0	0
1108	0	0	0	0	0	0	0	0
1109	0	0	0	0	0	0	0	0
1110	0	0	0	0	0	0	0	0
1111	0	0	0	0	0	0	0	0
1112	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
1101	0	0	0	0	0	0
1102	0	0	0	0	0	0
1103	0	0	0	0	0	0
1104	0	0	0	0	0	0
1105	0	0	0	0	0	0
1106	0	0	0	0	0	0
1107	0	0	0	0	0	0
1108	0	0	0	0	0	0
1109	0	0	0	0	0	0
1110	0	0	0	0	0	0
1111	0	0	0	0	0	0
1112	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

In-the-hand observation

Period : F0 before mating

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
2101	0	0	0	0	0	0	0	0
2102	0	0	0	0	0	0	0	0
2103	0	0	0	0	0	0	0	0
2104	0	0	0	0	0	0	0	0
2105	0	0	0	0	0	0	0	0
2106	0	0	0	0	0	0	0	0
2107	0	0	0	0	0	0	0	0
2108	0	0	0	0	0	0	0	0
2109	0	0	0	0	0	0	0	0
2110	0	0	0	0	0	0	0	0
2111	0	0	0	0	0	0	0	0
2112	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
2101	0	0	0	0	0	0
2102	0	0	0	0	0	0
2103	0	0	0	0	0	0
2104	0	0	0	0	0	0
2105	0	0	0	0	0	0
2106	0	0	0	0	0	0
2107	0	0	0	0	0	0
2108	0	0	0	0	0	0
2109	0	0	0	0	0	0
2110	0	0	0	0	0	0
2111	0	0	0	0	0	0
2112	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 before mating

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
3101	0	0	0	0	0	0	0	0
3102	0	0	0	0	0	0	0	0
3103	0	0	0	0	0	0	0	0
3104	0	0	0	0	0	0	0	0
3105	0	0	0	0	0	0	0	0
3106	0	0	0	0	0	0	0	0
3107	0	0	0	0	0	0	0	0
3108	0	0	0	0	0	0	0	0
3109	0	0	0	0	0	0	0	0
3110	0	0	0	0	0	0	0	0
3111	0	0	0	0	0	0	0	0
3112	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
3101	0	0	0	0	0	0
3102	0	0	0	0	0	0
3103	0	0	0	0	0	0
3104	0	0	0	0	0	0
3105	0	0	0	0	0	0
3106	0	0	0	0	0	0
3107	0	0	0	0	0	0
3108	0	0	0	0	0	0
3109	0	0	0	0	1	0
3110	0	0	0	0	0	0
3111	0	0	0	0	0	0
3112	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 before mating

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
4101	0	0	0	0	0	0	0	0
4102	0	0	0	0	0	0	0	0
4103	0	0	0	0	0	0	0	0
4104	0	0	0	0	0	0	0	0
4105	0	0	0	0	0	0	0	0
4106	0	0	0	0	0	0	0	0
4107	0	0	0	0	0	0	0	0
4108	0	0	0	0	0	0	0	0
4109	0	0	0	0	0	0	0	0
4110	0	0	0	0	0	0	0	0
4111	0	0	0	0	0	0	0	0
4112	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
4101	0	0	0	0	0	0
4102	0	0	0	0	0	0
4103	0	0	0	0	0	0
4104	0	0	0	0	0	0
4105	0	0	0	0	0	0
4106	0	0	0	0	0	0
4107	0	0	0	0	0	0
4108	0	0	0	0	0	0
4109	0	0	0	0	1	0
4110	0	0	0	0	1	1
4111	0	0	0	0	0	0
4112	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 1 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
1101	0	0	0	0	0	0	0	0
1102	0	0	0	0	0	0	0	0
1103	0	0	0	0	0	0	0	0
1104	0	0	0	0	0	0	0	0
1105	0	0	0	0	0	0	0	0
1106	0	0	0	0	0	0	0	0
1107	0	0	0	0	0	0	0	0
1108	0	0	0	0	0	0	0	0
1109	0	0	0	0	0	0	0	0
1110	0	0	0	0	0	0	0	0
1111	0	0	0	0	0	0	0	0
1112	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
1101	0	0	0	0	0	0
1102	0	0	0	0	0	0
1103	0	0	0	0	0	0
1104	0	0	0	0	0	0
1105	0	0	0	0	0	0
1106	0	0	0	0	0	0
1107	0	0	0	0	0	0
1108	0	0	0	0	0	0
1109	0	0	0	0	0	0
1110	0	0	0	0	0	0
1111	0	0	0	0	0	0
1112	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 1 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
2101	0	0	0	0	0	0	0	0
2102	0	0	0	0	0	0	0	0
2103	0	0	0	0	0	0	0	0
2104	0	0	0	0	0	0	0	0
2105	0	0	0	0	0	0	0	0
2106	0	0	0	0	0	0	0	0
2107	0	0	0	0	0	0	0	0
2108	0	0	0	0	0	0	0	0
2109	0	0	0	0	0	0	0	0
2110	0	0	0	0	0	0	0	0
2111	0	0	0	0	0	0	0	0
2112	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
2101	0	0	0	0	0	0
2102	0	0	0	0	0	0
2103	0	0	0	0	0	0
2104	0	0	0	0	0	0
2105	0	0	0	0	0	0
2106	0	0	0	0	0	0
2107	0	0	0	0	0	0
2108	0	0	0	0	0	0
2109	0	0	0	0	0	0
2110	0	0	0	0	0	0
2111	0	0	0	0	0	0
2112	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 1 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
3101	0	0	0	0	0	0	0	0
3102	0	0	0	0	0	0	0	0
3103	0	0	0	0	0	0	0	0
3104	0	0	0	0	0	0	0	0
3105	0	0	0	0	0	0	0	0
3106	0	0	0	0	0	0	0	0
3107	0	0	0	0	0	0	0	0
3108	0	0	0	0	0	0	0	0
3109	0	0	0	0	0	0	0	0
3110	0	0	0	0	0	0	0	0
3111	0	0	0	0	0	0	0	0
3112	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
3101	0	0	0	0	0	0
3102	0	0	0	0	0	0
3103	0	0	0	0	0	0
3104	0	0	0	0	0	0
3105	0	0	0	0	0	0
3106	0	0	0	0	0	0
3107	0	0	0	0	0	0
3108	0	0	0	0	0	0
3109	0	0	0	0	0	0
3110	0	0	0	0	0	0
3111	0	0	0	0	0	0
3112	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 1 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
4101	0	0	0	0	0	0	0	0
4102	0	0	0	0	0	0	0	0
4103	0	0	0	0	0	0	0	0
4104	0	0	0	0	0	0	0	0
4105	0	0	0	0	0	0	0	0
4106	0	0	0	0	0	0	0	0
4107	0	0	0	0	0	0	0	0
4108	0	0	0	0	0	0	0	0
4109	0	0	0	0	0	0	0	0
4110	0	0	0	0	0	0	0	0
4111	0	0	0	0	0	0	0	0
4112	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
4101	0	0	0	0	0	0
4102	0	0	0	0	0	0
4103	0	0	0	0	0	0
4104	0	0	0	0	0	0
4105	0	0	0	0	0	0
4106	0	0	0	0	0	0
4107	0	0	0	0	0	0
4108	0	0	0	0	0	0
4109	0	0	0	0	0	0
4110	0	0	0	0	0	0
4111	0	0	0	0	0	0
4112	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 7 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
1101	0	0	0	0	0	0	0	0
1102	0	0	0	0	0	0	0	0
1103	0	0	0	0	0	0	0	0
1104	0	0	0	0	0	0	0	0
1105	0	0	0	0	0	0	0	0
1106	0	0	0	0	0	0	0	0
1107	0	0	0	0	0	0	0	0
1108	0	0	0	0	0	0	0	0
1109	0	0	0	0	0	0	0	0
1110	0	0	0	0	0	0	0	0
1111	0	0	0	0	0	0	0	0
1112	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
1101	0	0	0	0	0	0
1102	0	0	0	0	0	0
1103	0	0	0	0	0	0
1104	0	0	0	0	0	0
1105	0	0	0	0	0	0
1106	0	0	0	0	0	0
1107	0	0	0	0	0	0
1108	0	0	0	0	0	0
1109	0	0	0	0	0	0
1110	0	0	0	0	0	0
1111	0	0	0	0	0	0
1112	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 7 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
2101	0	0	0	0	0	0	0	0
2102	0	0	0	0	0	0	0	0
2103	0	0	0	0	0	0	0	0
2104	0	0	0	0	0	0	0	0
2105	0	0	0	0	0	0	0	0
2106	0	0	0	0	0	0	0	0
2107	0	0	0	0	0	0	0	0
2108	0	0	0	0	0	0	0	0
2109	0	0	0	0	0	0	0	0
2110	0	0	0	0	0	0	0	0
2111	0	0	0	0	0	0	0	0
2112	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
2101	0	0	0	0	0	0
2102	0	0	0	0	0	0
2103	0	0	0	0	0	0
2104	0	0	0	0	0	0
2105	0	0	0	0	1	0
2106	0	0	0	0	0	0
2107	0	0	0	0	0	0
2108	0	0	0	0	0	0
2109	0	0	0	0	1	0
2110	0	0	0	0	0	0
2111	0	0	0	0	0	0
2112	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 7 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
3101	0	0	0	0	0	0	0	0
3102	0	0	0	0	0	0	0	0
3103	0	0	0	0	0	0	0	0
3104	0	0	0	0	0	0	0	0
3105	0	0	0	0	0	0	0	0
3106	0	0	0	0	0	0	0	0
3107	0	0	0	0	0	0	0	0
3108	0	0	0	0	0	0	0	0
3109	0	0	0	0	0	0	0	0
3110	0	0	0	0	0	0	0	0
3111	0	0	0	0	0	0	0	0
3112	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
3101	0	0	0	0	0	0
3102	0	0	0	0	0	0
3103	0	0	0	0	0	0
3104	0	0	0	0	0	0
3105	0	0	0	0	0	0
3106	0	0	0	0	0	0
3107	0	0	0	0	0	0
3108	0	0	0	0	0	0
3109	0	0	0	0	0	0
3110	0	0	0	0	0	0
3111	0	0	0	0	0	0
3112	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 7 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
4101	0	0	0	0	0	0	0	0
4102	0	0	0	0	0	0	0	0
4103	0	0	0	0	0	0	0	0
4104	0	0	0	0	0	0	0	0
4105	0	0	0	0	0	0	0	0
4106	0	0	0	0	0	0	0	0
4107	0	0	0	0	0	0	0	0
4108	0	0	0	0	0	0	0	0
4109	1	0	0	0	0	0	0	0
4110	0	0	0	0	0	0	0	0
4111	0	0	0	0	0	0	0	0
4112	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
4101	0	0	0	0	0	0
4102	0	0	0	0	0	0
4103	0	0	0	0	0	0
4104	0	0	0	0	0	0
4105	0	0	0	0	0	0
4106	0	0	0	0	0	0
4107	0	0	0	0	0	0
4108	0	0	0	0	0	0
4109	0	0	0	0	1	1
4110	0	0	0	0	0	0
4111	0	0	0	0	0	0
4112	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 14 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
1101	0	0	0	0	0	0	0	0
1102	0	0	0	0	0	0	0	0
1103	0	0	0	0	0	0	0	0
1104	0	0	0	0	0	0	0	0
1105	0	0	0	0	0	0	0	0
1106	0	0	0	0	0	0	0	0
1107	0	0	0	0	0	0	0	0
1108	0	0	0	0	0	0	0	0
1109	0	0	0	0	0	0	0	0
1110	0	0	0	0	0	0	0	0
1111	0	0	0	0	0	0	0	0
1112	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
1101	0	0	0	0	0	0
1102	0	0	0	0	0	0
1103	0	0	0	0	0	0
1104	0	0	0	0	0	0
1105	0	0	0	0	0	0
1106	0	0	0	0	0	0
1107	0	0	0	0	0	0
1108	0	0	0	0	0	0
1109	0	0	0	0	0	0
1110	0	0	0	0	0	0
1111	0	0	0	0	0	0
1112	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 14 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
2101	0	0	0	0	0	0	0	0
2102	0	0	0	0	0	0	0	0
2103	0	0	0	0	0	0	0	0
2104	0	0	0	0	0	0	0	0
2105	0	0	0	0	0	0	0	0
2106	0	0	0	0	0	0	0	0
2107	0	0	0	0	0	0	0	0
2108	0	0	0	0	0	0	0	0
2109	0	0	0	0	0	0	0	0
2110	0	0	0	0	0	0	0	0
2111	0	0	0	0	0	0	0	0
2112	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
2101	0	0	0	0	0	0
2102	0	0	0	0	0	0
2103	0	0	0	0	0	0
2104	0	0	0	0	0	0
2105	0	0	0	0	0	0
2106	0	0	0	0	0	0
2107	0	0	0	0	0	0
2108	0	0	0	0	0	0
2109	0	0	0	0	1	0
2110	0	0	0	0	0	0
2111	0	0	0	0	0	0
2112	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 14 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
3101	0	0	0	0	0	0	0	0
3102	0	0	0	0	0	0	0	0
3103	0	0	0	0	0	0	0	0
3104	0	0	0	0	0	0	0	0
3105	0	0	0	0	0	0	0	0
3106	0	0	0	0	0	0	0	0
3107	0	0	0	0	0	0	0	0
3108	0	0	0	0	0	0	0	0
3109	0	0	0	0	0	0	0	0
3110	0	0	0	0	0	0	0	0
3111	0	0	0	0	0	0	0	0
3112	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
3101	0	0	0	0	0	0
3102	0	0	0	0	0	0
3103	0	0	0	0	0	0
3104	0	0	0	0	0	0
3105	0	0	0	0	0	0
3106	0	0	0	0	0	0
3107	0	0	0	0	0	0
3108	0	0	0	0	0	0
3109	0	0	0	0	0	0
3110	0	0	0	0	0	0
3111	0	0	0	0	0	0
3112	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 14 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
4101	0	0	0	0	0	0	0	0
4102	0	0	0	0	0	0	0	0
4103	0	0	0	0	0	0	0	0
4104	0	0	0	0	0	0	0	0
4105	0	0	0	0	0	0	0	0
4106	0	0	0	0	0	0	0	0
4107	0	0	0	0	0	0	0	0
4108	0	0	0	0	0	0	0	0
4109	0	0	0	0	0	0	0	0
4110	0	0	0	0	0	0	0	0
4111	0	0	0	0	0	0	0	0
4112	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
4101	0	0	0	0	0	0
4102	0	0	0	0	0	0
4103	0	0	0	0	0	0
4104	0	0	0	0	0	0
4105	0	0	0	0	0	0
4106	0	0	0	0	0	0
4107	0	0	0	0	0	0
4108	0	0	0	0	0	0
4109	0	0	0	0	1	0
4110	0	0	0	0	0	0
4111	0	0	0	0	0	0
4112	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 20 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
1101	0	0	0	0	0	0	0	0
1102	0	0	0	0	0	0	0	0
1103	0	0	0	0	0	0	0	0
1104	0	0	0	0	0	0	0	0
1105	0	0	0	0	0	0	0	0
1106	0	0	0	0	0	0	0	0
1107	0	0	0	0	0	0	0	0
1108	0	0	0	0	0	0	0	0
1109	0	0	0	0	0	0	0	0
1110	0	0	0	0	0	0	0	0
1111	0	0	0	0	0	0	0	0
1112	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
1101	0	0	0	0	0	0
1102	0	0	0	0	0	0
1103	0	0	0	0	0	0
1104	0	0	0	0	0	0
1105	0	0	0	0	0	0
1106	0	0	0	0	0	0
1107	0	0	0	0	0	0
1108	0	0	0	0	0	0
1109	0	0	0	0	0	0
1110	0	0	0	0	0	0
1111	0	0	0	0	0	0
1112	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 20 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
2101	0	0	0	0	0	0	0	0
2102	0	0	0	0	0	0	0	0
2103	0	0	0	0	0	0	0	0
2104	0	0	0	0	0	0	0	0
2105	0	0	0	0	0	0	0	0
2106	0	0	0	0	0	0	0	0
2107	0	0	0	0	0	0	0	0
2108	0	0	0	0	0	0	0	0
2109	0	0	0	0	0	0	0	0
2110	0	0	0	0	0	0	0	0
2111	0	0	0	0	0	0	0	0
2112	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
2101	0	0	0	0	0	0
2102	0	0	0	0	0	0
2103	0	0	0	0	0	0
2104	0	0	0	0	0	0
2105	0	0	0	0	0	0
2106	0	0	0	0	0	0
2107	0	0	0	0	0	0
2108	0	0	0	0	0	0
2109	0	0	0	0	0	0
2110	0	0	0	0	0	0
2111	0	0	0	0	0	0
2112	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 20 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
3101	0	0	0	0	0	0	0	0
3102	0	0	0	0	0	0	0	0
3103	0	0	0	0	0	0	0	0
3104	0	0	0	0	0	0	0	0
3105	0	0	0	0	0	0	0	0
3106	0	0	0	0	0	0	0	0
3107	0	0	0	0	0	0	0	0
3108	0	0	0	0	0	0	0	0
3109	0	0	0	0	0	0	0	0
3110	0	0	0	0	0	0	0	0
3111	0	0	0	0	0	0	0	0
3112	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
3101	0	0	0	0	0	0
3102	0	0	0	0	0	0
3103	0	0	0	0	0	0
3104	0	0	0	0	0	0
3105	0	0	0	0	0	0
3106	0	0	0	0	0	0
3107	0	0	0	0	0	0
3108	0	0	0	0	0	0
3109	0	0	0	0	0	0
3110	0	0	0	0	0	0
3111	0	0	0	0	0	0
3112	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 20 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
4101	0	0	0	0	0	0	0	0
4102	0	0	0	0	0	0	0	0
4103	0	0	0	0	0	0	0	0
4104	0	0	0	0	0	0	0	0
4105	0	0	0	0	0	0	0	0
4106	0	0	0	0	0	0	0	0
4107	0	0	0	0	0	0	0	0
4108	0	0	0	0	0	0	0	0
4109	0	0	0	0	0	0	0	0
4110	0	0	0	0	0	0	0	0
4111	0	0	0	0	0	0	0	0
4112	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
4101	0	0	0	0	0	0
4102	0	0	0	0	0	0
4103	0	0	0	0	0	0
4104	0	0	0	0	0	0
4105	0	0	0	0	0	0
4106	0	0	0	0	0	0
4107	0	0	0	0	0	0
4108	0	0	0	0	0	0
4109	0	0	0	0	0	0
4110	0	0	0	0	0	0
4111	0	0	0	0	0	0
4112	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 lactation

Generation : F0 Sex : Female Day : 4 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
1101	0	0	0	0	0	0	0	0
1102	0	0	0	0	0	0	0	0
1103	0	0	0	0	0	0	0	0
1104	0	0	0	0	0	0	0	0
1105	0	0	0	0	0	0	0	0
1106	0	0	0	0	0	0	0	0
1107	0	0	0	0	0	0	0	0
1108	0	0	0	0	0	0	0	0
1109	0	0	0	0	0	0	0	0
1110	0	0	0	0	0	0	0	0
1111	0	0	0	0	0	0	0	0
1112	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
1101	0	0	0	0	0	0
1102	0	0	0	0	0	0
1103	0	0	0	0	0	0
1104	0	0	0	0	0	0
1105	0	0	0	0	0	0
1106	0	0	0	0	0	0
1107	0	0	0	0	0	0
1108	0	0	0	0	0	0
1109	0	0	0	0	0	0
1110	0	0	0	0	0	0
1111	0	0	0	0	0	0
1112	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

In-the-hand observation

Period : F0 lactation

Generation : F0 Sex : Female Day : 4 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
2101	0	0	0	0	0	0	0	0
2102	0	0	0	0	0	0	0	0
2103	0	0	0	0	0	0	0	0
2104	0	0	0	0	0	0	0	0
2105	0	0	0	0	0	0	0	0
2106	0	0	0	0	0	0	0	0
2107	0	0	0	0	0	0	0	0
2108	0	0	0	0	0	0	0	0
2109	0	0	0	0	0	0	0	0
2110	0	0	0	0	0	0	0	0
2111	0	0	0	0	0	0	0	0
2112	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
2101	0	0	0	0	0	0
2102	0	0	0	0	0	0
2103	0	0	0	0	0	0
2104	0	0	0	0	0	0
2105	0	0	0	0	0	0
2106	0	0	0	0	0	0
2107	0	0	0	0	0	0
2108	0	0	0	0	0	0
2109	0	0	0	0	0	0
2110	0	0	0	0	0	0
2111	0	0	0	0	0	0
2112	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : F0 lactation

Generation : F0 Sex : Female Day : 4 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
3101	0	0	0	0	0	0	0	0
3102	0	0	0	0	0	0	0	0
3103	0	0	0	0	0	0	0	0
3104	0	0	0	0	0	0	0	0
3105	0	0	0	0	0	0	0	0
3106	0	0	0	0	0	0	0	0
3107	0	0	0	0	0	0	0	0
3108	0	0	0	0	0	0	0	0
3109	0	0	0	0	0	0	0	0
3110	0	0	0	0	0	0	0	0
3111	0	0	0	0	0	0	0	0
3112	0	0	0	0	0	0	0	0
n	12	12	12	12	12	12	12	12

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
3101	0	0	0	0	0	0
3102	0	0	0	0	0	0
3103	0	0	0	0	0	0
3104	0	0	0	0	0	0
3105	0	0	0	0	0	0
3106	0	0	0	0	0	0
3107	0	0	0	0	0	0
3108	0	0	0	0	0	0
3109	0	0	0	0	0	0
3110	0	0	0	0	0	0
3111	0	0	0	0	0	0
3112	0	0	0	0	0	0
n	12	12	12	12	12	12

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : Administration

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
5101	0	0	0	0	0	0	0	0
5102	0	0	0	0	0	0	0	0
5103	0	0	0	0	0	0	0	0
5104	0	0	0	0	0	0	0	0
5105	0	0	0	0	0	0	0	0
5106	0	0	0	0	0	0	0	0
5107	0	0	0	0	0	0	0	0
5108	0	0	0	0	0	0	0	0
5109	0	0	0	0	0	0	0	0
5110	0	0	0	0	0	0	0	0
n	10	10	10	10	10	10	10	10

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
5101	0	0	0	0	0	0
5102	0	0	0	0	0	0
5103	0	0	0	0	0	0
5104	0	0	0	0	0	0
5105	0	0	0	0	0	0
5106	0	0	0	0	0	0
5107	0	0	0	0	0	0
5108	0	0	0	0	0	0
5109	0	0	0	0	0	0
5110	0	0	0	0	0	0
n	10	10	10	10	10	10

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : Administration

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
6101	0	0	0	0	0	0	0	0
6102	0	0	0	0	0	0	0	0
6103	0	0	0	0	0	0	0	0
6104	0	0	0	0	0	0	0	0
6105	0	0	0	0	0	0	0	0
6106	0	0	0	0	0	0	0	0
6107	0	0	0	0	0	0	0	0
6108	0	0	0	0	0	0	0	0
6109	0	0	0	0	0	0	0	0
6110	0	0	0	0	0	0	0	0
n	10	10	10	10	10	10	10	10

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
6101	0	0	0	0	0	0
6102	0	0	0	0	0	0
6103	0	0	0	0	0	0
6104	0	0	0	0	0	0
6105	0	0	0	0	0	0
6106	0	0	0	0	0	0
6107	0	0	0	0	0	0
6108	0	0	0	0	0	0
6109	0	0	0	0	0	0
6110	0	0	0	0	0	0
n	10	10	10	10	10	10

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : Administration

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
5101	0	0	0	0	0	0	0	0
5102	0	0	0	0	0	0	0	0
5103	0	0	0	0	0	0	0	0
5104	0	0	0	0	0	0	0	0
5105	0	0	0	0	0	0	0	0
5106	0	0	0	0	0	0	0	0
5107	0	0	0	0	0	0	0	0
5108	0	0	0	0	0	0	0	0
5109	0	0	0	0	0	0	0	0
5110	0	0	0	0	0	0	0	0
n	10	10	10	10	10	10	10	10

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
5101	0	0	0	0	0	0
5102	0	0	0	0	0	0
5103	0	0	0	0	0	0
5104	0	0	0	0	0	0
5105	0	0	0	0	0	0
5106	0	0	0	0	0	0
5107	0	0	0	0	0	0
5108	0	0	0	0	0	0
5109	0	0	0	0	0	0
5110	0	0	0	0	0	0
n	10	10	10	10	10	10

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : Administration

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
6101	0	0	0	0	0	0	0	0
6102	0	0	0	0	0	0	0	0
6103	0	0	0	0	0	0	0	0
6104	0	0	0	0	0	0	0	0
6105	0	0	0	0	0	0	0	0
6106	0	0	0	0	0	0	0	0
6107	0	0	0	0	0	0	0	0
6108	0	0	0	0	0	0	0	0
6109	0	0	0	0	0	0	0	0
6110	0	0	0	0	0	0	0	0
n	10	10	10	10	10	10	10	10

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
6101	0	0	0	0	0	0
6102	0	0	0	0	0	0
6103	0	0	0	0	0	0
6104	0	0	0	0	0	0
6105	0	0	0	0	0	0
6106	0	0	0	0	0	0
6107	0	0	0	0	0	0
6108	0	0	0	0	0	0
6109	0	0	0	0	0	0
6110	0	0	0	0	0	0
n	10	10	10	10	10	10

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : Administration

Generation : F0 Sex : Female Week : 3 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
5101	0	0	0	0	0	0	0	0
5102	0	0	0	0	0	0	0	0
5103	0	0	0	0	0	0	0	0
5104	0	0	0	0	0	0	0	0
5105	0	0	0	0	0	0	0	0
5106	0	0	0	0	0	0	0	0
5107	0	0	0	0	0	0	0	0
5108	0	0	0	0	0	0	0	0
5109	0	0	0	0	0	0	0	0
5110	0	0	0	0	0	0	0	0
n	10	10	10	10	10	10	10	10

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
5101	0	0	0	0	0	0
5102	0	0	0	0	0	0
5103	0	0	0	0	0	0
5104	0	0	0	0	0	0
5105	0	0	0	0	0	0
5106	0	0	0	0	0	0
5107	0	0	0	0	0	0
5108	0	0	0	0	0	0
5109	0	0	0	0	0	0
5110	0	0	0	0	0	0
n	10	10	10	10	10	10

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : Administration

Generation : F0 Sex : Female Week : 3 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
6101	0	0	0	0	0	0	0	0
6102	0	0	0	0	0	0	0	0
6103	0	0	0	0	0	0	0	0
6104	0	0	0	0	0	0	0	0
6105	0	0	0	0	0	0	0	0
6106	0	0	0	0	0	0	0	0
6107	0	0	0	0	0	0	0	0
6108	0	0	0	0	0	0	0	0
6109	0	0	0	0	0	0	0	0
6110	0	0	0	0	0	0	0	0
n	10	10	10	10	10	10	10	10

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
6101	0	0	0	0	0	0
6102	0	0	0	0	0	0
6103	0	0	0	0	0	0
6104	0	0	0	0	0	0
6105	0	0	0	0	0	0
6106	0	0	0	0	0	0
6107	0	0	0	0	1	0
6108	0	0	0	0	0	0
6109	0	0	0	0	0	0
6110	0	0	0	0	0	0
n	10	10	10	10	10	10

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : Administration

Generation : F0 Sex : Female Week : 4 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
5101	0	0	0	0	0	0	0	0
5102	0	0	0	0	0	0	0	0
5103	0	0	0	0	0	0	0	0
5104	0	0	0	0	0	0	0	0
5105	0	0	0	0	0	0	0	0
5106	0	0	0	0	0	0	0	0
5107	0	0	0	0	0	0	0	0
5108	0	0	0	0	0	0	0	0
5109	0	0	0	0	0	0	0	0
5110	0	0	0	0	0	0	0	0
n	10	10	10	10	10	10	10	10

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
5101	0	0	0	0	0	0
5102	0	0	0	0	0	0
5103	0	0	0	0	0	0
5104	0	0	0	0	0	0
5105	0	0	0	0	0	0
5106	0	0	0	0	0	0
5107	0	0	0	0	0	0
5108	0	0	0	0	0	0
5109	0	0	0	0	0	0
5110	0	0	0	0	0	0
n	10	10	10	10	10	10

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : Administration

Generation : F0 Sex : Female Week : 4 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
6101	0	0	0	0	0	0	0	0
6102	0	0	0	0	0	0	0	0
6103	0	0	0	0	0	0	0	0
6104	0	0	0	0	0	0	0	0
6105	0	0	0	0	0	0	0	0
6106	0	0	0	0	0	0	0	0
6107	0	0	0	0	0	0	0	0
6108	0	0	0	0	0	0	0	0
6109	0	0	0	0	0	0	0	0
6110	0	0	0	0	0	0	0	0
n	10	10	10	10	10	10	10	10

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
6101	0	0	0	0	0	0
6102	0	0	0	0	0	0
6103	0	0	0	0	0	0
6104	0	0	0	0	0	0
6105	0	0	0	0	0	0
6106	0	0	0	0	0	0
6107	0	0	0	0	0	0
6108	0	0	0	0	0	0
6109	0	0	0	0	0	0
6110	0	0	0	0	0	0
n	10	10	10	10	10	10

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : Administration

Generation : F0 Sex : Female Week : 5 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
5101	0	0	0	0	0	0	0	0
5102	0	0	0	0	0	0	0	0
5103	0	0	0	0	0	0	0	0
5104	0	0	0	0	0	0	0	0
5105	0	0	0	0	0	0	0	0
5106	0	0	0	0	0	0	0	0
5107	0	0	0	0	0	0	0	0
5108	0	0	0	0	0	0	0	0
5109	0	0	0	0	0	0	0	0
5110	0	0	0	0	0	0	0	0
n	10	10	10	10	10	10	10	10

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
5101	0	0	0	0	0	0
5102	0	0	0	0	0	0
5103	0	0	0	0	0	0
5104	0	0	0	0	0	0
5105	0	0	0	0	0	0
5106	0	0	0	0	0	0
5107	0	0	0	0	0	0
5108	0	0	0	0	0	0
5109	0	0	0	0	0	0
5110	0	0	0	0	0	0
n	10	10	10	10	10	10

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : Administration

Generation : F0 Sex : Female Week : 5 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
6101	0	0	0	0	0	0	0	0
6102	0	0	0	0	0	0	0	0
6103	0	0	0	0	0	0	0	0
6104	0	0	0	0	0	0	0	0
6105	0	0	0	0	0	0	0	0
6106	0	0	0	0	0	0	0	0
6107	0	0	0	0	0	0	0	0
6108	0	0	0	0	0	0	0	0
6109	0	0	0	0	0	0	0	0
6110	0	0	0	0	0	0	0	0
n	10	10	10	10	10	10	10	10

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
6101	0	0	0	0	1	0
6102	0	0	0	0	0	0
6103	0	0	0	0	0	0
6104	0	0	0	0	0	0
6105	0	0	0	0	0	0
6106	0	0	0	0	0	0
6107	0	0	0	0	1	0
6108	0	0	0	0	0	0
6109	0	0	0	0	0	0
6110	0	0	0	0	0	0
n	10	10	10	10	10	10

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : Administration

Generation : F0 Sex : Female Week : 6 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
5101	0	0	0	0	0	0	0	0
5102	0	0	0	0	0	0	0	0
5103	0	0	0	0	0	0	0	0
5104	0	0	0	0	0	0	0	0
5105	0	0	0	0	0	0	0	0
5106	0	0	0	0	0	0	0	0
5107	0	0	0	0	0	0	0	0
5108	0	0	0	0	0	0	0	0
5109	0	0	0	0	0	0	0	0
5110	0	0	0	0	0	0	0	0
n	10	10	10	10	10	10	10	10

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
5101	0	0	0	0	0	0
5102	0	0	0	0	0	0
5103	0	0	0	0	0	0
5104	0	0	0	0	0	0
5105	0	0	0	0	0	0
5106	0	0	0	0	0	0
5107	0	0	0	0	0	0
5108	0	0	0	0	0	0
5109	0	0	0	0	0	0
5110	0	0	0	0	0	0
n	10	10	10	10	10	10

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : Administration

Generation : F0 Sex : Female Week : 6 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
6101	0	0	0	0	0	0	0	0
6102	0	0	0	0	0	0	0	0
6103	0	0	0	0	0	0	0	0
6104	0	0	0	0	0	0	0	0
6105	0	0	0	0	0	0	0	0
6106	0	0	0	0	0	0	0	0
6107	0	0	0	0	0	0	0	0
6108	0	0	0	0	0	0	0	0
6109	0	0	0	0	0	0	0	0
6110	0	0	0	0	0	0	0	0
n	10	10	10	10	10	10	10	10

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
6101	0	0	0	0	0	0
6102	0	0	0	0	0	0
6103	0	0	0	0	0	0
6104	0	0	0	0	1	0
6105	0	0	0	0	0	0
6106	0	0	0	0	0	0
6107	0	0	0	0	0	0
6108	0	0	0	0	0	0
6109	0	0	0	0	0	0
6110	0	0	0	0	0	0
n	10	10	10	10	10	10

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : Recovery

Generation : F0 Sex : Male Week : 1 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
1008	0	0	0	0	0	0	0	0
1009	0	0	0	0	0	0	0	0
1010	0	0	0	0	0	0	0	0
1011	0	0	0	0	0	0	0	0
1012	0	0	0	0	0	0	0	0
n	5	5	5	5	5	5	5	5

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
1008	0	0	0	0	0	0
1009	0	0	0	0	0	0
1010	0	0	0	0	0	0
1011	0	0	0	0	0	0
1012	0	0	0	0	0	0
n	5	5	5	5	5	5

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : Recovery

Generation : F0 Sex : Male Week : 1 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
4008	0	0	0	0	0	0	0	0
4009	0	0	0	0	0	0	0	0
4010	0	0	0	0	0	0	0	0
4011	0	0	0	0	0	0	0	0
4012	0	0	0	0	0	0	0	0
n	5	5	5	5	5	5	5	5

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
4008	0	0	0	0	0	0
4009	0	0	0	0	0	0
4010	0	0	0	0	0	0
4011	0	0	0	0	0	0
4012	0	0	0	0	0	0
n	5	5	5	5	5	5

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : Recovery

Generation : F0 Sex : Male Week : 2 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
1008	0	0	0	0	0	0	0	0
1009	0	0	0	0	0	0	0	0
1010	0	0	0	0	0	0	0	0
1011	0	0	0	0	0	0	0	0
1012	0	0	0	0	0	0	0	0
n	5	5	5	5	5	5	5	5

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
1008	0	0	0	0	0	0
1009	0	0	0	0	0	0
1010	0	0	0	0	0	0
1011	0	0	0	0	0	0
1012	0	0	0	0	0	0
n	5	5	5	5	5	5

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : Recovery

Generation : F0 Sex : Male Week : 2 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
4008	0	0	0	0	0	0	0	0
4009	0	0	0	0	0	0	0	0
4010	0	0	0	0	0	0	0	0
4011	0	0	0	0	0	0	0	0
4012	0	0	0	0	0	0	0	0
n	5	5	5	5	5	5	5	5

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
4008	0	0	0	0	0	0
4009	0	0	0	0	0	0
4010	0	0	0	0	0	0
4011	0	0	0	0	0	0
4012	0	0	0	0	0	0
n	5	5	5	5	5	5

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : Recovery

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
5106	0	0	0	0	0	0	0	0
5107	0	0	0	0	0	0	0	0
5108	0	0	0	0	0	0	0	0
5109	0	0	0	0	0	0	0	0
5110	0	0	0	0	0	0	0	0
n	5	5	5	5	5	5	5	5

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
5106	0	0	0	0	0	0
5107	0	0	0	0	0	0
5108	0	0	0	0	0	0
5109	0	0	0	0	0	0
5110	0	0	0	0	0	0
n	5	5	5	5	5	5

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : Recovery

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
6106	0	0	0	0	0	0	0	0
6107	0	0	0	0	0	0	0	0
6108	0	0	0	0	0	0	0	0
6109	0	0	0	0	0	0	0	0
6110	0	0	0	0	0	0	0	0
n	5	5	5	5	5	5	5	5

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
6106	0	0	0	0	0	0
6107	0	0	0	0	0	0
6108	0	0	0	0	0	0
6109	0	0	0	0	0	0
6110	0	0	0	0	0	0
n	5	5	5	5	5	5

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : Recovery

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
5106	0	0	0	0	0	0	0	0
5107	0	0	0	0	0	0	0	0
5108	0	0	0	0	0	0	0	0
5109	0	0	0	0	0	0	0	0
5110	0	0	0	0	0	0	0	0
n	5	5	5	5	5	5	5	5

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
5106	0	0	0	0	0	0
5107	0	0	0	0	0	0
5108	0	0	0	0	0	0
5109	0	0	0	0	0	0
5110	0	0	0	0	0	0
n	5	5	5	5	5	5

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

In-the-hand observation

Period : Recovery

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Ease of removal from cage	Fur condition	Skin	Secretions-Eye, Nose	Exophthalmos	Palpebral closure	Mucosal membranes	Lacrimation
6106	0	0	0	0	0	0	0	0
6107	0	0	0	0	0	0	0	0
6108	0	0	0	0	0	0	0	0
6109	0	0	0	0	0	0	0	0
6110	0	0	0	0	0	0	0	0
n	5	5	5	5	5	5	5	5

Animal No.	Piloerection	Pupil size	Salivation	Abnormal respiration	Vocalization	Reactivity to handling
6106	0	0	0	0	0	0
6107	0	0	0	0	0	0
6108	0	0	0	0	0	0
6109	0	0	0	0	0	0
6110	0	0	0	0	0	0
n	5	5	5	5	5	5

Ease of removal from cage) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
Fur condition) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Skin) 0: Nomal, 1: Slight, 2: Moderate, 3: Severe
Secretions-Eye, Nose) 0: Absent, 1: Present
Exophthalmos) 0: Absent, 1: Present
Palpebral closure) 0: Nomal, 1: Slightly closed, 2: Half closed, 3: Completely closed
Mucosal membranes) 0: Nomal, 1: Slight, 2: Moderate, 3: Marked
Lacrimation) 0: Absent, 1: Present
Piloerection) 0: Absent, 1: Present
Pupil size) -1: Miosis, 0: Nomal, 1: Half opened pupil, 2: Mydriasis
Salivation) 0: None, 1: Slight, 2: Moderate, 3: Marked
Abnormal respiration) 0: None, 1: Slight, 2: Moderate, 3: Severe
Vocalization) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
Reactivity to handling) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Awkward, 3: Very Awkward

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 before mating

Generation : F0 Sex : Male Week : 1 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
1001	0	0	0	0	0	N	0	0
1002	0	0	0	0	0	N	0	0
1003	0	0	0	0	0	N	0	1
1004	0	0	0	0	0	N	0	0
1005	0	0	0	0	0	N	0	0
1006	0	0	0	0	0	N	0	0
1007	0	0	0	0	0	N	0	0
1008	0	0	0	0	0	N	0	0
1009	0	0	0	0	0	N	0	0
1010	0	0	0	0	0	N	0	0
1011	0	0	0	0	0	N	0	0
1012	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 before mating

Generation : F0 Sex : Male Week : 1 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
1001	6	0
1002	5	0
1003	2	0
1004	7	0
1005	4	0
1006	5	0
1007	3	0
1008	1	3
1009	2	4
1010	5	0
1011	2	1
1012	4	0
n	12	12
Mean	4	1
S.D.	2	1

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 before mating

Generation : F0 Sex : Male Week : 1 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
2001	0	0	0	0	0	N	0	0
2002	0	0	0	0	0	N	0	0
2003	0	0	0	0	0	N	0	0
2004	0	0	0	0	0	N	0	0
2005	0	0	0	0	0	N	0	0
2006	0	0	0	0	0	N	0	0
2007	0	0	0	0	0	N	0	0
2008	0	0	0	0	0	N	0	0
2009	0	0	0	0	0	N	0	0
2010	0	0	0	0	0	N	0	0
2011	0	0	0	0	0	N	0	0
2012	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 before mating

Generation : F0 Sex : Male Week : 1 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
2001	7	0
2002	8	0
2003	1	1
2004	7	0
2005	5	0
2006	5	0
2007	4	0
2008	3	2
2009	6	0
2010	5	0
2011	1	0
2012	1	3
n	12	12
Mean	4	1
S.D.	2	1

Appendix 2 - 147 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 before mating

Generation : F0 Sex : Male Week : 1 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
3001	0	0	0	0	0	N	0	0
3002	0	0	0	0	0	N	0	0
3003	0	0	0	0	0	N	0	0
3004	0	0	0	0	0	N	0	0
3005	0	0	0	0	0	N	0	0
3006	0	0	0	0	0	N	0	0
3007	0	0	0	0	0	N	0	0
3008	0	0	0	0	0	N	0	0
3009	0	0	0	0	0	N	0	0
3010	0	0	0	0	0	N	0	0
3011	0	0	0	0	0	N	0	0
3012	0	0	0	0	0	N	0	1
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 before mating

Generation : F0 Sex : Male Week : 1 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
3001	1	2
3002	10	0
3003	8	2
3004	3	0
3005	6	0
3006	3	0
3007	7	0
3008	6	0
3009	8	0
3010	1	0
3011	7	0
3012	2	1
n	12	12
Mean	5	0
S.D.	3	1

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 before mating

Generation : F0 Sex : Male Week : 1 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
4001	0	0	0	0	0	N	0	0
4002	0	0	0	0	0	N	0	0
4003	0	0	0	0	0	N	0	0
4004	0	0	0	0	0	N	0	0
4005	0	0	0	0	0	N	0	0
4006	0	0	0	0	0	N	0	0
4007	0	0	0	0	0	N	0	0
4008	0	0	0	0	0	N	0	0
4009	0	0	0	0	0	N	0	0
4010	0	0	0	0	0	N	0	0
4011	0	0	0	0	0	N	0	0
4012	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 before mating

Generation : F0 Sex : Male Week : 1 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
4001	2	0
4002	6	0
4003	3	0
4004	5	0
4005	6	0
4006	4	0
4007	1	6
4008	4	0
4009	7	0
4010	8	0
4011	2	0
4012	9	0
n	12	12
Mean	5	1
S.D.	3	2

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 before mating

Generation : F0 Sex : Male Week : 2 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
1001	0	0	0	0	0	N	0	0
1002	0	0	0	0	0	N	0	0
1003	0	0	0	0	0	N	0	0
1004	0	0	0	0	0	N	0	0
1005	0	0	0	0	0	N	0	0
1006	0	0	0	0	0	N	0	0
1007	0	0	0	0	0	N	0	1
1008	0	0	0	0	0	N	0	1
1009	0	0	0	0	0	N	0	0
1010	0	0	0	0	0	N	0	0
1011	0	0	0	0	0	N	0	0
1012	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 before mating

Generation : F0 Sex : Male Week : 2 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
1001	4	0
1002	7	0
1003	5	0
1004	7	0
1005	5	0
1006	6	0
1007	3	0
1008	1	4
1009	7	0
1010	3	0
1011	4	0
1012	7	0
n	12	12
Mean	5	0
S.D.	2	1

Appendix 2 - 153 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 before mating

Generation : F0 Sex : Male Week : 2 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
2001	0	0	0	0	0	N	0	0
2002	0	0	0	0	0	N	0	1
2003	0	0	0	0	0	N	0	0
2004	0	0	0	0	0	N	0	0
2005	0	0	0	0	0	N	0	0
2006	0	0	0	0	0	N	0	0
2007	0	0	0	0	0	N	0	1
2008	0	0	0	0	0	N	0	0
2009	0	0	0	0	0	N	0	0
2010	0	0	0	0	0	N	0	1
2011	0	0	0	0	0	N	0	0
2012	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

(1):0
Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 before mating

Generation : F0 Sex : Male Week : 2 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
2001	6	0
2002	1	0
2003	4	0
2004	7	0
2005	4	0
2006	4	0
2007	5	2
2008	5	0
2009	2	0
2010	5	0
2011	3	0
2012	4	0
n	12	12
Mean	4	0
S.D.	2	1

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 before mating

Generation : F0 Sex : Male Week : 2 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
3001	0	0	0	0	0	N	0	0
3002	0	0	0	0	0	N	0	0
3003	0	0	0	0	0	N	0	0
3004	0	0	0	0	0	N	0	0
3005	0	0	0	0	0	N	0	0
3006	0	0	0	0	0	N	0	1
3007	0	0	0	0	0	N	0	1
3008	0	0	0	0	0	N	0	0
3009	0	0	0	0	0	N	0	0
3010	0	0	0	0	0	N	0	0
3011	0	0	0	0	0	N	0	0
3012	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 before mating

Generation : F0 Sex : Male Week : 2 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
3001	3	1
3002	7	0
3003	5	0
3004	4	0
3005	6	0
3006	3	1
3007	3	0
3008	1	0
3009	3	1
3010	2	0
3011	2	0
3012	7	3
n	12	12
Mean	4	1
S.D.	2	1

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 before mating

Generation : F0 Sex : Male Week : 2 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
4001	0	0	0	0	0	N	0	0
4002	0	0	0	0	0	N	0	0
4003	0	0	0	0	0	N	0	0
4004	0	0	0	0	0	N	0	0
4005	0	0	0	0	0	N	0	0
4006	0	0	0	0	0	N	0	0
4007	0	0	0	0	0	N	0	0
4008	0	0	0	0	0	N	0	0
4009	0	0	0	0	0	N	0	0
4010	0	0	0	0	0	N	0	0
4011	0	0	0	0	0	N	0	0
4012	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 before mating

Generation : F0 Sex : Male Week : 2 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
4001	4	0
4002	6	0
4003	5	0
4004	5	0
4005	3	0
4006	6	0
4007	2	2
4008	5	1
4009	6	0
4010	3	0
4011	2	0
4012	8	0
n	12	12
Mean	5	0
S.D.	2	1

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 mating

Generation : F0 Sex : Male Week : 3 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
1001	0	0	0	0	0	N	0	0
1002	0	0	0	0	0	N	0	0
1003	0	0	0	0	0	N	0	0
1004	0	0	0	0	0	N	0	0
1005	0	0	0	0	0	N	0	0
1006	0	0	0	0	0	N	0	0
1007	0	0	0	0	0	N	0	0
1008	0	0	0	0	0	N	0	0
1009	0	0	0	0	0	N	0	0
1010	0	0	0	0	0	N	0	0
1011	0	0	0	0	0	N	0	0
1012	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 mating

Generation : F0 Sex : Male Week : 3 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
1001	3	0
1002	6	0
1003	4	0
1004	8	0
1005	7	0
1006	3	0
1007	4	0
1008	3	2
1009	3	0
1010	3	0
1011	3	0
1012	5	0
n	12	12
Mean	4	0
S.D.	2	1

Appendix 2 - 161 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 mating

Generation : F0 Sex : Male Week : 3 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
2001	0	0	0	0	0	N	0	0
2002	0	0	0	0	0	N	0	0
2003	0	0	0	0	0	N	0	0
2004	0	0	0	0	0	N	0	0
2005	0	0	0	0	0	N	0	0
2006	0	0	0	0	0	N	0	0
2007	0	0	0	0	0	N	0	0
2008	0	0	0	0	0	N	0	0
2009	0	0	0	0	0	N	0	0
2010	0	0	0	0	0	N	0	0
2011	0	0	0	0	0	N	0	0
2012	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 mating

Generation : F0 Sex : Male Week : 3 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
2001	6	0
2002	4	0
2003	4	0
2004	2	0
2005	3	0
2006	3	0
2007	5	0
2008	6	2
2009	6	0
2010	5	0
2011	7	0
2012	4	0
n	12	12
Mean	5	0
S.D.	2	1

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 mating

Generation : F0 Sex : Male Week : 3 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
3001	0	0	0	0	0	N	0	0
3002	0	0	0	0	0	N	0	0
3003	0	0	0	0	0	N	0	0
3004	0	0	0	0	0	N	0	0
3005	0	0	0	0	0	N	0	0
3006	0	0	0	0	0	N	0	0
3007	0	0	0	0	0	N	0	0
3008	0	0	0	0	U	N	0	0
3009	0	0	0	0	0	N	0	0
3010	0	0	0	0	0	N	0	0
3011	0	0	0	0	0	N	0	0
3012	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 mating

Generation : F0 Sex : Male Week : 3 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
3001	3	0
3002	9	0
3003	5	0
3004	3	0
3005	5	0
3006	4	0
3007	3	0
3008	0	0
3009	5	0
3010	3	0
3011	4	0
3012	7	0
n	12	12
Mean	4	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 mating

Generation : F0 Sex : Male Week : 3 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
4001	0	0	0	0	0	N	0	0
4002	0	0	0	0	0	N	0	0
4003	0	0	0	0	0	N	0	0
4004	0	0	0	0	0	N	0	0
4005	0	0	0	0	0	N	0	0
4006	0	0	0	0	0	N	0	0
4007	0	0	0	0	0	N	0	1
4008	0	0	0	0	0	N	0	0
4009	0	0	0	0	0	N	0	0
4010	0	0	0	0	0	N	0	0
4011	0	0	0	0	0	N	0	0
4012	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 mating

Generation : F0 Sex : Male Week : 3 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
4001	2	0
4002	4	0
4003	5	0
4004	4	0
4005	5	0
4006	5	0
4007	4	0
4008	4	0
4009	6	0
4010	5	0
4011	2	0
4012	7	0
n	12	12
Mean	4	0
S.D.	1	0

Appendix 2 - 167 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 mating

Generation : F0 Sex : Male Week : 4 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
1001	0	0	0	0	0	N	0	0
1002	0	0	0	0	0	N	0	0
1003	0	0	0	0	0	N	0	0
1004	0	0	0	0	0	N	0	0
1005	0	0	0	0	0	N	0	0
1006	0	0	0	0	0	N	0	0
1007	0	0	0	0	0	N	0	0
1008	0	0	0	0	0	N	0	1
1009	0	0	0	0	0	N	0	0
1010	0	0	0	0	0	N	0	0
1011	0	0	0	0	0	N	0	0
1012	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 mating

Generation : F0 Sex : Male Week : 4 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
1001	4	0
1002	5	0
1003	2	0
1004	7	0
1005	6	0
1006	5	0
1007	3	0
1008	6	0
1009	4	1
1010	6	0
1011	6	0
1012	3	0
n	12	12
Mean	5	0
S.D.	2	0

Appendix 2 - 169 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 mating

Generation : F0 Sex : Male Week : 4 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
2001	0	0	0	0	0	N	0	0
2002	0	0	0	0	0	N	0	0
2003	0	0	0	0	0	N	0	0
2004	0	0	0	0	0	N	0	0
2005	0	0	0	0	0	N	0	0
2006	0	0	0	0	0	N	0	0
2007	0	0	0	0	0	N	0	0
2008	0	0	0	0	0	N	0	0
2009	0	0	0	0	0	N	0	0
2010	0	0	0	0	0	N	0	0
2011	0	0	0	0	0	N	0	0
2012	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 mating

Generation : F0 Sex : Male Week : 4 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
2001	2	2
2002	2	0
2003	5	0
2004	5	0
2005	5	0
2006	4	0
2007	3	0
2008	5	1
2009	5	0
2010	3	0
2011	7	0
2012	5	0
n	12	12
Mean	4	0
S.D.	1	1

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 mating

Generation : F0 Sex : Male Week : 4 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
3001	0	0	0	0	0	N	0	0
3002	0	0	0	0	0	N	0	0
3003	0	0	0	0	0	N	0	0
3004	0	0	0	0	0	N	0	0
3005	0	0	0	0	0	N	0	1
3006	0	0	0	0	0	N	0	0
3007	0	0	0	0	0	N	0	0
3008	0	0	0	0	0	N	0	0
3009	0	0	0	0	0	N	0	1
3010	0	0	0	0	0	N	0	0
3011	0	0	0	0	0	N	0	0
3012	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 mating

Generation : F0 Sex : Male Week : 4 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
3001	3	0
3002	11	0
3003	4	0
3004	0	0
3005	6	0
3006	3	0
3007	6	0
3008	4	0
3009	3	0
3010	3	0
3011	4	0
3012	6	0
n	12	12
Mean	4	0
S.D.	3	0

Appendix 2 - 173 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 mating

Generation : F0 Sex : Male Week : 4 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
4001	0	0	0	0	0	N	0	0
4002	0	0	0	0	0	N	0	1
4003	0	0	0	0	0	N	0	0
4004	0	0	0	0	0	N	0	0
4005	0	0	0	0	0	N	0	0
4006	0	0	0	0	0	N	0	1
4007	0	0	0	0	0	N	0	0
4008	0	0	0	0	0	N	0	0
4009	0	0	0	0	0	N	0	0
4010	0	0	0	0	0	N	0	1
4011	0	0	0	0	0	N	0	1
4012	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 mating

Generation : F0 Sex : Male Week : 4 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
4001	3	0
4002	6	0
4003	3	0
4004	4	0
4005	6	0
4006	6	0
4007	4	0
4008	4	0
4009	7	0
4010	4	0
4011	3	0
4012	4	0
n	12	12
Mean	5	0
S.D.	1	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 mating

Generation : F0 Sex : Male Week : 5 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
1001	0	0	0	0	0	N	0	0
1002	0	0	0	0	0	N	0	0
1003	0	0	0	0	0	N	0	0
1004	0	0	0	0	0	N	0	0
1005	0	0	0	0	0	N	0	0
1006	0	0	0	0	0	N	0	0
1007	0	0	0	0	0	N	0	0
1008	0	0	0	0	0	N	0	1
1009	0	0	0	0	0	N	0	0
1010	0	0	0	0	0	N	0	0
1011	0	0	0	0	0	N	0	0
1012	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 mating

Generation : F0 Sex : Male Week : 5 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
1001	4	0
1002	6	0
1003	4	0
1004	7	0
1005	6	0
1006	4	0
1007	4	0
1008	6	0
1009	3	0
1010	4	0
1011	2	0
1012	5	0
n	12	12
Mean	5	0
S.D.	1	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 mating

Generation : F0 Sex : Male Week : 5 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
2001	0	0	0	0	0	N	0	0
2002	0	0	0	0	0	N	0	0
2003	0	0	0	0	0	N	0	0
2004	0	0	0	0	0	N	0	1
2005	0	0	0	0	0	N	0	0
2006	0	0	0	0	0	N	0	0
2007	0	0	0	0	0	N	0	0
2008	0	0	0	0	0	N	0	0
2009	0	0	0	0	0	N	0	0
2010	0	0	0	0	0	N	0	0
2011	0	0	0	0	0	N	0	1
2012	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 mating

Generation : F0 Sex : Male Week : 5 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
2001	2	0
2002	4	0
2003	4	1
2004	5	0
2005	7	0
2006	5	0
2007	3	0
2008	6	0
2009	5	0
2010	4	0
2011	6	0
2012	7	0
n	12	12
Mean	5	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 mating

Generation : F0 Sex : Male Week : 5 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
3001	0	0	0	0	0	N	0	0
3002	0	0	0	0	0	N	0	0
3003	0	0	0	0	0	N	0	0
3004	0	0	0	0	0	N	0	0
3005	0	0	0	0	0	N	0	0
3006	0	0	0	0	0	N	0	0
3007	0	0	0	0	0	N	0	1
3008	0	0	0	0	0	N	0	0
3009	0	0	0	0	0	N	0	0
3010	0	0	0	0	0	N	0	0
3011	0	0	0	0	0	N	0	0
3012	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 mating

Generation : F0 Sex : Male Week : 5 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
3001	5	0
3002	10	0
3003	4	0
3004	3	0
3005	5	0
3006	5	0
3007	3	0
3008	2	0
3009	1	0
3010	7	0
3011	4	0
3012	5	0
n	12	12
Mean	5	0
S.D.	2	0

Appendix 2 - 181 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 mating

Generation : F0 Sex : Male Week : 5 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
4001	0	0	0	0	0	N	0	1
4002	0	0	0	0	0	N	0	0
4003	0	0	0	0	0	N	0	0
4004	0	0	0	0	0	N	0	0
4005	0	0	0	0	0	N	0	0
4006	0	0	0	0	0	N	0	0
4007	0	0	0	0	0	N	0	0
4008	0	0	0	0	0	N	0	0
4009	0	0	0	0	0	N	0	0
4010	0	0	0	0	0	N	0	1
4011	0	0	0	0	0	N	0	0
4012	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 mating

Generation : F0 Sex : Male Week : 5 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
4001	5	0
4002	5	0
4003	1	0
4004	3	0
4005	3	0
4006	6	0
4007	6	0
4008	6	0
4009	5	0
4010	6	0
4011	5	1
4012	5	0
n	12	12
Mean	5	0
S.D.	2	0

Appendix 2 - 183 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 mating

Generation : F0 Sex : Male Week : 6 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
1001	0	0	0	0	0	N	0	0
1002	0	0	0	0	0	N	0	0
1003	0	0	0	0	0	N	0	0
1004	0	0	0	0	0	N	0	0
1005	0	0	0	0	0	N	0	0
1006	0	0	0	0	0	N	0	0
1007	0	0	0	0	0	N	0	0
1008	0	0	0	0	0	N	0	1
1009	0	0	0	0	0	N	0	0
1010	0	0	0	0	0	N	0	0
1011	0	0	0	0	0	N	0	0
1012	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 mating

Generation : F0 Sex : Male Week : 6 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
1001	6	0
1002	6	0
1003	6	0
1004	12	0
1005	6	0
1006	4	0
1007	5	0
1008	5	0
1009	4	0
1010	4	0
1011	2	0
1012	8	0
n	12	12
Mean	6	0
S.D.	2	0

Appendix 2 - 185 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 mating

Generation : F0 Sex : Male Week : 6 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
2001	0	0	0	0	0	N	0	0
2002	0	0	0	0	0	N	0	0
2003	0	0	0	0	0	N	0	0
2004	0	0	0	0	0	N	0	0
2005	0	0	0	0	0	N	0	0
2006	0	0	0	0	0	N	0	0
2007	0	0	0	0	0	N	0	1
2008	0	0	0	0	0	N	0	0
2009	0	0	0	0	0	N	0	1
2010	0	0	0	0	0	N	0	0
2011	0	0	0	0	0	N	0	0
2012	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 mating

Generation : F0 Sex : Male Week : 6 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
2001	5	0
2002	6	0
2003	3	0
2004	4	0
2005	2	0
2006	4	0
2007	5	0
2008	5	3
2009	3	0
2010	10	0
2011	6	0
2012	5	0
n	12	12
Mean	5	0
S.D.	2	1

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 mating

Generation : F0 Sex : Male Week : 6 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
3001	0	0	0	0	0	N	0	0
3002	0	0	0	0	0	N	0	0
3003	0	0	0	0	0	N	0	0
3004	0	0	0	0	0	N	0	0
3005	0	0	0	0	0	N	0	0
3006	0	0	0	0	0	N	0	0
3007	0	0	0	0	0	N	0	0
3008	0	0	0	0	0	N	0	0
3009	0	0	0	0	0	N	0	0
3010	0	0	0	0	0	N	0	0
3011	0	0	0	0	0	N	0	0
3012	0	0	0	0	0	N	0	1
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 mating

Generation : F0 Sex : Male Week : 6 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
3001	5	0
3002	7	0
3003	8	0
3004	3	0
3005	4	0
3006	4	0
3007	3	0
3008	2	0
3009	3	1
3010	2	0
3011	9	0
3012	5	0
n	12	12
Mean	5	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 mating

Generation : F0 Sex : Male Week : 6 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
4001	0	0	0	0	0	N	0	0
4002	0	0	0	0	0	N	0	1
4003	0	0	0	0	0	N	0	0
4004	0	0	0	0	0	N	0	0
4005	0	0	0	0	0	N	0	0
4006	0	0	0	0	0	N	0	1
4007	0	0	0	0	0	N	0	1
4008	0	0	0	0	0	N	0	0
4009	0	0	0	0	0	N	0	0
4010	0	0	0	0	0	N	0	1
4011	0	0	0	0	0	N	0	0
4012	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 mating

Generation : F0 Sex : Male Week : 6 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
4001	2	0
4002	4	0
4003	5	0
4004	5	0
4005	5	0
4006	3	0
4007	4	0
4008	5	0
4009	6	0
4010	6	0
4011	4	0
4012	3	0
n	12	12
Mean	4	0
S.D.	1	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 before mating

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
1101	0	0	0	0	0	N	0	0
1102	0	0	0	0	0	N	0	0
1103	0	0	0	0	0	N	0	0
1104	0	0	0	0	0	N	0	0
1105	0	0	0	0	0	N	0	0
1106	0	0	0	0	0	N	0	0
1107	0	0	0	0	0	N	0	0
1108	0	0	0	0	0	N	0	0
1109	0	0	0	0	0	N	0	0
1110	0	0	0	0	0	N	0	0
1111	0	0	0	0	0	N	0	0
1112	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 before mating

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
1101	7	0
1102	10	0
1103	6	0
1104	6	0
1105	8	0
1106	7	0
1107	5	0
1108	3	0
1109	11	0
1110	8	0
1111	7	0
1112	7	0
n	12	12
Mean	7	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 before mating

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
2101	0	0	0	0	0	N	0	0
2102	0	0	0	0	0	N	0	0
2103	0	0	0	0	0	N	0	0
2104	0	0	0	0	0	N	0	0
2105	0	0	0	0	0	N	0	0
2106	0	0	0	0	0	N	0	0
2107	0	0	0	0	0	N	0	0
2108	0	0	0	0	0	N	0	0
2109	0	0	0	0	0	N	0	0
2110	0	0	0	0	0	N	0	0
2111	0	0	0	0	0	N	0	0
2112	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 before mating

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
2101	6	0
2102	9	0
2103	10	0
2104	8	0
2105	7	0
2106	5	0
2107	8	0
2108	9	0
2109	7	0
2110	6	0
2111	7	0
2112	7	0
n	12	12
Mean	7	0
S.D.	1	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 before mating

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
3101	0	0	0	0	0	N	0	0
3102	0	0	0	0	0	N	0	0
3103	0	0	0	0	0	N	0	0
3104	0	0	0	0	0	N	0	0
3105	0	0	0	0	0	N	0	0
3106	0	0	0	0	0	N	0	0
3107	0	0	0	0	0	N	0	0
3108	0	0	0	0	0	N	0	0
3109	0	0	0	0	0	N	0	0
3110	0	0	0	0	0	N	0	0
3111	0	0	0	0	0	N	0	0
3112	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 before mating

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
3101	9	0
3102	7	0
3103	3	0
3104	9	0
3105	9	0
3106	7	0
3107	9	0
3108	8	0
3109	10	0
3110	9	0
3111	9	0
3112	9	0
n	12	12
Mean	8	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 before mating

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
4101	0	0	0	0	0	N	0	0
4102	0	0	0	0	0	N	0	0
4103	0	0	0	0	0	N	0	0
4104	0	0	0	0	0	N	0	0
4105	0	0	0	0	0	N	0	0
4106	0	0	0	0	0	N	0	0
4107	0	0	0	0	0	N	0	0
4108	0	0	0	0	0	N	0	0
4109	0	0	0	0	0	N	0	0
4110	0	0	0	0	0	N	0	0
4111	0	0	0	0	0	N	0	0
4112	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 before mating

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
4101	8	0
4102	6	0
4103	10	0
4104	6	0
4105	7	0
4106	7	0
4107	8	0
4108	4	0
4109	6	0
4110	8	0
4111	7	0
4112	3	0
n	12	12
Mean	7	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 before mating

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
1101	0	0	0	0	0	N	0	0
1102	0	0	0	0	0	N	0	0
1103	0	0	0	0	0	N	0	0
1104	0	0	0	0	0	N	0	0
1105	0	0	0	0	0	N	0	0
1106	0	0	0	0	0	N	0	0
1107	0	0	0	0	0	N	0	0
1108	0	0	0	0	0	N	0	0
1109	0	0	0	0	0	N	0	0
1110	0	0	0	0	0	N	0	0
1111	0	0	0	0	0	N	0	0
1112	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 before mating

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
1101	9	0
1102	9	0
1103	5	0
1104	9	0
1105	10	0
1106	8	0
1107	4	0
1108	6	0
1109	7	0
1110	4	0
1111	6	0
1112	11	0
n	12	12
Mean	7	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 before mating

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
2101	0	0	0	0	0	N	0	0
2102	0	0	0	0	0	N	0	0
2103	0	0	0	0	0	N	0	0
2104	0	0	0	0	0	N	0	0
2105	0	0	0	0	0	N	0	0
2106	0	0	0	0	0	N	0	0
2107	0	0	0	0	0	N	0	0
2108	0	0	0	0	0	N	0	0
2109	0	0	0	0	0	N	0	0
2110	0	0	0	0	0	N	0	0
2111	0	0	0	0	0	N	0	0
2112	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 before mating

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
2101	9	0
2102	5	0
2103	11	0
2104	8	0
2105	5	0
2106	6	0
2107	11	0
2108	11	0
2109	6	0
2110	9	0
2111	4	0
2112	8	0
n	12	12
Mean	8	0
S.D.	3	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 before mating

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
3101	0	0	0	0	0	N	0	0
3102	0	0	0	0	0	N	0	0
3103	0	0	0	0	0	N	0	0
3104	0	0	0	0	0	N	0	0
3105	0	0	0	0	0	N	0	0
3106	0	0	0	0	0	N	0	0
3107	0	0	0	0	0	N	0	0
3108	0	0	0	0	0	N	0	0
3109	0	0	0	0	0	N	0	0
3110	0	0	0	0	0	N	0	0
3111	0	0	0	0	0	N	0	0
3112	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 before mating

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
3101	10	0
3102	9	0
3103	5	0
3104	7	0
3105	9	0
3106	8	0
3107	7	0
3108	8	0
3109	10	0
3110	9	0
3111	10	0
3112	8	0
n	12	12
Mean	8	0
S.D.	1	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 before mating

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
4101	0	0	0	0	0	N	0	0
4102	0	0	0	0	0	N	0	0
4103	0	0	0	0	0	N	0	0
4104	0	0	0	0	0	N	0	0
4105	0	0	0	0	0	N	0	0
4106	0	0	0	0	0	N	0	0
4107	0	0	0	0	0	N	0	0
4108	0	0	0	0	0	N	0	0
4109	0	0	0	0	0	N	0	0
4110	0	0	0	0	0	N	0	0
4111	0	0	0	0	0	N	0	0
4112	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 before mating

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
4101	11	0
4102	4	0
4103	12	0
4104	8	0
4105	8	0
4106	8	0
4107	11	0
4108	6	0
4109	7	0
4110	6	0
4111	10	0
4112	7	0
n	12	12
Mean	8	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 1 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
1101	0	0	0	0	0	N	0	0
1102	0	0	0	0	0	N	0	0
1103	0	0	0	0	0	N	0	0
1104	0	0	0	0	0	N	0	0
1105	0	0	0	0	0	N	0	0
1106	0	0	0	0	0	N	0	0
1107	0	0	0	0	0	N	0	0
1108	0	0	0	0	0	N	0	0
1109	0	0	0	0	0	N	0	0
1110	0	0	0	0	0	N	0	0
1111	0	0	0	0	0	N	0	0
1112	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 1 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
1101	6	0
1102	7	0
1103	3	0
1104	5	0
1105	5	0
1106	7	0
1107	7	0
1108	5	0
1109	11	0
1110	6	0
1111	5	0
1112	6	0
n	12	12
Mean	6	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 1 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
2101	0	0	0	0	0	N	0	0
2102	0	0	0	0	0	N	0	0
2103	0	0	0	0	0	N	0	0
2104	0	0	0	0	0	N	0	0
2105	0	0	0	0	0	N	0	0
2106	0	0	0	0	0	N	0	0
2107	0	0	0	0	0	N	0	0
2108	0	0	0	0	0	N	0	0
2109	0	0	0	0	0	N	0	0
2110	0	0	0	0	0	N	0	0
2111	0	0	0	0	0	N	0	0
2112	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 1 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
2101	7	0
2102	5	0
2103	6	0
2104	6	0
2105	5	0
2106	7	0
2107	8	0
2108	6	0
2109	4	0
2110	9	0
2111	7	0
2112	5	0
n	12	12
Mean	6	0
S.D.	1	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 1 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
3101	0	0	0	0	0	N	0	0
3102	0	0	0	0	0	N	0	0
3103	0	0	0	0	0	N	0	0
3104	0	0	0	0	0	N	0	0
3105	0	0	0	0	0	N	0	0
3106	0	0	0	0	0	N	0	0
3107	0	0	0	0	0	N	0	0
3108	0	0	0	0	0	N	0	0
3109	0	0	0	0	0	N	0	0
3110	0	0	0	0	0	N	0	0
3111	0	0	0	0	0	N	0	0
3112	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 1 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
3101	9	0
3102	8	0
3103	6	0
3104	6	0
3105	12	0
3106	12	0
3107	7	0
3108	5	0
3109	14	0
3110	6	0
3111	5	0
3112	7	0
n	12	12
Mean	8	0
S.D.	3	0

Appendix 2 - 213 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 gestation

Generation : F0 Sex : Female Day : 1 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
4101	0	0	0	0	0	N	0	0
4102	0	0	0	0	0	N	0	0
4103	0	0	0	0	0	N	0	0
4104	0	0	0	0	0	N	0	0
4105	0	0	0	0	0	N	0	0
4106	0	0	0	0	0	N	0	0
4107	0	0	0	0	0	N	0	0
4108	0	0	0	0	0	N	0	0
4109	0	0	0	0	0	N	0	0
4110	0	0	0	0	0	N	0	0
4111	0	0	0	0	0	N	0	0
4112	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 1 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
4101	11	0
4102	5	0
4103	10	0
4104	7	0
4105	6	0
4106	6	0
4107	5	0
4108	4	0
4109	6	0
4110	4	0
4111	6	0
4112	4	0
n	12	12
Mean	6	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 7 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
1101	0	0	0	0	0	N	0	0
1102	0	0	0	0	0	N	0	0
1103	0	0	0	0	0	N	0	0
1104	0	0	0	0	0	N	0	0
1105	0	0	0	0	0	N	0	0
1106	0	0	0	0	0	N	0	0
1107	0	0	0	0	0	N	0	0
1108	0	0	0	0	0	N	0	0
1109	0	0	0	0	0	N	0	0
1110	0	0	0	0	0	N	0	0
1111	0	0	0	0	0	N	0	0
1112	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 7 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
1101	7	0
1102	4	0
1103	2	0
1104	6	0
1105	4	0
1106	6	0
1107	6	0
1108	4	0
1109	7	0
1110	5	0
1111	5	0
1112	4	0
n	12	12
Mean	5	0
S.D.	1	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 7 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
2101	0	0	0	0	0	N	0	0
2102	0	0	0	0	0	N	0	0
2103	0	0	0	0	0	N	0	0
2104	0	0	0	0	0	N	0	0
2105	0	0	0	0	0	N	0	0
2106	0	0	0	0	0	N	0	0
2107	0	0	0	0	0	N	0	0
2108	0	0	0	0	0	N	0	0
2109	0	0	0	0	0	N	0	0
2110	0	0	0	0	0	N	0	0
2111	0	0	0	0	0	N	0	0
2112	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 7 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
2101	4	0
2102	5	0
2103	4	0
2104	6	0
2105	6	0
2106	6	0
2107	9	0
2108	5	0
2109	8	0
2110	7	0
2111	3	0
2112	6	0
n	12	12
Mean	6	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 7 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
3101	0	0	0	0	0	N	0	0
3102	0	0	0	0	0	N	0	0
3103	0	0	0	0	0	N	0	0
3104	0	0	0	0	0	N	0	0
3105	0	0	0	0	0	N	0	0
3106	0	0	0	0	0	N	0	0
3107	0	0	0	0	0	N	0	0
3108	0	0	0	0	0	N	0	0
3109	0	0	0	0	0	N	0	0
3110	0	0	0	0	0	N	0	0
3111	0	0	0	0	0	N	0	0
3112	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 7 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
3101	10	0
3102	6	0
3103	8	0
3104	6	0
3105	8	0
3106	8	0
3107	3	0
3108	7	0
3109	8	0
3110	6	0
3111	3	0
3112	8	0
n	12	12
Mean	7	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 7 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
4101	0	0	0	0	0	N	0	0
4102	0	0	0	0	0	N	0	0
4103	0	0	0	0	0	N	0	0
4104	0	0	0	0	0	N	0	0
4105	0	0	0	0	0	N	0	0
4106	0	0	0	0	0	N	0	0
4107	0	0	0	0	0	N	0	0
4108	0	0	0	0	0	N	0	0
4109	0	0	0	0	0	N	0	0
4110	0	0	0	0	0	N	0	0
4111	0	0	0	0	0	N	0	0
4112	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 7 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
4101	10	0
4102	6	0
4103	8	0
4104	6	0
4105	5	0
4106	8	0
4107	5	0
4108	4	0
4109	6	0
4110	5	0
4111	6	0
4112	5	0
n	12	12
Mean	6	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 14 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
1101	0	0	0	0	0	N	0	0
1102	0	0	0	0	0	N	0	0
1103	0	0	0	0	0	N	0	0
1104	0	0	0	0	0	N	0	0
1105	0	0	0	0	0	N	0	0
1106	0	0	0	0	0	N	0	0
1107	0	0	0	0	0	N	0	0
1108	0	0	0	0	0	N	0	0
1109	0	0	0	0	0	N	0	0
1110	0	0	0	0	0	N	0	0
1111	0	0	0	0	0	N	0	0
1112	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 14 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
1101	7	0
1102	3	0
1103	3	0
1104	3	0
1105	4	0
1106	5	0
1107	3	0
1108	4	0
1109	9	0
1110	5	0
1111	4	0
1112	2	0
n	12	12
Mean	4	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 14 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
2101	0	0	0	0	0	N	0	0
2102	0	0	0	0	0	N	0	0
2103	0	0	0	0	0	N	0	0
2104	0	0	0	0	0	N	0	0
2105	0	0	0	0	0	N	0	0
2106	0	0	0	0	0	N	0	0
2107	0	0	0	0	0	N	0	0
2108	0	0	0	0	0	N	0	0
2109	0	0	0	0	0	N	0	0
2110	0	0	0	0	0	N	0	0
2111	0	0	0	0	0	N	0	0
2112	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 14 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
2101	2	0
2102	6	0
2103	3	0
2104	5	0
2105	4	0
2106	9	0
2107	5	0
2108	5	0
2109	5	0
2110	6	0
2111	6	0
2112	5	0
n	12	12
Mean	5	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 14 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
3101	0	0	0	0	0	N	0	0
3102	0	0	0	0	0	N	0	0
3103	0	0	0	0	0	N	0	0
3104	0	0	0	0	0	N	0	0
3105	0	0	0	0	0	N	0	0
3106	0	0	0	0	0	N	0	0
3107	0	0	0	0	0	N	0	0
3108	0	0	0	0	0	N	0	0
3109	0	0	0	0	0	N	0	1
3110	0	0	0	0	0	N	0	0
3111	0	0	0	0	0	N	0	0
3112	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 14 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
3101	6	0
3102	3	0
3103	4	0
3104	7	0
3105	6	0
3106	6	0
3107	5	0
3108	6	0
3109	6	0
3110	3	0
3111	8	0
3112	8	0
n	12	12
Mean	6	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 14 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
4101	0	0	0	0	0	N	0	0
4102	0	0	0	0	0	N	0	0
4103	0	0	0	0	0	N	0	0
4104	0	0	0	0	0	N	0	0
4105	0	0	0	0	0	N	0	0
4106	0	0	0	0	0	N	0	0
4107	0	0	0	0	0	N	0	0
4108	0	0	0	0	0	N	0	0
4109	0	0	0	0	0	N	0	0
4110	0	0	0	0	0	N	0	0
4111	0	0	0	0	0	N	0	0
4112	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 14 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
4101	8	0
4102	7	0
4103	4	0
4104	3	0
4105	4	0
4106	4	0
4107	4	0
4108	2	0
4109	6	0
4110	3	0
4111	1	0
4112	3	0
n	12	12
Mean	4	0
S.D.	2	0

Appendix 2 - 231 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 gestation

Generation : F0 Sex : Female Day : 20 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
1101	0	0	0	0	0	N	0	0
1102	0	0	0	0	0	N	0	0
1103	0	0	0	0	0	N	0	0
1104	0	0	0	0	0	N	0	0
1105	0	0	0	0	0	N	0	0
1106	0	0	0	0	0	N	0	0
1107	0	0	0	0	0	N	0	0
1108	0	0	0	0	0	N	0	0
1109	0	0	0	0	0	N	0	0
1110	0	0	0	0	0	N	0	0
1111	0	0	0	0	0	N	0	0
1112	0	0	0	0	0	N	0	1
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 20 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
1101	4	0
1102	7	0
1103	1	0
1104	5	0
1105	4	0
1106	7	0
1107	3	0
1108	3	0
1109	6	0
1110	3	0
1111	3	0
1112	4	0
n	12	12
Mean	4	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 20 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
2101	0	0	0	0	0	N	0	0
2102	0	0	0	0	0	N	0	0
2103	0	0	0	0	0	N	0	0
2104	0	0	0	0	0	N	0	0
2105	0	0	0	0	0	N	0	0
2106	0	0	0	0	0	N	0	0
2107	0	0	0	0	0	N	0	0
2108	0	0	0	0	0	N	0	0
2109	0	0	0	0	0	N	0	0
2110	0	0	0	0	0	N	0	0
2111	0	0	0	0	0	N	0	0
2112	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 20 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
2101	3	0
2102	2	0
2103	5	0
2104	5	0
2105	4	0
2106	5	0
2107	5	0
2108	5	0
2109	4	0
2110	5	0
2111	4	0
2112	2	0
n	12	12
Mean	4	0
S.D.	1	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 20 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
3101	0	0	0	0	0	N	0	0
3102	0	0	0	0	0	N	0	0
3103	0	0	0	0	0	N	0	0
3104	0	0	0	0	0	N	0	0
3105	0	0	0	0	0	N	0	0
3106	0	0	0	0	0	N	0	0
3107	0	0	0	0	0	N	0	0
3108	0	0	0	0	0	N	0	0
3109	0	0	0	0	0	N	0	0
3110	0	0	0	0	0	N	0	0
3111	0	0	0	0	0	N	0	0
3112	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 20 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
3101	8	0
3102	5	0
3103	4	0
3104	7	0
3105	6	0
3106	6	0
3107	3	0
3108	4	0
3109	8	0
3110	5	0
3111	6	0
3112	6	0
n	12	12
Mean	6	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 20 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
4101	0	0	0	0	0	N	0	0
4102	0	0	0	0	0	N	0	1
4103	0	0	0	0	0	N	0	0
4104	0	0	0	0	0	N	0	0
4105	0	0	0	0	0	N	0	0
4106	0	0	0	0	0	N	0	0
4107	0	0	0	0	0	N	0	0
4108	0	0	0	0	0	N	0	0
4109	0	0	0	0	0	N	0	0
4110	0	0	0	0	0	N	0	0
4111	0	0	0	0	0	N	0	0
4112	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 gestation

Generation : F0 Sex : Female Day : 20 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
4101	4	0
4102	4	0
4103	8	0
4104	4	0
4105	7	0
4106	7	0
4107	3	0
4108	2	0
4109	3	0
4110	1	0
4111	6	0
4112	5	0
n	12	12
Mean	5	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 lactation

Generation : F0 Sex : Female Day : 4 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
1101	0	0	0	0	0	N	0	0
1102	0	0	0	0	0	N	0	0
1103	0	0	0	0	0	N	0	0
1104	0	0	0	0	0	N	0	0
1105	0	0	0	0	0	N	0	0
1106	0	0	0	0	0	N	0	0
1107	0	0	0	0	0	N	0	0
1108	0	0	0	0	0	N	0	0
1109	0	0	0	0	0	N	0	0
1110	0	0	0	0	0	N	0	0
1111	0	0	0	0	0	N	0	0
1112	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 lactation

Generation : F0 Sex : Female Day : 4 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
1101	4	0
1102	4	0
1103	2	0
1104	8	0
1105	4	0
1106	5	0
1107	5	0
1108	4	0
1109	9	0
1110	3	0
1111	6	0
1112	3	0
n	12	12
Mean	5	0
S.D.	2	0

Appendix 2 - 241 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : F0 lactation

Generation : F0 Sex : Female Day : 4 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
2101	0	0	0	0	0	N	0	0
2102	0	0	0	0	0	N	0	0
2103	0	0	0	0	0	N	0	0
2104	0	0	0	0	0	N	0	0
2105	0	0	0	0	0	N	0	0
2106	0	0	0	0	0	N	0	0
2107	0	0	0	0	0	N	0	0
2108	0	0	0	0	0	N	0	0
2109	0	0	0	0	0	N	0	0
2110	0	0	0	0	0	N	0	0
2111	0	0	0	0	0	N	0	0
2112	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : F0 lactation

Generation : F0 Sex : Female Day : 4 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
2101	5	0
2102	3	0
2103	6	0
2104	2	0
2105	5	0
2106	4	0
2107	7	0
2108	5	0
2109	5	0
2110	6	0
2111	3	0
2112	5	0
n	12	12
Mean	5	0
S.D.	1	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 lactation

Generation : F0 Sex : Female Day : 4 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
3101	0	0	0	0	0	N	0	0
3102	0	0	0	0	0	N	0	0
3103	0	0	0	0	0	N	0	0
3104	0	0	0	0	0	N	0	0
3105	0	0	0	0	0	N	0	0
3106	0	0	0	0	0	N	0	0
3107	0	0	0	0	0	N	0	0
3108	0	0	0	0	0	N	0	0
3109	0	0	0	0	0	N	0	0
3110	0	0	0	0	0	N	0	0
3111	0	0	0	0	0	N	0	0
3112	0	0	0	0	0	N	0	0
n	12	12	12	12	12	12	12	12

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : F0 lactation

Generation : F0 Sex : Female Day : 4 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
3101	8	0
3102	4	0
3103	4	0
3104	7	0
3105	6	0
3106	9	0
3107	4	0
3108	8	0
3109	3	0
3110	4	0
3111	8	0
3112	6	0
n	12	12
Mean	6	0
S.D.	2	0

Appendix 2 - 245 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Administration

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
5101	0	0	0	0	0	N	0	0
5102	0	0	0	0	0	N	0	0
5103	0	0	0	0	0	N	0	0
5104	0	0	0	0	0	N	0	0
5105	0	0	0	0	0	N	0	0
5106	0	0	0	0	0	N	0	0
5107	0	0	0	0	0	N	0	0
5108	0	0	0	0	0	N	0	0
5109	0	0	0	0	0	N	0	0
5110	0	0	0	0	0	N	0	0
n	10	10	10	10	10	10	10	10

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : Administration

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
5101	9	0
5102	9	0
5103	11	0
5104	5	0
5105	8	0
5106	7	0
5107	9	0
5108	6	0
5109	7	0
5110	7	0
n	10	10
Mean	8	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : Administration

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
6101	0	0	0	0	0	N	0	0
6102	0	0	0	0	0	N	0	0
6103	0	0	0	0	0	N	0	0
6104	0	0	0	0	0	N	0	0
6105	0	0	0	0	0	N	0	0
6106	0	0	0	0	0	N	0	0
6107	0	0	0	0	0	N	0	0
6108	0	0	0	0	0	N	0	0
6109	0	0	0	0	0	N	0	0
6110	0	0	0	0	0	N	0	0
n	10	10	10	10	10	10	10	10

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : Administration

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
6101	6	0
6102	7	0
6103	11	0
6104	5	0
6105	7	0
6106	6	0
6107	6	0
6108	6	0
6109	4	0
6110	5	0
n	10	10
Mean	6	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : Administration

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
5101	0	0	0	0	0	N	0	0
5102	0	0	0	0	0	N	0	0
5103	0	0	0	0	0	N	0	0
5104	0	0	0	0	0	N	0	0
5105	0	0	0	0	0	N	0	0
5106	0	0	0	0	0	N	0	0
5107	0	0	0	0	0	N	0	0
5108	0	0	0	0	0	N	0	0
5109	0	0	0	0	0	N	0	1
5110	0	0	0	0	0	N	0	0
n	10	10	10	10	10	10	10	10

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : Administration

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
5101	7	0
5102	12	0
5103	9	0
5104	10	0
5105	11	0
5106	9	0
5107	6	0
5108	8	0
5109	6	0
5110	9	0
n	10	10
Mean	9	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : Administration

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
6101	0	0	0	0	0	N	0	0
6102	0	0	0	0	0	N	0	0
6103	0	0	0	0	0	N	0	0
6104	0	0	0	0	0	N	0	0
6105	0	0	0	0	0	N	0	0
6106	0	0	0	0	0	N	0	0
6107	0	0	0	0	0	N	0	1
6108	0	0	0	0	0	N	0	0
6109	0	0	0	0	0	N	0	0
6110	0	0	0	0	0	N	0	0
n	10	10	10	10	10	10	10	10

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : Administration

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
6101	7	0
6102	9	0
6103	10	0
6104	4	0
6105	10	0
6106	7	0
6107	6	0
6108	9	0
6109	8	0
6110	9	0
n	10	10
Mean	8	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : Administration

Generation : F0 Sex : Female Week : 3 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
5101	0	0	0	0	0	N	0	0
5102	0	0	0	0	0	N	0	0
5103	0	0	0	0	0	N	0	0
5104	0	0	0	0	0	N	0	0
5105	0	0	0	0	0	N	0	0
5106	0	0	0	0	0	N	0	0
5107	0	0	0	0	0	N	0	0
5108	0	0	0	0	0	N	0	0
5109	0	0	0	0	0	N	0	0
5110	0	0	0	0	0	N	0	0
n	10	10	10	10	10	10	10	10

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : Administration

Generation : F0 Sex : Female Week : 3 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
5101	8	0
5102	11	0
5103	7	0
5104	9	0
5105	11	0
5106	10	0
5107	6	0
5108	9	0
5109	7	0
5110	13	0
n	10	10
Mean	9	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : Administration

Generation : F0 Sex : Female Week : 3 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
6101	0	0	0	0	0	N	0	0
6102	0	0	0	0	0	N	0	0
6103	0	0	0	0	0	N	0	0
6104	0	0	0	0	0	N	0	0
6105	0	0	0	0	0	N	0	0
6106	0	0	0	0	0	N	0	0
6107	0	0	0	0	0	N	0	0
6108	0	0	0	0	0	N	0	0
6109	0	0	0	0	0	N	0	0
6110	0	0	0	0	0	N	0	0
n	10	10	10	10	10	10	10	10

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : Administration

Generation : F0 Sex : Female Week : 3 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
6101	5	0
6102	8	0
6103	10	0
6104	7	0
6105	9	0
6106	13	0
6107	4	0
6108	14	0
6109	10	0
6110	5	0
n	10	10
Mean	9	0
S.D.	3	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : Administration

Generation : F0 Sex : Female Week : 4 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
5101	0	0	0	0	0	N	0	0
5102	0	0	0	0	0	N	0	0
5103	0	0	0	0	0	N	0	0
5104	0	0	0	0	0	N	0	0
5105	0	0	0	0	0	N	0	0
5106	0	0	0	0	0	N	0	0
5107	0	0	0	0	0	N	0	0
5108	0	0	0	0	0	N	0	0
5109	0	0	0	0	0	N	0	0
5110	0	0	0	0	0	N	0	0
n	10	10	10	10	10	10	10	10

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : Administration

Generation : F0 Sex : Female Week : 4 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
5101	6	0
5102	11	0
5103	11	0
5104	7	0
5105	10	0
5106	7	0
5107	7	0
5108	15	0
5109	6	0
5110	8	0
n	10	10
Mean	9	0
S.D.	3	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : Administration

Generation : F0 Sex : Female Week : 4 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
6101	0	0	0	0	0	N	0	0
6102	0	0	0	0	0	N	0	0
6103	0	0	0	0	0	N	0	0
6104	0	0	0	0	0	N	0	0
6105	0	0	0	0	0	N	0	0
6106	0	0	0	0	0	N	0	1
6107	0	0	0	0	0	N	0	0
6108	0	0	0	0	0	N	0	0
6109	0	0	0	0	0	N	0	0
6110	0	0	0	0	0	N	0	0
n	10	10	10	10	10	10	10	10

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : Administration

Generation : F0 Sex : Female Week : 4 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
6101	9	0
6102	8	0
6103	9	0
6104	5	0
6105	6	0
6106	9	0
6107	5	0
6108	7	0
6109	12	0
6110	9	0
n	10	10
Mean	8	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : Administration

Generation : F0 Sex : Female Week : 5 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
5101	0	0	0	0	0	N	0	0
5102	0	0	0	0	0	N	0	0
5103	0	0	0	0	0	N	0	0
5104	0	0	0	0	0	N	0	0
5105	0	0	0	0	0	N	0	0
5106	0	0	0	0	0	N	0	0
5107	0	0	0	0	0	N	0	0
5108	0	0	0	0	0	N	0	0
5109	0	0	0	0	0	N	0	0
5110	0	0	0	0	0	N	0	0
n	10	10	10	10	10	10	10	10

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : Administration

Generation : F0 Sex : Female Week : 5 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
5101	8	0
5102	6	0
5103	8	0
5104	11	0
5105	9	0
5106	6	0
5107	6	0
5108	9	0
5109	6	0
5110	10	0
n	10	10
Mean	8	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : Administration

Generation : F0 Sex : Female Week : 5 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
6101	0	0	0	0	0	N	0	1
6102	0	0	0	0	0	N	0	0
6103	0	0	0	0	0	N	0	0
6104	0	0	0	0	0	N	0	0
6105	0	0	0	0	0	N	0	0
6106	0	0	0	0	0	N	0	0
6107	0	0	0	0	0	N	0	0
6108	0	0	0	0	0	N	0	0
6109	0	0	0	0	0	N	0	1
6110	0	0	0	0	0	N	0	0
n	10	10	10	10	10	10	10	10

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : Administration

Generation : F0 Sex : Female Week : 5 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
6101	6	0
6102	9	0
6103	7	0
6104	6	0
6105	5	0
6106	6	0
6107	2	0
6108	7	0
6109	11	0
6110	5	0
n	10	10
Mean	6	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : Administration

Generation : F0 Sex : Female Week : 6 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
5101	0	0	0	0	0	N	0	0
5102	0	0	0	0	0	N	0	0
5103	0	0	0	0	0	N	0	0
5104	0	0	0	0	0	N	0	0
5105	0	0	0	0	0	N	0	1
5106	0	0	0	0	0	N	0	0
5107	0	0	0	0	0	N	0	0
5108	0	0	0	0	0	N	0	0
5109	0	0	0	0	0	N	0	0
5110	0	0	0	0	0	N	0	0
n	10	10	10	10	10	10	10	10

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : Administration

Generation : F0 Sex : Female Week : 6 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
5101	7	0
5102	6	0
5103	5	0
5104	8	0
5105	9	0
5106	7	0
5107	8	0
5108	8	0
5109	7	0
5110	8	0
n	10	10
Mean	7	0
S.D.	1	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : Administration

Generation : F0 Sex : Female Week : 6 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
6101	0	0	0	0	0	N	0	0
6102	0	0	0	0	0	N	0	1
6103	0	0	0	0	0	N	0	0
6104	0	0	0	0	0	N	0	0
6105	0	0	0	0	0	N	0	0
6106	0	0	0	0	0	N	0	0
6107	0	0	0	0	0	N	0	1
6108	0	0	0	0	0	N	0	0
6109	0	0	0	0	0	N	0	0
6110	0	0	0	0	0	N	0	0
n	10	10	10	10	10	10	10	10

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : Administration

Generation : F0 Sex : Female Week : 6 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
6101	8	0
6102	5	0
6103	8	0
6104	5	0
6105	9	0
6106	6	0
6107	5	0
6108	8	0
6109	7	0
6110	5	0
n	10	10
Mean	7	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : Recovery

Generation : F0 Sex : Male Week : 1 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
1008	0	0	0	0	0	N	0	0
1009	0	0	0	0	0	N	0	0
1010	0	0	0	0	0	N	0	0
1011	0	0	0	0	0	N	0	0
1012	0	0	0	0	0	N	0	0
n	5	5	5	5	5	5	5	5

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : Recovery

Generation : F0 Sex : Male Week : 1 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
1008	2	3
1009	4	0
1010	2	0
1011	3	0
1012	6	0
n	5	5
Mean	3	1
S.D.	2	1

Appendix 2 - 271 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Recovery

Generation : F0 Sex : Male Week : 1 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
4008	0	0	0	0	0	N	0	0
4009	0	0	0	0	0	N	0	0
4010	0	0	0	0	0	N	0	1
4011	0	0	0	0	0	N	0	0
4012	0	0	0	0	0	N	0	0
n	5	5	5	5	5	5	5	5

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : Recovery

Generation : F0 Sex : Male Week : 1 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
4008	3	0
4009	3	0
4010	3	0
4011	3	0
4012	7	0
n	5	5
Mean	4	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : Recovery

Generation : F0 Sex : Male Week : 2 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
1008	0	0	0	0	0	N	0	0
1009	0	0	0	0	0	N	0	0
1010	0	0	0	0	0	N	0	0
1011	0	0	0	0	0	N	0	0
1012	0	0	0	0	0	N	0	0
n	5	5	5	5	5	5	5	5

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : Recovery

Generation : F0 Sex : Male Week : 2 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
1008	4	0
1009	7	0
1010	6	0
1011	4	0
1012	4	0
n	5	5
Mean	5	0
S.D.	1	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : Recovery

Generation : F0 Sex : Male Week : 2 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
4008	0	0	0	0	0	N	0	1
4009	0	0	0	0	0	N	0	0
4010	0	0	0	0	0	N	0	1
4011	0	0	0	0	0	N	0	0
4012	0	0	0	0	0	N	0	0
n	5	5	5	5	5	5	5	5

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : Recovery

Generation : F0 Sex : Male Week : 2 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
4008	4	0
4009	8	0
4010	7	0
4011	3	0
4012	4	0
n	5	5
Mean	5	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : Recovery

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
5106	0	0	0	0	0	N	0	0
5107	0	0	0	0	0	N	0	0
5108	0	0	0	0	0	N	0	0
5109	0	0	0	0	0	N	0	0
5110	0	0	0	0	0	N	0	0
n	5	5	5	5	5	5	5	5

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : Recovery

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
5106	7	0
5107	7	0
5108	6	0
5109	6	0
5110	10	0
n	5	5
Mean	7	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : Recovery

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
6106	0	0	0	0	0	N	0	0
6107	0	0	0	0	0	N	0	0
6108	0	0	0	0	0	N	0	0
6109	0	0	0	0	0	N	0	0
6110	0	0	0	0	0	N	0	0
n	5	5	5	5	5	5	5	5

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : Recovery

Generation : F0 Sex : Female Week : 1 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
6106	7	0
6107	5	0
6108	10	0
6109	9	0
6110	6	0
n	5	5
Mean	7	0
S.D.	2	0

Appendix 2 - 281 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Recovery

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
5106	0	0	0	0	0	N	0	0
5107	0	0	0	0	0	N	0	0
5108	0	0	0	0	0	N	0	1
5109	0	0	0	0	0	N	0	0
5110	0	0	0	0	0	N	0	0
n	5	5	5	5	5	5	5	5

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Open field observation

Period : Recovery

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
5106	5	0
5107	7	0
5108	9	0
5109	7	0
5110	7	0
n	5	5
Mean	7	0
S.D.	1	0

Appendix 2 - 283 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Open field observation Period : Recovery

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Arousal	Convulsion	Abnormal behavior	Stereotypy	Gait	Posture	Grooming	Urination
6106	0	0	0	0	0	N	0	0
6107	0	0	0	0	0	N	0	0
6108	0	0	0	0	0	N	0	0
6109	0	0	0	0	0	N	0	0
6110	0	0	0	0	0	N	0	0
n	5	5	5	5	5	5	5	5

Arousal) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Nomal, 1: Increased alertness, 2: Markedly alert
Convulsion) 0: None, 1: Minor, 2: Moderate, 3: Severe
Abnormal behavior) 0: None, 1: Minor, 2: Moderate, 3: Severe
Stereotypy) 0: None, 1: Minor, 2: Moderate, 3: Sevear
Gait) U: No/minimal location, 0: Nomal, 1: Slight, 2: Moderate, 3: Markedly
Posture) N: Normal, F: Flattened, H: Hunched
Grooming) 0: None, 1: Occasional bouts (up to four), 2: Numerous (more than four)
Urination) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Open field observation

Period : Recovery

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Rearing	Defecation count
6106	8	0
6107	7	0
6108	8	0
6109	12	0
6110	6	0
n	5	5
Mean	8	0
S.D.	2	0

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Manipulative test

Generation : F0 Sex : Male Week : 6 Period : F0 mating

Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Auditory response	Approach response	Touch response	Tail pinch response	Pupillary reflex
1008	0	0	0	0	P
1009	0	0	0	0	P
1010	0	0	0	0	P
1011	0	0	0	0	P
1012	0	0	0	0	P
n	5	5	5	5	5

Auditory response) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
Approach response) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
Touch response) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
Tail pinch response) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
Pupillary reflex) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Manipulative test

Generation : F0 Sex : Male Week : 6 Period : F0 mating

Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Aerial righting reflex	Landing foot splay mm
1008	0	86
1009	0	95
1010	0	64
1011	0	110
1012	0	60
n	5	5
Mean	0	83
S.D.	0	21

Aerial righting reflex) Total score

Appendix 2 - 287 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Manipulative test Period : F0 mating

Generation : F0 Sex : Male Week : 6 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Auditory response	Approach response	Touch response	Tail pinch response	Pupillary reflex
2008	0	0	0	0	P
2009	0	0	0	0	P
2010	0	0	0	0	P
2011	0	0	0	0	P
2012	0	0	0	0	P
n	5	5	5	5	5

Auditory response) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
Approach response) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
Touch response) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
Tail pinch response) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
Pupillary reflex) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Manipulative test

Generation : F0 Sex : Male Week : 6 Period : F0 mating

Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Aerial righting reflex	Landing foot splay mm
2008	0	63
2009	0	50
2010	0	95
2011	0	76
2012	0	69
n	5	5
Mean	0	71
S.D.	0	17

Aerial righting reflex) Total score

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Manipulative test

Period : F0 mating

Generation : F0 Sex : Male Week : 6 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Auditory response	Approach response	Touch response	Tail pinch response	Pupillary reflex
3008	0	0	0	0	P
3009	0	0	0	0	P
3010	0	0	0	0	P
3011	0	0	0	0	P
3012	0	0	0	0	P
n	5	5	5	5	5

Auditory response) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
Approach response) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
Touch response) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
Tail pinch response) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
Pupillary reflex) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Manipulative test

Generation : F0 Sex : Male Week : 6 Period : F0 mating

Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Aerial righting reflex	Landing foot splay mm
3008	0	84
3009	0	97
3010	0	91
3011	0	59
3012	0	53
n	5	5
Mean	0	77
S.D.	0	20

Aerial righting reflex) Total score

Appendix 2 - 291 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Manipulative test Period : F0 mating

Generation : F0 Sex : Male Week : 6 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Auditory response	Approach response	Touch response	Tail pinch response	Pupillary reflex
4008	0	0	0	0	P
4009	0	0	0	0	P
4010	0	0	0	0	P
4011	0	0	0	0	P
4012	0	0	0	0	P
n	5	5	5	5	5

Auditory response) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
Approach response) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
Touch response) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
Tail pinch response) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
Pupillary reflex) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Manipulative test

Generation : F0 Sex : Male Week : 6 Period : F0 mating

Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Aerial righting reflex	Landing foot splay mm
4008	0	95
4009	0	74
4010	0	109
4011	0	111
4012	0	75
n	5	5
Mean	0	93
S.D.	0	18

Aerial righting reflex) Total score

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Manipulative test

Period : F0 lactation

Generation : F0 Sex : Female Day : 4 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Auditory response	Approach response	Touch response	Tail pinch response	Pupillary reflex
1101	0	0	0	0	P
1102	0	0	0	0	P
1104	0	0	0	0	P
1107	0	0	0	0	P
1110	0	0	0	0	P
n	5	5	5	5	5

Auditory response) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
Approach response) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
Touch response) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
Tail pinch response) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
Pupillary reflex) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Manipulative test

Generation : F0 Sex : Female Day : 4 Period : F0 lactation

Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Aerial righting reflex	Landing foot splay mm
1101	0	53
1102	0	65
1104	0	62
1107	0	42
1110	0	53
n	5	5
Mean	0	55
S.D.	0	9

Aerial righting reflex) Total score

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Manipulative test

Period : F0 lactation

Generation : F0 Sex : Female Day : 4 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Auditory response	Approach response	Touch response	Tail pinch response	Pupillary reflex
2101	0	0	0	0	P
2102	0	0	0	0	P
2103	0	0	0	0	P
2107	0	0	0	0	P
2112	0	0	0	0	P
n	5	5	5	5	5

Auditory response) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
Approach response) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
Touch response) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
Tail pinch response) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
Pupillary reflex) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Manipulative test

Generation : F0 Sex : Female Day : 4 Period : F0 lactation

Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Aerial righting reflex	Landing foot splay mm
2101	0	46
2102	0	78
2103	0	52
2107	0	54
2112	0	70
n	5	5
Mean	0	60
S.D.	0	13

Aerial righting reflex) Total score

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Manipulative test

Period : F0 lactation

Generation : F0 Sex : Female Day : 4 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Auditory response	Approach response	Touch response	Tail pinch response	Pupillary reflex
3102	0	0	0	0	P
3103	0	0	0	0	P
3104	0	0	0	0	P
3105	0	0	0	0	P
3108	0	0	0	0	P
n	5	5	5	5	5

Auditory response) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
Approach response) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
Touch response) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
Tail pinch response) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
Pupillary reflex) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Manipulative test

Generation : F0 Sex : Female Day : 4 Period : F0 lactation

Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Aerial righting reflex	Landing foot splay mm
3102	0	48
3103	0	55
3104	0	90
3105	0	45
3108	0	41
n	5	5
Mean	0	56
S.D.	0	20

Aerial righting reflex) Total score

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Manipulative test

Period : Recovery

Generation : F0 Sex : Male Week : 2 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Auditory response	Approach response	Touch response	Tail pinch response	Pupillary reflex
1008	0	0	0	0	P
1009	0	0	0	0	P
1010	0	0	0	0	P
1011	0	0	0	0	P
1012	0	0	0	0	P
n	5	5	5	5	5

Auditory response) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
Approach response) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
Touch response) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
Tail pinch response) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
Pupillary reflex) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Manipulative test

Generation : F0 Sex : Male Week : 2 Period : Recovery

Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Aerial right-ing reflex	Landing foot splay mm
1008	0	97
1009	0	97
1010	0	81
1011	0	96
1012	0	66
n	5	5
Mean	0	87
S.D.	0	14

Aerial righting reflex) Total score

Appendix 2 - 301 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Manipulative test Period : Recovery

Generation : F0 Sex : Male Week : 2 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Auditory response	Approach response	Touch response	Tail pinch response	Pupillary reflex
4008	0	0	0	0	P
4009	0	0	0	0	P
4010	0	0	0	0	P
4011	0	0	0	0	P
4012	0	0	0	0	P
n	5	5	5	5	5

Auditory response) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
Approach response) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
Touch response) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
Tail pinch response) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
Pupillary reflex) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Manipulative test

Generation : F0 Sex : Male Week : 2 Period : Recovery

Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Aerial righting reflex	Landing foot splay mm
4008	0	65
4009	0	63
4010	0	107
4011	0	110
4012	0	91
n	5	5
Mean	0	87
S.D.	0	22

Aerial righting reflex) Total score

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Manipulative test

Period : Recovery

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Auditory response	Approach response	Touch response	Tail pinch response	Pupillary reflex
5106	0	0	0	0	P
5107	0	0	0	0	P
5108	0	0	0	0	P
5109	0	0	0	0	P
5110	0	0	0	0	P
n	5	5	5	5	5

Auditory response) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
Approach response) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
Touch response) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
Tail pinch response) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
Pupillary reflex) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Manipulative test

Generation : F0 Sex : Female Week : 2 Period : Recovery

Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Aerial right-ing reflex	Landing foot splay mm
5106	0	53
5107	0	54
5108	0	70
5109	0	88
5110	0	47
n	5	5
Mean	0	62
S.D.	0	17

Aerial righting reflex) Total score

Appendix 2 - 305 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Manipulative test Period : Recovery

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Auditory response	Approach response	Touch response	Tail pinch response	Pupillary reflex
6106	0	0	0	0	P
6107	0	0	0	0	P
6108	0	0	0	0	P
6109	0	0	0	0	P
6110	0	0	0	0	P
n	5	5	5	5	5

Auditory response) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
Approach response) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
Touch response) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
Tail pinch response) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
Pupillary reflex) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Manipulative test
Generation : F0 Sex : Female Week : 2 Period : Recovery
Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Aerial righting reflex	Landing foot splay mm
6106	0	33
6107	0	94
6108	0	35
6109	0	81
6110	0	31
n	5	5
Mean	0	55
S.D.	0	30

Aerial righting reflex) Total score

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Grip strength

Period : F0 mating

Generation : F0 Sex : Male Week : 6 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Grip strength of fore limb g	Grip strength of hind limb g
1008	1730	1006
1009	1870	1025
1010	1716	1034
1011	1591	1073
1012	1632	1090
n	5	5
Mean	1708	1046
S.D.	108	35

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Grip strength

Period : F0 mating

Generation : F0 Sex : Male Week : 6 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Grip strength of fore limb g	Grip strength of hind limb g
2008	1812	856
2009	1393	935
2010	1601	1116
2011	1874	1188
2012	1546	893
n	5	5
Mean	1645	998
S.D.	197	146

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Grip strength

Period : F0 mating

Generation : F0 Sex : Male Week : 6 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Grip strength of fore limb g	Grip strength of hind limb g
3008	1640	1056
3009	1888	1231
3010	1529	1109
3011	1883	1074
3012	1436	802
n	5	5
Mean	1675	1054
S.D.	205	157

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Grip strength

Period : F0 mating

Generation : F0 Sex : Male Week : 6 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Grip strength of fore limb g	Grip strength of hind limb g
4008	1890	1358
4009	1448	1170
4010	1864	1388
4011	1485	1071
4012	1737	1084
n	5	5
Mean	1685	1214
S.D.	208	150

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Grip strength

Period : F0 lactation

Generation : F0 Sex : Female Day : 4 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Grip strength of fore limb g	Grip strength of hind limb g
1101	1145	745
1102	1462	907
1104	1070	1184
1107	1109	662
1110	1454	774
n	5	5
Mean	1248	854
S.D.	194	204

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Grip strength

Generation : F0 Sex : Female Day : 4 Period : F0 lactation

Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Grip strength of fore limb g	Grip strength of hind limb g
2101	1038	976
2102	1115	975
2103	1414	880
2107	820	1033
2112	1112	671
n	5	5
Mean	1100	907
S.D.	213	143

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Grip strength

Generation : F0 Sex : Female Day : 4 Period : F0 lactation

Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Grip strength of fore limb g	Grip strength of hind limb g
3102	890	757
3103	1437	1070
3104	1311	1044
3105	1364	837
3108	1202	1136
n	5	5
Mean	1241	969
S.D.	214	163

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Grip strength

Period : Recovery

Generation : F0 Sex : Male Week : 2 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Grip strength of fore limb g	Grip strength of hind limb g
1008	2290	1407
1009	2113	829
1010	1454	1079
1011	1709	1029
1012	2087	1237
n	5	5
Mean	1931	1116
S.D.	340	218

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Grip strength

Period : Recovery

Generation : F0 Sex : Male Week : 2 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Grip strength of fore limb g	Grip strength of hind limb g
4008	1863	1223
4009	1420	894
4010	1918	1444
4011	1723	1242
4012	1997	1104
n	5	5
Mean	1784	1181
S.D.	227	202

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Grip strength

Period : Recovery

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Grip strength of fore limb g	Grip strength of hind limb g
5106	1467	661
5107	1367	910
5108	1193	503
5109	1213	815
5110	1064	829
n	5	5
Mean	1261	744
S.D.	158	162

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Grip strength

Period : Recovery

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Grip strength of fore limb g	Grip strength of hind limb g
6106	1222	877
6107	1139	870
6108	1150	858
6109	1219	660
6110	1218	710
n	5	5
Mean	1190	795
S.D.	41	102

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Motor activity

Period : F0 mating

Generation : F0 Sex : Male Week : 6 Dose : benzyl salicylate 0 mg/kg Species : Rat

	0'-10'	10'-20'	20'-30'	30'-40'	40'-50'	50'-60'	Total(0'-60')
Animal No.	Count	Count	Count	Count	Count	Count	Count
1008	522	400	277	324	365	255	2143
1009	436	394	233	291	171	234	1759
1010	449	219	46	29	248	249	1240
1011	413	248	181	172	211	38	1263
1012	452	299	313	354	253	332	2003
n	5	5	5	5	5	5	5
Mean	454	312	210	234	250	222	1682
S.D.	41	83	104	134	72	109	416

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Motor activity

Period : F0 mating

Generation : F0 Sex : Male Week : 6 Dose : benzyl salicylate 30 mg/kg Species : Rat

	0'-10'	10'-20'	20'-30'	30'-40'	40'-50'	50'-60'	Total(0'-60')
Animal No.	Count	Count	Count	Count	Count	Count	Count
2008	501	372	362	332	303	253	2123
2009	453	308	215	206	170	261	1613
2010	463	344	413	307	63	176	1766
2011	479	152	202	235	288	58	1414
2012	353	192	219	170	76	43	1053
n	5	5	5	5	5	5	5
Mean	450	274	282	250	180	158	1594
S.D.	57	97	98	68	113	104	398

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Motor activity

Period : F0 mating

Generation : F0 Sex : Male Week : 6 Dose : benzyl salicylate 100 mg/kg Species : Rat

	0'-10'	10'-20'	20'-30'	30'-40'	40'-50'	50'-60'	Total(0'-60')
Animal No.	Count	Count	Count	Count	Count	Count	Count
3008	449	383	264	151	12	38	1297
3009	341	112	8	265	359	340	1425
3010	310	449	50	55	371	27	1262
3011	492	303	330	285	282	224	1916
3012	264	164	335	52	45	136	996
n	5	5	5	5	5	5	5
Mean	371	282	197	162	214	153	1379
S.D.	96	143	157	111	173	132	338

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Motor activity

Period : F0 mating

Generation : F0 Sex : Male Week : 6 Dose : benzyl salicylate 300 mg/kg Species : Rat

	0'-10'	10'-20'	20'-30'	30'-40'	40'-50'	50'-60'	Total(0'-60')
Animal No.	Count	Count	Count	Count	Count	Count	Count
4008	491	349	390	330	348	374	2282
4009	430	361	356	367	366	11	1891
4010	260	324	132	326	276	40	1358
4011	398	405	249	253	310	165	1780
4012	257	269	291	273	270	145	1505
n	5	5	5	5	5	5	5
Mean	367	342	284	310	314	147	1763
S.D.	105	50	101	46	43	143	359

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Motor activity

Period : F0 lactation

Generation : F0 Sex : Female Day : 4 Dose : benzyl salicylate 0 mg/kg Species : Rat

	0'-10'	10'-20'	20'-30'	30'-40'	40'-50'	50'-60'	Total(0'-60')
Animal No.	Count	Count	Count	Count	Count	Count	Count
1101	413	341	294	300	323	222	1893
1102	336	108	149	92	146	337	1168
1104	322	90	46	16	51	337	862
1107	453	226	378	59	27	132	1275
1110	365	216	121	228	92	177	1199
n	5	5	5	5	5	5	5
Mean	378	196	198	139	128	241	1279
S.D.	55	102	135	120	118	93	377

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Motor activity

Period : F0 lactation

Generation : F0 Sex : Female Day : 4 Dose : benzyl salicylate 30 mg/kg Species : Rat

	0'-10'	10'-20'	20'-30'	30'-40'	40'-50'	50'-60'	Total(0'-60')
Animal No.	Count	Count	Count	Count	Count	Count	Count
2101	410	168	92	13	89	193	965
2102	373	168	213	59	140	280	1233
2103	361	131	5	65	171	162	895
2107	410	278	308	371	393	324	2084
2112	276	174	142	126	5	3	726
n	5	5	5	5	5	5	5
Mean	366	184	152	127	160	192	1181
S.D.	55	55	116	142	145	124	537

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Motor activity

Generation : F0 Sex : Female Day : 4 Period : F0 lactation

Dose : benzyl salicylate 100 mg/kg Species : Rat

	0'-10'	10'-20'	20'-30'	30'-40'	40'-50'	50'-60'	Total(0'-60')
Animal No.	Count	Count	Count	Count	Count	Count	Count
3102	314	147	35	55	200	120	871
3103	401	340	338	65	41	338	1523
3104	435	336	173	3	11	110	1068
3105	384	187	286	52	96	339	1344
3108	459	316	357	326	296	295	2049
n	5	5	5	5	5	5	5
Mean	399	265	238	100	129	240	1371
S.D.	56	91	134	128	118	116	454

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Motor activity

Period : Recovery

Generation : F0 Sex : Male Week : 2 Dose : benzyl salicylate 0 mg/kg Species : Rat

	0'-10'	10'-20'	20'-30'	30'-40'	40'-50'	50'-60'	Total(0'-60')
Animal No.	Count	Count	Count	Count	Count	Count	Count
1008	444	449	323	285	335	121	1957
1009	457	385	340	236	363	380	2161
1010	391	299	226	196	166	29	1307
1011	408	256	191	7	14	95	971
1012	427	370	317	277	346	262	1999
n	5	5	5	5	5	5	5
Mean	425	352	279	200	245	177	1679
S.D.	27	76	66	114	152	142	513

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Motor activity

Period : Recovery

Generation : F0 Sex : Male Week : 2 Dose : benzyl salicylate 300 mg/kg Species : Rat

	0'-10'	10'-20'	20'-30'	30'-40'	40'-50'	50'-60'	Total(0'-60')
Animal No.	Count	Count	Count	Count	Count	Count	Count
4008	433	441	375	364	301	366	2280
4009	418	360	260	407	142	2	1589
4010	399	143	34	8	299	220	1103
4011	409	405	290	269	290	253	1916
4012	323	341	287	228	253	326	1758
n	5	5	5	5	5	5	5
Mean	396	338	249	255	257	233	1729
S.D.	43	116	128	156	67	142	433

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Motor activity

Period : Recovery

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 0 mg/kg Species : Rat

	0'-10'	10'-20'	20'-30'	30'-40'	40'-50'	50'-60'	Total(0'-60')
Animal No.	Count	Count	Count	Count	Count	Count	Count
5106	461	102	238	16	55	58	930
5107	390	275	96	5	177	266	1209
5108	331	179	127	128	189	172	1126
5109	382	351	190	172	136	40	1271
5110	380	260	157	125	194	57	1173
n	5	5	5	5	5	5	5
Mean	389	233	162	89	150	119	1142
S.D.	47	96	55	74	58	98	130

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Motor activity

Period : Recovery

Generation : F0 Sex : Female Week : 2 Dose : benzyl salicylate 300 mg/kg Species : Rat

	0'-10'	10'-20'	20'-30'	30'-40'	40'-50'	50'-60'	Total(0'-60')
Animal No.	Count	Count	Count	Count	Count	Count	Count
6106	392	300	298	118	270	197	1575
6107	449	326	343	240	143	4	1505
6108	439	388	356	401	390	405	2379
6109	395	263	261	308	149	211	1587
6110	432	327	98	147	26	29	1059
n	5	5	5	5	5	5	5
Mean	421	321	271	243	196	169	1621
S.D.	26	46	104	116	139	162	476

Appendix 3 - 1 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight Period : F0 before mating Day 1-15, F0 mating Day 15-43

Sex : Male Dose : benzyl salicylate 0 mg/kg Unit : g Species : Rat

Animal No.	/Day 1	8	15	22	29	36	42	Body weight gain
1001	411	441	471	497	521	542	552	141
1002	387	422	456	478	511	539	555	168
1003	415	448	486	513	544	571	588	173
1004	392	420	450	466	489	501	511	119
1005	392	422	449	469	496	523	527	135
1006	403	427	458	468	489	515	528	125
1007	378	389	413	423	438	455	465	87
1008	384	411	436	461	494	515	512	128
1009	418	447	479	494	518	542	533	115
1010	412	445	483	505	534	566	578	166
1011	387	409	433	452	467	493	502	115
1012	384	410	428	435	451	471	482	98
n	12	12	12	12	12	12	12	12
Mean	397	424	454	472	496	519	528	131
S.D.	14	18	23	27	32	35	37	27

Appendix 3 - 2 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight Period : F0 before mating Day 1-15, F0 mating Day 15-43

Sex : Male Dose : benzyl salicylate 30 mg/kg Unit : g Species : Rat

Animal No.	/Day 1	8	15	22	29	36	42	Body weight gain
2001	411	448	481	504	522	554	559	148
2002	383	414	439	458	480	497	509	126
2003	388	404	422	439	452	462	473	85
2004	391	420	451	460	481	503	514	123
2005	409	440	469	490	506	519	504	95
2006	397	428	456	473	501	516	532	135
2007	420	447	470	492	522	543	550	130
2008	413	441	470	483	510	532	536	123
2009	389	426	452	467	482	495	500	111
2010	377	410	432	450	464	487	492	115
2011	399	436	463	478	497	512	514	115
2012	367	391	417	435	454	461	460	93
n	12	12	12	12	12	12	12	12
Mean	395	425	452	469	489	507	512	117
S.D.	16	18	20	22	24	29	29	18

Appendix 3 - 3 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight Period : F0 before mating Day 1-15, F0 mating Day 15-43

Sex : Male Dose : benzyl salicylate 100 mg/kg Unit : g Species : Rat

Animal No.	/Day 1	8	15	22	29	36	42	Body weight gain
3001	414	452	485	503	527	563	581	167
3002	410	442	479	507	542	568	585	175
3003	398	424	441	466	492	510	511	113
3004	389	415	440	455	470	486	493	104
3005	390	419	446	465	479	503	521	131
3006	385	421	441	457	475	499	506	121
3007	364	405	421	440	457	469	473	109
3008	380	413	448	475	496	519	522	142
3009	408	444	473	475	492	522	536	128
3010	380	420	456	467	495	511	524	144
3011	411	447	484	507	529	557	572	161
3012	397	432	472	487	512	540	545	148
n	12	12	12	12	12	12	12	12
Mean	394	428	457	475	497	521	531	137
S.D.	15	15	21	22	26	31	35	23

Appendix 3 - 4 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight Period : F0 before mating Day 1-15, F0 mating Day 15-43

Sex : Male Dose : benzyl salicylate 300 mg/kg Unit : g Species : Rat

Animal No.	/Day 1	8	15	22	29	36	42	Body weight gain
4001	370	391	414	428	454	468	478	108
4002	392	421	449	468	497	513	531	139
4003	405	423	459	465	478	498	508	103
4004	413	455	490	501	525	536	544	131
4005	396	415	451	469	497	523	539	143
4006	400	428	467	477	490	511	527	127
4007	376	400	423	441	466	481	488	112
4008	396	419	452	462	481	502	509	113
4009	381	392	416	439	462	482	490	109
4010	384	408	443	452	474	492	491	107
4011	419	438	452	460	476	479	481	62
4012	403	424	447	481	500	514	505	102
n	12	12	12	12	12	12	12	12
Mean	395	418	447	462	483	500	508	113
S.D.	15	19	22	20	20	20	23	21

Appendix 3 - 5 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight Period : F0 before mating Day 1-15

Sex : Female Dose : benzyl salicylate 0 mg/kg Unit : g Species : Rat

Animal No.	/Day 1	8	15	Body weight gain
1101	248	261	269	21
1102	247	262	273	26
1103	269	282	286	17
1104	251	253	260	9
1105	254	270	291	37
1106	262	259	273	11
1107	236	251	265	29
1108	256	278	290	34
1109	253	264	279	26
1110	261	269	287	26
1111	268	287	300	32
1112	231	240	247	16
n	12	12	12	12
Mean	253	265	277	24
S.D.	12	14	15	9

Appendix 3 - 6 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight Period : F0 before mating Day 1-15

Sex : Female Dose : benzyl salicylate 30 mg/kg Unit : g Species : Rat

Animal No.	/Day 1	8	15	Body weight gain
2101	245	250	259	14
2102	252	251	269	17
2103	264	266	283	19
2104	252	254	261	9
2105	264	284	295	31
2106	248	256	265	17
2107	225	246	259	34
2108	246	271	289	43
2109	247	268	278	31
2110	232	244	249	17
2111	266	277	285	19
2112	275	287	310	35
n	12	12	12	12
Mean	251	263	275	24
S.D.	14	15	18	10

Appendix 3 - 7 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight Period : F0 before mating Day 1-15

Sex : Female Dose : benzyl salicylate 100 mg/kg Unit : g Species : Rat

Animal No.	/Day 1	8	15	Body weight gain
3101	229	231	227	-2
3102	255	273	284	29
3103	257	270	287	30
3104	253	269	291	38
3105	244	262	271	27
3106	246	258	265	19
3107	256	272	280	24
3108	250	292	306	56
3109	247	250	250	3
3110	238	251	262	24
3111	260	278	293	33
3112	267	283	288	21
n	12	12	12	12
Mean	250	266	275	25
S.D.	10	17	22	15

Appendix 3 - 8 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight Period : F0 before mating Day 1-15

Sex : Female Dose : benzyl salicylate 300 mg/kg Unit : g Species : Rat

Animal No.	/Day 1	8	15	Body weight gain
4101	245	247	256	11
4102	266	277	280	14
4103	256	259	287	31
4104	250	265	286	36
4105	247	250	269	22
4106	250	269	278	28
4107	241	251	270	29
4108	254	258	290	36
4109	255	264	286	31
4110	232	245	254	22
4111	273	285	288	15
4112	238	244	268	30
n	12	12	12	12
Mean	251	260	276	25
S.D.	11	13	12	9

Appendix 3 - 9 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight Period : F0 gestation Day 0-25

Sex : Female Dose : benzyl salicylate 0 mg/kg Unit : g Species : Rat

Animal No.	/Day 0	7	14	20	Body weight gain
1101	275	311	342	425	150
1102	279	327	357	402	123
1103	307	336	376	458	151
1104	262	294	331	416	154
1105	298	358	408	499	201
1106	296	350	378	426	130
1107	264	303	343	429	165
1108	292	338	367	451	159
1109	294	345	387	451	157
1110	281	308	342	425	144
1111	311	351	380	455	144
1112	263	302	327	393	130
n	12	12	12	12	12
Mean	285	327	362	436	151
S.D.	17	22	25	29	20

Appendix 3 - 10 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight Period : F0 gestation Day 0-25

Sex : Female Dose : benzyl salicylate 30 mg/kg Unit : g Species : Rat

Animal No.	/Day 0	7	14	20	Body weight gain
2101	272	303	341	430	158
2102	271	303	340	416	145
2103	280	317	356	428	148
2104	282	327	357	456	174
2105	302	330	375	461	159
2106	261	304	332	426	165
2107	258	299	332	425	167
2108	288	324	352	431	143
2109	280	324	362	431	151
2110	260	291	325	419	159
2111	305	346	388	471	166
2112	305	352	389	477	172
n	12	12	12	12	12
Mean	280	318	354	439	159
S.D.	17	19	21	21	10

Appendix 3 - 11 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight Period : F0 gestation Day 0-25

Sex : Female Dose : benzyl salicylate 100 mg/kg Unit : g Species : Rat

Animal No.	/Day 0	7	14	20	Body weight gain
3101	243	286	321	404	161
3102	282	318	358	457	175
3103	289	325	352	434	145
3104	290	320	351	380	90
3105	269	310	339	414	145
3106	298	353	397	504	206
3107	286	319	354	430	144
3108	299	342	370	446	147
3109	263	295	324	394	131
3110	271	302	339	421	150
3111	297	324	359	463	166
3112	296	347	389	477	181
n	12	12	12	12	12
Mean	282	320	354	435	153
S.D.	17	20	23	36	29

Appendix 3 - 12 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight Period : F0 gestation Day 0-25

Sex : Female Dose : benzyl salicylate 300 mg/kg Unit : g Species : Rat

Animal No.	/Day 0	7	14	20	Body weight gain
4101	267	300	333	356	89
4102	302	346	381	422	120
4103	288	334	372	383	95
4104	287	318	352	361	74
4105	266	315	353	405	139
4106	273	316	355	392	119
4107	272	310	336	384	112
4108	286	332	375	402	116
4109	281	307	337	388	107
4110	259	293	315	353	94
4111	344	363	382	397	53
4112	261	310	338	385	124
n	12	12	12	12	12
Mean	282	320	352	386	104
S.D.	23	20	22	21	24

Appendix 3 - 13 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight Period : F0 lactation Day 0-5

Sex : Female Dose : benzyl salicylate 0 mg/kg Unit : g Species : Rat

Animal No.	/Day 0	4	Body weight gain
1101	343	332	-11
1102	358	359	1
1103	363	382	19
1104	340	349	9
1105	372	364	-8
1106	391	364	-27
1107	325	334	9
1108	363	367	4
1109	386	385	-1
1110	322	330	8
1111	363	357	-6
1112	328	320	-8
n	12	12	12
Mean	355	354	-1
S.D.	23	21	12

Appendix 3 - 14 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight Period : F0 lactation Day 0-5

Sex : Female Dose : benzyl salicylate 30 mg/kg Unit : g Species : Rat

Animal No.	/Day 0	4	Body weight gain
2101	337	331	-6
2102	340	332	-8
2103	345	355	10
2104	358	358	0
2105	362	365	3
2106	315	320	5
2107	332	319	-13
2108	340	338	-2
2109	361	349	-12
2110	319	313	-6
2111	376	372	-4
2112	378	354	-24
n	12	12	12
Mean	347	342	-5
S.D.	20	19	9

Appendix 3 - 15 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight Period : F0 lactation Day 0-5

Sex : Female Dose : benzyl salicylate 100 mg/kg Unit : g Species : Rat

Animal No.	/Day 0	4	Body weight gain
3101	333	321	-12
3102	340	356	16
3103	334	336	2
3104	375	363	-12
3105	346	333	-13
3106	375	385	10
3107	336	356	20
3108	355	355	0
3109	326	311	-15
3110	333	336	3
3111	362	373	11
3112	400	408	8
n	12	12	12
Mean	351	353	2
S.D.	23	28	12

Appendix 3 - 16 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight Period : F0 lactation Day 0-5

Sex : Female Dose : benzyl salicylate 300 mg/kg Unit : g Species : Rat

Animal No.	/Day 0	4	Body weight gain
4102 c)	371	...	:::
4105 b)	335	...	:::
4106 a)	...	...	:::
4107 b)	337	...	:::
4109 b)	350	...	:::
4110 b)	331	...	:::
n	5	0	0
Mean	345		
S.D.	16		

... : Mortality data, ::: : Impossible to calculate

Animal No. 4101,4103,4104,4108,4111,4112 : Not delivered

a) : Necropsied on lactaion day 0 because all offspring were stillborn

b) : Necropsied on lactaion day 1 because all offspring died

c) : Necropsied on lactaion day 2 because all offspring died

Appendix 3 - 17 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight Period : Administration

Sex : Female Dose : benzyl salicylate 0 mg/kg Unit : g Species : Rat

Animal No.	/Day 1	8	15	22	29	36	42	Body weight gain
5101	261	274	287	289	298	304	304	43
5102	248	248	250	263	268	280	282	34
5103	253	260	269	266	284	288	282	29
5104	239	254	264	257	273	269	280	41
5105	257	276	291	289	302	307	310	53
5106	242	255	261	280	295	298	302	60
5107	253	263	269	266	279	288	287	34
5108	246	255	266	278	295	299	308	62
5109	248	255	264	283	295	308	313	65
5110	249	272	288	290	309	311	316	67
n	10	10	10	10	10	10	10	10
Mean	250	261	271	276	290	295	298	49
S.D.	7	10	13	12	13	14	14	14

Appendix 3 - 18 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight Period : Administration

Sex : Female Dose : benzyl salicylate 300 mg/kg Unit : g Species : Rat

Animal No.	/Day 1	8	15	22	29	36	42	Body weight gain
6101	249	257	266	283	290	291	293	44
6102	240	246	259	280	299	305	314	74
6103	263	268	283	283	300	310	305	42
6104	237	255	268	278	286	296	300	63
6105	247	271	295	298	301	317	327	80
6106	256	262	286	302	312	318	332	76
6107	248	245	265	278	280	283	302	54
6108	246	257	265	266	265	279	281	35
6109	248	271	276	292	302	302	306	58
6110	223	245	253	263	267	276	279	56
n	10	10	10	10	10	10	10	10
Mean	246	258	272	282	290	298	304	58
S.D.	11	10	13	13	16	15	17	15

Appendix 3 - 19 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight Period : Recovery Day 1-15

Sex : Male Dose : benzyl salicylate 0 mg/kg Unit : g Species : Rat

Animal No.	/Day 1	8	14	Body weight gain
1008	520	531	525	5
1009	538	556	560	22
1010	580	601	610	30
1011	505	515	517	12
1012	484	498	499	15
n	5	5	5	5
Mean	525	540	542	17
S.D.	36	40	44	10

Appendix 3 - 20 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight Period : Recovery Day 1-15

Sex : Male Dose : benzyl salicylate 300 mg/kg Unit : g Species : Rat

Animal No.	/Day 1	8	14	Body weight gain
4008	512	519	537	25
4009	499	507	519	20
4010	495	498	513	18
4011	490	495	500	10
4012	505	524	533	28
n	5	5	5	5
Mean	500	509	520	20
S.D.	9	13	15	7

Appendix 3 - 21 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight Period : Recovery Day 1-15

Sex : Female Dose : benzyl salicylate 0 mg/kg Unit : g Species : Rat

Animal No.	/Day 1	8	14	Body weight gain
5106	299	311	307	8
5107	293	291	292	-1
5108	304	313	318	14
5109	310	320	322	12
5110	322	336	336	14
n	5	5	5	5
Mean	306	314	315	9
S.D.	11	16	17	6

Appendix 3 - 22 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight Period : Recovery Day 1-15

Sex : Female Dose : benzyl salicylate 300 mg/kg Unit : g Species : Rat

Animal No.	/Day 1	8	14	Body weight gain
6106	326	323	318	-8
6107	306	289	278	-28
6108	285	274	263	-22
6109	302	305	310	8
6110	285	277	279	-6
n	5	5	5	5
Mean	301	294	290	-11
S.D.	17	20	23	14

Appendix 4 - 1 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Food consumption Period : F0 before mating Day 1-15, F0 mating Day 15-43

Sex : Male Dose : benzyl salicylate 0 mg/kg Unit : g Species : Rat

Animal No.	/Day 2	8	15	30	36	42	Total food consumption
1001	21	25	21	22	21	22	132
1002	17	23	24	17	22	16	119
1003	20	23	24	24	24	24	139
1004	18	19	19	19	18	18	111
1005	16	21	19	19	20	18	113
1006	19	20	21	20	18	16	114
1007	15	16	17	16	16	15	95
1008	16	20	17	19	17	11	100
1009	25	24	25	21	23	17	135
1010	19	22	19	23	24	20	127
1011	18	17	19	20	21	18	113
1012	20	21	17	18	17	18	111
n	12	12	12	12	12	12	12
Mean	19	21	20	20	20	18	117
S.D.	3	3	3	2	3	3	14

Appendix 4 - 2 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Food consumption Period : F0 before mating Day 1-15, F0 mating Day 15-43

Sex : Male Dose : benzyl salicylate 30 mg/kg Unit : g Species : Rat

Animal No.	/Day 2	8	15	30	36	42	Total food consumption
2001	23	20	19	20	22	17	121
2002	21	21	19	16	19	17	113
2003	22	17	16	17	18	18	108
2004	20	23	19	21	18	19	120
2005	22	25	23	18	22	14	124
2006	20	22	19	21	22	20	124
2007	27	24	23	19	25	20	138
2008	22	19	17	17	18	16	109
2009	19	20	20	17	20	17	113
2010	21	24	19	19	20	18	121
2011	27	21	19	19	20	18	124
2012	19	19	20	17	18	16	109
n	12	12	12	12	12	12	12
Mean	22	21	19	18	20	18	119
S.D.	3	2	2	2	2	2	9

Appendix 4 - 3 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Food consumption Period : F0 before mating Day 1-15, F0 mating Day 15-43

Sex : Male Dose : benzyl salicylate 100 mg/kg Unit : g Species : Rat

Animal No.	/Day 2	8	15	30	36	42	Total food consumption
3001	19	24	19	21	24	24	131
3002	18	22	19	19	24	22	124
3003	24	23	20	19	22	18	126
3004	20	20	18	16	19	13	106
3005	20	19	19	19	22	21	120
3006	24	25	20	27	21	19	136
3007	7	19	18	17	17	15	93
3008	18	22	17	16	19	13	105
3009	21	23	22	20	22	21	129
3010	22	26	22	21	22	22	135
3011	18	22	22	22	24	19	127
3012	25	23	22	19	23	19	131
n	12	12	12	12	12	12	12
Mean	20	22	20	20	22	19	122
S.D.	5	2	2	3	2	4	14

Appendix 4 - 4 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Food consumption Period : F0 before mating Day 1-15, F0 mating Day 15-43

Sex : Male Dose : benzyl salicylate 300 mg/kg Unit : g Species : Rat

Animal No.	/Day 2	8	15	30	36	42	Total food consumption
4001	14	21	21	18	20	20	114
4002	20	24	22	21	26	22	135
4003	19	22	20	21	22	22	126
4004	23	25	24	20	23	21	136
4005	24	23	22	22	26	23	140
4006	21	23	22	21	21	24	132
4007	16	21	18	20	20	22	117
4008	17	23	22	22	21	20	125
4009	18	22	20	22	20	20	122
4010	18	22	21	20	21	18	120
4011	21	25	22	23	21	18	130
4012	21	23	20	21	22	20	127
n	12	12	12	12	12	12	12
Mean	19	23	21	21	22	21	127
S.D.	3	1	2	1	2	2	8

Appendix 4 - 5 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Food consumption Period : F0 before mating Day 1-15

Sex : Female Dose : benzyl salicylate 0 mg/kg Unit : g Species : Rat

Animal No.	/Day 2	8	15	Total food consumption
1101	12	16	14	42
1102	16	16	13	45
1103	15	18	11	44
1104	13	14	11	38
1105	17	18	18	53
1106	15	14	16	45
1107	14	16	15	45
1108	13	19	16	48
1109	17	17	16	50
1110	16	17	15	48
1111	12	18	14	44
1112	13	15	10	38
n	12	12	12	12
Mean	14	17	14	45
S.D.	2	2	2	4

Appendix 4 - 6 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Food consumption Period : F0 before mating Day 1-15

Sex : Female Dose : benzyl salicylate 30 mg/kg Unit : g Species : Rat

Animal No.	/Day 2	8	15	Total food consumption
2101	11	16	13	40
2102	14	10	13	37
2103	15	15	14	44
2104	14	15	10	39
2105	15	17	15	47
2106	9	18	18	45
2107	11	15	14	40
2108	13	18	16	47
2109	14	16	15	45
2110	11	15	12	38
2111	11	17	14	42
2112	16	12	16	44
n	12	12	12	12
Mean	13	15	14	42
S.D.	2	2	2	3

Appendix 4 - 7 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Food consumption Period : F0 before mating Day 1-15

Sex : Female Dose : benzyl salicylate 100 mg/kg Unit : g Species : Rat

Animal No.	/Day 2	8	15	Total food consumption
3101	5	14	7	26
3102	17	19	16	52
3103	17	12	15	44
3104	13	17	16	46
3105	16	16	14	46
3106	14	15	10	39
3107	11	16	15	42
3108	16	19	16	51
3109	16	16	14	46
3110	13	17	15	45
3111	14	17	16	47
3112	17	19	15	51
n	12	12	12	12
Mean	14	16	14	45
S.D.	3	2	3	7

Appendix 4 - 8 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Food consumption Period : F0 before mating Day 1-15

Sex : Female Dose : benzyl salicylate 300 mg/kg Unit : g Species : Rat

Animal No.	/Day 2	8	15	Total food consumption
4101	12	16	12	40
4102	17	18	14	49
4103	16	14	19	49
4104	13	16	20	49
4105	13	17	16	46
4106	18	20	17	55
4107	15	13	15	43
4108	17	14	17	48
4109	17	15	17	49
4110	9	15	15	39
4111	17	20	13	50
4112	15	12	18	45
n	12	12	12	12
Mean	15	16	16	47
S.D.	3	3	2	5

Appendix 4 - 9 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Food consumption Period : F0 gestation Day 0-25

Sex : Female Dose : benzyl salicylate 0 mg/kg Unit : g Species : Rat

Animal No.	/Day 1	7	14	20	Total food consumption
1101	8	25	20	21	74
1102	12	24	23	18	77
1103	12	19	20	24	75
1104	18	17	19	21	75
1105	21	26	22	17	86
1106	20	26	26	21	93
1107	15	21	18	25	79
1108	17	22	21	20	80
1109	20	28	28	21	97
1110	14	20	16	18	68
1111	20	22	24	24	90
1112	14	17	15	21	67
n	12	12	12	12	12
Mean	16	22	21	21	80
S.D.	4	4	4	3	10

Appendix 4 - 10 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Food consumption Period : F0 gestation Day 0-25

Sex : Female Dose : benzyl salicylate 30 mg/kg Unit : g Species : Rat

Animal No.	/Day 1	7	14	20	Total food consumption
2101	18	17	20	22	77
2102	13	15	17	21	66
2103	16	17	20	24	77
2104	19	22	21	24	86
2105	16	17	21	21	75
2106	17	22	22	20	81
2107	15	19	16	17	67
2108	13	19	16	18	66
2109	19	21	20	19	79
2110	15	18	19	22	74
2111	21	22	24	22	89
2112	18	21	17	21	77
n	12	12	12	12	12
Mean	17	19	19	21	76
S.D.	2	2	3	2	7

Appendix 4 - 11 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Food consumption Period : F0 gestation Day 0-25

Sex : Female Dose : benzyl salicylate 100 mg/kg Unit : g Species : Rat

Animal No.	/Day 1	7	14	20	Total food consumption
3101	14	17	18	24	73
3102	17	21	25	25	88
3103	19	20	18	20	77
3104	15	16	21	22	74
3105	19	19	17	24	79
3106	20	26	27	25	98
3107	17	17	19	18	71
3108	16	23	18	20	77
3109	15	19	18	19	71
3110	14	23	18	20	75
3111	16	18	20	28	82
3112	20	24	21	22	87
n	12	12	12	12	12
Mean	17	20	20	22	79
S.D.	2	3	3	3	8

Appendix 4 - 12 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Food consumption Period : F0 gestation Day 0-25

Sex : Female Dose : benzyl salicylate 300 mg/kg Unit : g Species : Rat

Animal No.	/Day 1	7	14	20	Total food consumption
4101	17	18	21	20	76
4102	21	29	27	23	100
4103	22	21	22	20	85
4104	19	20	23	18	80
4105	19	20	24	21	84
4106	19	20	22	25	86
4107	16	19	21	19	75
4108	20	20	23	23	86
4109	17	16	25	18	76
4110	15	17	17	17	66
4111	18	20	20	25	83
4112	18	21	19	22	80
n	12	12	12	12	12
Mean	18	20	22	21	81
S.D.	2	3	3	3	8

Appendix 4 - 13 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Food consumption Period : F0 lactation Day 0-5

Sex : Female Dose : benzyl salicylate 0 mg/kg Unit : g Species : Rat

Animal No.	/Day 2	4	Total food consumption
1101	31	40	71
1102	16	33	49
1103	26	39	65
1104	23	43	66
1105	15	39	54
1106	12	16	28
1107	22	38	60
1108	28	40	68
1109	21	31	52
1110	9	32	41
1111	21	30	51
1112	24	31	55
n	12	12	12
Mean	21	34	55
S.D.	7	7	12

Appendix 4 - 14 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Food consumption Period : F0 lactation Day 0-5

Sex : Female Dose : benzyl salicylate 30 mg/kg Unit : g Species : Rat

Animal No.	/Day 2	4	Total food consumption
2101	22	40	62
2102	23	28	51
2103	28	32	60
2104	23	32	55
2105	22	41	63
2106	22	39	61
2107	16	36	52
2108	23	33	56
2109	25	40	65
2110	27	38	65
2111	25	41	66
2112	17	25	42
n	12	12	12
Mean	23	35	58
S.D.	4	5	7

Appendix 4 - 15 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Food consumption Period : F0 lactation Day 0-5

Sex : Female Dose : benzyl salicylate 100 mg/kg Unit : g Species : Rat

Animal No.	/Day 2	4	Total food consumption
3101	18	30	48
3102	20	36	56
3103	22	38	60
3104	15	19	34
3105	21	32	53
3106	28	38	66
3107	25	39	64
3108	22	37	59
3109	29	40	69
3110	25	39	64
3111	18	47	65
3112	27	47	74
n	12	12	12
Mean	23	37	59
S.D.	4	7	11

Appendix 4 - 16 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Food consumption Period : F0 lactation Day 0-5

Sex : Female Dose : benzyl salicylate 300 mg/kg Unit : g Species : Rat

Animal No.	/Day 2	4	Total food consumption
4102 c)	...	...	:::
4105 b)	...	...	:::
4106 a)	...	...	:::
4107 b)	...	...	:::
4109 b)	...	...	:::
4110 b)	...	...	:::
n	0	0	0
Mean			
S.D.			

... : Mortality data, ::: : Impossible to calculate

Animal No. 4101,4103,4104,4108,4111,4112 : Not delivered

a) : Necropsied on lactation day 0 because all offspring were stillborn

b) : Necropsied on lactation day 1 because all offspring died

c) : Necropsied on lactation day 2 because all offspring died

Appendix 4 - 17 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Food consumption Period : Administration

Sex : Female Dose : benzyl salicylate 0 mg/kg Unit : g Species : Rat

Animal No.	/Day 2	8	15	30	36	42	Total food consumption
5101	13	17	12	13	15	13	83
5102	14	15	10	13	12	9	73
5103	11	18	15	12	12	11	79
5104	15	15	15	17	10	14	86
5105	13	16	15	14	13	14	85
5106	16	15	11	17	14	14	87
5107	12	16	13	11	14	8	74
5108	15	16	14	16	15	17	93
5109	14	16	11	15	16	13	85
5110	11	16	15	14	15	9	80
n	10	10	10	10	10	10	10
Mean	13	16	13	14	14	12	83
S.D.	2	1	2	2	2	3	6

Appendix 4 - 18 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Food consumption Period : Administration

Sex : Female Dose : benzyl salicylate 300 mg/kg Unit : g Species : Rat

Animal No.	/Day 2	8	15	30	36	42	Total food consumption
6101	12	17	11	13	14	13	80
6102	12	16	10	16	19	17	90
6103	10	19	18	15	18	14	94
6104	13	17	16	14	18	16	94
6105	16	17	20	18	19	18	108
6106	15	13	17	16	14	18	93
6107	14	13	19	20	15	21	102
6108	12	19	17	15	17	18	98
6109	12	16	13	16	16	14	87
6110	15	16	14	14	16	14	89
n	10	10	10	10	10	10	10
Mean	13	16	16	16	17	16	94
S.D.	2	2	3	2	2	3	8

Appendix 4 - 19 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Food consumption Period : Recovery Day 1-15

Sex : Male Dose : benzyl salicylate 0 mg/kg Unit : g Species : Rat

Animal No.	/Day 2	8	14	Total food consumption
1008	19	23	21	63
1009	22	26	27	75
1010	25	28	28	81
1011	24	23	22	69
1012	19	23	23	65
n	5	5	5	5
Mean	22	25	24	71
S.D.	3	2	3	7

Appendix 4 - 20 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Food consumption Period : Recovery Day 1-15

Sex : Male Dose : benzyl salicylate 300 mg/kg Unit : g Species : Rat

Animal No.	/Day 2	8	14	Total food consumption
4008	22	23	26	71
4009	23	22	24	69
4010	23	18	22	63
4011	21	26	22	69
4012	22	26	26	74
n	5	5	5	5
Mean	22	23	24	69
S.D.	1	3	2	4

Appendix 4 - 21 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Food consumption Period : Recovery Day 1-15

Sex : Female Dose : benzyl salicylate 0 mg/kg Unit : g Species : Rat

Animal No.	/Day 2	8	14	Total food consumption
5106	19	17	18	54
5107	17	13	16	46
5108	18	22	20	60
5109	15	19	18	52
5110	21	21	15	57
n	5	5	5	5
Mean	18	18	17	54
S.D.	2	4	2	5

Appendix 4 - 22 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Food consumption Period : Recovery Day 1-15

Sex : Female Dose : benzyl salicylate 300 mg/kg Unit : g Species : Rat

Animal No.	/Day 2	8	14	Total food consumption
6106	16	19	15	50
6107	16	17	12	45
6108	19	15	12	46
6109	17	18	17	52
6110	18	17	16	51
n	5	5	5	5
Mean	17	17	14	49
S.D.	1	1	2	3

Appendix 5 - 1 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 6 of administration

Sex : Male Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	pH	Protein	Ketones	Glucose	Occult Blood	Bilirubin	Urobilinogen	Color
1008	6.0	2+	1+	-	1+	-	+/-	Y
1009	8.5	+/-	+/-	-	+/-	-	+/-	Y
1010	>=9.0	2+	2+	1+	-	1+	+/-	Y
1011	7.0	+/-	2+	-	1+	1+	+/-	Y
1012	8.0	1+	-	-	1+	-	+/-	Y
n	5	5	5	5	5	5	5	5

Protein) -:Negative , +/-:15 , 1+:30 , 2+:100 , 3+:≥300 mg/dL
Ketones) -:Negative , +/-:5 , 1+:15 , 2+:40 , 3+:80 mg/dL
Glucose) -:Negative , 1+:100 , 2+:250 , 3+:500 , 4+:≥1000 mg/dL
Occult Blood) -:Negative , +/-:0.015 , 1+:0.062 , 2+:0.135 , 3+: 0.405 mg/dL
Bilirubin) -:Negative , 1+:0.8 , 2+:1.6 , 3+:3.2 mg/dL
Urobilinogen) +/-:0.1 - 1.0 , 1+:2.0 , 2+:4.0 , 3+:≥8.0 Ehrlich U/dL
Color LY: Light Yellow Y: Yellow DY: Dark Yellow BR: Brown RE: Red RB: Reddish brown WH: White BL: Blue CL: Colorless OT: Other

Appendix 5 - 2 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 6 of administration

Sex : Male Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	pH	Protein	Ketones	Glucose	Occult Blood	Bilirubin	Urobilinogen	Color
2008	>=9.0	+/-	+/-	-	-	-	+/-	Y
2009	8.5	+/-	-	-	+/-	-	+/-	Y
2010	>=9.0	1+	1+	-	-	-	+/-	Y
2011	8.5	2+	1+	-	+/-	-	+/-	Y
2012	8.5	+/-	+/-	-	+/-	-	+/-	Y
n	5	5	5	5	5	5	5	5

Protein) -:Negative , +/-:15 , 1+:30 , 2+:100 , 3+:≥300 mg/dL
Ketones) -:Negative , +/-:5 , 1+:15 , 2+:40 , 3+:80 mg/dL
Glucose) -:Negative , 1+:100 , 2+:250 , 3+:500 , 4+:≥1000 mg/dL
Occult Blood) -:Negative , +/-:0.015 , 1+:0.062 , 2+:0.135 , 3+: 0.405 mg/dL
Bilirubin) -:Negative , 1+:0.8 , 2+:1.6 , 3+:3.2 mg/dL
Urobilinogen) +/-:0.1 - 1.0 , 1+:2.0 , 2+:4.0 , 3+:≥8.0 Ehrlich U/dL
Color LY: Light Yellow Y: Yellow DY: Dark Yellow BR: Brown RE: Red RB: Reddish brown WH: White BL: Blue CL: Colorless OT: Other

Appendix 5 - 3 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 6 of administration

Sex : Male Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	pH	Protein	Ketones	Glucose	Occult Blood	Bilirubin	Urobilinogen	Color
3008	>=9.0	2+	2+	-	-	1+	+/-	Y
3009	>=9.0	+/-	1+	-	-	-	+/-	Y
3010	7.0	+/-	+/-	-	+/-	-	+/-	Y
3011	8.5	+/-	-	-	+/-	-	+/-	Y
3012	7.5	+/-	+/-	-	+/-	-	+/-	Y
n	5	5	5	5	5	5	5	5

Protein) -:Negative , +/-:15 , 1+:30 , 2+:100 , 3+:≥300 mg/dL
Ketones) -:Negative , +/-:5 , 1+:15 , 2+:40 , 3+:80 mg/dL
Glucose) -:Negative , 1+:100 , 2+:250 , 3+:500 , 4+:≥1000 mg/dL
Occult Blood) -:Negative , +/-:0.015 , 1+:0.062 , 2+:0.135 , 3+: 0.405 mg/dL
Bilirubin) -:Negative , 1+:0.8 , 2+:1.6 , 3+:3.2 mg/dL
Urobilinogen) +/-:0.1 - 1.0 , 1+:2.0 , 2+:4.0 , 3+:≥8.0 Ehrlich U/dL
Color LY: Light Yellow Y: Yellow DY: Dark Yellow BR: Brown RE: Red RB: Reddish brown WH: White BL: Blue CL: Colorless OT: Other

Appendix 5 - 4 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 6 of administration

Sex : Male Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	pH	Protein	Ketones	Glucose	Occult Blood	Bilirubin	Urobilinogen	Color
4008	7.5	1+	-	-	+/-	-	+/-	Y
4009	8.5	+/-	+/-	-	-	-	+/-	Y
4010	8.5	1+	1+	-	-	-	+/-	Y
4011	8.5	1+	1+	-	-	-	+/-	Y
4012	7.5	+/-	+/-	-	-	-	+/-	Y
n	5	5	5	5	5	5	5	5

Protein) -:Negative , +/-:15 , 1+:30 , 2+:100 , 3+:≥300 mg/dL
Ketones) -:Negative , +/-:5 , 1+:15 , 2+:40 , 3+:80 mg/dL
Glucose) -:Negative , 1+:100 , 2+:250 , 3+:500 , 4+:≥1000 mg/dL
Occult Blood) -:Negative , +/-:0.015 , 1+:0.062 , 2+:0.135 , 3+: 0.405 mg/dL
Bilirubin) -:Negative , 1+:0.8 , 2+:1.6 , 3+:3.2 mg/dL
Urobilinogen) +/-:0.1 - 1.0 , 1+:2.0 , 2+:4.0 , 3+:≥8.0 Ehrlich U/dL
Color LY: Light Yellow Y: Yellow DY: Dark Yellow BR: Brown RE: Red RB: Reddish brown WH: White BL: Blue CL: Colorless OT: Other

Appendix 5 - 5 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 6 of administration

Sex : Male Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	RBC	WBC	Squamous epithelial cells	Small round epithelial cells	Cast	Crystal phosphate salts	Crystal calcium oxalate
1008	-	-	+/-	-	-	-	-
1009	-	-	+/-	-	-	-	-
1010	-	-	+/-	-	-	+/-	-
1011	-	-	+/-	-	-	-	-
1012	-	-	+/-	-	-	-	-
n	5	5	5	5	5	5	5

RBC) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
WBC) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Squamous epithelial cells) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Small round epithelial cells) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Cast) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Crystal phosphate salts) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Crystal calcium oxalate) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe

Appendix 5 - 6 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 6 of administration

Sex : Male Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	RBC	WBC	Squamous epithelial cells	Small round epithelial cells	Cast	Crystal phosphate salts	Crystal calcium oxalate
2008	-	-	+/-	-	-	+/-	-
2009	-	-	+/-	-	-	-	-
2010	-	-	+/-	-	-	-	-
2011	-	-	+/-	-	-	-	-
2012	-	-	+/-	-	-	-	-
n	5	5	5	5	5	5	5

RBC) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
WBC) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Squamous epithelial cells) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Small round epithelial cells) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Cast) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Crystal phosphate salts) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Crystal calcium oxalate) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe

Appendix 5 - 7 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 6 of administration

Sex : Male Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	RBC	WBC	Squamous epithelial cells	Small round epithelial cells	Cast	Crystal phosphate salts	Crystal calcium oxalate
3008	-	-	+/-	-	-	-	-
3009	-	-	+/-	-	-	-	-
3010	-	-	+/-	-	-	-	-
3011	-	-	+/-	-	-	-	-
3012	-	-	+/-	-	-	-	-
n	5	5	5	5	5	5	5

RBC) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
WBC) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Squamous epithelial cells) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Small round epithelial cells) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Cast) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Crystal phosphate salts) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Crystal calcium oxalate) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe

Appendix 5 - 8 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 6 of administration

Sex : Male Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	RBC	WBC	Squamous epithelial cells	Small round epithelial cells	Cast	Crystal phosphate salts	Crystal calcium oxalate
4008	-	-	+/-	-	-	-	-
4009	-	-	+/-	-	-	-	-
4010	-	-	+/-	-	-	-	-
4011	-	-	+/-	-	-	-	-
4012	-	-	+/-	-	-	-	-
n	5	5	5	5	5	5	5

RBC) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
WBC) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Squamous epithelial cells) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Small round epithelial cells) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Cast) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Crystal phosphate salts) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Crystal calcium oxalate) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe

Appendix 5 - 9 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 6 of administration

Sex : Male Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Urine volume mL/24h	Osmotic pressure mOsm/kg	U-Na mmol/24h	U-K mmol/24h	U-Cl mmol/24h
1008	5.5	828	0.1	0.7	0.4
1009	11.9	1554	1.1	2.8	1.9
1010	6.5	2786	1.7	2.8	2.1
1011	9.8	934	0.7	1.3	1.0
1012	7.0	1786	0.6	1.9	1.2
n	5	5	5	5	5
Mean	8.1	1578	0.8	1.9	1.3
S.D.	2.6	787	0.6	0.9	0.7

Appendix 5 - 10 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 6 of administration

Sex : Male Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Urine volume mL/24h	Osmotic pressure mOsm/kg	U-Na mmol/24h	U-K mmol/24h	U-Cl mmol/24h
2008	5.4	1848	0.8	1.7	1.3
2009	14.7	972	1.0	2.2	1.5
2010	7.9	2084	1.2	2.4	1.8
2011	6.4	2026	1.0	2.0	1.6
2012	7.8	2370	1.4	2.7	2.0
n	5	5	5	5	5
Mean	8.4	1860	1.1	2.2	1.6
S.D.	3.7	531	0.2	0.4	0.3

Appendix 5 - 11 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 6 of administration

Sex : Male Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Urine volume mL/24h	Osmotic pressure mOsm/kg	U-Na mmol/24h	U-K mmol/24h	U-Cl mmol/24h
3008	5.9	1532	0.6	1.5	0.8
3009	12.8	1518	1.9	2.9	2.3
3010	19.4	884	1.2	2.6	1.7
3011	14.8	1484	1.3	3.5	2.2
3012	8.5	2120	1.3	2.9	2.2
n	5	5	5	5	5
Mean	12.3	1508	1.3	2.7	1.8
S.D.	5.3	437	0.5	0.7	0.6

Appendix 5 - 12 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 6 of administration

Sex : Male Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Urine volume mL/24h	Osmotic pressure mOsm/kg	U-Na mmol/24h	U-K mmol/24h	U-Cl mmol/24h
4008	15.5	1366	2.0	3.1	2.5
4009	25.5	1112	2.3	3.8	3.1
4010	10.7	1464	0.8	2.2	1.4
4011	8.8	2170	1.8	2.6	2.2
4012	26.5	940	2.2	3.4	3.2
n	5	5	5	5	5
Mean	17.4	1410	1.8	3.0	2.5
S.D.	8.2	472	0.6	0.6	0.7

Appendix 5 - 13 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 6 of administration

Sex : Female Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	pH	Protein	Ketones	Glucose	Occult Blood	Bilirubin	Urobilinogen	Color
5106	8.5	-	+/-	-	-	-	+/-	Y
5107	>=9.0	+/-	+/-	-	-	-	+/-	Y
5108	7.0	-	-	-	-	-	+/-	Y
5109	>=9.0	1+	+/-	-	-	1+	+/-	Y
5110	7.0	-	-	-	-	-	+/-	Y
n	5	5	5	5	5	5	5	5

Protein) -:Negative , +/-:15 , 1+:30 , 2+:100 , 3+:≥300 mg/dL
Ketones) -:Negative , +/-:5 , 1+:15 , 2+:40 , 3+:80 mg/dL
Glucose) -:Negative , 1+:100 , 2+:250 , 3+:500 , 4+:≥1000 mg/dL
Occult Blood) -:Negative , +/-:0.015 , 1+:0.062 , 2+:0.135 , 3+: 0.405 mg/dL
Bilirubin) -:Negative , 1+:0.8 , 2+:1.6 , 3+:3.2 mg/dL
Urobilinogen) +/-:0.1 - 1.0 , 1+:2.0 , 2+:4.0 , 3+:≥8.0 Ehrlich U/dL
Color LY: Light Yellow Y: Yellow DY: Dark Yellow BR: Brown RE: Red RB: Reddish brown WH: White BL: Blue CL: Colorless OT: Other

Appendix 5 - 14 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 6 of administration

Sex : Female Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	pH	Protein	Ketones	Glucose	Occult Blood	Bilirubin	Urobilinogen	Color
6106	5.5	1+	+/-	-	-	-	+/-	Y
6107	6.0	-	+/-	-	-	-	+/-	Y
6108	>=9.0	-	-	-	-	-	+/-	Y
6109	7.5	+/-	-	-	-	1+	+/-	Y
6110	8.5	-	-	-	-	-	+/-	Y
n	5	5	5	5	5	5	5	5

Protein) -:Negative , +/-:15 , 1+:30 , 2+:100 , 3+:≥300 mg/dL
Ketones) -:Negative , +/-:5 , 1+:15 , 2+:40 , 3+:80 mg/dL
Glucose) -:Negative , 1+:100 , 2+:250 , 3+:500 , 4+:≥1000 mg/dL
Occult Blood) -:Negative , +/-:0.015 , 1+:0.062 , 2+:0.135 , 3+: 0.405 mg/dL
Bilirubin) -:Negative , 1+:0.8 , 2+:1.6 , 3+:3.2 mg/dL
Urobilinogen) +/-:0.1 - 1.0 , 1+:2.0 , 2+:4.0 , 3+:≥8.0 Ehrlich U/dL
Color LY: Light Yellow Y: Yellow DY: Dark Yellow BR: Brown RE: Red RB: Reddish brown WH: White BL: Blue CL: Colorless OT: Other

Appendix 5 - 15 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 6 of administration

Sex : Female Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	RBC	WBC	Squamous epithelial cells	Small round epithelial cells	Cast	Crystal phosphate salts	Crystal calcium oxalate
5106	-	-	+/-	-	-	-	-
5107	-	-	+/-	-	-	-	-
5108	-	-	+/-	-	-	-	-
5109	-	-	+/-	-	-	+/-	-
5110	-	-	+/-	-	-	-	-
n	5	5	5	5	5	5	5

RBC) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
WBC) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Squamous epithelial cells) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Small round epithelial cells) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Cast) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Crystal phosphate salts) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Crystal calcium oxalate) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe

Appendix 5 - 16 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 6 of administration

Sex : Female Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	RBC	WBC	Squamous epithelial cells	Small round epithelial cells	Cast	Crystal phosphate salts	Crystal calcium oxalate
6106	-	-	+/-	-	-	-	-
6107	-	-	+/-	-	-	-	-
6108	-	-	+/-	-	-	-	-
6109	-	-	+/-	-	-	-	+/-
6110	-	-	+/-	-	-	-	-
n	5	5	5	5	5	5	5

RBC) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
WBC) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Squamous epithelial cells) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Small round epithelial cells) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Cast) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Crystal phosphate salts) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Crystal calcium oxalate) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe

Appendix 5 - 17 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 6 of administraion

Sex : Female Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Urine volume mL/24h	Osmotic pressure mOsm/kg	U-Na mmol/24h	U-K mmol/24h	U-Cl mmol/24h
5106	3.6	2670	0.7	1.5	1.2
5107	9.1	1544	1.0	2.2	1.5
5108	9.4	1526	1.6	2.0	1.9
5109	6.5	1914	1.0	1.8	1.3
5110	13.3	1206	1.2	2.5	1.8
n	5	5	5	5	5
Mean	8.4	1772	1.1	2.0	1.5
S.D.	3.6	561	0.3	0.4	0.3

Appendix 5 - 18 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 6 of administraion

Sex : Female Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Urine volume mL/24h	Osmotic pressure mOsm/kg	U-Na mmol/24h	U-K mmol/24h	U-Cl mmol/24h
6106	8.5	1610	1.3	1.8	1.5
6107	10.9	1280	0.9	1.9	1.1
6108	8.9	1360	1.2	1.6	1.4
6109	8.1	1506	1.0	1.6	1.2
6110	17.2	866	1.2	1.7	1.5
n	5	5	5	5	5
Mean	10.7	1324	1.1	1.7	1.3
S.D.	3.8	286	0.2	0.1	0.2

Appendix 5 - 19 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 2 of recovery

Sex : Male Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	pH	Protein	Ketones	Glucose	Occult Blood	Bilirubin	Urobilinogen	Color
1008	>=9.0	1+	1+	-	-	-	+/-	Y
1009	8.5	+/-	-	-	+/-	-	+/-	Y
1010	8.5	1+	1+	-	-	1+	+/-	Y
1011	8.5	1+	1+	-	+/-	-	+/-	Y
1012	8.5	+/-	-	-	+/-	-	+/-	Y
n	5	5	5	5	5	5	5	5

Protein) -:Negative , +/-:15 , 1+:30 , 2+:100 , 3+:≥300 mg/dL
Ketones) -:Negative , +/-:5 , 1+:15 , 2+:40 , 3+:80 mg/dL
Glucose) -:Negative , 1+:100 , 2+:250 , 3+:500 , 4+:≥1000 mg/dL
Occult Blood) -:Negative , +/-:0.015 , 1+:0.062 , 2+:0.135 , 3+: 0.405 mg/dL
Bilirubin) -:Negative , 1+:0.8 , 2+:1.6 , 3+:3.2 mg/dL
Urobilinogen) +/-:0.1 - 1.0 , 1+:2.0 , 2+:4.0 , 3+:≥8.0 Ehrlich U/dL
Color LY: Light Yellow Y: Yellow DY: Dark Yellow BR: Brown RE: Red RB: Reddish brown WH: White BL: Blue CL: Colorless OT: Other

Appendix 5 - 20 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 2 of recovery

Sex : Male Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	pH	Protein	Ketones	Glucose	Occult Blood	Bilirubin	Urobilinogen	Color
4008	8.5	1+	+/-	-	+/-	-	+/-	Y
4009	8.5	+/-	+/-	-	+/-	-	+/-	Y
4010	8.0	-	1+	-	+/-	-	+/-	Y
4011	>=9.0	1+	1+	-	+/-	-	+/-	Y
4012	8.5	+/-	1+	-	+/-	-	+/-	Y
n	5	5	5	5	5	5	5	5

Protein) -:Negative , +/-:15 , 1+:30 , 2+:100 , 3+:≥300 mg/dL
Ketones) -:Negative , +/-:5 , 1+:15 , 2+:40 , 3+:80 mg/dL
Glucose) -:Negative , 1+:100 , 2+:250 , 3+:500 , 4+:≥1000 mg/dL
Occult Blood) -:Negative , +/-:0.015 , 1+:0.062 , 2+:0.135 , 3+: 0.405 mg/dL
Bilirubin) -:Negative , 1+:0.8 , 2+:1.6 , 3+:3.2 mg/dL
Urobilinogen) +/-:0.1 - 1.0 , 1+:2.0 , 2+:4.0 , 3+:≥8.0 Ehrlich U/dL
Color LY: Light Yellow Y: Yellow DY: Dark Yellow BR: Brown RE: Red RB: Reddish brown WH: White BL: Blue CL: Colorless OT: Other

Appendix 5 - 21 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 2 of recovery

Sex : Male Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	RBC	WBC	Squamous epithelial cells	Small round epithelial cells	Cast	Crystal phosphate salts	Crystal calcium oxalate
1008	-	-	+/-	-	-	-	-
1009	-	-	+/-	-	-	-	-
1010	-	-	+/-	-	-	-	-
1011	-	-	+/-	-	-	-	-
1012	-	-	+/-	-	-	-	-
n	5	5	5	5	5	5	5

RBC) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
WBC) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Squamous epithelial cells) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Small round epithelial cells) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Cast) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Crystal phosphate salts) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Crystal calcium oxalate) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe

Appendix 5 - 22 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 2 of recovery

Sex : Male Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	RBC	WBC	Squamous epithelial cells	Small round epithelial cells	Cast	Crystal phosphate salts	Crystal calcium oxalate
4008	-	-	+/-	-	-	-	-
4009	-	-	+/-	-	-	-	-
4010	-	-	+/-	-	-	-	-
4011	-	-	+/-	-	-	-	-
4012	-	-	+/-	-	-	-	-
n	5	5	5	5	5	5	5

RBC) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
WBC) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Squamous epithelial cells) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Small round epithelial cells) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Cast) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Crystal phosphate salts) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Crystal calcium oxalate) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe

Appendix 5 - 23 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 2 of recovery

Sex : Male Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Urine volume mL/24h	Osmotic pressure mOsm/kg	U-Na mmol/24h	U-K mmol/24h	U-Cl mmol/24h
1008	11.5	1700	1.4	2.7	2.2
1009	18.6	1926	2.2	5.5	3.5
1010	12.5	2710	2.4	5.0	3.5
1011	10.0	2302	1.6	3.1	2.2
1012	12.1	2384	2.0	4.2	2.7
n	5	5	5	5	5
Mean	12.9	2204	1.9	4.1	2.8
S.D.	3.3	397	0.4	1.2	0.7

Appendix 5 - 24 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 2 of recovery

Sex : Male Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Urine volume mL/24h	Osmotic pressure mOsm/kg	U-Na mmol/24h	U-K mmol/24h	U-Cl mmol/24h
4008	15.4	1418	1.8	3.2	2.3
4009	18.4	1726	1.6	5.5	3.3
4010	13.8	1948	1.4	4.4	2.5
4011	8.8	2590	1.6	3.5	2.4
4012	12.5	2166	1.7	4.3	2.7
n	5	5	5	5	5
Mean	13.8	1970	1.6	4.2	2.6
S.D.	3.5	444	0.1	0.9	0.4

Appendix 5 - 25 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 2 of recovery

Sex : Female Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	pH	Protein	Ketones	Glucose	Occult Blood	Bilirubin	Urobilinogen	Color
5106	>=9.0	+/-	-	-	-	-	+/-	Y
5107	7.0	+/-	+/-	-	-	1+	+/-	Y
5108	8.5	-	-	-	-	-	+/-	Y
5109	6.5	1+	+/-	-	-	-	+/-	Y
5110	>=9.0	-	-	-	-	-	+/-	Y
n	5	5	5	5	5	5	5	5

Protein) -:Negative , +/-:15 , 1+:30 , 2+:100 , 3+:≥300 mg/dL
Ketones) -:Negative , +/-:5 , 1+:15 , 2+:40 , 3+:80 mg/dL
Glucose) -:Negative , 1+:100 , 2+:250 , 3+:500 , 4+:≥1000 mg/dL
Occult Blood) -:Negative , +/-:0.015 , 1+:0.062 , 2+:0.135 , 3+: 0.405 mg/dL
Bilirubin) -:Negative , 1+:0.8 , 2+:1.6 , 3+:3.2 mg/dL
Urobilinogen) +/-:0.1 - 1.0 , 1+:2.0 , 2+:4.0 , 3+:≥8.0 Ehrlich U/dL
Color LY: Light Yellow Y: Yellow DY: Dark Yellow BR: Brown RE: Red RB: Reddish brown WH: White BL: Blue CL: Colorless OT: Other

Appendix 5 - 26 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 2 of recovery

Sex : Female Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	pH	Protein	Ketones	Glucose	Occult Blood	Bilirubin	Urobilinogen	Color
6106	>=9.0	-	-	-	-	-	+/-	Y
6107	7.0	1+	+/-	-	-	-	+/-	Y
6108	7.0	+/-	+/-	-	-	-	+/-	Y
6109	8.0	-	-	-	-	-	+/-	Y
6110	8.5	-	-	-	-	-	+/-	Y
n	5	5	5	5	5	5	5	5

Protein) -:Negative , +/-:15 , 1+:30 , 2+:100 , 3+:≥300 mg/dL
Ketones) -:Negative , +/-:5 , 1+:15 , 2+:40 , 3+:80 mg/dL
Glucose) -:Negative , 1+:100 , 2+:250 , 3+:500 , 4+:≥1000 mg/dL
Occult Blood) -:Negative , +/-:0.015 , 1+:0.062 , 2+:0.135 , 3+: 0.405 mg/dL
Bilirubin) -:Negative , 1+:0.8 , 2+:1.6 , 3+:3.2 mg/dL
Urobilinogen) +/-:0.1 - 1.0 , 1+:2.0 , 2+:4.0 , 3+:≥8.0 Ehrlich U/dL
Color LY: Light Yellow Y: Yellow DY: Dark Yellow BR: Brown RE: Red RB: Reddish brown WH: White BL: Blue CL: Colorless OT: Other

Appendix 5 - 27 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 2 of recovery

Sex : Female Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	RBC	WBC	Squamous epithelial cells	Small round epithelial cells	Cast	Crystal phosphate salts	Crystal calcium oxalate
5106	-	-	+/-	-	-	-	-
5107	-	-	+/-	-	-	-	-
5108	-	-	+/-	-	-	-	-
5109	-	-	+/-	-	-	-	-
5110	-	-	+/-	-	-	-	-
n	5	5	5	5	5	5	5

RBC) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
WBC) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Squamous epithelial cells) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Small round epithelial cells) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Cast) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Crystal phosphate salts) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Crystal calcium oxalate) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe

Appendix 5 - 28 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 2 of recovery

Sex : Female Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	RBC	WBC	Squamous epithelial cells	Small round epithelial cells	Cast	Crystal phosphate salts	Crystal calcium oxalate
6106	-	-	+/-	-	-	-	-
6107	-	-	+/-	-	-	-	-
6108	-	-	+/-	-	-	-	-
6109	-	-	+/-	-	-	-	-
6110	-	-	+/-	-	-	+/-	-
n	5	5	5	5	5	5	5

RBC) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
WBC) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Squamous epithelial cells) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Small round epithelial cells) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Cast) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Crystal phosphate salts) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe
Crystal calcium oxalate) -:Negative , +/-:Slight , 1+:Mild , 2+:Moderate , 3+:Severe

Appendix 5 - 29 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 2 of recovery

Sex : Female Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Urine volume mL/24h	Osmotic pressure mOsm/kg	U-Na mmol/24h	U-K mmol/24h	U-Cl mmol/24h
5106	2.8	3492	0.7	1.3	1.0
5107	10.0	1914	1.5	2.8	2.0
5108	16.2	1342	1.5	3.1	2.2
5109	6.2	2212	1.2	2.0	1.4
5110	16.0	1466	2.0	3.4	2.9
n	5	5	5	5	5
Mean	10.2	2085	1.4	2.5	1.9
S.D.	5.9	860	0.5	0.9	0.7

Appendix 5 - 30 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Urinalysis Stage : Week 2 of recovery

Sex : Female Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Urine volume mL/24h	Osmotic pressure mOsm/kg	U-Na mmol/24h	U-K mmol/24h	U-Cl mmol/24h
6106	11.5	1596	1.5	2.6	1.8
6107	4.6	2658	0.7	1.8	1.1
6108	7.5	2152	1.1	2.4	1.5
6109	4.5	2782	0.8	1.7	1.1
6110	14.6	1314	1.2	2.9	1.9
n	5	5	5	5	5
Mean	8.5	2100	1.1	2.3	1.5
S.D.	4.4	642	0.3	0.5	0.4

Appendix 6 - 1 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Hematology Stage : End of administration

Sex : Male Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RETIC %	PLT $10^4/\mu L$	WBC $10^2/\mu L$	LYMP %	NEUT %
1001	790	15.1	44.5	56.3	19.2	34.0	2.5	103.5	64.3	82.1	14.0
1002	862	15.5	45.8	53.2	18.0	33.9	2.4	82.9	90.2	83.2	12.4
1003	814	15.2	42.8	52.6	18.7	35.5	2.5	105.2	101.4	70.1	24.7
1004	809	15.2	44.1	54.5	18.7	34.4	2.3	106.1	92.7	63.9	31.8
1005	861	16.0	46.1	53.5	18.6	34.8	1.8	89.9	70.8	74.2	21.5
n	5	5	5	5	5	5	5	5	5	5	5
Mean	827	15.4	44.7	54.0	18.6	34.5	2.3	97.5	83.9	74.7	20.9
S.D.	33	0.4	1.3	1.4	0.4	0.7	0.3	10.5	15.6	8.1	8.0

Animal No.	EOS %	BASO %	MONO %	LUC %	#LYMP $10^2/\mu L$	#NEUT $10^2/\mu L$	#EOS $10^2/\mu L$	#BASO $10^2/\mu L$	#MONO $10^2/\mu L$	#LUC $10^2/\mu L$	PT s
1001	0.9	0.1	2.0	0.8	52.8	9.0	0.6	0.1	1.3	0.5	12.1
1002	1.1	0.2	2.5	0.6	75.1	11.2	1.0	0.2	2.2	0.5	12.4
1003	1.9	0.3	2.6	0.5	71.0	25.0	1.9	0.3	2.6	0.5	10.9
1004	1.1	0.3	2.3	0.6	59.2	29.5	1.0	0.3	2.1	0.6	15.5
1005	1.3	0.2	2.4	0.4	52.5	15.2	0.9	0.1	1.7	0.3	13.1
n	5	5	5	5	5	5	5	5	5	5	5
Mean	1.3	0.2	2.4	0.6	62.1	18.0	1.1	0.2	2.0	0.5	12.8
S.D.	0.4	0.1	0.2	0.1	10.4	8.9	0.5	0.1	0.5	0.1	1.7

Animal No.	APTT s	FIB mg/dL
1001	15.9	265
1002	18.5	268
1003	12.6	267
1004	18.9	255
1005	18.5	268
n	5	5
Mean	16.9	265
S.D.	2.7	6

Appendix 6 - 2 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Hematology Stage : End of administration

Sex : Male Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RETIC %	PLT $10^4/\mu L$	WBC $10^2/\mu L$	LYMP %	NEUT %
2001	840	15.3	45.5	54.2	18.2	33.6	2.4	107.1	95.9	78.7	16.6
2002	865	16.1	46.4	53.6	18.6	34.7	2.3	89.9	82.1	81.5	13.8
2003	866	15.0	44.4	51.2	17.3	33.8	1.9	100.8	85.5	60.2	33.0
2004	832	15.0	43.8	52.6	18.0	34.2	2.3	82.0	67.2	86.7	10.0
2005	860	15.8	45.7	53.2	18.3	34.5	1.5	82.0	59.7	71.2	23.4
n	5	5	5	5	5	5	5	5	5	5	5
Mean	853	15.4	45.2	53.0	18.1	34.2	2.1	92.4	78.1	75.7	19.4
S.D.	16	0.5	1.0	1.1	0.5	0.5	0.4	11.3	14.5	10.3	9.1

Animal No.	EOS %	BASO %	MONO %	LUC %	#LYMP $10^2/\mu L$	#NEUT $10^2/\mu L$	#EOS $10^2/\mu L$	#BASO $10^2/\mu L$	#MONO $10^2/\mu L$	#LUC $10^2/\mu L$	PT s
2001	1.0	0.2	2.9	0.5	75.5	16.0	0.9	0.2	2.8	0.5	13.0
2002	1.0	0.2	3.0	0.5	66.9	11.4	0.8	0.2	2.5	0.4	12.4
2003	1.4	0.2	4.3	0.8	51.5	28.2	1.2	0.2	3.7	0.7	13.5
2004	1.0	0.2	1.7	0.5	58.3	6.7	0.7	0.1	1.1	0.4	12.2
2005	0.4	0.1	4.2	0.6	42.5	14.0	0.3	0.1	2.5	0.4	14.4
n	5	5	5	5	5	5	5	5	5	5	5
Mean	1.0	0.2	3.2	0.6	58.9	15.3	0.8	0.2	2.5	0.5	13.1
S.D.	0.4	0.0	1.1	0.1	12.9	8.0	0.3	0.1	0.9	0.1	0.9

Animal No.	APTT s	FIB mg/dL
2001	16.2	259
2002	17.4	260
2003	17.8	259
2004	17.2	265
2005	18.0	240
n	5	5
Mean	17.3	257
S.D.	0.7	10

Appendix 6 - 3 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Hematology Stage : End of administration

Sex : Male Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RETIC %	PLT $10^4/\mu L$	WBC $10^2/\mu L$	LYMP %	NEUT %
3001	806	15.4	44.7	55.5	19.1	34.4	2.4	84.4	79.9	74.1	22.7
3002	868	15.9	46.8	54.0	18.3	34.0	2.0	89.5	112.3	73.5	22.2
3003	831	15.8	46.3	55.6	19.1	34.3	2.4	89.2	70.8	71.2	23.5
3004	852	15.9	45.5	53.4	18.7	34.9	2.4	91.8	64.3	65.7	30.9
3005	833	15.4	44.4	53.2	18.5	34.8	1.8	112.5	48.3	70.6	24.6
n	5	5	5	5	5	5	5	5	5	5	5
Mean	838	15.7	45.5	54.3	18.7	34.5	2.2	93.5	75.1	71.0	24.8
S.D.	23	0.3	1.0	1.1	0.4	0.4	0.3	11.0	23.8	3.3	3.5

Animal No.	EOS %	BASO %	MONO %	LUC %	#LYMP $10^2/\mu L$	#NEUT $10^2/\mu L$	#EOS $10^2/\mu L$	#BASO $10^2/\mu L$	#MONO $10^2/\mu L$	#LUC $10^2/\mu L$	PT s
3001	0.4	0.3	2.3	0.2	59.2	18.2	0.3	0.3	1.8	0.2	13.0
3002	0.9	0.4	2.5	0.5	82.6	25.0	1.0	0.4	2.8	0.6	15.4
3003	0.5	0.2	4.3	0.3	50.4	16.6	0.3	0.1	3.0	0.2	16.3
3004	1.2	0.2	1.6	0.3	42.3	19.9	0.8	0.2	1.0	0.2	19.3
3005	0.9	0.2	2.7	0.9	34.1	11.9	0.5	0.1	1.3	0.4	13.0
n	5	5	5	5	5	5	5	5	5	5	5
Mean	0.8	0.3	2.7	0.4	53.7	18.3	0.6	0.2	2.0	0.3	15.4
S.D.	0.3	0.1	1.0	0.3	18.6	4.8	0.3	0.1	0.9	0.2	2.6

Animal No.	APTT s	FIB mg/dL
3001	16.9	283
3002	20.6	306
3003	19.3	267
3004	21.7	257
3005	15.9	267
n	5	5
Mean	18.9	276
S.D.	2.4	19

Appendix 6 - 4 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Hematology Stage : End of administration

Sex : Male Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RETIC %	PLT $10^4/\mu L$	WBC $10^2/\mu L$	LYMP %	NEUT %
4001	858	15.8	47.6	55.4	18.4	33.2	2.8	67.6	89.9	69.0	26.4
4002	833	15.4	46.1	55.4	18.5	33.4	2.6	85.1	63.1	73.9	22.4
4003	816	15.0	43.9	53.8	18.4	34.2	2.4	77.7	47.6	61.6	36.0
4004	832	15.1	44.1	53.1	18.2	34.2	2.7	75.6	73.5	50.7	44.8
4005	808	14.7	43.2	53.5	18.2	33.9	2.7	76.0	73.0	58.1	37.4
n	5	5	5	5	5	5	5	5	5	5	5
Mean	829	15.2	45.0	54.2	18.3	33.8	2.6	76.4	69.4	62.7	33.4
S.D.	19	0.4	1.8	1.1	0.1	0.5	0.2	6.2	15.5	9.1	9.0

Animal No.	EOS %	BASO %	MONO %	LUC %	#LYMP $10^2/\mu L$	#NEUT $10^2/\mu L$	#EOS $10^2/\mu L$	#BASO $10^2/\mu L$	#MONO $10^2/\mu L$	#LUC $10^2/\mu L$	PT s
4001	0.7	0.3	3.1	0.6	62.0	23.7	0.6	0.2	2.8	0.5	27.2
4002	0.9	0.2	2.2	0.4	46.6	14.1	0.6	0.1	1.4	0.3	21.9
4003	0.4	0.2	1.4	0.3	29.3	17.1	0.2	0.1	0.7	0.2	42.8
4004	1.0	0.1	3.0	0.2	37.3	33.0	0.8	0.1	2.2	0.2	25.6
4005	0.9	0.1	3.1	0.4	42.4	27.3	0.7	0.1	2.2	0.3	21.1
n	5	5	5	5	5	5	5	5	5	5	5
Mean	0.8	0.2	2.6	0.4	43.5	23.0	0.6	0.1	1.9	0.3	27.7
S.D.	0.2	0.1	0.8	0.1	12.2	7.6	0.2	0.0	0.8	0.1	8.8

Animal No.	APTT s	FIB mg/dL
4001	27.1	334
4002	24.0	333
4003	41.0	438
4004	30.2	373
4005	25.9	339
n	5	5
Mean	29.6	363
S.D.	6.7	45

Appendix 6 - 5 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Hematology Stage : Lactaion day 5

Sex : Female Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RETIC %	PLT $10^4/\mu L$	WBC $10^2/\mu L$	LYMP %	NEUT %
1101	622	12.1	36.1	58.1	19.5	33.5	6.6	131.1	116.0	53.6	42.1
1102	746	14.4	41.3	55.3	19.3	34.9	2.9	147.6	112.6	64.0	30.2
1104	729	13.9	41.2	56.5	19.1	33.8	5.4	130.2	100.7	66.2	29.4
1107	681	13.0	38.4	56.4	19.2	33.9	6.5	125.9	103.9	47.2	48.2
1110	660	13.2	38.6	58.4	20.0	34.2	4.9	109.5	104.0	50.6	41.8
n	5	5	5	5	5	5	5	5	5	5	5
Mean	688	13.3	39.1	56.9	19.4	34.1	5.3	128.9	107.4	56.3	38.3
S.D.	51	0.9	2.2	1.3	0.4	0.5	1.5	13.6	6.5	8.4	8.2

Animal No.	EOS %	BASO %	MONO %	LUC %	#LYMP $10^2/\mu L$	#NEUT $10^2/\mu L$	#EOS $10^2/\mu L$	#BASO $10^2/\mu L$	#MONO $10^2/\mu L$	#LUC $10^2/\mu L$	PT s
1101	0.6	0.2	3.2	0.4	62.2	48.8	0.7	0.2	3.7	0.5	14.9
1102	1.0	0.3	3.4	1.1	72.0	34.1	1.1	0.3	3.8	1.3	13.0
1104	0.5	0.3	2.7	0.8	66.7	29.6	0.6	0.3	2.7	0.8	14.7
1107	0.9	0.1	3.0	0.5	49.1	50.1	0.9	0.1	3.2	0.5	11.7
1110	0.8	0.2	6.1	0.5	52.6	43.5	0.8	0.2	6.4	0.6	14.6
n	5	5	5	5	5	5	5	5	5	5	5
Mean	0.8	0.2	3.7	0.7	60.5	41.2	0.8	0.2	4.0	0.7	13.8
S.D.	0.2	0.1	1.4	0.3	9.6	9.0	0.2	0.1	1.4	0.3	1.4

Animal No.	APTT s	FIB mg/dL
1101	18.3	269
1102	11.6	269
1104	17.3	314
1107	13.3	373
1110	18.8	395
n	5	5
Mean	15.9	324
S.D.	3.2	58

Appendix 6 - 6 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Hematology Stage : Lactaion day 5

Sex : Female Dose : benzyl salicylate 30 mg/kg Species : Rat

	RBC	HGB	HCT	MCV	MCH	MCHC	RETIC	PLT	WBC	LYMP	NEUT
Animal No.	10^4/μL	g/dL	%	fL	pg	g/dL	%	10^4/μL	10^2/μL	%	%
2101	710	13.2	38.7	54.6	18.6	34.0	4.9	156.8	137.2	72.3	22.8
2102	616	12.2	35.8	58.1	19.7	34.0	10.1	155.7	126.1	53.1	41.9
2103	735	14.1	40.8	55.5	19.2	34.6	3.5	120.6	78.9	60.9	32.0
2107	692	13.0	38.2	55.2	18.8	34.0	5.4	157.7	152.1	70.3	24.8
2112	688	13.0	38.4	55.8	18.9	33.9	6.4	137.5	83.8	54.6	38.6
n	5	5	5	5	5	5	5	5	5	5	5
Mean	688	13.1	38.4	55.8	19.0	34.1	6.1	145.7	115.6	62.2	32.0
S.D.	44	0.7	1.8	1.3	0.4	0.3	2.5	16.3	32.7	8.8	8.3

	EOS	BASO	MONO	LUC	#LYMP	#NEUT	#EOS	#BASO	#MONO	#LUC	PT
Animal No.	%	%	%	%	10^2/μL	10^2/μL	10^2/μL	10^2/μL	10^2/μL	10^2/μL	s
2101	0.9	0.4	2.7	1.0	99.2	31.3	1.2	0.5	3.7	1.3	11.4
2102	1.0	0.2	3.5	0.3	67.0	52.8	1.2	0.3	4.5	0.4	11.1
2103	1.5	0.3	4.0	1.2	48.1	25.3	1.2	0.2	3.2	1.0	12.0
2107	0.3	0.4	3.4	0.8	106.8	37.8	0.5	0.7	5.1	1.2	12.8
2112	0.4	0.2	5.8	0.5	45.7	32.3	0.3	0.2	4.9	0.4	10.8
n	5	5	5	5	5	5	5	5	5	5	5
Mean	0.8	0.3	3.9	0.8	73.4	35.9	0.9	0.4	4.3	0.9	11.6
S.D.	0.5	0.1	1.2	0.4	28.4	10.4	0.4	0.2	0.8	0.4	0.8

	APTT	FIB
Animal No.	s	mg/dL
2101	14.1	400
2102	12.8	279
2103	12.3	315
2107	14.5	279
2112	13.5	285
n	5	5
Mean	13.4	312
S.D.	0.9	52

Appendix 6 - 7 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Hematology Stage : Lactaion day 5

Sex : Female Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RETIC %	PLT $10^4/\mu L$	WBC $10^2/\mu L$	LYMP %	NEUT %
3102	682	12.6	37.2	54.5	18.5	33.9	7.4	145.3	118.5	55.5	39.0
3103	653	12.9	37.0	56.6	19.8	34.9	6.5	124.7	104.8	45.8	47.3
3104	650	13.3	38.7	59.5	20.4	34.3	8.8	163.6	74.1	81.0	13.0
3105	665	13.3	39.0	58.7	20.0	34.1	4.8	134.6	118.3	65.5	30.3
3108	638	12.5	36.3	56.8	19.5	34.4	7.3	142.7	106.7	63.6	32.1
n	5	5	5	5	5	5	5	5	5	5	5
Mean	658	12.9	37.6	57.2	19.6	34.3	7.0	142.2	104.5	62.3	32.3
S.D.	17	0.4	1.2	2.0	0.7	0.4	1.5	14.4	18.1	13.0	12.7

Animal No.	EOS %	BASO %	MONO %	LUC %	#LYMP $10^2/\mu L$	#NEUT $10^2/\mu L$	#EOS $10^2/\mu L$	#BASO $10^2/\mu L$	#MONO $10^2/\mu L$	#LUC $10^2/\mu L$	PT s
3102	1.1	0.2	3.6	0.6	65.8	46.2	1.3	0.2	4.3	0.7	14.0
3103	0.4	0.2	5.0	1.3	48.0	49.6	0.4	0.2	5.2	1.4	11.1
3104	1.3	0.4	3.7	0.6	60.0	9.6	1.0	0.3	2.7	0.4	11.8
3105	0.7	0.2	3.0	0.3	77.5	35.8	0.9	0.2	3.6	0.4	12.9
3108	0.3	0.3	2.9	0.8	67.9	34.3	0.3	0.3	3.1	0.8	11.6
n	5	5	5	5	5	5	5	5	5	5	5
Mean	0.8	0.3	3.6	0.7	63.8	35.1	0.8	0.2	3.8	0.7	12.3
S.D.	0.4	0.1	0.8	0.4	10.9	15.7	0.4	0.1	1.0	0.4	1.2

Animal No.	APTT s	FIB mg/dL
3102	15.2	301
3103	13.0	327
3104	13.7	243
3105	12.2	316
3108	15.3	336
n	5	5
Mean	13.9	305
S.D.	1.4	37

Appendix 6 - 8 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Hematology Stage : End of administration

Sex : Female Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RETIC %	PLT $10^4/\mu L$	WBC $10^2/\mu L$	LYMP %	NEUT %
5101	784	14.6	42.1	53.7	18.6	34.6	1.8	102.0	67.5	88.2	7.7
5102	757	14.3	42.3	55.8	18.9	33.8	2.7	143.0	149.9	49.6	43.2
5103	775	14.8	43.4	56.0	19.1	34.2	2.7	96.7	53.0	84.5	11.4
5104	759	13.8	40.5	53.3	18.2	34.1	2.6	90.9	50.4	77.4	18.6
5105	728	14.0	40.5	55.7	19.2	34.5	2.0	103.1	37.5	67.4	29.0
n	5	5	5	5	5	5	5	5	5	5	5
Mean	761	14.3	41.8	54.9	18.8	34.2	2.4	107.1	71.7	73.4	22.0
S.D.	21	0.4	1.3	1.3	0.4	0.3	0.4	20.6	45.0	15.5	14.4

Animal No.	EOS %	BASO %	MONO %	LUC %	#LYMP $10^2/\mu L$	#NEUT $10^2/\mu L$	#EOS $10^2/\mu L$	#BASO $10^2/\mu L$	#MONO $10^2/\mu L$	#LUC $10^2/\mu L$	PT s
5101	1.1	0.4	2.2	0.5	59.6	5.2	0.7	0.3	1.5	0.3	12.5
5102	0.6	0.2	5.7	0.7	74.3	64.7	0.9	0.4	8.6	1.0	13.9
5103	1.4	0.0	1.9	0.8	44.7	6.0	0.7	0.0	1.0	0.4	12.2
5104	1.0	0.2	1.8	0.9	39.0	9.4	0.5	0.1	0.9	0.5	12.6
5105	1.1	0.1	2.0	0.4	25.3	10.9	0.4	0.1	0.7	0.2	12.1
n	5	5	5	5	5	5	5	5	5	5	5
Mean	1.0	0.2	2.7	0.7	48.6	19.2	0.6	0.2	2.5	0.5	12.7
S.D.	0.3	0.1	1.7	0.2	18.9	25.5	0.2	0.2	3.4	0.3	0.7

Animal No.	APTT s	FIB mg/dL
5101	14.3	215
5102	13.8	394
5103	11.8	182
5104	13.4	226
5105	14.6	180
n	5	5
Mean	13.6	239
S.D.	1.1	89

Appendix 6 - 9 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Hematology Stage : End of administration

Sex : Female Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RETIC %	PLT $10^4/\mu L$	WBC $10^2/\mu L$	LYMP %	NEUT %
6101	696	14.2	40.3	57.9	20.4	35.2	3.2	90.5	65.5	81.1	15.6
6102	733	13.9	41.2	56.3	19.0	33.7	2.2	65.9	83.7	85.3	12.2
6103	716	13.7	40.3	56.2	19.1	33.9	2.8	81.8	55.4	80.5	16.3
6104	822	15.7	45.0	54.8	19.0	34.8	1.9	90.9	45.8	69.6	24.1
6105	767	14.6	42.6	55.5	19.0	34.2	2.9	82.4	64.4	70.2	25.9
n	5	5	5	5	5	5	5	5	5	5	5
Mean	747	14.4	41.9	56.1	19.3	34.4	2.6	82.3	63.0	77.3	18.8
S.D.	49	0.8	2.0	1.2	0.6	0.6	0.5	10.1	14.1	7.0	5.9

Animal No.	EOS %	BASO %	MONO %	LUC %	#LYMP $10^2/\mu L$	#NEUT $10^2/\mu L$	#EOS $10^2/\mu L$	#BASO $10^2/\mu L$	#MONO $10^2/\mu L$	#LUC $10^2/\mu L$	PT s
6101	0.3	0.2	2.4	0.5	53.1	10.2	0.2	0.1	1.6	0.3	11.3
6102	0.6	0.1	1.1	0.6	71.4	10.2	0.5	0.1	0.9	0.5	13.3
6103	0.6	0.1	1.7	0.7	44.6	9.1	0.4	0.1	1.0	0.4	11.4
6104	1.5	0.1	4.2	0.4	31.9	11.0	0.7	0.0	1.9	0.2	12.1
6105	0.8	0.1	2.4	0.6	45.2	16.7	0.5	0.1	1.5	0.4	13.6
n	5	5	5	5	5	5	5	5	5	5	5
Mean	0.8	0.1	2.4	0.6	49.2	11.4	0.5	0.1	1.4	0.4	12.3
S.D.	0.5	0.0	1.2	0.1	14.5	3.0	0.2	0.0	0.4	0.1	1.1

Animal No.	APTT s	FIB mg/dL
6101	13.9	279
6102	17.3	253
6103	15.4	246
6104	18.0	235
6105	17.7	238
n	5	5
Mean	16.5	250
S.D.	1.8	18

Appendix 6 - 10 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Hematology Stage : End of recovery

Sex : Male Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RETIC %	PLT $10^4/\mu L$	WBC $10^2/\mu L$	LYMP %	NEUT %
1008	822	15.1	44.2	53.8	18.4	34.2	1.8	89.2	51.7	79.0	16.9
1009	917	15.8	46.4	50.6	17.2	34.1	1.7	90.5	63.0	68.0	27.5
1010	810	14.8	43.1	53.3	18.2	34.2	2.4	87.6	58.0	68.2	26.3
1011	889	15.6	45.9	51.6	17.6	34.0	1.7	111.8	92.5	79.5	15.9
1012	827	15.4	43.8	53.0	18.6	35.2	2.0	101.5	118.3	75.0	21.1
n	5	5	5	5	5	5	5	5	5	5	5
Mean	853	15.3	44.7	52.5	18.0	34.3	1.9	96.1	76.7	73.9	21.5
S.D.	47	0.4	1.4	1.3	0.6	0.5	0.3	10.3	28.0	5.6	5.3

Animal No.	EOS %	BASO %	MONO %	LUC %	#LYMP $10^2/\mu L$	#NEUT $10^2/\mu L$	#EOS $10^2/\mu L$	#BASO $10^2/\mu L$	#MONO $10^2/\mu L$	#LUC $10^2/\mu L$	PT s
1008	2.4	0.1	1.3	0.3	40.8	8.7	1.2	0.1	0.7	0.1	17.3
1009	2.2	0.2	1.8	0.3	42.8	17.3	1.4	0.1	1.1	0.2	15.6
1010	2.1	0.3	2.5	0.6	39.5	15.3	1.2	0.2	1.5	0.4	11.7
1011	1.7	0.4	2.0	0.5	73.6	14.7	1.6	0.3	1.9	0.4	15.8
1012	1.2	0.3	1.8	0.7	88.7	24.9	1.4	0.3	2.1	0.9	15.9
n	5	5	5	5	5	5	5	5	5	5	5
Mean	1.9	0.3	1.9	0.5	57.1	16.2	1.4	0.2	1.5	0.4	15.3
S.D.	0.5	0.1	0.4	0.2	22.6	5.8	0.2	0.1	0.6	0.3	2.1

Animal No.	APTT s	FIB mg/dL
1008	19.6	287
1009	19.8	246
1010	15.6	297
1011	19.6	316
1012	19.6	348
n	5	5
Mean	18.8	299
S.D.	1.8	38

Appendix 6 - 11 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Hematology Stage : End of recovery

Sex : Male Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RETIC %	PLT $10^4/\mu L$	WBC $10^2/\mu L$	LYMP %	NEUT %
4008	842	15.1	44.3	52.6	18.0	34.1	2.6	124.9	83.2	68.2	27.2
4009	794	15.3	45.5	57.3	19.3	33.7	2.3	88.9	67.8	65.8	27.6
4010	876	16.3	48.7	55.5	18.7	33.6	2.1	86.8	81.5	53.5	42.6
4011	861	16.1	47.4	55.1	18.8	34.0	1.8	88.8	104.1	84.9	11.3
4012	876	16.3	48.1	54.9	18.7	34.0	2.1	101.1	114.2	81.3	13.8
n	5	5	5	5	5	5	5	5	5	5	5
Mean	850	15.8	46.8	55.1	18.7	33.9	2.2	98.1	90.2	70.7	24.5
S.D.	34	0.6	1.8	1.7	0.5	0.2	0.3	16.0	18.7	12.7	12.6

Animal No.	EOS %	BASO %	MONO %	LUC %	#LYMP $10^2/\mu L$	#NEUT $10^2/\mu L$	#EOS $10^2/\mu L$	#BASO $10^2/\mu L$	#MONO $10^2/\mu L$	#LUC $10^2/\mu L$	PT s
4008	0.7	0.2	3.3	0.4	56.7	22.6	0.6	0.2	2.7	0.3	13.0
4009	1.6	0.2	4.0	0.7	44.6	18.7	1.1	0.1	2.7	0.5	11.6
4010	0.8	0.2	2.2	0.7	43.6	34.7	0.6	0.2	1.8	0.6	14.3
4011	1.0	0.2	2.0	0.5	88.4	11.8	1.1	0.3	2.1	0.5	14.7
4012	1.5	0.4	2.4	0.7	92.9	15.7	1.7	0.4	2.7	0.8	14.2
n	5	5	5	5	5	5	5	5	5	5	5
Mean	1.1	0.2	2.8	0.6	65.2	20.7	1.0	0.2	2.4	0.5	13.6
S.D.	0.4	0.1	0.8	0.1	23.8	8.8	0.5	0.1	0.4	0.2	1.3

Animal No.	APTT s	FIB mg/dL
4008	15.8	266
4009	17.6	226
4010	18.5	230
4011	20.2	261
4012	17.2	321
n	5	5
Mean	17.9	261
S.D.	1.6	38

Appendix 6 - 12 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Hematology Stage : End of recovery

Sex : Female Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RETIC %	PLT $10^4/\mu L$	WBC $10^2/\mu L$	LYMP %	NEUT %
5106	813	15.0	43.3	53.3	18.5	34.7	1.5	104.5	61.9	78.7	16.1
5107	807	14.8	43.0	53.3	18.4	34.5	1.9	106.9	37.6	82.2	13.7
5108	781	15.0	43.1	55.1	19.2	34.9	1.7	102.5	48.6	83.2	11.4
5109	695	14.3	39.8	57.3	20.6	36.0	1.9	158.8	67.0	69.4	24.1
5110	774	14.7	41.6	53.8	19.0	35.3	1.7	111.5	40.1	77.8	16.1
n	5	5	5	5	5	5	5	5	5	5	5
Mean	774	14.8	42.2	54.6	19.1	35.1	1.7	116.8	51.0	78.3	16.3
S.D.	47	0.3	1.5	1.7	0.9	0.6	0.2	23.7	13.0	5.5	4.8

Animal No.	EOS %	BASO %	MONO %	LUC %	#LYMP $10^2/\mu L$	#NEUT $10^2/\mu L$	#EOS $10^2/\mu L$	#BASO $10^2/\mu L$	#MONO $10^2/\mu L$	#LUC $10^2/\mu L$	PT s
5106	1.6	0.2	2.6	0.7	48.7	10.0	1.0	0.1	1.6	0.4	11.0
5107	1.3	0.1	2.2	0.4	30.9	5.1	0.5	0.1	0.8	0.2	11.0
5108	1.6	0.1	3.3	0.4	40.4	5.5	0.8	0.1	1.6	0.2	10.6
5109	2.2	0.2	3.8	0.3	46.5	16.2	1.5	0.1	2.5	0.2	10.3
5110	3.3	0.2	2.0	0.5	31.2	6.5	1.3	0.1	0.8	0.2	11.7
n	5	5	5	5	5	5	5	5	5	5	5
Mean	2.0	0.2	2.8	0.5	39.5	8.7	1.0	0.1	1.5	0.2	10.9
S.D.	0.8	0.1	0.8	0.2	8.3	4.6	0.4	0.0	0.7	0.1	0.5

Animal No.	APTT s	FIB mg/dL
5106	17.1	166
5107	13.0	182
5108	14.8	190
5109	12.2	193
5110	14.7	207
n	5	5
Mean	14.4	188
S.D.	1.9	15

Appendix 6 - 13 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Hematology Stage : End of recovery

Sex : Female Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RETIC %	PLT $10^4/\mu L$	WBC $10^2/\mu L$	LYMP %	NEUT %
6106	800	15.2	43.4	54.3	19.0	35.0	1.9	93.5	75.3	78.5	16.7
6107	764	14.1	41.3	54.0	18.5	34.2	1.3	103.3	64.2	46.0	47.4
6108	740	14.0	40.1	54.2	18.9	34.9	1.6	109.8	35.9	72.3	20.7
6109	790	14.8	42.8	54.2	18.7	34.6	1.2	117.1	38.9	78.0	16.9
6110	778	14.9	42.6	54.7	19.1	34.9	2.3	106.7	73.2	84.3	10.4
n	5	5	5	5	5	5	5	5	5	5	5
Mean	774	14.6	42.0	54.3	18.8	34.7	1.7	106.1	57.5	71.8	22.4
S.D.	23	0.5	1.3	0.3	0.2	0.3	0.5	8.7	18.8	15.0	14.4

Animal No.	EOS %	BASO %	MONO %	LUC %	#LYMP $10^2/\mu L$	#NEUT $10^2/\mu L$	#EOS $10^2/\mu L$	#BASO $10^2/\mu L$	#MONO $10^2/\mu L$	#LUC $10^2/\mu L$	PT s
6106	1.4	0.1	2.9	0.4	59.1	12.6	1.1	0.1	2.2	0.3	10.6
6107	1.6	0.1	4.2	0.5	29.5	30.4	1.0	0.1	2.7	0.3	9.6
6108	1.4	0.2	4.5	1.0	25.9	7.4	0.5	0.1	1.6	0.3	10.3
6109	1.6	0.1	2.8	0.5	30.4	6.6	0.6	0.0	1.1	0.2	12.0
6110	1.2	0.3	3.0	0.9	61.7	7.6	0.9	0.2	2.2	0.6	11.8
n	5	5	5	5	5	5	5	5	5	5	5
Mean	1.4	0.2	3.5	0.7	41.3	12.9	0.8	0.1	2.0	0.3	10.9
S.D.	0.2	0.1	0.8	0.3	17.5	10.1	0.3	0.1	0.6	0.2	1.0

Animal No.	APTT s	FIB mg/dL
6106	13.8	176
6107	12.1	281
6108	16.1	203
6109	16.8	208
6110	13.1	185
n	5	5
Mean	14.4	211
S.D.	2.0	41

Appendix 6 - 14 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Hematology Stage : All littermates died

Sex : Female Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RETIC %	PLT $10^4/\mu L$	WBC $10^2/\mu L$	LYMP %	NEUT %
4102	653	12.7	37.5	57.4	19.4	33.8	4.4	117.2	98.0	60.9	33.9
4105	517	10.8	31.0	60.1	20.9	34.8	4.7	66.4	119.6	63.4	33.7
4106	604	12.5	36.2	60.0	20.7	34.6	5.0	84.2	105.0	60.6	35.3
4107	611	11.8	35.1	57.4	19.3	33.7	4.0	83.1	121.5	63.6	33.3
4109	521	10.2	30.0	57.6	19.5	33.9	4.1	58.9	98.0	66.6	29.9
4110	611	12.8	37.1	60.8	20.9	34.4	4.3	89.2	71.5	52.1	43.3
n	6	6	6	6	6	6	6	6	6	6	6
Mean	586	11.8	34.5	58.9	20.1	34.2	4.4	83.2	102.3	61.2	34.9
S.D.	55	1.1	3.2	1.6	0.8	0.5	0.4	20.3	18.2	5.0	4.5

Animal No.	EOS %	BASO %	MONO %	LUC %	#LYMP $10^2/\mu L$	#NEUT $10^2/\mu L$	#EOS $10^2/\mu L$	#BASO $10^2/\mu L$	#MONO $10^2/\mu L$	#LUC $10^2/\mu L$	PT s
4102	0.4	0.2	3.9	0.7	59.7	33.2	0.4	0.2	3.8	0.7	13.1
4105	0.5	0.2	1.8	0.4	75.9	40.3	0.5	0.3	2.1	0.4	11.7
4106	0.4	0.3	2.5	0.9	63.7	37.0	0.4	0.3	2.7	0.9	11.8
4107	0.4	0.2	2.1	0.4	77.2	40.5	0.5	0.3	2.6	0.4	14.1
4109	0.3	0.2	2.3	0.6	65.3	29.3	0.3	0.2	2.3	0.6	12.2
4110	0.7	0.2	3.4	0.3	37.3	31.0	0.5	0.1	2.4	0.2	12.3
n	6	6	6	6	6	6	6	6	6	6	6
Mean	0.5	0.2	2.7	0.6	63.2	35.2	0.4	0.2	2.7	0.5	12.5
S.D.	0.1	0.0	0.8	0.2	14.5	4.8	0.1	0.1	0.6	0.3	0.9

Animal No.	APTT s	FIB mg/dL
4102	16.1	354
4105	21.2	329
4106	13.5	275
4107	17.5	301
4109	16.6	336
4110	18.7	297
n	6	6
Mean	17.3	315
S.D.	2.6	29

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Hematology

Stage : Undelivered

Sex : Female

Dose : benzyl salicylate 300 mg/kg

Species : Rat

Animal No.	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RETIC %	PLT $10^4/\mu L$	WBC $10^2/\mu L$	LYMP %	NEUT %
4101	618	11.7	34.1	55.3	19.0	34.4	4.8	82.2	122.9	64.9	28.0
4103	575	12.1	34.7	60.4	21.0	34.8	3.9	65.5	88.1	79.5	16.4
4104	707	14.0	41.3	58.4	19.8	33.8	2.4	70.5	60.4	74.6	19.2
4108	661	13.2	40.0	60.5	20.0	33.1	6.1	74.5	115.2	65.3	29.1
4111	657	13.1	39.3	59.8	20.0	33.3	2.9	83.0	72.5	74.5	21.4
4112	643	12.9	37.5	58.3	20.1	34.6	3.8	85.0	71.5	77.6	16.6
n	6	6	6	6	6	6	6	6	6	6	6
Mean	644	12.8	37.8	58.8	20.0	34.0	4.0	76.8	88.4	72.7	21.8
S.D.	44	0.8	2.9	2.0	0.6	0.7	1.3	7.8	25.4	6.2	5.6

Animal No.	EOS %	BASO %	MONO %	LUC %	#LYMP $10^2/\mu L$	#NEUT $10^2/\mu L$	#EOS $10^2/\mu L$	#BASO $10^2/\mu L$	#MONO $10^2/\mu L$	#LUC $10^2/\mu L$	PT s
4101	0.6	0.3	4.5	1.7	79.8	34.4	0.7	0.3	5.5	2.1	14.3
4103	0.2	0.3	2.4	1.2	70.1	14.4	0.1	0.3	2.1	1.1	12.1
4104	0.7	0.2	3.7	1.5	45.1	11.6	0.4	0.1	2.3	0.9	13.1
4108	0.9	0.2	3.3	1.1	75.2	33.6	1.0	0.3	3.8	1.3	14.2
4111	0.5	0.2	3.0	0.4	54.0	15.5	0.3	0.1	2.2	0.3	12.6
4112	0.5	0.2	4.2	0.8	55.5	11.9	0.4	0.1	3.0	0.6	13.7
n	6	6	6	6	6	6	6	6	6	6	6
Mean	0.6	0.2	3.5	1.1	63.3	20.2	0.5	0.2	3.2	1.1	13.3
S.D.	0.2	0.1	0.8	0.5	13.7	10.8	0.3	0.1	1.3	0.6	0.9

Animal No.	APTT s	FIB mg/dL
4101	20.7	293
4103	14.1	248
4104	20.8	271
4108	12.7	277
4111	17.9	235
4112	14.6	236
n	6	6
Mean	16.8	260
S.D.	3.5	24

Appendix 7 - 1 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Blood chemistry Stage : End of administration

Sex : Male Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	AST IU/L	ALT IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	T-BA μmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
1001	75	40	100	1	547	45.7	51	23	88	0.1	129
1002	52	37	38	1	410	110.1	68	28	108	0.1	134
1003	67	40	62	0	365	16.9	69	48	97	0.1	133
1004	67	41	55	1	498	6.5	53	33	85	0.1	143
1005	56	30	33	0	323	10.1	56	31	85	0.1	136
n	5	5	5	5	5	5	5	5	5	5	5
Mean	63	38	58	1	429	37.9	59	33	93	0.1	135
S.D.	9	5	27	1	93	43.2	9	9	10	0.0	5

Animal No.	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
1001	12	0.23	142	4.2	106	9.9	5.5	5.9	3.1	1.1
1002	14	0.28	143	4.3	106	10.1	6.3	5.6	3.1	1.2
1003	11	0.23	143	4.2	106	10.1	5.7	6.1	3.1	1.0
1004	15	0.25	143	4.6	105	9.5	6.4	5.4	2.9	1.2
1005	11	0.22	142	4.0	106	9.8	4.8	5.9	3.1	1.1
n	5	5	5	5	5	5	5	5	5	5
Mean	13	0.24	143	4.3	106	9.9	5.7	5.8	3.1	1.1
S.D.	2	0.02	1	0.2	0	0.2	0.7	0.3	0.1	0.1

Appendix 7 - 2 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Blood chemistry Stage : End of administration

Sex : Male Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	AST IU/L	ALT IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	T-BA μmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
2001	66	29	58	0	415	5.7	47	22	79	0.1	141
2002	52	28	35	0	349	10.5	47	15	75	0.1	143
2003	66	41	39	0	411	14.3	56	48	87	0.1	133
2004	59	34	30	0	367	6.5	52	28	80	0.1	134
2005	63	39	46	0	410	8.1	42	37	77	0.1	137
n	5	5	5	5	5	5	5	5	5	5	5
Mean	61	34	42	0	390	9.0	49	30	80	0.1	138
S.D.	6	6	11	0	30	3.5	5	13	5	0.0	4

Animal No.	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
2001	10	0.28	142	4.7	106	9.6	5.8	5.7	3.0	1.1
2002	13	0.27	145	4.0	108	10.0	6.3	5.6	2.9	1.1
2003	13	0.25	143	4.1	107	9.7	4.8	5.5	3.0	1.2
2004	11	0.22	144	4.2	108	10.0	5.6	5.7	3.1	1.2
2005	11	0.18	144	4.3	107	9.9	5.6	5.7	3.2	1.3
n	5	5	5	5	5	5	5	5	5	5
Mean	12	0.24	144	4.3	107	9.8	5.6	5.6	3.0	1.2
S.D.	1	0.04	1	0.3	1	0.2	0.5	0.1	0.1	0.1

Appendix 7 - 3 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Blood chemistry Stage : End of administration

Sex : Male Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	AST IU/L	ALT IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	T-BA μmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
3001	62	38	54	0	381	30.5	59	49	100	0.1	136
3002	69	52	44	0	783	50.2	38	65	80	0.0	143
3003	73	33	35	0	379	9.5	45	18	75	0.0	131
3004	50	29	40	0	348	21.2	50	63	88	0.0	116
3005	64	28	53	0	400	5.5	44	28	74	0.1	138
n	5	5	5	5	5	5	5	5	5	5	5
Mean	64	36	45	0	458	23.4	47	45	83	0.0	133
S.D.	9	10	8	0	183	17.9	8	21	11	0.1	10

Animal No.	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
3001	13	0.26	142	4.7	106	10.2	6.3	5.7	3.2	1.3
3002	20	0.34	142	4.9	105	10.0	8.0	5.8	3.2	1.2
3003	12	0.23	144	4.2	109	9.9	6.5	5.4	3.0	1.3
3004	14	0.23	143	4.6	106	9.8	5.8	5.6	3.2	1.3
3005	10	0.20	144	4.0	106	9.6	5.2	5.6	3.1	1.2
n	5	5	5	5	5	5	5	5	5	5
Mean	14	0.25	143	4.5	106	9.9	6.4	5.6	3.1	1.3
S.D.	4	0.05	1	0.4	2	0.2	1.0	0.1	0.1	0.1

Appendix 7 - 4 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Blood chemistry Stage : End of administration

Sex : Male Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	AST IU/L	ALT IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	T-BA μmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
4001	97	65	46	1	747	19.1	57	50	108	0.0	123
4002	75	51	41	1	784	18.0	51	39	94	0.0	138
4003	89	67	47	0	817	17.1	56	43	98	0.0	116
4004	159	99	102	0	805	66.3	48	59	88	0.0	109
4005	78	53	48	0	449	13.0	59	84	112	0.0	119
n	5	5	5	5	5	5	5	5	5	5	5
Mean	100	67	57	0	720	26.7	54	55	100	0.0	121
S.D.	34	19	25	1	154	22.3	5	18	10	0.0	11

Animal No.	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
4001	13	0.31	145	4.2	109	9.7	6.7	5.2	3.2	1.6
4002	13	0.33	142	4.4	107	9.9	5.5	5.4	3.3	1.6
4003	19	0.27	146	3.7	110	9.6	5.4	5.2	3.2	1.6
4004	15	0.29	143	3.7	104	10.0	6.4	5.6	3.3	1.4
4005	13	0.30	143	4.1	105	10.2	6.8	5.6	3.2	1.3
n	5	5	5	5	5	5	5	5	5	5
Mean	15	0.30	144	4.0	107	9.9	6.2	5.4	3.2	1.5
S.D.	3	0.02	2	0.3	3	0.2	0.7	0.2	0.1	0.1

Appendix 7 - 5 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Blood chemistry Stage : Lactation day 5

Sex : Female Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	AST IU/L	ALT IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	T-BA μmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
1101	70	52	53	0	299	11.0	58	32	112	0.1	128
1102	70	70	48	0	368	34.8	81	64	132	0.1	143
1104	78	37	56	0	458	19.5	42	28	82	0.1	118
1107	77	69	36	0	288	14.9	56	84	114	0.1	125
1110	66	56	33	1	245	25.7	68	63	121	0.1	119
n	5	5	5	5	5	5	5	5	5	5	5
Mean	72	57	45	0	332	21.2	61	54	112	0.1	127
S.D.	5	14	10	0	83	9.4	15	24	19	0.0	10

Animal No.	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
1101	17	0.28	141	3.7	105	10.6	8.4	6.0	3.3	1.2
1102	22	0.38	141	4.5	104	10.7	6.8	5.8	3.2	1.2
1104	13	0.25	140	4.0	107	10.3	7.5	5.6	3.2	1.3
1107	19	0.28	142	3.6	107	10.4	6.7	5.5	3.1	1.3
1110	26	0.38	142	3.8	106	10.8	7.7	6.0	3.1	1.1
n	5	5	5	5	5	5	5	5	5	5
Mean	19	0.31	141	3.9	106	10.6	7.4	5.8	3.2	1.2
S.D.	5	0.06	1	0.4	1	0.2	0.7	0.2	0.1	0.1

Appendix 7 - 6 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Blood chemistry Stage : Lactation day 5

Sex : Female Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	AST IU/L	ALT IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	T-BA μmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
2101	72	62	41	1	395	169.4	73	66	161	0.1	96
2102	67	40	66	1	218	18.7	52	57	97	0.1	124
2103	64	62	42	1	426	34.0	72	59	130	0.1	114
2107	69	47	53	0	187	29.1	53	126	124	0.1	123
2112	58	38	60	0	230	14.7	68	155	142	0.1	124
n	5	5	5	5	5	5	5	5	5	5	5
Mean	66	50	52	1	291	53.2	64	93	131	0.1	116
S.D.	5	12	11	1	111	65.4	10	45	24	0.0	12

Animal No.	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
2101	31	0.32	139	4.7	105	10.9	8.9	6.0	3.3	1.2
2102	19	0.33	142	4.0	105	10.9	8.3	5.5	3.1	1.3
2103	22	0.32	142	4.4	107	10.6	6.6	6.0	3.4	1.3
2107	14	0.22	141	3.8	103	10.8	7.5	6.2	3.5	1.3
2112	12	0.27	140	4.2	104	11.1	8.0	6.3	3.5	1.3
n	5	5	5	5	5	5	5	5	5	5
Mean	20	0.29	141	4.2	105	10.9	7.9	6.0	3.4	1.3
S.D.	8	0.05	1	0.3	1	0.2	0.9	0.3	0.2	0.0

Appendix 7 - 7 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Blood chemistry Stage : Lactation day 5

Sex : Female Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	AST IU/L	ALT IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	T-BA μmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
3102	73	50	73	1	254	22.6	58	113	119	0.0	96
3103	87	60	76	1	284	41.2	83	137	155	0.1	123
3104	63	30	43	1	228	31.7	52	26	100	0.0	118
3105	64	56	36	1	173	18.8	77	152	151	0.0	124
3108	68	59	35	1	162	23.3	69	93	134	0.0	106
n	5	5	5	5	5	5	5	5	5	5	5
Mean	71	51	53	1	220	27.5	68	104	132	0.0	113
S.D.	10	12	20	0	52	9.0	13	49	23	0.0	12

Animal No.	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
3102	17	0.29	142	3.9	106	10.5	7.0	5.6	3.2	1.3
3103	18	0.35	142	4.0	103	11.0	9.8	5.8	3.4	1.4
3104	20	0.37	140	4.1	104	10.7	5.8	5.8	3.3	1.3
3105	15	0.31	141	4.0	104	10.9	5.9	6.1	3.4	1.3
3108	23	0.32	142	4.7	105	10.8	8.6	6.0	3.4	1.3
n	5	5	5	5	5	5	5	5	5	5
Mean	19	0.33	141	4.1	104	10.8	7.4	5.9	3.3	1.3
S.D.	3	0.03	1	0.3	1	0.2	1.7	0.2	0.1	0.0

Appendix 7 - 8 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Blood chemistry Stage : End of administration

Sex : Female Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	AST IU/L	ALT IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	T-BA μmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
5101	57	36	42	1	179	16.8	71	15	130	0.1	120
5102	47	20	44	1	201	13.3	29	20	64	0.1	112
5103	54	35	37	1	171	34.3	61	15	120	0.1	113
5104	52	23	40	0	311	26.1	67	19	124	0.1	144
5105	48	25	47	0	163	16.6	88	24	168	0.1	140
n	5	5	5	5	5	5	5	5	5	5	5
Mean	52	28	42	1	205	21.4	63	19	121	0.1	126
S.D.	4	7	4	1	61	8.6	22	4	37	0.0	15

Animal No.	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
5101	16	0.31	140	4.3	108	10.2	4.5	6.6	3.8	1.4
5102	10	0.28	138	4.2	106	9.8	4.3	5.6	2.4	0.8
5103	16	0.32	140	4.0	108	10.0	4.0	6.0	3.6	1.5
5104	15	0.32	141	4.3	109	10.1	4.2	6.2	3.4	1.2
5105	12	0.25	141	3.9	106	11.0	3.7	7.1	4.3	1.5
n	5	5	5	5	5	5	5	5	5	5
Mean	14	0.30	140	4.1	107	10.2	4.1	6.3	3.5	1.3
S.D.	3	0.03	1	0.2	1	0.5	0.3	0.6	0.7	0.3

Appendix 7 - 9 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Blood chemistry Stage : End of administration

Sex : Female Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	AST IU/L	ALT IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	T-BA μmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
6101	70	34	35	1	265	32.4	63	41	129	0.0	137
6102	93	70	42	1	377	23.2	53	62	121	0.0	132
6103	76	67	33	1	363	28.7	81	97	161	0.0	92
6104	68	52	37	1	378	27.1	53	22	113	0.0	116
6105	110	92	40	0	300	30.8	62	49	117	0.0	104
n	5	5	5	5	5	5	5	5	5	5	5
Mean	83	63	37	1	337	28.4	62	54	128	0.0	116
S.D.	18	22	4	0	51	3.6	11	28	19	0.0	19

Animal No.	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
6101	13	0.41	142	4.3	109	9.8	4.4	5.8	3.6	1.6
6102	22	0.35	142	4.1	109	9.2	4.1	5.4	3.4	1.7
6103	13	0.28	142	4.1	106	9.6	4.8	5.7	3.6	1.7
6104	9	0.25	141	3.6	105	10.0	4.8	5.8	3.7	1.8
6105	15	0.30	142	4.2	111	9.4	4.9	5.6	3.3	1.4
n	5	5	5	5	5	5	5	5	5	5
Mean	14	0.32	142	4.1	108	9.6	4.6	5.7	3.5	1.6
S.D.	5	0.06	0	0.3	2	0.3	0.3	0.2	0.2	0.2

Appendix 7 - 10 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Blood chemistry Stage : End of recovery

Sex : Male Dose : benzyl salicylate 0 mg/kg Species : Rat

	AST	ALT	LDH	γ-GTP	ALP	T-BA	T-CHO	TG	PL	T-BIL	GLU
Animal No.	IU/L	IU/L	IU/L	IU/L	IU/L	μmol/L	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL
1008	63	30	37	0	306	8.3	57	37	90	0.1	148
1009	70	33	44	1	506	9.8	68	42	99	0.1	150
1010	50	32	41	0	198	3.7	71	68	105	0.1	143
1011	84	36	44	0	316	5.7	60	36	90	0.1	127
1012	77	32	32	0	312	8.4	62	31	91	0.1	128
n	5	5	5	5	5	5	5	5	5	5	5
Mean	69	33	40	0	328	7.2	64	43	95	0.1	139
S.D.	13	2	5	0	111	2.4	6	15	7	0.0	11

	BUN	CRNN	Na	K	Cl	Ca	P	TP	ALB	A/G
Animal No.	mg/dL	mg/dL	mmol/L	mmol/L	mmol/L	mg/dL	mg/dL	g/dL	g/dL	
1008	16	0.25	142	4.6	106	9.7	6.2	5.9	3.1	1.1
1009	18	0.22	145	4.3	109	9.7	5.6	5.9	3.1	1.1
1010	17	0.19	145	4.4	107	10.2	5.4	6.5	3.2	1.0
1011	17	0.23	145	4.5	108	9.8	6.6	5.8	3.1	1.1
1012	17	0.26	144	4.1	108	9.5	5.9	6.1	3.1	1.0
n	5	5	5	5	5	5	5	5	5	5
Mean	17	0.23	144	4.4	108	9.8	5.9	6.0	3.1	1.1
S.D.	1	0.03	1	0.2	1	0.3	0.5	0.3	0.0	0.1

Appendix 7 - 11 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Blood chemistry Stage : End of recovery

Sex : Male Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	AST IU/L	ALT IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	T-BA μmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
4008	60	33	36	1	391	7.6	52	91	91	0.1	113
4009	57	43	45	0	264	12.8	78	84	120	0.1	132
4010	60	27	35	1	389	7.7	64	38	99	0.1	132
4011	58	35	37	0	318	9.1	52	20	78	0.1	119
4012	60	38	30	0	320	10.6	58	38	89	0.1	122
n	5	5	5	5	5	5	5	5	5	5	5
Mean	59	35	37	0	336	9.6	61	54	95	0.1	124
S.D.	1	6	5	1	54	2.2	11	31	16	0.0	8

Animal No.	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
4008	11	0.19	144	4.3	108	10.3	6.1	5.9	3.1	1.1
4009	17	0.19	144	4.4	109	10.5	6.7	5.9	3.2	1.2
4010	16	0.23	145	4.3	108	9.8	7.0	5.8	3.0	1.1
4011	16	0.18	143	4.4	106	10.1	7.2	5.6	3.2	1.3
4012	15	0.19	143	4.4	108	10.2	7.6	5.9	3.2	1.2
n	5	5	5	5	5	5	5	5	5	5
Mean	15	0.20	144	4.4	108	10.2	6.9	5.8	3.1	1.2
S.D.	2	0.02	1	0.1	1	0.3	0.6	0.1	0.1	0.1

Appendix 7 - 12 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Blood chemistry Stage : End of recovery

Sex : Female Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	AST IU/L	ALT IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	T-BA μmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
5106	63	36	44	0	96	20.1	86	30	161	0.1	119
5107	52	29	39	0	129	27.2	79	37	146	0.1	117
5108	65	29	36	0	163	8.4	88	15	144	0.1	134
5109	48	32	47	0	131	17.5	75	76	157	0.1	146
5110	61	27	37	0	139	6.7	70	14	123	0.1	114
n	5	5	5	5	5	5	5	5	5	5	5
Mean	58	31	41	0	132	16.0	80	34	146	0.1	126
S.D.	7	4	5	0	24	8.5	8	25	15	0.0	14

Animal No.	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
5106	19	0.27	143	4.0	109	10.4	3.4	6.8	3.9	1.3
5107	24	0.32	142	4.3	109	10.2	4.0	6.8	3.7	1.2
5108	15	0.35	141	4.3	105	10.0	4.9	6.4	3.4	1.1
5109	19	0.26	143	4.1	109	10.7	4.4	7.3	4.1	1.3
5110	16	0.30	143	4.3	109	9.9	3.4	6.3	3.6	1.3
n	5	5	5	5	5	5	5	5	5	5
Mean	19	0.30	142	4.2	108	10.2	4.0	6.7	3.7	1.2
S.D.	4	0.04	1	0.1	2	0.3	0.6	0.4	0.3	0.1

Appendix 7 - 13 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Blood chemistry Stage : End of recovery

Sex : Female Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	AST IU/L	ALT IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	T-BA μmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
6106	48	20	33	0	101	12.2	99	21	152	0.1	119
6107	105	26	71	0	129	9.7	95	13	145	0.1	138
6108	91	33	86	1	196	11.5	77	18	150	0.1	140
6109	67	38	52	0	143	10.1	50	11	97	0.1	111
6110	53	22	33	1	176	11.2	71	26	134	0.1	127
n	5	5	5	5	5	5	5	5	5	5	5
Mean	73	28	55	0	149	10.9	78	18	136	0.1	127
S.D.	25	8	23	1	38	1.0	20	6	23	0.0	12

Animal No.	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
6106	22	0.31	142	4.3	108	10.1	4.4	5.8	3.4	1.4
6107	14	0.24	143	4.3	109	10.4	4.5	6.2	3.4	1.2
6108	15	0.30	142	3.6	107	10.3	4.7	6.5	3.6	1.2
6109	16	0.27	143	4.0	108	10.1	5.2	6.1	3.5	1.3
6110	25	0.39	142	4.0	106	10.2	6.0	6.3	3.8	1.5
n	5	5	5	5	5	5	5	5	5	5
Mean	18	0.30	142	4.0	108	10.2	5.0	6.2	3.5	1.3
S.D.	5	0.06	1	0.3	1	0.1	0.7	0.3	0.2	0.1

Appendix 7 - 14 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Blood chemistry Stage : All littermates died

Sex : Female Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	AST IU/L	ALT IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	T-BA μmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
4102	83	50	50	1	404	33.6	73	87	142	0.0	130
4105	102	74	97	1	238	21.4	65	158	149	0.0	116
4106	62	35	42	0	248	33.0	65	129	137	0.0	144
4107	77	69	66	1	607	17.0	63	218	148	0.0	115
4109	85	52	44	1	396	15.9	64	221	144	0.0	127
4110	48	33	36	1	337	33.3	64	99	128	0.0	129
n	6	6	6	6	6	6	6	6	6	6	6
Mean	76	52	56	1	372	25.7	66	152	141	0.0	127
S.D.	19	17	23	0	135	8.5	4	58	8	0.0	11

Animal No.	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
4102	23	0.29	142	4.0	100	11.8	7.7	6.1	3.6	1.4
4105	23	0.31	141	3.1	103	11.2	6.9	5.7	3.3	1.4
4106	25	0.27	144	4.5	103	11.2	7.0	5.7	3.5	1.6
4107	29	0.31	143	3.3	105	11.0	4.5	5.9	3.5	1.5
4109	27	0.30	143	3.7	100	11.1	6.2	6.1	3.4	1.3
4110	18	0.30	143	3.8	98	11.5	8.5	6.3	3.8	1.5
n	6	6	6	6	6	6	6	6	6	6
Mean	24	0.30	143	3.7	102	11.3	6.8	6.0	3.5	1.5
S.D.	4	0.02	1	0.5	3	0.3	1.4	0.2	0.2	0.1

Appendix 7 - 15 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Blood chemistry Stage : Undelivered

Sex : Female Dose : benzyl salicylate 300 mg/kg Species : Rat

	AST	ALT	LDH	γ-GTP	ALP	T-BA	T-CHO	TG	PL	T-BIL	GLU
Animal No.	IU/L	IU/L	IU/L	IU/L	IU/L	μmol/L	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL
4101	73	45	38	0	292	22.9	63	110	135	0.0	140
4103	85	62	47	1	511	42.0	79	226	149	0.0	138
4104	145	65	51	1	216	15.1	68	94	118	0.0	149
4108	74	36	51	1	338	32.9	56	119	121	0.0	143
4111	78	50	58	1	191	11.0	59	100	120	0.0	133
4112	83	40	41	1	285	14.5	47	169	116	0.0	144
n	6	6	6	6	6	6	6	6	6	6	6
Mean	90	50	48	1	306	23.1	62	136	127	0.0	141
S.D.	28	12	7	0	114	12.1	11	51	13	0.0	5

	BUN	CRNN	Na	K	Cl	Ca	P	TP	ALB	A/G
Animal No.	mg/dL	mg/dL	mmol/L	mmol/L	mmol/L	mg/dL	mg/dL	g/dL	g/dL	
4101	20	0.29	142	4.1	102	11.1	7.1	5.9	3.6	1.6
4103	26	0.37	142	4.4	107	10.7	5.9	5.0	2.7	1.2
4104	15	0.37	144	3.9	111	9.8	2.8	5.3	3.4	1.8
4108	18	0.32	141	4.5	104	10.8	6.6	5.9	3.6	1.6
4111	25	0.35	143	4.0	109	9.9	4.0	5.4	3.3	1.6
4112	21	0.30	141	4.6	106	10.6	4.6	5.4	3.4	1.7
n	6	6	6	6	6	6	6	6	6	6
Mean	21	0.33	142	4.3	107	10.5	5.2	5.5	3.3	1.6
S.D.	4	0.04	1	0.3	3	0.5	1.7	0.4	0.3	0.2

Appendix 8 - 1 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Organ weight Stage : End of administration

Sex : Male Dose : benzyl salicylate 0 mg/kg Species : Rat

	Body weight	Brain		Pituitary		Thyroid-R		Thyroid-L	
		AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	g	g	g/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g
1001	539	2.18	0.40	12.7	2.4	9.3	1.7	7.9	1.5
1002	543	2.27	0.42	12.8	2.4	4.6	0.8	5.8	1.1
1003	571	2.19	0.38	13.1	2.3	13.4	2.3	13.7	2.4
1004	491	2.19	0.45	12.7	2.6	5.3	1.1	8.9	1.8
1005	513	2.05	0.40	13.1	2.6	12.0	2.3	13.7	2.7
1006	512	2.14	0.42	15.1	2.9	9.9	1.9	11.4	2.2
1007	451	2.07	0.46	11.2	2.5	7.5	1.7	5.3	1.2
n	7	7	7	7	7	7	7	7	7
Mean	517	2.16	0.42	13.0	2.5	8.9	1.7	9.5	1.8
S.D.	39	0.08	0.03	1.1	0.2	3.3	0.6	3.5	0.6

	Thyroid-RL		Thymus		Heart		Liver		Spleen	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	mg	mg/100g	g	g/100g	g	g/100g	g	g/100g
1001	17.2	3.2	458	85	1.46	0.27	13.60	2.52	0.63	0.12
1002	10.4	1.9	317	58	1.71	0.31	13.47	2.48	0.92	0.17
1003	27.1	4.7	348	61	1.48	0.26	16.22	2.84	0.92	0.16
1004	14.2	2.9	348	71	1.31	0.27	12.43	2.53	0.78	0.16
1005	25.7	5.0	264	51	1.38	0.27	13.71	2.67	0.70	0.14
1006	21.3	4.2	340	66	1.50	0.29	12.87	2.51	0.73	0.14
1007	12.8	2.8	323	72	1.30	0.29	11.63	2.58	0.74	0.16
n	7	7	7	7	7	7	7	7	7	7
Mean	18.4	3.5	343	66	1.45	0.28	13.42	2.59	0.77	0.15
S.D.	6.5	1.1	59	11	0.14	0.02	1.44	0.13	0.11	0.02

	Kidney-R		Kidney-L		Kidney-RL		Adrenal-R		Adrenal-L	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	g	g/100g	g	g/100g	g	g/100g	mg	mg/100g	mg	mg/100g
1001	1.63	0.30	1.57	0.29	3.20	0.59	25	5	27	5
1002	1.69	0.31	1.84	0.34	3.53	0.65	34	6	34	6
1003	1.90	0.33	1.88	0.33	3.78	0.66	33	6	32	6
1004	1.64	0.33	1.71	0.35	3.35	0.68	25	5	29	6
1005	1.69	0.33	1.76	0.34	3.45	0.67	32	6	35	7
1006	1.59	0.31	1.68	0.33	3.27	0.64	31	6	32	6
1007	1.46	0.32	1.60	0.35	3.06	0.68	25	6	25	6
n	7	7	7	7	7	7	7	7	7	7
Mean	1.66	0.32	1.72	0.33	3.38	0.65	29	6	31	6
S.D.	0.13	0.01	0.12	0.02	0.24	0.03	4	0	4	1

AB : Absolute weight, RE : Relative weight by body weight

Appendix 8 - 2 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Organ weight Stage : End of administration

Sex : Male Dose : benzyl salicylate 0 mg/kg Species : Rat

	Adrenal-RL		Testis-R		Testis-L		Testis-RL		Epididymis-R	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	g	g/100g	g	g/100g	g	g/100g	mg	mg/100g
1001	52	10	1.68	0.31	1.74	0.32	3.42	0.63	703	130
1002	68	13	1.83	0.34	1.84	0.34	3.67	0.68	802	148
1003	65	11	1.55	0.27	1.57	0.27	3.12	0.55	676	118
1004	54	11	1.64	0.33	1.62	0.33	3.26	0.66	655	133
1005	67	13	1.68	0.33	1.68	0.33	3.36	0.65	684	133
1006	63	12	1.66	0.32	1.66	0.32	3.32	0.65	687	134
1007	50	11	1.71	0.38	1.73	0.38	3.44	0.76	645	143
n	7	7	7	7	7	7	7	7	7	7
Mean	60	12	1.68	0.33	1.69	0.33	3.37	0.65	693	134
S.D.	8	1	0.08	0.03	0.09	0.03	0.17	0.06	52	10

	Epididymis-L		Epididymis-RL		Prostate		Seminal vesicle	
	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	mg	mg/100g	g	g/100g	g	g/100g
1001	662	123	1365	253	1.41	0.26	1.97	0.37
1002	704	130	1506	277	1.90	0.35	1.98	0.36
1003	639	112	1315	230	1.33	0.23	1.95	0.34
1004	608	124	1263	257	1.28	0.26	2.09	0.43
1005	734	143	1418	276	1.19	0.23	1.79	0.35
1006	722	141	1409	275	1.46	0.29	2.07	0.40
1007	670	149	1315	292	1.27	0.28	1.57	0.35
n	7	7	7	7	7	7	7	7
Mean	677	132	1370	266	1.41	0.27	1.92	0.37
S.D.	46	13	81	21	0.24	0.04	0.18	0.03

AB : Absolute weight, RE : Relative weight by body weight

Appendix 8 - 3 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Organ weight Stage : End of administration

Sex : Male Dose : benzyl salicylate 30 mg/kg Species : Rat

	Body weight	Brain		Pituitary		Thyroid-R		Thyroid-L	
		AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	g	g	g/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g
2001	540	2.09	0.39	12.6	2.3	12.8	2.4	11.6	2.1
2002	494	2.10	0.43	13.1	2.7	11.9	2.4	8.6	1.7
2003	458	2.09	0.46	12.5	2.7	15.3	3.3	12.3	2.7
2004	502	2.14	0.43	14.1	2.8	9.0	1.8	9.2	1.8
2005	497	2.09	0.42	10.3	2.1	15.2	3.1	15.9	3.2
2006	518	2.18	0.42	13.7	2.6	14.5	2.8	10.7	2.1
2007	527	2.23	0.42	13.8	2.6	9.5	1.8	10.9	2.1
2008	518	2.13	0.41	11.2	2.2	7.5	1.4	3.3	0.6
2009	488	2.23	0.46	13.6	2.8	11.9	2.4	10.5	2.2
2010	476	2.11	0.44	14.1	3.0	6.0	1.3	6.6	1.4
2011	495	2.23	0.45	13.3	2.7	15.5	3.1	15.2	3.1
2012	448	2.05	0.46	11.2	2.5	11.9	2.7	7.7	1.7
n	12	12	12	12	12	12	12	12	12
Mean	497	2.14	0.43	12.8	2.6	11.8	2.4	10.2	2.1
S.D.	27	0.06	0.02	1.3	0.3	3.2	0.7	3.5	0.7

	Thyroid-RL		Thymus		Heart		Liver		Spleen	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	mg	mg/100g	g	g/100g	g	g/100g	g	g/100g
2001	24.4	4.5	308	57	1.30	0.24	12.64	2.34	0.83	0.15
2002	20.5	4.1	557	113	1.23	0.25	13.11	2.65	0.76	0.15
2003	27.6	6.0	236	52	1.40	0.31	10.63	2.32	0.70	0.15
2004	18.2	3.6	293	58	1.45	0.29	13.53	2.70	0.83	0.17
2005	31.1	6.3	283	57	1.32	0.27	11.09	2.23	0.60	0.12
2006	25.2	4.9	436	84	1.72	0.33	13.79	2.66	0.71	0.14
2007	20.4	3.9	243	46	1.46	0.28	12.98	2.46	0.63	0.12
2008	10.8	2.1	217	42	1.60	0.31	11.05	2.13	0.63	0.12
2009	22.4	4.6	441	90	1.51	0.31	12.97	2.66	0.68	0.14
2010	12.6	2.6	326	68	1.38	0.29	12.14	2.55	0.60	0.13
2011	30.7	6.2	286	58	1.47	0.30	11.96	2.42	0.81	0.16
2012	19.6	4.4	261	58	1.45	0.32	10.92	2.44	0.73	0.16
n	12	12	12	12	12	12	12	12	12	12
Mean	22.0	4.4	324	65	1.44	0.29	12.23	2.46	0.71	0.14
S.D.	6.4	1.3	102	21	0.13	0.03	1.10	0.19	0.09	0.02

AB : Absolute weight, RE : Relative weight by body weight

Appendix 8 - 4 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Organ weight Stage : End of administration

Sex : Male Dose : benzyl salicylate 30 mg/kg Species : Rat

	Kidney-R		Kidney-L		Kidney-RL		Adrenal-R		Adrenal-L	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	g	g/100g	g	g/100g	g	g/100g	mg	mg/100g	mg	mg/100g
2001	1.48	0.27	1.52	0.28	3.00	0.56	39	7	36	7
2002	1.60	0.32	1.75	0.35	3.35	0.68	20	4	24	5
2003	1.42	0.31	1.49	0.33	2.91	0.64	24	5	26	6
2004	1.65	0.33	1.75	0.35	3.40	0.68	36	7	38	8
2005	1.69	0.34	1.74	0.35	3.43	0.69	26	5	28	6
2006	1.63	0.31	1.64	0.32	3.27	0.63	31	6	30	6
2007	1.84	0.35	1.86	0.35	3.70	0.70	31	6	38	7
2008	1.50	0.29	1.72	0.33	3.22	0.62	26	5	28	5
2009	1.64	0.34	1.62	0.33	3.26	0.67	32	7	33	7
2010	1.52	0.32	1.66	0.35	3.18	0.67	34	7	30	6
2011	1.67	0.34	1.79	0.36	3.46	0.70	30	6	28	6
2012	1.59	0.35	1.58	0.35	3.17	0.71	29	6	35	8
n	12	12	12	12	12	12	12	12	12	12
Mean	1.60	0.32	1.68	0.34	3.28	0.66	30	6	31	6
S.D.	0.11	0.02	0.11	0.02	0.21	0.04	5	1	5	1

	Adrenal-RL		Testis-R		Testis-L		Testis-RL		Epididymis-R	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	g	g/100g	g	g/100g	g	g/100g	mg	mg/100g
2001	75	14	1.57	0.29	1.63	0.30	3.20	0.59	659	122
2002	44	9	1.57	0.32	1.59	0.32	3.16	0.64	675	137
2003	50	11	1.65	0.36	1.64	0.36	3.29	0.72	618	135
2004	74	15	1.64	0.33	1.63	0.32	3.27	0.65	603	120
2005	54	11	1.85	0.37	1.81	0.36	3.66	0.74	671	135
2006	61	12	1.83	0.35	1.90	0.37	3.73	0.72	667	129
2007	69	13	1.64	0.31	1.62	0.31	3.26	0.62	677	128
2008	54	10	1.69	0.33	1.64	0.32	3.33	0.64	700	135
2009	65	13	1.75	0.36	1.74	0.36	3.49	0.72	724	148
2010	64	13	1.62	0.34	1.57	0.33	3.19	0.67	683	143
2011	58	12	1.56	0.32	1.57	0.32	3.13	0.63	655	132
2012	64	14	1.66	0.37	1.67	0.37	3.33	0.74	682	152
n	12	12	12	12	12	12	12	12	12	12
Mean	61	12	1.67	0.34	1.67	0.34	3.34	0.67	668	135
S.D.	9	2	0.10	0.03	0.10	0.03	0.19	0.05	33	10

AB : Absolute weight, RE : Relative weight by body weight

Appendix 8 - 5 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Organ weight Stage : End of administration

Sex : Male Dose : benzyl salicylate 30 mg/kg Species : Rat

	Epididymis-L		Epididymis-RL		Prostate		Seminal vesicle	
	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	mg	mg/100g	g	g/100g	g	g/100g
2001	640	119	1299	241	1.41	0.26	1.64	0.30
2002	619	125	1294	262	1.19	0.24	1.35	0.27
2003	588	128	1206	263	1.28	0.28	1.61	0.35
2004	609	121	1212	241	1.19	0.24	1.76	0.35
2005	668	134	1339	269	0.89	0.18	1.78	0.36
2006	672	130	1339	258	1.49	0.29	1.74	0.34
2007	603	114	1280	243	1.28	0.24	2.68	0.51
2008	683	132	1383	267	1.14	0.22	1.87	0.36
2009	736	151	1460	299	1.62	0.33	2.11	0.43
2010	641	135	1324	278	1.67	0.35	1.26	0.26
2011	646	131	1301	263	1.28	0.26	1.96	0.40
2012	626	140	1308	292	1.41	0.31	1.69	0.38
n	12	12	12	12	12	12	12	12
Mean	644	130	1312	265	1.32	0.27	1.79	0.36
S.D.	41	10	68	19	0.22	0.05	0.37	0.07

AB : Absolute weight, RE : Relative weight by body weight

Appendix 8 - 6 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Organ weight Stage : End of administration

Sex : Male Dose : benzyl salicylate 100 mg/kg Species : Rat

	Body weight	Brain		Pituitary		Thyroid-R		Thyroid-L	
		AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	g	g	g/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g
3001	561	2.09	0.37	15.4	2.7	10.0	1.8	11.1	2.0
3002	563	2.10	0.37	12.6	2.2	8.9	1.6	9.8	1.7
3003	495	2.16	0.44	12.3	2.5	9.4	1.9	12.5	2.5
3004	481	2.08	0.43	11.8	2.5	8.1	1.7	8.3	1.7
3005	504	2.15	0.43	11.6	2.3	8.2	1.6	10.3	2.0
3006	498	2.17	0.44	13.4	2.7	10.4	2.1	8.5	1.7
3007	458	2.09	0.46	11.1	2.4	9.4	2.1	9.7	2.1
3008	510	2.12	0.42	13.8	2.7	10.5	2.1	10.5	2.1
3009	517	2.17	0.42	12.4	2.4	11.5	2.2	9.1	1.8
3010	510	2.09	0.41	13.0	2.5	10.4	2.0	10.8	2.1
3011	555	2.17	0.39	11.8	2.1	12.4	2.2	12.7	2.3
3012	526	2.19	0.42	11.5	2.2	14.3	2.7	10.0	1.9
n	12	12	12	12	12	12	12	12	12
Mean	515	2.13	0.42	12.6	2.4	10.3	2.0	10.3	2.0
S.D.	32	0.04	0.03	1.2	0.2	1.8	0.3	1.4	0.3

	Thyroid-RL		Thymus		Heart		Liver		Spleen	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	mg	mg/100g	g	g/100g	g	g/100g	g	g/100g
3001	21.1	3.8	337	60	1.74	0.31	14.26	2.54	0.84	0.15
3002	18.7	3.3	367	65	1.37	0.24	12.61	2.24	0.79	0.14
3003	21.9	4.4	196	40	1.41	0.28	12.10	2.44	0.69	0.14
3004	16.4	3.4	249	52	1.43	0.30	11.96	2.49	0.68	0.14
3005	18.5	3.7	307	61	1.34	0.27	12.33	2.45	0.73	0.14
3006	18.9	3.8	198	40	1.54	0.31	13.10	2.63	0.75	0.15
3007	19.1	4.2	200	44	1.41	0.31	11.84	2.59	0.77	0.17
3008	21.0	4.1	329	65	1.37	0.27	11.70	2.29	0.64	0.13
3009	20.6	4.0	188	36	1.54	0.30	13.03	2.52	0.89	0.17
3010	21.2	4.2	220	43	1.24	0.24	12.73	2.50	0.70	0.14
3011	25.1	4.5	352	63	1.58	0.28	13.98	2.52	0.60	0.11
3012	24.3	4.6	274	52	1.37	0.26	13.69	2.60	0.75	0.14
n	12	12	12	12	12	12	12	12	12	12
Mean	20.6	4.0	268	52	1.45	0.28	12.78	2.48	0.74	0.14
S.D.	2.5	0.4	68	11	0.13	0.03	0.86	0.12	0.08	0.02

AB : Absolute weight, RE : Relative weight by body weight

Appendix 8 - 7 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Organ weight Stage : End of administration

Sex : Male Dose : benzyl salicylate 100 mg/kg Species : Rat

	Kidney-R		Kidney-L		Kidney-RL		Adrenal-R		Adrenal-L	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	g	g/100g	g	g/100g	g	g/100g	mg	mg/100g	mg	mg/100g
3001	1.74	0.31	1.64	0.29	3.38	0.60	29	5	29	5
3002	1.61	0.29	1.70	0.30	3.31	0.59	29	5	33	6
3003	1.75	0.35	1.85	0.37	3.60	0.73	38	8	40	8
3004	1.51	0.31	1.62	0.34	3.13	0.65	30	6	35	7
3005	1.69	0.34	1.75	0.35	3.44	0.68	26	5	29	6
3006	1.75	0.35	1.83	0.37	3.58	0.72	30	6	33	7
3007	1.61	0.35	1.56	0.34	3.17	0.69	32	7	37	8
3008	1.57	0.31	1.64	0.32	3.21	0.63	36	7	41	8
3009	1.92	0.37	2.01	0.39	3.93	0.76	35	7	38	7
3010	1.55	0.30	1.60	0.31	3.15	0.62	30	6	35	7
3011	1.68	0.30	1.73	0.31	3.41	0.61	24	4	27	5
3012	1.65	0.31	1.61	0.31	3.26	0.62	29	6	31	6
n	12	12	12	12	12	12	12	12	12	12
Mean	1.67	0.32	1.71	0.33	3.38	0.66	31	6	34	7
S.D.	0.11	0.03	0.13	0.03	0.23	0.06	4	1	4	1

	Adrenal-RL		Testis-R		Testis-L		Testis-RL		Epididymis-R	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	g	g/100g	g	g/100g	g	g/100g	mg	mg/100g
3001	58	10	1.71	0.30	1.68	0.30	3.39	0.60	596	106
3002	62	11	1.68	0.30	1.59	0.28	3.27	0.58	667	118
3003	78	16	1.52	0.31	1.50	0.30	3.02	0.61	571	115
3004	65	14	1.97	0.41	1.98	0.41	3.95	0.82	727	151
3005	55	11	1.73	0.34	1.72	0.34	3.45	0.68	702	139
3006	63	13	1.22	0.24	1.25	0.25	2.47	0.50	557	112
3007	69	15	1.81	0.40	1.78	0.39	3.59	0.78	750	164
3008	77	15	1.67	0.33	1.64	0.32	3.31	0.65	656	129
3009	73	14	1.78	0.34	1.71	0.33	3.49	0.68	680	132
3010	65	13	1.65	0.32	1.71	0.34	3.36	0.66	630	124
3011	51	9	1.52	0.27	1.57	0.28	3.09	0.56	527	95
3012	60	11	1.57	0.30	1.55	0.29	3.12	0.59	621	118
n	12	12	12	12	12	12	12	12	12	12
Mean	65	13	1.65	0.32	1.64	0.32	3.29	0.64	640	125
S.D.	8	2	0.19	0.05	0.18	0.05	0.36	0.09	69	19

AB : Absolute weight, RE : Relative weight by body weight

Appendix 8 - 8 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Organ weight Stage : End of administration

Sex : Male Dose : benzyl salicylate 100 mg/kg Species : Rat

	Epididymis-L		Epididymis-RL		Prostate		Seminal vesicle	
	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	mg	mg/100g	g	g/100g	g	g/100g
3001	593	106	1189	212	1.26	0.22	1.62	0.29
3002	653	116	1320	234	1.45	0.26	1.57	0.28
3003	525	106	1096	221	1.30	0.26	1.98	0.40
3004	744	155	1471	306	1.18	0.25	1.77	0.37
3005	719	143	1421	282	1.22	0.24	1.56	0.31
3006	485	97	1042	209	1.35	0.27	1.54	0.31
3007	712	155	1462	319	1.12	0.24	1.94	0.42
3008	634	124	1290	253	1.15	0.23	2.05	0.40
3009	606	117	1286	249	1.39	0.27	1.29	0.25
3010	669	131	1299	255	1.50	0.29	1.66	0.33
3011	590	106	1117	201	1.01	0.18	1.35	0.24
3012	607	115	1228	233	1.07	0.20	1.41	0.27
n	12	12	12	12	12	12	12	12
Mean	628	123	1268	248	1.25	0.24	1.65	0.32
S.D.	77	20	141	38	0.15	0.03	0.25	0.06

AB : Absolute weight, RE : Relative weight by body weight

Appendix 8 - 9 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Organ weight Stage : End of administration

Sex : Male Dose : benzyl salicylate 300 mg/kg Species : Rat

	Body weight	Brain		Pituitary		Thyroid-R		Thyroid-L	
		AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	g	g	g/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g
4001	454	2.22	0.49	12.8	2.8	11.2	2.5	9.1	2.0
4002	511	2.15	0.42	13.5	2.6	10.0	2.0	9.5	1.9
4003	482	2.16	0.45	11.3	2.3	9.9	2.1	10.3	2.1
4004	519	2.22	0.43	12.0	2.3	13.4	2.6	13.6	2.6
4005	510	2.20	0.43	13.6	2.7	11.4	2.2	8.6	1.7
4006	506	2.06	0.41	11.8	2.3	12.2	2.4	14.1	2.8
4007	464	2.20	0.47	12.5	2.7	9.6	2.1	10.6	2.3
n	7	7	7	7	7	7	7	7	7
Mean	492	2.17	0.44	12.5	2.5	11.1	2.3	10.8	2.2
S.D.	26	0.06	0.03	0.9	0.2	1.4	0.2	2.2	0.4

	Thyroid-RL		Thymus		Heart		Liver		Spleen	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	mg	mg/100g	g	g/100g	g	g/100g	g	g/100g
4001	20.3	4.5	309	68	1.38	0.30	11.65	2.57	0.83	0.18
4002	19.5	3.8	259	51	1.46	0.29	14.49	2.84	0.72	0.14
4003	20.2	4.2	109	23	1.40	0.29	13.08	2.71	0.67	0.14
4004	27.0	5.2	312	60	1.42	0.27	14.80	2.85	0.67	0.13
4005	20.0	3.9	176	35	1.30	0.25	14.99	2.94	0.72	0.14
4006	26.3	5.2	375	74	1.38	0.27	14.70	2.91	0.68	0.13
4007	20.2	4.4	171	37	1.30	0.28	12.34	2.66	0.61	0.13
n	7	7	7	7	7	7	7	7	7	7
Mean	21.9	4.5	244	50	1.38	0.28	13.72	2.78	0.70	0.14
S.D.	3.2	0.6	95	19	0.06	0.02	1.35	0.14	0.07	0.02

	Kidney-R		Kidney-L		Kidney-RL		Adrenal-R		Adrenal-L	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	g	g/100g	g	g/100g	g	g/100g	mg	mg/100g	mg	mg/100g
4001	1.41	0.31	1.59	0.35	3.00	0.66	29	6	30	7
4002	1.70	0.33	1.76	0.34	3.46	0.68	27	5	24	5
4003	1.67	0.35	1.86	0.39	3.53	0.73	31	6	32	7
4004	1.84	0.35	2.00	0.39	3.84	0.74	27	5	29	6
4005	1.70	0.33	1.73	0.34	3.43	0.67	35	7	35	7
4006	1.62	0.32	1.58	0.31	3.20	0.63	27	5	28	6
4007	1.59	0.34	1.62	0.35	3.21	0.69	29	6	34	7
n	7	7	7	7	7	7	7	7	7	7
Mean	1.65	0.33	1.73	0.35	3.38	0.69	29	6	30	6
S.D.	0.13	0.01	0.16	0.03	0.27	0.04	3	1	4	1

AB : Absolute weight, RE : Relative weight by body weight

Appendix 8 - 10 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Organ weight Stage : End of administration

Sex : Male Dose : benzyl salicylate 300 mg/kg Species : Rat

	Adrenal-RL		Testis-R		Testis-L		Testis-RL		Epididymis-R	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	g	g/100g	g	g/100g	g	g/100g	mg	mg/100g
4001	59	13	1.75	0.39	1.76	0.39	3.51	0.77	630	139
4002	51	10	1.61	0.32	1.64	0.32	3.25	0.64	636	124
4003	63	13	1.94	0.40	1.92	0.40	3.86	0.80	630	131
4004	56	11	1.57	0.30	1.59	0.31	3.16	0.61	588	113
4005	70	14	1.55	0.30	1.55	0.30	3.10	0.61	672	132
4006	55	11	1.66	0.33	1.62	0.32	3.28	0.65	645	127
4007	63	14	1.61	0.35	1.53	0.33	3.14	0.68	607	131
n	7	7	7	7	7	7	7	7	7	7
Mean	60	12	1.67	0.34	1.66	0.34	3.33	0.68	630	128
S.D.	6	2	0.14	0.04	0.14	0.04	0.27	0.08	27	8

	Epididymis-L		Epididymis-RL		Prostate		Seminal vesicle	
	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	mg	mg/100g	g	g/100g	g	g/100g
4001	586	129	1216	268	1.24	0.27	1.97	0.43
4002	626	123	1262	247	1.08	0.21	1.89	0.37
4003	652	135	1282	266	1.34	0.28	1.71	0.35
4004	572	110	1160	224	1.11	0.21	1.66	0.32
4005	598	117	1270	249	1.24	0.24	2.27	0.45
4006	621	123	1266	250	1.04	0.21	1.60	0.32
4007	575	124	1182	255	1.27	0.27	2.34	0.50
n	7	7	7	7	7	7	7	7
Mean	604	123	1234	251	1.19	0.24	1.92	0.39
S.D.	30	8	48	15	0.11	0.03	0.29	0.07

AB : Absolute weight, RE : Relative weight by body weight

Appendix 8 - 11 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Organ weight Stage : Lactation day 5

Sex : Female Dose : benzyl salicylate 0 mg/kg Species : Rat

	Body weight	Brain		Pituitary		Thyroid-R		Thyroid-L	
		AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	g	g	g/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g
1101	325	1.99	0.61	19.0	5.8	6.0	1.8	6.1	1.9
1102	340	2.03	0.60	17.3	5.1	8.7	2.6	7.5	2.2
1103	361	1.98	0.55	16.1	4.5	9.0	2.5	9.4	2.6
1104	324	1.97	0.61	15.9	4.9	7.2	2.2	7.5	2.3
1105	349	2.24	0.64	20.2	5.8	5.9	1.7	7.0	2.0
1106	349	2.07	0.59	18.6	5.3	9.3	2.7	8.3	2.4
1107	330	1.96	0.59	14.6	4.4	9.9	3.0	8.3	2.5
1108	345	2.05	0.59	14.1	4.1	9.5	2.8	8.3	2.4
1109	371	2.05	0.55	16.8	4.5	7.8	2.1	9.1	2.5
1110	319	2.01	0.63	16.8	5.3	14.1	4.4	10.9	3.4
1111	340	2.03	0.60	19.1	5.6	14.6	4.3	11.7	3.4
1112	308	1.96	0.64	17.7	5.7	9.8	3.2	11.8	3.8
n	12	12	12	12	12	12	12	12	12
Mean	338	2.03	0.60	17.2	5.1	9.3	2.8	8.8	2.6
S.D.	18	0.08	0.03	1.9	0.6	2.7	0.9	1.8	0.6

	Thyroid-RL		Thymus		Heart		Liver		Spleen	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	mg	mg/100g	g	g/100g	g	g/100g	g	g/100g
1101	12.1	3.7	176	54	0.98	0.30	9.80	3.02	0.57	0.18
1102	16.2	4.8	214	63	0.96	0.28	10.49	3.09	0.61	0.18
1103	18.4	5.1	329	91	1.20	0.33	12.50	3.46	0.85	0.24
1104	14.7	4.5	188	58	1.08	0.33	9.50	2.93	0.64	0.20
1105	12.9	3.7	152	44	1.18	0.34	11.49	3.29	0.70	0.20
1106	17.6	5.0	336	96	1.11	0.32	10.20	2.92	0.58	0.17
1107	18.2	5.5	172	52	0.97	0.29	10.15	3.08	0.62	0.19
1108	17.8	5.2	229	66	1.22	0.35	12.08	3.50	0.65	0.19
1109	16.9	4.6	256	69	1.27	0.34	10.76	2.90	0.61	0.16
1110	25.0	7.8	211	66	1.11	0.35	10.07	3.16	0.67	0.21
1111	26.3	7.7	174	51	1.10	0.32	10.58	3.11	0.97	0.29
1112	21.6	7.0	213	69	0.97	0.31	10.11	3.28	0.59	0.19
n	12	12	12	12	12	12	12	12	12	12
Mean	18.1	5.4	221	65	1.10	0.32	10.64	3.15	0.67	0.20
S.D.	4.3	1.4	59	16	0.11	0.02	0.92	0.20	0.12	0.03

AB : Absolute weight, RE : Relative weight by body weight

Appendix 8 - 12 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Organ weight Stage : Lactation day 5

Sex : Female Dose : benzyl salicylate 0 mg/kg Species : Rat

	Kidney-R		Kidney-L		Kidney-RL		Adrenal-R		Adrenal-L	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	g	g/100g	g	g/100g	g	g/100g	mg	mg/100g	mg	mg/100g
1101	1.06	0.33	1.08	0.33	2.14	0.66	37	11	38	12
1102	0.93	0.27	0.96	0.28	1.89	0.56	37	11	40	12
1103	1.23	0.34	1.23	0.34	2.46	0.68	43	12	44	12
1104	1.09	0.34	1.06	0.33	2.15	0.66	41	13	41	13
1105	1.03	0.30	1.05	0.30	2.08	0.60	44	13	49	14
1106	1.10	0.32	1.03	0.30	2.13	0.61	29	8	32	9
1107	1.03	0.31	1.11	0.34	2.14	0.65	37	11	41	12
1108	1.03	0.30	1.12	0.32	2.15	0.62	34	10	34	10
1109	1.08	0.29	1.06	0.29	2.14	0.58	33	9	38	10
1110	1.03	0.32	1.05	0.33	2.08	0.65	42	13	49	15
1111	1.05	0.31	1.04	0.31	2.09	0.61	30	9	35	10
1112	1.11	0.36	1.06	0.34	2.17	0.70	35	11	36	12
n	12	12	12	12	12	12	12	12	12	12
Mean	1.06	0.32	1.07	0.32	2.14	0.63	37	11	40	12
S.D.	0.07	0.02	0.06	0.02	0.13	0.04	5	2	5	2

	Adrenal-RL		Ovary-R		Ovary-L		Ovary-RL		Uterus	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g
1101	75	23	58.1	17.9	30.9	9.5	89.0	27.4	687	211
1102	77	23	51.9	15.3	58.3	17.1	110.2	32.4	700	206
1103	87	24	65.8	18.2	65.2	18.1	131.0	36.3	670	186
1104	82	25	48.2	14.9	31.8	9.8	80.0	24.7	721	223
1105	93	27	72.1	20.7	72.8	20.9	144.9	41.5	951	272
1106	61	17	48.2	13.8	53.1	15.2	101.3	29.0	645	185
1107	78	24	46.1	14.0	38.0	11.5	84.1	25.5	656	199
1108	68	20	63.6	18.4	40.8	11.8	104.4	30.3	892	259
1109	71	19	56.5	15.2	64.5	17.4	121.0	32.6	676	182
1110	91	29	53.9	16.9	40.7	12.8	94.6	29.7	724	227
1111	65	19	75.0	22.1	54.8	16.1	129.8	38.2	708	208
1112	71	23	41.0	13.3	49.6	16.1	90.6	29.4	607	197
n	12	12	12	12	12	12	12	12	12	12
Mean	77	23	56.7	16.7	50.0	14.7	106.7	31.4	720	213
S.D.	10	3	10.6	2.8	13.7	3.6	20.8	5.1	101	28

AB : Absolute weight, RE : Relative weight by body weight

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weight

Stage : Lactation day 5

Sex : Female

Dose : benzyl salicylate 30 mg/kg

Species : Rat

Animal No.	Body weight	Brain		Pituitary		Thyroid-R		Thyroid-L	
		AB	RE	AB	RE	AB	RE	AB	RE
	g	g	g/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g
2101	317	2.24	0.71	18.6	5.9	9.5	3.0	9.7	3.1
2102	321	1.94	0.60	16.1	5.0	11.6	3.6	6.7	2.1
2103	334	1.97	0.59	13.0	3.9	7.6	2.3	7.6	2.3
2104	343	1.94	0.57	16.1	4.7	8.0	2.3	7.7	2.2
2105	359	2.13	0.59	23.1	6.4	10.4	2.9	9.2	2.6
2106	320	1.89	0.59	16.8	5.3	9.8	3.1	6.4	2.0
2107	310	2.23	0.72	20.4	6.6	7.5	2.4	8.8	2.8
2108	331	1.97	0.60	16.7	5.0	9.4	2.8	12.1	3.7
2109	339	1.91	0.56	20.7	6.1	8.6	2.5	7.8	2.3
2110	300	1.91	0.64	17.2	5.7	9.2	3.1	7.7	2.6
2111	352	2.06	0.59	19.1	5.4	8.6	2.4	8.6	2.4
2112	346	2.03	0.59	17.8	5.1	10.2	2.9	9.5	2.7
n	12	12	12	12	12	12	12	12	12
Mean	331	2.02	0.61	18.0	5.4	9.2	2.8	8.5	2.6
S.D.	18	0.12	0.05	2.6	0.8	1.2	0.4	1.5	0.5

Animal No.	Thyroid-RL		Thymus		Heart		Liver		Spleen	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
	mg	mg/100g	mg	mg/100g	g	g/100g	g	g/100g	g	g/100g
2101	19.2	6.1	185	58	0.98	0.31	9.84	3.10	0.66	0.21
2102	18.3	5.7	186	58	1.27	0.40	9.62	3.00	0.79	0.25
2103	15.2	4.6	252	75	0.99	0.30	9.49	2.84	0.58	0.17
2104	15.7	4.6	264	77	1.29	0.38	10.84	3.16	0.70	0.20
2105	19.6	5.5	242	67	1.18	0.33	11.91	3.32	1.04	0.29
2106	16.2	5.1	115	36	1.06	0.33	11.45	3.58	0.63	0.20
2107	16.3	5.3	231	75	1.06	0.34	10.10	3.26	0.63	0.20
2108	21.5	6.5	242	73	0.95	0.29	9.93	3.00	0.58	0.18
2109	16.4	4.8	261	77	1.11	0.33	11.58	3.42	0.65	0.19
2110	16.9	5.6	171	57	0.95	0.32	10.47	3.49	0.54	0.18
2111	17.2	4.9	193	55	1.07	0.30	10.85	3.08	0.79	0.22
2112	19.7	5.7	207	60	1.02	0.29	10.06	2.91	0.61	0.18
n	12	12	12	12	12	12	12	12	12	12
Mean	17.7	5.4	212	64	1.08	0.33	10.51	3.18	0.68	0.21
S.D.	1.9	0.6	44	12	0.12	0.03	0.81	0.24	0.14	0.03

AB : Absolute weight, RE : Relative weight by body weight

Appendix 8 - 14 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Organ weight Stage : Lactation day 5

Sex : Female Dose : benzyl salicylate 30 mg/kg Species : Rat

	Kidney-R		Kidney-L		Kidney-RL		Adrenal-R		Adrenal-L	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	g	g/100g	g	g/100g	g	g/100g	mg	mg/100g	mg	mg/100g
2101	1.11	0.35	0.98	0.31	2.09	0.66	37	12	38	12
2102	0.99	0.31	1.01	0.31	2.00	0.62	33	10	34	11
2103	1.15	0.34	1.12	0.34	2.27	0.68	29	9	31	9
2104	1.06	0.31	0.98	0.29	2.04	0.59	32	9	32	9
2105	1.21	0.34	1.20	0.33	2.41	0.67	42	12	48	13
2106	1.26	0.39	1.27	0.40	2.53	0.79	36	11	39	12
2107	1.02	0.33	0.97	0.31	1.99	0.64	33	11	37	12
2108	1.08	0.33	1.06	0.32	2.14	0.65	34	10	40	12
2109	1.19	0.35	1.20	0.35	2.39	0.71	37	11	38	11
2110	1.01	0.34	1.00	0.33	2.01	0.67	33	11	37	12
2111	0.99	0.28	0.97	0.28	1.96	0.56	41	12	49	14
2112	0.99	0.29	0.95	0.27	1.94	0.56	40	12	42	12
n	12	12	12	12	12	12	12	12	12	12
Mean	1.09	0.33	1.06	0.32	2.15	0.65	36	11	39	12
S.D.	0.10	0.03	0.11	0.03	0.20	0.06	4	1	6	1

	Adrenal-RL		Ovary-R		Ovary-L		Ovary-RL		Uterus	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g
2101	75	24	57.2	18.0	43.5	13.7	100.7	31.8	729	230
2102	67	21	54.9	17.1	64.5	20.1	119.4	37.2	836	260
2103	60	18	64.9	19.4	43.8	13.1	108.7	32.5	601	180
2104	64	19	45.5	13.3	48.9	14.3	94.4	27.5	702	205
2105	90	25	52.9	14.7	52.2	14.5	105.1	29.3	710	198
2106	75	23	45.6	14.3	61.1	19.1	106.7	33.3	975	305
2107	70	23	61.4	19.8	43.5	14.0	104.9	33.8	757	244
2108	74	22	61.5	18.6	46.9	14.2	108.4	32.7	684	207
2109	75	22	57.1	16.8	59.1	17.4	116.2	34.3	875	258
2110	70	23	42.6	14.2	50.9	17.0	93.5	31.2	784	261
2111	90	26	52.6	14.9	52.5	14.9	105.1	29.9	753	214
2112	82	24	45.9	13.3	52.9	15.3	98.8	28.6	840	243
n	12	12	12	12	12	12	12	12	12	12
Mean	74	23	53.5	16.2	51.7	15.6	105.2	31.8	771	234
S.D.	9	2	7.3	2.4	7.0	2.2	7.8	2.7	99	35

AB : Absolute weight, RE : Relative weight by body weight

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weight

Stage : Lactation day 5

Sex : Female

Dose : benzyl salicylate 100 mg/kg

Species : Rat

	Body weight	Brain		Pituitary		Thyroid-R		Thyroid-L	
		AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	g	g	g/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g
3101	306	1.97	0.64	17.7	5.8	9.3	3.0	6.3	2.1
3102	335	2.01	0.60	17.3	5.2	9.0	2.7	7.1	2.1
3103	322	1.96	0.61	18.1	5.6	10.7	3.3	9.1	2.8
3104	342	1.91	0.56	15.2	4.4	10.9	3.2	9.0	2.6
3105	322	1.92	0.60	18.6	5.8	9.5	3.0	8.4	2.6
3106	359	2.07	0.58	18.4	5.1	14.2	4.0	8.7	2.4
3107	329	2.06	0.63	18.3	5.6	8.9	2.7	7.8	2.4
3108	342	2.06	0.60	18.4	5.4	8.8	2.6	7.4	2.2
3109	304	2.07	0.68	17.3	5.7	10.7	3.5	9.2	3.0
3110	319	1.95	0.61	24.7	7.7	8.5	2.7	5.0	1.6
3111	345	2.07	0.60	16.6	4.8	9.4	2.7	9.4	2.7
3112	378	2.07	0.55	22.7	6.0	12.2	3.2	8.4	2.2
n	12	12	12	12	12	12	12	12	12
Mean	334	2.01	0.61	18.6	5.6	10.2	3.1	8.0	2.4
S.D.	21	0.06	0.03	2.6	0.8	1.7	0.4	1.3	0.4

	Thyroid-RL		Thymus		Heart		Liver		Spleen	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	mg	mg/100g	g	g/100g	g	g/100g	g	g/100g
3101	15.6	5.1	156	51	1.05	0.34	9.85	3.22	0.60	0.20
3102	16.1	4.8	257	77	1.15	0.34	9.74	2.91	0.76	0.23
3103	19.8	6.1	202	63	1.04	0.32	10.33	3.21	0.66	0.20
3104	19.9	5.8	274	80	1.07	0.31	9.60	2.81	0.68	0.20
3105	17.9	5.6	260	81	1.03	0.32	11.05	3.43	0.91	0.28
3106	22.9	6.4	215	60	1.10	0.31	12.17	3.39	0.69	0.19
3107	16.7	5.1	259	79	1.00	0.30	10.78	3.28	0.65	0.20
3108	16.2	4.7	191	56	1.00	0.29	10.02	2.93	0.58	0.17
3109	19.9	6.5	166	55	0.97	0.32	10.01	3.29	0.59	0.19
3110	13.5	4.2	146	46	1.37	0.43	10.03	3.14	0.68	0.21
3111	18.8	5.4	204	59	1.12	0.32	10.89	3.16	0.72	0.21
3112	20.6	5.4	283	75	1.14	0.30	11.82	3.13	0.62	0.16
n	12	12	12	12	12	12	12	12	12	12
Mean	18.2	5.4	218	65	1.09	0.33	10.52	3.16	0.68	0.20
S.D.	2.6	0.7	48	13	0.11	0.04	0.83	0.19	0.09	0.03

AB : Absolute weight, RE : Relative weight by body weight

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weight

Stage : Lactation day 5

Sex : Female

Dose : benzyl salicylate 100 mg/kg

Species : Rat

	Kidney-R		Kidney-L		Kidney-RL		Adrenal-R		Adrenal-L	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	g	g/100g	g	g/100g	g	g/100g	mg	mg/100g	mg	mg/100g
3101	1.04	0.34	0.97	0.32	2.01	0.66	27	9	26	8
3102	1.12	0.33	1.12	0.33	2.24	0.67	30	9	27	8
3103	1.04	0.32	1.02	0.32	2.06	0.64	33	10	35	11
3104	0.97	0.28	0.94	0.27	1.91	0.56	30	9	27	8
3105	1.09	0.34	1.03	0.32	2.12	0.66	36	11	40	12
3106	1.17	0.33	1.19	0.33	2.36	0.66	35	10	33	9
3107	1.04	0.32	1.10	0.33	2.14	0.65	28	9	31	9
3108	0.98	0.29	0.97	0.28	1.95	0.57	34	10	39	11
3109	1.13	0.37	1.10	0.36	2.23	0.73	34	11	36	12
3110	1.20	0.38	1.13	0.35	2.33	0.73	29	9	32	10
3111	1.19	0.34	1.24	0.36	2.43	0.70	43	12	44	13
3112	1.12	0.30	1.13	0.30	2.25	0.60	42	11	49	13
n	12	12	12	12	12	12	12	12	12	12
Mean	1.09	0.33	1.08	0.32	2.17	0.65	33	10	35	10
S.D.	0.08	0.03	0.09	0.03	0.17	0.05	5	1	7	2

	Adrenal-RL		Ovary-R		Ovary-L		Ovary-RL		Uterus	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g
3101	53	17	54.6	17.8	39.0	12.7	93.6	30.6	728	238
3102	57	17	39.9	11.9	60.8	18.1	100.7	30.1	580	173
3103	68	21	50.9	15.8	49.2	15.3	100.1	31.1	743	231
3104	57	17	88.6	25.9	63.4	18.5	152.0	44.4	558	163
3105	76	24	50.5	15.7	50.5	15.7	101.0	31.4	655	203
3106	68	19	72.6	20.2	54.6	15.2	127.2	35.4	735	205
3107	59	18	41.8	12.7	68.2	20.7	110.0	33.4	615	187
3108	73	21	53.5	15.6	49.1	14.4	102.6	30.0	652	191
3109	70	23	51.3	16.9	53.1	17.5	104.4	34.3	591	194
3110	61	19	54.6	17.1	37.5	11.8	92.1	28.9	727	228
3111	87	25	64.9	18.8	51.8	15.0	116.7	33.8	715	207
3112	91	24	44.5	11.8	37.4	9.9	81.9	21.7	707	187
n	12	12	12	12	12	12	12	12	12	12
Mean	68	20	55.6	16.7	51.2	15.4	106.9	32.1	667	201
S.D.	12	3	13.8	3.9	9.9	3.0	18.4	5.2	67	23

AB : Absolute weight, RE : Relative weight by body weight

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weight

Stage : End of administration

Sex : Female

Dose : benzyl salicylate 0 mg/kg

Species : Rat

	Body weight	Brain		Pituitary		Thyroid-R		Thyroid-L	
		AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	g	g	g/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g
5101	302	1.80	0.60	18.6	6.2	8.0	2.6	8.1	2.7
5102	269	2.07	0.77	13.7	5.1	7.9	2.9	8.7	3.2
5103	283	1.95	0.69	14.1	5.0	5.4	1.9	5.6	2.0
5104	269	2.01	0.75	15.0	5.6	6.4	2.4	7.2	2.7
5105	300	1.84	0.61	20.0	6.7	7.8	2.6	4.1	1.4
n	5	5	5	5	5	5	5	5	5
Mean	285	1.93	0.68	16.3	5.7	7.1	2.5	6.7	2.4
S.D.	16	0.11	0.08	2.8	0.7	1.2	0.4	1.9	0.7

	Thyroid-RL		Thymus		Heart		Liver		Spleen	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	mg	mg/100g	g	g/100g	g	g/100g	g	g/100g
5101	16.1	5.3	194	64	0.93	0.31	7.06	2.34	0.55	0.18
5102	16.6	6.2	162	60	1.28	0.48	8.13	3.02	1.05	0.39
5103	11.0	3.9	262	93	0.84	0.30	6.71	2.37	0.49	0.17
5104	13.6	5.1	250	93	0.86	0.32	6.56	2.44	0.53	0.20
5105	11.9	4.0	332	111	0.93	0.31	7.72	2.57	0.42	0.14
n	5	5	5	5	5	5	5	5	5	5
Mean	13.8	4.9	240	84	0.97	0.34	7.24	2.55	0.61	0.22
S.D.	2.5	1.0	66	22	0.18	0.08	0.67	0.28	0.25	0.10

	Kidney-R		Kidney-L		Kidney-RL		Adrenal-R		Adrenal-L	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	g	g/100g	g	g/100g	g	g/100g	mg	mg/100g	mg	mg/100g
5101	0.88	0.29	0.94	0.31	1.82	0.60	24	8	26	9
5102	0.98	0.36	0.96	0.36	1.94	0.72	43	16	44	16
5103	0.94	0.33	0.97	0.34	1.91	0.67	28	10	28	10
5104	0.84	0.31	0.87	0.32	1.71	0.64	35	13	35	13
5105	1.00	0.33	0.97	0.32	1.97	0.66	29	10	34	11
n	5	5	5	5	5	5	5	5	5	5
Mean	0.93	0.32	0.94	0.33	1.87	0.66	32	11	33	12
S.D.	0.07	0.03	0.04	0.02	0.11	0.04	7	3	7	3

AB : Absolute weight, RE : Relative weight by body weight

Appendix 8 - 18 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Organ weight Stage : End of administration

Sex : Female Dose : benzyl salicylate 0 mg/kg Species : Rat

	Adrenal-RL		Ovary-R		Ovary-L		Ovary-RL		Uterus	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g
5101	50	17	41.4	13.7	41.7	13.8	83.1	27.5	501	166
5102	87	32	40.6	15.1	50.5	18.8	91.1	33.9	526	196
5103	56	20	35.2	12.4	32.4	11.4	67.6	23.9	388	137
5104	70	26	33.6	12.5	36.8	13.7	70.4	26.2	763	284
5105	63	21	37.4	12.5	38.1	12.7	75.5	25.2	611	204
n	5	5	5	5	5	5	5	5	5	5
Mean	65	23	37.6	13.2	39.9	14.1	77.5	27.3	558	197
S.D.	14	6	3.4	1.2	6.8	2.8	9.6	3.9	140	55

AB : Absolute weight, RE : Relative weight by body weight

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weight

Stage : End of administration

Sex : Female

Dose : benzyl salicylate 300 mg/kg

Species : Rat

	Body weight	Brain		Pituitary		Thyroid-R		Thyroid-L	
		AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	g	g	g/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g
6101	276	1.97	0.71	17.1	6.2	6.6	2.4	7.9	2.9
6102	300	2.01	0.67	18.3	6.1	10.0	3.3	10.4	3.5
6103	292	1.99	0.68	18.6	6.4	8.6	2.9	6.6	2.3
6104	284	1.91	0.67	15.9	5.6	8.1	2.9	5.6	2.0
6105	302	2.12	0.70	13.6	4.5	9.3	3.1	8.3	2.7
n	5	5	5	5	5	5	5	5	5
Mean	291	2.00	0.69	16.7	5.8	8.5	2.9	7.8	2.7
S.D.	11	0.08	0.02	2.0	0.8	1.3	0.3	1.8	0.6

	Thyroid-RL		Thymus		Heart		Liver		Spleen	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	mg	mg/100g	g	g/100g	g	g/100g	g	g/100g
6101	14.5	5.3	161	58	0.98	0.36	7.32	2.65	0.58	0.21
6102	20.4	6.8	204	68	0.96	0.32	8.11	2.70	0.57	0.19
6103	15.2	5.2	142	49	0.88	0.30	8.26	2.83	0.59	0.20
6104	13.7	4.8	211	74	0.97	0.34	7.46	2.63	0.53	0.19
6105	17.6	5.8	205	68	0.98	0.32	8.13	2.69	0.50	0.17
n	5	5	5	5	5	5	5	5	5	5
Mean	16.3	5.6	185	63	0.95	0.33	7.86	2.70	0.55	0.19
S.D.	2.7	0.8	31	10	0.04	0.02	0.43	0.08	0.04	0.01

	Kidney-R		Kidney-L		Kidney-RL		Adrenal-R		Adrenal-L	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	g	g/100g	g	g/100g	g	g/100g	mg	mg/100g	mg	mg/100g
6101	0.82	0.30	0.78	0.28	1.60	0.58	21	8	30	11
6102	1.01	0.34	1.02	0.34	2.03	0.68	26	9	27	9
6103	1.12	0.38	1.09	0.37	2.21	0.76	25	9	31	11
6104	1.05	0.37	1.02	0.36	2.07	0.73	31	11	29	10
6105	1.10	0.36	1.09	0.36	2.19	0.73	32	11	36	12
n	5	5	5	5	5	5	5	5	5	5
Mean	1.02	0.35	1.00	0.34	2.02	0.70	27	10	31	11
S.D.	0.12	0.03	0.13	0.04	0.25	0.07	5	1	3	1

AB : Absolute weight, RE : Relative weight by body weight

Appendix 8 - 20 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Organ weight Stage : End of administration

Sex : Female Dose : benzyl salicylate 300 mg/kg Species : Rat

	Adrenal-RL		Ovary-R		Ovary-L		Ovary-RL		Uterus	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g
6101	51	18	31.5	11.4	42.9	15.5	74.4	27.0	526	191
6102	53	18	32.8	10.9	33.8	11.3	66.6	22.2	704	235
6103	56	19	35.4	12.1	32.7	11.2	68.1	23.3	607	208
6104	60	21	31.9	11.2	32.4	11.4	64.3	22.6	582	205
6105	68	23	42.4	14.0	42.0	13.9	84.4	27.9	385	127
n	5	5	5	5	5	5	5	5	5	5
Mean	58	20	34.8	11.9	36.8	12.7	71.6	24.6	561	193
S.D.	7	2	4.5	1.2	5.2	1.9	8.1	2.7	117	40

AB : Absolute weight, RE : Relative weight by body weight

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weight

Stage : End of recovery

Sex : Male

Dose : benzyl salicylate 0 mg/kg

Species : Rat

	Body weight	Brain		Pituitary		Thyroid-R		Thyroid-L	
		AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	g	g	g/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g
1008	508	2.26	0.44	11.7	2.3	15.2	3.0	12.0	2.4
1009	543	2.09	0.38	12.9	2.4	9.2	1.7	8.9	1.6
1010	594	2.14	0.36	11.3	1.9	14.2	2.4	14.3	2.4
1011	500	2.14	0.43	12.5	2.5	11.6	2.3	11.5	2.3
1012	481	2.18	0.45	13.2	2.7	11.2	2.3	10.0	2.1
n	5	5	5	5	5	5	5	5	5
Mean	525	2.16	0.41	12.3	2.4	12.3	2.3	11.3	2.2
S.D.	45	0.06	0.04	0.8	0.3	2.4	0.5	2.1	0.3

	Thyroid-RL		Thymus		Heart		Liver		Spleen	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	mg	mg/100g	g	g/100g	g	g/100g	g	g/100g
1008	27.2	5.4	272	54	1.46	0.29	11.68	2.30	0.56	0.11
1009	18.1	3.3	307	57	1.37	0.25	13.49	2.48	0.63	0.12
1010	28.5	4.8	347	58	1.41	0.24	16.85	2.84	0.73	0.12
1011	23.1	4.6	307	61	1.45	0.29	11.75	2.35	0.59	0.12
1012	21.2	4.4	345	72	1.39	0.29	10.33	2.15	0.67	0.14
n	5	5	5	5	5	5	5	5	5	5
Mean	23.6	4.5	316	60	1.42	0.27	12.82	2.42	0.64	0.12
S.D.	4.3	0.8	31	7	0.04	0.02	2.52	0.26	0.07	0.01

	Kidney-R		Kidney-L		Kidney-RL		Adrenal-R		Adrenal-L	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	g	g/100g	g	g/100g	g	g/100g	mg	mg/100g	mg	mg/100g
1008	1.59	0.31	1.71	0.34	3.30	0.65	27	5	31	6
1009	1.52	0.28	1.74	0.32	3.26	0.60	36	7	38	7
1010	1.79	0.30	1.82	0.31	3.61	0.61	24	4	27	5
1011	1.59	0.32	1.75	0.35	3.34	0.67	34	7	33	7
1012	1.39	0.29	1.49	0.31	2.88	0.60	32	7	33	7
n	5	5	5	5	5	5	5	5	5	5
Mean	1.58	0.30	1.70	0.33	3.28	0.63	31	6	32	6
S.D.	0.14	0.02	0.13	0.02	0.26	0.03	5	1	4	1

AB : Absolute weight, RE : Relative weight by body weight

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weight

Stage : End of recovery

Sex : Male

Dose : benzyl salicylate 0 mg/kg

Species : Rat

	Adrenal-RL		Testis-R		Testis-L		Testis-RL		Epididymis-R	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	g	g/100g	g	g/100g	g	g/100g	mg	mg/100g
1008	58	11	1.70	0.33	1.72	0.34	3.42	0.67	668	131
1009	74	14	1.57	0.29	1.55	0.29	3.12	0.57	559	103
1010	51	9	1.67	0.28	1.57	0.26	3.24	0.55	655	110
1011	67	13	1.78	0.36	1.72	0.34	3.50	0.70	672	134
1012	65	14	1.49	0.31	1.45	0.30	2.94	0.61	566	118
n	5	5	5	5	5	5	5	5	5	5
Mean	63	12	1.64	0.31	1.60	0.31	3.24	0.62	624	119
S.D.	9	2	0.11	0.03	0.12	0.03	0.23	0.06	57	13

	Epididymis-L		Epididymis-RL		Prostate		Seminal vesicle	
	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	mg	mg/100g	g	g/100g	g	g/100g
1008	656	129	1324	261	1.15	0.23	1.80	0.35
1009	557	103	1116	206	1.34	0.25	1.54	0.28
1010	609	103	1264	213	1.28	0.22	1.73	0.29
1011	621	124	1293	259	1.08	0.22	1.79	0.36
1012	543	113	1109	231	1.10	0.23	1.69	0.35
n	5	5	5	5	5	5	5	5
Mean	597	114	1221	234	1.19	0.23	1.71	0.33
S.D.	47	12	102	25	0.11	0.01	0.11	0.04

AB : Absolute weight, RE : Relative weight by body weight

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weight

Stage : End of recovery

Sex : Male

Dose : benzyl salicylate 300 mg/kg

Species : Rat

Animal No.	Body weight g	Brain AB g	Brain RE g/100g	Pituitary AB mg	Pituitary RE mg/100g	Thyroid-R AB mg	Thyroid-R RE mg/100g	Thyroid-L AB mg	Thyroid-L RE mg/100g
4008	522	2.09	0.40	11.9	2.3	15.9	3.0	11.0	2.1
4009	500	2.08	0.42	12.6	2.5	12.3	2.5	11.1	2.2
4010	497	2.20	0.44	13.6	2.7	11.1	2.2	11.2	2.3
4011	485	2.21	0.46	11.5	2.4	8.4	1.7	9.2	1.9
4012	515	2.05	0.40	14.2	2.8	12.1	2.3	14.3	2.8
n	5	5	5	5	5	5	5	5	5
Mean	504	2.13	0.42	12.8	2.5	12.0	2.3	11.4	2.3
S.D.	15	0.07	0.03	1.1	0.2	2.7	0.5	1.8	0.3

Animal No.	Thyroid-RL AB mg	Thyroid-RL RE mg/100g	Thymus AB mg	Thymus RE mg/100g	Heart AB g	Heart RE g/100g	Liver AB g	Liver RE g/100g	Spleen AB g	Spleen RE g/100g
4008	26.9	5.2	343	66	1.40	0.27	12.22	2.34	0.86	0.16
4009	23.4	4.7	383	77	1.70	0.34	13.04	2.61	0.62	0.12
4010	22.3	4.5	273	55	1.70	0.34	11.59	2.33	0.57	0.11
4011	17.6	3.6	331	68	1.33	0.27	12.22	2.52	0.86	0.18
4012	26.4	5.1	366	71	1.52	0.30	13.16	2.56	0.76	0.15
n	5	5	5	5	5	5	5	5	5	5
Mean	23.3	4.6	339	67	1.53	0.30	12.45	2.47	0.73	0.14
S.D.	3.7	0.6	42	8	0.17	0.04	0.65	0.13	0.13	0.03

Animal No.	Kidney-R AB g	Kidney-R RE g/100g	Kidney-L AB g	Kidney-L RE g/100g	Kidney-RL AB g	Kidney-RL RE g/100g	Adrenal-R AB mg	Adrenal-R RE mg/100g	Adrenal-L AB mg	Adrenal-L RE mg/100g
4008	1.68	0.32	1.81	0.35	3.49	0.67	28	5	29	6
4009	1.55	0.31	1.87	0.37	3.42	0.68	24	5	31	6
4010	1.53	0.31	1.58	0.32	3.11	0.63	25	5	26	5
4011	1.72	0.35	1.80	0.37	3.52	0.73	30	6	35	7
4012	1.67	0.32	1.89	0.37	3.56	0.69	26	5	29	6
n	5	5	5	5	5	5	5	5	5	5
Mean	1.63	0.32	1.79	0.36	3.42	0.68	27	5	30	6
S.D.	0.08	0.02	0.12	0.02	0.18	0.04	2	0	3	1

AB : Absolute weight, RE : Relative weight by body weight

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weight

Stage : End of recovery

Sex : Male

Dose : benzyl salicylate 300 mg/kg

Species : Rat

	Adrenal-RL		Testis-R		Testis-L		Testis-RL		Epididymis-R	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	g	g/100g	g	g/100g	g	g/100g	mg	mg/100g
4008	57	11	1.56	0.30	1.51	0.29	3.07	0.59	641	123
4009	55	11	1.51	0.30	1.47	0.29	2.98	0.60	619	124
4010	51	10	1.53	0.31	1.52	0.31	3.05	0.61	632	127
4011	65	13	1.67	0.34	1.68	0.35	3.35	0.69	672	139
4012	55	11	1.59	0.31	1.58	0.31	3.17	0.62	645	125
n	5	5	5	5	5	5	5	5	5	5
Mean	57	11	1.57	0.31	1.55	0.31	3.12	0.62	642	128
S.D.	5	1	0.06	0.02	0.08	0.02	0.14	0.04	20	7

	Epididymis-L		Epididymis-RL		Prostate		Seminal vesicle	
	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	mg	mg/100g	g	g/100g	g	g/100g
4008	587	112	1228	235	1.36	0.26	1.97	0.38
4009	611	122	1230	246	1.16	0.23	1.61	0.32
4010	624	126	1256	253	1.50	0.30	2.20	0.44
4011	687	142	1359	280	1.67	0.34	2.01	0.41
4012	625	121	1270	247	1.34	0.26	2.46	0.48
n	5	5	5	5	5	5	5	5
Mean	627	125	1269	252	1.41	0.28	2.05	0.41
S.D.	37	11	54	17	0.19	0.04	0.31	0.06

AB : Absolute weight, RE : Relative weight by body weight

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weight

Stage : End of recovery

Sex : Female

Dose : benzyl salicylate 0 mg/kg

Species : Rat

Animal No.	Body weight g	Brain AB g	Brain RE g/100g	Pituitary AB mg	Pituitary RE mg/100g	Thyroid-R AB mg	Thyroid-R RE mg/100g	Thyroid-L AB mg	Thyroid-L RE mg/100g
5106	298	1.96	0.66	16.5	5.5	7.7	2.6	7.9	2.7
5107	283	2.00	0.71	16.2	5.7	9.3	3.3	7.4	2.6
5108	304	1.99	0.65	14.7	4.8	7.6	2.5	6.0	2.0
5109	314	2.04	0.65	15.5	4.9	7.6	2.4	7.8	2.5
5110	325	1.99	0.61	15.4	4.7	7.8	2.4	8.6	2.6
n	5	5	5	5	5	5	5	5	5
Mean	305	2.00	0.66	15.7	5.1	8.0	2.6	7.5	2.5
S.D.	16	0.03	0.04	0.7	0.4	0.7	0.4	1.0	0.3

Animal No.	Thyroid-RL AB mg	Thyroid-RL RE mg/100g	Thymus AB mg	Thymus RE mg/100g	Heart AB g	Heart RE g/100g	Liver AB g	Liver RE g/100g	Spleen AB g	Spleen RE g/100g
5106	15.6	5.2	311	104	1.01	0.34	7.83	2.63	0.56	0.19
5107	16.7	5.9	245	87	0.96	0.34	6.52	2.30	0.43	0.15
5108	13.6	4.5	215	71	1.26	0.41	7.18	2.36	0.43	0.14
5109	15.4	4.9	374	119	1.01	0.32	8.39	2.67	0.54	0.17
5110	16.4	5.0	242	74	0.95	0.29	7.46	2.30	0.47	0.14
n	5	5	5	5	5	5	5	5	5	5
Mean	15.5	5.1	277	91	1.04	0.34	7.48	2.45	0.49	0.16
S.D.	1.2	0.5	65	20	0.13	0.04	0.70	0.18	0.06	0.02

Animal No.	Kidney-R AB g	Kidney-R RE g/100g	Kidney-L AB g	Kidney-L RE g/100g	Kidney-RL AB g	Kidney-RL RE g/100g	Adrenal-R AB mg	Adrenal-R RE mg/100g	Adrenal-L AB mg	Adrenal-L RE mg/100g
5106	1.16	0.39	1.08	0.36	2.24	0.75	38	13	38	13
5107	0.84	0.30	0.92	0.33	1.76	0.62	25	9	28	10
5108	0.92	0.30	0.94	0.31	1.86	0.61	37	12	40	13
5109	1.07	0.34	1.09	0.35	2.16	0.69	28	9	32	10
5110	1.01	0.31	1.07	0.33	2.08	0.64	34	10	37	11
n	5	5	5	5	5	5	5	5	5	5
Mean	1.00	0.33	1.02	0.34	2.02	0.66	32	11	35	11
S.D.	0.13	0.04	0.08	0.02	0.20	0.06	6	2	5	2

AB : Absolute weight, RE : Relative weight by body weight

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weight

Stage : End of recovery

Sex : Female

Dose : benzyl salicylate 0 mg/kg

Species : Rat

	Adrenal-RL		Ovary-R		Ovary-L		Ovary-RL		Uterus	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g
5106	76	26	38.4	12.9	33.6	11.3	72.0	24.2	573	192
5107	53	19	46.4	16.4	37.0	13.1	83.4	29.5	692	245
5108	77	25	37.1	12.2	43.0	14.1	80.1	26.3	650	214
5109	60	19	38.7	12.3	44.9	14.3	83.6	26.6	523	167
5110	71	22	66.4	20.4	57.8	17.8	124.2	38.2	490	151
n	5	5	5	5	5	5	5	5	5	5
Mean	67	22	45.4	14.8	43.3	14.1	88.7	29.0	586	194
S.D.	11	3	12.3	3.6	9.3	2.4	20.4	5.5	85	37

AB : Absolute weight, RE : Relative weight by body weight

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weight

Stage : End of recovery

Sex : Female

Dose : benzyl salicylate 300 mg/kg

Species : Rat

	Body weight	Brain		Pituitary		Thyroid-R		Thyroid-L	
		AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	g	g	g/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g
6106	304	1.90	0.63	16.3	5.4	8.5	2.8	7.7	2.5
6107	276	1.84	0.67	16.3	5.9	7.7	2.8	6.4	2.3
6108	254	1.95	0.77	16.7	6.6	8.0	3.1	7.6	3.0
6109	294	2.00	0.68	14.6	5.0	5.6	1.9	7.4	2.5
6110	268	1.90	0.71	16.9	6.3	6.8	2.5	6.9	2.6
n	5	5	5	5	5	5	5	5	5
Mean	279	1.92	0.69	16.2	5.8	7.3	2.6	7.2	2.6
S.D.	20	0.06	0.05	0.9	0.7	1.1	0.5	0.5	0.3

	Thyroid-RL		Thymus		Heart		Liver		Spleen	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	mg	mg/100g	g	g/100g	g	g/100g	g	g/100g
6106	16.2	5.3	292	96	0.89	0.29	7.31	2.40	0.54	0.18
6107	14.1	5.1	254	92	1.05	0.38	7.49	2.71	0.53	0.19
6108	15.6	6.1	151	59	0.93	0.37	6.81	2.68	0.42	0.17
6109	13.0	4.4	343	117	0.89	0.30	6.67	2.27	0.48	0.16
6110	13.7	5.1	333	124	0.84	0.31	7.04	2.63	0.50	0.19
n	5	5	5	5	5	5	5	5	5	5
Mean	14.5	5.2	275	98	0.92	0.33	7.06	2.54	0.49	0.18
S.D.	1.3	0.6	78	25	0.08	0.04	0.34	0.19	0.05	0.01

	Kidney-R		Kidney-L		Kidney-RL		Adrenal-R		Adrenal-L	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	g	g/100g	g	g/100g	g	g/100g	mg	mg/100g	mg	mg/100g
6106	1.08	0.36	1.12	0.37	2.20	0.72	25	8	30	10
6107	1.09	0.39	1.08	0.39	2.17	0.79	29	11	31	11
6108	0.95	0.37	0.98	0.39	1.93	0.76	35	14	36	14
6109	0.91	0.31	0.91	0.31	1.82	0.62	34	12	34	12
6110	0.86	0.32	0.87	0.32	1.73	0.65	37	14	36	13
n	5	5	5	5	5	5	5	5	5	5
Mean	0.98	0.35	0.99	0.36	1.97	0.71	32	12	33	12
S.D.	0.10	0.03	0.11	0.04	0.21	0.07	5	2	3	2

AB : Absolute weight, RE : Relative weight by body weight

Appendix 8 - 28 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Organ weight Stage : End of recovery

Sex : Female Dose : benzyl salicylate 300 mg/kg Species : Rat

	Adrenal-RL		Ovary-R		Ovary-L		Ovary-RL		Uterus	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g
6106	55	18	36.7	12.1	38.6	12.7	75.3	24.8	451	148
6107	60	22	38.3	13.9	40.3	14.6	78.6	28.5	543	197
6108	71	28	35.1	13.8	36.7	14.4	71.8	28.3	659	259
6109	68	23	43.9	14.9	39.9	13.6	83.8	28.5	459	156
6110	73	27	39.6	14.8	37.5	14.0	77.1	28.8	711	265
n	5	5	5	5	5	5	5	5	5	5
Mean	65	24	38.7	13.9	38.6	13.9	77.3	27.8	565	205
S.D.	8	4	3.4	1.1	1.5	0.8	4.4	1.7	117	55

AB : Absolute weight, RE : Relative weight by body weight

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weight

Stage : All littermates died

Sex : Female

Dose : benzyl salicylate 300 mg/kg

Species : Rat

	Body weight	Brain		Pituitary		Thyroid-R		Thyroid-L	
		AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	g	g	g/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g
4102	356	1.96	0.55	16.1	4.5	12.5	3.5	10.0	2.8
4105	320	1.87	0.58	14.9	4.7	8.1	2.5	8.5	2.7
4106	348	1.89	0.54	15.2	4.4	7.1	2.0	8.9	2.6
4107	337	1.92	0.57	17.9	5.3	10.5	3.1	11.3	3.4
4109	337	2.03	0.60	17.4	5.2	11.8	3.5	9.4	2.8
4110	319	1.88	0.59	13.3	4.2	10.4	3.3	9.0	2.8
n	6	6	6	6	6	6	6	6	6
Mean	336	1.93	0.57	15.8	4.7	10.1	3.0	9.5	2.9
S.D.	15	0.06	0.02	1.7	0.4	2.1	0.6	1.0	0.3

	Thyroid-RL		Thymus		Heart		Liver		Spleen	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	mg	mg/100g	g	g/100g	g	g/100g	g	g/100g
4102	22.5	6.3	145	41	1.02	0.29	15.46	4.34	0.78	0.22
4105	16.6	5.2	122	38	1.01	0.32	14.95	4.67	0.71	0.22
4106	16.0	4.6	172	49	1.03	0.30	14.21	4.08	0.66	0.19
4107	21.8	6.5	273	81	1.20	0.36	17.19	5.10	0.86	0.26
4109	21.2	6.3	220	65	1.07	0.32	14.33	4.25	0.92	0.27
4110	19.4	6.1	174	55	1.00	0.31	13.44	4.21	0.73	0.23
n	6	6	6	6	6	6	6	6	6	6
Mean	19.6	5.8	184	55	1.06	0.32	14.93	4.44	0.78	0.23
S.D.	2.7	0.8	54	16	0.08	0.02	1.30	0.38	0.10	0.03

	Kidney-R		Kidney-L		Kidney-RL		Adrenal-R		Adrenal-L	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	g	g/100g	g	g/100g	g	g/100g	mg	mg/100g	mg	mg/100g
4102	1.18	0.33	1.14	0.32	2.32	0.65	33	9	34	10
4105	1.23	0.38	1.20	0.38	2.43	0.76	36	11	39	12
4106	1.03	0.30	1.01	0.29	2.04	0.59	26	7	26	7
4107	1.16	0.34	1.27	0.38	2.43	0.72	37	11	39	12
4109	1.12	0.33	1.13	0.34	2.25	0.67	35	10	37	11
4110	1.02	0.32	1.03	0.32	2.05	0.64	28	9	34	11
n	6	6	6	6	6	6	6	6	6	6
Mean	1.12	0.33	1.13	0.34	2.25	0.67	33	10	35	11
S.D.	0.08	0.03	0.10	0.04	0.18	0.06	5	2	5	2

AB : Absolute weight, RE : Relative weight by body weight

Appendix 8 - 30 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Organ weight Stage : All littermates died

Sex : Female Dose : benzyl salicylate 300 mg/kg Species : Rat

	Adrenal-RL		Ovary-R		Ovary-L		Ovary-RL		Uterus	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g
4102	67	19	57.2	16.1	58.5	16.4	115.7	32.5	1897	533
4105	75	23	69.6	21.8	71.6	22.4	141.2	44.1	2844	889
4106	52	15	61.0	17.5	54.1	15.5	115.1	33.1	1774	510
4107	76	23	43.1	12.8	44.1	13.1	87.2	25.9	3004	891
4109	72	21	54.9	16.3	46.9	13.9	101.8	30.2	2416	717
4110	62	19	39.0	12.2	53.7	16.8	92.7	29.1	1762	552
n	6	6	6	6	6	6	6	6	6	6
Mean	67	20	54.1	16.1	54.8	16.4	109.0	32.5	2283	682
S.D.	9	3	11.4	3.5	9.7	3.3	19.6	6.3	553	177

AB : Absolute weight, RE : Relative weight by body weight

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weight

Stage : Undelivered

Sex : Female

Dose : benzyl salicylate 300 mg/kg

Species : Rat

	Body weight	Brain		Pituitary		Thyroid-R		Thyroid-L	
		AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	g	g	g/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g
4101	321	1.95	0.61	18.2	5.7	8.2	2.6	6.3	2.0
4103	350	1.91	0.55	15.8	4.5	7.7	2.2	9.7	2.8
4104	317	2.04	0.64	12.1	3.8	10.8	3.4	7.8	2.5
4108	368	1.93	0.52	16.0	4.3	5.6	1.5	10.8	2.9
4111	366	2.11	0.58	17.4	4.8	11.1	3.0	10.6	2.9
4112	324	1.89	0.58	15.2	4.7	8.8	2.7	11.7	3.6
n	6	6	6	6	6	6	6	6	6
Mean	341	1.97	0.58	15.8	4.6	8.7	2.6	9.5	2.8
S.D.	23	0.09	0.04	2.1	0.6	2.1	0.7	2.0	0.5

	Thyroid-RL		Thymus		Heart		Liver		Spleen	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	mg	mg/100g	g	g/100g	g	g/100g	g	g/100g
4101	14.5	4.5	127	40	1.11	0.35	12.92	4.02	0.53	0.17
4103	17.4	5.0	214	61	1.09	0.31	14.44	4.13	0.89	0.25
4104	18.6	5.9	193	61	1.10	0.35	10.71	3.38	0.62	0.20
4108	16.4	4.5	138	38	1.13	0.31	15.12	4.11	0.71	0.19
4111	21.7	5.9	200	55	1.09	0.30	13.32	3.64	0.74	0.20
4112	20.5	6.3	214	66	1.06	0.33	13.03	4.02	0.51	0.16
n	6	6	6	6	6	6	6	6	6	6
Mean	18.2	5.4	181	54	1.10	0.33	13.26	3.88	0.67	0.20
S.D.	2.7	0.8	39	12	0.02	0.02	1.52	0.30	0.14	0.03

	Kidney-R		Kidney-L		Kidney-RL		Adrenal-R		Adrenal-L	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	g	g/100g	g	g/100g	g	g/100g	mg	mg/100g	mg	mg/100g
4101	1.08	0.34	1.08	0.34	2.16	0.67	29	9	30	9
4103	1.21	0.35	1.21	0.35	2.42	0.69	21	6	34	10
4104	1.06	0.33	1.08	0.34	2.14	0.68	33	10	36	11
4108	1.09	0.30	1.12	0.30	2.21	0.60	34	9	35	10
4111	1.27	0.35	1.38	0.38	2.65	0.72	38	10	42	11
4112	1.09	0.34	1.06	0.33	2.15	0.66	28	9	31	10
n	6	6	6	6	6	6	6	6	6	6
Mean	1.13	0.34	1.16	0.34	2.29	0.67	31	9	35	10
S.D.	0.09	0.02	0.12	0.03	0.21	0.04	6	1	4	1

AB : Absolute weight, RE : Relative weight by body weight

Appendix 8 - 32 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Organ weight Stage : Undelivered

Sex : Female Dose : benzyl salicylate 300 mg/kg Species : Rat

	Adrenal-RL		Ovary-R		Ovary-L		Ovary-RL		Uterus	
	AB	RE	AB	RE	AB	RE	AB	RE	AB	RE
Animal No.	mg	mg/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g	mg	mg/100g
4101	59	18	44.7	13.9	27.2	8.5	71.9	22.4	1039	324
4103	55	16	40.1	11.5	39.3	11.2	79.4	22.7	1691	483
4104	69	22	30.8	9.7	30.8	9.7	61.6	19.4	1158	365
4108	69	19	66.6	18.1	50.1	13.6	116.7	31.7	1068	290
4111	80	22	38.2	10.4	51.5	14.1	89.7	24.5	801	219
4112	59	18	56.7	17.5	56.7	17.5	113.4	35.0	982	303
n	6	6	6	6	6	6	6	6	6	6
Mean	65	19	46.2	13.5	42.6	12.4	88.8	26.0	1123	331
S.D.	9	2	13.2	3.6	12.0	3.3	22.4	6.1	302	89

AB : Absolute weight, RE : Relative weight by body weight

Appendix 9-1(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 1001 Male 0 mg/kg Day 43 End of administration

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Parathyroid, Pancreas, Pituitary, Prostate
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral
Seminal vesicle(coagulating gland), Spinal cord,thoracic, Testis, Thymus, Trachea
Thyroid, Urinary bladder

Appendix 9-2(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 1002 Male 0 mg/kg Day 43 End of administration

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Parathyroid, Pancreas, Pituitary, Prostate
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral
Seminal vesicle(coagulating gland), Spinal cord,thoracic, Testis, Thymus, Trachea
Thyroid, Urinary bladder

Appendix 9-3(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 1003 Male 0 mg/kg Day 43 End of administration

Gross pathology:

All tissues	Not remarkable

Histopathology:

Heart	Cell infiltration,focal: minimal
Kidney	Basophilia,tubular: minimal
Prostate	Cell infiltration: minimal, lymphocytic ventral

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Mammary gland,inguinal
Optic nerve, Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular
Salivary gland,sublingual, Skin,inguinal, Sciatic nerve, Spleen, Stomach
Skeletal muscle,femoral, Seminal vesicle(coagulating gland), Spinal cord,thoracic
Testis, Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-4(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 1004 Male 0 mg/kg Day 43 End of administration

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Necrosis,focal: minimal
Testis	Atrophy,seminiferous tubular: minimal, focal, unilateral

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Parathyroid, Pancreas, Pituitary, Prostate
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral
Seminal vesicle(coagulating gland), Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder

Appendix 9-5(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 1005 Male 0 mg/kg Day 43 End of administration

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Prostate	Cell infiltration: mild, lymphocytic ventral

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral
Seminal vesicle(coagulating gland), Spinal cord,thoracic, Testis, Thymus, Trachea
Thyroid, Urinary bladder

Appendix 9-6(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 1006 Male 0 mg/kg Day 43 End of administration

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-7(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 1007 Male 0 mg/kg Day 43 End of administration

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-8(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 1008 Male 0 mg/kg Day 57 End of recovery

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Parathyroid, Pancreas, Pituitary, Prostate
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral
Seminal vesicle(coagulating gland), Spinal cord,thoracic, Testis, Thymus, Trachea
Thyroid, Urinary bladder

Appendix 9-9(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 1009 Male 0 mg/kg Day 57 End of recovery

Gross pathology:

All tissues	Not remarkable

Histopathology:

Prostate	Cell infiltration: minimal, lymphocytic ventral

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral
Seminal vesicle(coagulating gland), Spinal cord,thoracic, Testis, Thymus, Trachea
Thyroid, Urinary bladder

Appendix 9-10(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 1010 Male 0 mg/kg Day 57 End of recovery

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Parathyroid, Pancreas, Pituitary, Prostate
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral
Seminal vesicle(coagulating gland), Spinal cord,thoracic, Testis, Thymus, Trachea
Thyroid, Urinary bladder

Appendix 9-11(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 1011 Male 0 mg/kg Day 57 End of recovery

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Parathyroid, Pancreas, Pituitary, Prostate
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral
Seminal vesicle(coagulating gland), Spinal cord,thoracic, Testis, Thymus, Trachea
Thyroid, Urinary bladder

Appendix 9-12(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 1012 Male 0 mg/kg Day 57 End of recovery

Gross pathology:

All tissues	Not remarkable

Histopathology:

Epididymis	Hypospermia: mild, bilateral
Prostate	Cell infiltration: minimal, lymphocytic ventral
Testis	Atrophy,seminiferous tubular: moderate, bilateral Granuloma,spermatic: mild, bilateral

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral
Seminal vesicle(coagulating gland), Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder

Appendix 9-13(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 2001 Male 30 mg/kg Day 43 End of administration

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Pituitary, Thyroid

Appendix 9-14(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 2002 Male 30 mg/kg Day 43 End of administration

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Pituitary, Thyroid

Appendix 9-15(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 2003 Male 30 mg/kg Day 43 End of administration

Gross pathology:

All tissues	Not remarkable

Histopathology:

Pituitary	Cyst,pars distalis: minimal

Following tissues : Not remarkable

Thyroid

Appendix 9-16(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 2004 Male 30 mg/kg Day 43 End of administration

Gross pathology:

Stomach	Focus,dark red,glandular stomach: 1 present 1x1 mm
Other tissues	Not remarkable

Histopathology:

Following tissues : Not remarkable

Pituitary, Thyroid

Appendix 9-17(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 2005 Male 30 mg/kg Day 43 End of administration

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Pituitary, Thyroid

Appendix 9-18(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 2006 Male 30 mg/kg Day 43 End of administration

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-19(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 2007 Male 30 mg/kg Day 43 End of administration

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-20(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 2008 Male 30 mg/kg Day 43 End of administration

Gross pathology:

Lung(bronchus)	Focus,dark red: 1 present 1x1 mm
Other tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-21(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 2009 Male 30 mg/kg Day 43 End of administration

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-22(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 2010 Male 30 mg/kg Day 43 End of administration

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-23(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 2011 Male 30 mg/kg Day 43 End of administration

Gross pathology:

Stomach	Focus,dark red,glandular stomach: 1 present 2x1 mm
Other tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-24(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 2012 Male 30 mg/kg Day 43 End of administration

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-25(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 3001 Male 100 mg/kg Day 43 End of administration

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Bone+Bone marrow,femoral, Pituitary, Thymus, Thyroid

Appendix 9-26(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 3002 Male 100 mg/kg Day 43 End of administration

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Bone+Bone marrow,femoral, Pituitary, Thymus, Thyroid

Appendix 9-27(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 3003 Male 100 mg/kg Day 43 End of administration

Gross pathology:

Stomach	Focus,dark red,glandular stomach: 1 present 2x1 mm
Other tissues	Not remarkable

Histopathology:

Following tissues : Not remarkable

Bone+Bone marrow,femoral, Pituitary, Thymus, Thyroid

Appendix 9-28(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 3004 Male 100 mg/kg Day 43 End of administration

Gross pathology:

Liver	Hepatodiaphragmatic nodule: 1 present 8x8x4 mm
Other tissues	Not remarkable

Histopathology:

Following tissues : Not remarkable

Bone+Bone marrow,femoral, Pituitary, Thymus, Thyroid

Appendix 9-29(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 3005 Male 100 mg/kg Day 43 End of administration

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Bone+Bone marrow,femoral, Pituitary, Thymus, Thyroid

Appendix 9-30(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 3006 Male 100 mg/kg Day 43 End of administration

Gross pathology:

Lung(bronchus)	Focus,dark red: 1 present 2x2 mm
Other tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-31(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 3007 Male 100 mg/kg Day 43 End of administration

Gross pathology:

Epididymis	Focus,yellow: 1 present, left caudal, 8x5 mm
Other tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-32(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 3008 Male 100 mg/kg Day 43 End of administration

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-33(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 3009 Male 100 mg/kg Day 43 End of administration

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-34(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 3010 Male 100 mg/kg Day 43 End of administration

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-35(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 3011 Male 100 mg/kg Day 43 End of administration

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-36(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 3012 Male 100 mg/kg Day 43 End of administration

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-37(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 4001 Male 300 mg/kg Day 43 End of administration

Gross pathology:

All tissues	Not remarkable

Histopathology:

Bone+Bone marrow,femoral	Increased trabecular bone: minimal
Parathyroid	No sample

Following tissues : Not remarkable

Adrenal, Cerebellum(pons), Cerebrum, Epididymis, Eye, Heart, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Mammary gland,inguinal
Optic nerve, Pancreas, Pituitary, Prostate, Salivary gland,submandibular
Salivary gland,sublingual, Skin,inguinal, Sciatic nerve, Spleen, Stomach
Skeletal muscle,femoral, Seminal vesicle(coagulating gland), Spinal cord,thoracic
Testis, Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-38(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 4002 Male 300 mg/kg Day 43 End of administration

Gross pathology:

All tissues	Not remarkable

Histopathology:

Bone+Bone marrow,femoral	Increased trabecular bone: minimal
Heart	Cell infiltration,focal: minimal

Following tissues : Not remarkable

Adrenal, Cerebellum(pons), Cerebrum, Epididymis, Eye, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Mammary gland,inguinal
Optic nerve, Parathyroid, Pancreas, Pituitary, Prostate
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral
Seminal vesicle(coagulating gland), Spinal cord,thoracic, Testis, Thymus, Trachea
Thyroid, Urinary bladder

Appendix 9-39(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 4003 Male 300 mg/kg Day 43 End of administration

Gross pathology:

Lung(bronchus)	Focus,dark red: 1 present 1x1 mm
Other tissues	Not remarkable

Histopathology:

Bone+Bone marrow,femoral	Increased trabecular bone: minimal
Heart	Cell infiltration,focal: minimal
Lung(bronchus)	Hemorrhage,focal: minimal
Thymus	Atrophy: minimal

Following tissues : Not remarkable

Adrenal, Cerebellum(pons), Cerebrum, Epididymis, Eye, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Liver, Mammary gland,inguinal, Optic nerve
Parathyroid, Pancreas, Pituitary, Prostate, Salivary gland,submandibular
Salivary gland,sublingual, Skin,inguinal, Sciatic nerve, Spleen, Stomach
Skeletal muscle,femoral, Seminal vesicle(coagulating gland), Spinal cord,thoracic
Testis, Trachea, Thyroid, Urinary bladder

Appendix 9-40(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 4004 Male 300 mg/kg Day 43 End of administration

Gross pathology:

All tissues	Not remarkable

Histopathology:

Bone+Bone marrow,femoral	Increased trabecular bone: minimal
Prostate	Cell infiltration: minimal, lymphocytic ventral
Testis	Atrophy,seminiferous tubular: minimal, focal, unilateral

Following tissues : Not remarkable

Adrenal, Cerebellum(pons), Cerebrum, Epididymis, Eye, Heart, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Mammary gland,inguinal
Optic nerve, Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular
Salivary gland,sublingual, Skin,inguinal, Sciatic nerve, Spleen, Stomach
Skeletal muscle,femoral, Seminal vesicle(coagulating gland), Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-41(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 4005 Male 300 mg/kg Day 43 End of administration

Gross pathology:

All tissues	Not remarkable

Histopathology:

Bone+Bone marrow,femoral	Increased trabecular bone: minimal
Heart	Cell infiltration,focal: minimal
Kidney	Basophilia,tubular: minimal
Pituitary	Cyst,pars distalis: minimal

Following tissues : Not remarkable

Adrenal, Cerebellum(pons), Cerebrum, Epididymis, Eye, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Mammary gland,inguinal
Optic nerve, Parathyroid, Pancreas, Prostate, Salivary gland,submandibular
Salivary gland,sublingual, Skin,inguinal, Sciatic nerve, Spleen, Stomach
Skeletal muscle,femoral, Seminal vesicle(coagulating gland), Spinal cord,thoracic
Testis, Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-42(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 4006 Male 300 mg/kg Day 43 End of administration

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-43(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 4007 Male 300 mg/kg Day 43 End of administration

Gross pathology:

Stomach	Focus,dark red,glandular stomach: 2 present 1x1 mm, 1x1 mm
Other tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-44(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 4008 Male 300 mg/kg Day 57 End of recovery

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Parathyroid, Pancreas, Pituitary, Prostate
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral
Seminal vesicle(coagulating gland), Spinal cord,thoracic, Testis, Thymus, Trachea
Thyroid, Urinary bladder

Appendix 9-45(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 4009 Male 300 mg/kg Day 57 End of recovery

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Basophilia,tubular: minimal
Pituitary	Cyst,pars intermedia: mild

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Mammary gland,inguinal
Optic nerve, Parathyroid, Pancreas, Prostate, Salivary gland,submandibular
Salivary gland,sublingual, Skin,inguinal, Sciatic nerve, Spleen, Stomach
Skeletal muscle,femoral, Seminal vesicle(coagulating gland), Spinal cord,thoracic
Testis, Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-46(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 4010 Male 300 mg/kg Day 57 End of recovery

Gross pathology:

All tissues	Not remarkable

Histopathology:

Heart	Cell infiltration,focal: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Parathyroid, Pancreas, Pituitary, Prostate
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral
Seminal vesicle(coagulating gland), Spinal cord,thoracic, Testis, Thymus, Trachea
Thyroid, Urinary bladder

Appendix 9-47(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 4011 Male 300 mg/kg Day 57 End of recovery

Gross pathology:

Stomach	Focus,dark red,glandular stomach: 1 present 1x1 mm
Other tissues	Not remarkable

Histopathology:

Kidney	Basophilia,tubular: minimal
Stomach	Erosion/Ulcer,glandular stomach: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Mammary gland,inguinal
Optic nerve, Parathyroid, Pancreas, Pituitary, Prostate
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Skeletal muscle,femoral, Seminal vesicle(coagulating gland)
Spinal cord,thoracic, Testis, Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-48(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 4012 Male 300 mg/kg Day 57 End of recovery

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Parathyroid, Pancreas, Pituitary, Prostate
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral
Seminal vesicle(coagulating gland), Spinal cord,thoracic, Testis, Thymus, Trachea
Thyroid, Urinary bladder

Appendix 9-49(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 1101 Female 0 mg/kg Day 45 End of administration,Dams

Gross pathology:

All tissues Not remarkable

Histopathology:

Lung(bronchus) Aggregation,alveolar macrophage: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Mammary gland,inguinal
Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-50(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 1102 Female 0 mg/kg Day 45 End of administration,Dams

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-51(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 1103 Female 0 mg/kg Day 47 End of administration,Dams

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-52(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 1104 Female 0 mg/kg Day 42 End of administration,Dams

Gross pathology:

Stomach	Focus,dark red,glandular stomach: 1 present 1x2 mm
Other tissues	Not remarkable

Histopathology:

Stomach	Erosion/Ulcer,glandular stomach: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus
Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-53(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 1105 Female 0 mg/kg Day 45 End of administration,Dams

Gross pathology:

Stomach	Focus,dark red,glandular stomach: 1 present 2x1 mm
Other tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-54(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 1106 Female 0 mg/kg Day 47 End of administration,Dams

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-55(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 1107 Female 0 mg/kg Day 44 End of administration,Dams

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-56(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 1108 Female 0 mg/kg Day 45 End of administration,Dams

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-57(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 1109 Female 0 mg/kg Day 46 End of administration,Dams

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-58(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 1110 Female 0 mg/kg Day 44 End of administration,Dams

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-59(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 1111 Female 0 mg/kg Day 45 End of administration,Dams

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-60(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 1112 Female 0 mg/kg Day 46 End of administration,Dams

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-61(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 2101 Female 30 mg/kg Day 44 End of administration,Dams

Gross pathology:

All tissues	Not remarkable

Histopathology:

Pituitary	Cyst,pars intermedia: mild

Following tissues : Not remarkable

Thyroid

Appendix 9-62(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 2102 Female 30 mg/kg Day 43 End of administration,Dams

Gross pathology:

Lung(bronchus)	Focus,dark red: 1 present 1x1 mm
Other tissues	Not remarkable

Histopathology:

Following tissues : Not remarkable

Pituitary, Thyroid

Appendix 9-63(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 2103 Female 30 mg/kg Day 43 End of administration,Dams

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Pituitary, Thyroid

Appendix 9-64(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 2104 Female 30 mg/kg Day 46 End of administration,Dams

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-65(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 2105 Female 30 mg/kg Day 44 End of administration,Dams

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-66(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 2106 Female 30 mg/kg Day 45 End of administration,Dams

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-67(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 2107 Female 30 mg/kg Day 43 End of administration,Dams

Gross pathology:

Stomach	Focus,dark red,glandular stomach: 1 present 1x1 mm
Other tissues	Not remarkable

Histopathology:

Following tissues : Not remarkable

Pituitary, Thyroid

Appendix 9-68(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 2108 Female 30 mg/kg Day 44 End of administration,Dams

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-69(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 2109 Female 30 mg/kg Day 44 End of administration,Dams

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-70(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 2110 Female 30 mg/kg Day 44 End of administration,Dams

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-71(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 2111 Female 30 mg/kg Day 45 End of administration,Dams

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-72(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 2112 Female 30 mg/kg Day 43 End of administration,Dams

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Pituitary, Thyroid

Appendix 9-73(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 3101 Female 100 mg/kg Day 46 End of administration,Dams

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-74(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 3102 Female 100 mg/kg Day 44 End of administration,Dams

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-75(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 3103 Female 100 mg/kg Day 43 End of administration,Dams

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-76(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 3104 Female 100 mg/kg Day 44 End of administration,Dams

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-77(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 3105 Female 100 mg/kg Day 44 End of administration,Dams

Gross pathology:

All tissues Not remarkable

Histopathology:

Kidney Cyst: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Mammary gland,inguinal
Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-78(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 3106 Female 100 mg/kg Day 46 End of administration,Dams

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-79(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 3107 Female 100 mg/kg Day 45 End of administration,Dams

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-80(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 3108 Female 100 mg/kg Day 43 End of administration,Dams

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-81(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 3109 Female 100 mg/kg Day 46 End of administration,Dams

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-82(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 3110 Female 100 mg/kg Day 46 End of administration,Dams

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-83(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 3111 Female 100 mg/kg Day 44 End of administration,Dams

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-84(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 3112 Female 100 mg/kg Day 46 End of administration,Dams

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-85(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 4101 Female 300 mg/kg Day 44 Undelivered

Gross pathology:

All tissues Not remarkable

Histopathology:

Bone+Bone marrow,femoral Increased trabecular bone: minimal

Following tissues : Not remarkable

Adrenal, Cerebellum(pons), Cerebrum, Eye, Heart, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Mammary gland,inguinal
Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-86(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 4102 Female 300 mg/kg Day 43 All littermates died

Gross pathology:

Liver	Large: mild No microscopic findings corresponding to necropsy observation
Other tissues	Not remarkable

Histopathology:

Bone+Bone marrow,femoral	Increased trabecular bone: minimal with osteoblast atrophy

Following tissues : Not remarkable

Adrenal, Cerebellum(pons), Cerebrum, Eye, Heart, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Mammary gland,inguinal
Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-87(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 4103 Female 300 mg/kg Day 41 Undelivered

Gross pathology:

Mammary gland,inguinal	Poor development: systemic No abnormal microscopic findings corresponding to necropsy observation
Uterus	Retention,conceptus: 3 present right horn: 2 present, left horn: 1 present
Other tissues	Not remarkable

Histopathology:

Bone+Bone marrow,femoral	Increased trabecular bone: minimal
Uterus	Retention,conceptus

Following tissues : Not remarkable

Adrenal, Cerebellum(pons), Cerebrum, Eye, Heart, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Mammary gland,inguinal
Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Vagina

Appendix 9-88(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 4104 Female 300 mg/kg Day 42 Undelivered

Gross pathology:

Mammary gland,inguinal	Poor development: systemic No abnormal microscopic findings corresponding to necropsy observation
Other tissues	Not remarkable

Histopathology:

Bone+Bone marrow,femoral	Increased trabecular bone: minimal

Following tissues : Not remarkable

Adrenal, Cerebellum(pons), Cerebrum, Eye, Heart, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Mammary gland,inguinal
Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-89(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 4105 Female 300 mg/kg Day 39 All littermates died

Gross pathology:

All tissues	Not remarkable

Histopathology:

Bone+Bone marrow,femoral	Increased trabecular bone: minimal with osteoblast atrophy
Thymus	Atrophy: minimal

Following tissues : Not remarkable

Adrenal, Cerebellum(pons), Cerebrum, Eye, Heart, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Mammary gland,inguinal
Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-90(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 4106 Female 300 mg/kg Day 41 All littermates died

Gross pathology:

All tissues Not remarkable

Histopathology:

Bone+Bone marrow,femoral Increased trabecular bone: minimal

Following tissues : Not remarkable

Adrenal, Cerebellum(pons), Cerebrum, Eye, Heart, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Mammary gland,inguinal
Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-91(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 4107 Female 300 mg/kg Day 40 All littermates died

Gross pathology:

All tissues	Not remarkable

Histopathology:

Bone+Bone marrow,femoral	Increased trabecular bone: minimal with osteoblast atrophy

Following tissues : Not remarkable

Adrenal, Cerebellum(pons), Cerebrum, Eye, Heart, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Mammary gland,inguinal
Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-92(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 4108 Female 300 mg/kg Day 41 Undelivered

Gross pathology:

All tissues	Not remarkable

Histopathology:

Bone+Bone marrow,femoral	Increased trabecular bone: minimal
Heart	Cell infiltration,focal: minimal

Following tissues : Not remarkable

Adrenal, Cerebellum(pons), Cerebrum, Eye, Intestine,duodenum, Intestine,jejunum
Intestine,ileum(Peyer's patch), Intestine,cecum, Intestine,colon
Intestine,rectum, Kidney, Lymph node,mesenteric, Lymph node,submandibular, Liver
Lung(bronchus), Mammary gland,inguinal, Optic nerve, Ovary, Parathyroid
Pancreas, Pituitary, Salivary gland,submandibular, Salivary gland,sublingual
Skin,inguinal, Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral
Spinal cord,thoracic, Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-93(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 4109 Female 300 mg/kg Day 40 All littermates died

Gross pathology:

All tissues	Not remarkable

Histopathology:

Bone+Bone marrow,femoral	Increased trabecular bone: minimal with osteoblast atrophy
Thymus	Atrophy: minimal

Following tissues : Not remarkable

Adrenal, Cerebellum(pons), Cerebrum, Eye, Heart, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Mammary gland,inguinal
Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-94(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 4110 Female 300 mg/kg Day 42 All littermates died

Gross pathology:

All tissues	Not remarkable

Histopathology:

Bone+Bone marrow,femoral	Increased trabecular bone: minimal
Kidney	Urinary cast,hyaline: minimal
Pituitary	Cyst,pars distalis: minimal

Following tissues : Not remarkable

Adrenal, Cerebellum(pons), Cerebrum, Eye, Heart, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Mammary gland,inguinal
Optic nerve, Ovary, Parathyroid, Pancreas, Salivary gland,submandibular
Salivary gland,sublingual, Skin,inguinal, Sciatic nerve, Spleen, Stomach
Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-95(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 4111 Female 300 mg/kg Day 54 Undelivered

Gross pathology:

Mammary gland,inguinal	Poor development: systemic No abnormal microscopic findings corresponding to necropsy observation
Other tissues	Not remarkable

Histopathology:

Bone+Bone marrow,femoral	Increased trabecular bone: minimal with osteoblast atrophy

Following tissues : Not remarkable

Adrenal, Cerebellum(pons), Cerebrum, Eye, Heart, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Mammary gland,inguinal
Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-96(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 4112 Female 300 mg/kg Day 41 Undelivered

Gross pathology:

All tissues Not remarkable

Histopathology:

Bone+Bone marrow,femoral Increased trabecular bone: minimal

Following tissues : Not remarkable

Adrenal, Cerebellum(pons), Cerebrum, Eye, Heart, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Mammary gland,inguinal
Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-97(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 5101 Female 0 mg/kg Day 43 End of administration

Gross pathology:

All tissues	Not remarkable

Histopathology:

Lung(bronchus)	Aggregation,alveolar macrophage: minimal
Parathyroid	No sample

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Mammary gland,inguinal
Optic nerve, Ovary, Pancreas, Pituitary, Salivary gland,submandibular
Salivary gland,sublingual, Skin,inguinal, Sciatic nerve, Spleen, Stomach
Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-98(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 5102 Female 0 mg/kg Day 43 End of administration

Gross pathology:

All tissues	Not remarkable

Histopathology:

Intestine,colon	Arteritis: mild
Intestine,rectum	Arteritis: mild
Pancreas	Arteritis: mild
Stomach	Arteritis: mild
Uterus	Arteritis: mild cervical

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Kidney, Lymph node,mesenteric, Lymph node,submandibular, Liver
Lung(bronchus), Mammary gland,inguinal, Optic nerve, Ovary, Parathyroid
Pituitary, Salivary gland,submandibular, Salivary gland,sublingual
Skin,inguinal, Sciatic nerve, Spleen, Skeletal muscle,femoral
Spinal cord,thoracic, Thymus, Trachea, Thyroid, Urinary bladder, Vagina

Appendix 9-99(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 5103 Female 0 mg/kg Day 43 End of administration

Gross pathology:

All tissues	Not remarkable

Histopathology:

Eye	Dysplasia,retinal: minimal
Heart	Cell infiltration,focal: minimal
Kidney	Pyelitis: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Mammary gland,inguinal
Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-100(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 5104 Female 0 mg/kg Day 43 End of administration

Gross pathology:

All tissues	Not remarkable

Histopathology:

Vagina	Thickening,mucus cell layer: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus

Appendix 9-101(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 5105 Female 0 mg/kg Day 43 End of administration

Gross pathology:

All tissues	Not remarkable

Histopathology:

Ovary	Atrophy: minimal, bilateral
Vagina	Thickening,squamous cell layer: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus

Appendix 9-102(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 5106 Female 0 mg/kg Day 57 End of recovery

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-103(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 5107 Female 0 mg/kg Day 57 End of recovery

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Urinary cast,hyaline: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Mammary gland,inguinal
Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-104(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 5108 Female 0 mg/kg Day 57 End of recovery

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-105(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 5109 Female 0 mg/kg Day 57 End of recovery

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-106(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 5110 Female 0 mg/kg Day 57 End of recovery

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-107(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 6101 Female 300 mg/kg Day 43 End of administration

Gross pathology:

All tissues	Not remarkable

Histopathology:

Bone+Bone marrow,femoral	Increased trabecular bone: minimal

Following tissues : Not remarkable

Adrenal, Cerebellum(pons), Cerebrum, Eye, Heart, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Mammary gland,inguinal
Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-108(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 6102 Female 300 mg/kg Day 43 End of administration

Gross pathology:

All tissues	Not remarkable

Histopathology:

Bone+Bone marrow,femoral	Increased trabecular bone: minimal

Following tissues : Not remarkable

Adrenal, Cerebellum(pons), Cerebrum, Eye, Heart, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Mammary gland,inguinal
Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-109(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 6103 Female 300 mg/kg Day 43 End of administration

Gross pathology:

All tissues	Not remarkable

Histopathology:

Bone+Bone marrow,femoral	Increased trabecular bone: minimal

Following tissues : Not remarkable

Adrenal, Cerebellum(pons), Cerebrum, Eye, Heart, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Mammary gland,inguinal
Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-110(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 6104 Female 300 mg/kg Day 43 End of administration

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-111(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 6105 Female 300 mg/kg Day 43 End of administration

Gross pathology:

All tissues	Not remarkable

Histopathology:

Bone+Bone marrow,femoral	Increased trabecular bone: minimal
Intestine,duodenum	Erosion/ulcer: minimal

Following tissues : Not remarkable

Adrenal, Cerebellum(pons), Cerebrum, Eye, Heart, Intestine,jejunum
Intestine,ileum(Peyer's patch), Intestine,cecum, Intestine,colon
Intestine,rectum, Kidney, Lymph node,mesenteric, Lymph node,submandibular, Liver
Lung(bronchus), Mammary gland,inguinal, Optic nerve, Ovary, Parathyroid
Pancreas, Pituitary, Salivary gland,submandibular, Salivary gland,sublingual
Skin,inguinal, Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral
Spinal cord,thoracic, Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-112(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 6106 Female 300 mg/kg Day 57 End of recovery

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-113(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 6107 Female 300 mg/kg Day 57 End of recovery

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-114(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 6108 Female 300 mg/kg Day 57 End of recovery

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-115(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 6109 Female 300 mg/kg Day 57 End of recovery

Gross pathology:

All tissues	Not remarkable

Histopathology:

Eye	Dysplasia,retinal: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-116(1/1) Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Individual gross and histopathological findings

Animal No. 6110 Female 300 mg/kg Day 57 End of recovery

Gross pathology:

Stomach	Focus,dark red,glandular stomach: 1 present 2x1 mm
Other tissues	Not remarkable

Histopathology:

Stomach	Erosion/Ulcer,glandular stomach: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus
Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 10 - 1

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Estrus cycles and copulation

Study No. : R-1190

Generation : F0 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	/Before mating (day) 1	2	3	4	5	6	7	8	9	10	11	12	13	14
1101	P	E	M	D	P	E	M	D	P	E	M	D	P	E
1102	M	D	P	E	M	D	D	P	E	M	D	D	P	E
1103	D	P	E	M	D	P	E	M	D	P	E	M	D	P
1104	M	D	P	E	M	D	P	E	M	D	P	E	M	D
1105	M	D	P	E	E	M	D	P	E	M	D	P	E	E
1106	M	D	P	E	M	D	P	E	M	D	P	E	M	D
1107	E	M	D	P	E	M	D	P	E	M	D	P	E	M
1108	P	E	M	D	P	E	M	D	P	E	M	D	P	E
1109	M	D	P	E	E	M	D	P	E	E	M	D	P	E
1110	E	M	D	P	E	M	D	P	E	M	D	P	E	M
1111	P	E	M	D	P	E	M	D	P	E	M	D	P	E
1112	D	P	E	M	D	P	E	M	D	P	E	M	D	P

P : Proestrus, E : Estrus, M : Metestrus, D : Diestrus

Appendix 10 - 2

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Estrus cycles and copulation

Study No. : R-1190

Generation : F0 Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	/Before mating (day) 15	Length of estrous cycle (days)			Mean	Number of estrus	Animal with abnormal estrous cycle
1101	M	4	4	4	4.0	4	-
1102	M	5	5		5.0	3	-
1103	E	4	4	4	4.0	4	-
1104	P	4	4		4.0	3	-
1105	M	5	4		4.5	3	-
1106	P	4	4		4.0	3	-
1107	D	4	4	4	4.0	4	-
1108	M	4	4	4	4.0	4	-
1109	M	5	5		5.0	3	-
1110	D	4	4	4	4.0	4	-
1111	M	4	4	4	4.0	4	-
1112	E	4	4	4	4.0	4	-

P : Proestrus, E : Estrus, M : Metestrus, D : Diestrus
+ : Animal with abnormal estrous cycle, - : Animal with normal and regular cycle

Appendix 10 - 3

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Estrus cycles and copulation

Study No. : R-1190

Generation : F0

Dose : benzyl salicylate 30 mg/kg

Species : Rat

Animal No.	/Before mating (day) 1	2	3	4	5	6	7	8	9	10	11	12	13	14
2101	P	E	M	D	P	E	M	D	P	E	M	D	P	E
2102	M	D	P	E	M	D	P	E	M	D	P	E	M	D
2103	M	D	P	E	M	D	P	E	M	D	P	E	M	D
2104	D	P	E	M	D	P	E	M	D	P	E	M	D	P
2105	E	M	D	P	E	M	D	P	E	M	D	P	E	M
2106	P	E	M	D	P	E	M	D	P	E	M	D	P	E
2107	E	M	D	P	E	M	D	P	E	M	D	P	E	M
2108	E	M	D	P	E	M	D	P	E	M	D	P	E	M
2109	E	M	D	P	E	M	D	P	E	M	D	P	E	M
2110	P	E	M	D	P	E	M	D	P	E	M	D	P	E
2111	P	E	M	D	P	E	M	D	P	E	M	D	P	E
2112	M	D	P	E	M	D	P	E	M	D	P	E	M	D

P : Proestrus, E : Estrus, M : Metestrus, D : Diestrus

Appendix 10 - 4

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Estrus cycles and copulation

Study No. : R-1190

Generation : F0 Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	/Before mating (day) 15	Length of estrous cycle (days)			Mean	Number of estrus	Animal with abnormal estrous cycle
2101	M	4	4	4	4.0	4	-
2102	P	4	4		4.0	3	-
2103	P	4	4		4.0	3	-
2104	E	4	4	4	4.0	4	-
2105	D	4	4	4	4.0	4	-
2106	M	4	4	4	4.0	4	-
2107	D	4	4	4	4.0	4	-
2108	D	4	4	4	4.0	4	-
2109	D	4	4	4	4.0	4	-
2110	M	4	4	4	4.0	4	-
2111	M	4	4	4	4.0	4	-
2112	P	4	4		4.0	3	-

P : Proestrus, E : Estrus, M : Metestrus, D : Diestrus

+ : Animal with abnormal estrous cycle, - : Animal with normal and regular cycle

Appendix 10 - 5

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Estrus cycles and copulation

Study No. : R-1190

Generation : F0

Dose : benzyl salicylate 100 mg/kg

Species : Rat

Animal No.	/Before mating (day) 1	2	3	4	5	6	7	8	9	10	11	12	13	14
3101	P	E	M	D	P	E	M	D	D	P	E	M	D	P
3102	E	M	D	P	E	M	D	P	E	M	D	P	E	M
3103	M	D	P	E	M	D	P	E	M	D	P	E	M	D
3104	E	E	M	D	P	E	E	M	D	P	E	E	M	D
3105	E	M	D	P	E	M	D	P	E	M	D	P	E	M
3106	D	P	E	M	D	P	E	M	D	P	E	M	D	P
3107	P	E	M	D	P	E	M	D	P	E	M	D	P	E
3108	D	D	D	D	D	D	D	D	D	D	D	D	D	D
3109	D	P	E	M	D	P	E	M	D	P	E	M	D	P
3110	P	E	M	D	P	E	M	D	P	E	E	M	D	P
3111	E	M	D	P	E	M	D	P	E	M	D	P	E	M
3112	D	P	E	M	D	P	E	M	D	P	E	M	D	P

P : Proestrus, E : Estrus, M : Metestrus, D : Diestrus

Appendix 10 - 6

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Estrus cycles and copulation

Study No. : R-1190

Generation : F0 Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	/Before mating (day) 15	Length of estrous cycle (days)			Mean	Number of estrus	Animal with abnormal estrous cycle
3101	E	4	5	4	4.3	4	-
3102	D	4	4	4	4.0	4	-
3103	P	4	4		4.0	3	-
3104	P	5	5		5.0	3	-
3105	D	4	4	4	4.0	4	-
3106	E	4	4	4	4.0	4	-
3107	M	4	4	4	4.0	4	-
3108	P					0	+
3109	E	4	4	4	4.0	4	-
3110	E	4	4	5	4.3	4	-
3111	D	4	4	4	4.0	4	-
3112	E	4	4	4	4.0	4	-

P : Proestrus, E : Estrus, M : Metestrus, D : Diestrus

+ : Animal with abnormal estrous cycle, - : Animal with normal and regular cycle

Appendix 10 - 7

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Estrus cycles and copulation

Study No. : R-1190

Generation : F0

Dose : benzyl salicylate 300 mg/kg

Species : Rat

Animal No.	/Before mating (day) 1	2	3	4	5	6	7	8	9	10	11	12	13	14
4101	D	P	E	M	D	P	E	M	D	P	E	M	D	P
4102	D	P	E	M	D	P	E	M	D	P	E	M	D	P
4103	M	D	P	E	M	D	P	E	M	D	P	E	M	D
4104	E	M	D	P	E	M	D	P	E	M	D	P	E	M
4105	D	P	E	E	M	D	P	E	M	D	P	E	M	D
4106	E	M	D	P	E	M	D	P	E	M	D	P	E	M
4107	E	M	D	P	E	M	D	P	E	M	D	P	E	M
4108	M	D	P	E	M	D	P	E	M	D	P	E	M	D
4109	M	D	P	E	M	D	P	E	M	D	P	E	M	D
4110	P	E	M	D	P	E	M	D	P	E	M	D	P	E
4111	D	P	E	M	D	P	E	M	D	P	E	M	D	P
4112	M	D	P	E	M	D	P	E	M	D	P	E	M	D

P : Proestrus, E : Estrus, M : Metestrus, D : Diestrus

Appendix 10 - 8

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Estrus cycles and copulation

Study No. : R-1190

Generation : F0 Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	/Before mating (day) 15	Length of estrous cycle (days)			Mean	Number of estrus	Animal with abnormal estrous cycle
4101	E	4	4	4	4.0	4	-
4102	E	4	4	4	4.0	4	-
4103	P	4	4		4.0	3	-
4104	D	4	4	4	4.0	4	-
4105	P	5	4		4.5	3	-
4106	D	4	4	4	4.0	4	-
4107	D	4	4	4	4.0	4	-
4108	P	4	4		4.0	3	-
4109	P	4	4		4.0	3	-
4110	M	4	4	4	4.0	4	-
4111	E	4	4	4	4.0	4	-
4112	P	4	4		4.0	3	-

P : Proestrus, E : Estrus, M : Metestrus, D : Diestrus

+ : Animal with abnormal estrous cycle, - : Animal with normal and regular cycle

Appendix 11 - 1 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Reproductive performance

Generation : F0 Sex : Male Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Elapsed day of conceiving	1st mating Paired animal	Copulation a)	Fertility b)
1001	3	1101	+	+
1002	3	1102	+	+
1003	5	1103	+	+
1004	1	1104	+	+
1005	3	1105	+	+
1006	5	1106	+	+
1007	2	1107	+	+
1008	3	1108	+	+
1009	3	1109	+	+
1010	2	1110	+	+
1011	3	1111	+	+
1012	4	1112	+	+
n	12		12	12
Mean	3.1			
S.D.	1.2			
No. of positives			12	12
%			100.0 c)	100.0 d)

a) + : Copulation
b) + : Pregnant
c): (Number of copulated animals / Number of mated animals)×100
d): (Number of males which impregnated females / Number of copulated males)×100

Appendix 11 - 2 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Reproductive performance

Generation : F0 Sex : Male Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Elapsed day of conceiving	1st mating Paired animal	Copulation a)	Fertility b)
2001	3	2101	+	+
2002	1	2102	+	+
2003	1	2103	+	+
2004	4	2104	+	+
2005	2	2105	+	+
2006	3	2106	+	+
2007	2	2107	+	+
2008	2	2108	+	+
2009	2	2109	+	+
2010	3	2110	+	+
2011	3	2111	+	+
2012	1	2112	+	+
n	12		12	12
Mean	2.3			
S.D.	1.0			
No. of positives			12	12
%			100.0 c)	100.0 d)

a) + : Copulation
b) + : Pregnant
c): (Number of copulated animals / Number of mated animals)×100
d): (Number of males which impregnated females / Number of copulated males)×100

Appendix 11 - 3 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Reproductive performance

Generation : F0 Sex : Male Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Elapsed day of conceiving	1st mating Paired animal	Copulation a)	Fertility b)
3001	4	3101	+	+
3002	2	3102	+	+
3003	1	3103	+	+
3004	1	3104	+	+
3005	2	3105	+	+
3006	4	3106	+	+
3007	3	3107	+	+
3008	1	3108	+	+
3009	4	3109	+	+
3010	4	3110	+	+
3011	2	3111	+	+
3012	4	3112	+	+
n	12		12	12
Mean	2.7			
S.D.	1.3			
No. of positives			12	12
%			100.0 c)	100.0 d)

a) + : Copulation
b) + : Pregnant
c): (Number of copulated animals / Number of mated animals)×100
d): (Number of males which impregnated females / Number of copulated males)×100

Appendix 11 - 4 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Reproductive performance

Generation : F0 Sex : Male Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Elapsed day of conceiving	1st mating Paired animal	Copulation a)	Fertility b)
4001	4	4101	+	+
4002	4	4102	+	+
4003	1	4103	+	+
4004	2	4104	+	+
4005	1	4105	+	+
4006	2	4106	+	+
4007	2	4107	+	+
4008	1	4108	+	+
4009	1	4109	+	+
4010	3	4110	+	+
4011	14	4111	+	+
4012	1	4112	+	+
n	12		12	12
Mean	3.0			
S.D.	3.6			
No. of positives			12	12
%			100.0 c)	100.0 d)

a) + : Copulation
b) + : Pregnant
c): (Number of copulated animals / Number of mated animals)×100
d): (Number of males which impregnated females / Number of copulated males)×100

Appendix 11 - 5 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Reproductive performance

Generation : F0 Sex : Female Dose : benzyl salicylate 0 mg/kg Species : Rat

Animal No.	Elapsed day of conceiving	1st mating Paired animal	Copulation a)	Fertility b)
1101	3	1001	+	+
1102	3	1002	+	+
1103	5	1003	+	+
1104	1	1004	+	+
1105	3	1005	+	+
1106	5	1006	+	+
1107	2	1007	+	+
1108	3	1008	+	+
1109	3	1009	+	+
1110	2	1010	+	+
1111	3	1011	+	+
1112	4	1012	+	+
n	12		12	12
Mean	3.1			
S.D.	1.2			
No. of positives			12	12
%			100.0 c)	100.0 d)

a) + : Copulation
b) + : Pregnant
c): (Number of copulated animals / Number of mated animals)×100
d): (Number of pregnant females / Number of copulated females)×100

Appendix 11 - 6 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Reproductive performance

Generation : F0 Sex : Female Dose : benzyl salicylate 30 mg/kg Species : Rat

Animal No.	Elapsed day of conceiving	1st mating Paired animal	Copulation a)	Fertility b)
2101	3	2001	+	+
2102	1	2002	+	+
2103	1	2003	+	+
2104	4	2004	+	+
2105	2	2005	+	+
2106	3	2006	+	+
2107	2	2007	+	+
2108	2	2008	+	+
2109	2	2009	+	+
2110	3	2010	+	+
2111	3	2011	+	+
2112	1	2012	+	+
n	12		12	12
Mean	2.3			
S.D.	1.0			
No. of positives			12	12
%			100.0 c)	100.0 d)

a) + : Copulation
b) + : Pregnant
c): (Number of copulated animals / Number of mated animals)×100
d): (Number of pregnant females / Number of copulated females)×100

Appendix 11 - 7 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Reproductive performance

Generation : F0 Sex : Female Dose : benzyl salicylate 100 mg/kg Species : Rat

Animal No.	Elapsed day of conceiving	1st mating Paired animal	Copulation a)	Fertility b)
3101	4	3001	+	+
3102	2	3002	+	+
3103	1	3003	+	+
3104	1	3004	+	+
3105	2	3005	+	+
3106	4	3006	+	+
3107	3	3007	+	+
3108	1	3008	+	+
3109	4	3009	+	+
3110	4	3010	+	+
3111	2	3011	+	+
3112	4	3012	+	+
n	12		12	12
Mean	2.7			
S.D.	1.3			
No. of positives			12	12
%			100.0 c)	100.0 d)

a) + : Copulation
b) + : Pregnant
c): (Number of copulated animals / Number of mated animals)×100
d): (Number of pregnant females / Number of copulated females)×100

Appendix 11 - 8 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Reproductive performance

Generation : F0 Sex : Female Dose : benzyl salicylate 300 mg/kg Species : Rat

Animal No.	Elapsed day of conceiving	1st mating Paired animal	Copulation a)	Fertility b)
4101	4	4001	+	+
4102	4	4002	+	+
4103	1	4003	+	+
4104	2	4004	+	+
4105	1	4005	+	+
4106	2	4006	+	+
4107	2	4007	+	+
4108	1	4008	+	+
4109	1	4009	+	+
4110	3	4010	+	+
4111	14	4011	+	+
4112	1	4012	+	+
n	12		12	12
Mean	3.0			
S.D.	3.6			
No. of positives			12	12
%			100.0 c)	100.0 d)

a) + : Copulation
b) + : Pregnant
c): (Number of copulated animals / Number of mated animals)×100
d): (Number of pregnant females / Number of copulated females)×100

Appendix 12 - 1

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Delivery data

Generation : F0

Dose : benzyl salicylate 0 mg/kg

Species : Rat

Dam No.	Gestation period (day)	Number of corpora lutea	Number of implan-tation	Preimplan-tation loss (%) a)	Implantation index (%) b)	Delivery index (%) c)	Live birth index (%) d)	Number of offspring	Number of live newborns			Number of dead newborns			
									M	F	Total	M	F	U	Total
1101	22.5	15(10/5)	14(9/5)	6.7	93.3	92.9	100.0	13	7	6	13	0	0	0	0
1102	22.5	9(5/4)	9(5/4)	0.0	100.0	100.0	100.0	9	3	6	9	0	0	0	0
1103	22	16(8/8)	16(8/8)	0.0	100.0	87.5	92.9	14	9	4	13	0	1	0	1
1104	21.5	15(8/7)	14(8/6)	6.7	93.3	100.0	100.0	14	8	6	14	0	0	0	0
1105	22.5	21(11/10)	21(11/10)	0.0	100.0	81.0	88.2	17	12	3	15	1	1	0	2
1106	22.5	6(0/6)	6(0/6)	0.0	100.0	100.0	83.3	6	3	2	5	0	1	0	1
1107	22	14(9/5)	14(9/5)	0.0	100.0	100.0	100.0	14	7	7	14	0	0	0	0
1108	22	16(10/6)	16(10/6)	0.0	100.0	93.8	100.0	15	8	7	15	0	0	0	0
1109	23	9(9/0)	8(8/0)	11.1	88.9	100.0	100.0	8	5	3	8	0	0	0	0
1110	22	15(9/6)	15(9/6)	0.0	100.0	93.3	100.0	14	6	8	14	0	0	0	0
1111	22.5	15(11/4)	15(11/4)	0.0	100.0	100.0	100.0	15	4	11	15	0	0	0	0
1112	22.5	15(7/8)	15(7/8)	0.0	100.0	66.7	100.0	10	5	5	10	0	0	0	0
n	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
Mean	22.3	13.8	13.6	2.0	98.0	92.9	97.0	12.4	6.4	5.7	12.1	0.1	0.3	0.0	0.3
S.D.	0.4	4.0	4.1	3.8	3.8	10.3	5.7	3.3	2.6	2.5	3.3	0.3	0.5	0.0	0.7

(/) : Right/Left, M : Male, F : Female, U : Unable to be sexed

a): [(Number of corpora lutea - Number of implantation) / Number of corpora lutea]×100

b): (Number of implantation / Number of corpora lutea)×100

c): (Number of delivered pups / Number of implantation)×100

d): (Number of live borns / Number of delivered pups)×100

Appendix 12 - 2

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Delivery data

Generation : F0 | Dose : benzyl salicylate 30 mg/kg | Species : Rat

Dam No.	Gestation period (day)	Number of corpora lutea	Number of implan-tation	Preimplan-tation loss (%) a)	Implantation index (%) b)	Delivery index (%) c)	Live birth index (%) d)	Number of offspring	Number of live newborns			Number of dead newborns			
									M	F	Total	M	F	U	Total
2101	21.5	16(8/8)	16(8/8)	0.0	100.0	100.0	100.0	16	9	7	16	0	0	0	0
2102	22.5	15(8/7)	15(8/7)	0.0	100.0	86.7	100.0	13	8	5	13	0	0	0	0
2103	22	15(9/6)	15(9/6)	0.0	100.0	80.0	100.0	12	5	7	12	0	0	0	0
2104	22	15(5/10)	15(5/10)	0.0	100.0	93.3	100.0	14	6	8	14	0	0	0	0
2105	22.5	15(9/6)	15(9/6)	0.0	100.0	100.0	100.0	15	7	8	15	0	0	0	0
2106	22	17(6/11)	17(6/11)	0.0	100.0	88.2	100.0	15	7	8	15	0	0	0	0
2107	21.5	17(13/4)	17(13/4)	0.0	100.0	94.1	100.0	16	9	7	16	0	0	0	0
2108	22.5	16(10/6)	16(10/6)	0.0	100.0	100.0	100.0	16	7	9	16	0	0	0	0
2109	22	16(8/8)	16(8/8)	0.0	100.0	75.0	100.0	12	6	6	12	0	0	0	0
2110	21.5	19(8/11)	19(8/11)	0.0	100.0	100.0	100.0	19	9	10	19	0	0	0	0
2111	22.5	18(9/9)	18(9/9)	0.0	100.0	88.9	100.0	16	6	10	16	0	0	0	0
2112	22.5	15(8/7)	15(8/7)	0.0	100.0	100.0	93.3	15	7	7	14	1	0	0	1
n	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
Mean	22.1	16.2	16.2	0.0	100.0	92.2	99.4	14.9	7.2	7.7	14.8	0.1	0.0	0.0	0.1
S.D.	0.4	1.3	1.3	0.0	0.0	8.6	1.9	2.0	1.3	1.5	2.0	0.3	0.0	0.0	0.3

(/) : Right/Left, M : Male, F : Female, U : Unable to be sexed

a): [(Number of corpora lutea - Number of implantation) / Number of corpora lutea]×100

b): (Number of implantation / Number of corpora lutea)×100

c): (Number of delivered pups / Number of implantation)×100

d): (Number of live borns / Number of delivered pups)×100

Appendix 12 - 3

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Delivery data

Generation : F0

Dose : benzyl salicylate 100 mg/kg

Species : Rat

Dam No.	Gestation period (day)	Number of corpora lutea	Number of implan-tation	Preimplan-tation loss (%) a)	Implantation index (%) b)	Delivery index (%) c)	Live birth index (%) d)	Number of offspring	Number of live newborns			Number of dead newborns			
									M	F	Total	M	F	U	Total
3101	22.5	16(9/7)	15(9/6)	6.3	93.8	93.3	92.9	14	4	9	13	0	1	0	1
3102	22	17(8/9)	17(8/9)	0.0	100.0	94.1	100.0	16	9	7	16	0	0	0	0
3103	22	16(8/8)	16(8/8)	0.0	100.0	100.0	100.0	16	11	5	16	0	0	0	0
3104	23.5	16(12/4)	3(0/3)	81.3	18.8	100.0	100.0	3	3	0	3	0	0	0	0
3105	22.5	17(8/9)	17(8/9)	0.0	100.0	64.7	100.0	11	4	7	11	0	0	0	0
3106	22	16(8/8)	16(8/8)	0.0	100.0	100.0	100.0	16	9	7	16	0	0	0	0
3107	22	16(3/13)	16(3/13)	0.0	100.0	87.5	100.0	14	7	7	14	0	0	0	0
3108	22.5	15(9/6)	15(9/6)	0.0	100.0	100.0	100.0	15	8	7	15	0	0	0	0
3109	22	15(8/7)	15(8/7)	0.0	100.0	93.3	100.0	14	8	6	14	0	0	0	0
3110	22	15(10/5)	15(10/5)	0.0	100.0	93.3	100.0	14	6	8	14	0	0	0	0
3111	22	15(8/7)	15(8/7)	0.0	100.0	93.3	100.0	14	8	6	14	0	0	0	0
3112	22.5	16(11/5)	14(10/4)	12.5	87.5	100.0	100.0	14	6	8	14	0	0	0	0
n	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
Mean	22.3	15.8	14.5	8.3	91.7	93.3	99.4	13.4	6.9	6.4	13.3	0.0	0.1	0.0	0.1
S.D.	0.5	0.7	3.7	23.3	23.3	9.9	2.0	3.6	2.4	2.3	3.6	0.0	0.3	0.0	0.3

(/) : Right/Left, M : Male, F : Female, U : Unable to be sexed

a): [(Number of corpora lutea - Number of implantation) / Number of corpora lutea]×100

b): (Number of implantation / Number of corpora lutea)×100

c): (Number of delivered pups / Number of implantation)×100

d): (Number of live borns / Number of delivered pups)×100

Appendix 12 - 4

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Delivery data

Generation : F0

Dose : benzyl salicylate 300 mg/kg

Species : Rat

Dam No.	Gestation period (day)	Number of corpora lutea	Number of implan-tation	Preimplan-tation loss (%) a)	Implantation index (%) b)	Delivery index (%) c)	Live birth index (%) d)	Number of offspring	Number of live newborns			Number of dead newborns			
									M	F	Total	M	F	U	Total
4102	22.5	17(10/7)	17(10/7)	0.0	100.0	52.9	66.7	9	2	4	6	1	2	0	3
4105	22.5	15(8/7)	15(8/7)	0.0	100.0	86.7	30.8	13	2	2	4	7	2	0	9
4106	24	18(9/9)	17(8/9)	5.6	94.4	11.8	0.0	2	0	0	0	1	1	0	2
4107	22.5	14(7/7)	14(7/7)	0.0	100.0	50.0	28.6	7	1	1	2	2	3	0	5
4109	23	17(10/7)	17(10/7)	0.0	100.0	35.3	66.7	6	4	0	4	1	1	0	2
4110	23.5	13(4/9)	13(4/9)	0.0	100.0	23.1	33.3	3	1	0	1	1	1	0	2
n	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
Mean	23.0	15.7	15.5	0.9	99.1	43.3	37.7	6.7	1.7	1.2	2.8	2.2	1.7	0.0	3.8
S.D.	0.6	2.0	1.8	2.3	2.3	26.4	25.5	4.0	1.4	1.6	2.2	2.4	0.8	0.0	2.8

(/) : Right/Left, M : Male, F : Female, U : Unable to be sexed

Animal No. 4101,4103,4104,4108,4111,4112 : Not delivered

a): [(Number of corpora lutea - Number of implantation) / Number of corpora lutea]×100

b): (Number of implantation / Number of corpora lutea)×100

c): (Number of delivered pups / Number of implantation)×100

d): (Number of live borns / Number of delivered pups)×100

Appendix 13 - 1 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

External examination of offspring Unit : Number of anomalous offspring (incidence %) Days after birth : 0

Generation : F0 Dose : benzyl salicylate 0 mg/kg Species : Rat

Dam No.	Number of offspring examined	/Findings (Number of offspring with anomalies)	Number of offspring with any anomaly (%)a)
1101	13	No anomaly	0 (0.0)
1102	9	No anomaly	0 (0.0)
1103	14	No anomaly	0 (0.0)
1104	14	No anomaly	0 (0.0)
1105	17	Acaudia (1)	1 (5.9)
1106	6	Acaudia (1)	1 (16.7)
1107	14	No anomaly	0 (0.0)
1108	15	No anomaly	0 (0.0)
1109	8	No anomaly	0 (0.0)
1110	14	No anomaly	0 (0.0)
1111	15	No anomaly	0 (0.0)
1112	10	No anomaly	0 (0.0)
Total	149		2
n	12		12
Mean			(1.9)
S.D.			(5.0)

Mean : Average of incidence (%)

a) : (Number of offspring with any anomaly / Number of offspring) x 100

Appendix 13 - 2 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

External examination of offspring Unit : Number of anomalous offspring (incidence %) Days after birth : 0

Generation : F0 Dose : benzyl salicylate 30 mg/kg Species : Rat

Dam No.	Number of offspring examined	/Findings (Number of offspring with anomalies)	Number of offspring with any anomaly (%)a)
2101	16	No anomaly	0 (0.0)
2102	13	No anomaly	0 (0.0)
2103	12	No anomaly	0 (0.0)
2104	14	No anomaly	0 (0.0)
2105	15	No anomaly	0 (0.0)
2106	15	No anomaly	0 (0.0)
2107	16	No anomaly	0 (0.0)
2108	16	No anomaly	0 (0.0)
2109	12	No anomaly	0 (0.0)
2110	19	No anomaly	0 (0.0)
2111	16	No anomaly	0 (0.0)
2112	15	No anomaly	0 (0.0)
Total	179		0
n	12		12
Mean			(0.0)
S.D.			(0.0)

Mean : Average of incidence (%)

a) : (Number of offspring with any anomaly / Number of offspring) x 100

Appendix 13 - 3 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

External examination of offspring Unit : Number of anomalous offspring (incidence %) Days after birth : 0

Generation : F0 Dose : benzyl salicylate 100 mg/kg Species : Rat

Dam No.	Number of offspring examined	/Findings (Number of offspring with anomalies)	Number of offspring with any anomaly (%)a)
3101	14	No anomaly	0 (0.0)
3102	16	No anomaly	0 (0.0)
3103	16	No anomaly	0 (0.0)
3104	3	No anomaly	0 (0.0)
3105	11	No anomaly	0 (0.0)
3106	16	No anomaly	0 (0.0)
3107	14	No anomaly	0 (0.0)
3108	15	No anomaly	0 (0.0)
3109	14	No anomaly	0 (0.0)
3110	14	No anomaly	0 (0.0)
3111	14	No anomaly	0 (0.0)
3112	14	No anomaly	0 (0.0)
Total	161		0
n	12		12
Mean			(0.0)
S.D.			(0.0)

Mean : Average of incidence (%)

a) : (Number of offspring with any anomaly / Number of offspring) x 100

Appendix 13 - 4 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

External examination of offspring Unit : Number of anomalous offspring (incidence %) Days after birth : 0

Generation : F0 Dose : benzyl salicylate 300 mg/kg Species : Rat

Dam No.	Number of offspring examined	/Findings (Number of offspring with anomalies)	Number of offspring with any anomaly (%)a)
4102	9	No anomaly	0 (0.0)
4105	13	No anomaly	0 (0.0)
4106	2	No anomaly	0 (0.0)
4107	7	Exencephaly (3)	5 (71.4)
		Exencephaly and Holorachischisis (2)	
4109	6	No anomaly	0 (0.0)
4110	3	No anomaly	0 (0.0)
Total	40		5
n	6		6
Mean			(11.9)
S.D.			(29.1)

Mean : Average of incidence (%)

a) : (Number of offspring with any anomaly / Number of offspring) x 100

Animal No. 4101, 4103, 4104, 4108, 4111, 4112 : Not delivered

Appendix 13 - 5 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

External examination of offspring Unit : Number of anomalous offspring Days after birth : 4

Generation : F0 Dose : benzyl salicylate 0 mg/kg Species : Rat

Dam No.	Number of offspring examined	/Findings (Number of offspring with anomalies)
1101	13	No anomaly
1102	9	No anomaly
1103	13	No anomaly
1104	14	No anomaly
1105	15	Acaudia (1)
1106	5	No anomaly
1107	14	No anomaly
1108	15	No anomaly
1109	8	No anomaly
1110	14	No anomaly
1111	14	No anomaly
1112	10	No anomaly
Total	144	
n	12	

Appendix 13 - 6 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

External examination of offspring Unit : Number of anomalous offspring Days after birth : 4

Generation : F0 Dose : benzyl salicylate 30 mg/kg Species : Rat

Dam No.	Number of offspring examined	/Findings (Number of offspring with anomalies)
2101	16	No anomaly
2102	13	No anomaly
2103	12	No anomaly
2104	14	No anomaly
2105	15	No anomaly
2106	15	No anomaly
2107	16	No anomaly
2108	16	No anomaly
2109	12	No anomaly
2110	19	No anomaly
2111	14	No anomaly
2112	14	No anomaly
Total	176	
n	12	

Appendix 13 - 7 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

External examination of offspring Unit : Number of anomalous offspring Days after birth : 4

Generation : F0 Dose : benzyl salicylate 100 mg/kg Species : Rat

Dam No.	Number of offspring examined	/Findings (Number of offspring with anomalies)
3101	12	No anomaly
3102	16	No anomaly
3103	16	No anomaly
3104	3	No anomaly
3105	11	No anomaly
3106	16	No anomaly
3107	14	No anomaly
3108	15	No anomaly
3109	14	No anomaly
3110	13	No anomaly
3111	14	No anomaly
3112	14	No anomaly
Total	158	
n	12	

Appendix 14 - 1

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Viability index and sex ratio of offspring on day 4 after birth

Study No. : R-1190

Generation : F0 | Dose : benzyl salicylate 0 mg/kg | Species : Rat

Dam No.	Number of live offspring		Viability index	Day 4 Number of live offspring		Sex ratio
	Day 0	Day 4	(%)a)	Male	Female	(%)b)
1101	13	13	100.0	7	6	
1102	9	9	100.0	3	6	
1103	13	13	100.0	9	4	
1104	14	14	100.0	8	6	
1105	15	15	100.0	12	3	
1106	5	5	100.0	3	2	
1107	14	14	100.0	7	7	
1108	15	15	100.0	8	7	
1109	8	8	100.0	5	3	
1110	14	14	100.0	6	8	
1111	15	14	93.3	4	10	
1112	10	10	100.0	5	5	
n	12	12	12			77/144
Mean	12.1	12.0	99.4			53.5
S.D.	3.3	3.2	1.9			

a) : (Number of live offspring on day 4 after birth / Number of live newborns) × 100

b) : (Number of live males on day 4 after birth / Number of live offspring on day 4 after birth) × 100

Appendix 14 - 2

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Viability index and sex ratio of offspring on day 4 after birth

Study No. : R-1190

Generation : F0 | Dose : benzyl salicylate 30 mg/kg | Species : Rat

Dam No.	Number of live offspring		Viability index	Day 4 Number of live offspring		Sex ratio
	Day 0	Day 4	(%)a)	Male	Female	(%)b)
2101	16	16	100.0	9	7	
2102	13	13	100.0	8	5	
2103	12	12	100.0	5	7	
2104	14	14	100.0	6	8	
2105	15	15	100.0	7	8	
2106	15	15	100.0	7	8	
2107	16	16	100.0	9	7	
2108	16	16	100.0	7	9	
2109	12	12	100.0	6	6	
2110	19	19	100.0	9	10	
2111	16	14	87.5	5	9	
2112	14	14	100.0	7	7	
n	12	12	12			85/176
Mean	14.8	14.7	99.0			48.3
S.D.	2.0	2.0	3.6			

a) : (Number of live offspring on day 4 after birth / Number of live newborns) × 100

b) : (Number of live males on day 4 after birth / Number of live offspring on day 4 after birth) × 100

Appendix 14 - 3

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Viability index and sex ratio of offspring on day 4 after birth

Study No. : R-1190

Generation : F0 | Dose : benzyl salicylate 100 mg/kg | Species : Rat

Dam No.	Number of live offspring		Viability index	Day 4 Number of live offspring		Sex ratio
	Day 0	Day 4	(%)a)	Male	Female	(%)b)
3101	13	12	92.3	3	9	
3102	16	16	100.0	9	7	
3103	16	16	100.0	11	5	
3104	3	3	100.0	3	0	
3105	11	11	100.0	4	7	
3106	16	16	100.0	9	7	
3107	14	14	100.0	7	7	
3108	15	15	100.0	8	7	
3109	14	14	100.0	8	6	
3110	14	13	92.9	5	8	
3111	14	14	100.0	8	6	
3112	14	14	100.0	6	8	
n	12	12	12			81/158
Mean	13.3	13.2	98.8			51.3
S.D.	3.6	3.6	2.9			

a) : (Number of live offspring on day 4 after birth / Number of live newborns) × 100

b) : (Number of live males on day 4 after birth / Number of live offspring on day 4 after birth) × 100

Appendix 14 - 4

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Viability index and sex ratio of offspring on day 4 after birth

Generation : F0 Dose : benzyl salicylate 300 mg/kg Species : Rat

Dam No.	Number of live offspring Day 0	Number of live offspring Day 4	Viability index (%)a)
4102	6	0	0.0
4105	4	0	0.0
4106	0		
4107	2	0	0.0
4109	4	0	0.0
4110	1	0	0.0
n	6	5	5
Mean	2.8	0.0	0.0
S.D.	2.2	0.0	0.0

a) : (Number of live offspring on day 4 after birth / Number of live newborns) × 100

b) : (Number of live males on day 4 after birth / Number of live offspring on day 4 after birth) × 100

Animal No. 4101, 4103, 4104, 4108, 4111, 4112 : Not delivered

Animal No. 4106 : All offspring were stillborn.

Appendix 15 - 1 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight of offspring

Generation : F0 Dose : benzyl salicylate 0 mg/kg Unit : g Species : Rat

/Days after birth

		0		4/Pre-culled	
Dam No.	Sex	n	B.W.	n	B.W.
1101	Male	7	7.5	7	11.5
	Female	6	7.0	6	10.8
1102	Male	3	7.1	3	12.4
	Female	6	6.9	6	12.0
1103	Male	9	6.7	9	10.9
	Female	4	5.8	4	9.5
1104	Male	8	6.4	8	10.0
	Female	6	5.9	6	9.3
1105	Male	12	7.0	12	10.6
	Female	3	6.3	3	9.9
1106	Male	3	7.4	3	12.6
	Female	2	7.3	2	12.3
1107	Male	7	6.8	7	10.9
	Female	7	6.1	7	9.6
1108	Male	8	7.4	8	11.7
	Female	7	6.8	7	11.0
1109	Male	5	7.4	5	13.3
	Female	3	8.1	3	14.8
1110	Male	6	6.7	6	10.5
	Female	8	6.2	8	10.2
1111	Male	4	6.4	4	10.1
	Female	11	6.1	10	9.7
1112	Male	5	7.9	5	13.4
	Female	5	7.3	5	12.5
n	Male	77		77	
	Female	68		67	
Mean	Male		7.1		11.5
	Female		6.7		11.0
S.D.	Male		0.5		1.2
	Female		0.7		1.7

Appendix 15 - 2

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Body weight of offspring

Generation : F0 | Dose : benzyl salicylate 30 mg/kg | Unit : g | Species : Rat

Dam No.	Sex	/Days after birth 0 n	0 B.W.	4/Pre-culled n	4/Pre-culled B.W.
2101	Male	9	5.8	9	9.3
	Female	7	5.4	7	8.5
2102	Male	8	6.8	8	11.0
	Female	5	6.5	5	10.2
2103	Male	5	6.6	5	10.8
	Female	7	6.1	7	10.0
2104	Male	6	7.0	6	10.6
	Female	8	6.8	8	10.3
2105	Male	7	7.2	7	11.7
	Female	8	6.8	8	10.3
2106	Male	7	6.7	7	10.7
	Female	8	6.4	8	10.6
2107	Male	9	5.8	9	8.8
	Female	7	5.6	7	8.7
2108	Male	7	6.6	7	9.7
	Female	9	5.9	9	8.9
2109	Male	6	7.3	6	11.7
	Female	6	6.9	6	11.5
2110	Male	9	5.7	9	8.5
	Female	10	5.3	10	8.0
2111	Male	6	7.1	5	11.7
	Female	10	6.5	9	10.7
2112	Male	7	6.7	7	10.3
	Female	7	6.6	7	9.4
n	Male	86		85	
	Female	92		91	
Mean	Male		6.6		10.4
	Female		6.2		9.8
S.D.	Male		0.6		1.1
	Female		0.6		1.1

Appendix 15 - 3

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Body weight of offspring

Generation : F0 | Dose : benzyl salicylate 100 mg/kg | Unit : g | Species : Rat

		/Days after birth			
		0		4/Pre-culled	
Dam No.	Sex	n	B.W.	n	B.W.
3101	Male	4	7.0	3	11.7
	Female	9	6.2	9	10.5
3102	Male	9	5.8	9	9.2
	Female	7	5.6	7	8.7
3103	Male	11	6.1	11	9.9
	Female	5	5.5	5	9.4
3104	Male	3	7.5	3	11.4
	Female	0		0	
3105	Male	4	6.6	4	11.6
	Female	7	6.5	7	11.2
3106	Male	9	6.6	9	10.5
	Female	7	6.4	7	10.4
3107	Male	7	6.1	7	10.4
	Female	7	5.7	7	10.2
3108	Male	8	6.4	8	10.5
	Female	7	6.1	7	10.5
3109	Male	8	6.3	8	10.7
	Female	6	5.8	6	9.8
3110	Male	6	5.7	5	9.9
	Female	8	5.6	8	9.2
3111	Male	8	6.4	8	10.4
	Female	6	6.1	6	10.3
3112	Male	6	6.9	6	12.0
	Female	8	6.5	8	11.2
n	Male	83		81	
	Female	77		77	
Mean	Male		6.5		10.7
	Female		6.0		10.1
S.D.	Male		0.5		0.8
	Female		0.4		0.8

Appendix 15 - 4 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight of offspring

Generation : F0 Dose : benzyl salicylate 300 mg/kg Unit : g Species : Rat

/Days after birth

		0		4/Pre-culled	
Dam No.	Sex	n	B.W.	n	B.W.
4102	Male	2	4.8	a)	
	Female	4	4.5	a)	
4105	Male	2	4.2	a)	
	Female	2	3.6	a)	
4107	Male	1	5.2	a)	
	Female	1	4.9	a)	
4109	Male	4	4.7	a)	
	Female	0			
4110	Male	1	5.8	a)	
	Female	0			
n	Male	10			
	Female	7			
Mean	Male		4.9		
	Female		4.3		
S.D.	Male		0.6		
	Female		0.7		

Animal No. 4101,4103,4104,4108,4111,4112 : Not delivered

Animal No. 4106 : All offspring were stillborn

a) : All offspring died

Appendix 15 - 5

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Body weight gain of offspring

Base : Day 4 after birth

Generation : F0 | Dose : benzyl salicylate 0 mg/kg | Unit : g | Species : Rat

Dam No.	Sex	/Days after birth /Before culling n	0-4
1101	Male	7	4.0
	Female	6	3.8
1102	Male	3	5.3
	Female	6	5.1
1103	Male	9	4.2
	Female	4	3.7
1104	Male	8	3.6
	Female	6	3.4
1105	Male	12	3.6
	Female	3	3.6
1106	Male	3	5.2
	Female	2	5.0
1107	Male	7	4.1
	Female	7	3.5
1108	Male	8	4.3
	Female	7	4.2
1109	Male	5	5.9
	Female	3	6.7
1110	Male	6	3.8
	Female	8	4.0
1111	Male	4	3.7
	Female	10	3.6
1112	Male	5	5.5
	Female	5	5.2
n	Male	77	
	Female	67	
Mean	Male		4.4
	Female		4.3
S.D.	Male		0.8
	Female		1.0

Appendix 15 - 6

Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Study No. : R-1190

Body weight gain of offspring

Base : Day 4 after birth

Generation : F0

Dose : benzyl salicylate 30 mg/kg

Unit : g

Species : Rat

Dam No.	Sex	/Days after birth /Before culling n	0-4
2101	Male	9	3.5
	Female	7	3.1
2102	Male	8	4.2
	Female	5	3.7
2103	Male	5	4.2
	Female	7	3.9
2104	Male	6	3.6
	Female	8	3.5
2105	Male	7	4.5
	Female	8	3.5
2106	Male	7	4.0
	Female	8	4.2
2107	Male	9	3.0
	Female	7	3.1
2108	Male	7	3.1
	Female	9	3.0
2109	Male	6	4.4
	Female	6	4.6
2110	Male	9	2.8
	Female	10	2.7
2111	Male	5	4.6
	Female	9	4.2
2112	Male	7	3.6
	Female	7	2.8
n	Male	85	
	Female	91	
Mean	Male		3.8
	Female		3.5
S.D.	Male		0.6
	Female		0.6

Appendix 15 - 7 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

Body weight gain of offspring Base : Day 4 after birth

Generation : F0 Dose : benzyl salicylate 100 mg/kg Unit : g Species : Rat

Dam No.	Sex	/Days after birth /Before culling n	0-4
3101	Male	3	4.7
	Female	9	4.3
3102	Male	9	3.4
	Female	7	3.1
3103	Male	11	3.8
	Female	5	3.9
3104	Male	3	3.9
	Female	0	
3105	Male	4	5.0
	Female	7	4.7
3106	Male	9	3.9
	Female	7	4.0
3107	Male	7	4.3
	Female	7	4.5
3108	Male	8	4.1
	Female	7	4.4
3109	Male	8	4.4
	Female	6	4.0
3110	Male	5	4.2
	Female	8	3.6
3111	Male	8	4.0
	Female	6	4.2
3112	Male	6	5.1
	Female	8	4.7
n	Male	81	
	Female	77	
Mean	Male		4.2
	Female		4.1
S.D.	Male		0.5
	Female		0.5

Appendix 16 - 1 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

External examination of dead offspring Unit : Number of anomalous offspring

Generation : F0 Dose : benzyl salicylate 0 mg/kg Species : Rat

Dam No.	Number of offspring examined	/Findings
1101	0	
1102	0	
1103	0	
1104	0	
1105	0	
1106	0	
1107	0	
1108	0	
1109	0	
1110	0	
1111	1	No anomaly
1112	0	
Total	1	
n	12	

Appendix 16 - 2 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

External examination of dead offspring Unit : Number of anomalous offspring

Generation : F0 Dose : benzyl salicylate 30 mg/kg Species : Rat

Dam No.	Number of offspring examined	/Findings
2101	0	
2102	0	
2103	0	
2104	0	
2105	0	
2106	0	
2107	0	
2108	0	
2109	0	
2110	0	
2111	2	No anomaly
2112	0	
Total	2	
n	12	

Appendix 16 - 3 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

External examination of dead offspring Unit : Number of anomalous offspring

Generation : F0 Dose : benzyl salicylate 100 mg/kg Species : Rat

Dam No.	Number of offspring examined	/Findings
3101	0	
3102	0	
3103	0	
3104	0	
3105	0	
3106	0	
3107	0	
3108	0	
3109	0	
3110	0	
3111	0	
3112	0	
Total	0	
n	12	

Appendix 16 - 4 Benzyl salicylate: An oral combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats Study No. : R-1190

External examination of dead offspring Unit : Number of anomalous offspring

Generation : F0 Dose : benzyl salicylate 300 mg/kg Species : Rat

Dam No.	Number of offspring examined	/Findings
4102	0	
4105	1	No anomaly
4107	0	
4109	1	No anomaly
4110	1	No anomaly
Total	3	
n	5	

Animal No. 4101, 4103, 4104, 4108, 4111, 4112 : Not delivered

Animal No. 4106 : All offspring were stillborn.

信頼性保証書（1/4）

試験番号　：　R-1190

試験表題　：　サリチル酸ベンジル:ラットを用いた経口投与による
反復投与毒性・生殖発生毒性併合試験

本試験は以下に示す基準を遵守して実施されたことを保証致します。
なお、一部委託部分（血中ホルモン測定）については試験場所信頼性保証部門により保証されていることを確認致しております。

- 「新規化学物質等に係る試験を実施する試験施設に関する基準」
（平成 23 年 3 月 31 日：薬食発 0331 第 8 号、平成 23･03･29 製局第 6 号、環保企発第 110331010 号）

なお、調査は下記の通り実施致しました。

2017 年 3 月 30 日
株式会社ボゾリサーチセンター
主信頼性保証部門 [redacted]

試験における調査

項　目	担当者	調　査　日	試験責任者及び運営管理者への報告日
試験計画書	[redacted]	2016 年 10 月 4 日	2016 年 10 月 4 日
試験計画書変更書（1）		2016 年 10 月 11 日	2016 年 10 月 11 日
作業予定表・コンピュータプロトコール		2016 年 10 月 12 日	2016 年 10 月 12 日
改善確認		2016 年 10 月 19 日	2016 年 10 月 19 日
調製・保存（被験物質）		2016 年 10 月 24 日	2016 年 10 月 24 日
投与液の濃度確認		2016 年 10 月 24 日	2016 年 10 月 24 日
群分け		2016 年 10 月 26 日	2016 年 10 月 26 日

信頼性保証書（2/4）

項　目	担当者	調　査　日	試験責任者及び運営管理者への報告日
体重・摂餌量測定・投与・一般状態の観察・腟垢検査	[redacted]	2016年 10月 27日	2016年 10月 28日
詳細な一般状態の観察		2016年 10月 28日	2016年 10月 28日
交配		2016年 11月 11日	2016年 11月 11日
機能検査・握力・自発運動量の測定		2016年 12月 2日	2016年 12月 2日
分娩・哺育観察・体重測定		2016年 12月 2日	2016年 12月 2日
尿検査（尿量・色調・定性・沈渣）		2016年 12月 5日	2016年 12月 6日
採血・剖検		2016年 12月 7日	2016年 12月 7日
病理組織学検査（切り出し）		2016年 12月 22日	2016年 12月 26日
被験物質の安定性		2016年 12月 26日	2016年 12月 26日
試験計画書変更書（2）		2016年 12月 27日	2016年 12月 27日
試験計画書変更書（3）		2017年 1月 24日	2017年 1月 24日
試験計画書変更書（4）		2017年 2月 6日	2017年 2月 6日
試験計画書変更書（5）		2017年 3月 1日	2017年 3月 1日
生データ		2017年 3月 13日	
		2017年 3月 14日	
		2017年 3月 15日	
		2017年 3月 16日	
		2017年 3月 17日	
		2017年 3月 18日	
		2017年 3月 28日	2017年 3月 29日
改善確認		2017年 3月 29日	2017年 3月 29日

信頼性保証書（3/4）

項　目	担当者	調　査　日	試験責任者及び運営管理者への報告日
図・表・付表	[redacted]	2017年　3月 13日	
		2017年　3月 14日	
		2017年　3月 15日	
		2017年　3月 16日	
		2017年　3月 17日	
		2017年　3月 25日	2017年　3月 27日
改善確認		2017年　3月 28日	2017年　3月 28日
最終報告書草案		2017年　3月 16日	
		2017年　3月 17日	
		2017年　3月 18日	
		2017年　3月 19日	
		2017年　3月 27日	2017年　3月 28日
改善確認		2017年　3月 30日	2017年　3月 30日
最終報告書		2017年　3月 30日	2017年　3月 30日

信頼性保証書（4/4）

プロセス調査

項　目	試験番号	担当者	調　査　日	試験責任者及び運営管理者への報告日
動物入荷	B-8043	[redacted]	2016年　8月　8日	2016年　8月　8日
検疫・馴化	B-8043		2016年　8月　8日	2016年　8月　8日
	B-8043		2016年　8月 15日	2016年　8月 15日
尿検査 （浸透圧・電解質）	B-8044		2016年 10月 17日	2016年 10月 17日
血液学検査・ 血液化学検査	B-8123		2016年 10月 13日	2016年 10月 14日
病理組織学検査	B-8082		2016年 10月　3日	2016年 10月　3日
（包埋・薄切・染色）	B-8082		2016年 10月　4日	2016年 10月　4日
	B-8082		2016年 10月　6日	2016年 10月　7日
	R-1192		2017年　1月　4日	2017年　1月　4日
	R-1192		2017年　1月　5日	2017年　1月　6日
	R-1192		2017年　1月　6日	2017年　1月　6日