

最 終 報 告 書

(訂正版)

試験表題 : 1,3-Propanediol,2-butyl-2-ethyl 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

試験番号 : R-1088

作成日 : 2013 年 4 月 4 日

試験期間 : 2011 年 10 月 21 日~2012 年 3 月 28 日

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

試験委託者

厚生労働省 医薬食品局 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

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

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2. 試験実施概要

2.1 試験計画書

試験番号 : R-1088
試験表題 : 1,3-Propanediol,2-butyl-2-ethyl 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
(A combined repeated dose toxicity study with the
reproduction/developmental toxicity screening test of
1,3-Propanediol, 2-butyl-2-ethyl by oral administration
in rats)

2.2 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。

2.3 試験委託者

厚生労働省 医薬食品局 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

2.4 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

2.5 試験実施施設

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

2.6 被験物質

製造者 : 
名称 : 1,3-Propanediol,2-butyl-2-ethyl
和名 : 1,3-プロパンジオール,2-ブチル-2-エチル
CAS 番号 : 115-84-4
官報公示整理番号 : 2-240
入手日 : 2011 年 9 月 15 日

2.7 試験日程

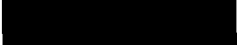
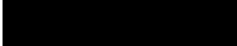
試験開始日 : 2011 年 10 月 21 日
被験物質出庫日 : 2011 年 11 月 1 日

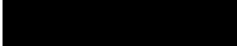
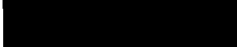
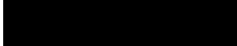
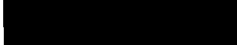
動物入荷日 : 2011 年 10 月 24 日
実験開始日（投与開始日）
: 2011 年 11 月 9 日
交配開始日 : 2011 年 11 月 23 日
分娩開始日 : 2011 年 12 月 15 日
母動物剖検開始日 : 2011 年 12 月 20 日
投与終了剖検日 : 2011 年 12 月 21 日（雄及び非交配群）
回復開始日 : 2011 年 12 月 21 日
回復終了剖検日 : 2012 年 1 月 4 日
動物試験終了日 : 2012 年 1 月 4 日
実験終了日（病理組織学検査終了日）
: 2012 年 2 月 22 日
試験終了日 : 2012 年 3 月 28 日

2.8 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

2.9 試験担当者

試験主担当者 : 
被験物質保存責任者 :  (2012 年 2 月 29 日まで)
:  (2012 年 3 月 1 日から)

臨床検査責任者 : 
化学分析責任者 : 
病理検査責任者 : 
統計解析責任者 : 

2.10 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。

2.11 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

- (1) 血液化学検査において低及び中用量群の雌各 1 例（動物番号：2106 及び 3106）の総胆汁酸が同群の他個体に比べ高値を示したことから、確認のため再測定を実施した。その結果、初回測定値とほぼ同様の結果を示したため初回測定値を採用した。
- (2) 動物番号 3008 の上皮小体が標本作製時に欠落したが、当該個体は検索対象動物ではないことから病理評価上の問題はないと判断されたため、試験成績へ及ぼす

影響はなかった。

2.12 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（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5年間保存する。期間終了後の保存については、厚生労働省医薬食品局審査管理課化学物質安全対策室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、血清）及び腔垢標本については、試験終了までに廃棄した。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なかったため試験終了までに廃棄した。

2.13 試験責任者の記名・なつ印



2013 年 4 月 4 日



3. 要約

1,3-Propanediol, 2-butyl-2-ethyl の 0 (対照群: 0.5 w/v%メチルセルロース溶液)、20、100 及び 500 mg/kg を Sprague-Dawley 系 SPF ラット (交配群として雌雄各 12 匹/群、雌には非交配群として対照群及び 500 mg/kg 投与群に各 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)、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 500 mg/kg 投与群の一部の動物 (交配群雄 5 匹と非交配群雌 5 匹) については非交配群雌及び雄ともに 42 日間投与した後 14 日間の回復期間を設け、毒性変化の可逆性を検討した。

3.1 反復投与毒性

いずれの投与群においても死亡動物はみられず、機能検査、握力、体重及び摂餌量には被験物質投与の影響は認められなかった。雄では、500 mg/kg 群でよろめき歩行、尿 pH 低値傾向、摂水量高値、リンパ球比率高値、好中球比率低値、肝臓及び腎臓重量高値、胃に境界縁扁平上皮細胞過形成及び腎臓に顆粒円柱、尿細管の再生、上皮細胞内好酸性小体増加、拡張及び上皮細胞壊死/剥離がみられた。また、100 mg/kg 群で腎臓に重量高値、顆粒円柱、尿細管の再生及び上皮細胞内好酸性小体増加がみられた。交配群雌では、500 mg/kg 群でよろめき歩行、腹臥/横臥、自発運動量低値、肝臓重量高値がみられた。また、20 mg/kg 以上の群でリンパ球比率高値、好中球比率低値がみられた。非交配群雌では、500 mg/kg 群でよろめき歩行、尿 pH 低値傾向、グルコース低値、肝臓重量高値、胃に境界縁扁平上皮細胞過形成がみられた。なお、摂水量、リンパ球比率、好中球比率、グルコースの変動の毒性学的意義は低いと考えられた。また、14 日間の投与の休止により投与期間中にみられた変化は、尿細管の再生を除き、消失するか、頻度及び程度が軽減したことから回復性がみられた。

3.2 生殖発生毒性

性周期、交尾までに要した日数、交尾率、授精率及び受胎率、出産率、妊娠期間、黄体数、着床痕数、着床率、死産児率、死産児の外表観察、出生児数及び出生率に被験物質投与の影響は認められず、授乳期間中の哺育状態にも異常が認められなかった。

出生児では、出生時の外表観察、出生時及び生後 4 日の雌雄体重並びに性比、生後 4 日の生存率及び肉眼観察所見に被験物質投与による影響は認められなかった。

これらの結果から、本試験条件下において、本被験物質の雌雄動物における反復投与毒性に対する無影響量及び無毒性量はいずれも雄で 20 mg/kg、雌で 100 mg/kg と判断した。また、雌雄親動物と児動物における生殖発生毒性に対する無影響量及び無毒性量は、雌雄親動物及び児動物でいずれも 500 mg/kg と判断した。

4. 緒言

厚生労働省医薬食品局審査管理課化学物質安全対策室の委託により、1,3-Propanediol,2-butyl-2-ethyl 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。また、本試験は動物実験委員会の承認を受けている（承認番号：G110147）。

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」
（平成 23 年 3 月 31 日：薬食発 0331 第 8 号、平成 23・3・29 製局第 6 号、
環境企発第 110331010 号）

4.2 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、
環境企発第 110331009 号）

4.3 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、最終改正平成 23 年 6 月 24 日法律第 74 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）

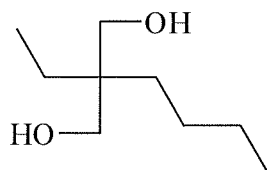
5. 試験材料及び方法

5.1 被験物質及び媒体

5.1.1 被験物質

1,3-Propanediol,2-butyl-2-ethyl は三立ケミー株式会社から以下の情報とともに購入した。また、試験開始前に赤外吸収スペクトルの測定により特性が確認されている(試験番号：A-2425、添付資料 1)。

製造者	:	東京化成工業株式会社
名称	:	1,3-Propanediol,2-butyl-2-ethyl
和名	:	1,3-プロパンジオール,2-ブチル-2-エチル
CAS 番号	:	115-84-4
官報公示整理番号	:	2-240
構造式又は示性式	:	



分子式	:	$C_9H_{20}O_2$
分子量	:	160.25
常温における性状(外観)	:	白色結晶性粉末
沸点	:	178°C/6.7kPa
オクタノール/水分配係数	:	2.01
ロット番号	:	BLODO
純度(GC)	:	99.8%
不純物	:	不明
融点	:	44.7°C
メタノール溶状	:	澄明
入手量	:	1500 g
保存条件	:	密栓、冷暗所
保存方法	:	気密容器に入れ冷蔵庫内(許容値：1~10°C、実測値：2~8°C)に保存した。
保存場所	:	御殿場研究所被験物質保存室、第2研究棟4階被験物質調製室及び生化学部標準物質保存場所
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、実験実施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。（添付資料 2）。
- 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、直接の接触を防ぐ。取り扱い後は、手、顔等を良く洗い、うがいをする。
- 残量の処理 : 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。動物試験及び分析終了後の残量は全て焼却処分した。

5.1.2 媒体

- 名称 : 0.5 w/v%メチルセルロース溶液（略称：0.5 w/v%MC 溶液）

なお、媒体については、本試験に先立って実施した被験液中濃度測定法バリデーション及び均一性・安定性試験（試験番号：A-2425）[1]において、0.5 w/v%MC 溶液中での被験物質の安定性に良好な結果が得られていることから、0.5 w/v%MC 溶液を選択した。

5.2 投与液の調製及び保存方法

5.2.1 媒体の調製及び保存

メチルセルロース（METOLOSE SM-400、日本薬局方、信越化学工業株式会社、ロット番号：0055301）を注射用水（日本薬局方、株式会社大塚製薬工場、ロット番号：1C80、1C94）に溶解して 0.5 w/v%MC 溶液とした。調製した媒体は、調製当日に被験液の調製に使用した。また、被験液調製当日の被験物質を取り扱う前に対照群投与液として、必要量の媒体を褐色ガラス瓶に分注し、投与に使用するまで被験液と同様に保存した。

5.2.2 被験液の調製及び保存

濃度ごとに必要量の被験物質を正確に秤取した。媒体を少量ずつ添加し、乳鉢及び乳棒を用いて被験物質を媒体に懸濁させた。懸濁液をメスシリンダーに移すとともに、乳鉢及び乳棒を少量の媒体で数回洗い、その液もメスシリンダーに加えた。更に媒体をメスシリンダーに加えて規定量にメスアップし、所定の濃度液を調製した。調製は 7 日に 1 回以上の頻度で最大 7 日分を一括して行い、調製した被験液は褐色ガラス瓶に入れて冷所（冷蔵庫内、許容値：1~10°C、実測値：4~8°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。残液はポリ瓶に回収又はペーパータオル等に吸着させて焼却処分した。

5.2.3 被験液の安定性

本被験物質の 1.00 及び 200 mg/mL 懸濁液（媒体：0.5 w/v%MC 溶液）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、その後室温で 24 時間安定であることが株式会社ボゾリサーチセンターで確認されている（試験番号：A-2425、添付資料 3）[1]。

5.2.4 被験液の濃度・均一性確認

初回投与及び投与 6 週の 2 回、投与に用いる各濃度の被験液（上・中・下層より各 10 mL 採取）について、投与に使用する前に株式会社ボゾリサーチセンター御殿場研究所で GC により濃度及び均一性確認を実施した。その結果、各濃度液における表示値に対する被験物質の割合は 94.5~107.0%、変動係数は 5.7%以下であり、いずれも許容範囲内（濃度：表示値に対する割合；100.0±10.0%、均一性：CV10.0%以下）であった（添付資料 4、5）ことから、被験液の調製に問題はなかったと考えられた。なお、GC 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-2425）[1]で実施された。分析法の概略を以下に示した。

[標準物質]

被験物質から一部分配したものをを用いた。

名称	:	1,3-Propanediol,2-butyl-2-ethyl
ロット番号	:	BLODO
保存条件	:	密栓、冷暗所
保存方法	:	気密容器に入れ冷蔵庫内（許容値：1~10°C、実測値：2~8°C）に保存した。
保存場所	:	御殿場研究所 被験物質保存室及び生化学部標準物質保存場所

[測定実測試料の調製]

マグネチックスターラーで攪拌しながら各測定試料を任意の場所から n=1 で採取し、以下の表に従ってアセトンで溶解・希釈した溶液をシリンジフィルターでろ過（最初の 1 mL は使用せず廃棄）した測定実測試料を用時調製した。なお、全ての測定試料において、凝固していなかったため、微温で溶解・再分散は行わなかった。

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)	
4	1	20	2	20	—	—	200
20	1	20	1	50	—	—	1000
100	1	20	2	50	2	20	5000

溶媒：アセトン

[GC システム]

機器名及び型式		メーカー
GC	HP6890N	Agilent Technologies, Inc.
インジェクタ	G2613A	
オートサンプラトレイ	G2614A	
データ処理ソフト	GC ChemStation G2070AJ	

[GC 測定条件]

カラム	:	DB-5 (0.53 mm I.D.×25 m、膜厚 5 μm、 Agilent Technologies Inc.)
キャリアガス	:	He
流量モード	:	コンスタントフローモード
流量	:	5.0 mL/min
注入口	:	スプリットレス注入口
注入口温度	:	250°C
検出器	:	Flame ionization detector (FID)
検出器温度	:	250°C
H ₂ 流量	:	40 mL/min
Air 流量	:	450 mL/min
オーブン温度	:	150°C (Hold 0 分) → 250°C (20°C/min、Hold 2 分)
注入量	:	1 μL

5.3 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よりげっ歯類を用いた試験が必要とされていることからラットを選択した。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。

5.4 試験動物

Sprague-Dawley 系 SPF ラット [CrI: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 8 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 16 日間の馴化飼育を行った。その間、一般状態の観察 (1 回/日)、体重測定 (馴化 1、3、9 及び 16 日の 4 回)、詳細な一般状態の観察 (群分け 4 日前の馴化 12 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、雌については腔垢を検疫期間終了後群分け日まで採取して性周期を調べた。その結果、1 例 (耳標番号: 371) で性周期の異常がみられ、1 例 (耳標番号: 341) で精巣の小型化が疑われた。また、馴化 3 日 (検疫終了日) に給水ノズルの不備がみられ雄 1 例 (耳標番号: 336) で体重減少が認められた。それらの異常例を除き、検疫・馴化期間中の一般状態、詳細な一

般状態、体重推移、精巣の触診結果及び性周期（検疫期間終了後 12 日間）に異常がなく、性成熟に達した陰茎龟头であり、健康と思われる雄 60 匹中 48 匹及び雌 82 匹中 68 匹を選択し、10 週齢で投与に使用した。投与開始時（10 週齢）の体重の変動範囲は雄で 353~416 g（平均体重：378 g）、雌は 209~265 g（平均体重：233 g）であり、雌雄それぞれ平均体重の $\pm 20\%$ 以内であった。

なお、動物は検疫・馴化期間中の体重増加量（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無処置動物として継続飼育し、使用しなかった無処置動物は交配期間終了後に試験から除外した。その他の雌雄残余動物は投与開始後に試験から除外した。なお、試験から除外された動物は、有効利用を目的として動物管理責任者に移管した。

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。

5.5 飼育条件

動物は、温度 $23\pm 3^{\circ}\text{C}$ （実測値：22~24 $^{\circ}\text{C}$ ）、相対湿度 $50\pm 20\%$ （実測値：40~60%）、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：904 号室）で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）に交配中を除いて個別に収容した。なお、妊娠 17 日から授乳 4 日までは、床敷（ホワイトフレック：日本チャールス・リバー株式会社、ロット番号：2011-2）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。

飼料は NMF 固形（放射線滅菌、オリエンタル酵母工業株式会社、ロット番号：110613、110714、110817、111114）をステンレス製給餌器により自由に摂取させた。

飲料水は御殿場市営水道水を自動給水装置（ブラケット式金属製網ケージでの飼育時）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。

飼料及び床敷中の混入物質の分析に関しては、使用したロットについて Eurofins Scientific Analytics で実施した分析結果を入手した。また、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て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。

5.6 動物の識別

動物は番号（雄：301~362、雌：363~445）が刻印された耳標を入荷時に装着し、個体識別を行った。群分け後は、1000 の位は群（対照群、低、中及び高用量の順）、100 の位は性別（0 番を雄、1 番を雌）、10 と 1 の位は個体番号を示す 4 桁の動物番号を設定した。各飼育ケージに投与量（群）ごとに色分けしたケージラベルを付け、試験番号、投与経路、投与量、性別、動物番号、耳標番号、剖検予定日（雄及び非交配群の雌）、交尾成立日（交配群の雌雄）及び分娩日（交配群の雌）を明記した。

5.7 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。投与期間は雄で 42 日間（交配前 14 日間、交配期間 14 日間、その後 14 日間）、交配群の雌で 41~46 日間（交配前 14 日間、交配期間及び妊娠期間を通して授乳 4 日まで）、非交配群の雌で 42 日間とした。また、不妊であった動物（動物番号：2109）については 40 日間、交尾が成立しなかった動物（動物番号：3111）については 53 日間とした。回復期間は投与終了後 14 日間とし、その間投与を行わなかった。投与回数は反復投与試験で一般的に行われている 1 回/日（7 回/週）とした。

5.8 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 mL/kg 体重とし、フレキシブル胃ゾンデを用いて投与液を 1 日 1 回、08:40~11:16 の間に強制経口投与した。ただし、投与時に分娩中であった動物は分娩終了を待って、14:03~14:48 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。投与に際しては被験液の状態を確認し、凝固していた場合は、微温で溶解・再分散した後に使用した。

5.9 投与量及び群構成

投与量は 20、100 及び 500 mg/kg の 3 用量とし、試験群はこれらの用量群に媒体を投与する対照群を加え 4 群構成とした。1 群当たりの動物数は交配を行う交配群として各群で雌雄各 12 匹、交配しない非交配群として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群内番号 8 番以降、雌の群内番号 18 番以降の各 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. 群構成表 (雄)

試験群	投与量 (mg/kg)	被験液濃度 (mg/mL)	投与容量 (mL/kg)	交配群	
				動物数	動物番号
対照群	0	0	5	12	1001~1012 ^{注1}
低用量群	20	4	5	12	2001~2012
中用量群	100	20	5	12	3001~3012
高用量群	500	100	5	12	4001~4012 ^{注1}

注1： 群内番号 8 番以降の 5 匹は、最終投与終了日以降、回復動物とした。

表 1-2. 群構成表 (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	
				動物数	動物番号	動物数	動物番号
対照群	0	0	5	12	1101~1112	10	1113~1122 ^{注2}
低用量群	20	4	5	12	2101~2112	—	—
中用量群	100	20	5	12	3101~3112	—	—
高用量群	500	100	5	12	4101~4112	10	4113~4122 ^{注2}

注2： 群内番号 18 番以降の 5 匹は、最終投与終了日以降、回復動物とした。

5.10 投与量の設定根拠

本試験の投与量は、先に実施した「1,3-Propanediol, 2-butyl-2-ethyl」のラットを用いた 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-R028、投与量：250、500 及び 1000 mg/kg/day」[2]の結果（添付資料 6）を参考に設定した。すなわち、投与量設定試験では、高用量の 1000 mg/kg 投与群においても死亡例はみられず、体重及び摂餌量に被験物質投与の影響はみられなかった。しかし、1000 mg/kg 投与群では、雌雄でよろめき歩行及び腹臥/横臥がみられ、雄で血小板数の高値、AST 及びグルコースの低値が認められた。また、雌雄で肝臓重量の高値、雄で胸腺重量の低値、雌で腎臓相対重量の高値が認められ、雌雄で前胃に隆起巣が、雄で腎臓の大型化（軽度）がみられた。500 mg/kg 投与群では、雌でよろめき歩行がみられ、雄で胸腺重量の低値が認められた。250 mg/kg 投与群では、雄で胸腺重量の低値が認められた。今回実施する反復投与毒性・生殖発生毒性併合試験の投与期間は投与量設定試験の 3 倍以上になること、当試験が生殖発生毒性試験との併合試験であることを考慮すると、1000 mg/kg は本試験の投与量には高すぎると考えられた。したがって、本試験では 500 mg/kg を高用量とし、以下公比 5 で除して 100 及び 20 mg/kg をそれぞれ中及び低用量に設定した。

5.11 観察及び検査の方法

試験日の起算は、投与開始日を投与 1 日、投与 1 日から 7 日を投与 1 週、回復開始日（投与期間終了の翌日）を回復 1 日、回復 1 日から 7 日を回復 1 週、交尾成立日を妊娠 0 日、分娩終了日を授乳 0 日、出産日（出生日）を哺育 0 日（生後 0 日）とし、以下に示す項目について、それぞれ記載の時期に観察及び検査を実施した。

5.11.1 一般状態の観察

全個体について、検疫・馴化期間中は毎日 1 回、投与期間中は毎日 4 回（投与前、投与直後、投与後 30 分及び投与後 1~3 時間）、回復期間中は毎日 1 回（午前中）、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 週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。

5.11.2 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。投与開始前（馴化期間中）に 1 回、また、雄及び非交配群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、未交尾動物は交配開始後 6 及び 13 日、分娩動物は授乳 4 日）にそれぞれ行った。

機能検査、握力測定及び自発運動量の測定は、各群の 5 匹（雄の群内番号 8~12 番、交配群雌の各群の分娩順で動物番号が若い順^注、非交配群の群内番号 18~22 番）について行った。投与期間中は交配群の雌で授乳 4 日（投与 41~43 日）に、その他は投与期間終了週（投与 6 週、投与 38 日）に、回復期間中は対照群及び高用量群の雌雄で回復期間終了週（回復 2 週、雌雄ともに回復 10 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、自発運動量の測定に関しては、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、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：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、1103、1104、1108、1110
低用量群	2102、2103、2106、2108、2111
中用量群	3102、3104、3106、3107、3112
高用量群	4101、4102、4103、4104、4111

1) 詳細な一般状態の観察

ケージ内観察として姿勢、痙攣、異常行動、手に持つての観察として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、オープンフィールド内観察として覚醒状態、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）について観察した。

2) 機能検査

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

について検査した。

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。

5.11.3 体重測定

全個体について、馴化 1、3、9 及び 16 日に体重を測定した。交配群の雄及び非交配群の雌は投与 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、交配群の雌は投与 1、8、15 日（未交尾動物は交配期間中の投与 22 日）、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。なお、午後の分娩観察時に分娩の終了が確認された個体の授乳 0 日の体重測定（13:44~16:56 の間）を除き、測定当日の投与前、08:00~10:07 の間に体重測定を行った。剖検日には、前日から約 16 時間絶食させた後、相対器官重量算出に備えて体重を 07:40~08:58 の間に測定した。また、未交尾雌動物及び妊娠 25 日未分娩動物については、搬出前に体重を測定した。

5.11.4 摂餌量測定

全個体について、交配群の雄及び非交配群の雌は投与 1、8、15、30、36 及び 42 日に、回復動物は更に回復 1、8 及び 14 日に、交配群の雌は投与 1、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当日の投与前、08:15~11:41 の間に行った。

5.11.5 膣垢検査

馴化期間中は入手した雌全個体について、検疫期間終了後から群分け日まで毎日膣垢を採取し、性周期異常の有無について調べた。

交配前投与期間中は交配群の雌の全個体について、投与開始日から交尾成立まで毎日膣垢を採取し、多数の角化上皮細胞から成る膣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）を調べた。

交配期間中は膣垢内の精子の有無を調べるとともに膣垢像を発情前期、発情期、発情後期及び発情休止期に分類した。

非交配群及び交尾の認められなかった雌については、剖検時における性周期ステージを調べるため、剖検 6 日前から剖検日まで毎日膣垢を採取し、鏡検した。なお、鏡検結果については、解剖日の性周期の判別のための参考データとした。

5.11.6 交配方法

交配前投与期間終了後、交配群の同じ投与群の雌雄を 1:1 で終夜同居させ、翌朝、膣栓形成あるいは膣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を調べた。同一雌雄による同居期間は最長 14 日間であった。交尾が確認されなかった 100 mg/kg 投与群の 1 例（動物番号：3111）は交配期間終了日を妊娠 0 日と仮定して一般状態の観察、体重・摂餌量測定及び投与を継続し、25 日後に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、病理学検査に供した。妊娠の有無を確認した結果、着床は認められなかったため、交尾不成立とみなした。

5.11.7 分娩及び哺育観察

1) 母動物の観察

交尾の確認された雌動物は妊娠 21 日から妊娠 25 日の午前中まで 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の異常の有無を観察した。分娩が 17 時までには終了していた場合、その日を授乳 0 日とした。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 日単位で算出、1 日単位で集計した。

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。なお、妊娠 25 日の 10 時までには分娩が終了しなかった 20 mg/kg 投与群の 1 例（動物番号：2109）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、病理学検査に供した。妊娠の有無を確認した結果、着床が認められなかったため不妊とみなした。

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、それぞれ外表異常の有無を観察^{注)}し、性別を判定して体重を測定した。出生児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。死亡児は肉眼による異常の有無を観察した後、ブアン液で固定し保存した。

生後 4 日に全生存児の性別を判定し、個体別に体重を測定後、肉眼による異常の有無を観察した後、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、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。

5.11.8 尿検査（摂水量測定を含む）

投与期間終了週（投与 6 週、投与 36~37 日）及び回復期間終了週（回復 2 週、回復 8~9 日）に検査を実施した。投与期間中は検査当日の投与後に、雄では群内番号 8~12 番、非交配群では群内番号 18~22 番の各群それぞれ 5 匹を、回復期間中は回復動物の全個体を、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、その後得られた 20 時間尿について浸透圧及び電解質（ナトリウム、カリウム、塩素）と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。摂水量は、採尿器をセットしたケージに収容した状態で前日からの 1 日の摂取量を、給水瓶を用いて測定した。

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	マルティステックス試験紙 [シーメンスヘルスケア・タグ・イアグ・ノスティクス株式会社] a)
たん白質	マルティステックス試験紙 [シーメンスヘルスケア・タグ・イアグ・ノスティクス株式会社] a)
ケトン体	マルティステックス試験紙 [シーメンスヘルスケア・タグ・イアグ・ノスティクス株式会社] a)
グルコース	マルティステックス試験紙 [シーメンスヘルスケア・タグ・イアグ・ノスティクス株式会社] a)
潜血	マルティステックス試験紙 [シーメンスヘルスケア・タグ・イアグ・ノスティクス株式会社] a)
ビリルビン	マルティステックス試験紙 [シーメンスヘルスケア・タグ・イアグ・ノスティクス株式会社] a)
ウロビリノーゲン	マルティステックス試験紙 [シーメンスヘルスケア・タグ・イアグ・ノスティクス株式会社] 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）	メスシリンダーを用いた容量測定（単位：mL）
摂水量（24 時間量）	重量測定
使用測定機器	
a)：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-6030 (アークレイ株式会社)	
c)：臨床化学自動分析装置 TBA-I20FR 形 (東芝メディカルシステムズ株式会社)	

5.11.9 血液学検査

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（16~21 時間）絶食させた。各群雌雄各 5 匹（動物番号が若い順、但し、交配群雌は分娩順の 5 匹^注）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。得られた血液について、次の表 3.-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、1,600×g、10 分間）し、得られた血漿について表 3.-2)に記載の項目及び方法により検査した。未交尾雌動物及び妊娠 25 日未分娩動物についても採血し同様に検査した。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。

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、1103、1104、1108、1110
低用量群	2102、2103、2106、2108、2111
中用量群	3102、3104、3106、3107、3112
高用量群	4101、4102、4103、4104、4111

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(Hb)	シアンメトヘモグロビン変法 ^{a)}	g/dL
ヘマトクリット値(Ht)	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(Reticulocyte)	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(Platelet)	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(Fibrinogen)	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 420 (Siemens Healthcare Diagnostics Inc., Illinois, USA)		
b)：血液凝固自動測定装置 ACL Elite Pro (Instrumentation Laboratory, MA, USA)		
注)：好中球(Neut.)、好酸球(Eosino.)、好塩基球(Baso.)、リンパ球(Lymph.)、単球(Mono.) 及び大型非染色球(LUC)		

5.11.10 血液化学検査

血液学検査用試料と同時に採取した血液（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、1,670×g、10 分間）し、得られた血清について表 4.-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（約 2 mL）を遠心分離（3,000 rpm、1,600×g、10 分間）して得られた血漿について表 4.-2)に記載の項目及び方法により検査した。未交尾雌動物及び妊娠 25 日未分娩動物についても同様に検査した。血清の一部は血中ホルモン測定に備え、約 0.5 mL×3 本をサンプルチューブに分注し、-80℃の冷凍庫（許容範囲：-70℃以下）に保存した。

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 (TBA)	3 α -ヒドロキシステロイドデヒドロゲナーゼ ^{a)}	μ mol/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.bilirubin)	ビリルビンオキシダーゼ法 ^{a)}	mg/dL
グルコース(Glucose)	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(Creatinine)	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)	モリブデン酸法 ^{a)}	mg/dL
総たん白質(TP)	Biuret 法 ^{a)}	g/dL
アルブミン(Albumin)	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(GOT)	UV-rate 法 ^{a)}	IU/L
ALT(GPT)	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）		

5.11.11 血中ホルモン測定

他の観察及び検査結果から下垂体-甲状腺系への影響が認められなかったため 6.11.10 で得られた血清について血中ホルモン（T₃、T₄及び TSH）測定は実施しなかった。

5.11.12 病理学検査

1) 剖検及び器官重量測定

最終投与翌日及び回復期間終了日に全ての生存動物について、採血した動物は採血後に、その他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、それぞれ体外表並びに頭部、胸部及び腹部の器官・組織の肉眼検査を行った。なお、母動物については剖検時に黄体数及び着床痕数を数えた。次いで、全例について、以下に示す器官の重量を測定した。それら器官重量（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。未交尾雌動物及び妊娠 25 日未分娩動物については、採血して放血致死させた後、同様に剖検を行い器官の重量を測定した。

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）、卵巢*、子宮

2) 病理組織学検査

全ての個体について、以下に示す全検査対象器官/組織をリン酸緩衝 10 vol%ホルマリン液で固定し、保存した。固定時に肺にはリン酸緩衝 10 vol%ホルマリン液を注入した。ただし、眼球、視神経はリン酸緩衝液で調製した 3 vol%グルタルアルデヒド・2.5 vol%ホルマリン液で固定後、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 vol%ホルマリン液に置換し保存した。次いで、パラフィン包埋した後、切片とし（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）染色標本作製した。鏡検は、まず投与終了時剖検群における対照群及び高用量群の採血を行った動物、妊娠 25 日未分娩動物及び未交尾雌雄の全検査対象器官/組織について行った。両側性の器官については両側を摘出し、坐骨神経、眼球、甲状腺、上皮小体、副腎、顎下腺、腎臓、大腿骨（骨髄を含む）及び大腿部骨格筋は片側、精巣、卵巢、精巣上体及び精嚢（凝固腺含む）は両側並びに子宮は両角部を鏡検した。なお、舌下腺及び視神経は H・E 染色標本作製までとし、病理組織学検査は実施しなかった。その結果、高用量群の雄の腎臓及び雌雄の胃に被験物質投与による影響が疑われたため、中及び低用量群並びに回復終了時剖検群の当該組織について鏡検した。また、回復期間終了時の器官重量測定において対照群と比べ 500 mg/kg 投与群の雄で胸腺重量に有意な低値、雌で子宮重量に有意な高値が認められたことから、回復動物の雄の胸腺及び雌の子宮の病理組織学検査を実施した。

大脳、小脳（橋を含む）、坐骨神経、脊髄（胸部）、眼球、視神経、ハーダー腺、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、胸大動脈、気管、肺（気管支を含む）、舌、喉頭、食道、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、脾臓、腎臓、膀胱、精巣、卵巢、精巣上体、子宮、陰、前立腺、精嚢（凝固腺を

含む)、皮膚(鼠径部)、乳腺(鼠径部)、胸骨(骨髄を含む)、大腿骨(骨髄を含む)、大腿部骨格筋、個体識別部(耳標を装着した耳介)

5.12 統計解析

5.12.1 パラメータの算出

以下の式により交尾率、授精率、受胎率及び出産率を群ごとに、妊娠期間、着床率、死産児率、外表異常率、出生率、生後4日生存率、生後0及び4日の出生児の性比を母動物ごとに算出した。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。

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

着床率(%) = (着床痕数/黄体数) × 100

死産児率(%) = (死産児数/出生児数及び死産児数) × 100

外表異常率(%) = (外表異常児数/出生児数及び死産児数) × 100

出生率(%) = (出生児数/着床痕数) × 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日の性比 = 雄出生児数/出生児数

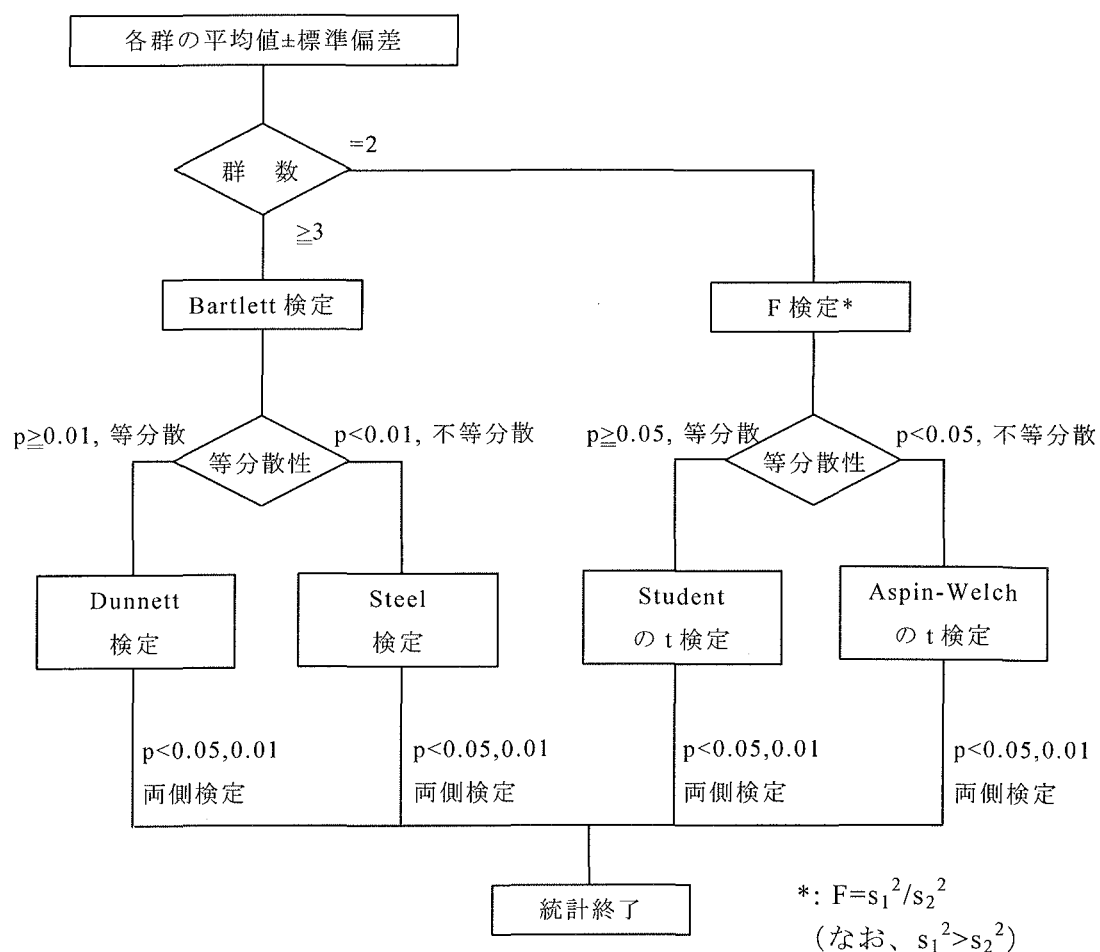
生後4日の性比 = 生後4日の雄生存児数/生後4日の生存児数

5.12.2 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。

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、摂水量、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、出生児の性比(生後0及び4日)、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]。

なお、交尾不成立あるいは不妊と判断された雌の交配開始後の交配成績を除くデータは統計解析より除外した。



着床率、死産児率、外表異常率、出生率及び生後4日生存率については、群ごとに平均値及び標準偏差を求め、Steel検定(有意水準0.05及び0.01、両側)を行った[5]。

交尾率、授精率、受胎率、出産率、聴覚反応、接近反応、接触反応、痛覚反応、瞳孔反射、空中正向反射は、各群の交尾動物数、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、正常反射のみられた動物数より算出し、期待度数が5以下のセルがみられたため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[6]。

6. 試験結果

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

500 mg/kg 投与群では、よろめき歩行が雄で投与 38 日に 1 例、交配群雌で投与 2 日以降、1 例に散見され、腹臥/横臥が交配群雌で投与 10 日以降 1~2 例に散見された。

その他いずれの動物にも投与期間及び回復期間を通じて異常はみられなかった。

6.2 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. 1~5、Table 2-1~2-84、Appendix 2-1~2-258)

6.2.1 ホームケージ内観察 (Table 2-1~2-23、Appendix 2-1~2-72)

いずれの動物にも異常はみられなかった。

6.2.2 手に持つての観察 (Table 2-24~2-46、Appendix 2-73~2-144)

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。

6.2.3 オープンフィールド内観察 (Table 2-47~2-69、Appendix 2-145~2-216)

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。また、排糞の個数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。

20 mg/kg 投与群の雄で投与 3 週に立ち上がり回数が対照群と比べ有意な高値を示したが、用量に依存性のない変化であった。

6.2.4 機能検査 (Table 2-70~2-74、Appendix 2-217~2-230)

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に異常はみられず、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に異常はみられず、着地開脚幅には対照群と 500 mg/kg 投与群との間に有意差は認められなかった。

6.2.5 握力 (Table 2-75~2-79、Appendix 2-231~2-244)

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 500 mg/kg 投与群との間に有意差は認められなかった。

6.2.6 自発運動量 (Fig. 1~5、Table 2-80~2-84、Appendix 2-245~2-258)

1) 投与期間終了週測定

20 mg/kg 投与群の雄で 40-50 分の間の運動量に对照群と比べ有意な高値、100 mg/kg 投与群の雄で 30-40 分の運動量に对照群と比べ有意な低値が認められたが、いずれも用量に依存性のない変化であった。

交配群雌の 500 mg/kg 投与群で 0-10 及び 10-20 分の間の運動量に对照群と比べ有意な低値が認められた。

非交配群雌では对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

对照群と 500 mg/kg 投与群との間に有意差は認められなかった。

6.3 体重 (Fig. 6~8、Table 3-1~3-7、Appendix 3-1~3-22)

1) 投与期間

雄及び非交配群雌では、各被験物質投与群ともに对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。

交配群雌では、交配前、妊娠及び授乳の各期間中、各被験物質投与群ともに对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

对照群と 500 mg/kg 投与群との間に有意差は認められなかった。

6.4 摂餌量 (Fig. 9~11、Table 4-1~4-7、Appendix 4-1~4-22)

1) 投与期間

500 mg/kg 投与群の雄で投与 15 日に、非交配群雌で投与 8 及び 36 日に对照群と比べ有意な高値、非交配群雌で投与 42 日に对照群と比べ有意な低値が認められたが、軽度な一過性の変化であり、偶発性と判断した。

交配群雌では、各被験物質投与群ともに妊娠及び授乳期間を含め投与期間中の各測定時点の摂餌量は对照群と同等な値を示し、有意差は認められなかった。

2) 回復期間

对照群と 500 mg/kg 投与群との間に有意差は認められなかった。

6.5 尿検査 (摂水量測定を含む) (Table 5-1~5-16、Appendix 5-1~5-30)

1) 投与期間終了週検査

定性項目については、500 mg/kg 投与群の雌雄で尿 pH の低値傾向がみられた。その他の項目には異常はみられなかった。

定量項目については、500 mg/kg 投与群の雄で对照群と比べ摂水量に有意な高値が認められた。雌ではいずれの検査項目においても被験物質投与群と对照群との間に有意差は認められなかった。

2) 回復期間終了時検査

定性項目については、500 mg/kg 投与群の雌雄ともに異常はみられなかった。

定量項目については、500 mg/kg 投与群の雌で対照群と比べナトリウム、カリウム及び塩素の排泄量に有意な低値が認められたが、軽微な変化であり投与期間終了時検査には異常はないことから生理的変動範囲内の変化性と判断した。雄ではいずれの検査項目においても 500 mg/kg 投与群と対照群との間に有意差は認められなかった。

6.6 血液学検査 (Table 6-1~6-10、Appendix 6-1~6-10)

1) 投与期間終了時検査

雄では 500 mg/kg 投与群で対照群と比べ白血球分画におけるリンパ球比率の有意な高値、好中球比率の有意な低値が認められた。

交配群雌では 20、100 及び 500 mg/kg 投与群で対照群と比べ白血球分画におけるリンパ球比率の有意な高値、好中球比率の有意な低値が認められた。他に 20 mg/kg 投与群で平均赤血球血色素濃度、白血球分画における大型非染色球比率に対照群と比べ有意な高値が認められたが、用量に依存性のない変化であった。

非交配群雌では 500 mg/kg 投与群で好塩基球の比率及び絶対数に対照群と比べ有意な低値が認められたが、白血球に占める割合の少ない分画におけるわずかな変動であり白血球数等の関連項目に異常はないことから偶発性と判断した。

2) 回復期間終了時検査

500 mg/kg 投与群の雄ではいずれの検査項目においても対照群との間に有意差は認められなかった。

500 mg/kg 投与群の雌でフィブリノーゲン量に対照群と比べ有意な高値が認められたが、投与期間終了時検査にみられない軽微な変化であり、他の血液凝固系項目に異常はみられないことから偶発性と判断した。

6.7 血液化学検査 (Table 7-1~7-10、Appendix 7-1~7-10)

1) 投与期間終了時検査

雄では 20 mg/kg 投与群で対照群と比べ LDH に有意な高値、100 mg/kg 投与群で無機リンに有意な高値が認められたが、いずれも軽微な変化であり用量に依存性のない変化であることから偶発性と判断した。

交配群雌ではいずれの検査項目においても各被験物質投与群と対照群との間に有意差は認められなかった。

非交配群雌では 500 mg/kg 投与群でグルコースに対照群と比べ有意な低値が認められた。同群でナトリウムの有意な低値が認められたが、軽微な変化でありカリウム及び塩素に変動はないことから偶発性と判断した。

2) 回復期間終了時検査

500 mg/kg 投与群の雄ではいずれの検査項目においても対照群との間に有意差は認

められなかった。

500 mg/kg 投与群の雌で総コレステロール及びリン脂質に対照群と比べ有意な高値が認められたが、軽微な変化であり投与期間終了時検査に同変化はみられないことから偶発性と判断した。

6.8 器官重量 (Table 8-1~8-12、Appendix 8-1~8-42)

1) 投与期間終了時検査

被験物質投与との関連性が疑われる変化が肝臓、腎臓、副腎及び子宮に認められた。

肝臓	:	500 mg/kg 投与群の雌雄で対照群と比べ相対重量に有意な高値が認められた。
腎臓	:	雄の 100 mg/kg 投与群で対照群と比べ相対重量に、500 mg/kg 投与群で絶対及び相対重量に有意な高値が認められた。
副腎	:	非交配群雌の 500 mg/kg 投与群で対照群と比べ絶対及び相対重量に有意な高値が認められた。
子宮	:	非交配群雌の 500 mg/kg 投与群で対照群と比べ絶対及び相対重量に有意な低値が認められた。

その他に対照群と比べ雄の 100 mg/kg 投与群で心臓の絶対及び相対重量に有意な低値が認められたが用量に依存性のない変化であることから偶発性と判断した。交配群雌の 20 及び 500mg/kg 投与群で脳の絶対重量に有意な低値が認められたが、相対重量に変動はなく明確な用量との相関性はみられないため偶発性と判断した。

2) 回復期間終了時検査

500 mg/kg 投与群の雄で対照群と比べ胸腺の絶対及び相対重量に有意な低値が認められた。他に脾臓の相対重量に有意な低値が認められたが、軽微な変化であり投与期間終了時には異常はみられていないため偶発性と判断した。

500 mg/kg 投与群の雌で対照群と比べ肝臓の相対重量に有意な高値、子宮の絶対及び相対重量に有意な高値が認められた。

6.9 剖検所見 (Table 9-1~9-5、Appendix 9-1~9-116)

1) 投与期間終了時検査

被験物質投与の影響と考えられる変化として 500 mg/kg 投与群の雄で胃に境界縁の肥厚が 6/7 例にみられた。なお、100 mg/kg 群の雄 1 例で肉眼的にみられた胃の境界縁の肥厚については、病理組織学的変化がなんら認められず、また、標本作製時にも病変の確認ができなかったことから、被験物質投与の影響としなかった。

その他に Table 及び Appendix に示したいくつかの器官・組織に肉眼的異常がみられたが、その発現状況あるいは病理学的性状から偶発性変化と判断した。

妊娠 25 日未分娩 (不妊) であった 20 mg/kg 投与群の 1 例 (動物番号: 2109) と未交尾 (不妊) であった 100 mg/kg 投与群の雌 1 例 (動物番号: 3111) では肉眼的異常

はみられなかった。

2) 回復期間終了時検査

Table 及び Appendix に示す所見がみられたが、いずれもその発現状況あるいは病理学的性状から偶発性変化と判断した。

6.10 病理組織学検査 (Table 10-1~10-13、Appendix 9-1~9-116)

1) 投与期間終了時検査

被験物質投与に起因する考えられる変化が腎臓及び胃にみられた。

- 腎臓 : 100 及び 500 mg/kg 投与群の雄で軽微又は軽度な顆粒円柱がみられ、尿細管の再生及び上皮細胞内の好酸性小体の発生頻度及び程度が増加した。500 mg/kg 投与群の雄では加えて軽微な尿細管の拡張及び上皮細胞の壊死/剥離がみられた。なお、尿細管の再生、尿細管上皮細胞内の好酸性小体及び壊死/剥離は、近位尿細管にみられ、顆粒円柱は髄質外帯にみられた。
- 胃 : 500 mg/kg 群の雄及び非交配群雌で軽微な境界縁の扁平上皮細胞過形成がみられた。

妊娠 25 日未分娩 (不妊) であった 20 mg/kg 投与群の 1 例 (動物番号 : 2109) と交尾の成立しなかった 100 mg/kg 投与群の 1 組 (動物番号 : 3011 及び 3111) については、いずれも被験物質投与の影響並びに不妊及び交尾不成立の原因と考えられる組織学的変化はみられなかった。

なお、500 mg/kg 投与群のみに眼球で網膜異形成、盲腸及び脾臓で細胞浸潤、精巣で精細管の萎縮がみられたが、いずれも 1 例のみ発現であり、時折、背景的にみられる変化であることから、偶発性変化と判断した。

Table 及び Appendix に示すその他の所見は、出現状況あるいは病理組織学的性状から偶発性変化と判断した。

2) 回復期間終了時検査

- 腎臓 : 尿細管の拡張及び上皮細胞の壊死/剥離は認められなかったが、尿細管上皮細胞内の好酸性小体及び顆粒円柱は依然として観察された。しかし、その発生頻度及び程度は減少した。尿細管の再生は、投与期間終了時検査と同程度にみられた。
- 胃 : 境界縁の扁平上皮細胞過形成は雄の対照群及び 500 mg/kg 投与群に各 1 例ずつみられ、雌では観察されなかった。

器官重量において変化のみられた 500 mg/kg 群の雄の胸腺及び雌の子宮については、対照群との間に組織学的差異は認められなかった。

Table 及び Appendix に示す所見がみられたが、いずれもその発現状況あるいは病理

組織学的性状から偶発性変化と判断した。

6.11 性周期 (Table 11、Appendix 10-1~10-4)

性周期異常の動物はみられず、発情期像発現回数及び平均性周期日数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。

6.12 交配成績 (Table 12、Appendix 11-1~11-4)

交尾までに要した日数、交尾率、授精率及び受胎率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。

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

出産率、妊娠期間、黄体数、着床痕数、着床率、死産児率、出生児数、外表異常率及び出生率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。

妊娠動物の分娩状態では妊娠 21~23 日の間に全例が分娩し、胎盤及び羊膜の処理は正常に行われ、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。

6.14 出生児の生存率 (Table 14、Appendix 13-1~13-4)

生後 4 日の生存率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。

6.15 出生児の性比 (Table 15、Appendix 14-1~14-4)

生後 0 及び 4 日の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。

6.16 出生児の体重 (Table 16、Appendix 15-1~15-4)

生後 0 及び 4 日の雌雄体重並びに生後 0~4 日の間の体重増加量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。

6.17 出生児の生後 4 日肉眼観察所見 (Table 17、Appendix 16-1~16-4)

いずれの出生児にも肉眼的異常はみられなかった。

7. 考察

1,3-Propanediol, 2-butyl-2-ethyl の 0 (対照群 : 0.5 w/v%MC 溶液)、20、100 及び 500 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)、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 500 mg/kg 投与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、毒性変化の可逆性を検討した。

7.1 反復投与毒性

いずれの投与群においても死亡動物はみられず、詳細な一般状態、機能検査、握力、体重及び摂餌量には被験物質投与の影響は認められなかった。

一般状態観察では、よろめき歩行が 500 mg/kg 投与群の雌雄で、腹臥/横臥が交配群雌で散見された。回復期間ではこれらの変化はみられず、回復性が認められた。

自発運動量測定では、交配群雌の 500 mg/kg 投与群で 0-20 分の間の運動量に低値が認められた。本試験では一般状態の異常として捉えることが出来得る程度の自発運動の減少はみられなかったが、自発運動量測定で認められた変化は、一般状態観察でみられたよろめき歩行及び腹臥/横臥に関連した変化と推察され、被験物質投与による影響と考えられた。回復期間ではこれらの変化はみられず、回復性が認められた。

尿検査では、投与期間終了時検査で 500 mg/kg 投与群の雌雄で尿 pH の低値傾向、雄で摂水量に高値が認められた。尿 pH の低下の機序は不明だが、被験物質投与の影響と判断した。摂水量の高値については、尿量、尿浸透圧並びに尿及び血中電解質バランスに異常はみられないことから毒性学的意義は低いと考えられた。回復期間ではこれらの変化はみられず、回復性が認められた。

血液学検査では、雄の 500 mg/kg 投与群と交配群雌の 20、100 及び 500 mg/kg 投与群でリンパ球比率の高値及び好中球比率の低値が認められた。いずれも絶対数に統計学的有意差はないものの変化がみられることから、被験物質投与の影響と判断したが、白血球数等の関連項目に異常はないため、毒性学的意義は低いと考えられた。回復期間ではこれらの変化はみられず、回復性が認められた。

血液化学検査では、非交配群雌の 500 mg/kg 投与群でグルコースに低値が認められたが、軽微な変化であり血糖調節に関連する下垂体、甲状腺、副腎、肝臓などの病理組織に異常はみられないことから、毒性学的意義は低いと考えられた。回復期間ではこれらの変化はみられず、回復性が認められた。

器官重量では、投与期間終了時検査で 500 mg/kg 投与群の雌雄で肝臓重量に高値が認められたが、血液学及び血液化学検査の関連パラメータに異常はなく重量増加を示唆する組織学的変化もみられないことから、毒性学的意義は低いと考えられた。回復期間終了時検査でも 500 mg/kg 投与群の雌で肝臓重量の高値が認められたが、程度は

減弱し回復性が窺われた。非交配群雌の 500 mg/kg 投与群で副腎重量に高値、子宮重量に低値が認められたが、いずれも重量変動を示唆する組織学的変化はみられないことから、偶発性と判断した。回復期間終了時に 500 mg/kg 投与群の雄で胸腺重量に低値及び雌で子宮重量に高値が認められたが、いずれも重量変動を示唆する組織学的変化はなく、対照群との間に組織学的差異は認められないことから、偶発性と判断した。

病理学検査では、肉眼的に 500 mg/kg 投与群の雄で胃に境界縁の肥厚がみられ、組織学的に 500 mg/kg 投与群の雄及び非交配群雌で境界縁の扁平上皮細胞過形成がみられた。扁平上皮細胞過形成は、化学物質などを経口投与した際に様々な刺激に対する反応性変化としてみられることがある。本被験物質の刺激性は不明であるが、類似物質において皮膚への軽微な刺激性が報告されていることから[7]、本被験物質が胃粘膜に対し、何らかの刺激性を有する可能性が疑われ、本変化はそれに起因するものと推察された。また、交配群の雌では扁平上皮の過形成がみられなかったが、その原因として、妊娠、分娩及び授乳などの母動物に特有な生理的環境が何らかの影響を及ぼした可能性が考えられた。なお、回復群では雄で対照群と共に各 1 例ずつにみられ、雌では認められなくなり、明らかな回復性を示した。100 及び 500 mg/kg 投与群の雄で腎臓重量に高値が認められ、組織学的に顆粒円柱がみられ、尿細管の再生及び上皮細胞内の好酸性小体の発生頻度及び程度の増加、500 mg/kg 投与群の雄では加えて尿細管の拡張及び上皮細胞の壊死/剥離がみられた。腎臓の組織変化はいずれも雄のみに認められる変化であった。好酸性小体は、背景的に雄ラットの近位尿細管曲部にもしばしばみられ、 $\alpha 2\mu$ グロブリンを含み、様々な化学物質の投与により増加することが知られている[8]。本試験においても、個々の上皮細胞内における好酸性小体の異常な蓄積と、近位尿細管直部までにわたる広範囲な発現が認められ、腎重量増加の一因と考えられた。髓質外帯にみられた顆粒円柱は、上記の好酸性小体を含む尿細管上皮細胞の壊死/剥離による細胞残渣が、尿細管径が細くなるヘンレループにて充満することにより生じるものと考えられた。尿細管の再生の増加及び尿細管の拡張も、雄のみで認められていることから、多量に蓄積した好酸性小体との関連性が窺われた。また、尿細管障害を伴う好酸性小体の増加及び髓質外帯における顆粒円柱の出現は、 $\alpha 2\mu$ グロブリン腎症と類似していることから、同様の機序が疑われた[9][10]。回復群では、尿細管の再生像が投与終了時剖検群と同程度にみられたものの、尿細管上皮細胞の壊死/剥離及び尿細管の拡張が認められなくなり、好酸性小体及び顆粒円柱の程度が減少したことから、回復傾向が窺われた。

7.2 生殖発生毒性

性周期、交尾までに要した日数、交尾率、授精率及び受胎率には被験物質投与の影響は認められなかった。更に、出産率、妊娠期間、黄体数、着床痕数、着床率、死産児率、死産児の外表観察、出生児数及び出生率に被験物質投与の影響は認められず、授乳期間中の哺育状態にも異常が認められないことから、500 mg/kg 投与群においても雌雄動物の交尾能、授精能及び受胎能、母動物の妊娠維持、分娩及び哺育行動など

の生殖機能への影響はないと判断した。

出生児では、生後 0 日の外表観察、生後 0 及び 4 日の雌雄体重並びに性比、生後 4 日の生存率及び肉眼観察所見に被験物質投与による影響は認められなかった。

これらの結果から、本試験条件下で 1,3-Propanediol, 2-butyl-2-ethyl を反復経口投与することにより、500 mg/kg 投与群の雌雄でよろめき歩行がみられ、100 mg/kg 以上の雄で顆粒円柱、尿細管の再生及び尿細管上皮細胞内の好酸性小体の増加が、500 mg/kg の雄で尿細管の拡張及び尿細管上皮細胞の壊死/剥離が、500 mg/kg の雌雄（雌については非交配群のみ）の胃で、境界縁の扁平上皮細胞過形成が惹起された。一方、雌雄親動物及び児動物において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。したがって、本被験物質の雌雄動物における反復投与毒性に対する無影響量及び無毒性量はいずれも雄で 20 mg/kg、雌で 100 mg/kg と判断した。また、雌雄親動物と児動物における生殖発生毒性に対する無影響量及び無毒性量は、雌雄親動物及び児動物でいずれも 500 mg/kg と判断した。

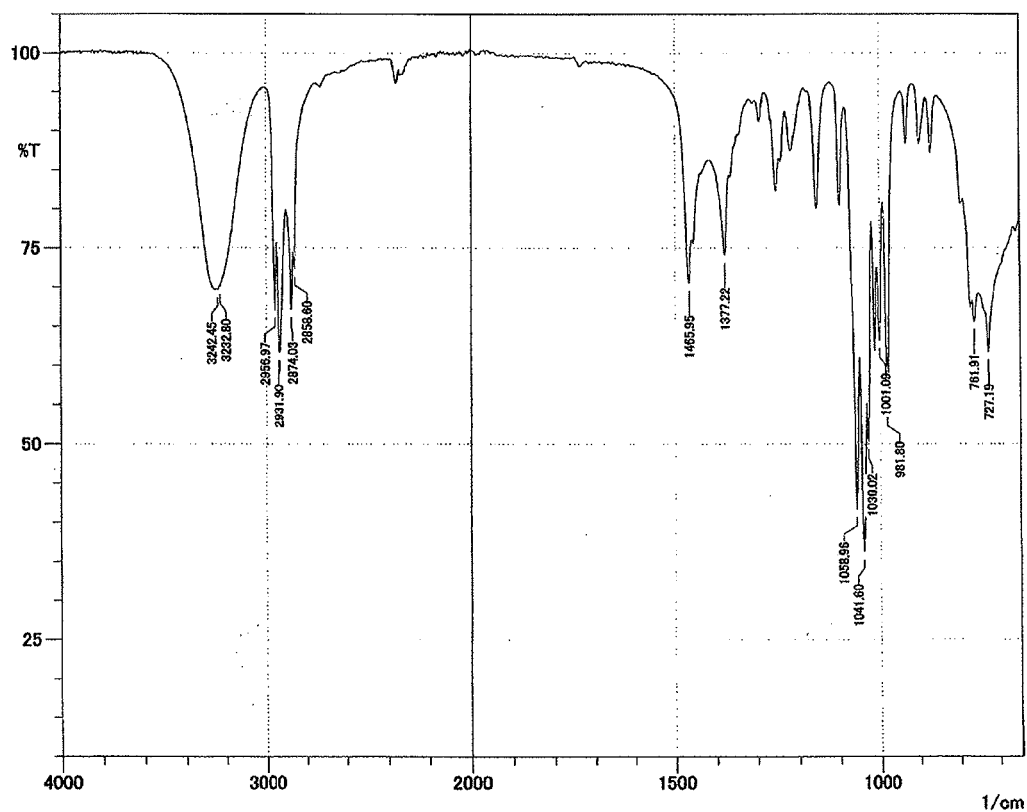
8. 文献

- [1] [REDACTED] 1,3-Propanediol, 2-butyl-2-ethyl の GC を用いた被験液中濃度測定法バリデーション及び均一性・安定性試験（媒体：0.5 w/v%メチルセルローズ溶液）並びに IR を用いた特性及び安定性試験（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-2425、2011 年）
- [2] [REDACTED] 1,3-Propanediol, 2-butyl-2-ethyl のラットを用いた 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-R028、2011 年）
- [3] Snedecor GW, Cochran WG. Statistical methods, 8th ed. Ames: Iowa State University Press; 1989.
- [4] Dunnett CW. A multiple comparison procedure for comparing several treatments with a control. J Am Stat Assoc 1955; 50: 1096-121.
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- [8] Haschek WM, Rousseaux CG, Walling MA. (eds.) Handbook of Toxicologic Pathology. 2nd ed. Academic Press, 2002.
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- [10] Hamamura M, Hirose A, Kamata E, Katoku K, Kuwasaki E, Oshikata T, Nakahara Y, Ema M, Hasegawa R, Semi-quantitative immunohistochemical analysis of male rat-specific α 2u-globulin accumulation for chemical toxicity evaluation, J Toxicol Sci. 2006 Feb;31(1):35-47.

試験番号：A-2425

試験成績書
[被験物質の特性]

ステージ : 実験の実施前
測定日 : 2011 年 10 月 4 日
被験物質 : 1,3-Propanediol, 2-butyl-2-ethyl (ロット番号 BLODO)
試験項目 : 赤外吸収スペクトルの確認 (ATR 法)
結果 : 赤外吸収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)

試験責任者
株式会社ボヅリサーチセンター 御殿場研究所

2011 年 11 月 18 日

測定成績書
(被験物質の安定性)

試験番号 : R-1088

被験物質 : 1,3-Propanediol, 2-butyl-2-ethyl (ロット番号 : BLODO)

測定項目 : 赤外吸収スペクトルの確認 (ATR 法)

ステージ : 投与期間終了後

測定日 : 2012 年 1 月 6 日

判定基準 : 参照スペクトル¹⁾と同一波数のところに同様な強度の吸収を認める。

1) [REDACTED] : 1,3-Propanediol, 2-butyl-2-ethyl の GC を用いた被験液中濃度測定法バリデーション及び均一性・安定性試験 (媒体 : 0.5 w/v% メチルセルロース溶液) 並びに IR を用いた特性及び安定性試験 (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-2425)

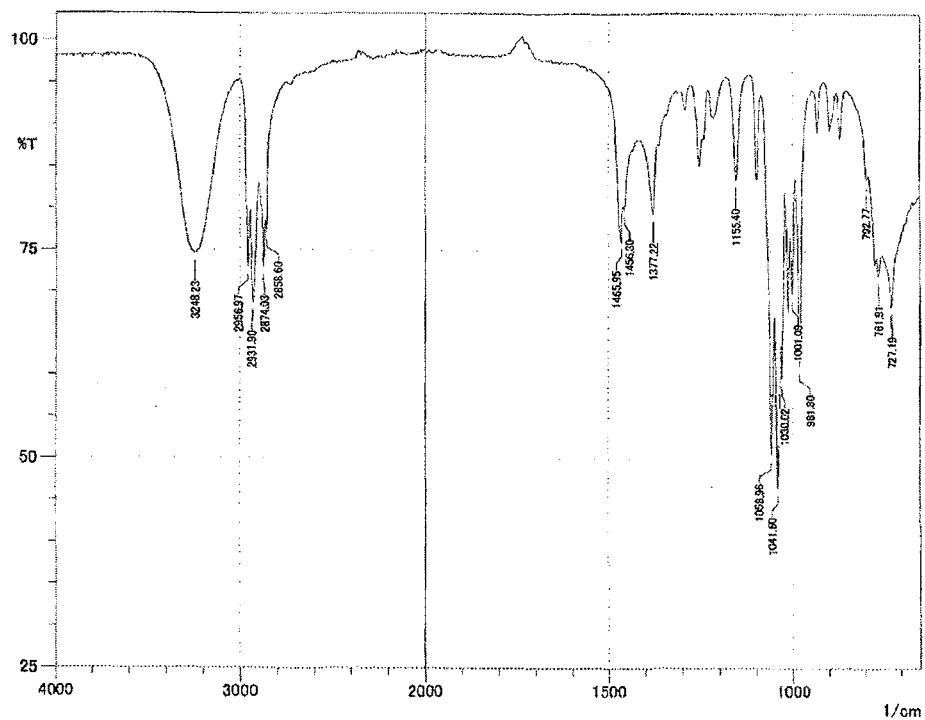
結果 : 参照スペクトルと同一波数のところに同様な強度の吸収を認めた。
なお、赤外吸収スペクトルは次のページに示す。

判定 : 適

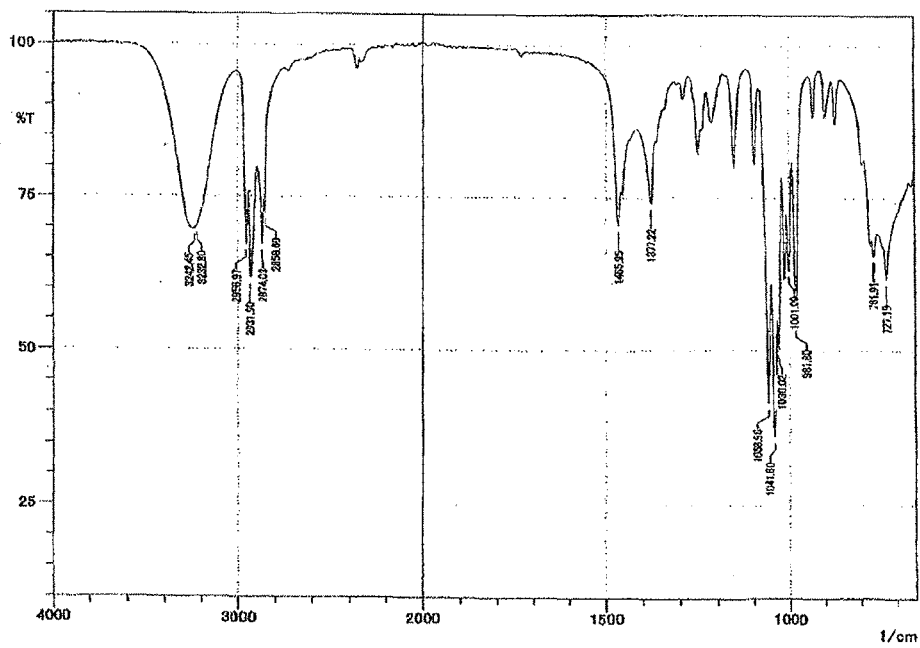
基準 : 「新規化学物質等に係る試験を実施する試験施設に関する基準」 (平成 23 年 3 月 31 日 : 薬食発 0331 第 8 号、平成 23・3・29 製局第 6 号、環保企発第 110331010 号)

[REDACTED] 2012 年 1 月 13 日
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

結果 : 赤外吸収スペクトル



(投与期間終了後)



(参照スペクトル)

試験番号：A-2425

試験成績書

[被験液中 1,3-Propanediol, 2-butyl-2-ethyl の均一性・安定性]

被験物質 : 1,3-Propanediol, 2-butyl-2-ethyl (ロット番号：BLODO)
形態 (媒体) : 懸濁液 (0.5 w/v%メチルセルロース溶液)
評価基準
安定性 : 残存率 {調製直後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 $100.0 \pm 10.0\%$ 以内。
均一性 : 変動係数が 10.0% 以下。
結果：

調製濃度 (mg/mL)	測定濃度 (mg/mL)	
	調製直後	冷所 8 日間 + 室温 24 時間
1.00	0.949	0.891
	0.940	0.911
	0.940	0.877
平均値	0.943	0.893
標準偏差	0.005	0.017
残存率 (%)	100	94.7
変動係数 (%)	0.5	1.9

調製濃度 (mg/mL)	測定濃度 (mg/mL)	
	調製直後	冷所 8 日間 + 室温 24 時間
200	211	203
	211	210
	215	207
平均値	212	207
標準偏差	2	4
残存率 (%)	100	97.5
変動係数 (%)	0.9	1.9

判定 : 被験液中の 1,3-Propanediol, 2-butyl-2-ethyl は、褐色ガラスビン中で冷所 8 日間 + 室温 24 時間保存後の均一性及び安定性が確認された。
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)

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

2021 年 11 月 18 日

分析結果

試験番号 : R-1088
測定項目 : 濃度・均一性
ステージ : 初回投与
分析日 : 2011 年 11 月 4 日

測定試料

被験物質 : 1,3-propanediol,2-butyl-2-ethyl (ロット番号 ; BLODO)
形態 (媒体) : 懸濁液 (0.5 w/v%メチルセルロース溶液)
調製日 : 2011 年 11 月 4 日

評価基準

濃度 : 表示値に対する割合 ; $100.0 \pm 10.0\%$
均一性 : 変動係数 (CV) ; 10.0%以下

結果 :

濃度 (mg/mL)	採取層	測定濃度 (mg/mL)	平均値±標準偏差	表示値に 対する割合 (%)	変動係数 (%)
4	上層	4.02	4.04 ± 0.04	101.0	1.0
	中層	4.08			
	下層	4.01			
20	上層	21.4	21.1 ± 0.3	105.5	1.4
	中層	21.2			
	下層	20.8			
100	上層	107	107 ± 1	107.0	0.9
	中層	108			
	下層	106			

判定 : 適

分析結果

試験番号 : R-1088
測定項目 : 濃度・均一性
ステージ : 投与 6 週
分析日 : 2011 年 12 月 8 日

測定試料

被験物質 : 1,3-propanediol,2-butyl-2-ethyl (ロット番号 ; BLODO)
形態 (媒体) : 懸濁液 (0.5 w/v%メチルセルロース溶液)
調製日 : 2011 年 12 月 8 日

評価基準

濃度 : 表示値に対する割合 ; $100.0 \pm 10.0\%$
均一性 : 変動係数 (CV) ; 10.0%以下

結果 :

濃度 (mg/mL)	採取層	測定濃度 (mg/mL)	平均値±標準偏差	表示値に 対する割合 (%)	変動係数 (%)
4	上層	4.31	4.23 ± 0.08	105.8	1.9
	中層	4.16			
	下層	4.21			
20	上層	19.0	18.9 ± 0.1	94.5	0.5
	中層	18.8			
	下層	18.9			
100	上層	111	106 ± 6	106.0	5.7
	中層	107			
	下層	99.2			

判定 : 適

1,3-Propanediol, 2-butyl-2-ethyl のラットを用いた
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-R028

被験物質		媒体 ^{a)}	1,3-Propanediol, 2-butyl-2-ethyl		
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	0/0	0/0
死亡発現時期		—	—	—	—
一般状態	生存	—	—	よろめき歩行(♀)	よろめき歩行(♂♀) 腹臥/横臥(♂♀)
	死亡	/	/	/	/
体重		/	—	—	—
摂餌量		/	—	—	—
血液学検査		/	—	Retic : ↓↓(♂)	PLT : ↑↑(♂)
血液化学検査		/	—	BUN : ↓↓(♂) TP : ↑(♂)	AST : ↓↓(♂) GLU : ↓(♂)
器官重量	絶対	/	胸腺 : ↓(♂)	胸腺 : ↓(♂)	胸腺 : ↓(♂) 肝臓 : ↑(♂)、↑↑(♀)
	相対	/	胸腺 : ↓(♂)	胸腺 : ↓(♂)	胸腺 : ↓(♂) 肝臓 : ↑(♂)、↑↑(♀) 腎臓 : ↑(♀)
剖検	生存	—	肝臓 : 横隔膜 ヘルニア結節(♀ 1/5)	—	胃(前胃) : 隆起巣(♂2/5、♀4/5) 腎臓 : 大型化(左右、軽度)(♂1/5)
	死亡	/	/	/	/

a) : 0.5w/v%メチルセルロース水溶液

— : 著変なし

/ : データなし又は判別不明あるいは検定不能

↑又は↓ ; p<0.05, ↑↑又は↓↓ ; p<0.01, (対照群との間に有意差あり)

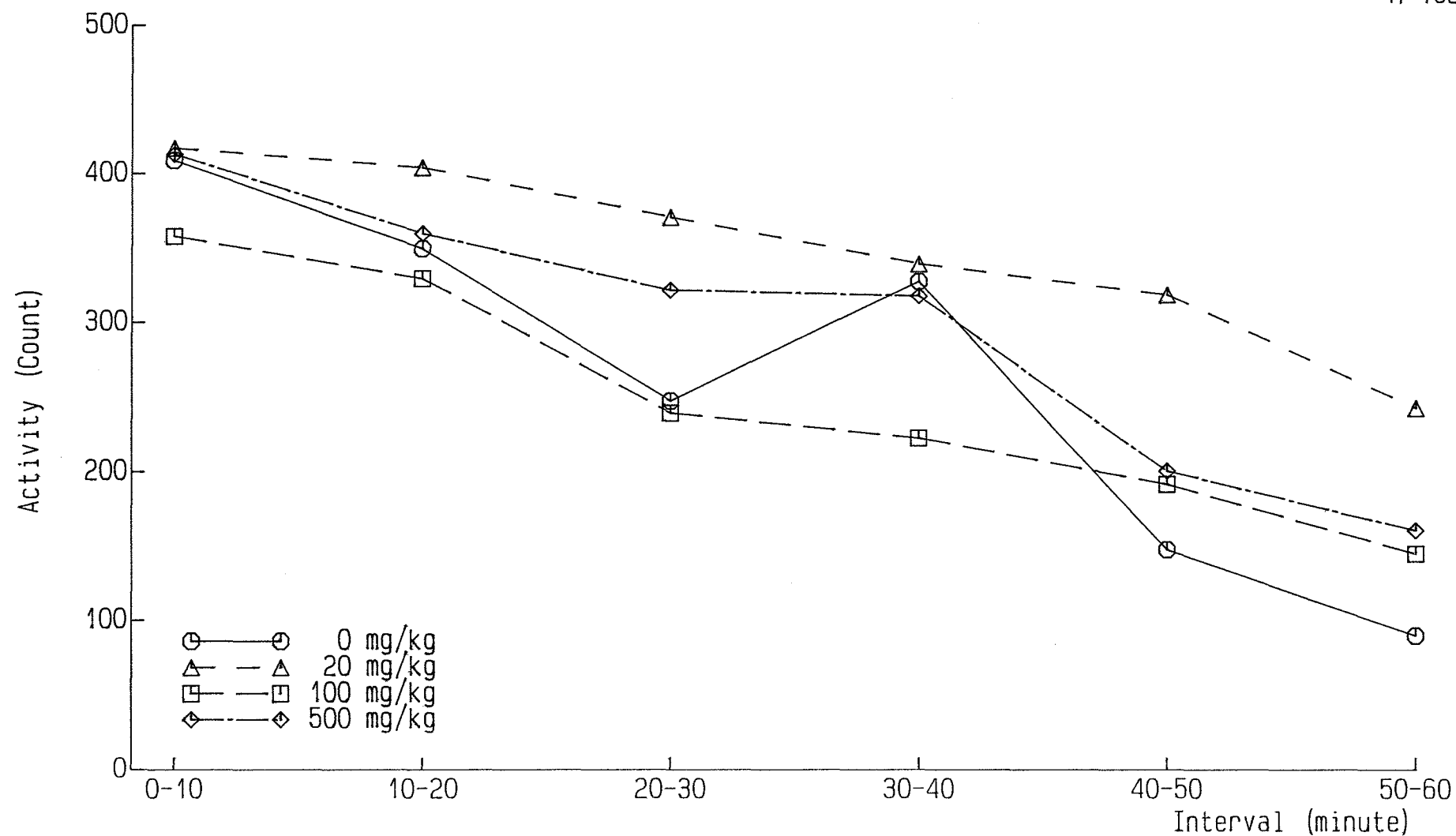


Fig.1 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats
Motor activity of male rats (Week 6 of administration)

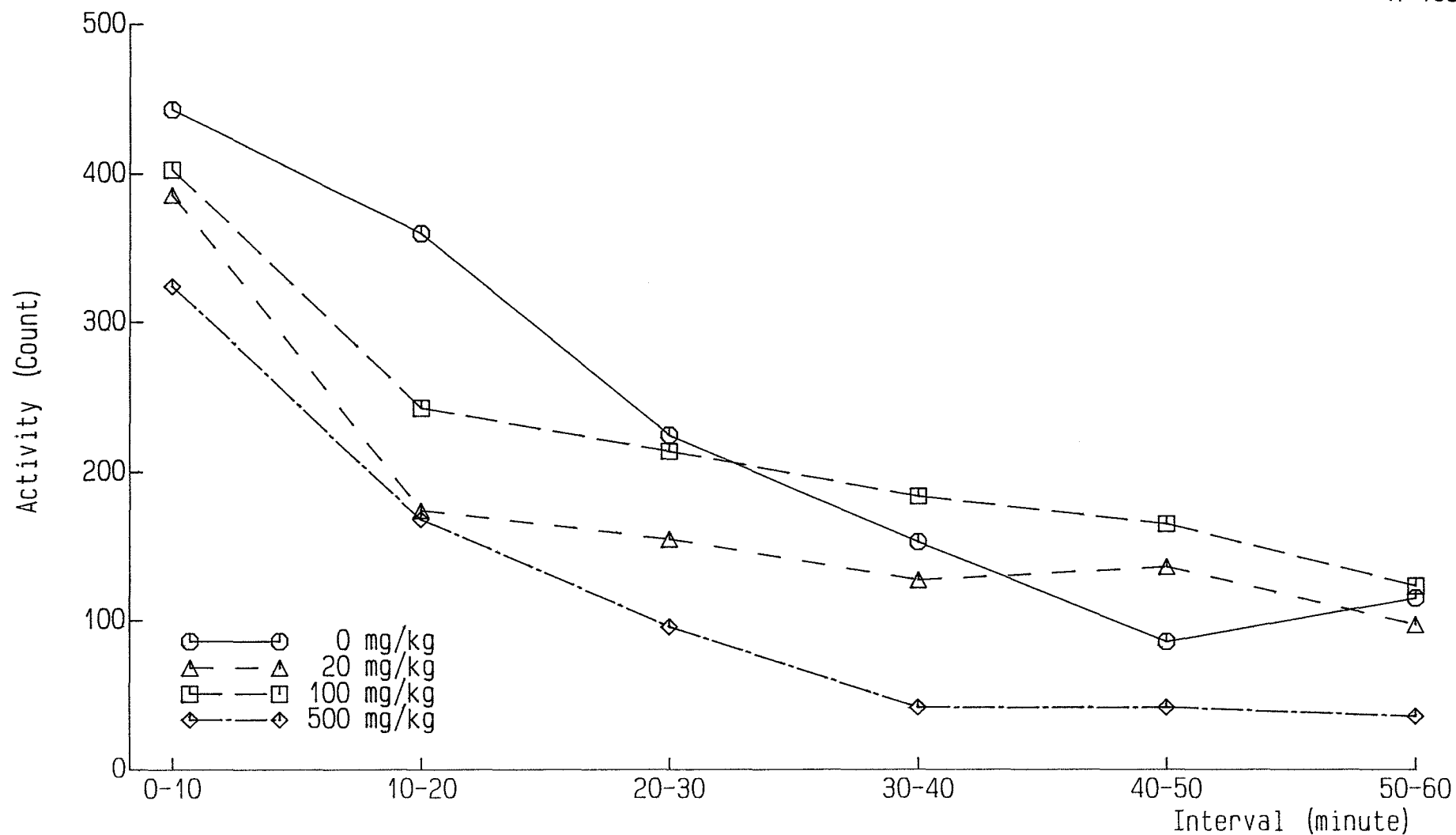


Fig.2 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats
Motor activity of female rats (Main group, Lactation day 4)

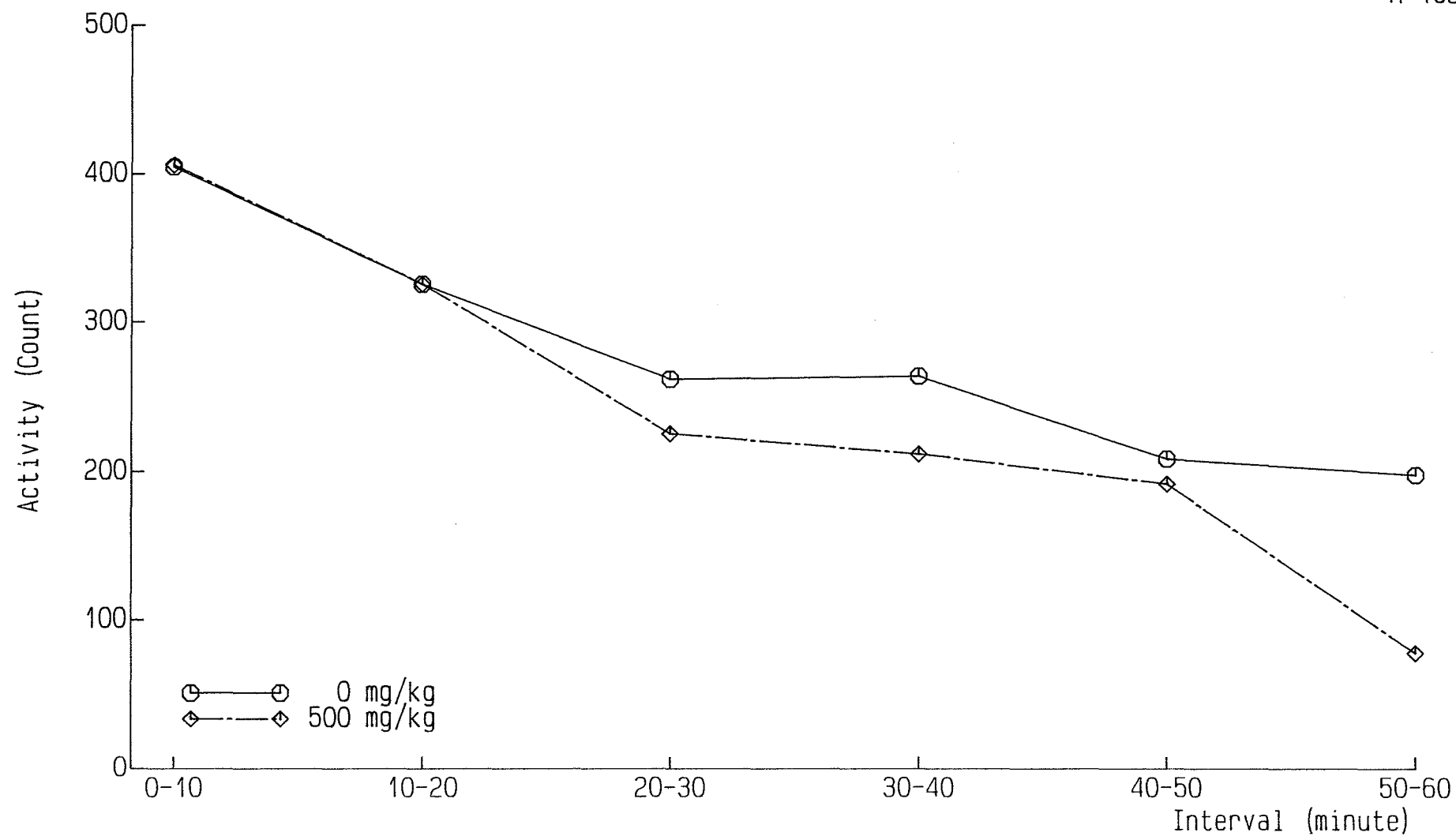


Fig.3 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats
Motor activity of female rats (Satellite group, Week 6 of administration)

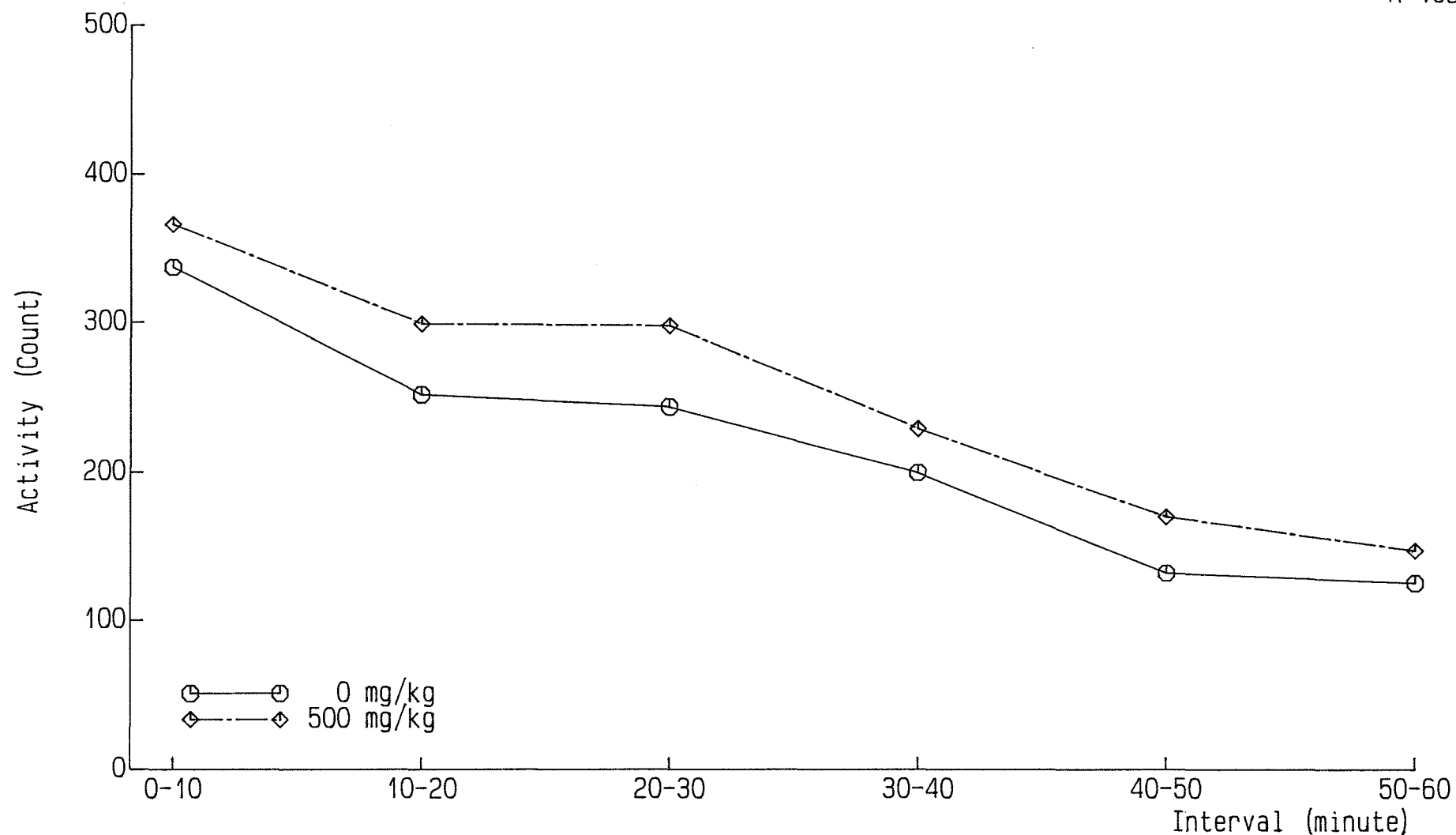


Fig.4 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats
Motor activity of male rats (Week 2 of recovery)

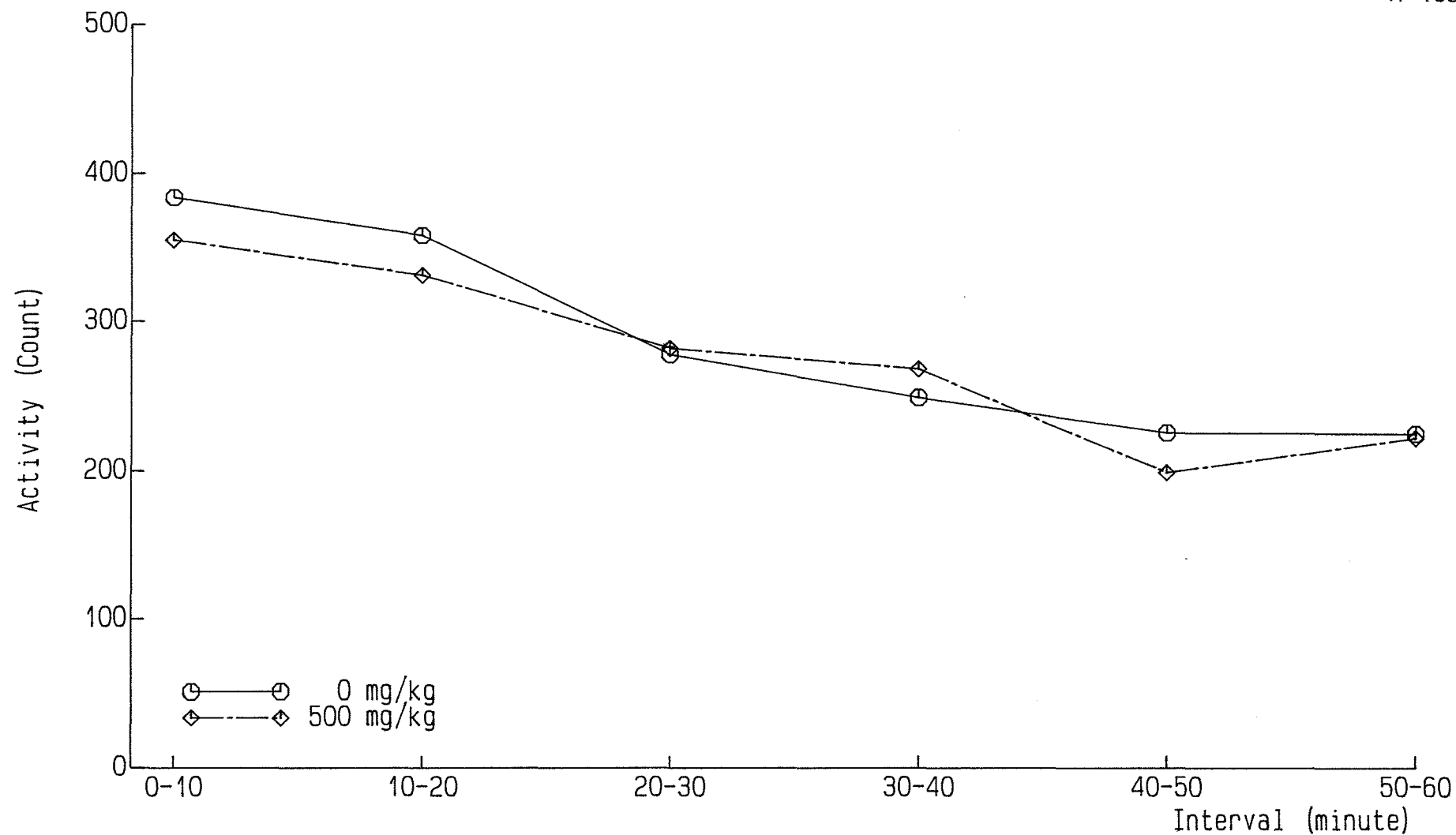


Fig.5 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats
Motor activity of female rats (Week 2 of recovery)

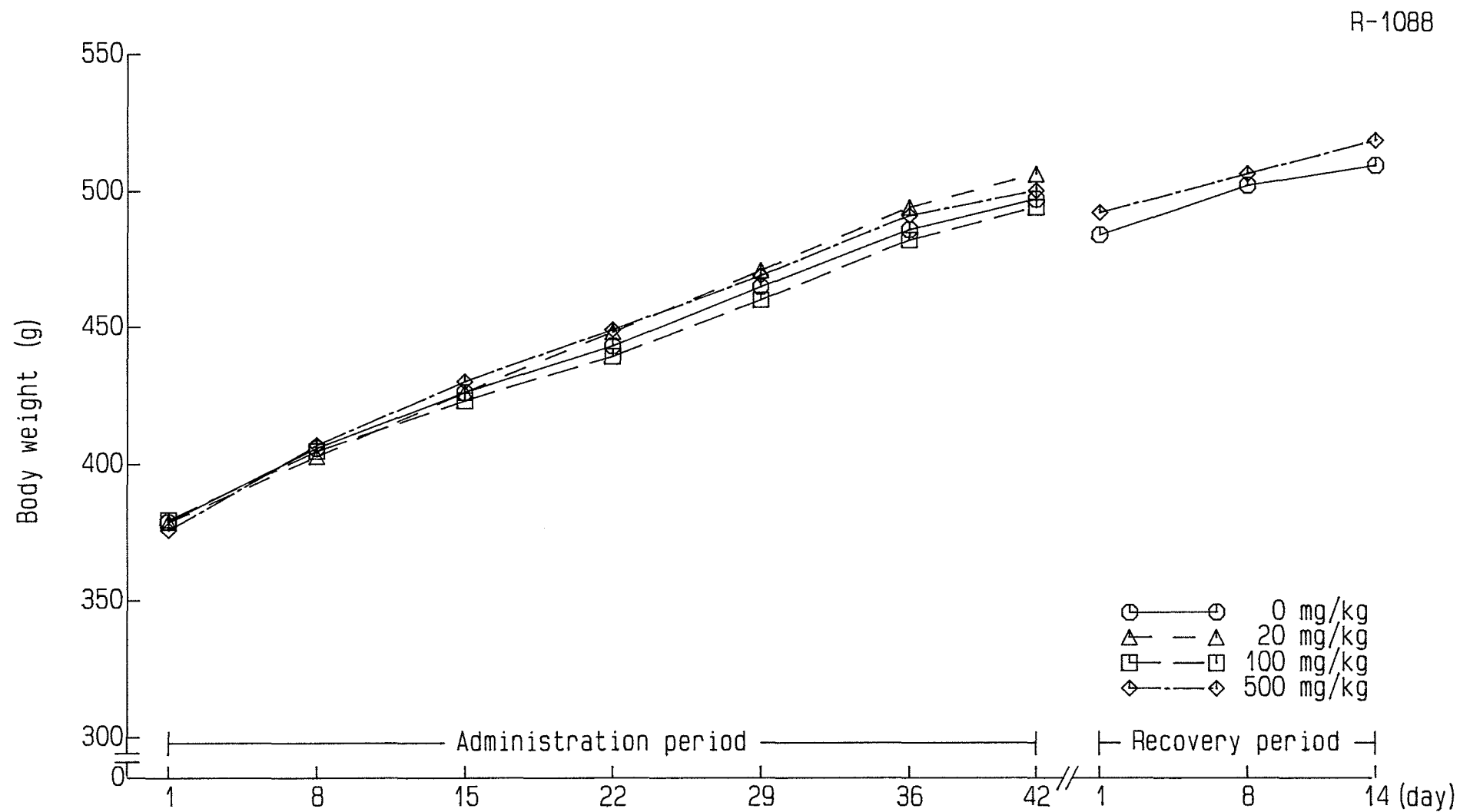


Fig.6 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Body weight of male rats

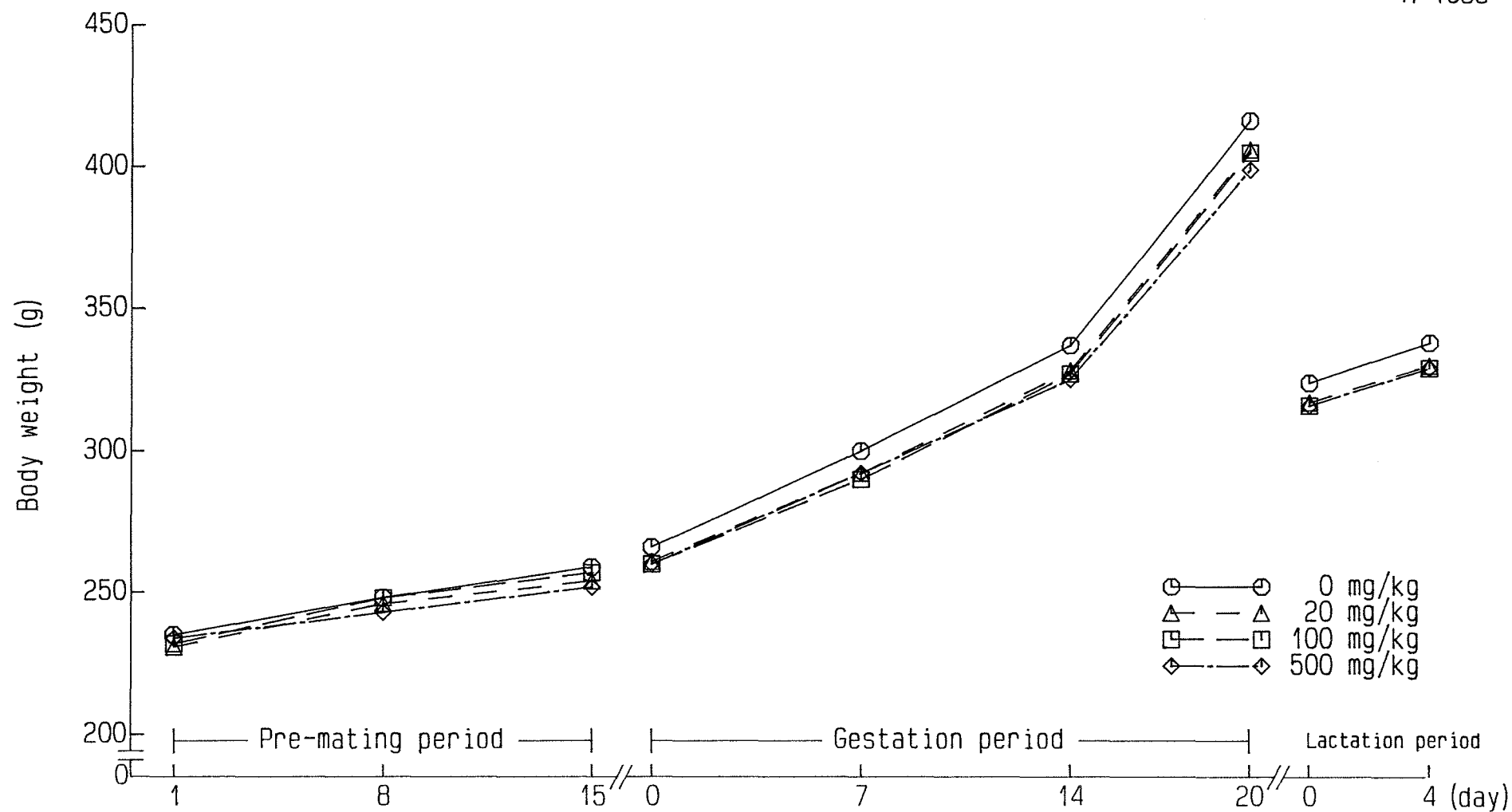


Fig.7 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Body weight of female rats (Main group)

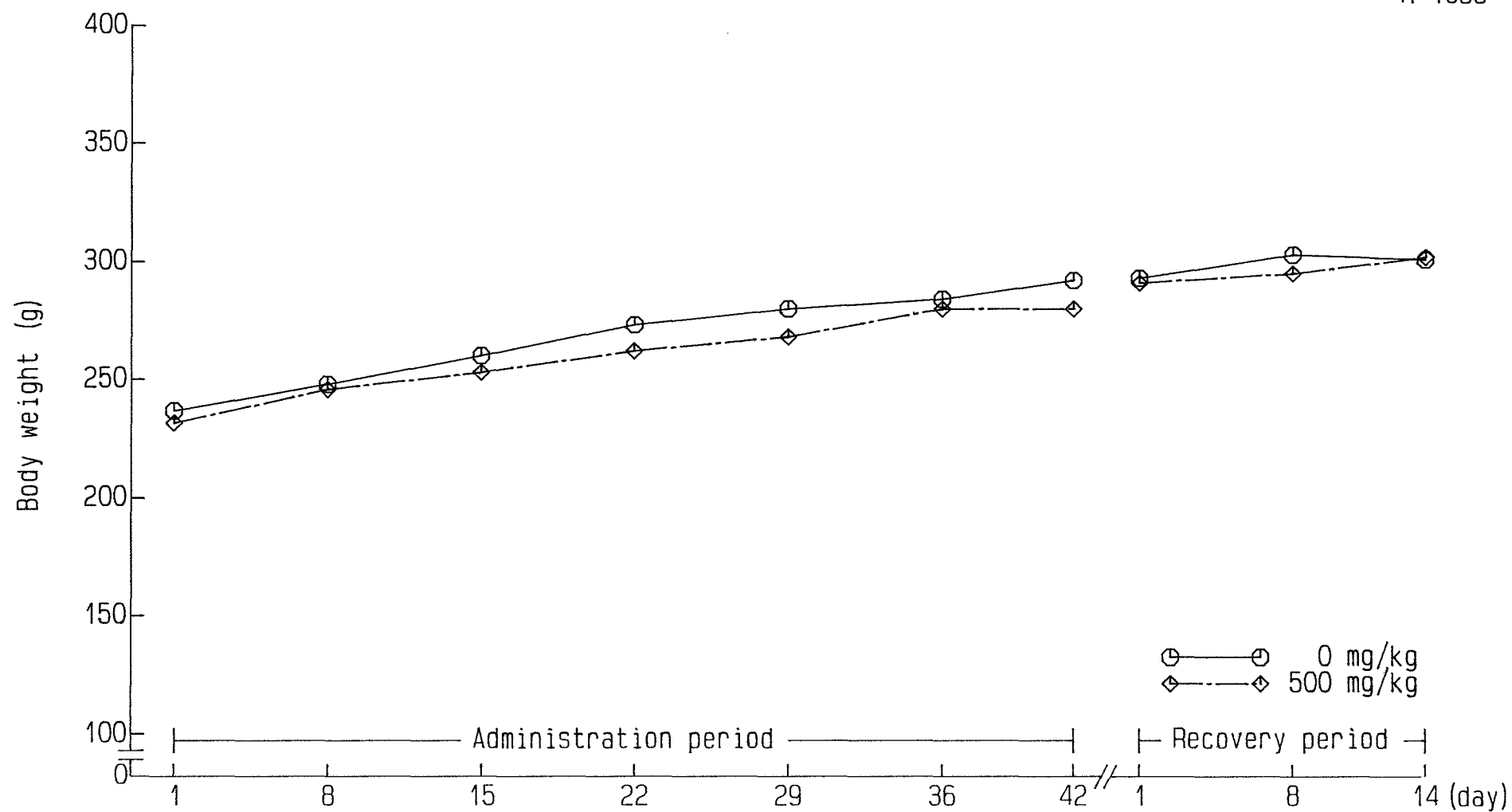


Fig.8 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Body weight of female rats (Satellite group)

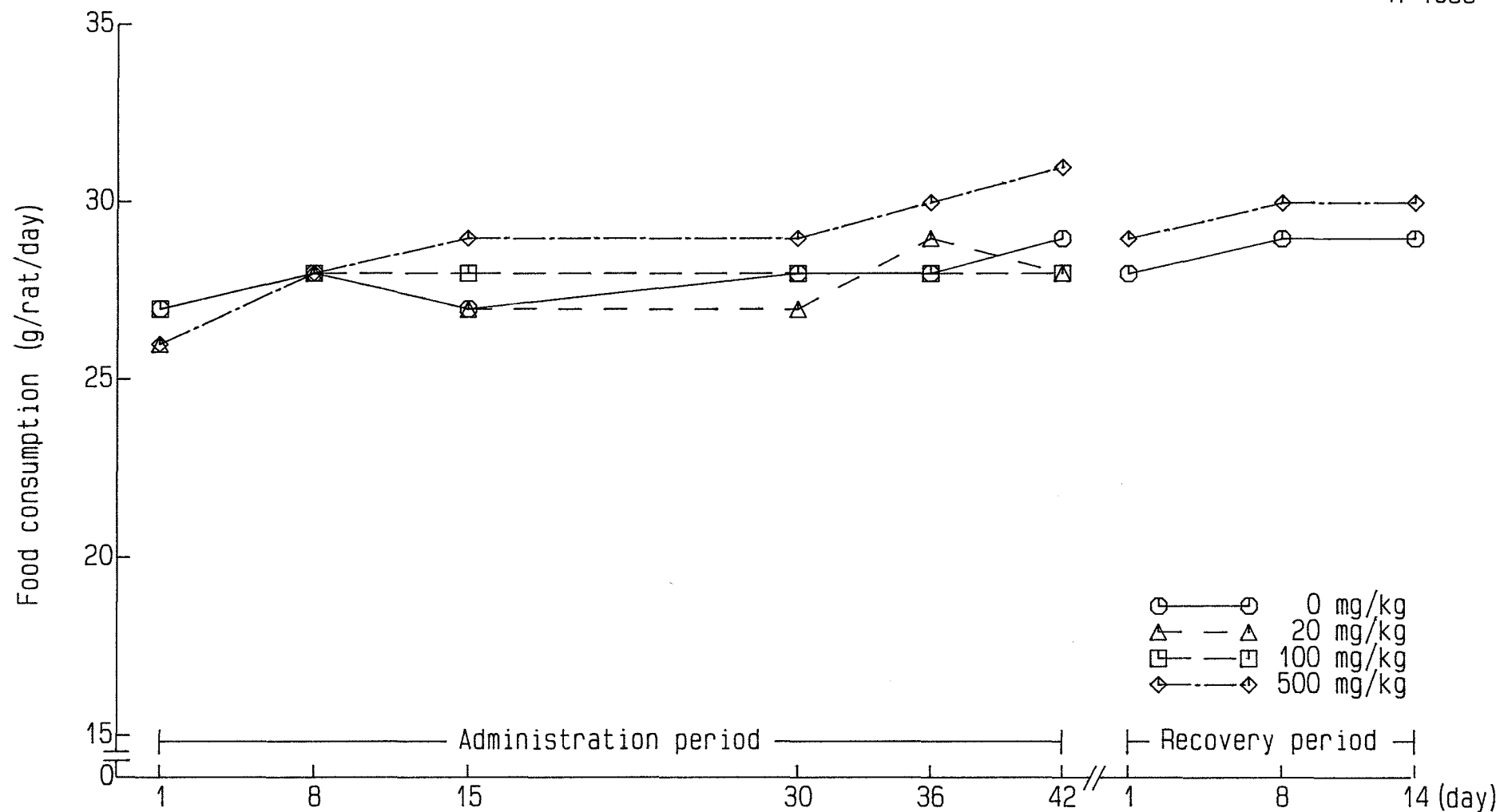


Fig.9 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Food consumption of male rats

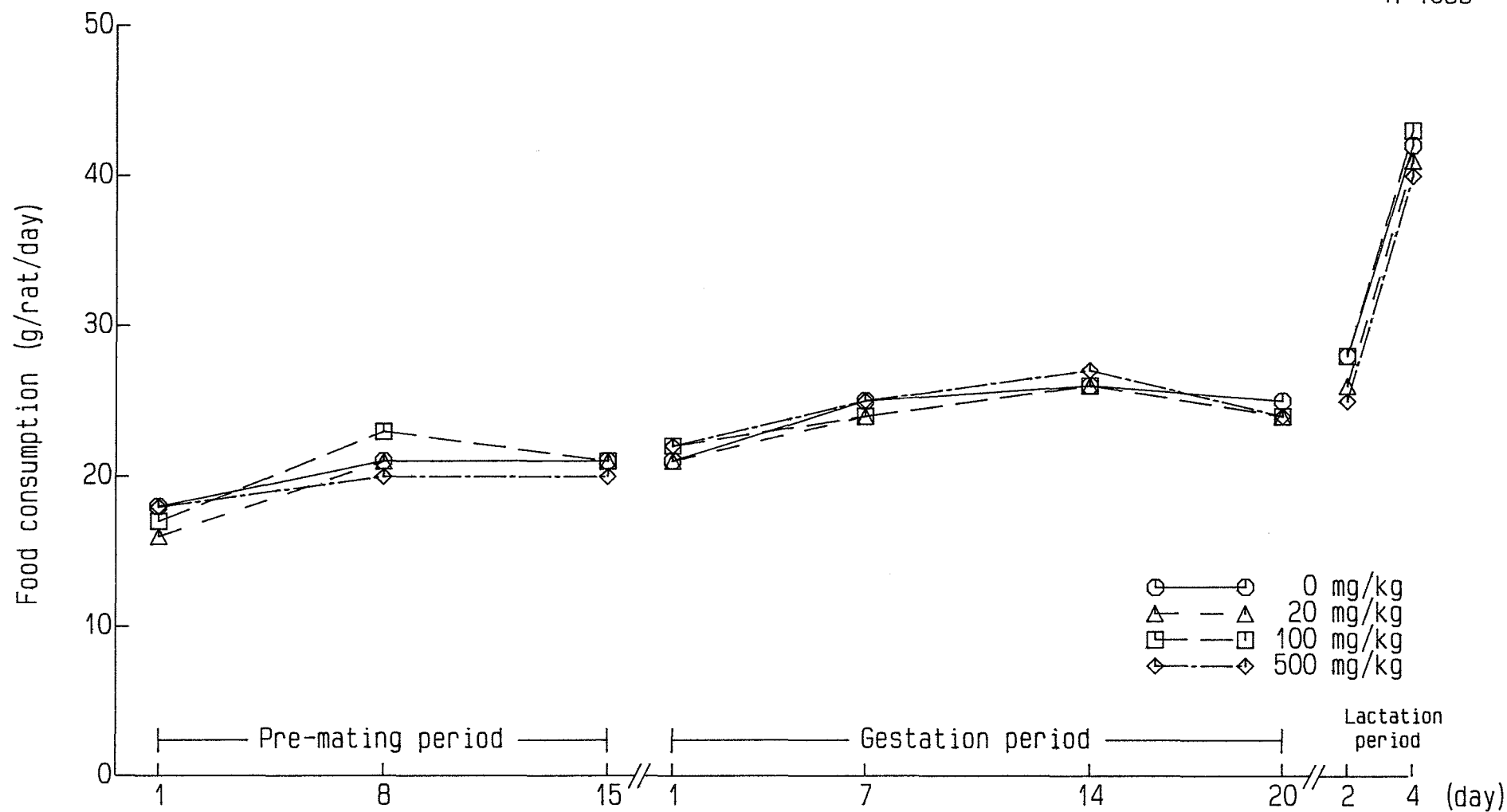


Fig.10 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Food consumption of female rats (Main group)

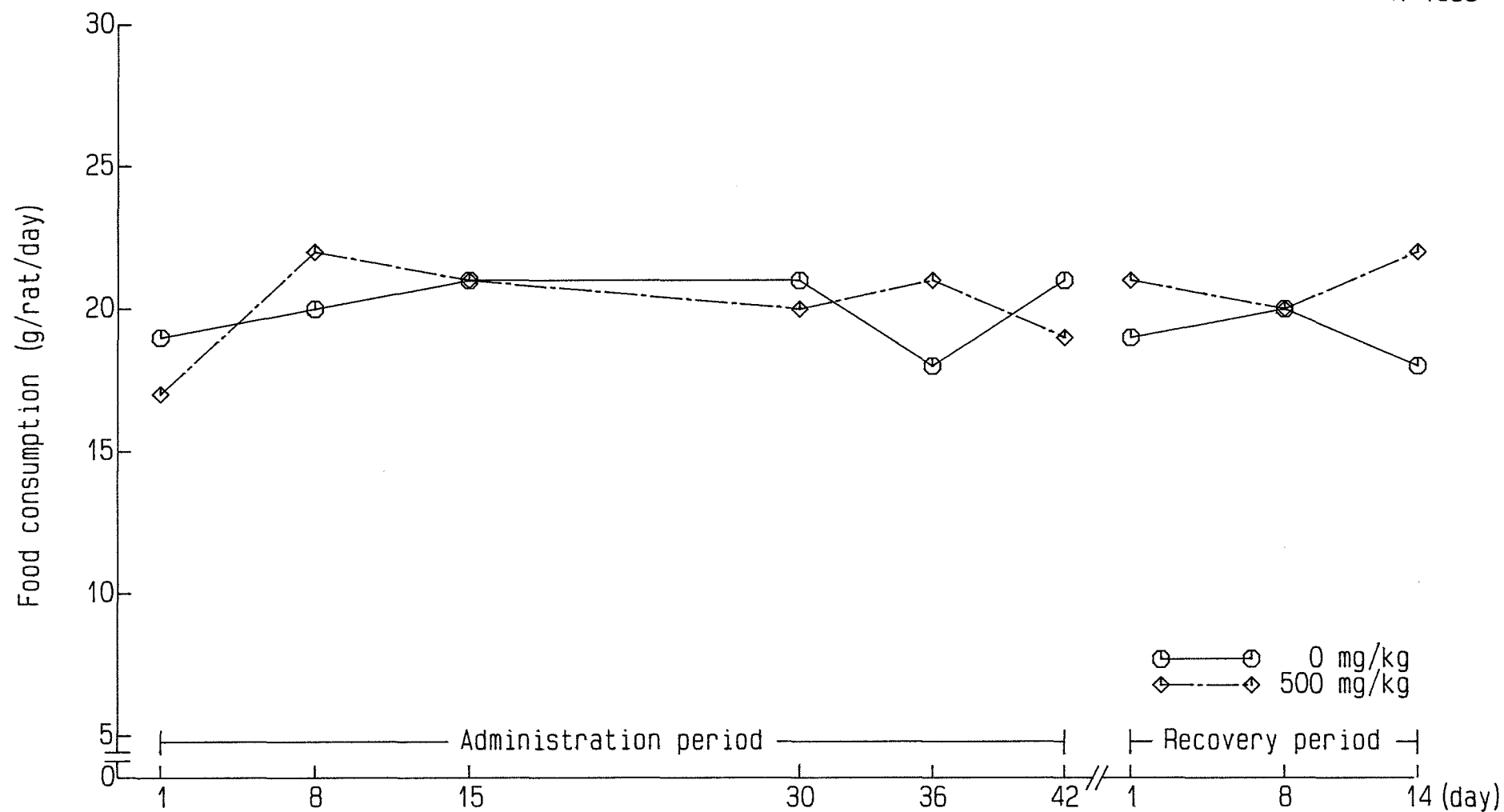


Fig.11 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Food consumption of female rats (Satellite group)

Table 1-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Clinical signs in male rats (Administration period)

[illegible]

Table 1-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Clinical signs in male rats (Administration period)

[illegible]

Table 1-3 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Clinical signs in male rats (Administration period)

Dose mg/kg	Signs	Day of administration														
		29	30	31	32	33	34	35	36	37	38	39	40	41	42	43a)
0	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	7
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
100	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
500	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	7
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
	Ataxia	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0

a): Day of necropsy

Table 1-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Clinical signs in female rats during the pre-mating period (Main group)

Dose mg/kg	Signs	Day of administration														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
0	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
100	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
500	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	No. of animals with abnormal findings	0	0	0	0	0	0	1	0	0	1	1	0	0	0	0
	Ataxia	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0
	Prone/Lateral position	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0

Table 1-5

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Clinical signs in dams during the gestation period (Main group)

Dose mg/kg	Signs	Administration																							
		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23a)
0	No. of dams	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	1	0
	No. of dams 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
20	No. of dams	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	2	0
	No. of dams 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
100	No. of dams	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	2	0
	No. of dams 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
500	No. of dams	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	4	0
	No. of dams with abnormal findings	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0	1	0	0	1	0	
	Ataxia	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	Prone/Lateral position	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0	1	0	

a): Gestation day

Table 1-6 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Clinical signs in dams during the lactation period (Main group)

Dose mg/kg	Signs	Administration					
		0	1	2	3	4a)	5b)
0	No. of dams	12	12	12	12	12	12
	No. of dams with abnormal findings	0	0	0	0	0	0
20	No. of dams	11	11	11	11	11	11
	No. of dams with abnormal findings	0	0	0	0	0	0
100	No. of dams	11	11	11	11	11	11
	No. of dams with abnormal findings	0	0	0	0	0	0
500	No. of dams	12	12	12	12	12	12
	No. of dams with abnormal findings	1	2	3	1	0	0
	Ataxia	0	0	1	1	0	0
	Prone/Lateral position	1	2	2	0	0	0

a): Lactation day
b): Day of necropsy

Table 1-7

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Clinical signs in female rats (Satellite group, administration period)

[illegible]

Clinical signs in female rats (Satellite group, administration period)

[illegible]

Table 1-9

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Clinical signs in female rats (Satellite group, administration period)

Dose mg/kg	Signs	Day of administration														
		29	30	31	32	33	34	35	36	37	38	39	40	41	42	43a)
0	No. of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
500	No. of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5
	No. of animals with abnormal findings	0	0	1	0	0	0	0	0	0	0	0	0	1	0	0
	Ataxia	0	0	1	0	0	0	0	0	0	0	0	0	1	0	0

a): Day of necropsy

Table 1-10

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Clinical signs in male rats (Recovery period)

Dose mg/kg	Signs	Day of recovery														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)
0	No. of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
500	No. of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	No. 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 1-11 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Clinical signs in female rats (Recovery period)

Dose mg/kg	Signs	Day of recovery														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)
0	No. of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
500	No. of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	No. 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

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in male rats: home cage observation (Week 1 of administration)

Parameter	Dose (mg/kg)	0	20	100	500
	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in male rats: home cage observation (Week 2 of administration)

Parameter	Dose (mg/kg)	0	20	100	500
	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in male rats: home cage observation (Week 3 of administration)

Parameter	Dose (mg/kg)	0	20	100	500
	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in male rats: home cage observation (Week 4 of administration)

Parameter	Dose (mg/kg)	0	20	100	500
	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-5

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in male rats: home cage observation (Week 5 of administration)

Parameter	Dose (mg/kg)	0	20	100	500
	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-6

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in male rats: home cage observation (Week 6 of administration)

Parameter	Dose (mg/kg)	0	20	100	500
	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-7

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: home cage observation (Main group, Week 1 of administration)

Parameter	Dose (mg/kg)	0	20	100	500
	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-8

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: home cage observation (Main group, Week 2 of administration)

Parameter	Dose (mg/kg)	0	20	100	500
	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-9

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: home cage observation (Main group, Gestation day 1)

Parameter	Dose (mg/kg)	0	20	100	500
	No. of animals	12	11	11	12
Posture					
Normal		12	11	11	12
Convulsion					
None		12	11	11	12
Abnormal behavior					
None		12	11	11	12

Table 2-10

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: home cage observation (Main group, Gestation day 7)

Parameter	Dose (mg/kg)	0	20	100	500
	No. of animals	12	11	11	12
Posture					
Normal		12	11	11	12
Convulsion					
None		12	11	11	12
Abnormal behavior					
None		12	11	11	12

Table 2-11

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: home cage observation (Main group, Gestation day 14)

Parameter	Dose (mg/kg)	0	20	100	500
	No. of animals	12	11	11	12
Posture					
Normal		12	11	11	12
Convulsion					
None		12	11	11	12
Abnormal behavior					
None		12	11	11	12

Table 2-12

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: home cage observation (Main group, Gestation day 20)

	Dose (mg/kg)	0	20	100	500
Parameter	No. of animals	12	11	11	12
Posture					
Normal		12	11	11	12
Convulsion					
None		12	11	11	12
Abnormal behavior					
None		12	11	11	12

Table 2-13

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: home cage observation (Main group, Lactation day 4)

Parameter	Dose (mg/kg)	0	20	100	500
	No. of animals	12	11	11	12
Posture					
Normal		12	11	11	12
Convulsion					
None		12	11	11	12
Abnormal behavior					
None		12	11	11	12

Table 2-14

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: home cage observation (Satellite group, Week 1 of administration)

Parameter	Dose (mg/kg)	0	500
	No. of animals	10	10
Posture			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10

Table 2-15

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: home cage observation (Satellite group, Week 2 of administration)

Parameter	Dose (mg/kg)	0	500
	No. of animals	10	10
Posture			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10

Table 2-16

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: home cage observation (Satellite group, Week 3 of administration)

Parameter	Dose (mg/kg)	0	500
	No. of animals	10	10
Posture			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10

Table 2-17

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: home cage observation (Satellite group, Week 4 of administration)

Parameter	Dose (mg/kg)	0	500
	No. of animals	10	10
Posture			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10

Table 2-18

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: home cage observation (Satellite group, Week 5 of administration)

Parameter	Dose (mg/kg)	0	500
	No. of animals	10	10
Posture			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10

Table 2-19

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: home cage observation (Satellite group, Week 6 of administration)

Parameter	Dose (mg/kg)	0	500
	No. of animals	10	10
Posture			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10

Table 2-20

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in male rats: home cage observation (Week 1 of recovery)

Parameter	Dose (mg/kg)	0	500
	No. of animals	5	5
Posture			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5

Table 2-21

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in male rats: home cage observation (Week 2 of recovery)

Parameter	Dose (mg/kg)	0	500
	No. of animals	5	5
Posture			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5

Table 2-22

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: home cage observation (Week 1 of recovery)

Parameter	Dose (mg/kg)	0	500
	No. of animals	5	5
Posture			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5

Table 2-23

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: home cage observation (Week 2 of recovery)

Parameter	Dose (mg/kg)	0	500
	No. of animals	5	5
Posture			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5

Table 2-24

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in male rats: in-the-hand observation (Week 1 of administration)

Parameter	Dose (mg/kg)	0	20	100	500
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	12	12
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	12	11	12
Soft		0	0	1	0
Reactivity to handling					
Easy		12	12	12	12

Table 2-25

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in male rats: in-the-hand observation (Week 2 of administration)

Dose (mg/kg)		0	20	100	500
Parameter	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	12	12
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	12	12	12
Reactivity to handling					
Easy		11	12	12	12
Slightly awkward		1	0	0	0

Table 2-26

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in male rats: in-the-hand observation (Week 3 of administration)

		Dose (mg/kg)	0	20	100	500
Parameter	No. of animals	12	12	12	12	12
Ease of removal from cage						
Easy		12	12	12	12	12
Fur condition						
Normal		12	12	12	12	12
Skin						
Normal		12	12	12	12	12
Secretions-Eye, Nose						
Absent		12	12	12	12	12
Exophthalmos						
Absent		12	12	12	12	12
Palpebral closure						
Normal		12	12	12	12	12
Mucosal membranes						
Normal		12	12	12	12	12
Lacrimation						
Normal		12	12	12	12	12
Piloerection						
Absent		12	12	12	12	12
Pupil size						
Normal		12	12	12	12	12
Salivation						
None		12	12	12	12	12
Abnormal respiration						
Absent		12	12	12	12	12
Vocalization						
None		12	12	11	12	12
Soft		0	0	1	0	0
Reactivity to handling						
Easy		12	12	12	12	12

Table 2-27

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in male rats: in-the-hand observation (Week 4 of administration)

Parameter	Dose (mg/kg)	0	20	100	500
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	12	12
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	10	12	11
Soft		0	2	0	1
Reactivity to handling					
Easy		12	12	12	12

Table 2-28

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in male rats: in-the-hand observation (Week 5 of administration)

Parameter	Dose (mg/kg)	0	20	100	500
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	12	12
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	11	9	12
Soft		0	1	3	0
Reactivity to handling					
Easy		12	12	11	12
Slightly awkward		0	0	1	0

Table 2-29

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in male rats: in-the-hand observation (Week 6 of administration)

Parameter	Dose (mg/kg)	0	20	100	500
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	12	12
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		11	12	12	12
Soft		1	0	0	0
Reactivity to handling					
Easy		12	12	12	12

Table 2-30

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: in-the-hand observation (Main group, Week 1 of administration)

Parameter	Dose (mg/kg)	0	20	100	500
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	12	12
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	12	12	12
Reactivity to handling					
Easy		12	12	12	12

Table 2-31

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: in-the-hand observation (Main group, Week 2 of administration)

Dose (mg/kg)		0	20	100	500
Parameter	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	12	12
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	11	12	12
Soft		0	1	0	0
Reactivity to handling					
Easy		12	12	12	12

Table 2-32

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: in-the-hand observation (Main group, Gestation day 1)

Parameter	Dose (mg/kg)	0	20	100	500
	No. of animals	12	11	11	12
Ease of removal from cage					
Easy		12	11	11	12
Fur condition					
Normal		12	11	11	12
Skin					
Normal		12	11	11	12
Secretions-Eye, Nose					
Absent		12	11	11	12
Exophthalmos					
Absent		12	11	11	12
Palpebral closure					
Normal		12	11	11	12
Mucosal membranes					
Normal		12	11	11	12
Lacrimation					
Normal		12	11	11	12
Piloerection					
Absent		12	11	11	12
Pupil size					
Normal		12	11	11	12
Salivation					
None		12	11	11	12
Abnormal respiration					
Absent		12	11	11	12
Vocalization					
None		12	11	11	12
Reactivity to handling					
Easy		12	11	11	12

Table 2-33

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: in-the-hand observation (Main group, Gestation day 7)

Parameter	Dose (mg/kg)	0	20	100	500
	No. of animals	12	11	11	12
Ease of removal from cage					
Easy		12	11	11	12
Fur condition					
Normal		12	11	11	12
Skin					
Normal		12	11	11	12
Secretions-Eye, Nose					
Absent		12	11	11	12
Exophthalmos					
Absent		12	11	11	12
Palpebral closure					
Normal		12	11	11	12
Mucosal membranes					
Normal		12	11	11	12
Lacrimation					
Normal		12	11	11	12
Piloerection					
Absent		12	11	11	12
Pupil size					
Normal		12	11	11	12
Salivation					
None		12	11	11	12
Abnormal respiration					
Absent		12	11	11	12
Vocalization					
None		11	11	11	12
Soft		1	0	0	0
Reactivity to handling					
Easy		12	11	11	12

Table 2-34

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: in-the-hand observation (Main group, Gestation day 14)

Parameter	Dose (mg/kg)	0	20	100	500
	No. of animals	12	11	11	12
Ease of removal from cage					
Easy		12	11	11	12
Fur condition					
Normal		12	11	11	12
Skin					
Normal		12	11	11	12
Secretions-Eye, Nose					
Absent		12	11	11	12
Exophthalmos					
Absent		12	11	11	12
Palpebral closure					
Normal		12	11	11	12
Mucosal membranes					
Normal		12	11	11	12
Lacrimation					
Normal		12	11	11	12
Piloerection					
Absent		12	11	11	12
Pupil size					
Normal		12	11	11	12
Salivation					
None		12	11	11	12
Abnormal respiration					
Absent		12	11	11	12
Vocalization					
None		12	11	11	12
Reactivity to handling					
Easy		12	11	11	12

Table 2-35

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: in-the-hand observation (Main group, Gestation day 20)

Parameter	Dose (mg/kg)	0	20	100	500
	No. of animals	12	11	11	12
Ease of removal from cage					
Easy		12	11	11	12
Fur condition					
Normal		12	11	11	12
Skin					
Normal		12	11	11	12
Secretions-Eye, Nose					
Absent		12	11	11	12
Exophthalmos					
Absent		12	11	11	12
Palpebral closure					
Normal		12	11	11	12
Mucosal membranes					
Normal		12	11	11	12
Lacrimation					
Normal		12	11	11	12
Piloerection					
Absent		12	11	11	12
Pupil size					
Normal		12	11	11	12
Salivation					
None		12	11	11	12
Abnormal respiration					
Absent		12	11	11	12
Vocalization					
None		12	11	11	12
Reactivity to handling					
Easy		12	11	11	12

Table 2-36

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: in-the-hand observation (Main group, Lactation day 4)

Parameter	Dose (mg/kg)	0	20	100	500
	No. of animals	12	11	11	12
Ease of removal from cage					
Easy		12	11	11	12
Fur condition					
Normal		12	11	11	12
Skin					
Normal		12	11	11	12
Secretions-Eye, Nose					
Absent		12	11	11	12
Exophthalmos					
Absent		12	11	11	12
Palpebral closure					
Normal		12	11	11	12
Mucosal membranes					
Normal		12	11	11	12
Lacrimation					
Normal		12	11	11	12
Piloerection					
Absent		12	11	11	12
Pupil size					
Normal		12	11	11	12
Salivation					
None		12	11	11	12
Abnormal respiration					
Absent		12	11	11	12
Vocalization					
None		12	11	11	12
Reactivity to handling					
Easy		12	11	11	12

Table 2-37

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: in-the-hand observation (Satellite group, Week 1 of administration)

Parameter	Dose (mg/kg)	0	500
	No. of animals	10	10
Ease of removal from cage			
Easy		10	10
Fur condition			
Normal		10	10
Skin			
Normal		10	10
Secretions-Eye, Nose			
Absent		10	10
Exophthalmos			
Absent		10	10
Palpebral closure			
Normal		10	10
Mucosal membranes			
Normal		10	10
Lacrimation			
Normal		10	10
Piloerection			
Absent		10	10
Pupil size			
Normal		10	10
Salivation			
None		10	10
Abnormal respiration			
Absent		10	10
Vocalization			
None		10	10
Reactivity to handling			
Easy		10	10

Table 2-38

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: in-the-hand observation (Satellite group, Week 2 of administration)

Parameter	Dose (mg/kg)	0	500
	No. of animals	10	10
Ease of removal from cage			
Easy		10	10
Fur condition			
Normal		10	10
Skin			
Normal		10	10
Secretions-Eye, Nose			
Absent		10	10
Exophthalmos			
Absent		10	10
Palpebral closure			
Normal		10	10
Mucosal membranes			
Normal		10	10
Lacrimation			
Normal		10	10
Piloerection			
Absent		10	10
Pupil size			
Normal		10	10
Salivation			
None		10	10
Abnormal respiration			
Absent		10	10
Vocalization			
None		10	10
Reactivity to handling			
Easy		10	9
Slightly awkward		0	1

Table 2-39

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: in-the-hand observation (Satellite group, Week 3 of administration)

Parameter	Dose (mg/kg)	0	500
	No. of animals	10	10
Ease of removal from cage			
Easy		10	10
Fur condition			
Normal		10	10
Skin			
Normal		10	10
Secretions-Eye, Nose			
Absent		10	10
Exophthalmos			
Absent		10	10
Palpebral closure			
Normal		10	10
Mucosal membranes			
Normal		10	10
Lacrimation			
Normal		10	10
Piloerection			
Absent		10	10
Pupil size			
Normal		10	10
Salivation			
None		10	10
Abnormal respiration			
Absent		10	10
Vocalization			
None		10	10
Reactivity to handling			
Easy		10	10

Table 2-40

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: in-the-hand observation (Satellite group, Week 4 of administration)

Parameter	Dose (mg/kg)	0	500
	No. of animals	10	10
Ease of removal from cage			
Easy		10	10
Fur condition			
Normal		10	10
Skin			
Normal		10	10
Secretions-Eye, Nose			
Absent		10	10
Exophthalmos			
Absent		10	10
Palpebral closure			
Normal		10	10
Mucosal membranes			
Normal		10	10
Lacrimation			
Normal		10	10
Piloerection			
Absent		10	10
Pupil size			
Normal		10	10
Salivation			
None		10	10
Abnormal respiration			
Absent		10	10
Vocalization			
None		10	10
Reactivity to handling			
Easy		10	10

Table 2-41

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: in-the-hand observation (Satellite group, Week 5 of administration)

Parameter	Dose (mg/kg)	0	500
	No. of animals	10	10
Ease of removal from cage			
Easy		10	10
Fur condition			
Normal		10	10
Skin			
Normal		10	10
Secretions-Eye, Nose			
Absent		10	10
Exophthalmos			
Absent		10	10
Palpebral closure			
Normal		10	10
Mucosal membranes			
Normal		10	10
Lacrimation			
Normal		10	10
Piloerection			
Absent		10	10
Pupil size			
Normal		10	10
Salivation			
None		10	10
Abnormal respiration			
Absent		10	10
Vocalization			
None		10	10
Reactivity to handling			
Easy		10	10

Table 2-42

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: in-the-hand observation (Satellite group, Week 6 of administration)

Parameter	Dose (mg/kg)	0	500
	No. of animals	10	10
Ease of removal from cage			
Easy		10	10
Fur condition			
Normal		10	10
Skin			
Normal		10	10
Secretions-Eye, Nose			
Absent		10	10
Exophthalmos			
Absent		10	10
Palpebral closure			
Normal		10	10
Mucosal membranes			
Normal		10	10
Lacrimation			
Normal		10	10
Piloerection			
Absent		10	10
Pupil size			
Normal		10	10
Salivation			
None		10	10
Abnormal respiration			
Absent		10	10
Vocalization			
None		10	10
Reactivity to handling			
Easy		10	10

Table 2-43

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in male rats: in-the-hand observation (Week 1 of recovery)

Parameter	Dose (mg/kg)	0	500
	No. of animals	5	5
Ease of removal from cage			
Easy		5	5
Fur condition			
Normal		5	5
Skin			
Normal		5	5
Secretions-Eye, Nose			
Absent		5	5
Exophthalmos			
Absent		5	5
Palpebral closure			
Normal		5	5
Mucosal membranes			
Normal		5	5
Lacrimation			
Normal		5	5
Piloerection			
Absent		5	5
Pupil size			
Normal		5	5
Salivation			
None		5	5
Abnormal respiration			
Absent		5	5
Vocalization			
None		5	5
Reactivity to handling			
Easy		5	5

Table 2-44

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in male rats: in-the-hand observation (Week 2 of recovery)

Parameter	Dose (mg/kg)	0	500
	No. of animals	5	5
Ease of removal from cage			
Easy		5	5
Fur condition			
Normal		5	5
Skin			
Normal		5	5
Secretions-Eye, Nose			
Absent		5	5
Exophthalmos			
Absent		5	5
Palpebral closure			
Normal		5	5
Mucosal membranes			
Normal		5	5
Lacrimation			
Normal		5	5
Piloerection			
Absent		5	5
Pupil size			
Normal		5	5
Salivation			
None		5	5
Abnormal respiration			
Absent		5	5
Vocalization			
None		2	4
Soft		3	1
Reactivity to handling			
Easy		5	4
Slightly awkward		0	1

Table 2-45

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: in-the-hand observation (Week 1 of recovery)

Parameter	Dose (mg/kg)	0	500
	No. of animals	5	5
Ease of removal from cage			
Easy		5	5
Fur condition			
Normal		5	5
Skin			
Normal		5	5
Secretions-Eye, Nose			
Absent		5	5
Exophthalmos			
Absent		5	5
Palpebral closure			
Normal		5	5
Mucosal membranes			
Normal		5	5
Lacrimation			
Normal		5	5
Piloerection			
Absent		5	5
Pupil size			
Normal		5	5
Salivation			
None		5	5
Abnormal respiration			
Absent		5	5
Vocalization			
None		5	5
Reactivity to handling			
Easy		5	5

Table 2-46

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: in-the-hand observation (Week 2 of recovery)

Parameter	Dose (mg/kg)	0	500
	No. of animals	5	5
Ease of removal from cage			
Easy		5	5
Fur condition			
Normal		5	5
Skin			
Normal		5	5
Secretions-Eye, Nose			
Absent		5	5
Exophthalmos			
Absent		5	5
Palpebral closure			
Normal		5	5
Mucosal membranes			
Normal		5	5
Lacrimation			
Normal		5	5
Piloerection			
Absent		5	5
Pupil size			
Normal		5	5
Salivation			
None		5	5
Abnormal respiration			
Absent		5	5
Vocalization			
None		5	5
Reactivity to handling			
Easy		5	5

Table 2-47

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in male rats: open field observation (Week 1 of administration)

	Dose (mg/kg)	0	20	100	500
Parameter	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		4± 1	4± 2	5± 2	4± 1
Defecation count (Mean±S.D.)		0± 1	0± 0	0± 0	1± 1
Urination					
None		11	10	11	11
Small amount		1	2	1	1

No significant difference in any treated groups from control group.

Table 2-48

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in male rats: open field observation (Week 2 of administration)

Parameter	Dose (mg/kg)	0	20	100	500
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
No/minimal location		1	0	0	0
Normal		11	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		4± 2	5± 2	5± 2	4± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		11	10	12	11
Small amount		1	2	0	1

No significant difference in any treated groups from control group.

Table 2-49

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in male rats: open field observation (Week 3 of administration)

	Dose (mg/kg)	0	20	100	500
Parameter	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
No/minimal location		1	0	0	0
Normal		11	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean+S.D.)		4 ₊ 2	6 ₊ 2*D	4 ₊ 1	4 ₊ 2
Defecation count (Mean+S.D.)		0 ₊ 1	0 ₊ 0	0 ₊ 0	0 ₊ 0
Urination					
None		9	11	11	10
Small amount		3	1	1	2

* : p<0.05 (Significant difference from control group)

D : Dunnett's test

Table 2-50

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in male rats: open field observation (Week 4 of administration)

	Dose (mg/kg)	0	20	100	500
Parameter	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		4± 2	6± 2	5± 2	5± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		9	9	10	9
Small amount		3	3	2	3

No significant difference in any treated groups from control group.

Table 2-51

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in male rats: open field observation (Week 5 of administration)

	Dose (mg/kg)	0	20	100	500
Parameter	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		4± 1	5± 2	4± 2	5± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		10	8	8	11
Small amount		2	4	4	1

No significant difference in any treated groups from control group.

Table 2-52

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in male rats: open field observation (Week 6 of administration)

	Dose (mg/kg)	0	20	100	500
Parameter	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		4± 2	5± 2	4± 1	4± 1
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		10	9	9	10
Small amount		2	3	3	2

No significant difference in any treated groups from control group.

Table 2-53

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: open field observation (Main group, Week 1 of administration)

	Dose (mg/kg)	0	20	100	500
Parameter	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		6± 2	6± 2	7± 3	6± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 1
Urination					
None		12	12	12	11
Small amount		0	0	0	1

No significant difference in any treated groups from control group.

Table 2-54

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: open field observation (Main group, Week 2 of administration)

	Dose (mg/kg)	0	20	100	500
Parameter	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		6± 2	7± 2	9± 3	6± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	12	12	12

No significant difference in any treated groups from control group.

Table 2-55

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: open field observation (Main group, Gestation day 1)

	Dose (mg/kg)	0	20	100	500
Parameter	No. of animals	12	11	11	12
Arousal					
Normal		12	11	11	12
Convulsion					
None		12	11	11	12
Abnormal behavior					
None		12	11	11	12
Stereotypy					
None		12	11	11	12
Gait					
Normal		12	11	11	12
Posture					
Normal		12	11	11	12
Grooming					
None		12	11	11	12
Rearing (Mean±S.D.)		7± 2	7± 2	8± 2	6± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	11	11	12

No significant difference in any treated groups from control group.

Table 2-56

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: open field observation (Main group, Gestation day 7)

	Dose (mg/kg)	0	20	100	500
Parameter	No. of animals	12	11	11	12
Arousal					
Normal		12	11	11	12
Convulsion					
None		12	11	11	12
Abnormal behavior					
None		12	11	11	12
Stereotypy					
None		12	11	11	12
Gait					
Normal		12	11	11	12
Posture					
Normal		12	11	11	12
Grooming					
None		12	11	11	12
Rearing (Mean±S.D.)		6± 2	6± 2	7± 2	5± 3
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		11	10	9	12
Small amount		1	1	2	0

No significant difference in any treated groups from control group.

Table 2-57

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: open field observation (Main group, Gestation day 14)

	Dose (mg/kg)	0	20	100	500
Parameter	No. of animals	12	11	11	12
Arousal					
Normal		12	11	11	12
Convulsion					
None		12	11	11	12
Abnormal behavior					
None		12	11	11	12
Stereotypy					
None		12	11	11	12
Gait					
Normal		12	11	11	12
Posture					
Normal		12	11	11	12
Grooming					
None		12	11	11	12
Rearing (Mean+S.D.)		6 $\pm$ 1	5 $\pm$ 1	7 $\pm$ 1	5 $\pm$ 2
Defecation count (Mean+S.D.)		0 $\pm$ 0	0 $\pm$ 0	0 $\pm$ 0	0 $\pm$ 0
Urination					
None		12	11	11	12

No significant difference in any treated groups from control group.

Table 2-58

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: open field observation (Main group, Gestation day 20)

	Dose (mg/kg)	0	20	100	500
Parameter	No. of animals	12	11	11	12
Arousal					
Normal		12	11	11	12
Convulsion					
None		12	11	11	12
Abnormal behavior					
None		12	11	11	12
Stereotypy					
None		12	11	11	12
Gait					
Normal		12	11	11	12
Posture					
Normal		12	11	11	12
Grooming					
None		12	11	11	12
Rearing (Mean±S.D.)		6± 1	5± 1	6± 1	5± 1
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	11	11	12

No significant difference in any treated groups from control group.

Table 2-59

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: open field observation (Main group, Lactation day 4)

	Dose (mg/kg)	0	20	100	500
Parameter	No. of animals	12	11	11	12
Arousal					
Normal		12	11	11	12
Convulsion					
None		12	11	11	12
Abnormal behavior					
None		12	11	11	12
Stereotypy					
None		12	11	11	12
Gait					
Normal		12	11	11	12
Posture					
Normal		12	11	11	12
Grooming					
None		12	11	11	12
Rearing (Mean±S.D.)		6± 2	6± 2	6± 1	6± 1
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	11	11	11
Small amount		0	0	0	1

No significant difference in any treated groups from control group.

Table 2-60

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: open field observation (Satellite group, Week 1 of administration)

Parameter	Dose (mg/kg)	0	500
	No. of animals	10	10
Arousal			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10
Stereotypy			
None		10	10
Gait			
Normal		10	10
Posture			
Normal		10	10
Grooming			
None		10	10
Rearing (Mean±S.D.)		7± 3	6± 2
Defecation count (Mean±S.D.)		0± 0	0± 1
Urination			
None		9	10
Small amount		1	0

No significant difference between treated group and control group.

Table 2-61

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: open field observation (Satellite group, Week 2 of administration)

Parameter	Dose (mg/kg)	0	500
	No. of animals	10	10
Arousal			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10
Stereotypy			
None		10	10
Gait			
Normal		10	10
Posture			
Normal		10	10
Grooming			
None		10	10
Rearing (Mean±S.D.)		8± 3	7± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	10

No significant difference between treated group and control group.

Table 2-62

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: open field observation (Satellite group, Week 3 of administration)

Parameter	Dose (mg/kg)	0	500
	No. of animals	10	10
Arousal			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10
Stereotypy			
None		10	10
Gait			
Normal		10	10
Posture			
Normal		10	10
Grooming			
None		10	10
Rearing (Mean±S.D.)		9± 2	8± 3
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	10

No significant difference between treated group and control group.

Table 2-63

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: open field observation (Satellite group, Week 4 of administration)

Parameter	Dose (mg/kg)	0	500
	No. of animals	10	10
Arousal			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10
Stereotypy			
None		10	10
Gait			
Normal		10	10
Posture			
Normal		10	10
Grooming			
None		10	10
Rearing (Mean±S.D.)		8± 3	7± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	10

No significant difference between treated group and control group.

Table 2-64

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: open field observation (Satellite group, Week 5 of administration)

Parameter	Dose (mg/kg)	0	500
	No. of animals	10	10
Arousal			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10
Stereotypy			
None		10	10
Gait			
Normal		10	10
Posture			
Normal		10	10
Grooming			
None		10	10
Rearing (Mean±S.D.)		9± 3	7± 3
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	10

No significant difference between treated group and control group.

Table 2-65

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: open field observation (Satellite group, Week 6 of administration)

Parameter	Dose (mg/kg)	0	500
	No. of animals	10	10
Arousal			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10
Stereotypy			
None		10	10
Gait			
Normal		10	10
Posture			
Normal		10	10
Grooming			
None		10	10
Rearing (Mean±S.D.)		8± 2	8± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	10

No significant difference between treated group and control group.

Table 2-66

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in male rats: open field observation (Week 1 of recovery)

Parameter	Dose (mg/kg)	0	500
	No. of animals	5	5
Arousal			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5
Stereotypy			
None		5	5
Gait			
Normal		5	5
Posture			
Normal		5	5
Grooming			
None		5	5
Rearing (Mean±S.D.)		3± 2	4± 1
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		5	3
Small amount		0	2

No significant difference between treated group and control group.

Table 2-67

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in male rats: open field observation (Week 2 of recovery)

Parameter	Dose (mg/kg)	0	500
	No. of animals	5	5
Arousal			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5
Stereotypy			
None		5	5
Gait			
Normal		5	5
Posture			
Normal		5	5
Grooming			
None		5	5
Rearing (Mean±S.D.)		3± 1	3± 1
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		5	5

No significant difference between treated group and control group.

Table 2-68

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: open field observation (Week 1 of recovery)

Parameter	Dose (mg/kg)	0	500
	No. of animals	5	5
Arousal			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5
Stereotypy			
None		5	5
Gait			
Normal		5	5
Posture			
Normal		5	5
Grooming			
None		5	5
Rearing (Mean+S.D.)		8 $\pm$ 2	7 $\pm$ 2
Defecation count (Mean+S.D.)		0 $\pm$ 0	0 $\pm$ 0
Urination			
None		5	5

No significant difference between treated group and control group.

Table 2-69

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Detailed clinical signs in female rats: open field observation (Week 2 of recovery)

Parameter	Dose (mg/kg)	0	500
	No. of animals	5	5
Arousal			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5
Stereotypy			
None		5	5
Gait			
Normal		5	5
Posture			
Normal		5	5
Grooming			
None		5	5
Rearing (Mean±S.D.)		7± 2	7± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		5	5

No significant difference between treated group and control group.

Table 2-70

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Manipulative test of male rats (Week 6 of administration)

	Dose (mg/kg)	0	20	100	500
Parameter	No. of animals	5	5	5	5
Auditory response					
Normal		5	5	5	5
Approach response					
Normal		5	5	5	5
Touch response					
Normal		5	5	5	5
Tail pinch response					
Normal		5	5	5	5
Pupillary reflex					
Pass, both		5	5	5	5
Aerial righting reflex					
(Total score: Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Landing foot splay (mm: Mean±S.D.)		96±29	86±16	91±17	73±14

No significant difference in any treated groups from control group.

Table 2-71

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Manipulative test of female rats (Main group, Lactation day 4)

	Dose (mg/kg)	0	20	100	500
Parameter	No. of animals	5	5	5	5
Auditory response Normal		5	5	5	5
Approach response Normal		5	5	5	5
Touch response Normal		5	5	5	5
Tail pinch response Normal		5	5	5	5
Pupillary reflex Pass, both		5	5	5	5
Aerial righting reflex (Total score: Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Landing foot splay (mm: Mean±S.D.)		58±11	65±22	60±16	51±15

No significant difference in any treated groups from control group.

Table 2-72

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Manipulative test of female rats (Satellite group, Week 6 of administration)

Parameter	Dose (mg/kg)	0	500
	No. of animals	5	5
Auditory response Normal		5	5
Approach response Normal		5	5
Touch response Normal		5	5
Tail pinch response Normal		5	5
Pupillary reflex Pass, both		5	5
Aerial righting reflex (Total score: Mean+S.D.)		0± 0	0± 0
Landing foot splay (mm: Mean+S.D.)		64±16	71±22

No significant difference between treated group and control group.

Table 2-73

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Manipulative test of male rats (Week 2 of recovery)

Parameter	Dose (mg/kg)	0	500
	No. of animals	5	5
Auditory response Normal		5	5
Approach response Normal		5	5
Touch response Normal		5	5
Tail pinch response Normal		5	5
Pupillary reflex Pass, both		5	5
Aerial righting reflex (Total score: Mean+S.D.)		0± 0	0± 0
Landing foot splay (mm: Mean+S.D.)		97±24	88±21

No significant difference between treated group and control group.

Table 2-74

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Manipulative test of female rats (Week 2 of recovery)

Parameter	Dose (mg/kg)	0	500
	No. of animals	5	5
Auditory response Normal		5	5
Approach response Normal		5	5
Touch response Normal		5	5
Tail pinch response Normal		5	5
Pupillary reflex Pass, both		5	5
Aerial righting reflex (Total score: Mean±S.D.)		0± 0	0± 0
Landing foot splay (mm: Mean±S.D.)		66±11	67±25

No significant difference between treated group and control group.

Table 2-75

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Grip strength of male rats (Week 6 of administration)

Dose mg/kg		Fore limb g	Hind limb g
0	No.	5	5
	Mean	1616	983
	S.D.	129	171
20	No.	5	5
	Mean	1651	962
	S.D.	181	44
100	No.	5	5
	Mean	1626	1016
	S.D.	208	83
500	No.	5	5
	Mean	1675	1121
	S.D.	212	168

No.: No. of animals

No significant difference in any treated groups from control group.

Table 2-76

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Grip strength of female rats (Main group, Lactation day 4)

Dose mg/kg		Fore limb g	Hind limb g
0	No.	5	5
	Mean	1422	730
	S.D.	284	122
20	No.	5	5
	Mean	1496	809
	S.D.	238	95
100	No.	5	5
	Mean	1340	842
	S.D.	186	106
500	No.	5	5
	Mean	1295	672
	S.D.	156	49

No.: No. of animals

No significant difference in any treated groups from control group.

Table 2-77

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Grip strength of female rats (Satellite group, Week 6 of administration)

Dose mg/kg		Fore limb g	Hind limb g
0	No.	5	5
	Mean	1241	719
	S.D.	131	73
500	No.	5	5
	Mean	1081	670
	S.D.	178	99

No.: No. of animals

No significant difference between treated group and control group.

Table 2-78

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Grip strength of male rats (Week 2 of recovery)

Dose mg/kg		Fore limb g	Hind limb g
0	No.	5	5
	Mean	1723	1002
	S.D.	323	183
500	No.	5	5
	Mean	1731	1064
	S.D.	174	202

No.: No. of animals

No significant difference between treated group and control group.

Table 2-79

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Grip strength of female rats (Week 2 of recovery)

Dose mg/kg		Fore limb g	Hind limb g
0	No.	5	5
	Mean	1386	770
	S.D.	187	113
500	No.	5	5
	Mean	1235	706
	S.D.	163	122

No.: No. of animals

No significant difference between treated group and control group.

Table 2-80

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Motor activity of male rats (Week 6 of administration)

Dose mg/kg		Interval (minutes)						
		0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
0	No.	5	5	5	5	5	5	5
	Mean	409	350	248	328	148	90	1574
	S.D.	37	110	173	74	122	73	499
20	No.	5	5	5	5	5	5	5
	Mean	417	404	371	340	319*	243	2094
	S.D.	53	27	45	56	33D	127	213
100	No.	5	5	5	5	5	5	5
	Mean	358	330	240	223*	192	145	1489
	S.D.	18	41	83	41D	96	93	305
500	No.	5	5	5	5	5	5	5
	Mean	413	360	322	318	201	161	1775
	S.D.	49	68	48	42	67	114	278

Unit : Count

No.: No. of animals

* : p<0.05 (Significant difference from control group)

D: Dunnett's test

Table 2-81

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Motor activity of female rats (Main group, Lactation day 4)

Dose mg/kg		Interval (minutes)						Total(0-60)
		0-10	10-20	20-30	30-40	40-50	50-60	
0	No.	5	5	5	5	5	5	5
	Mean	443	360	225	153	86	115	1382
	S.D.	35	54	144	183	121	133	499
20	No.	5	5	5	5	5	5	5
	Mean	386	174	155	127	136	97	1076
	S.D.	56	126	121	115	142	164	634
100	No.	5	5	5	5	5	5	5
	Mean	403	243	214	184	165	123	1333
	S.D.	43	86	68	107	129	98	364
500	No.	5	5	5	5	5	5	5
	Mean	324**	168*	96	42	42	36	708
	S.D.	71D	166D	94	71	43	66	316

Unit : Count

No.: No. of animals

* : $p < 0.05$; ** : $p < 0.01$ (Significant difference from control group)

D: Dunnett's test

Table 2-82

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Motor activity of female rats (Satellite group, Week 6 of administration)

Dose mg/kg	Interval (minutes)						
	0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
0	No.	5	5	5	5	5	5
	Mean	405	326	262	264	209	1664
	S.D.	26	39	185	156	120	362
500	No.	5	5	5	5	5	5
	Mean	406	326	226	212	192	1440
	S.D.	24	48	131	104	134	232

Unit : Count

No.: No. of animals

No significant difference between treated group and control group.

Table 2-83

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Motor activity of male rats (Week 2 of recovery)

Dose mg/kg		Interval (minutes)						Total(0-60)
		0-10	10-20	20-30	30-40	40-50	50-60	
0	No.	5	5	5	5	5	5	5
	Mean	337	252	244	200	132	125	1290
	S.D.	34	54	60	60	47	89	271
500	No.	5	5	5	5	5	5	5
	Mean	366	299	298	230	170	147	1510
	S.D.	30	65	77	74	116	102	387

Unit : Count

No.: No. of animals

No significant difference between treated group and control group.

Table 2-84

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Motor activity of female rats (Week 2 of recovery)

Dose mg/kg	Interval (minutes)						
	0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
0	No.	5	5	5	5	5	5
	Mean	384	358	278	249	226	1720
	S.D.	73	88	76	63	35	222
500	No.	5	5	5	5	5	5
	Mean	355	331	282	268	199	1658
	S.D.	82	62	58	164	163	460

Unit : Count

No.: No. of animals

No significant difference between treated group and control group.

Table 3-1 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Body weight of male rats (Administration period)

Dose mg/kg		Day of administration							Gain 1-42
		1	8	15	22	29	36	42	
0	No.	12	12	12	12	12	12	12	12
	Mean	379	406	426	443	465	486	497	119
	S.D.	18	22	27	30	34	37	40	25
20	No.	12	12	12	12	12	12	12	12
	Mean	379	403	426	448	471	494	506	127
	S.D.	18	23	26	29	34	37	40	27
100	No.	12	12	12	12	12	12	12	12
	Mean	380	405	423	439	460	482	494	114
	S.D.	19	18	20	21	25	25	26	16
500	No.	12	12	12	12	12	12	12	12
	Mean	376	407	430	449	469	491	500	124
	S.D.	17	21	27	31	34	35	38	25

Unit: g

No.: No. of animals

No significant difference in any treated groups from control group.

Table 3-2 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Body weight of female rats during the pre-mating period (Main group)

Dose mg/kg		Day of administration			Gain 1-15
		1	8	15	
0	No.	12	12	12	12
	Mean	235	248	259	24
	S.D.	15	14	17	9
20	No.	12	12	12	12
	Mean	231	246	254	23
	S.D.	9	11	13	10
100	No.	12	12	12	12
	Mean	232	248	257	25
	S.D.	8	11	12	9
500	No.	12	12	12	12
	Mean	234	243	252	18
	S.D.	13	12	14	9

Unit: g

No.: No. of animals

No significant difference in any treated groups from control group.

Table 3-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Body weight of dams during the gestation period (Main group)

Dose mg/kg		Administration				Gain 0-20
		0	7	14	20a)	
0	No.	12	12	12	12	12
	Mean	266	300	337	416	150
	S.D.	16	15	18	30	24
20	No.	11	11	11	11	11
	Mean	261	292	328	406	145
	S.D.	13	16	20	30	19
100	No.	11	11	11	11	11
	Mean	260	290	327	405	145
	S.D.	15	18	20	24	13
500	No.	12	12	12	12	12
	Mean	260	292	325	399	139
	S.D.	14	16	20	30	22

Unit: g

No.: No. of dams

a): Gestation day

No significant difference in any treated groups from control group.

Table 3-4 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Body weight of dams during the lactation period (Main group)

Dose mg/kg		Administration		Gain 0-4
		0	4a)	
0	No.	12	12	12
	Mean	324	338	14
	S.D.	22	24	14
20	No.	11	11	11
	Mean	317	330	13
	S.D.	21	14	10
100	No.	11	11	11
	Mean	316	329	13
	S.D.	19	17	16
500	No.	12	12	12
	Mean	316	329	13
	S.D.	20	20	11

Unit: g

No.: No. of dams

a): Lactation day

No significant difference in any treated groups from control group.

Table 3-5

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Body weight of female rats (Satellite group, administration period)

Dose mg/kg		Day of administration							Gain 1-42
		1	8	15	22	29	36	42	
0	No.	10	10	10	10	10	10	10	10
	Mean	237	248	260	273	280	284	292	56
	S.D.	10	10	9	11	12	13	11	9
500	No.	10	10	10	10	10	10	10	10
	Mean	232	246	253	262	268	280	280	48
	S.D.	8	12	18	20	15	20	20	15

Unit: g

No.: No. of animals

No significant difference between treated group and control group.

Table 3-6

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Body weight of male rats (Recovery period)

Dose mg/kg		Day of recovery			Gain 1-14
		1	8	14	
0	No.	5	5	5	5
	Mean	484	502	509	25
	S.D.	20	20	19	12
500	No.	5	5	5	5
	Mean	492	506	518	25
	S.D.	40	41	46	10

Unit: g

No.: No. of animals

No significant difference between treated group and control group.

Table 3-7

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Body weight of female rats (Recovery period)

Dose mg/kg		Day of recovery			Gain 1-14
		1	8	14	
0	No.	5	5	5	5
	Mean	293	303	301	8
	S.D.	3	4	6	5
500	No.	5	5	5	5
	Mean	291	295	302	11
	S.D.	18	18	19	4

Unit: g

No.: No. of animals

No significant difference between treated group and control group.

Table 4-1 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Food consumption of male rats (Administration period)

Dose mg/kg		Day of administration					
		1	8	15	30	36	42
0	No.	12	12	12	12	12	12
	Mean	27	28	27	28	28	29
	S.D.	2	2	2	2	3	2
20	No.	12	12	12	12	12	12
	Mean	26	28	27	27	29	28
	S.D.	3	2	2	2	3	3
100	No.	12	12	12	12	12	12
	Mean	27	28	28	28	28	28
	S.D.	4	2	2	2	2	1
500	No.	12	12	12	12	12	12
	Mean	26	28	29*	29	30	31
	S.D.	2	2	3D	3	3	3

Unit: g/rat/day

No.: No. of animals

*: p<0.05 (Significant difference from control group)

D: Dunnett's test

Table 4-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Food consumption of female rats during the pre-mating period (Main group)

Dose mg/kg		Day of administration		
		1	8	15
0	No.	12	12	12
	Mean	18	21	21
	S.D.	4	2	3
20	No.	12	12	12
	Mean	16	21	21
	S.D.	3	2	4
100	No.	12	12	12
	Mean	17	23	21
	S.D.	2	1	2
500	No.	12	12	12
	Mean	18	20	20
	S.D.	2	3	3

Unit: g/rat/day

No.: No. of animals

No significant difference in any treated groups from control group.

Table 4-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Food consumption of dams during the gestation period (Main group)

Dose mg/kg		Administration			
		1	7	14	20a)
0	No.	12	12	12	12
	Mean	21	25	26	25
	S.D.	3	3	3	4
20	No.	11	11	11	11
	Mean	21	24	26	24
	S.D.	3	3	3	3
100	No.	11	11	11	11
	Mean	22	24	26	24
	S.D.	3	3	2	4
500	No.	12	12	12	12
	Mean	22	25	27	24
	S.D.	3	3	3	2

Unit: g/rat/day

No.: No. of dams

a): Gestation day

No significant difference in any treated groups from control group.

Table 4-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Food consumption of dams during the lactation period (Main group)

Dose mg/kg		Administration	
		2	4a)
0	No.	12	12
	Mean	28	42
	S.D.	6	5
20	No.	11	11
	Mean	26	41
	S.D.	6	5
100	No.	11	11
	Mean	28	43
	S.D.	4	4
500	No.	12	12
	Mean	25	40
	S.D.	10	5

Unit: g/rat/day

No.: No. of dams

a): Lactation day

No significant difference in any treated groups from control group.

Table 4-5

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Food consumption of female rats (Satellite group, administration period)

Dose mg/kg		Day of administration					
		1	8	15	30	36	42
0	No.	10	10	10	10	10	10
	Mean	19	20	21	21	18	21
	S.D.	2	3	2	1	2	1
500	No.	10	10	10	10	10	10
	Mean	17	22*	21	20	21*	19*
	S.D.	2	1AT	4	4	3T	3AT

Unit: g/rat/day

No.: No. of animals

*: $p < 0.05$ (Significant difference from control group)

T: Student's t-test

AT: Aspin-Welch t-test

Table 4-6 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Food consumption of male rats (Recovery period)

Dose mg/kg		Day of recovery		
		1	8	14
0	No.	5	5	5
	Mean	28	29	29
	S.D.	2	3	4
500	No.	5	5	5
	Mean	29	30	30
	S.D.	2	3	3

Unit: g/rat/day

No.: No. of animals

No significant difference between treated group and control group.

Table 4-7

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Food consumption of female rats (Recovery period)

Dose mg/kg		Day of recovery		
		1	8	14
0	No.	5	5	5
	Mean	19	20	18
	S.D.	3	2	4
500	No.	5	5	5
	Mean	21	20	22
	S.D.	3	2	3

Unit: g/rat/day

No.: No. of animals

No significant difference between treated group and control group.

Table 5-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Urinalysis of male rats (Week 6 of administration)

Dose mg/kg	No.	pH										1) Protein					2) Ketone body					3) Glucose				
		5.0	5.5	6.0	6.5	7.0	7.5	8.0	8.5	>=9.0	-	+-	+	++	+++	-	+-	+	++	+++	-	+	++	+++	++++	
0	5	0	0	0	0	0	0	0	3	2	2	3	0	0	0	1	1	3	0	0	5	0	0	0	0	
20	5	0	0	0	0	0	1	1	2	1	3	1	0	1	0	0	3	2	0	0	5	0	0	0	0	
100	5	0	0	0	0	0	1	0	3	1	2	1	2	0	0	0	1	4	0	0	5	0	0	0	0	
500	5	0	0	0	4	1	0	0	0	0	1	2	2	0	0	1	3	1	0	0	5	0	0	0	0	
1)	-	: 0 mg/dL				+- : 15 mg/dL				+ : 30 mg/dL				++ : 100 mg/dL				+++ : >=300 mg/dL								
2)	-	: 0 mg/dL				+- : 5 mg/dL				+ : 15 mg/dL				++ : 40 mg/dL				+++ : 80 mg/dL								
3)	-	: 0 mg/dL				+ : 100 mg/dL				++ : 250 mg/dL				+++ : 500 mg/dL				++++ : >=1000 mg/dL								

Table 5-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Urinalysis of male rats (Week 6 of administration)

Dose mg/kg	No.	4) Occult blood					5) Bilirubin				6) Urobilinogen				7) Color		
		-	+-	+	++	+++	-	+	++	+++	+-	+	++	+++	LY	Y	DY
0	5	4	1	0	0	0	5	0	0	0	5	0	0	0	0	5	0
20	5	5	0	0	0	0	4	1	0	0	5	0	0	0	0	5	0
100	5	5	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0
500	5	5	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0

4)	-	: 0 mg/dL	+-	: 0.015 mg/dL	+	: 0.062 mg/dL	++	: 0.135 mg/dL	+++	: 0.405 mg/dL
5)	-	: 0 mg/dL	+	: 0.8 mg/dL	++	: 1.6 mg/dL	+++	: 3.2 mg/dL		
6)	+-	: 0.1-1.0 E.U./dL	+	: 2.0 E.U./dL	++	: 4.0 E.U./dL	+++	: >=8.0 E.U./dL		
7)	LY	: Light yellow	Y	: Yellow	DY	: Dark yellow				

Table 5-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Urinalysis of male rats (Week 6 of administration)

		URINE SEDIMENT															CRYSTALLIZATION																	
Dose mg/kg	No.	RBC					WBC					SEC					SREC					Cast			PS					CO				
		-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	-	+-	+	++	+++	-	+-	+	++	+++
0	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	0	5	0	0	5	0	0	2	1	2	0	0	5	0	0	0	0	
20	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	0	5	0	0	5	0	0	2	2	1	0	0	5	0	0	0	0	
100	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	0	5	0	0	5	0	0	2	1	2	0	0	5	0	0	0	0	
500	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	0	5	0	0	5	0	0	3	2	0	0	0	5	0	0	0	0	
SEC		: Squamous Epithelial Cell					-					: Negative																						
SREC		: Small Round Epithelial Cell					+-					: Slight																						
PS		: Phosphate Salts					+					: Mild																						
CO		: Calcium Oxalate					++					: Moderate																						
							+++					: Severe																						

Table 5-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Water intake and urinalysis of male rats (Week 6 of administration)

Dose mg/kg	No.		Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
0	5	Mean	35	13.8	2087	1.51	4.58	1.96
		S.D.	6	3.5	277	0.32	0.96	0.39
20	5	Mean	35	11.8	2228	1.44	4.14	1.83
		S.D.	5	1.7	299	0.31	0.38	0.34
100	5	Mean	37	14.7	1846	1.52	4.28	1.89
		S.D.	5	4.2	202	0.34	0.98	0.33
500	5	Mean	45*	16.8	1843	1.59	4.76	2.01
		S.D.	6D	5.4	258	0.34	0.80	0.37

*: p<0.05 (Significant difference from control group)

D: Dunnett's test

Table 5-5

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Urinalysis of female rats (Satellite group, Week 6 of administration)

Dose mg/kg	No.	pH									1) Protein					2) Ketone body					3) Glucose				
		5.0	5.5	6.0	6.5	7.0	7.5	8.0	8.5	>=9.0	-	+-	+	++	+++	-	+-	+	++	+++	-	+	++	+++	++++
0	5	0	0	0	0	0	0	3	1	1	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0
500	5	0	0	1	1	1	1	1	0	0	3	1	1	0	0	3	2	0	0	0	5	0	0	0	0
1)	-	: 0 mg/dL				+- : 15 mg/dL				+ : 30 mg/dL				++ : 100 mg/dL				+++ : >=300 mg/dL							
2)	-	: 0 mg/dL				+- : 5 mg/dL				+ : 15 mg/dL				++ : 40 mg/dL				+++ : 80 mg/dL							
3)	-	: 0 mg/dL				+ : 100 mg/dL				++ : 250 mg/dL				+++ : 500 mg/dL				++++ : >=1000 mg/dL							

Table 5-6

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Urinalysis of female rats (Satellite group, Week 6 of administration)

Dose mg/kg	No.	4) Occult blood					5) Bilirubin				6) Urobilinogen				7) Color		
		-	+	++	+++	++++	-	+	++	+++	+	++	+++	++++	LY	Y	DY
0	5	5	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0
500	5	5	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0

4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
 5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
 6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
 7) LY : Light yellow Y : Yellow DY : Dark yellow

Urinalysis of female rats (Satellite group, Week 6 of administration)

		URINE SEDIMENT															CRYSTALLIZATION																		
Dose mg/kg	No.	RBC					WBC					SEC					SREC					Cast			PS					CO					
		-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	-	+-	+	++	+++	-	+-	+	++	+++	
0	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	5	0	0	0	0	5	0	0	0	0
500	5	5	0	0	0	0	4	1	0	0	0	1	4	0	0	0	5	0	0	0	0	5	0	0	4	1	0	0	0	5	0	0	0	0	

SEC	:	Squamous Epithelial Cell	-	:	Negative
SREC	:	Small Round Epithelial Cell	+-	:	Slight
PS	:	Phosphate Salts	+	:	Mild
CO	:	Calcium Oxalate	++	:	Moderate
			+++	:	Severe

Table 5-8

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Water intake and urinalysis of female rats (Satellite group, Week 6 of administration)

Dose mg/kg	No.		Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
0	5	Mean	31	12.5	1640	1.05	2.97	1.37
		S.D.	9	4.8	224	0.25	0.96	0.38
500	5	Mean	30	10.1	2080	1.04	2.98	1.23
		S.D.	4	3.7	430	0.15	0.62	0.34

No significant difference between treated group and control group.

Table 5-9

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Urinalysis of male rats (Week 2 of recovery)

Dose mg/kg	No.	pH										1) Protein					2) Ketone body					3) Glucose				
		5.0	5.5	6.0	6.5	7.0	7.5	8.0	8.5	>=9.0	-	+-	+	++	+++	-	+-	+	++	+++	-	+	++	+++	++++	
0	5	0	0	0	0	0	0	0	1	4	0	1	4	0	0	1	0	4	0	0	5	0	0	0	0	
500	5	0	0	0	0	0	0	0	2	3	0	0	5	0	0	0	0	5	0	0	5	0	0	0	0	
1)	-	:	0	mg/dL		+-	:	15	mg/dL		+	:	30	mg/dL		++	:	100	mg/dL		+++	:	>=300	mg/dL		
2)	-	:	0	mg/dL		+-	:	5	mg/dL		+	:	15	mg/dL		++	:	40	mg/dL		+++	:	80	mg/dL		
3)	-	:	0	mg/dL		+	:	100	mg/dL		++	:	250	mg/dL		+++	:	500	mg/dL		++++	:	>=1000	mg/dL		

Table 5-10

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Urinalysis of male rats (Week 2 of recovery)

Dose mg/kg	No.	4) Occult blood					5) Bilirubin				6) Urobilinogen				7) Color		
		-	+	++	+++	++++	-	+	++	+++	+	+	++	+++	LY	Y	DY
0	5	2	2	1	0	0	5	0	0	0	5	0	0	0	0	5	0
500	5	3	2	0	0	0	5	0	0	0	5	0	0	0	0	5	0

4)	-	:	0 mg/dL		+-	:	0.015 mg/dL		+	:	0.062 mg/dL		++	:	0.135 mg/dL		+++	:	0.405 mg/dL
5)	-	:	0 mg/dL		+	:	0.8 mg/dL		++	:	1.6 mg/dL		+++	:	3.2 mg/dL				
6)	+-	:	0.1-1.0 E.U./dL		+	:	2.0 E.U./dL		++	:	4.0 E.U./dL		+++	:	>=8.0 E.U./dL				
7)	LY	:	Light yellow		Y	:	Yellow		DY	:	Dark yellow								

Table 5-11

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Urinalysis of male rats (Week 2 of recovery)

		URINE SEDIMENT																										
														CRYSTALLIZATION														
Dose mg/kg	No.	RBC				WBC				SEC				SREC				Cast			PS				CO			
		-	+	++	+++	-	+	++	+++	-	+	++	+++	-	+	++	+++	-	+	++	-	+	++	+++	-	+	++	+++
0	5	4	1	0	0	0	5	0	0	0	0	0	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	0
500	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	0	5	0	0	0	0	1	4	0	0	0	0
SEC : Squamous Epithelial Cell						- : Negative																						
SREC : Small Round Epithelial Cell						+- : Slight																						
PS : Phosphate Salts						+ : Mild																						
CO : Calcium Oxalate						++ : Moderate																						
						+++ : Severe																						

Table 5-12

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Water intake and urinalysis of male rats (Week 2 of recovery)

Dose mg/kg	No.		Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
0	5	Mean	38	15.1	2074	1.56	4.76	2.06
		S.D.	6	4.1	345	0.44	0.82	0.35
500	5	Mean	39	15.2	1876	1.47	4.28	1.86
		S.D.	7	4.4	220	0.25	1.10	0.38

No significant difference between treated group and control group.

Table 5-13

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Urinalysis of female rats (Week 2 of recovery)

Dose mg/kg	No.	pH									1) Protein					2) Ketone body					3) Glucose				
		5.0	5.5	6.0	6.5	7.0	7.5	8.0	8.5	>=9.0	-	+-	+	++	+++	-	+-	+	++	+++	-	+	++	+++	++++
0	5	0	0	0	0	0	1	0	2	2	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0
500	5	0	0	0	0	1	0	1	3	0	4	1	0	0	0	2	3	0	0	0	5	0	0	0	0
1)	- : 0 mg/dL	+- : 15 mg/dL									+ : 30 mg/dL					++ : 100 mg/dL					+++ : >=300 mg/dL				
2)	- : 0 mg/dL	+- : 5 mg/dL									+ : 15 mg/dL					++ : 40 mg/dL					+++ : 80 mg/dL				
3)	- : 0 mg/dL	+ : 100 mg/dL									++ : 250 mg/dL					+++ : 500 mg/dL					++++ : >=1000 mg/dL				

Table 5-14

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Urinalysis of female rats (Week 2 of recovery)

Dose mg/kg	No.	4) Occult blood					5) Bilirubin				6) Urobilinogen				7) Color		
		-	+	++	+++	++++	-	+	++	+++	++	+	++	+++	LY	Y	DY
0	5	5	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0
500	5	5	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0

4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
 5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
 6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
 7) LY : Light yellow Y : Yellow DY : Dark yellow

Table 5-15

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Urinalysis of female rats (Week 2 of recovery)

		URINE SEDIMENT																				CRYSTALLIZATION													
Dose mg/kg	No.	RBC					WBC					SEC					SREC					Cast			PS					CO					
		-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	-	+-	+	++	+++						
0	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	2	3	0	0	0	5	0	0	0	0
500	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	2	3	0	0	0	5	0	0	0	0

SEC	: Squamous Epithelial Cell	-	: Negative
SREC	: Small Round Epithelial Cell	+-	: Slight
PS	: Phosphate Salts	+	: Mild
CO	: Calcium Oxalate	++	: Moderate
		+++	: Severe

Table 5-16

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Water intake and urinalysis of female rats (Week 2 of recovery)

Dose mg/kg	No.		Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
0	5	Mean	37	16.1	1664	1.39	3.82	1.58
		S.D.	10	6.0	342	0.16	0.67	0.34
500	5	Mean	34	9.1	2045	0.93**	2.77*	1.13*
		S.D.	3	1.4	231	0.16T	0.38T	0.22T

*: $p < 0.05$; **: $p < 0.01$ (Significant difference from control group)

T: Student's t-test

Table 6-1 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Hematology of male rats (End of administration)

Dose mg/kg	No.		RBC ×10 ⁴ /μL	Hb g/dL	Ht %	MCV fL	MCH pg	MCHC g/dL	Reticu- loocyte %	Plate- let ×10 ⁴ /μL	PT s	APTT s	Fibri- nogen mg/dL
0	5	Mean	891	15.5	44.5	50.0	17.5	35.0	2.1	113.6	17.8	25.3	277
		S.D.	45	0.5	2.1	2.2	0.7	0.4	0.5	13.1	3.3	4.4	20
20	5	Mean	891	15.5	44.5	49.9	17.4	34.8	2.1	112.9	17.1	23.5	275
		S.D.	7	0.6	1.9	2.0	0.6	0.3	0.4	13.8	2.4	4.7	22
100	5	Mean	902	15.2	43.5	48.3	16.9	35.0	2.1	116.2	16.6	25.5	273
		S.D.	50	0.5	1.9	0.9	0.6	0.6	0.5	12.3	1.8	4.0	19
500	5	Mean	887	15.3	43.7	49.2	17.2	35.0	1.9	117.5	19.5	26.5	327
		S.D.	25	0.7	2.1	1.6	0.5	0.2	0.4	14.1	3.2	3.5	56

No significant difference in any treated groups from control group.

Table 6-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Hematology of male rats (End of administration)

Dose mg/kg	No.		WBC	Differential leukocyte counts (%)						Differential leukocyte counts ($\times 10^2/\mu\text{L}$)					
			$\times 10^2/\mu\text{L}$	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	5	Mean	75.7	69.0	25.5	1.7	0.3	2.9	0.6	52.2	19.0	1.3	0.2	2.4	0.5
		S.D.	26.4	3.9	3.6	0.4	0.1	1.4	0.6	18.1	5.8	0.4	0.2	2.1	0.7
20	5	Mean	82.6	71.6	23.2	1.7	0.5	2.6	0.5	59.7	18.7	1.3	0.4	2.1	0.4
		S.D.	27.2	4.8	4.6	0.4	0.2	0.7	0.2	22.5	4.7	0.3	0.3	0.6	0.2
100	5	Mean	90.5	76.4	18.4	1.4	0.4	2.7	0.8	69.3	16.5	1.3	0.4	2.3	0.7
		S.D.	17.6	6.7	6.5	0.2	0.1	0.7	0.2	16.5	6.6	0.3	0.2	0.5	0.2
500	5	Mean	73.4	79.1*	16.3*	1.6	0.3	2.1	0.5	58.7	11.4	1.2	0.2	1.5	0.4
		S.D.	18.6	5.6D	5.0D	0.2	0.1	0.7	0.3	18.0	1.7	0.3	0.1	0.3	0.3

LUC: Large unstained cells

*: $p < 0.05$ (Significant difference from control group)

D: Dunnett's test

Table 6-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Hematology of female rats (Lactation day 5)

Dose mg/kg	No.		RBC ×10 ⁴ /μL	Hb g/dL	Ht %	MCV fL	MCH pg	MCHC g/dL	Reticu- locyte %	Plate- let ×10 ⁴ /μL	PT s	APTT s	Fibri- nogen mg/dL
0	5	Mean	730	13.7	40.1	54.9	18.8	34.2	7.1	148.9	12.9	17.1	275
		S.D.	18	0.5	1.6	1.6	0.3	0.4	1.2	23.4	0.6	1.4	62
20	5	Mean	768	14.2	40.4	52.7	18.5	35.1*	5.4	139.6	12.4	16.9	301
		S.D.	45	0.6	1.6	1.6	0.5	0.4D	0.9	32.3	1.0	3.4	58
100	5	Mean	775	14.3	41.2	53.2	18.4	34.7	6.3	149.1	13.0	17.3	291
		S.D.	14	0.3	1.5	1.8	0.3	0.6	0.9	27.0	1.2	2.7	36
500	5	Mean	739	13.8	39.6	53.7	18.7	34.9	7.0	177.9	12.8	15.5	313
		S.D.	32	0.3	0.5	1.9	0.5	0.6	1.1	34.4	0.5	2.3	58

*: p<0.05 (Significant difference from control group)

D: Dunnett's test

Table 6-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Hematology of female rats (Lactation day 5)

Dose mg/kg	No.		WBC	Differential leukocyte counts (%)						Differential leukocyte counts ($\times 10^2/\mu\text{L}$)					
			$\times 10^2/\mu\text{L}$	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	5	Mean	101.1	58.4	36.9	0.9	0.3	3.1	0.4	58.3	38.1	0.9	0.3	3.2	0.4
		S.D.	22.9	4.8	4.6	0.7	0.1	0.9	0.1	9.1	12.7	0.6	0.1	1.6	0.1
20	5	Mean	102.3	68.0*	27.5*	0.9	0.3	2.8	0.6*	69.2	28.5	0.9	0.3	2.6	0.6
		S.D.	39.5	3.1D	2.5D	0.4	0.1	1.3	0.2D	25.5	13.1	0.6	0.2	1.0	0.3
100	5	Mean	103.6	70.3**	25.6**	1.0	0.3	2.3	0.5	73.4	25.9	1.0	0.3	2.5	0.5
		S.D.	14.0	6.6D	7.2D	0.3	0.1	0.7	0.0	15.4	5.2	0.3	0.1	0.8	0.1
500	5	Mean	102.6	72.3**	24.0**	0.7	0.3	2.2	0.6	74.1	24.7	0.7	0.3	2.2	0.6
		S.D.	10.9	2.7D	2.4D	0.2	0.0	0.4	0.2	8.5	3.4	0.2	0.1	0.6	0.2

LUC: Large unstained cells

*: $p < 0.05$; **: $p < 0.01$ (Significant difference from control group)

D: Dunnett's test

Table 6-5

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Hematology of female rats (Satellite group, End of administration)

Dose mg/kg	No.		RBC ×10 ⁴ /μL	Hb g/dL	Ht %	MCV fL	MCH pg	MCHC g/dL	Reticu- loocyte %	Plate- let ×10 ⁴ /μL	PT s	APTT s	Fibri- nogen mg/dL
0	5	Mean	869	15.7	44.1	50.7	18.0	35.5	2.1	109.9	13.9	19.4	223
		S.D.	12	0.6	1.9	1.8	0.5	0.4	0.4	7.8	0.4	2.4	17
500	5	Mean	840	15.1	42.5	50.5	18.0	35.6	1.8	120.2	13.4	19.0	245
		S.D.	34	0.5	1.7	0.6	0.3	0.4	0.2	14.3	0.5	3.4	34

No significant difference between treated group and control group.

Table 6-6

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Hematology of female rats (Satellite group, End of administration)

Dose mg/kg	No.		WBC	Differential leukocyte counts (%)						Differential leukocyte counts ($\times 10^2/\mu\text{L}$)					
			$\times 10^2/\mu\text{L}$	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	5	Mean	51.5	71.0	24.6	1.8	0.3	2.0	0.3	36.7	12.7	0.9	0.2	1.0	0.2
		S.D.	21.0	5.3	5.3	0.4	0.0	0.6	0.1	15.7	6.0	0.3	0.1	0.5	0.1
500	5	Mean	38.4	75.5	18.9	3.7	0.2*	1.5	0.3	29.0	7.4	1.3	0.1*	0.6	0.1
		S.D.	5.3	4.3	3.6	3.7	0.1T	0.4	0.1	3.4	2.5	1.2	0.0T	0.2	0.1

LUC: Large unstained cells

*: $p < 0.05$ (Significant difference from control group)

T: Student's t-test

Table 6-7

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Hematology of male rats (End of recovery)

Dose mg/kg	No.		RBC ×10 ⁴ /μL	Hb g/dL	Ht %	MCV fL	MCH pg	MCHC g/dL	Reticu- locyte %	Plate- let ×10 ⁴ /μL	PT s	APTT s	Fibri- nogen mg/dL
0	5	Mean	945	16.5	46.5	49.2	17.4	35.4	1.8	98.7	17.6	24.1	296
		S.D.	24	0.3	1.2	0.3	0.3	0.8	0.3	10.2	3.0	1.9	19
500	5	Mean	951	16.5	46.6	49.0	17.4	35.5	1.6	98.6	19.3	22.3	341
		S.D.	28	0.4	1.4	0.7	0.3	0.3	0.4	7.2	1.7	1.2	41

No significant difference between treated group and control group.

Table 6-8

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Hematology of male rats (End of recovery)

Dose mg/kg	No.		WBC	Differential leukocyte counts (%)						Differential leukocyte counts ($\times 10^2/\mu\text{L}$)					
			$\times 10^2/\mu\text{L}$	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	5	Mean	82.8	71.7	23.2	1.7	0.4	2.7	0.5	59.3	19.3	1.3	0.4	2.2	0.4
		S.D.	29.4	1.3	1.3	0.6	0.1	0.3	0.2	20.7	7.5	0.4	0.2	0.8	0.2
500	5	Mean	71.8	75.3	20.4	1.3	0.3	2.2	0.5	53.8	14.9	1.0	0.2	1.6	0.4
		S.D.	20.7	7.2	7.2	0.6	0.1	0.4	0.2	16.1	8.1	0.5	0.1	0.3	0.1

LUC: Large unstained cells

No significant difference between treated group and control group.

Table 6-9

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Hematology of female rats (End of recovery)

Dose mg/kg	No.		RBC ×10 ⁴ /μL	Hb g/dL	Ht %	MCV fL	MCH pg	MCHC g/dL	Reticu- locyte %	Plate- let ×10 ⁴ /μL	PT s	APTT s	Fibri- nogen mg/dL
0	5	Mean	865	15.8	43.2	49.9	18.2	36.6	1.7	116.9	12.6	19.2	208
		S.D.	31	0.9	2.2	2.4	1.0	0.4	0.5	6.3	1.0	2.5	26
500	5	Mean	870	16.1	44.3	50.9	18.5	36.3	2.0	123.3	12.6	19.5	241*
		S.D.	26	0.5	1.8	1.6	0.5	0.4	0.4	13.1	0.7	1.2	19T

*: p<0.05 (Significant difference from control group)

T: Student's t-test

Table 6-10

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Hematology of female rats (End of recovery)

Dose mg/kg	No.		WBC	Differential leukocyte counts (%)						Differential leukocyte counts ($\times 10^2/\mu\text{L}$)					
			$\times 10^2/\mu\text{L}$	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	5	Mean	69.0	79.3	16.4	1.8	0.3	1.6	0.6	54.2	11.9	1.2	0.2	1.1	0.4
		S.D.	19.2	4.4	4.7	0.4	0.1	0.2	0.2	13.0	6.3	0.5	0.1	0.4	0.2
500	5	Mean	53.3	76.9	19.2	1.4	0.2	1.7	0.6	40.7	10.4	0.8	0.1	0.9	0.3
		S.D.	11.2	6.7	5.7	1.0	0.1	0.6	0.1	7.8	4.5	0.8	0.0	0.4	0.1

LUC: Large unstained cells

No significant difference between treated group and control group.

Table 7-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Blood chemistry of male rats (End of administration)

Dose mg/kg	No.		AST (GOT) IU/L	ALT (GPT) IU/L	LDH IU/L	γ -GTP IU/L	ALP IU/L	TBA μ mol/L	T.cho mg/dL	TG mg/dL	PL mg/dL	T.bili- rubin mg/dL	Glucose mg/dL
0	5	Mean	65	31	42	1	363	6.8	52	36	83	0.1	133
		S.D.	4	3	7	0	76	1.8	11	10	13	0.0	19
20	5	Mean	68	33	58*	1	387	11.7	49	34	83	0.1	135
		S.D.	4	12	10D	0	73	2.9	8	17	11	0.0	14
100	5	Mean	61	28	46	1	381	11.0	48	33	79	0.1	139
		S.D.	7	4	7	1	70	8.6	10	19	15	0.0	20
500	5	Mean	58	24	47	1	362	5.6	50	33	80	0.1	129
		S.D.	8	3	6	0	39	3.1	10	15	14	0.0	16

*: p<0.05 (Significant difference from control group)

D: Dunnett's test

Table 7-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Blood chemistry of male rats (End of administration)

Dose mg/kg	No.		BUN mg/dL	Crea- tinine mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	Albumin g/dL	A/G
0	5	Mean	16	0.26	144	4.4	107	9.3	5.6	5.5	3.0	1.18
		S.D.	1	0.02	2	0.3	2	0.3	0.3	0.1	0.1	0.10
20	5	Mean	15	0.25	144	4.5	107	9.4	5.8	5.6	3.1	1.22
		S.D.	2	0.02	1	0.2	2	0.4	0.3	0.3	0.2	0.08
100	5	Mean	17	0.25	143	4.6	106	9.5	6.1*	5.8	3.0	1.10
		S.D.	3	0.02	1	0.1	1	0.2	0.4D	0.2	0.1	0.04
500	5	Mean	17	0.25	144	4.7	105	9.7	6.0	5.8	3.1	1.15
		S.D.	3	0.04	1	0.1	1	0.3	0.2	0.3	0.1	0.03

*: p<0.05 (Significant difference from control group)

D: Dunnett's test

Table 7-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Blood chemistry of female rats (Lactation day 5)

Dose mg/kg	No.		AST (GOT) IU/L	ALT (GPT) IU/L	LDH IU/L	γ -GTP IU/L	ALP IU/L	TBA μ mol/L	T.cho mg/dL	TG mg/dL	PL mg/dL	T.bili- rubin mg/dL	Glucose mg/dL
0	5	Mean	83	44	47	1	189	14.0	56	49	111	0.1	114
		S.D.	17	6	11	0	30	6.7	8	9	12	0.0	9
20	5	Mean	85	53	41	1	256	36.9	59	50	116	0.1	117
		S.D.	33	27	14	0	140	52.3	14	15	23	0.0	6
100	5	Mean	93	55	52	1	226	50.7	56	48	116	0.1	116
		S.D.	37	18	22	0	38	60.6	16	21	22	0.0	5
500	5	Mean	72	41	50	1	263	13.0	56	52	115	0.1	106
		S.D.	8	7	16	0	103	2.6	5	23	12	0.0	7

No significant difference in any treated groups from control group.

Table 7-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Blood chemistry of female rats (Lactation day 5)

Dose mg/kg	No.		BUN mg/dL	Crea- tinine mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	Albumin g/dL	A/G
0	5	Mean	15	0.27	142	4.2	108	10.0	6.2	5.8	3.3	1.30
		S.D.	2	0.06	1	0.4	0	0.2	0.1	0.2	0.2	0.06
20	5	Mean	17	0.25	141	4.5	105	10.4	6.8	6.0	3.3	1.25
		S.D.	2	0.05	1	0.4	3	0.5	0.5	0.4	0.2	0.07
100	5	Mean	17	0.26	141	4.3	108	10.2	6.5	5.9	3.4	1.32
		S.D.	1	0.03	1	0.2	2	0.2	0.3	0.2	0.1	0.07
500	5	Mean	16	0.22	141	4.5	106	10.2	6.7	5.9	3.3	1.27
		S.D.	3	0.01	2	0.2	1	0.3	0.6	0.2	0.2	0.07

No significant difference in any treated groups from control group.

Table 7-5

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Blood chemistry of female rats (Satellite group, End of administration)

Dose mg/kg	No.		AST (GOT) IU/L	ALT (GPT) IU/L	LDH IU/L	γ -GTP IU/L	ALP IU/L	TBA μ mol/L	T.cho mg/dL	TG mg/dL	PL mg/dL	T.bili- rubin mg/dL	Glucose mg/dL
0	5	Mean	65	33	43	1	213	11.0	56	22	110	0.1	134
		S.D.	10	12	9	0	39	2.7	15	12	25	0.0	11
500	5	Mean	62	27	44	1	169	9.0	63	21	119	0.1	106**
		S.D.	3	0	9	0	35	3.1	8	11	14	0.0	13T

** : $p < 0.01$ (Significant difference from control group)

T: Student's t-test

Table 7-6

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Blood chemistry of female rats (Satellite group, End of administration)

Dose mg/kg	No.		BUN mg/dL	Crea- tinine mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	Albumin g/dL	A/G
0	5	Mean	17	0.29	143	4.2	109	9.6	3.6	6.1	3.5	1.34
		S.D.	2	0.03	1	0.2	2	0.3	0.2	0.3	0.2	0.09
500	5	Mean	17	0.30	142*	4.3	107	9.8	4.5	6.3	3.5	1.24
		S.D.	1	0.02	1T	0.3	1	0.2	1.1	0.1	0.2	0.12

*: p<0.05 (Significant difference from control group)

T: Student's t-test

Table 7-7

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Blood chemistry of male rats (End of recovery)

Dose mg/kg	No.		AST (GOT) IU/L	ALT (GPT) IU/L	LDH IU/L	γ -GTP IU/L	ALP IU/L	TBA μ mol/L	T.cho mg/dL	TG mg/dL	PL mg/dL	T.bili- rubin mg/dL	Glucose mg/dL
0	5	Mean	63	32	45	1	335	20.1	50	32	83	0.1	122
		S.D.	7	3	5	0	20	17.4	8	21	14	0.0	9
500	5	Mean	62	37	49	1	344	16.3	51	38	88	0.1	131
		S.D.	9	11	12	0	41	8.2	8	14	10	0.0	15

No significant difference between treated group and control group.

Table 7-8

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Blood chemistry of male rats (End of recovery)

Dose mg/kg	No.		BUN mg/dL	Crea- tinine mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	Albumin g/dL	A/G
0	5	Mean	16	0.23	142	4.4	106	9.4	5.8	5.7	3.0	1.10
		S.D.	2	0.03	1	0.2	3	0.1	0.6	0.1	0.1	0.04
500	5	Mean	15	0.23	144	4.5	106	9.4	5.8	5.8	3.1	1.14
		S.D.	2	0.02	1	0.2	2	0.1	0.5	0.3	0.1	0.11

No significant difference between treated group and control group.

Table 7-9

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Blood chemistry of female rats (End of recovery)

Dose mg/kg	No.		AST (GOT) IU/L	ALT (GPT) IU/L	LDH IU/L	γ -GTP IU/L	ALP IU/L	TBA μ mol/L	T.cho mg/dL	TG mg/dL	PL mg/dL	T.bili- rubin mg/dL	Glucose mg/dL
0	5	Mean	64	27	41	1	174	9.0	55	13	104	0.1	121
		S.D.	3	2	10	1	58	3.3	10	2	17	0.0	12
500	5	Mean	62	29	36	1	199	10.9	74*	18	137*	0.1	131
		S.D.	5	6	4	1	34	7.8	9T	9	18T	0.0	14

*: $p < 0.05$ (Significant difference from control group)

T: Student's t-test

Table 7-10

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Blood chemistry of female rats (End of recovery)

Dose mg/kg	No.		BUN mg/dL	Crea- tinine mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	Albumin g/dL	A/G
0	5	Mean	19	0.32	143	4.2	109	9.8	4.6	6.0	3.5	1.41
		S.D.	3	0.05	1	0.4	1	0.3	0.6	0.2	0.2	0.12
500	5	Mean	16	0.30	142	4.2	108	9.8	4.6	6.3	3.5	1.29
		S.D.	2	0.04	1	0.3	1	0.3	0.9	0.4	0.3	0.12

No significant difference between treated group and control group.

Table 8-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Organ weight of male rats (End of administration)

			Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)
Absolute	0	No.	7	7	7	7	7	7
		Mean	476	2.07	12.9	23.4	324	1.50
		S.D.	48	0.07	1.6	3.8	132	0.16
	20	No.	12	12	12	12	12	12
		Mean	478	2.14	13.1	23.0	288	1.44
		S.D.	38	0.07	1.1	3.6	39	0.16
	100	No.	12	12	12	12	12	12
		Mean	466	2.09	12.3	21.7	285	1.31*
		S.D.	25	0.06	1.3	4.0	45	0.06D
	500	No.	7	7	7	7	7	7
		Mean	476	2.07	12.7	22.4	269	1.41
		S.D.	34	0.04	1.2	4.3	62	0.12
Relative	0	No.		7	7	7	7	7
		Mean		0.44	2.7	4.9	68	0.31
		S.D.		0.04	0.2	0.8	25	0.02
	20	No.		12	12	12	12	12
		Mean		0.45	2.8	4.8	61	0.30
		S.D.		0.03	0.2	0.6	8	0.04
	100	No.		12	12	12	12	12
		Mean		0.45	2.6	4.7	62	0.28**
		S.D.		0.02	0.2	0.9	12	0.01ST
	500	No.		7	7	7	7	7
		Mean		0.44	2.7	4.7	56	0.29
		S.D.		0.04	0.2	0.7	11	0.02

*: p<0.05; **: p<0.01 (Significant difference from control group)

D: Dunnett's test

ST: Steel's test

Table 8-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Organ weight of male rats (End of administration)

			Liver	Spleen	Kidney (R+L)	Adrenal (R+L)	Seminal vesicle	Prostate
		Dose mg/kg	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	mg(mg/100g BW)	g(g/100g BW)	g(g/100g BW)
Absolute	0	No.	7	7	7	7	7	7
		Mean	12.38	0.78	3.24	61	1.79	1.28
		S.D.	1.71	0.13	0.37	15	0.18	0.13
	20	No.	12	12	12	12	12	12
		Mean	11.97	0.77	3.27	63	1.78	1.26
		S.D.	1.66	0.13	0.30	10	0.32	0.20
	100	No.	12	12	12	12	12	12
		Mean	12.59	0.77	3.59	64	1.80	1.35
		S.D.	1.19	0.12	0.38	13	0.21	0.18
	500	No.	7	7	7	7	7	7
		Mean	14.18	0.76	3.78*	69	1.91	1.35
		S.D.	1.30	0.12	0.36D	9	0.30	0.15
Relative	0	No.	7	7	7	7	7	7
		Mean	2.59	0.16	0.68	13	0.38	0.27
		S.D.	0.16	0.03	0.05	3	0.06	0.05
	20	No.	12	12	12	12	12	12
		Mean	2.50	0.16	0.68	13	0.37	0.26
		S.D.	0.18	0.02	0.04	3	0.05	0.04
	100	No.	12	12	12	12	12	12
		Mean	2.70	0.17	0.77**	14	0.39	0.29
		S.D.	0.15	0.03	0.07D	2	0.05	0.04
	500	No.	7	7	7	7	7	7
		Mean	2.98**	0.16	0.79**	15	0.40	0.28
		S.D.	0.17D	0.02	0.05D	2	0.08	0.04

*: $p < 0.05$; **: $p < 0.01$ (Significant difference from control group)
D: Dunnett's test

Table 8-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Organ weight of male rats (End of administration)

		Testis (R+L) g(g/100g BW)		Epididymis (R+L) mg(mg/100g BW)	
Dose mg/kg					
Absolute	0	No.	7	7	
		Mean	3.11	1333	
		S.D.	0.32	178	
	20	No.	12	12	
		Mean	3.28	1280	
		S.D.	0.27	117	
	100	No.	12	12	
		Mean	3.32	1311	
		S.D.	0.19	52	
	500	No.	7	7	
		Mean	3.14	1329	
		S.D.	0.22	77	
Relative	0	No.	7	7	
		Mean	0.66	282	
		S.D.	0.12	49	
	20	No.	12	12	
		Mean	0.69	269	
		S.D.	0.07	32	
	100	No.	12	12	
		Mean	0.72	282	
		S.D.	0.07	20	
	500	No.	7	7	
		Mean	0.67	280	
		S.D.	0.09	20	

No significant difference in any treated groups from control group.

Table 8-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Organ weight of female rats (Lactation day 5)

			Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)
Absolute	0	No.	12	12	12	12	12	12
		Mean	303	1.97	17.5	16.5	221	1.03
		S.D.	21	0.08	2.4	2.0	69	0.05
	20	No.	11	11	11	11	11	11
		Mean	296	1.91*	18.5	15.5	230	1.01
		S.D.	14	0.04D	3.2	2.3	78	0.08
	100	No.	11	11	11	11	11	11
		Mean	293	1.93	17.8	15.3	246	1.00
		S.D.	15	0.05	2.4	2.4	57	0.06
	500	No.	12	12	12	12	12	12
		Mean	289	1.91*	17.9	15.7	198	0.97
		S.D.	15	0.05D	2.3	2.8	53	0.10
Relative	0	No.		12	12	12	12	12
		Mean		0.65	5.8	5.5	73	0.34
		S.D.		0.05	0.7	0.7	23	0.03
	20	No.		11	11	11	11	11
		Mean		0.65	6.3	5.2	78	0.34
		S.D.		0.03	1.2	0.7	28	0.03
	100	No.		11	11	11	11	11
		Mean		0.66	6.1	5.2	84	0.34
		S.D.		0.04	0.7	0.8	19	0.01
	500	No.		12	12	12	12	12
		Mean		0.67	6.2	5.4	69	0.34
		S.D.		0.03	0.7	0.9	18	0.02

*: p<0.05 (Significant difference from control group)

D: Dunnett's test

Table 8-5

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Organ weight of female rats (Lactation day 5)

			Liver	Spleen	Kidney (R+L)	Adrenal (R+L)	Ovary (R+L)	Uterus
		Dose mg/kg	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)
Absolute	0	No.	12	12	12	12	12	12
		Mean	9.68	0.67	2.14	79	108.1	749
		S.D.	0.78	0.06	0.18	11	12.5	103
	20	No.	11	11	11	11	11	11
		Mean	9.82	0.69	2.57	79	104.0	686
		S.D.	0.74	0.07	1.45	8	13.0	100
	100	No.	11	11	11	11	11	11
		Mean	9.84	0.67	2.16	85	110.5	801
		S.D.	0.66	0.08	0.13	9	11.3	109
	500	No.	12	12	12	12	12	12
		Mean	10.24	0.66	2.16	77	106.6	724
		S.D.	0.70	0.09	0.19	11	14.7	98
Relative	0	No.	12	12	12	12	12	12
		Mean	3.19	0.22	0.71	26	35.8	248
		S.D.	0.18	0.03	0.07	4	4.7	39
	20	No.	11	11	11	11	11	11
		Mean	3.32	0.23	0.86	27	35.1	231
		S.D.	0.19	0.03	0.48	3	4.1	29
	100	No.	11	11	11	11	11	11
		Mean	3.36	0.23	0.74	29	37.8	274
		S.D.	0.15	0.02	0.06	3	4.1	38
	500	No.	12	12	12	12	12	12
		Mean	3.55**	0.23	0.75	27	37.0	251
		S.D.	0.24D	0.02	0.06	4	5.3	31

** : $p < 0.01$ (Significant difference from control group)

D: Dunnett's test

Table 8-6

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Organ weight of female rats (Satellite group, End of administration)

			Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)
Absolute	0	No.	5	5	5	5	5	5
		Mean	270	1.92	16.2	15.6	316	0.87
		S.D.	12	0.04	1.5	3.0	46	0.05
	500	No.	5	5	5	5	5	5
		Mean	257	1.96	16.3	15.3	286	0.88
		S.D.	19	0.05	1.7	2.9	46	0.07
Relative	0	No.		5	5	5	5	5
		Mean		0.72	6.0	5.8	117	0.32
		S.D.		0.04	0.6	1.4	15	0.01
	500	No.		5	5	5	5	5
		Mean		0.76	6.4	6.0	111	0.34
		S.D.		0.04	0.9	1.3	11	0.04

No significant difference between treated group and control group.

Table 8-7

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Organ weight of female rats (Satellite group, End of administration)

			Liver	Spleen	Kidney (R+L)	Adrenal (R+L)	Ovary (R+L)	Uterus
		Dose mg/kg	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)
Absolute	0	No.	5	5	5	5	5	5
		Mean	6.73	0.53	1.84	67	89.5	664
		S.D.	0.68	0.09	0.08	5	12.4	116
	500	No.	5	5	5	5	5	5
		Mean	7.38	0.46	1.88	84*	91.9	466*
		S.D.	0.60	0.05	0.19	10T	16.4	44AT
Relative	0	No.	5	5	5	5	5	5
		Mean	2.49	0.19	0.68	25	33.3	246
		S.D.	0.15	0.03	0.04	3	5.2	44
	500	No.	5	5	5	5	5	5
		Mean	2.87**	0.18	0.73	33*	35.7	182*
		S.D.	0.11T	0.01	0.04	5T	4.9	23T

*: p<0.05; **: p<0.01 (Significant difference from control group)

T: Student's t-test

AT: Aspin-Welch t-test

Table 8-8

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Organ weight of male rats (End of recovery)

			Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)
Absolute	0	No.	5	5	5	5	5	5
		Mean	478	2.13	12.5	22.1	255	1.45
		S.D.	21	0.06	0.6	4.0	26	0.12
	500	No.	5	5	5	5	5	5
		Mean	483	2.09	13.3	22.0	187**	1.42
		S.D.	44	0.08	1.3	2.6	35T	0.17
Relative	0	No.		5	5	5	5	5
		Mean		0.45	2.6	4.6	53	0.30
		S.D.		0.02	0.2	0.7	6	0.02
	500	No.		5	5	5	5	5
		Mean		0.43	2.8	4.6	39**	0.30
		S.D.		0.03	0.3	0.3	5T	0.03

** : p<0.01 (Significant difference from control group)

T: Student's t-test

Table 8-9

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Organ weight of male rats (End of recovery)

			Liver	Spleen	Kidney (R+L)	Adrenal (R+L)	Seminal vesicle	Prostate
		Dose mg/kg	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	mg(mg/100g BW)	g(g/100g BW)	g(g/100g BW)
Absolute	0	No.	5	5	5	5	5	5
		Mean	11.99	0.79	3.29	64	1.78	1.39
		S.D.	1.52	0.08	0.21	10	0.21	0.13
	500	No.	5	5	5	5	5	5
		Mean	13.12	0.67	3.38	61	1.85	1.29
		S.D.	1.89	0.09	0.38	3	0.23	0.23
Relative	0	No.	5	5	5	5	5	5
		Mean	2.51	0.17	0.69	13	0.37	0.29
		S.D.	0.28	0.02	0.04	2	0.05	0.02
	500	No.	5	5	5	5	5	5
		Mean	2.71	0.14*	0.70	13	0.39	0.27
		S.D.	0.18	0.02T	0.05	1	0.05	0.04

*: p<0.05 (Significant difference from control group)

T: Student's t-test

Table 8-10

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Organ weight of male rats (End of recovery)

Dose mg/kg		Testis (R+L) g(g/100g BW)		Epididymis (R+L) mg(mg/100g BW)	
Absolute	0	No.	5	5	
		Mean	3.49	1380	
		S.D.	0.27	118	
	500	No.	5	5	
		Mean	3.16	1296	
		S.D.	0.27	77	
Relative	0	No.	5	5	
		Mean	0.73	289	
		S.D.	0.05	22	
	500	No.	5	5	
		Mean	0.66	270	
		S.D.	0.07	24	

No significant difference between treated group and control group.

Table 8-11

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Organ weight of female rats (End of recovery)

			Body weight	Brain	Pituitary	Thyroid (R+L)	Thymus	Heart
			g	g(g/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	g(g/100g BW)
Absolute	0	No.	5	5	5	5	5	5
		Mean	284	1.94	16.7	14.9	259	0.87
		S.D.	3	0.09	2.7	2.6	85	0.05
	500	No.	5	5	5	5	5	5
		Mean	281	1.90	17.2	15.3	230	0.92
		S.D.	17	0.08	3.9	3.9	22	0.08
Relative	0	No.		5	5	5	5	5
		Mean		0.68	5.9	5.2	91	0.31
		S.D.		0.03	0.9	0.8	28	0.02
	500	No.		5	5	5	5	5
		Mean		0.68	6.1	5.4	82	0.33
		S.D.		0.03	1.0	1.2	7	0.02

No significant difference between treated group and control group.

Table 8-12

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Organ weight of female rats (End of recovery)

			Liver	Spleen	Kidney (R+L)	Adrenal (R+L)	Ovary (R+L)	Uterus
		Dose mg/kg	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)
Absolute	0	No.	5	5	5	5	5	5
		Mean	6.80	0.54	1.84	66	89.4	479
		S.D.	0.27	0.13	0.11	9	8.4	108
	500	No.	5	5	5	5	5	5
		Mean	7.45	0.55	1.92	76	89.8	662*
		S.D.	0.63	0.04	0.13	10	19.6	136T
Relative	0	No.	5	5	5	5	5	5
		Mean	2.39	0.19	0.65	23	31.4	168
		S.D.	0.11	0.04	0.04	3	2.8	37
	500	No.	5	5	5	5	5	5
		Mean	2.65**	0.19	0.69	27	32.4	236*
		S.D.	0.09T	0.01	0.02	3	8.5	49T

*: $p < 0.05$; **: $p < 0.01$ (Significant difference from control group)

T: Student's t-test

Table 9-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Gross pathological findings (End of administration period (D42))

Organs	Sex:	M	M	M	M
Findings	Dose(mg/kg): Number:	0 7	20 12	100 12	500 7
Epididymis					
Focus, white		1	0	0	0
Intestine, ileum(Peyer's patch)					
Diverticulum		0	0	1	0
Stomach					
Focus, dark red, glandular stomach		1	1	1	0
Thickening, limiting ridge		0	0	1	6

M : Male

Table 9-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Gross pathological findings (End of administration period (D42))

Organs	Sex:	F	F
Findings	Dose(mg/kg): Number:	0 5	500 5
All tissues			
Not remarkable		5	5

F : Female

Table 9-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Gross pathological findings (End of administration period (L4))

Organs	Sex:	F	F	F	F
Findings	Dose(mg/kg): Number:	0 12	20 11	100 11	500 12
Kidney					
Nodule		0	1	0	0
Spleen					
Small		0	0	0	1
Stomach					
Focus, dark red, glandular stomach		3	1	1	4

F : Female

Table 9-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Gross pathological findings (End of recovery period)

Organs	Sex:	M	M	F	F
Findings	Dose(mg/kg): Number:	0 5	500 5	0 5	500 5
Stomach					
Focus, dark red, glandular stomach		0	1	0	1

M : Male, F : Female

Table 9-5

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Gross pathological findings (Undelivered/Not copulated)

Organs	Sex:	F	F
Findings	Dose(mg/kg): Number:	20 1	100 1
All tissues			
Not remarkable		1	1

F : Female

Table 10-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Histopathological findings (End of administration period (D42))

Organs	Sex: Dose(mg/kg): Number:	M 0 5	M 20 5	M 100 6	M 500 5
Findings					
Adrenal					
Number examined		5	0	1	5
Not remarkable		5	0	1	5
Bone+Bone marrow,femoral					
Number examined		5	0	1	5
Not remarkable		5	0	1	5
Cerebellum(Pons)					
Number examined		5	0	1	5
Not remarkable		5	0	1	5
Cerebrum					
Number examined		5	0	1	5
Not remarkable		5	0	1	5
Epididymis					
Number examined		5	0	1	5
Not remarkable		4	0	1	5
Granuloma,spermatic		1	0	0	0
mild		1	0	0	0
Eye					
Number examined		5	0	1	5
Not remarkable		5	0	1	5
Heart					
Number examined		5	0	1	5
Not remarkable		4	0	1	4
Cell infiltration		1	0	0	1
minimal		1	0	0	1
Intestine,duodenum					
Number examined		5	0	1	5
Not remarkable		5	0	1	5
Intestine,jejunum					
Number examined		5	0	1	5
Not remarkable		5	0	1	5
Intestine,ileum(Peyer's patch)					
Number examined		5	0	1	5
Not remarkable		5	0	1	5
Intestine,cecum					
Number examined		5	0	1	5
Not remarkable		5	0	1	4
Cell infiltration		0	0	0	1
mild		0	0	0	1
Intestine,colon					
Number examined		5	0	1	5
Not remarkable		5	0	1	5
Intestine,rectum					
Number examined		5	0	1	5
Not remarkable		5	0	1	5
Kidney					
Number examined		5	5	6	5
Not remarkable		3	2	0	0
Dilatation,tubular		0	0	0	2
minimal		0	0	0	2

M : Male

Table 10-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Histopathological findings (End of administration period (D42))

Organs	Sex: Dose(mg/kg): Number:	M 0 5	M 20 5	M 100 6	M 500 5
Findings					
Kidney (continued)					
Regeneration, tubular		2	2	6	5
minimal		2	2	1	1
mild		0	0	5	4
Eosinophilic body, tubular cell		1	2	6	5
minimal		1	2	1	0
mild		0	0	5	3
moderate		0	0	0	2
Urinary cast, granular		0	0	2	1
minimal		0	0	2	0
mild		0	0	0	1
Necrosis/Desquamation, tubular cell		0	0	0	2
minimal		0	0	0	2
Liver					
Number examined		5	0	1	5
Not remarkable		1	0	0	2
Necrosis, focal		1	0	0	0
minimal		1	0	0	0
Microgranuloma		4	0	1	3
minimal		4	0	1	3
Lung (bronchus)					
Number examined		5	0	1	5
Not remarkable		3	0	1	5
Aggregation, foamy cell		2	0	0	0
minimal		2	0	0	0
Lymph node, mesenteric					
Number examined		5	0	1	5
Not remarkable		5	0	1	5
Lymph node, submandibular					
Number examined		5	0	1	5
Not remarkable		5	0	1	5
Pancreas					
Number examined		5	0	1	5
Not remarkable		5	0	1	4
Cell infiltration		0	0	0	1
minimal		0	0	0	1
Parathyroid					
Number examined		5	0	1	5
Not remarkable		5	0	1	5
Pituitary					
Number examined		5	0	1	5
Not remarkable		5	0	1	5
Prostate					
Number examined		5	0	1	5
Not remarkable		0	0	0	1
Cell infiltration		5	0	1	4
minimal		5	0	0	3
mild		0	0	1	1
Salivary gland, submandibular					
Number examined		5	0	1	5
Not remarkable		5	0	1	5

M : Male

Table 10-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Histopathological findings (End of administration period (D42))

Organs	Sex: Dose(mg/kg): Number:	M 0 5	M 20 5	M 100 6	M 500 5
Findings					
Sciatic nerve					
Number examined		5	0	1	5
Not remarkable		5	0	1	5
Seminal vesicle(Coagulating gland)					
Number examined		5	0	1	5
Not remarkable		5	0	1	5
Skeletal muscle,femoral					
Number examined		5	0	1	5
Not remarkable		5	0	1	5
Spinal cord,thoracic					
Number examined		5	0	1	5
Not remarkable		5	0	1	5
Spleen					
Number examined		5	0	1	5
Not remarkable		0	0	1	1
Hematopoiesis,extramedullary		5	0	0	4
minimal		5	0	0	4
Stomach					
Number examined		5	5	6	5
Not remarkable		5	5	6	0
Hyperplasia,squamous,limiting ridge		0	0	0	5
minimal		0	0	0	5
Testis					
Number examined		5	0	1	5
Not remarkable		5	0	1	4
Atrophy,seminiferous tubular		0	0	0	1
minimal		0	0	0	1
Thymus					
Number examined		5	0	1	5
Not remarkable		5	0	1	5
Thyroid					
Number examined		5	0	1	5
Not remarkable		5	0	1	5
Trachea					
Number examined		5	0	1	5
Not remarkable		5	0	1	5
Urinary bladder					
Number examined		5	0	1	5
Not remarkable		5	0	1	5

M : Male

Table 10-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Histopathological findings (End of administration period (D42))

Organs	Sex:	F	F
Findings	Dose(mg/kg): Number:	0 5	500 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		5	5
Liver			
Number examined		5	5
Not remarkable		0	2
Microgranuloma		5	3
minimal		5	3

F : Female

Table 10-5

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Histopathological findings (End of administration period (D42))

Organs	Sex: Dose(mg/kg): Number:	F 0 5	F 500 5
Findings			
Lung(bronchus)			
Number examined		5	5
Not remarkable		4	5
Aggregation,foamy cell		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
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,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
Spinal cord,thoracic			
Number examined		5	5
Not remarkable		5	5
Spleen			
Number examined		5	5
Not remarkable		3	5
Hematopoiesis,extramedullary		2	0
minimal		2	0
Stomach			
Number examined		5	5
Not remarkable		5	3
Hyperplasia,squamous,limiting ridge		0	2
minimal		0	2
Thymus			
Number examined		5	5
Not remarkable		5	5

F : Female

Table 10-6

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Histopathological findings (End of administration period (D42))

Organs	Sex:	F	F
Findings	Dose(mg/kg): Number:	0 5	500 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

Table 10-7

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Histopathological findings (End of administration period (L4))

Organs	Sex: Dose(mg/kg): Number:	F 0 5	F 20 5	F 100 5	F 500 5
Findings					
Adrenal					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Bone+Bone marrow,femoral					
Number examined		5	0	0	5
Not remarkable		5	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
Eye					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Heart					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
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
Regeneration,tubular		1	0	0	1
minimal		1	0	0	1
Liver					
Number examined		5	0	0	5
Not remarkable		1	0	0	3
Microgranuloma		4	0	0	2
minimal		4	0	0	2

F : Female

Table 10-8

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Histopathological findings (End of administration period (L4))

Organs	Sex:	F	F	F	F
Findings	Dose(mg/kg): Number:	0 5	20 5	100 5	500 5
Lung(bronchus)					
Number examined		5	0	0	5
Not remarkable		5	0	0	4
Aggregation,foamy cell		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
Ovary					
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	5
Not remarkable		5	0	0	5
Pituitary					
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
Skeletal muscle,femoral					
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
Hematopoiesis,extramedullary		5	0	0	5
minimal		0	0	0	1
mild		5	0	0	4
Stomach					
Number examined		5	5	5	5
Not remarkable		4	4	4	4
Erosion,glandular stomach		1	1	1	1
minimal		1	1	1	1
Thymus					
Number examined		5	0	0	5
Not remarkable		5	0	0	5

F : Female

Table 10-9

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Histopathological findings (End of administration period (L4))

Organs	Sex:	F	F	F	F
Findings	Dose(mg/kg): Number:	0 5	20 5	100 5	500 5
Thyroid					
Number examined		5	0	0	5
Not remarkable		5	0	0	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
Uterus					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Vagina					
Number examined		5	0	0	5
Not remarkable		5	0	0	5

F : Female

Table 10-10

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Histopathological findings (End of recovery period)

Organs	Sex:	M	M	F	F
Findings	Dose(mg/kg): Number:	0 5	500 5	0 5	500 5
Kidney					
Number examined		5	5	0	0
Not remarkable		1	0	0	0
Regeneration,tubular		4	5	0	0
minimal		4	0	0	0
mild		0	5	0	0
Eosinophilic body,tubular cell		1	4	0	0
minimal		1	4	0	0
Urinary cast,granular		0	2	0	0
minimal		0	2	0	0
Stomach					
Number examined		5	5	5	5
Not remarkable		4	3	5	4
Erosion,glandular stomach		0	1	0	1
minimal		0	1	0	1
Hyperplasia,squamous,limiting ridge		1	1	0	0
minimal		1	1	0	0
Thymus					
Number examined		5	5	0	0
Not remarkable		5	5	0	0
Uterus					
Number examined		-	-	5	5
Not remarkable		-	-	5	5

M : Male, F : Female

- : Not applicable

Table 10-11

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Histopathological findings (Undelivered/Not copulated)

Organs	Sex: Dose(mg/kg): Number:	F 20 1	F 100 1
Findings			
Adrenal			
Number examined		1	1
Not remarkable		1	1
Bone+Bone marrow, femoral			
Number examined		1	1
Not remarkable		1	1
Cerebellum(Pons)			
Number examined		1	1
Not remarkable		1	1
Cerebrum			
Number examined		1	1
Not remarkable		1	1
Eye			
Number examined		1	1
Not remarkable		1	1
Heart			
Number examined		1	1
Not remarkable		1	1
Intestine, duodenum			
Number examined		1	1
Not remarkable		1	1
Intestine, jejunum			
Number examined		1	1
Not remarkable		1	1
Intestine, ileum(Peyer's patch)			
Number examined		1	1
Not remarkable		1	1
Intestine, cecum			
Number examined		1	1
Not remarkable		1	1
Intestine, colon			
Number examined		1	1
Not remarkable		1	1
Intestine, rectum			
Number examined		1	1
Not remarkable		1	1
Kidney			
Number examined		1	1
Not remarkable		1	1
Liver			
Number examined		1	1
Not remarkable		1	0
Microgranuloma		0	1
minimal		0	1
Lung(bronchus)			
Number examined		1	1
Not remarkable		1	0
Aggregation, foamy cell		0	1
minimal		0	1

F : Female

Table 10-12

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Histopathological findings (Undelivered/Not copulated)

Organs	Sex: Dose(mg/kg): Number:	F 20 1	F 100 1
Findings			
Lymph node,mesenteric			
Number examined		1	1
Not remarkable		1	1
Lymph node,submandibular			
Number examined		1	1
Not remarkable		1	1
Ovary			
Number examined		1	1
Not remarkable		1	1
Pancreas			
Number examined		1	1
Not remarkable		1	1
Parathyroid			
Number examined		1	1
Not remarkable		1	1
Pituitary			
Number examined		1	1
Not remarkable		1	1
Salivary gland,submandibular			
Number examined		1	1
Not remarkable		1	1
Sciatic nerve			
Number examined		1	1
Not remarkable		1	1
Skeletal muscle,femoral			
Number examined		1	1
Not remarkable		1	1
Spinal cord,thoracic			
Number examined		1	1
Not remarkable		1	1
Spleen			
Number examined		1	1
Hematopoiesis,extramedullary		1	1
minimal		1	1
Stomach			
Number examined		1	1
Not remarkable		1	1
Thymus			
Number examined		1	1
Not remarkable		1	1
Thyroid			
Number examined		1	1
Not remarkable		1	1

F : Female

Table 10-13

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Histopathological findings (Undelivered/Not copulated)

Organs	Sex: Dose(mg/kg): Number:	F 20 1	F 100 1
Findings			
Trachea			
Number examined		1	1
Not remarkable		1	1
Urinary bladder			
Number examined		1	1
Not remarkable		1	1
Uterus			
Number examined		1	1
Not remarkable		1	1
Vagina			
Number examined		1	1
Not remarkable		1	1

F : Female

Table 11

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Estrous cycle in female rats during the pre-mating period

Dose mg/kg	No. of animals	Count of estrus					Mean duration of cycles Mean±S.D.
		0	1	2	3	4	
0	12	0	0	0	4	8	3.7±0.5
20	12	0	0	0	3	9	3.8±0.5
100	12	0	0	0	2	10	3.8±0.4
500	12	0	0	0	5	7	3.6±0.5

No significant difference in any treated groups from control group.

Table 12

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Mating and fertility of animals

Dose mg/kg	Male				Female			
	No. of males	Days until copulation Mean±S.D.	Copulation index (%) a)	Insemination index (%) b)	No. of females	Days until copulation Mean±S.D.	Copulation index (%) a)	Fertility index (%) c)
0	12	2.5±1.6	12/12(100.0)	12/12(100.0)	12	2.5±1.6	12/12(100.0)	12/12(100.0)
20	12	2.1±1.0	12/12(100.0)	11/12(91.7)	12	2.1±1.0	12/12(100.0)	11/12(91.7)
100	12	2.4±1.1	11/12(91.7)	11/11(100.0)	12	2.4±1.1	11/12(91.7)	11/11(100.0)
500	12	2.3±1.2	12/12(100.0)	12/12(100.0)	12	2.3±1.2	12/12(100.0)	12/12(100.0)

a): (No. of copulated animals / No. of mated animals) × 100

b): (No. of males which impregnated females / No. of copulated males) × 100

c): (No. of pregnant females / No. of copulated females) × 100

No significant difference in any treated groups from control group.

Table 13 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Delivery data on dams

Dose mg/kg		No. of pregnant females	No. of females with liveborns	Delivery index % a)	Gestation length in days	No. of corpora lutea	No. of implan- tation sites	Implan- tation index % b)	No. of still- borns (%)c)	No. of live- borns	External d) abnor- malities(%)e)	Live birth index % f)
0	Total	12	12	100.0		202	182		2	164	0	
	Mean				21.7	16.8	15.2	90.4	(0.9)	13.7	(0.0)	89.4
	S.D.				0.5	2.4	2.6	11.3	(2.2)	3.3	(0.0)	13.1
20	Total	11	11	100.0		168	160		1	152	0	
	Mean				21.7	15.3	14.5	95.1	(0.6)	13.8	(0.0)	94.9
	S.D.				0.5	1.8	2.0	5.8	(1.9)	2.4	(0.0)	8.5
100	Total	11	11	100.0		179	166		0	151	0	
	Mean				21.5	16.3	15.1	93.0	(0.0)	13.7	(0.0)	91.1
	S.D.				0.5	1.6	1.5	8.0	(0.0)	1.7	(0.0)	8.3
500	Total	12	12	100.0		190	179		1	163	0	
	Mean				21.8	15.8	14.9	94.6	(0.6)	13.6	(0.0)	90.5
	S.D.				0.6	1.7	1.7	8.5	(1.9)	3.1	(0.0)	16.9

a): (No. of females which delivered liveborns / No. of pregnant females) × 100

b): (No. of implantation sites / No. of corpora lutea) × 100

c): (No. of stillborns / No. of liveborns and stillborns) × 100

d): No. of delivered pups with external abnormalities

e): (No. of delivered pups with external abnormalities / No. of liveborns and stillborns) × 100

f): (No. of liveborns / No. of implantation sites) × 100

No significant difference in any treated groups from control group.

Table 14

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Viability index of pups

Dose mg/kg		No. of dams	No. of live pups		Viability index on postnatal day 4 % a)
			Day 0	Day 4	
0	Total	12	164	160	
	Mean		13.7	13.3	97.9
	S.D.		3.3	3.1	4.2
20	Total	11	152	149	
	Mean		13.8	13.5	98.3
	S.D.		2.4	2.3	4.0
100	Total	11	151	149	
	Mean		13.7	13.5	98.7
	S.D.		1.7	1.7	2.9
500	Total	12	163	161	
	Mean		13.6	13.4	98.9
	S.D.		3.1	3.0	2.7

a): (No. of live pups on postnatal day 4 / No. of liveborns) × 100
No significant difference in any treated groups from control group.

Table 15 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Sex ratio of pups

Dose mg/kg	No. of dams		Liveborns		Sex ratio of liveborns at birth a)	No. of dams	Postnatal day 4		Sex ratio of live pups on day 4 b)
			No. of males	No. of females			No. of males	No. of females	
0	12	Total	75	89		12	74	86	
		Mean	6.3	7.4	0.46		6.2	7.2	0.47
		S.D.	2.9	3.2	0.21		2.8	3.0	0.21
20	11	Total	64	88		11	62	87	
		Mean	5.8	8.0	0.42		5.6	7.9	0.42
		S.D.	2.1	2.6	0.15		2.1	2.4	0.15
100	11	Total	74	77		11	74	75	
		Mean	6.7	7.0	0.49		6.7	6.8	0.50
		S.D.	1.8	2.1	0.12		1.8	2.3	0.12
500	12	Total	90	73		12	88	73	
		Mean	7.5	6.1	0.56		7.3	6.1	0.55
		S.D.	2.4	2.3	0.13		2.3	2.3	0.13

a): No. of liveborn males / No. of liveborns

b): No. of live males on day 4 / No. of live pups on day 4

No significant difference in any treated groups from control group.

Table 16

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Body weight of pups

Dose mg/kg	Male			Female		
	0	4a)	Gain	0	4a)	Gain
0	No.	11 ^{b)}	11	11	12	12
	Mean	6.6	10.3	3.7	6.2	9.7
	S.D.	0.6	1.5	1.1	0.5	1.4
20	No.	11	11	11	11	11
	Mean	6.5	9.8	3.2	6.2	9.3
	S.D.	0.5	1.0	0.7	0.3	1.0
100	No.	11	11	11	11	11
	Mean	6.5	10.0	3.5	6.1	9.4
	S.D.	0.4	0.9	0.6	0.4	0.9
500	No.	12	12	12	12	12
	Mean	6.6	9.7	3.1	6.2	9.3
	S.D.	0.6	1.6	1.3	0.8	2.0

Unit: g

No.: No. of dams

a): Postnatal day

b): Male pups were not born in one dam.

No significant difference in any treated groups from control group.

Table 17

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Externally for gross abnormalities in pups on postnatal day 4

	Dose (mg/kg)	0	20	100	500
Male					
No. of pups examined		74	62	74	88
No. of pups with abnormal findings		0	0	0	0
Female					
No. of pups examined		86	87	75	73
No. of pups with abnormal findings		0	0	0	0

Appendix 1-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in male rats (Administration period)

Dose (mg/kg): 0

Animal number	Day of administration													
	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

Appendix 1-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in male rats (Administration period)

Dose (mg/kg): 0

Animal number	Day of administration													
	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

Appendix 1-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in male rats (Administration period)

Dose (mg/kg): 0

Animal number	Day of administration														43a)
	29	30	31	32	33	34	35	36	37	38	39	40	41	42	
1001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1002	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1003	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1004	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1005	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1006	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1007	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1008	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1009	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1010	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1011	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

a): Day of necropsy
-: No abnormal findings

Appendix 1-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in male rats (Administration period)

Dose (mg/kg): 20

Animal number	Day of administration													
	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

Appendix 1-5

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in male rats (Administration period)

Dose (mg/kg): 20

Animal number	Day of administration													
	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

Appendix 1-6

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in male rats (Administration period)

Dose (mg/kg): 20

Animal number	Day of administration														43a)
	29	30	31	32	33	34	35	36	37	38	39	40	41	42	
2001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2002	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2003	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2004	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2005	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2006	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2007	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2008	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2009	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2010	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2011	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

a): Day of necropsy
-: No abnormal findings

Appendix 1-7

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in male rats (Administration period)

Dose (mg/kg): 100

Animal number	Day of administration													
	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

Appendix 1-8

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in male rats (Administration period)

Dose (mg/kg): 100

Animal number	Day of administration													
	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

Appendix 1-9

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in male rats (Administration period)

Dose (mg/kg): 100

Animal number	Day of administration														43a)
	29	30	31	32	33	34	35	36	37	38	39	40	41	42	
3001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3002	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3003	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3004	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3005	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3006	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3007	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3008	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3009	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3010	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3011	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

a): Day of necropsy
-: No abnormal findings

Appendix 1-10

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in male rats (Administration period)

Dose (mg/kg): 500

Animal number	Day of administration													
	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

Appendix 1-11

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in male rats (Administration period)

Dose (mg/kg): 500

Animal number	Day of administration													
	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

Appendix 1-12

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in male rats (Administration period)

Dose (mg/kg): 500

Animal number	Day of administration														43a)
	29	30	31	32	33	34	35	36	37	38	39	40	41	42	
4001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4002	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4003	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4004	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4005	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4006	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4007	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4008	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4009	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4010	-	-	-	-	-	-	-	-	-	A	-	-	-	-	-
4011	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

a): Day of necropsy
 -: No abnormal findings
 A: Ataxia

Appendix 1-13

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in female rats during the pre-mating period (Main group)

Dose (mg/kg): 0

Animal number	Day of administration														
	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

Appendix 1-14

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in female rats during the pre-mating period (Main group)

Dose (mg/kg): 20

Animal number	Day of administration														
	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

Appendix 1-15

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in female rats during the pre-mating period (Main group)

Dose (mg/kg): 100

Animal number	Day of administration														
	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

Appendix 1-16

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in female rats during the pre-mating period (Main group)

Dose (mg/kg): 500

Animal number	Day of administration														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
4101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4103	-	-	-	-	-	-	-	-	-	-	A	-	-	-	-
4104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4107	-	-	-	-	-	-	A	-	-	-	-	-	-	-	-
4108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4109	-	-	-	-	-	-	-	-	-	B	-	-	-	-	-
4110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4111	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4112	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-: No abnormal findings

A: Ataxia

B: Prone/Lateral position

Appendix 1-17

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in dams during the gestation period (Main group)

Dose (mg/kg): 0

Dam number	Administration																							
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23a)
1101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
1102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
1103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1111	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1112	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

a): Gestation day

-: No abnormal findings

d: Delivery

/d: Found delivery after the observation of general conditions.

Appendix 1-18

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in dams during the gestation period (Main group)

Dose (mg/kg): 20

Dam number	Administration																							
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23a)
2101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
2102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
2103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
2104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
2105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
2106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
2107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
2108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
2109	Non-pregnant																							
2110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
2111	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2112	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

a): Gestation day

-: No abnormal findings

d: Delivery

/d: Found delivery after the observation of general conditions.

Appendix 1-19

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in dams during the gestation period (Main group)

Dose (mg/kg): 100

Dam number	Administration																							
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23a)
3101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
3102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
3103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3111	Not copulated																							
3112	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

a): Gestation day

-: No abnormal findings

d: Delivery

/d: Found delivery after the observation of general conditions.

Appendix 1-20

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in dams during the gestation period (Main group)

Dose (mg/kg): 500

Dam number	Administration																								
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23a)	
4101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d	d
4102	-	-	-	-	-	-	-	-	A	-	-	-	-	B	-	-	-	-	B	-	-	B	-	-/d	
4103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d	
4104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d	
4105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
4106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
4107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
4108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
4109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
4110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
4111	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
4112	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	

a): Gestation day

-: No abnormal findings

A: Ataxia

B: Prone/Lateral position

d: Delivery

/d: Found delivery after the observation of general conditions.

Appendix 1-21

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in dams during the lactation period (Main group)

Dose (mg/kg): 0

Dam number	Administration					5b)
	0	1	2	3	4a)	
1101	-	-	-	-	-	-
1102	-	-	-	-	-	-
1103	-	-	-	-	-	-
1104	-	-	-	-	-	-
1105	-	-	-	-	-	-
1106	-	-	-	-	-	-
1107	-	-	-	-	-	-
1108	-	-	-	-	-	-
1109	-	-	-	-	-	-
1110	-	-	-	-	-	-
1111	-	-	-	-	-	-
1112	-	-	-	-	-	-

a): Lactation day

b): Day of necropsy

-: No abnormal findings

Appendix 1-22

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in dams during the lactation period (Main group)

Dose (mg/kg): 20

Dam number	Administration					5b)
	0	1	2	3	4a)	
2101	-	-	-	-	-	-
2102	-	-	-	-	-	-
2103	-	-	-	-	-	-
2104	-	-	-	-	-	-
2105	-	-	-	-	-	-
2106	-	-	-	-	-	-
2107	-	-	-	-	-	-
2108	-	-	-	-	-	-
2109	Non-pregnant					-
2110	-	-	-	-	-	-
2111	-	-	-	-	-	-
2112	-	-	-	-	-	-

a): Lactation day
b): Day of necropsy
-: No abnormal findings

Appendix 1-23

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in dams during the lactation period (Main group)

Dose (mg/kg): 100

Dam number	Administration					5b)
	0	1	2	3	4a)	
3101	-	-	-	-	-	-
3102	-	-	-	-	-	-
3103	-	-	-	-	-	-
3104	-	-	-	-	-	-
3105	-	-	-	-	-	-
3106	-	-	-	-	-	-
3107	-	-	-	-	-	-
3108	-	-	-	-	-	-
3109	-	-	-	-	-	-
3110	-	-	-	-	-	-
3111	Not copulated					-
3112	-	-	-	-	-	-

a): Lactation day
b): Day of necropsy
-: No abnormal findings

Appendix 1-24

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in dams during the lactation period (Main group)

Dose (mg/kg): 500

Dam number	Administration					
	0	1	2	3	4a)	5b)
4101	-	-	-	-	-	-
4102	B	B	B	-	-	-
4103	-	-	-	-	-	-
4104	-	B	B	-	-	-
4105	-	-	-	-	-	-
4106	-	-	A	-	-	-
4107	-	-	-	A	-	-
4108	-	-	-	-	-	-
4109	-	-	-	-	-	-
4110	-	-	-	-	-	-
4111	-	-	-	-	-	-
4112	-	-	-	-	-	-

a): Lactation day

b): Day of necropsy

-: No abnormal findings

A: Ataxia

B: Prone/Lateral position

Appendix 1-25

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in female rats (Satellite group, administration period)

Dose (mg/kg): 0

Animal number	Day of administration													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1113	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1114	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1115	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1116	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1117	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1118	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1119	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1120	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1121	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1122	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-: No abnormal findings

Appendix 1-26

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in female rats (Satellite group, administration period)

Dose (mg/kg): 0

Animal number	Day of administration													
	15	16	17	18	19	20	21	22	23	24	25	26	27	28
1113	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1114	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1115	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1116	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1117	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1118	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1119	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1120	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1121	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1122	-	-	-	-	-	-	-	-	-	-	-	-	-	-

∴ No abnormal findings

Appendix 1-27

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in female rats (Satellite group, administration period)

Dose (mg/kg): 0

Animal number	Day of administration														43a)
	29	30	31	32	33	34	35	36	37	38	39	40	41	42	
1113	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1114	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1115	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1116	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1117	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1118	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1119	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1120	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1121	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1122	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

a): Day of necropsy
 -: No abnormal findings

Appendix 1-28

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in female rats (Satellite group, administration period)

Dose (mg/kg): 500

Animal number	Day of administration													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
4113	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4114	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4115	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4116	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4117	-	A	-	-	-	-	-	-	-	-	-	-	-	-
4118	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4119	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4120	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4121	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4122	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-: No abnormal findings

A: Ataxia

Appendix 1-29

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in female rats (Satellite group, administration period)

Dose (mg/kg): 500

Animal number	Day of administration													
	15	16	17	18	19	20	21	22	23	24	25	26	27	28
4113	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4114	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4115	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4116	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4117	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4118	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4119	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4120	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4121	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4122	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-: No abnormal findings

Appendix 1-30

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in female rats (Satellite group, administration period)

Dose (mg/kg): 500

Animal number	Day of administration														43a)
	29	30	31	32	33	34	35	36	37	38	39	40	41	42	
4113	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4114	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4115	-	-	A	-	-	-	-	-	-	-	-	-	A	-	-
4116	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4117	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4118	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4119	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4120	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4121	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4122	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

a): Day of necropsy
 -: No abnormal findings
 A: Ataxia

Appendix 1-31

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in male rats (Recovery period)

Dose (mg/kg): 0

Animal number	Day of recovery														15a)
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
1008	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1009	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1010	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1011	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

a): Day of necropsy
-: No abnormal findings

Appendix 1-32

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in male rats (Recovery period)

Dose (mg/kg): 500

Animal number	Day of recovery														15a)
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
4008	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4009	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4010	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4011	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

a): Day of necropsy

-: No abnormal findings

Appendix 1-33

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in female rats (Recovery period)

Dose (mg/kg): 0

Animal number	Day of recovery														15a)
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
1118	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1119	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1120	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1121	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1122	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

a): Day of necropsy

-: No abnormal findings

Appendix 1-34

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual clinical signs in female rats (Recovery period)

Dose (mg/kg): 500

Animal number	Day of recovery														15a)
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
4118	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4119	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4120	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4121	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4122	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

a): Day of necropsy

-: No abnormal findings

Appendix 2-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 1 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 1 of administration)

Dose (mg/kg) : 20

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 1 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 1 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-5

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 2 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-6

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 2 of administration)

Dose (mg/kg) : 20

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-7

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 2 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-8

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 2 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-9

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 3 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-10

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 3 of administration)

Dose (mg/kg) : 20

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-11

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 3 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-12

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 3 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-13

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 4 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-14

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 4 of administration)

Dose (mg/kg) : 20

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-15

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 4 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-16

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 4 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-17

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 5 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-18

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 5 of administration)

Dose (mg/kg) : 20

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-19

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 5 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-20

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 5 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-21

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 6 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-22

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 6 of administration)

Dose (mg/kg) : 20

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-23

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 6 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-24

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 6 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-25

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 1 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-26

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 1 of administration)

Dose (mg/kg) : 20

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-27

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 1 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-28

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 1 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-29

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 2 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-30

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 2 of administration)

Dose (mg/kg) : 20

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-31

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 2 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-32

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 2 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-33

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 1)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-34

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 1)

Dose (mg/kg) : 20

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9 NP	10	11	12
Posture a)	N	N	N	N	N	N	N	N		N	N	N
Convulsion b)	0	0	0	0	0	0	0	0		0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0		0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

NP: Non-pregnant

Appendix 2-35

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 1)

Dose (mg/kg) : 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 NC	12
Posture a)	N	N	N	N	N	N	N	N	N	N		N
Convulsion b)	0	0	0	0	0	0	0	0	0	0		0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0		0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

NC: Not copulated

Appendix 2-36

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 1)

Dose (mg/kg) : 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-37

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 7)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-38

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 7)

Dose (mg/kg) : 20

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9 NP	10	11	12
Posture a)	N	N	N	N	N	N	N	N		N	N	N
Convulsion b)	0	0	0	0	0	0	0	0		0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0		0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

NP: Non-pregnant

Appendix 2-39

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 7)

Dose (mg/kg) : 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 NC	12
Posture a)	N	N	N	N	N	N	N	N	N	N		N
Convulsion b)	0	0	0	0	0	0	0	0	0	0		0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0		0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

NC: Not copulated

Appendix 2-40

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 7)

Dose (mg/kg) : 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-41

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 14)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-42

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 14)

Dose (mg/kg) : 20

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9 NP	10	11	12
Posture a)	N	N	N	N	N	N	N	N		N	N	N
Convulsion b)	0	0	0	0	0	0	0	0		0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0		0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

NP: Non-pregnant

Appendix 2-43

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 14)

Dose (mg/kg) : 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 NC	12
Posture a)	N	N	N	N	N	N	N	N	N	N		N
Convulsion b)	0	0	0	0	0	0	0	0	0	0		0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0		0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

NC: Not copulated

Appendix 2-44

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 14)

Dose (mg/kg) : 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-45

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 20)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-46

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 20)

Dose (mg/kg) : 20

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9 NP	10	11	12
Posture a)	N	N	N	N	N	N	N	N		N	N	N
Convulsion b)	0	0	0	0	0	0	0	0		0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0		0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

NP: Non-pregnant

Appendix 2-47

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 20)

Dose (mg/kg) : 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 NC	12
Posture a)	N	N	N	N	N	N	N	N	N	N		N
Convulsion b)	0	0	0	0	0	0	0	0	0	0		0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0		0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

NC: Not copulated

Appendix 2-48

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 20)

Dose (mg/kg) : 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-49

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Lactation day 4)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-50

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Lactation day 4)

Dose (mg/kg) : 20

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9 NP	10	11	12
Posture a)	N	N	N	N	N	N	N	N		N	N	N
Convulsion b)	0	0	0	0	0	0	0	0		0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0		0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

NP: Non-pregnant

Appendix 2-51

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Lactation day 4)

Dose (mg/kg) : 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 NC	12
Posture a)	N	N	N	N	N	N	N	N	N	N		N
Convulsion b)	0	0	0	0	0	0	0	0	0	0		0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0		0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

NC: Not copulated

Appendix 2-52

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Lactation day 4)

Dose (mg/kg) : 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-53

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 1 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-54

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 1 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-55

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 2 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-56

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 2 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-57

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 3 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-58

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 3 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-59

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 4 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-60

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 4 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-61

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 5 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-62

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 5 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-63

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 6 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-64

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 6 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-65

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 1 of recovery)

Dose (mg/kg) : 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-66

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 1 of recovery)

Dose (mg/kg) : 500

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-67

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 2 of recovery)

Dose (mg/kg) : 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-68

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 2 of recovery)

Dose (mg/kg) : 500

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-69

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Week 1 of recovery)

Dose (mg/kg) : 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-70

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Week 1 of recovery)

Dose (mg/kg) : 500

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-71

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Week 2 of recovery)

Dose (mg/kg) : 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-72

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Week 2 of recovery)

Dose (mg/kg) : 500

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-73

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 1 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-74

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 1 of administration)

Dose (mg/kg) : 20

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-75

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 1 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	1	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-76

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 1 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-77

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 2 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	1	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-78

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 2 of administration)

Dose (mg/kg) : 20

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-79

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 2 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-80

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 2 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-81

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 3 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-82

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 3 of administration)

Dose (mg/kg) : 20

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-83

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 3 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	1	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-84

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 3 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-85

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 4 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-86

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 4 of administration)

Dose (mg/kg) : 20

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	1	0	0	0	0	0	0	1	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-87

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 4 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-88

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 4 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	1	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-89

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 5 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-90

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 5 of administration)

Dose (mg/kg) : 20

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	1	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-91

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 5 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	1	1	0	1	0	0	0	0
Reactivity to handling n)	0	0	0	0	1	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-92

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 5 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-93

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 6 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	1	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-94

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 6 of administration)

Dose (mg/kg) : 20

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-95

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 6 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-96

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 6 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-97

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 1 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-98

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 1 of administration)

Dose (mg/kg) : 20

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-99

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 1 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-100

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 1 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-101

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 2 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-102

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 2 of administration)

Dose (mg/kg) : 20

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	1	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-103

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 2 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-104

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 2 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-105

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 1)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-106

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 1)

Dose (mg/kg) : 20

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9 NP	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0		0	0	0
Fur condition b)	0	0	0	0	0	0	0	0		0	0	0
Skin c)	0	0	0	0	0	0	0	0		0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0		0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0		0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0		0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0		0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0		0	0	0
Piloerection i)	0	0	0	0	0	0	0	0		0	0	0
Pupil size j)	0	0	0	0	0	0	0	0		0	0	0
Salivation k)	0	0	0	0	0	0	0	0		0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0		0	0	0
Vocalization m)	0	0	0	0	0	0	0	0		0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0		0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

NP: Non-pregnant

Appendix 2-107

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 1)

Dose (mg/kg) : 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 NC	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0		0
Fur condition b)	0	0	0	0	0	0	0	0	0	0		0
Skin c)	0	0	0	0	0	0	0	0	0	0		0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0		0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0		0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0		0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0		0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0		0
Piloerection i)	0	0	0	0	0	0	0	0	0	0		0
Pupil size j)	0	0	0	0	0	0	0	0	0	0		0
Salivation k)	0	0	0	0	0	0	0	0	0	0		0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0		0
Vocalization m)	0	0	0	0	0	0	0	0	0	0		0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0		0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

NC: Not copulated

Appendix 2-108

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 1)

Dose (mg/kg) : 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-109

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 7)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	1	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-110

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 7)

Dose (mg/kg) : 20

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9 NP	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0		0	0	0
Fur condition b)	0	0	0	0	0	0	0	0		0	0	0
Skin c)	0	0	0	0	0	0	0	0		0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0		0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0		0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0		0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0		0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0		0	0	0
Piloerection i)	0	0	0	0	0	0	0	0		0	0	0
Pupil size j)	0	0	0	0	0	0	0	0		0	0	0
Salivation k)	0	0	0	0	0	0	0	0		0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0		0	0	0
Vocalization m)	0	0	0	0	0	0	0	0		0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0		0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

NP: Non-pregnant

Appendix 2-111

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 7)

Dose (mg/kg) : 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 NC	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0		0
Fur condition b)	0	0	0	0	0	0	0	0	0	0		0
Skin c)	0	0	0	0	0	0	0	0	0	0		0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0		0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0		0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0		0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0		0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0		0
Piloerection i)	0	0	0	0	0	0	0	0	0	0		0
Pupil size j)	0	0	0	0	0	0	0	0	0	0		0
Salivation k)	0	0	0	0	0	0	0	0	0	0		0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0		0
Vocalization m)	0	0	0	0	0	0	0	0	0	0		0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0		0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult
NC: Not copulated

Appendix 2-112

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 7)

Dose (mg/kg) : 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-113

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 14)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-114

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 14)

Dose (mg/kg) : 20

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9 NP	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0		0	0	0
Fur condition b)	0	0	0	0	0	0	0	0		0	0	0
Skin c)	0	0	0	0	0	0	0	0		0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0		0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0		0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0		0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0		0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0		0	0	0
Piloerection i)	0	0	0	0	0	0	0	0		0	0	0
Pupil size j)	0	0	0	0	0	0	0	0		0	0	0
Salivation k)	0	0	0	0	0	0	0	0		0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0		0	0	0
Vocalization m)	0	0	0	0	0	0	0	0		0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0		0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

NP: Non-pregnant

Appendix 2-115

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 14)

Dose (mg/kg) : 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 NC	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0		0
Fur condition b)	0	0	0	0	0	0	0	0	0	0		0
Skin c)	0	0	0	0	0	0	0	0	0	0		0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0		0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0		0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0		0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0		0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0		0
Piloerection i)	0	0	0	0	0	0	0	0	0	0		0
Pupil size j)	0	0	0	0	0	0	0	0	0	0		0
Salivation k)	0	0	0	0	0	0	0	0	0	0		0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0		0
Vocalization m)	0	0	0	0	0	0	0	0	0	0		0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0		0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult
NC: Not copulated

Appendix 2-116

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 14)

Dose (mg/kg) : 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-117

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 20)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-118

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 20)

Dose (mg/kg) : 20

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9 NP	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0		0	0	0
Fur condition b)	0	0	0	0	0	0	0	0		0	0	0
Skin c)	0	0	0	0	0	0	0	0		0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0		0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0		0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0		0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0		0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0		0	0	0
Piloerection i)	0	0	0	0	0	0	0	0		0	0	0
Pupil size j)	0	0	0	0	0	0	0	0		0	0	0
Salivation k)	0	0	0	0	0	0	0	0		0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0		0	0	0
Vocalization m)	0	0	0	0	0	0	0	0		0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0		0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

NP: Non-pregnant

Appendix 2-119

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 20)

Dose (mg/kg) : 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 NC	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0		0
Fur condition b)	0	0	0	0	0	0	0	0	0	0		0
Skin c)	0	0	0	0	0	0	0	0	0	0		0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0		0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0		0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0		0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0		0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0		0
Piloerection i)	0	0	0	0	0	0	0	0	0	0		0
Pupil size j)	0	0	0	0	0	0	0	0	0	0		0
Salivation k)	0	0	0	0	0	0	0	0	0	0		0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0		0
Vocalization m)	0	0	0	0	0	0	0	0	0	0		0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0		0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

NC: Not copulated

Appendix 2-120

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 20)

Dose (mg/kg) : 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-121

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Lactation day 4)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-122

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Lactation day 4)

Dose (mg/kg) : 20

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9 NP	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0		0	0	0
Fur condition b)	0	0	0	0	0	0	0	0		0	0	0
Skin c)	0	0	0	0	0	0	0	0		0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0		0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0		0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0		0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0		0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0		0	0	0
Piloerection i)	0	0	0	0	0	0	0	0		0	0	0
Pupil size j)	0	0	0	0	0	0	0	0		0	0	0
Salivation k)	0	0	0	0	0	0	0	0		0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0		0	0	0
Vocalization m)	0	0	0	0	0	0	0	0		0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0		0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

NP: Non-pregnant

Appendix 2-123

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Lactation day 4)

Dose (mg/kg) : 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 NC	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0		0
Fur condition b)	0	0	0	0	0	0	0	0	0	0		0
Skin c)	0	0	0	0	0	0	0	0	0	0		0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0		0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0		0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0		0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0		0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0		0
Piloerection i)	0	0	0	0	0	0	0	0	0	0		0
Pupil size j)	0	0	0	0	0	0	0	0	0	0		0
Salivation k)	0	0	0	0	0	0	0	0	0	0		0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0		0
Vocalization m)	0	0	0	0	0	0	0	0	0	0		0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0		0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult
NC: Not copulated

Appendix 2-124

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Lactation day 4)

Dose (mg/kg) : 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-125

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 1 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-126

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 1 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-127

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 2 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-128

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 2 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	1	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-129

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 3 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-130

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 3 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-131

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 4 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-132

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 4 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-133

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 5 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-134

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 5 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-135

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 6 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-136

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 6 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-137

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 1 of recovery)

Dose (mg/kg) : 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-138

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 1 of recovery)

Dose (mg/kg) : 500

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-139

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 2 of recovery)

Dose (mg/kg) : 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	1	0	0	1	1
Reactivity to handling n)	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-140 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 2 of recovery)

Dose (mg/kg) : 500

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	1	0	0	0
Reactivity to handling n)	0	1	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-141

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Week 1 of recovery)

Dose (mg/kg) : 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-142

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Week 1 of recovery)

Dose (mg/kg) : 500

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-143

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Week 2 of recovery)

Dose (mg/kg) : 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-144

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Week 2 of recovery)

Dose (mg/kg) : 500

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-145

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 1 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	3	3	5	5	4	4	4	5	5	5	3	3
Defecation count	0	0	0	0	0	0	2	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	1	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-146

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 1 of administration)

Dose (mg/kg) : 20

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	2	2	3	6	7	2	5	6	4	4	8	3
Defecation count	0	0	1	0	0	0	0	0	0	0	0	1
Urination h)	1	0	0	0	0	0	0	0	0	0	0	1

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-147

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 1 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	5	5	2	5	6	7	8	1	3	6	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	1	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-148

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 1 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	4	5	6	5	4	3	3	5	6	3	4
Defecation count	0	0	0	0	0	5	0	0	0	0	0	1
Urination h)	0	0	0	0	0	0	0	0	1	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-149

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 2 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	U	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	3	4	6	4	4	1	6	5	4	0	3	3
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	1	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-150

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 2 of administration)

Dose (mg/kg) : 20

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	2	6	4	4	6	1	3	7	6	6	6	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	1	0	0	0	0	0	0	0	0	1	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-151

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 2 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	6	6	1	5	5	4	5	4	3	4	7
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-152

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 2 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	3	5	8	7	2	5	4	3	2	6	2	3
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	1	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-153

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 3 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	U	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	5	4	5	3	1	5	3	5	0	4	2
Defecation count	0	1	0	0	0	0	0	0	0	2	0	0
Urination h)	0	0	0	1	1	0	0	0	1	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-154

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 3 of administration)

Dose (mg/kg) : 20

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	5	4	5	4	5	5	9	4	4	10	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	1	0	0	0	0	0	0	0	0	0	0

- a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-155

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 3 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	1	5	4	3	6	4	4	3	2	4	4	2
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	1	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-156

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 3 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	3	8	4	4	3	7	4	4	5	1	3
Defecation count	0	0	0	0	0	0	1	0	0	0	0	1
Urination h)	0	1	0	0	0	0	0	0	0	0	1	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-157

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 4 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	7	3	5	4	3	6	6	4	0	3	3
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	1	0	0	1	1	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-158

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 4 of administration)

Dose (mg/kg) : 20

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	4	3	5	6	6	4	7	6	5	8	9
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	1	0	0	0	1	0	0	0	1	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-159

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 4 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	4	6	6	5	6	5	3	3	1	4	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	1	0	0	0	0	0	0	1	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-160

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 4 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	6	7	4	2	3	5	4	3	6	2	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	1	1	0	0	0	0	0	0	0	1

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-161

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 5 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	5	5	6	3	4	5	4	6	3	1	4
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	1	0	0	0	1	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-162

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 5 of administration)

Dose (mg/kg) : 20

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	3	6	3	6	5	2	8	5	7	7	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	1	0	0	0	1	0	0	0	1	1	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-163

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 5 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	3	7	4	3	5	6	1	2	3	5	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	1	0	0	1	0	0	0	1	1

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-164

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 5 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	8	4	4	7	2	3	7	4	5	5	3	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	1

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-165

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 6 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	2	2	8	3	4	3	3	8	1	4	4
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	1	0	0	1	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-166

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 6 of administration)

Dose (mg/kg) : 20

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	3	5	8	3	5	6	4	6	5	7	7	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	1	0	0	0	1	0	0	0	0	1	0

- a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-167

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 6 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	4	3	4	3	6	4	4	2	2	5	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	1	0	0	1	0	0	0	1	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-168

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 6 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	4	3	6	1	4	4	4	4	6	2	4
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	1	0	0	0	0	0	0	0	0	1

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-169

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Week 1 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	3	6	4	5	8	10	7	6	6	6	7	7
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-170

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Week 1 of administration)

Dose (mg/kg) : 20

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	3	6	5	6	7	2	5	7	8	3	9	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-171

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Week 1 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	4	11	9	4	8	15	4	7	5	4	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-172

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Week 1 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	6	11	8	4	5	7	3	7	6	2	7
Defecation count	0	0	0	0	0	0	0	0	0	0	2	0
Urination h)	0	0	0	0	0	0	0	0	0	0	1	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-173

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Week 2 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	8	5	6	4	9	7	5	7	9	5	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert.

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-174

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Week 2 of administration)

Dose (mg/kg) : 20

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	4	4	6	8	7	8	7	9	6	10	7
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-175

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Week 2 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	9	9	14	12	5	8	14	6	10	9	3	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-176

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Week 2 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	12	6	6	5	7	6	4	9	4	5	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-177

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 1)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	7	5	6	7	6	4	7	7	10	9	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-178

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 1)

Dose (mg/kg) : 20

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9 NP	10	11	12
Arousal a)	0	0	0	0	0	0	0	0		0	0	0
Convulsion b)	0	0	0	0	0	0	0	0		0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0		0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0		0	0	0
Gait e)	0	0	0	0	0	0	0	0		0	0	0
Posture f)	N	N	N	N	N	N	N	N		N	N	N
Grooming g)	0	0	0	0	0	0	0	0		0	0	0
Rearing	5	8	7	8	8	6	6	6		6	5	10
Defecation count	0	0	0	0	0	0	0	0		0	0	0
Urination h)	0	0	0	0	0	0	0	0		0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

NP: Non-pregnant

Appendix 2-179

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 1)

Dose (mg/kg) : 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 NC	12
Arousal a)	0	0	0	0	0	0	0	0	0	0		0
Convulsion b)	0	0	0	0	0	0	0	0	0	0		0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0		0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0		0
Gait e)	0	0	0	0	0	0	0	0	0	0		0
Posture f)	N	N	N	N	N	N	N	N	N	N		N
Grooming g)	0	0	0	0	0	0	0	0	0	0		0
Rearing	8	7	10	7	7	10	10	5	7	9		6
Defecation count	0	0	0	0	0	0	0	0	0	0		0
Urination h)	0	0	0	0	0	0	0	0	0	0		0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

NC: Not copulated

Appendix 2-180

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 1)

Dose (mg/kg) : 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	8	5	11	8	6	10	5	3	4	6	4	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-181

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 7)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	8	7	5	5	5	9	3	5	5	6	8	8
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	1	0	0	0	0	0	0	0	0	0	0

- a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-182

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 7)

Dose (mg/kg) : 20

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
	NP											
Arousal a)	0	0	0	0	0	0	0	0		0	0	0
Convulsion b)	0	0	0	0	0	0	0	0		0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0		0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0		0	0	0
Gait e)	0	0	0	0	0	0	0	0		0	0	0
Posture f)	N	N	N	N	N	N	N	N		N	N	N
Grooming g)	0	0	0	0	0	0	0	0		0	0	0
Rearing	5	8	3	6	8	4	8	7		4	6	8
Defecation count	0	0	0	0	0	0	0	0		0	0	0
Urination h)	0	0	0	0	0	0	0	0		1	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

NP: Non-pregnant

Appendix 2-183

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 7)

Dose (mg/kg) : 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 NC	12
Arousal a)	0	0	0	0	0	0	0	0	0	0		0
Convulsion b)	0	0	0	0	0	0	0	0	0	0		0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0		0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0		0
Gait e)	0	0	0	0	0	0	0	0	0	0		0
Posture f)	N	N	N	N	N	N	N	N	N	N		N
Grooming g)	0	0	0	0	0	0	0	0	0	0		0
Rearing	7	9	10	5	6	7	7	4	7	7		5
Defecation count	0	0	0	0	0	0	0	0	0	0		0
Urination h)	0	0	0	0	0	0	0	1	1	0		0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

NC: Not copulated

Appendix 2-184

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 7)

Dose (mg/kg) : 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	9	5	5	5	6	4	1	11	3	4	7
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

- a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-185

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 14)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	8	7	4	4	8	6	5	4	6	5	5	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-186

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 14)

Dose (mg/kg) : 20

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9 NP	10	11	12
Arousal a)	0	0	0	0	0	0	0	0		0	0	0
Convulsion b)	0	0	0	0	0	0	0	0		0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0		0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0		0	0	0
Gait e)	0	0	0	0	0	0	0	0		0	0	0
Posture f)	N	N	N	N	N	N	N	N		N	N	N
Grooming g)	0	0	0	0	0	0	0	0		0	0	0
Rearing	4	6	4	5	7	3	7	4		6	6	7
Defecation count	0	0	0	0	0	0	0	0		0	0	0
Urination h)	0	0	0	0	0	0	0	0		0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

NP: Non-pregnant

Appendix 2-187

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 14)

Dose (mg/kg) : 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 NC	12
Arousal a)	0	0	0	0	0	0	0	0	0	0		0
Convulsion b)	0	0	0	0	0	0	0	0	0	0		0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0		0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0		0
Gait e)	0	0	0	0	0	0	0	0	0	0		0
Posture f)	N	N	N	N	N	N	N	N	N	N		N
Grooming g)	0	0	0	0	0	0	0	0	0	0		0
Rearing	6	8	7	8	6	5	7	7	8	5		6
Defecation count	0	0	0	0	0	0	0	0	0	0		0
Urination h)	0	0	0	0	0	0	0	0	0	0		0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

NC: Not copulated

Appendix 2-188

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 14)

Dose (mg/kg) : 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	3	5	6	5	6	3	4	1	7	6	5	4
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

- a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-189

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 20)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	6	4	5	8	6	5	5	5	5	4	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-190

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 20)

Dose (mg/kg) : 20

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9 NP	10	11	12
Arousal a)	0	0	0	0	0	0	0	0		0	0	0
Convulsion b)	0	0	0	0	0	0	0	0		0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0		0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0		0	0	0
Gait e)	0	0	0	0	0	0	0	0		0	0	0
Posture f)	N	N	N	N	N	N	N	N		N	N	N
Grooming g)	0	0	0	0	0	0	0	0		0	0	0
Rearing	5	5	3	6	5	2	6	5		4	6	3
Defecation count	0	0	0	0	0	0	0	0		0	0	0
Urination h)	0	0	0	0	0	0	0	0		0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

NP: Non-pregnant

Appendix 2-191

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 20)

Dose (mg/kg) : 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 NC	12
Arousal a)	0	0	0	0	0	0	0	0	0	0		0
Convulsion b)	0	0	0	0	0	0	0	0	0	0		0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0		0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0		0
Gait e)	0	0	0	0	0	0	0	0	0	0		0
Posture f)	N	N	N	N	N	N	N	N	N	N		N
Grooming g)	0	0	0	0	0	0	0	0	0	0		0
Rearing	7	6	7	6	7	5	6	4	6	3		4
Defecation count	0	0	0	0	0	0	0	0	0	0		0
Urination h)	0	0	0	0	0	0	0	0	0	0		0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

NC: Not copulated

Appendix 2-192

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 20)

Dose (mg/kg) : 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	6	4	3	5	4	3	5	4	6	5	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-193

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Lactation day 4)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	5	8	7	5	8	4	6	3	6	6	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-194

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Lactation day 4)

Dose (mg/kg) : 20

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9 NP	10	11	12
Arousal a)	0	0	0	0	0	0	0	0		0	0	0
Convulsion b)	0	0	0	0	0	0	0	0		0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0		0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0		0	0	0
Gait e)	0	0	0	0	0	0	0	0		0	0	0
Posture f)	N	N	N	N	N	N	N	N		N	N	N
Grooming g)	0	0	0	0	0	0	0	0		0	0	0
Rearing	5	7	3	5	9	3	6	6		8	6	5
Defecation count	1	0	0	0	0	0	0	0		0	0	0
Urination h)	0	0	0	0	0	0	0	0		0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

NP: Non-pregnant

Appendix 2-195

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Lactation day 4)

Dose (mg/kg) : 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 NC	12
Arousal a)	0	0	0	0	0	0	0	0	0	0		0
Convulsion b)	0	0	0	0	0	0	0	0	0	0		0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0		0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0		0
Gait e)	0	0	0	0	0	0	0	0	0	0		0
Posture f)	N	N	N	N	N	N	N	N	N	N		N
Grooming g)	0	0	0	0	0	0	0	0	0	0		0
Rearing	6	6	6	8	8	5	8	6	7	6		4
Defecation count	0	0	0	0	0	0	0	0	0	0		0
Urination h)	0	0	0	0	0	0	0	0	0	0		0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

NC: Not copulated

Appendix 2-196

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Lactation day 4)

Dose (mg/kg) : 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	6	5	7	5	6	5	5	9	4	5	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	1	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-197

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 1 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	10	10	3	9	4	6	9	8	1	5
Defecation count	0	0	0	0	0	0	0	0	1	0
Urination h)	0	0	0	0	0	0	0	0	1	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-198

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 1 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	5	6	5	7	5	6	6	3	6	9
Defecation count	0	0	0	0	0	0	0	3	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-199

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 2 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	10	6	8	8	7	11	10	11	4	4
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-200

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 2 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	6	8	5	8	3	7	6	6	8	10
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

- a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-201

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 3 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	9	8	5	8	11	11	9	13	7	6
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

- a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-202

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 3 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	4	12	9	9	7	8	7	5	6	12
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-203

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 4 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	6	7	8	13	10	8	8	8	12	4
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-204

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 4 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	5	11	7	8	6	7	7	3	8	7
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

- a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-205

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 5 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	6	7	6	11	5	10	9	13	13	7
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-206

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 5 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	2	12	5	8	5	6	8	5	6	8
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

- a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-207

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 6 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	6	8	5	13	8	8	8	9	10	7
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-208

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 6 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	6	7	6	10	11	10	9	6	8	8
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

- a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-209

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 1 of recovery)

Dose (mg/kg) : 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	3	6	0	4	3
Defecation count	0	0	0	0	0
Urination h)	0	0	0	0	0

- a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-210

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 1 of recovery)

Dose (mg/kg) : 500

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	5	4	4	3	3
Defecation count	0	0	0	0	0
Urination h)	0	0	0	1	1

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-211

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 2 of recovery)

Dose (mg/kg) : 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	2	5	4	2	2
Defecation count	0	0	0	0	0
Urination h)	0	0	0	0	0

- a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-212

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 2 of recovery)

Dose (mg/kg) : 500

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	4	2	5	2	4
Defecation count	0	0	0	0	0
Urination h)	0	0	0	0	0

- a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-213

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Week 1 of recovery)

Dose (mg/kg) : 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	4	9	8	8	9
Defecation count	0	0	0	0	0
Urination h)	0	0	0	0	0

- a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-214

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Week 1 of recovery)

Dose (mg/kg) : 500

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	10	5	6	7	8
Defecation count	0	0	0	0	0
Urination h)	0	0	0	0	0

- a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-215

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Week 2 of recovery)

Dose (mg/kg) : 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	6	7	5	9	6
Defecation count	0	0	0	0	0
Urination h)	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

d) 0: None, 1: Minor, 2: Moderate, 3: Severe

e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly

f) N: Normal, F: Flattened, H: Hunched

g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)

h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-216

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Week 2 of recovery)

Dose (mg/kg) : 500

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	6	6	6	8	11
Defecation count	0	0	0	0	0
Urination h)	0	0	0	0	0

- a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-217

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual manipulative test of male rats (Week 6 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	105	113	46	116	101

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate

b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction

c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction

d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate

e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-218

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual manipulative test of male rats (Week 6 of administration)

Dose (mg/kg) : 20

Parameter	Animal number (2008-2012)				
	8	9	10	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	85	92	68	75	109

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate

b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction

c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction

d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate

e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-219

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual manipulative test of male rats (Week 6 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (3008-3012)				
	8	9	10	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	80	98	67	105	105

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate

b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction

c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction

d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate

e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-220

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual manipulative test of male rats (Week 6 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	72	75	59	96	63

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate

b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction

c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction

d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate

e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-221

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual manipulative test of female rats (Main group, Lactation day 4)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1110)				
	1	3	4	8	10
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	56	57	58	74	43

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate

b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction

c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction

d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate

e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-222

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual manipulative test of female rats (Main group, Lactation day 4)

Dose (mg/kg) : 20

Parameter	Animal number (2102-2111)				
	2	3	6	8	11
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	43	41	69	81	90

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate

b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction

c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction

d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate

e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-223

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual manipulative test of female rats (Main group, Lactation day 4)

Dose (mg/kg) : 100

Parameter	Animal number (3102-3112)				
	2	4	6	7	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	73	56	74	34	61

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate

b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction

c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction

d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate

e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-224

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual manipulative test of female rats (Main group, Lactation day 4)

Dose (mg/kg) : 500

Parameter	Animal number (4101-4111)				
	1	2	3	4	11
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	48	61	66	27	54

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate

b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction

c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction

d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate

e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-225

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual manipulative test of female rats (Satellite group, Week 6 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	70	71	43	85	53

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate

b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction

c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction

d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate

e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-226

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual manipulative test of female rats (Satellite group, Week 6 of administration)

Dose (mg/kg) : 500

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	77	84	74	34	88

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate

b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction

c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction

d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate

e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-227

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual manipulative test of male rats (Week 2 of recovery)

Dose (mg/kg) : 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	97	115	57	114	104

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate

b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction

c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction

d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate

e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-228

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual manipulative test of male rats (Week 2 of recovery)

Dose (mg/kg) : 500

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	71	108	61	103	96

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate

b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction

c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction

d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate

e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-229

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual manipulative test of female rats (Week 2 of recovery)

Dose (mg/kg) : 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	69	73	50	79	61

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate

b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction

c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction

d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate

e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-230

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual manipulative test of female rats (Week 2 of recovery)

Dose (mg/kg) : 500

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	96	82	72	36	48

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate

b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction

c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction

d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate

e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-231

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual grip strength of male rats (Week 6 of administration)

Dose (mg/kg) : 0

Animal number	Fore limb g	Hind limb g
1008	1789	1239
1009	1613	875
1010	1451	810
1011	1546	1062
1012	1681	928
Mean	1616	983
S.D.	129	171

Appendix 2-232

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual grip strength of male rats (Week 6 of administration)

Dose (mg/kg) : 20

Animal number	Fore limb g	Hind limb g
2008	1943	964
2009	1602	978
2010	1634	889
2011	1444	972
2012	1634	1008
Mean	1651	962
S.D.	181	44

Appendix 2-233

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual grip strength of male rats (Week 6 of administration)

Dose (mg/kg) : 100

Animal number	Fore limb g	Hind limb g
3008	1468	1047
3009	1394	980
3010	1597	951
3011	1894	953
3012	1775	1148
Mean	1626	1016
S.D.	208	83

Appendix 2-234

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual grip strength of male rats (Week 6 of administration)

Dose (mg/kg) : 500

Animal number	Fore limb g	Hind limb g
4008	1779	957
4009	1831	1343
4010	1751	1148
4011	1303	1207
4012	1711	951
Mean	1675	1121
S.D.	212	168

Appendix 2-235

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual grip strength of female rats (Main group, Lactation day 4)

Dose (mg/kg) : 0

Animal number	Fore limb g	Hind limb g
1101	1883	803
1103	1435	864
1104	1400	686
1108	1263	752
1110	1131	546
Mean	1422	730
S.D.	284	122

Appendix 2-236

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual grip strength of female rats (Main group, Lactation day 4)

Dose (mg/kg) : 20

Animal number	Fore limb g	Hind limb g
2102	1187	828
2103	1829	699
2106	1587	953
2108	1391	757
2111	1484	809
Mean	1496	809
S.D.	238	95

Appendix 2-237

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual grip strength of female rats (Main group, Lactation day 4)

Dose (mg/kg) : 100

Animal number	Fore limb g	Hind limb g
3102	1515	982
3104	1187	889
3106	1522	856
3107	1115	706
3112	1359	776
Mean	1340	842
S.D.	186	106

Appendix 2-238

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual grip strength of female rats (Main group, Lactation day 4)

Dose (mg/kg) : 500

Animal number	Fore limb g	Hind limb g
4101	1044	650
4102	1458	744
4103	1379	624
4104	1290	698
4111	1304	643
Mean	1295	672
S.D.	156	49

Appendix 2-239

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual grip strength of female rats (Satellite group, Week 6 of administration)

Dose (mg/kg) : 0

Animal number	Fore limb g	Hind limb g
1118	1378	741
1119	1265	593
1120	1149	772
1121	1346	766
1122	1067	724
Mean	1241	719
S.D.	131	73

Appendix 2-240

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual grip strength of female rats (Satellite group, Week 6 of administration)

Dose (mg/kg) : 500

Animal number	Fore limb g	Hind limb g
4118	1163	747
4119	1346	782
4120	958	560
4121	1038	578
4122	901	685
Mean	1081	670
S.D.	178	99

Appendix 2-241

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual grip strength of male rats (Week 2 of recovery)

Dose (mg/kg) : 0

Animal number	Fore limb g	Hind limb g
1008	1613	1182
1009	1343	977
1010	1545	701
1011	2107	1090
1012	2008	1059
Mean	1723	1002
S.D.	323	183

Appendix 2-242

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual grip strength of male rats (Week 2 of recovery)

Dose (mg/kg) : 500

Animal number	Fore limb g	Hind limb g
4008	1808	917
4009	1816	1287
4010	1931	1101
4011	1517	1213
4012	1581	804
Mean	1731	1064
S.D.	174	202

Appendix 2-243

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual grip strength of female rats (Week 2 of recovery)

Dose (mg/kg) : 0

Animal number	Fore limb g	Hind limb g
1118	1536	941
1119	1588	710
1120	1312	656
1121	1373	821
1122	1119	720
Mean	1386	770
S.D.	187	113

Appendix 2-244

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual grip strength of female rats (Week 2 of recovery)

Dose (mg/kg) : 500

Animal number	Fore limb g	Hind limb g
4118	1205	740
4119	1482	779
4120	1028	523
4121	1252	837
4122	1209	653
Mean	1235	706
S.D.	163	122

Appendix 2-245

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual motor activity of male rats (Week 6 of administration)

Dose (mg/kg) : 0

Animal number	Interval (minutes)						Total(0-60)
	0-10	10-20	20-30	30-40	40-50	50-60	
1008	385	387	398	267	272	187	1896
1009	407	445	261	355	124	115	1707
1010	363	169	9	233	13	33	820
1011	453	418	424	403	276	111	2085
1012	438	333	150	382	54	3	1360
Mean	409	350	248	328	148	90	1574
S.D.	37	110	173	74	122	73	499

Unit : Count

Appendix 2-246

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual motor activity of male rats (Week 6 of administration)

Dose (mg/kg) : 20

Animal number	Interval (minutes)						Total(0-60)
	0-10	10-20	20-30	30-40	40-50	50-60	
2008	424	411	350	327	268	340	2120
2009	351	359	301	303	327	185	1826
2010	446	412	403	372	332	49	2014
2011	380	431	405	279	310	290	2095
2012	485	406	395	418	357	353	2414
Mean	417	404	371	340	319	243	2094
S.D.	53	27	45	56	33	127	213

Unit : Count

Appendix 2-247

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual motor activity of male rats (Week 6 of administration)

Dose (mg/kg) : 100

Animal number	Interval (minutes)						Total(0-60)
	0-10	10-20	20-30	30-40	40-50	50-60	
3008	352	313	327	252	315	229	1788
3009	362	348	307	278	220	240	1755
3010	357	389	222	204	235	157	1564
3011	384	323	116	179	112	68	1182
3012	333	278	229	203	79	32	1154
Mean	358	330	240	223	192	145	1489
S.D.	18	41	83	41	96	93	305

Unit : Count

Appendix 2-248

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual motor activity of male rats (Week 6 of administration)

Dose (mg/kg) : 500

Animal number	Interval (minutes)						Total(0-60)
	0-10	10-20	20-30	30-40	40-50	50-60	
4008	372	308	311	322	149	294	1756
4009	495	383	301	290	188	64	1721
4010	416	410	308	369	298	207	2008
4011	377	271	284	263	133	21	1349
4012	405	429	406	344	237	218	2039
Mean	413	360	322	318	201	161	1775
S.D.	49	68	48	42	67	114	278

Unit : Count

Appendix 2-249

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual motor activity of female rats (Main group, Lactation day 4)

Dose (mg/kg) : 0

Animal number	Interval (minutes)						Total(0-60)
	0-10	10-20	20-30	30-40	40-50	50-60	
1101	478	440	288	384	66	211	1867
1103	404	304	395	27	13	9	1152
1104	462	323	72	17	20	18	912
1108	464	382	76	19	33	34	1008
1110	407	351	293	319	300	301	1971
Mean	443	360	225	153	86	115	1382
S.D.	35	54	144	183	121	133	499

Unit : Count

Appendix 2-250

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual motor activity of female rats (Main group, Lactation day 4)

Dose (mg/kg) : 20

Animal number	Interval (minutes)						Total(0-60)
	0-10	10-20	20-30	30-40	40-50	50-60	
2102	455	339	319	306	310	390	2119
2103	400	216	199	50	268	21	1154
2106	304	42	49	6	22	36	459
2108	405	221	23	125	72	32	878
2111	367	53	187	147	10	6	770
Mean	386	174	155	127	136	97	1076
S.D.	56	126	121	115	142	164	634

Unit : Count

Appendix 2-251

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual motor activity of female rats (Main group, Lactation day 4)

Dose (mg/kg) : 100

Animal number	Interval (minutes)						Total(0-60)
	0-10	10-20	20-30	30-40	40-50	50-60	
3102	384	193	265	135	7	9	993
3104	338	139	153	179	71	63	943
3106	438	352	171	39	204	263	1467
3107	438	308	308	253	338	167	1812
3112	418	225	174	315	203	115	1450
Mean	403	243	214	184	165	123	1333
S.D.	43	86	68	107	129	98	364

Unit : Count

Appendix 2-252

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual motor activity of female rats (Main group, Lactation day 4)

Dose (mg/kg) : 500

Animal number	Interval (minutes)						Total(0-60)
	0-10	10-20	20-30	30-40	40-50	50-60	
4101	237	76	4	5	96	154	572
4102	380	84	7	1	16	5	493
4103	405	420	109	167	81	7	1189
4104	330	248	227	31	16	8	860
4111	270	12	132	6	0	6	426
Mean	324	168	96	42	42	36	708
S.D.	71	166	94	71	43	66	316

Unit : Count

Appendix 2-253

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual motor activity of female rats (Satellite group, Week 6 of administration)

Dose (mg/kg) : 0

Animal number	Interval (minutes)						Total(0-60)
	0-10	10-20	20-30	30-40	40-50	50-60	
1118	383	338	280	330	233	108	1672
1119	377	301	294	263	225	151	1611
1120	410	282	189	310	295	194	1680
1121	441	383	20	2	2	320	1168
1122	414	324	529	415	290	216	2188
Mean	405	326	262	264	209	198	1664
S.D.	26	39	185	156	120	80	362

Unit : Count

Appendix 2-254

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual motor activity of female rats (Satellite group, Week 6 of administration)

Dose (mg/kg) : 500

Animal number	Interval (minutes)						Total(0-60)
	0-10	10-20	20-30	30-40	40-50	50-60	
4118	380	353	318	249	88	10	1398
4119	436	363	248	50	303	371	1771
4120	383	315	245	250	11	1	1205
4121	406	354	319	182	302	5	1568
4122	423	246	2	329	254	4	1258
Mean	406	326	226	212	192	78	1440
S.D.	24	48	131	104	134	164	232

Unit : Count

Appendix 2-255

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual motor activity of male rats (Week 2 of recovery)

Dose (mg/kg) : 0

Animal number	Interval (minutes)						Total(0-60)
	0-10	10-20	20-30	30-40	40-50	50-60	
1008	376	289	329	290	195	240	1719
1009	344	237	166	192	78	22	1039
1010	358	165	228	123	95	114	1083
1011	317	301	232	209	150	61	1270
1012	291	269	266	187	141	187	1341
Mean	337	252	244	200	132	125	1290
S.D.	34	54	60	60	47	89	271

Unit : Count

Appendix 2-256

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual motor activity of male rats (Week 2 of recovery)

Dose (mg/kg) : 500

Animal number	Interval (minutes)						Total(0-60)
	0-10	10-20	20-30	30-40	40-50	50-60	
4008	400	303	241	261	266	85	1556
4009	395	274	319	259	231	220	1698
4010	353	340	333	211	41	186	1464
4011	330	204	202	113	47	0	896
4012	352	375	396	306	267	242	1938
Mean	366	299	298	230	170	147	1510
S.D.	30	65	77	74	116	102	387

Unit : Count

Appendix 2-257

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual motor activity of female rats (Week 2 of recovery)

Dose (mg/kg) : 0

Animal number	Interval (minutes)						Total(0-60)
	0-10	10-20	20-30	30-40	40-50	50-60	
1118	403	229	317	182	215	287	1633
1119	287	378	340	267	200	240	1712
1120	474	422	341	290	192	217	1936
1121	420	313	202	184	243	37	1399
1122	338	448	188	321	278	345	1918
Mean	384	358	278	249	226	225	1720
S.D.	73	88	76	63	35	116	222

Unit : Count

Appendix 2-258

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual motor activity of female rats (Week 2 of recovery)

Dose (mg/kg) : 500

Animal number	Interval (minutes)						Total(0-60)
	0-10	10-20	20-30	30-40	40-50	50-60	
4118	320	340	275	520	330	334	2119
4119	397	332	312	191	82	338	1652
4120	253	320	238	210	167	88	1276
4121	337	245	221	92	16	219	1130
4122	470	419	364	329	400	132	2114
Mean	355	331	282	268	199	222	1658
S.D.	82	62	58	164	163	114	460

Unit : Count

Appendix 3-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual body weight of male rats (Administration period)

Dose (mg/kg): 0

Animal number	Day of administration							Gain 1-42
	1	8	15	22	29	36	42	
1001	381	408	429	461	488	515	531	150
1002	367	383	406	420	454	474	487	120
1003	353	372	377	382	394	406	413	60
1004	408	446	475	490	514	532	539	131
1005	376	403	426	442	464	490	510	134
1006	387	417	433	447	466	494	507	120
1007	412	443	471	491	517	539	562	150
1008	382	416	426	448	465	480	492	110
1009	353	385	406	417	428	444	452	99
1010	374	395	411	427	450	469	474	100
1011	366	399	420	441	468	481	495	129
1012	383	403	428	445	472	507	505	122
Mean	379	406	426	443	465	486	497	119
S.D.	18	22	27	30	34	37	40	25

Unit: g

Appendix 3-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual body weight of male rats (Administration period)

Dose (mg/kg): 20

Animal number	Day of administration							Gain 1-42
	1	8	15	22	29	36	42	
2001	368	394	407	429	449	481	499	131
2002	386	417	447	484	519	547	562	176
2003	395	417	428	447	460	481	492	97
2004	400	441	474	493	528	552	567	167
2005	414	437	459	487	516	540	558	144
2006	369	406	429	453	469	493	499	130
2007	366	384	405	416	428	449	458	92
2008	388	415	445	462	485	512	523	135
2009	358	366	386	406	427	444	446	88
2010	380	401	426	443	465	483	504	124
2011	366	385	411	437	467	483	492	126
2012	356	375	400	421	442	457	467	111
Mean	379	403	426	448	471	494	506	127
S.D.	18	23	26	29	34	37	40	27

Unit: g

Appendix 3-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual body weight of male rats (Administration period)

Dose (mg/kg): 100

Animal number	Day of administration							Gain 1-42
	1	8	15	22	29	36	42	
3001	369	394	402	422	435	459	468	99
3002	383	416	443	455	478	505	518	135
3003	355	391	414	428	446	469	479	124
3004	365	386	399	415	434	448	463	98
3005	374	391	415	432	461	494	510	136
3006	385	403	420	432	449	470	485	100
3007	416	448	462	481	515	524	539	123
3008	402	425	442	462	479	502	521	119
3009	387	417	447	464	487	510	520	133
3010	366	396	419	422	437	458	466	100
3011	360	388	405	425	443	460	475	115
3012	400	404	413	433	454	482	489	89
Mean	380	405	423	439	460	482	494	114
S.D.	19	18	20	21	25	25	26	16

Unit: g

Appendix 3-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual body weight of male rats (Administration period)

Dose (mg/kg): 500

Animal number	Day of administration							Gain 1-42
	1	8	15	22	29	36	42	
4001	384	410	436	462	484	505	517	133
4002	357	388	417	426	462	485	502	145
4003	389	425	443	463	481	500	511	122
4004	380	420	450	472	488	514	516	136
4005	359	389	392	407	410	422	431	72
4006	376	413	445	461	476	506	527	151
4007	404	442	470	496	522	542	557	153
4008	370	395	410	429	443	472	480	110
4009	364	391	417	438	457	474	480	116
4010	405	439	474	496	520	543	551	146
4011	372	394	414	425	454	474	474	102
4012	353	377	395	408	427	451	451	98
Mean	376	407	430	449	469	491	500	124
S.D.	17	21	27	31	34	35	38	25

Unit: g

Appendix 3-5

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual body weight of female rats during the pre-mating period (Main group)

Dose (mg/kg): 0

Animal number	Day of administration			Gain 1-15
	1	8	15	
1101	222	249	260	38
1102	229	242	251	22
1103	244	251	267	23
1104	239	249	263	24
1105	209	221	230	21
1106	244	266	266	22
1107	239	239	242	3
1108	237	242	266	29
1109	243	258	272	29
1110	265	275	296	31
1111	215	237	245	30
1112	235	247	249	14
Mean	235	248	259	24
S.D.	15	14	17	9

Unit: g

Appendix 3-6

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual body weight of female rats during the pre-mating period (Main group)

Dose (mg/kg): 20

Animal number	Day of administration			Gain 1-15
	1	8	15	
2101	228	240	248	20
2102	228	233	254	26
2103	233	237	247	14
2104	225	246	251	26
2105	233	248	250	17
2106	251	266	280	29
2107	242	257	259	17
2108	233	256	263	30
2109	238	244	240	2
2110	218	233	243	25
2111	218	234	241	23
2112	230	259	273	43
Mean	231	246	254	23
S.D.	9	11	13	10

Unit: g

Appendix 3-7

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual body weight of female rats during the pre-mating period (Main group)

Dose (mg/kg): 100

Animal number	Day of administration			Gain 1-15
	1	8	15	
3101	237	259	273	36
3102	219	236	259	40
3103	239	244	250	11
3104	218	237	239	21
3105	239	258	266	27
3106	238	250	258	20
3107	228	254	254	26
3108	241	268	280	39
3109	225	237	244	19
3110	239	251	253	14
3111	234	250	255	21
3112	224	235	248	24
Mean	232	248	257	25
S.D.	8	11	12	9

Unit: g

Appendix 3-8

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual body weight of female rats during the pre-mating period (Main group)

Dose (mg/kg): 500

Animal number	Day of administration			Gain 1-15
	1	8	15	
4101	219	234	243	24
4102	264	269	289	25
4103	232	235	245	13
4104	226	237	245	19
4105	217	231	239	22
4106	228	229	258	30
4107	229	240	233	4
4108	238	249	254	16
4109	250	257	263	13
4110	244	247	246	2
4111	234	241	254	20
4112	228	243	257	29
Mean	234	243	252	18
S.D.	13	12	14	9

Unit: g

Appendix 3-9

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual body weight of dams during the gestation period (Main group)

Dose (mg/kg): 0

Dam number	Administration				Gain 0-20
	0	7	14	20a)	
1101	263	302	351	440	177
1102	252	282	307	349	97
1103	275	301	344	416	141
1104	267	293	334	405	138
1105	232	285	323	400	168
1106	273	290	322	385	112
1107	261	293	333	429	168
1108	268	302	335	422	154
1109	276	317	356	440	164
1110	297	334	374	464	167
1111	253	291	326	409	156
1112	269	308	342	432	163
Mean	266	300	337	416	150
S.D.	16	15	18	30	24

Unit: g

a): Gestation day

Appendix 3-10

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual body weight of dams during the gestation period (Main group)

Dose (mg/kg): 20

Dam number	Administration				Gain 0-20
	0	7	14	20a)	
2101	257	297	326	415	158
2102	258	290	330	410	152
2103	261	286	326	410	149
2104	255	285	324	399	144
2105	248	274	300	361	113
2106	278	313	359	444	166
2107	274	308	347	431	157
2108	263	294	329	409	146
2109	Non-pregnant				
2110	242	274	303	376	134
2111	250	275	307	361	111
2112	282	318	358	451	169
Mean	261	292	328	406	145
S.D.	13	16	20	30	19

Unit: g

a): Gestation day

Appendix 3-11

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual body weight of dams during the gestation period (Main group)

Dose (mg/kg): 100

Dam number	Administration				Gain 0-20
	0	7	14	20a)	
3101	281	318	364	453	172
3102	253	279	316	390	137
3103	259	278	308	395	136
3104	247	274	309	377	130
3105	267	292	333	427	160
3106	261	297	342	415	154
3107	255	296	327	402	147
3108	290	311	341	421	131
3109	237	263	298	371	134
3110	265	308	345	413	148
3111	Not copulated				
3112	250	273	312	394	144
Mean	260	290	327	405	145
S.D.	15	18	20	24	13

Unit: g

a): Gestation day

Appendix 3-12

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual body weight of dams during the gestation period (Main group)

Dose (mg/kg): 500

Dam number	Administration				Gain 0-20
	0	7	14	20a)	
4101	247	277	311	373	126
4102	292	319	359	444	152
4103	253	291	326	418	165
4104	254	292	327	416	162
4105	244	271	295	336	92
4106	264	294	324	389	125
4107	248	287	319	400	152
4108	272	310	347	407	135
4109	271	307	351	431	160
4110	265	300	327	414	149
4111	251	269	297	362	111
4112	257	282	319	392	135
Mean	260	292	325	399	139
S.D.	14	16	20	30	22

Unit: g

a): Gestation day

Appendix 3-13

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual body weight of dams during the lactation period (Main group)

Dose (mg/kg): 0

Dam number	Administration		Gain 0-4
	0	4a)	
1101	341	348	7
1102	297	312	15
1103	342	359	17
1104	329	316	-13
1105	286	314	28
1106	314	339	25
1107	300	325	25
1108	316	322	6
1109	336	359	23
1110	360	393	33
1111	335	336	1
1112	330	333	3
Mean	324	338	14
S.D.	22	24	14

Unit: g

a): Lactation day

Appendix 3-14

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual body weight of dams during the lactation period (Main group)

Dose (mg/kg): 20

Dam number	Administration		Gain 0-4
	0	4a)	
2101	311	322	11
2102	323	333	10
2103	318	322	4
2104	295	324	29
2105	300	315	15
2106	353	360	7
2107	327	336	9
2108	336	335	-1
2109	Non-pregnant		
2110	281	313	32
2111	309	327	18
2112	333	346	13
Mean	317	330	13
S.D.	21	14	10

Unit: g

a): Lactation day

Appendix 3-15

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual body weight of dams during the lactation period (Main group)

Dose (mg/kg): 100

Dam number	Administration		Gain 0-4
	0	4a)	
3101	320	341	21
3102	295	329	34
3103	304	293	-11
3104	314	319	5
3105	308	332	24
3106	337	355	18
3107	314	334	20
3108	340	349	9
3109	282	313	31
3110	346	334	-12
3111	Not copulated		
3112	321	322	1
Mean	316	329	13
S.D.	19	17	16

Unit: g

a): Lactation day

Appendix 3-16

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual body weight of dams during the lactation period (Main group)

Dose (mg/kg): 500

Dam number	Administration		Gain 0-4
	0	4a)	
4101	285	309	24
4102	347	357	10
4103	325	320	-5
4104	312	334	22
4105	303	309	6
4106	313	346	33
4107	316	334	18
4108	331	344	13
4109	348	354	6
4110	306	302	-4
4111	290	300	10
4112	319	339	20
Mean	316	329	13
S.D.	20	20	11

Unit: g

a): Lactation day

Appendix 3-17

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual body weight of female rats (Satellite group, administration period)

Dose (mg/kg): 0

Animal number	Day of administration							Gain 1-42
	1	8	15	22	29	36	42	
1113	224	231	243	252	263	264	279	55
1114	234	245	259	273	277	285	298	64
1115	230	244	251	268	280	296	300	70
1116	240	251	267	282	292	291	307	67
1117	220	236	249	257	263	265	270	50
1118	251	266	274	288	299	305	302	51
1119	238	252	264	275	277	287	289	51
1120	245	249	260	275	278	283	290	45
1121	240	246	264	273	279	273	297	57
1122	245	261	266	282	294	293	292	47
Mean	237	248	260	273	280	284	292	56
S.D.	10	10	9	11	12	13	11	9

Unit: g

Appendix 3-18

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual body weight of female rats (Satellite group, administration period)

Dose (mg/kg): 500

Animal number	Day of administration							Gain 1-42
	1	8	15	22	29	36	42	
4113	228	243	244	249	256	267	266	38
4114	233	247	240	254	268	264	265	32
4115	239	265	284	295	289	311	312	73
4116	221	231	239	239	247	252	257	36
4117	230	239	245	245	253	264	262	32
4118	242	244	255	264	274	290	283	41
4119	243	261	275	287	291	307	310	67
4120	223	237	248	255	270	280	274	51
4121	231	257	271	283	279	290	296	65
4122	225	231	231	246	257	270	271	46
Mean	232	246	253	262	268	280	280	48
S.D.	8	12	18	20	15	20	20	15

Unit: g

Appendix 3-19

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual body weight of male rats (Recovery period)

Dose (mg/kg): 0

Animal number	Day of recovery			Gain 1-14
	1	8	14	
1008	492	511	516	24
1009	454	466	476	22
1010	474	507	520	46
1011	499	513	518	19
1012	502	513	516	14
Mean	484	502	509	25
S.D.	20	20	19	12

Unit: g

Appendix 3-20

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual body weight of male rats (Recovery period)

Dose (mg/kg): 500

Animal number	Day of recovery			Gain 1-14
	1	8	14	
4008	479	490	497	18
4009	488	500	506	18
4010	560	575	594	34
4011	479	497	517	38
4012	455	466	474	19
Mean	492	506	518	25
S.D.	40	41	46	10

Unit: g

Appendix 3-21

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual body weight of female rats (Recovery period)

Dose (mg/kg): 0

Animal number	Day of recovery			Gain 1-14
	1	8	14	
1118	297	308	307	10
1119	293	298	304	11
1120	289	300	298	9
1121	292	303	292	0
1122	293	306	305	12
Mean	293	303	301	8
S.D.	3	4	6	5

Unit: g

Appendix 3-22

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual body weight of female rats (Recovery period)

Dose (mg/kg): 500

Animal number	Day of recovery			Gain 1-14
	1	8	14	
4118	291	294	309	18
4119	316	321	327	11
4120	277	279	285	8
4121	300	305	309	9
4122	271	278	280	9
Mean	291	295	302	11
S.D.	18	18	19	4

Unit: g

Appendix 4-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual food consumption of male rats (Administration period)

Dose (mg/kg): 0

Animal number	Day of administration					
	1	8	15	30	36	42
1001	26	26	28	29	29	30
1002	28	27	27	28	26	26
1003	23	27	22	25	24	27
1004	30	31	25	29	29	27
1005	29	28	29	27	27	31
1006	28	29	25	26	29	29
1007	29	30	29	29	29	33
1008	28	32	29	30	31	32
1009	24	27	25	24	26	27
1010	28	28	28	28	32	28
1011	27	28	26	29	26	30
1012	29	26	26	29	32	27
Mean	27	28	27	28	28	29
S.D.	2	2	2	2	3	2

Unit: g/rat/day

Appendix 4-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual food consumption of male rats (Administration period)

Dose (mg/kg): 20

Animal number	Day of administration					
	1	8	15	30	36	42
2001	25	26	24	27	29	29
2002	26	29	28	31	32	29
2003	28	26	26	26	29	27
2004	27	32	29	30	35	33
2005	30	30	27	29	29	29
2006	23	29	28	27	30	28
2007	22	24	26	26	24	23
2008	30	28	28	27	30	26
2009	19	28	27	25	30	31
2010	26	26	26	28	24	28
2011	26	26	30	26	29	29
2012	25	28	26	26	27	25
Mean	26	28	27	27	29	28
S.D.	3	2	2	2	3	3

Unit: g/rat/day

Appendix 4-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual food consumption of male rats (Administration period)

Dose (mg/kg): 100

Animal number	Day of administration					
	1	8	15	30	36	42
3001	24	27	26	25	27	28
3002	23	29	30	29	29	29
3003	23	28	27	26	30	27
3004	27	27	27	26	26	28
3005	28	26	29	33	32	28
3006	26	27	25	26	27	29
3007	29	30	29	30	29	31
3008	35	30	30	29	28	31
3009	30	31	28	27	30	28
3010	23	29	29	26	30	28
3011	24	23	25	27	23	26
3012	29	27	26	27	28	27
Mean	27	28	28	28	28	28
S.D.	4	2	2	2	2	1

Unit: g/rat/day

Appendix 4-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual food consumption of male rats (Administration period)

Dose (mg/kg): 500

Animal number	Day of administration					
	1	8	15	30	36	42
4001	22	23	28	30	28	30
4002	26	30	29	27	31	29
4003	28	29	30	28	29	30
4004	27	32	31	32	32	34
4005	22	26	24	23	25	26
4006	26	28	31	31	31	33
4007	29	29	33	34	37	37
4008	25	28	24	30	31	28
4009	24	28	29	27	25	28
4010	29	28	32	31	28	35
4011	27	27	32	28	33	28
4012	24	27	28	29	28	28
Mean	26	28	29	29	30	31
S.D.	2	2	3	3	3	3

Unit: g/rat/day

Appendix 4-5

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual food consumption of female rats during the pre-mating period (Main group)

Dose (mg/kg): 0

Animal number	Day of administration		
	1	8	15
1101	14	22	20
1102	14	21	20
1103	22	20	22
1104	17	17	22
1105	14	19	20
1106	18	22	19
1107	19	21	16
1108	19	19	24
1109	21	25	25
1110	22	18	26
1111	12	21	21
1112	21	25	17
Mean	18	21	21
S.D.	4	2	3

Unit: g/rat/day

Appendix 4-6

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual food consumption of female rats during the pre-mating period (Main group)

Dose (mg/kg): 20

Animal number	Day of administration		
	1	8	15
2101	13	21	23
2102	19	18	20
2103	17	17	20
2104	12	23	21
2105	17	22	20
2106	16	24	22
2107	19	21	20
2108	14	23	21
2109	20	23	15
2110	17	20	21
2111	14	19	18
2112	16	25	30
Mean	16	21	21
S.D.	3	2	4

Unit: g/rat/day

Appendix 4-7

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual food consumption of female rats during the pre-mating period (Main group)

Dose (mg/kg): 100

Animal number	Day of administration		
	1	8	15
3101	19	25	26
3102	13	23	22
3103	19	20	17
3104	19	21	20
3105	15	21	20
3106	18	23	20
3107	15	24	20
3108	15	24	24
3109	17	23	22
3110	17	23	18
3111	19	22	19
3112	19	22	20
Mean	17	23	21
S.D.	2	1	2

Unit: g/rat/day

Appendix 4-8

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual food consumption of female rats during the pre-mating period (Main group)

Dose (mg/kg): 500

Animal number	Day of administration		
	1	8	15
4101	17	22	21
4102	20	22	24
4103	18	17	19
4104	16	24	22
4105	19	15	21
4106	18	15	23
4107	20	22	16
4108	21	22	16
4109	21	23	22
4110	20	21	17
4111	15	18	21
4112	14	21	20
Mean	18	20	20
S.D.	2	3	3

Unit: g/rat/day

Appendix 4-9

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual food consumption of dams during the gestation period (Main group)

Dose (mg/kg): 0

Dam number	Administration			
	1	7	14	20a)
1101	21	25	28	29
1102	21	23	24	20
1103	21	27	30	28
1104	19	21	25	22
1105	20	27	25	24
1106	16	19	25	19
1107	20	23	24	23
1108	24	24	26	25
1109	20	27	29	29
1110	25	28	32	31
1111	23	22	24	24
1112	24	28	24	26
Mean	21	25	26	25
S.D.	3	3	3	4

Unit: g/rat/day

a): Gestation day

Appendix 4-10

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual food consumption of dams during the gestation period (Main group)

Dose (mg/kg): 20

Dam number	Administration			
	1	7	14	20a)
2101	23	27	26	27
2102	18	27	29	29
2103	19	21	28	28
2104	19	24	25	22
2105	20	22	21	19
2106	18	26	28	25
2107	25	27	29	27
2108	23	24	23	22
2109	Non-pregnant			
2110	21	22	22	22
2111	20	19	25	21
2112	25	27	26	26
Mean	21	24	26	24
S.D.	3	3	3	3

Unit: g/rat/day
a): Gestation day

Appendix 4-11

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual food consumption of dams during the gestation period (Main group)

Dose (mg/kg): 100

Dam number	Administration			
	1	7	14	20a)
3101	26	32	30	30
3102	22	23	23	19
3103	24	21	25	23
3104	20	23	25	18
3105	23	22	24	23
3106	25	27	28	25
3107	21	25	27	29
3108	25	25	24	22
3109	15	21	24	24
3110	23	27	27	23
3111	Not copulated			
3112	22	23	27	26
Mean	22	24	26	24
S.D.	3	3	2	4

Unit: g/rat/day

a): Gestation day

Appendix 4-12

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual food consumption of dams during the gestation period (Main group)

Dose (mg/kg): 500

Dam number	Administration			
	1	7	14	20a)
4101	20	24	29	23
4102	19	24	30	27
4103	22	24	27	28
4104	22	28	28	25
4105	19	24	26	20
4106	22	22	25	23
4107	26	28	24	22
4108	25	30	29	24
4109	26	27	29	26
4110	22	26	28	21
4111	17	21	20	22
4112	22	22	23	22
Mean	22	25	27	24
S.D.	3	3	3	2

Unit: g/rat/day
a): Gestation day

Appendix 4-13

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual food consumption of dams during the lactation period (Main group)

Dose (mg/kg): 0

Dam number	Administration	
	2	4a)
1101	30	45
1102	24	30
1103	27	43
1104	20	41
1105	35	44
1106	33	40
1107	25	47
1108	22	44
1109	35	44
1110	34	48
1111	28	36
1112	21	45
Mean	28	42
S.D.	6	5

Unit: g/rat/day
a): Lactation day

Appendix 4-14

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual food consumption of dams during the lactation period (Main group)

Dose (mg/kg): 20

Dam number	Administration	
	2	4a)
2101	31	38
2102	27	36
2103	22	41
2104	35	41
2105	28	33
2106	18	42
2107	30	47
2108	24	41
2109	Non-pregnant	
2110	30	47
2111	27	39
2112	15	51
Mean	26	41
S.D.	6	5

Unit: g/rat/day

a): Lactation day

Appendix 4-15

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual food consumption of dams during the lactation period (Main group)

Dose (mg/kg): 100

Dam number	Administration	
	2	4a)
3101	34	52
3102	32	44
3103	21	37
3104	26	37
3105	29	44
3106	28	44
3107	26	45
3108	33	42
3109	31	40
3110	24	39
3111	Not copulated	
3112	23	45
Mean	28	43
S.D.	4	4

Unit: g/rat/day

a): Lactation day

Appendix 4-16

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual food consumption of dams during the lactation period (Main group)

Dose (mg/kg): 500

Dam number	Administration	
	2	4a)
4101	34	42
4102	25	36
4103	19	41
4104	24	44
4105	18	32
4106	28	48
4107	31	48
4108	25	41
4109	35	36
4110	1	34
4111	18	35
4112	39	40
Mean	25	40
S.D.	10	5

Unit: g/rat/day
a): Lactation day

Appendix 4-17

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual food consumption of female rats (Satellite group, administration period)

Dose (mg/kg): 0

Animal number	Day of administration					
	1	8	15	30	36	42
1113	21	16	21	22	17	22
1114	18	17	20	20	18	22
1115	20	23	17	20	23	22
1116	23	19	25	22	17	23
1117	15	20	23	20	18	19
1118	21	23	19	22	21	19
1119	17	21	24	23	18	20
1120	19	19	21	21	17	19
1121	19	17	19	22	14	21
1122	21	25	21	22	20	21
Mean	19	20	21	21	18	21
S.D.	2	3	2	1	2	1

Unit: g/rat/day

Appendix 4-18

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual food consumption of female rats (Satellite group, administration period)

Dose (mg/kg): 500

Animal number	Day of administration					
	1	8	15	30	36	42
4113	17	24	21	17	24	17
4114	21	23	14	19	18	19
4115	15	23	25	26	22	22
4116	16	20	21	16	19	18
4117	16	20	21	16	18	15
4118	21	23	24	19	24	17
4119	18	23	26	28	25	23
4120	17	23	21	17	22	15
4121	15	23	23	21	18	21
4122	17	21	17	21	20	18
Mean	17	22	21	20	21	19
S.D.	2	1	4	4	3	3

Unit: g/rat/day

Appendix 4-19

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual food consumption of male rats (Recovery period)

Dose (mg/kg): 0

Animal number	Day of recovery		
	1	8	14
1008	30	31	35
1009	26	26	26
1010	29	34	31
1011	28	29	27
1012	27	27	26
Mean	28	29	29
S.D.	2	3	4

Unit: g/rat/day

Appendix 4-20

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual food consumption of male rats (Recovery period)

Dose (mg/kg): 500

Animal number	Day of recovery		
	1	8	14
4008	28	31	28
4009	26	29	27
4010	29	32	33
4011	32	31	32
4012	28	25	29
Mean	29	30	30
S.D.	2	3	3

Unit: g/rat/day

Appendix 4-21

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual food consumption of female rats (Recovery period)

Dose (mg/kg): 0

Animal number	Day of recovery		
	1	8	14
1118	16	18	18
1119	24	20	23
1120	19	19	17
1121	20	20	12
1122	17	23	19
Mean	19	20	18
S.D.	3	2	4

Unit: g/rat/day

Appendix 4-22

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual food consumption of female rats (Recovery period)

Dose (mg/kg): 500

Animal number	Day of recovery		
	1	8	14
4118	21	19	24
4119	25	23	26
4120	21	18	21
4121	19	22	22
4122	17	18	19
Mean	21	20	22
S.D.	3	2	3

Unit: g/rat/day

Appendix 5-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual urinalysis of male rats (Week 6 of administration)

Dose (mg/kg): 0

Animal number	pH	1) Pro- tein	2) Ketone body	3) Glu- cose	4) Occult blood	5) Bili- rubin	6) Urobi- linogen	7) Color
1008	>=9.0	+-	+	-	-	-	+-	Y
1009	>=9.0	-	-	-	-	-	+-	Y
1010	8.5	+-	+	-	-	-	+-	Y
1011	8.5	+-	+-	-	+-	-	+-	Y
1012	8.5	-	+	-	-	-	+-	Y

1)	- : 0 mg/dL	+- : 15 mg/dL	+	: 30 mg/dL	++ : 100 mg/dL	+++ : >=300 mg/dL
2)	- : 0 mg/dL	+- : 5 mg/dL	+	: 15 mg/dL	++ : 40 mg/dL	+++ : 80 mg/dL
3)	- : 0 mg/dL	+	: 100 mg/dL	++ : 250 mg/dL	+++ : 500 mg/dL	++++ : >=1000 mg/dL
4)	- : 0 mg/dL	+- : 0.015 mg/dL	+	: 0.062 mg/dL	++ : 0.135 mg/dL	+++ : 0.405 mg/dL
5)	- : 0 mg/dL	+	: 0.8 mg/dL	++ : 1.6 mg/dL	+++ : 3.2 mg/dL	
6)	+- : 0.1-1.0 E.U./dL	+	: 2.0 E.U./dL	++ : 4.0 E.U./dL	+++ : >=8.0 E.U./dL	
7)	LY : Light yellow	Y : Yellow	DY : Dark yellow			

Appendix 5-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual urinalysis of male rats (Week 6 of administration)

Dose (mg/kg): 0

Animal number	URINE SEDIMENT					CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
1008	-	-	+-	-	-	+-	-
1009	-	-	+-	-	-	-	-
1010	-	-	+-	-	-	+	-
1011	-	-	+-	-	-	-	-
1012	-	-	+-	-	-	+	-

SEC	: Squamous Epithelial Cell	-	: Negative
SREC	: Small Round Epithelial Cell	+-	: Slight
PS	: Phosphate Salts	+	: Mild
CO	: Calcium Oxalate	++	: Moderate
		+++	: Severe

Appendix 5-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual water intake and urinalysis of male rats (Week 6 of administration)

Dose (mg/kg): 0

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
1008	30	11.6	2374	1.30	4.37	1.93
1009	43	16.9	1648	1.62	4.29	2.10
1010	39	11.9	2242	1.45	4.21	1.81
1011	36	10.4	2152	1.16	3.79	1.46
1012	29	18.2	2020	2.00	6.25	2.51
Mean	35	13.8	2087	1.51	4.58	1.96
S.D.	6	3.5	277	0.32	0.96	0.39

Appendix 5-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual urinalysis of male rats (Week 6 of administration)

Dose (mg/kg): 20

Animal number	pH	1) Pro- tein	2) Ketone body	3) Glu- cose	4) Occult blood	5) Bili- rubin	6) Urobi- linogen	7) Color
2008	8.5	+-	+	-	-	-	+-	Y
2009	7.5	-	+-	-	-	-	+-	Y
2010	>=9.0	-	+-	-	-	-	+-	Y
2011	8.5	++	+	-	-	+	+-	Y
2012	8.0	-	+-	-	-	-	+-	Y

1)	- : 0 mg/dL	+- : 15 mg/dL	+	: 30 mg/dL	++ : 100 mg/dL	+++ : >=300 mg/dL
2)	- : 0 mg/dL	+- : 5 mg/dL	+	: 15 mg/dL	++ : 40 mg/dL	+++ : 80 mg/dL
3)	- : 0 mg/dL	+	: 100 mg/dL	++ : 250 mg/dL	+++ : 500 mg/dL	++++ : >=1000 mg/dL
4)	- : 0 mg/dL	+- : 0.015 mg/dL	+	: 0.062 mg/dL	++ : 0.135 mg/dL	+++ : 0.405 mg/dL
5)	- : 0 mg/dL	+	: 0.8 mg/dL	++ : 1.6 mg/dL	+++ : 3.2 mg/dL	
6)	+- : 0.1-1.0 E.U./dL	+	: 2.0 E.U./dL	++ : 4.0 E.U./dL	+++ : >=8.0 E.U./dL	
7)	LY : Light yellow	Y : Yellow	DY : Dark yellow			

Appendix 5-5

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual urinalysis of male rats (Week 6 of administration)

Dose (mg/kg): 20

Animal number	URINE SEDIMENT					CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
2008	-	-	+-	-	-	+	-
2009	-	-	+-	-	-	-	-
2010	-	-	+-	-	-	+-	-
2011	-	-	+-	-	-	+-	-
2012	-	-	+-	-	-	-	-

SEC	: Squamous Epithelial Cell	-	: Negative
SREC	: Small Round Epithelial Cell	+-	: Slight
PS	: Phosphate Salts	+	: Mild
CO	: Calcium Oxalate	++	: Moderate
		+++	: Severe

Appendix 5-6

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual water intake and urinalysis of male rats (Week 6 of administration)

Dose (mg/kg): 20

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
2008	34	11.9	1964	1.12	3.94	1.64
2009	42	12.2	1970	1.15	4.04	1.54
2010	34	13.9	2112	1.70	4.41	2.11
2011	29	9.1	2594	1.40	3.69	1.60
2012	38	11.9	2502	1.81	4.63	2.28
Mean	35	11.8	2228	1.44	4.14	1.83
S.D.	5	1.7	299	0.31	0.38	0.34

Appendix 5-7

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual urinalysis of male rats (Week 6 of administration)

Dose (mg/kg): 100

Animal number	pH	1) Pro- tein	2) Ketone body	3) Glu- cose	4) Occult blood	5) Bili- rubin	6) Urobi- linogen	7) Color
3008	8.5	-	+	-	-	-	+-	Y
3009	7.5	+-	+	-	-	-	+-	Y
3010	>=9.0	-	+	-	-	-	+-	Y
3011	8.5	+	+-	-	-	-	+-	Y
3012	8.5	+	+	-	-	-	+-	Y

1)	- : 0 mg/dL	+- : 15 mg/dL	+	: 30 mg/dL	++ : 100 mg/dL	+++ : >=300 mg/dL
2)	- : 0 mg/dL	+- : 5 mg/dL	+	: 15 mg/dL	++ : 40 mg/dL	+++ : 80 mg/dL
3)	- : 0 mg/dL	+	: 100 mg/dL	++ : 250 mg/dL	+++ : 500 mg/dL	++++ : >=1000 mg/dL
4)	- : 0 mg/dL	+- : 0.015 mg/dL	+	: 0.062 mg/dL	++ : 0.135 mg/dL	+++ : 0.405 mg/dL
5)	- : 0 mg/dL	+	: 0.8 mg/dL	++ : 1.6 mg/dL	+++ : 3.2 mg/dL	
6)	+- : 0.1-1.0 E.U./dL	+	: 2.0 E.U./dL	++ : 4.0 E.U./dL	+++ : >=8.0 E.U./dL	
7)	LY : Light yellow	Y : Yellow	DY : Dark yellow			

Individual urinalysis of male rats (Week 6 of administration)

Dose (mg/kg): 100

Animal number	URINE SEDIMENT						CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast		PS	CO
3008	-	-	+-	-	-		+	-
3009	-	-	+-	-	-		+	-
3010	-	-	+-	-	-		-	-
3011	-	-	+-	-	-		-	-
3012	-	-	+-	-	-		+-	-

SEC	: Squamous Epithelial Cell	-	: Negative
SREC	: Small Round Epithelial Cell	+-	: Slight
PS	: Phosphate Salts	+	: Mild
CO	: Calcium Oxalate	++	: Moderate
		+++	: Severe

Appendix 5-9

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual water intake and urinalysis of male rats (Week 6 of administration)

Dose (mg/kg): 100

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
3008	46	18.0	1774	1.66	5.18	2.12
3009	35	19.8	1542	1.70	4.97	2.10
3010	36	9.6	1862	1.08	2.70	1.40
3011	35	11.8	2032	1.25	4.05	1.68
3012	33	14.4	2020	1.90	4.48	2.13
Mean	37	14.7	1846	1.52	4.28	1.89
S.D.	5	4.2	202	0.34	0.98	0.33

Appendix 5-10

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual urinalysis of male rats (Week 6 of administration)

Dose (mg/kg): 500

Animal number	pH	1) Pro- tein	2) Ketone body	3) Glu- cose	4) Occult blood	5) Bili- rubin	6) Urobi- linogen	7) Color
4008	6.5	+-	+-	-	-	-	+-	Y
4009	6.5	+	+	-	-	-	+-	Y
4010	7.0	-	-	-	-	-	+-	Y
4011	6.5	+	+-	-	-	-	+-	Y
4012	6.5	+-	+-	-	-	-	+-	Y

1)	- : 0 mg/dL	+- : 15 mg/dL	+	: 30 mg/dL	++ :	100 mg/dL	+++ :	>=300 mg/dL
2)	- : 0 mg/dL	+- : 5 mg/dL	+	: 15 mg/dL	++ :	40 mg/dL	+++ :	80 mg/dL
3)	- : 0 mg/dL	+	: 100 mg/dL	++ :	250 mg/dL	+++ :	500 mg/dL	++++ : >=1000 mg/dL
4)	- : 0 mg/dL	+- : 0.015 mg/dL	+	: 0.062 mg/dL	++ :	0.135 mg/dL	+++ :	0.405 mg/dL
5)	- : 0 mg/dL	+	: 0.8 mg/dL	++ :	1.6 mg/dL	+++ :	3.2 mg/dL	
6)	+- : 0.1-1.0 E.U./dL	+	: 2.0 E.U./dL	++ :	4.0 E.U./dL	+++ :	>=8.0 E.U./dL	
7)	LY : Light yellow	Y : Yellow		DY : Dark yellow				

Individual urinalysis of male rats (Week 6 of administration)

Dose (mg/kg): 500

SEC	: Squamous Epithelial Cell	-	: Negative
SREC	: Small Round Epithelial Cell	+-	: Slight
PS	: Phosphate Salts	+	: Mild
CO	: Calcium Oxalate	++	: Moderate
		+++	: Severe

Appendix 5-12

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual water intake and urinalysis of male rats (Week 6 of administration)

Dose (mg/kg): 500

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
4008	42	25.5	1390	2.14	5.57	2.45
4009	38	15.5	2002	1.46	5.01	2.02
4010	52	18.1	1898	1.70	5.35	2.28
4011	50	12.0	1920	1.37	3.72	1.63
4012	41	13.0	2004	1.30	4.14	1.66
Mean	45	16.8	1843	1.59	4.76	2.01
S.D.	6	5.4	258	0.34	0.80	0.37

Appendix 5-13

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual urinalysis of female rats (Satellite group, Week 6 of administration)

Dose (mg/kg): 0

Animal number	pH	1) Pro- tein	2) Ketone body	3) Glu- cose	4) Occult blood	5) Bili- rubin	6) Urobi- linogen	7) Color
1118	>=9.0	-	-	-	-	-	+-	Y
1119	8.0	-	-	-	-	-	+-	Y
1120	8.5	-	-	-	-	-	+-	Y
1121	8.0	-	-	-	-	-	+-	Y
1122	8.0	-	-	-	-	-	+-	Y

1)	- : 0 mg/dL	+- : 15 mg/dL	+	: 30 mg/dL	++ : 100 mg/dL	+++ : >=300 mg/dL
2)	- : 0 mg/dL	+- : 5 mg/dL	+	: 15 mg/dL	++ : 40 mg/dL	+++ : 80 mg/dL
3)	- : 0 mg/dL	+	: 100 mg/dL	++ : 250 mg/dL	+++ : 500 mg/dL	++++ : >=1000 mg/dL
4)	- : 0 mg/dL	+- : 0.015 mg/dL	+	: 0.062 mg/dL	++ : 0.135 mg/dL	+++ : 0.405 mg/dL
5)	- : 0 mg/dL	+	: 0.8 mg/dL	++ : 1.6 mg/dL	+++ : 3.2 mg/dL	
6)	+- : 0.1-1.0 E.U./dL	+	: 2.0 E.U./dL	++ : 4.0 E.U./dL	+++ : >=8.0 E.U./dL	
7)	LY : Light yellow	Y : Yellow	DY : Dark yellow			

Appendix 5-14

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual urinalysis of female rats (Satellite group, Week 6 of administration)

Dose (mg/kg): 0

Animal number	URINE SEDIMENT					CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
1118	-	-	+-	-	-	-	-
1119	-	-	+-	-	-	-	-
1120	-	-	+-	-	-	-	-
1121	-	-	+-	-	-	-	-
1122	-	-	+-	-	-	-	-

SEC	: Squamous Epithelial Cell	-	: Negative
SREC	: Small Round Epithelial Cell	+-	: Slight
PS	: Phosphate Salts	+	: Mild
CO	: Calcium Oxalate	++	: Moderate
		+++	: Severe

Appendix 5-15

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual water intake and urinalysis of female rats (Satellite group, Week 6 of administration)

Dose (mg/kg): 0

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
1118	26	12.4	1466	0.97	2.60	1.12
1119	24	7.0	1822	0.70	1.86	0.95
1120	25	8.7	1930	0.99	2.58	1.24
1121	44	15.8	1424	1.30	3.43	1.64
1122	36	18.4	1556	1.29	4.38	1.88
Mean	31	12.5	1640	1.05	2.97	1.37
S.D.	9	4.8	224	0.25	0.96	0.38

Appendix 5-16

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual urinalysis of female rats (Satellite group, Week 6 of administration)

Dose (mg/kg): 500

Animal number	pH	1) Pro- tein	2) Ketone body	3) Glu- cose	4) Occult blood	5) Bili- rubin	6) Urobi- linogen	7) Color
4118	8.0	-	-	-	-	-	+-	Y
4119	7.0	+	+-	-	-	-	+-	Y
4120	6.5	-	-	-	-	-	+-	Y
4121	6.0	-	-	-	-	-	+-	Y
4122	7.5	+-	+-	-	-	-	+-	Y

1)	- : 0 mg/dL	+- : 15 mg/dL	+	: 30 mg/dL	++	: 100 mg/dL	+++	: >=300 mg/dL	
2)	- : 0 mg/dL	+- : 5 mg/dL	+	: 15 mg/dL	++	: 40 mg/dL	+++	: 80 mg/dL	
3)	- : 0 mg/dL	+	: 100 mg/dL	++	: 250 mg/dL	+++	: 500 mg/dL	++++	: >=1000 mg/dL
4)	- : 0 mg/dL	+- : 0.015 mg/dL	+	: 0.062 mg/dL	++	: 0.135 mg/dL	+++	: 0.405 mg/dL	
5)	- : 0 mg/dL	+	: 0.8 mg/dL	++	: 1.6 mg/dL	+++	: 3.2 mg/dL		
6)	+- : 0.1-1.0 E.U./dL	+	: 2.0 E.U./dL	++	: 4.0 E.U./dL	+++	: >=8.0 E.U./dL		
7)	LY : Light yellow	Y : Yellow	DY	: Dark yellow					

Appendix 5-17

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual urinalysis of female rats (Satellite group, Week 6 of administration)

Dose (mg/kg): 500

Animal number	URINE SEDIMENT					CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
4118	-	-	+-	-	-	-	-
4119	-	-	+-	-	-	-	-
4120	-	-	+-	-	-	-	-
4121	-	-	+-	-	-	-	-
4122	-	+-	-	-	-	+-	-

SEC	: Squamous Epithelial Cell	-	: Negative
SREC	: Small Round Epithelial Cell	+-	: Slight
PS	: Phosphate Salts	+	: Mild
CO	: Calcium Oxalate	++	: Moderate
		+++	: Severe

Appendix 5-18

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual water intake and urinalysis of female rats (Satellite group, Week 6 of administration)

Dose (mg/kg): 500

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
4118	32	8.9	2012	1.00	2.78	1.19
4119	26	5.9	2712	0.83	2.31	0.81
4120	36	14.7	1572	1.15	3.65	1.44
4121	26	7.7	2246	1.02	2.53	1.03
4122	32	13.2	1858	1.21	3.61	1.69
Mean	30	10.1	2080	1.04	2.98	1.23
S.D.	4	3.7	430	0.15	0.62	0.34

Appendix 5-19

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual urinalysis of male rats (Week 2 of recovery)

Dose (mg/kg): 0

Animal number	pH	1) Pro- tein	2) Ketone body	3) Glu- cose	4) Occult blood	5) Bili- rubin	6) Urobi- linogen	7) Color
1008	8.5	+	+	-	-	-	+-	Y
1009	>=9.0	+-	-	-	-	-	+-	Y
1010	>=9.0	+	+	-	+-	-	+-	Y
1011	>=9.0	+	+	-	+	-	+-	Y
1012	>=9.0	+	+	-	+-	-	+-	Y

1)	- : 0 mg/dL	+- : 15 mg/dL	+	: 30 mg/dL	++ : 100 mg/dL	+++ : >=300 mg/dL
2)	- : 0 mg/dL	+- : 5 mg/dL	+	: 15 mg/dL	++ : 40 mg/dL	+++ : 80 mg/dL
3)	- : 0 mg/dL	+	: 100 mg/dL	++ : 250 mg/dL	+++ : 500 mg/dL	++++ : >=1000 mg/dL
4)	- : 0 mg/dL	+- : 0.015 mg/dL	+	: 0.062 mg/dL	++ : 0.135 mg/dL	+++ : 0.405 mg/dL
5)	- : 0 mg/dL	+	: 0.8 mg/dL	++ : 1.6 mg/dL	+++ : 3.2 mg/dL	
6)	+- : 0.1-1.0 E.U./dL	+	: 2.0 E.U./dL	++ : 4.0 E.U./dL	+++ : >=8.0 E.U./dL	
7)	LY : Light yellow	Y : Yellow		DY : Dark yellow		

Individual urinalysis of male rats (Week 2 of recovery)

Dose (mg/kg): 0

Animal number	URINE SEDIMENT					CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
1008	-	-	+-	-	-	+-	-
1009	-	-	+-	-	-	+-	-
1010	-	-	+-	-	-	+-	-
1011	+-	-	+-	-	-	+-	-
1012	-	-	+-	-	-	+-	-

SEC	: Squamous Epithelial Cell	-	: Negative
SREC	: Small Round Epithelial Cell	+-	: Slight
PS	: Phosphate Salts	+	: Mild
CO	: Calcium Oxalate	++	: Moderate
		+++	: Severe

Appendix 5-21

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual water intake and urinalysis of male rats (Week 2 of recovery)

Dose (mg/kg): 0

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
1008	34	9.4	2360	1.00	3.59	1.58
1009	49	20.0	1498	1.72	4.60	2.28
1010	39	15.9	2020	1.78	5.01	2.29
1011	34	12.9	2244	1.21	4.72	1.78
1012	36	17.1	2248	2.09	5.88	2.36
Mean	38	15.1	2074	1.56	4.76	2.06
S.D.	6	4.1	345	0.44	0.82	0.35

Appendix 5-22

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual urinalysis of male rats (Week 2 of recovery)

Dose (mg/kg): 500

Animal number	pH	1) Pro- tein	2) Ketone body	3) Glu- cose	4) Occult blood	5) Bili- rubin	6) Urobi- linogen	7) Color
4008	>=9.0	+	+	-	-	-	+-	Y
4009	8.5	+	+	-	+-	-	+-	Y
4010	>=9.0	+	+	-	+-	-	+-	Y
4011	>=9.0	+	+	-	-	-	+-	Y
4012	8.5	+	+	-	-	-	+-	Y

1)	- : 0 mg/dL	+- : 15 mg/dL	+	: 30 mg/dL	++ : 100 mg/dL	+++ : >=300 mg/dL
2)	- : 0 mg/dL	+- : 5 mg/dL	+	: 15 mg/dL	++ : 40 mg/dL	+++ : 80 mg/dL
3)	- : 0 mg/dL	+	: 100 mg/dL	++ : 250 mg/dL	+++ : 500 mg/dL	++++ : >=1000 mg/dL
4)	- : 0 mg/dL	+- : 0.015 mg/dL	+	: 0.062 mg/dL	++ : 0.135 mg/dL	+++ : 0.405 mg/dL
5)	- : 0 mg/dL	+	: 0.8 mg/dL	++ : 1.6 mg/dL	+++ : 3.2 mg/dL	
6)	+- : 0.1-1.0 E.U./dL	+	: 2.0 E.U./dL	++ : 4.0 E.U./dL	+++ : >=8.0 E.U./dL	
7)	LY : Light yellow	Y : Yellow		DY : Dark yellow		

Appendix 5-23

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual urinalysis of male rats (Week 2 of recovery)

Dose (mg/kg): 500

Animal number	URINE SEDIMENT					CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
4008	-	-	+-	-	-	+-	-
4009	-	-	+-	-	-	+-	-
4010	-	-	+-	-	-	+-	-
4011	-	-	+-	-	-	+-	-
4012	-	-	+-	-	-	-	-

SEC	: Squamous Epithelial Cell	-	: Negative
SREC	: Small Round Epithelial Cell	+-	: Slight
PS	: Phosphate Salts	+	: Mild
CO	: Calcium Oxalate	++	: Moderate
		+++	: Severe

Appendix 5-24

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual water intake and urinalysis of male rats (Week 2 of recovery)

Dose (mg/kg): 500

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
4008	36	17.1	1684	1.68	4.35	2.12
4009	49	17.2	1662	1.31	4.60	1.79
4010	43	19.8	1838	1.66	5.62	2.22
4011	39	13.6	2028	1.58	4.26	1.93
4012	30	8.5	2170	1.11	2.57	1.26
Mean	39	15.2	1876	1.47	4.28	1.86
S.D.	7	4.4	220	0.25	1.10	0.38

Appendix 5-25

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual urinalysis of female rats (Week 2 of recovery)

Dose (mg/kg): 0

Animal number	pH	1) Pro- tein	2) Ketone body	3) Glu- cose	4) Occult blood	5) Bili- rubin	6) Urobi- linogen	7) Color
1118	8.5	-	-	-	-	-	+-	Y
1119	8.5	-	-	-	-	-	+-	Y
1120	>=9.0	-	-	-	-	-	+-	Y
1121	7.5	-	-	-	-	-	+-	Y
1122	>=9.0	-	-	-	-	-	+-	Y

1)	- : 0 mg/dL	+- : 15 mg/dL	+	: 30 mg/dL	++ : 100 mg/dL	+++ : >=300 mg/dL
2)	- : 0 mg/dL	+- : 5 mg/dL	+	: 15 mg/dL	++ : 40 mg/dL	+++ : 80 mg/dL
3)	- : 0 mg/dL	+	: 100 mg/dL	++ : 250 mg/dL	+++ : 500 mg/dL	++++ : >=1000 mg/dL
4)	- : 0 mg/dL	+- : 0.015 mg/dL	+	: 0.062 mg/dL	++ : 0.135 mg/dL	+++ : 0.405 mg/dL
5)	- : 0 mg/dL	+	: 0.8 mg/dL	++ : 1.6 mg/dL	+++ : 3.2 mg/dL	
6)	+- : 0.1-1.0 E.U./dL	+	: 2.0 E.U./dL	++ : 4.0 E.U./dL	+++ : >=8.0 E.U./dL	
7)	LY : Light yellow	Y : Yellow	DY : Dark yellow			

Appendix 5-26

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual urinalysis of female rats (Week 2 of recovery)

Dose (mg/kg): 0

Animal number	URINE SEDIMENT					CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
1118	-	-	+-	-	-	+-	-
1119	-	-	+-	-	-	+-	-
1120	-	-	+-	-	-	+-	-
1121	-	-	+-	-	-	-	-
1122	-	-	+-	-	-	-	-

SEC	: Squamous Epithelial Cell	-	: Negative
SREC	: Small Round Epithelial Cell	+-	: Slight
PS	: Phosphate Salts	+	: Mild
CO	: Calcium Oxalate	++	: Moderate
		+++	: Severe

Appendix 5-27

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual water intake and urinalysis of female rats (Week 2 of recovery)

Dose (mg/kg): 0

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
1118	24	10.8	1936	1.19	3.09	1.14
1119	38	19.6	1450	1.57	4.17	1.96
1120	31	11.3	2052	1.27	3.70	1.65
1121	50	24.7	1220	1.53	4.78	1.83
1122	43	14.0	1660	1.37	3.37	1.32
Mean	37	16.1	1664	1.39	3.82	1.58
S.D.	10	6.0	342	0.16	0.67	0.34

Appendix 5-28

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual urinalysis of female rats (Week 2 of recovery)

Dose (mg/kg): 500

Animal number	pH	1) Pro- tein	2) Ketone body	3) Glu- cose	4) Occult blood	5) Bili- rubin	6) Urobi- linogen	7) Color
4118	7.0	-	+-	-	-	-	+-	Y
4119	8.5	-	-	-	-	-	+-	Y
4120	8.5	+-	+-	-	-	-	+-	Y
4121	8.5	-	-	-	-	-	+-	Y
4122	8.0	-	+-	-	-	-	+-	Y

1)	- : 0 mg/dL	+- : 15 mg/dL	+	: 30 mg/dL	++ : 100 mg/dL	+++ : >=300 mg/dL
2)	- : 0 mg/dL	+- : 5 mg/dL	+	: 15 mg/dL	++ : 40 mg/dL	+++ : 80 mg/dL
3)	- : 0 mg/dL	+	: 100 mg/dL	++ : 250 mg/dL	+++ : 500 mg/dL	++++ : >=1000 mg/dL
4)	- : 0 mg/dL	+- : 0.015 mg/dL	+	: 0.062 mg/dL	++ : 0.135 mg/dL	+++ : 0.405 mg/dL
5)	- : 0 mg/dL	+	: 0.8 mg/dL	++ : 1.6 mg/dL	+++ : 3.2 mg/dL	
6)	+- : 0.1-1.0 E.U./dL	+	: 2.0 E.U./dL	++ : 4.0 E.U./dL	+++ : >=8.0 E.U./dL	
7)	LY : Light yellow	Y : Yellow	DY : Dark yellow			

Appendix 5-29

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual urinalysis of female rats (Week 2 of recovery)

Dose (mg/kg): 500

Animal number	URINE SEDIMENT					CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
4118	-	-	+-	-	-	-	-
4119	-	-	+-	-	-	+-	-
4120	-	-	+-	-	-	+-	-
4121	-	-	+-	-	-	+-	-
4122	-	-	+-	-	-	-	-

SEC	: Squamous Epithelial Cell	-	: Negative
SREC	: Small Round Epithelial Cell	+-	: Slight
PS	: Phosphate Salts	+	: Mild
CO	: Calcium Oxalate	++	: Moderate
		+++	: Severe

Appendix 5-30

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual water intake and urinalysis of female rats (Week 2 of recovery)

Dose (mg/kg): 500

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
4118	35	7.8	2352	0.95	2.78	1.12
4119	34	8.9	2178	0.94	2.92	1.16
4120	34	10.5	2020	1.18	3.25	1.49
4121	37	10.7	1752	0.73	2.68	0.98
4122	28	7.8	1924	0.86	2.21	0.92
Mean	34	9.1	2045	0.93	2.77	1.13
S.D.	3	1.4	231	0.16	0.38	0.22

Appendix 6-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual hematology of male rats (End of administration)

Dose mg/kg	Animal number	RBC ×10 ⁴ /μL	Hb g/dL	Ht %	MCV fL	MCH pg	MCHC g/dL	Reticu- locyte %	Plate- let ×10 ⁴ /μL	PT s	APTT s	Fibri- nogen mg/dL
0	1001	918	15.4	43.8	47.7	16.8	35.2	2.0	113.4	18.5	21.2	272
	1002	828	15.0	42.2	51.0	18.1	35.5	2.2	121.0	16.9	23.4	267
	1003	938	16.4	47.8	50.9	17.5	34.4	2.0	91.0	23.0	32.7	298
	1004	911	15.2	43.5	47.8	16.7	34.9	1.3	120.8	16.6	25.0	296
	1005	860	15.7	45.2	52.6	18.3	34.8	2.8	121.6	14.2	24.4	251
	Mean	891	15.5	44.5	50.0	17.5	35.0	2.1	113.6	17.8	25.3	277
	S.D.	45	0.5	2.1	2.2	0.7	0.4	0.5	13.1	3.3	4.4	20
20	2001	881	14.7	42.1	47.8	16.6	34.8	2.1	102.1	15.2	19.5	264
	2002	890	15.4	44.0	49.4	17.3	35.1	2.1	103.9	15.8	21.4	241
	2003	891	15.9	45.6	51.1	17.9	35.0	2.0	102.9	21.1	22.0	296
	2004	898	15.2	43.8	48.7	16.9	34.7	1.6	124.4	16.0	22.9	283
	2005	896	16.2	47.2	52.7	18.1	34.3	2.8	131.0	17.6	31.6	289
	Mean	891	15.5	44.5	49.9	17.4	34.8	2.1	112.9	17.1	23.5	275
	S.D.	7	0.6	1.9	2.0	0.6	0.3	0.4	13.8	2.4	4.7	22
100	3001	896	15.0	43.2	48.2	16.8	34.8	2.4	119.6	15.9	27.7	259
	3002	908	15.0	43.1	47.4	16.5	34.8	1.4	113.5	18.7	23.4	305
	3003	909	15.6	44.6	49.1	17.2	35.0	1.8	96.8	16.5	19.5	262
	3004	968	15.8	45.8	47.3	16.3	34.5	2.0	120.8	17.8	29.0	267
	3005	827	14.7	40.8	49.3	17.8	36.1	2.8	130.1	14.0	27.9	271
	Mean	902	15.2	43.5	48.3	16.9	35.0	2.1	116.2	16.6	25.5	273
	S.D.	50	0.5	1.9	0.9	0.6	0.6	0.5	12.3	1.8	4.0	19
500	4001	875	14.4	41.1	47.0	16.5	35.1	2.2	111.1	15.8	24.3	268
	4002	855	14.9	42.4	49.5	17.4	35.2	2.3	141.9	17.1	23.8	270
	4003	887	15.2	43.5	49.1	17.2	35.0	1.8	117.1	18.9	31.4	374
	4004	899	16.0	46.4	51.6	17.8	34.6	1.8	110.9	22.9	29.1	336
	4005	921	15.8	45.1	48.9	17.1	35.0	1.4	106.7	22.6	23.8	386
	Mean	887	15.3	43.7	49.2	17.2	35.0	1.9	117.5	19.5	26.5	327
	S.D.	25	0.7	2.1	1.6	0.5	0.2	0.4	14.1	3.2	3.5	56

Appendix 6-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual hematology of male rats (End of administration)

Dose mg/kg	Animal number	WBC	Differential leukocyte counts (%)						Differential leukocyte counts (X10 ² /μL)					
		X10 ² /μL	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	1001	88.0	70.2	25.0	2.1	0.3	2.1	0.3	61.7	22.0	1.9	0.3	1.8	0.3
	1002	72.6	71.4	24.7	1.3	0.3	2.1	0.2	51.8	17.9	1.0	0.2	1.5	0.1
	1003	54.5	72.9	22.5	1.6	0.1	2.6	0.3	39.7	12.3	0.9	0.1	1.4	0.2
	1004	49.1	63.0	31.7	2.3	0.3	2.3	0.4	30.9	15.6	1.1	0.1	1.1	0.2
	1005	114.1	67.4	23.8	1.4	0.4	5.3	1.6	76.9	27.2	1.6	0.5	6.1	1.8
	Mean	75.7	69.0	25.5	1.7	0.3	2.9	0.6	52.2	19.0	1.3	0.2	2.4	0.5
	S.D.	26.4	3.9	3.6	0.4	0.1	1.4	0.6	18.1	5.8	0.4	0.2	2.1	0.7
20	2001	73.8	71.6	22.4	1.3	0.4	3.6	0.7	52.8	16.5	1.0	0.3	2.6	0.5
	2002	95.9	73.8	21.6	1.6	0.4	1.8	0.8	70.8	20.8	1.5	0.4	1.7	0.7
	2003	66.3	63.5	31.3	2.0	0.5	2.5	0.3	42.1	20.7	1.3	0.3	1.6	0.2
	2004	54.1	73.0	21.4	2.1	0.3	3.0	0.3	39.5	11.6	1.1	0.1	1.6	0.2
	2005	122.9	76.0	19.4	1.4	0.7	2.3	0.3	93.4	23.8	1.7	0.9	2.8	0.4
	Mean	82.6	71.6	23.2	1.7	0.5	2.6	0.5	59.7	18.7	1.3	0.4	2.1	0.4
	S.D.	27.2	4.8	4.6	0.4	0.2	0.7	0.2	22.5	4.7	0.3	0.3	0.6	0.2
100	3001	113.6	82.4	13.2	1.2	0.5	2.0	0.7	93.7	15.0	1.4	0.6	2.2	0.8
	3002	66.5	77.8	16.9	1.2	0.3	2.9	0.9	51.7	11.2	0.8	0.2	1.9	0.6
	3003	81.5	72.3	21.5	1.5	0.3	3.6	0.8	58.9	17.5	1.2	0.2	3.0	0.6
	3004	93.3	82.5	12.4	1.5	0.5	2.8	0.4	77.0	11.5	1.4	0.5	2.6	0.4
	3005	97.4	67.1	28.1	1.5	0.4	2.0	1.0	65.3	27.4	1.5	0.3	1.9	1.0
	Mean	90.5	76.4	18.4	1.4	0.4	2.7	0.8	69.3	16.5	1.3	0.4	2.3	0.7
	S.D.	17.6	6.7	6.5	0.2	0.1	0.7	0.2	16.5	6.6	0.3	0.2	0.5	0.2
500	4001	79.8	83.5	12.5	1.9	0.3	1.4	0.5	66.6	9.9	1.5	0.2	1.1	0.4
	4002	74.7	80.7	14.3	1.5	0.4	2.1	1.0	60.3	10.7	1.2	0.3	1.6	0.8
	4003	100.2	83.1	13.1	1.5	0.4	1.6	0.3	83.2	13.1	1.5	0.4	1.6	0.3
	4004	58.9	78.7	16.9	1.8	0.3	2.2	0.2	46.3	9.9	1.0	0.2	1.3	0.1
	4005	53.2	69.7	24.8	1.3	0.2	3.3	0.7	37.0	13.2	0.7	0.1	1.8	0.4
	Mean	73.4	79.1	16.3	1.6	0.3	2.1	0.5	58.7	11.4	1.2	0.2	1.5	0.4
	S.D.	18.6	5.6	5.0	0.2	0.1	0.7	0.3	18.0	1.7	0.3	0.1	0.3	0.3

LUC: Large unstained cells

Appendix 6-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual hematology of female rats (Lactation day 5)

Dose mg/kg	Animal number	RBC ×10 ⁴ /μL	Hb g/dL	Ht %	MCV fL	MCH pg	MCHC g/dL	Reticu- locyte %	Plate- let ×10 ⁴ /μL	PT s	APTT s	Fibri- nogen mg/dL
0	1101	759	14.6	42.7	56.2	19.2	34.2	6.9	113.7	13.1	17.9	281
	1103	737	13.7	39.8	54.0	18.5	34.3	6.4	168.6	12.3	15.5	225
	1104	717	13.4	39.0	54.3	18.7	34.5	8.3	146.8	12.4	15.7	253
	1108	715	13.6	40.6	56.9	19.0	33.5	8.4	171.8	13.6	18.6	237
	1110	723	13.3	38.5	53.2	18.4	34.6	5.6	143.6	13.3	17.8	380
	Mean	730	13.7	40.1	54.9	18.8	34.2	7.1	148.9	12.9	17.1	275
	S.D.	18	0.5	1.6	1.6	0.3	0.4	1.2	23.4	0.6	1.4	62
20	2102	829	15.0	42.8	51.6	18.0	35.0	4.7	86.0	12.1	17.7	286
	2103	758	13.7	39.0	51.4	18.0	35.1	6.3	153.5	12.9	16.1	314
	2106	710	13.6	39.3	55.3	19.1	34.5	6.4	162.5	10.7	11.4	377
	2108	751	14.1	39.8	53.0	18.8	35.4	5.0	162.8	12.8	19.4	217
	2109a)	807Z	15.3Z	43.9Z	54.5Z	18.9Z	34.8Z	3.7Z	107.5Z	13.3Z	19.2Z	287Z
	2111	794	14.6	41.3	52.1	18.4	35.4	4.7	133.3	13.4	20.0	312
	Mean	768	14.2	40.4	52.7	18.5	35.1	5.4	139.6	12.4	16.9	301
100	S.D.	45	0.6	1.6	1.6	0.5	0.4	0.9	32.3	1.0	3.4	58
	3102	783	14.3	41.6	53.1	18.3	34.5	6.5	150.9	13.7	17.0	299
	3104	791	14.3	40.3	51.0	18.1	35.5	5.6	152.8	14.3	19.1	278
	3106	768	14.1	40.8	53.1	18.3	34.5	7.7	117.2	12.0	16.0	240
	3107	754	13.9	39.7	52.7	18.5	35.1	5.5	134.5	11.5	13.8	340
	3111b)	892Z	15.7Z	43.6Z	48.9Z	17.6Z	36.0Z	1.3Z	121.5Z	13.5Z	20.3Z	181Z
	3112	778	14.8	43.6	56.0	19.0	33.9	6.4	190.0	13.4	20.8	299
500	Mean	775	14.3	41.2	53.2	18.4	34.7	6.3	149.1	13.0	17.3	291
	S.D.	14	0.3	1.5	1.8	0.3	0.6	0.9	27.0	1.2	2.7	36
	4101	785	14.3	40.3	51.4	18.2	35.5	5.6	195.5	13.0	16.3	374
	4102	702	13.4	39.2	55.9	19.1	34.2	8.4	227.5	12.5	16.9	220
	4103	717	13.9	39.8	55.5	19.3	34.8	7.5	168.7	13.6	18.0	308
	4104	750	13.7	39.7	52.9	18.2	34.5	7.3	158.7	12.5	12.4	345
	4111	740	13.9	39.1	52.9	18.8	35.5	6.0	139.0	12.3	14.1	318
500	Mean	739	13.8	39.6	53.7	18.7	34.9	7.0	177.9	12.8	15.5	313
	S.D.	32	0.3	0.5	1.9	0.5	0.6	1.1	34.4	0.5	2.3	58

a): Non-pregnant

b): Not copulated

Z: Data was excluded from statistical analysis.

Appendix 6-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual hematology of female rats (Lactation day 5)

Dose mg/kg	Animal number	WBC	Differential leukocyte counts (%)						Differential leukocyte counts (X10 ² /μL)					
		X10 ² /μL	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	1101	86.9	61.2	33.3	2.0	0.4	2.7	0.4	53.2	29.0	1.8	0.4	2.3	0.3
	1103	93.1	57.6	37.6	0.4	0.2	3.7	0.5	53.6	35.0	0.4	0.2	3.4	0.4
	1104	110.6	54.3	41.7	0.5	0.1	3.1	0.3	60.0	46.1	0.5	0.2	3.4	0.4
	1108	136.3	53.8	40.9	0.5	0.3	4.1	0.3	73.4	55.7	0.7	0.4	5.6	0.5
	1110	78.7	65.1	31.2	1.1	0.3	1.8	0.5	51.2	24.6	0.9	0.2	1.4	0.4
	Mean	101.1	58.4	36.9	0.9	0.3	3.1	0.4	58.3	38.1	0.9	0.3	3.2	0.4
	S.D.	22.9	4.8	4.6	0.7	0.1	0.9	0.1	9.1	12.7	0.6	0.1	1.6	0.1
20	2102	93.5	66.1	28.7	0.8	0.3	3.7	0.5	61.8	26.8	0.7	0.3	3.5	0.4
	2103	165.0	66.3	30.2	0.8	0.4	1.6	0.7	109.4	49.8	1.4	0.6	2.6	1.1
	2106	80.3	73.5	23.4	0.5	0.3	1.4	0.9	59.1	18.8	0.4	0.2	1.1	0.7
	2108	111.2	67.3	27.4	1.5	0.2	3.0	0.6	74.8	30.4	1.7	0.2	3.4	0.6
	2109a)	71.5Z	82.5Z	13.6Z	1.4Z	0.5Z	1.3Z	0.7Z	59.0Z	9.7Z	1.0Z	0.3Z	1.0Z	0.5Z
	2111	61.4	66.6	27.6	0.8	0.2	4.3	0.5	40.9	16.9	0.5	0.1	2.6	0.3
	Mean	102.3	68.0	27.5	0.9	0.3	2.8	0.6	69.2	28.5	0.9	0.3	2.6	0.6
100	S.D.	39.5	3.1	2.5	0.4	0.1	1.3	0.2	25.5	13.1	0.6	0.2	1.0	0.3
	3102	93.0	71.0	24.4	0.7	0.2	3.2	0.5	66.0	22.7	0.7	0.2	3.0	0.5
	3104	105.2	67.7	28.0	1.4	0.3	2.0	0.5	71.3	29.5	1.5	0.3	2.1	0.5
	3106	105.4	76.7	19.1	1.0	0.3	2.5	0.5	80.8	20.1	1.0	0.3	2.7	0.5
	3107	89.3	60.5	36.7	0.8	0.1	1.4	0.4	54.0	32.8	0.8	0.1	1.3	0.3
	3111b)	97.1Z	87.3Z	7.2Z	2.0Z	0.4Z	2.6Z	0.6Z	84.8Z	7.0Z	2.0Z	0.3Z	2.5Z	0.5Z
	3112	125.0	75.8	19.7	1.0	0.4	2.6	0.5	94.7	24.6	1.2	0.5	3.2	0.7
500	Mean	103.6	70.3	25.6	1.0	0.3	2.3	0.5	73.4	25.9	1.0	0.3	2.5	0.5
	S.D.	14.0	6.6	7.2	0.3	0.1	0.7	0.0	15.4	5.2	0.3	0.1	0.8	0.1
	4101	96.4	74.2	22.7	0.4	0.3	1.8	0.7	71.5	21.9	0.4	0.3	1.7	0.6
	4102	87.6	72.9	23.7	1.0	0.2	1.8	0.4	63.9	20.8	0.8	0.2	1.6	0.3
	4103	115.9	75.0	21.5	0.6	0.3	2.0	0.6	86.9	25.0	0.7	0.4	2.4	0.6
	4104	107.9	71.0	24.4	0.8	0.3	2.6	0.9	76.6	26.4	0.9	0.3	2.8	1.0
	4111	105.0	68.4	27.8	0.5	0.3	2.6	0.5	71.8	29.2	0.5	0.3	2.7	0.6
500	Mean	102.6	72.3	24.0	0.7	0.3	2.2	0.6	74.1	24.7	0.7	0.3	2.2	0.6
	S.D.	10.9	2.7	2.4	0.2	0.0	0.4	0.2	8.5	3.4	0.2	0.1	0.6	0.2

LUC: Large unstained cells

a): Non-pregnant

b): Not copulated

Z: Data was excluded from statistical analysis.

Appendix 6-5

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual hematology of female rats (Satellite group, End of administration)

Dose mg/kg	Animal number	RBC ×10 ⁴ /μL	Hb g/dL	Ht %	MCV fL	MCH pg	MCHC g/dL	Reticu- locyte %	Plate- let ×10 ⁴ /μL	PT s	APTT s	Fibri- nogen mg/dL
0	1113	866	15.3	42.8	49.4	17.7	35.8	2.2	105.9	13.6	18.2	219
	1114	853	14.8	41.8	49.0	17.3	35.4	2.0	101.4	13.5	21.7	200
	1115	875	16.3	46.6	53.3	18.6	35.0	2.6	112.9	13.7	18.9	221
	1116	864	15.9	44.7	51.7	18.4	35.6	2.2	121.7	14.1	16.3	228
	1117	886	16.0	44.6	50.3	18.0	35.9	1.4	107.7	14.5	22.0	246
	Mean	869	15.7	44.1	50.7	18.0	35.5	2.1	109.9	13.9	19.4	223
	S.D.	12	0.6	1.9	1.8	0.5	0.4	0.4	7.8	0.4	2.4	17
500	4113	822	15.1	42.1	51.1	18.4	36.0	1.9	102.4	13.0	17.2	240
	4114	798	14.3	40.3	50.6	18.0	35.6	2.1	118.7	13.2	19.2	203
	4115	846	15.0	41.9	49.6	17.8	35.8	1.6	116.6	13.4	15.5	273
	4116	890	15.7	44.8	50.3	17.6	35.0	1.7	121.1	14.2	18.4	225
	4117	845	15.4	43.2	51.1	18.2	35.6	1.8	142.3	13.4	24.5	285
	Mean	840	15.1	42.5	50.5	18.0	35.6	1.8	120.2	13.4	19.0	245
	S.D.	34	0.5	1.7	0.6	0.3	0.4	0.2	14.3	0.5	3.4	34

Appendix 6-6

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual hematology of female rats (Satellite group, End of administration)

Dose mg/kg	Animal number	WBC $\times 10^2/\mu\text{L}$	Differential leukocyte counts (%)						Differential leukocyte counts ($\times 10^2/\mu\text{L}$)					
			Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	1113	24.6	73.2	21.3	2.4	0.3	2.5	0.3	18.0	5.2	0.6	0.1	0.6	0.1
	1114	64.4	64.3	31.5	1.3	0.4	2.4	0.2	41.4	20.3	0.9	0.2	1.5	0.1
	1115	33.0	68.3	27.5	1.9	0.3	1.8	0.2	22.5	9.1	0.6	0.1	0.6	0.1
	1116	67.3	70.8	24.6	1.9	0.3	2.1	0.3	47.7	16.6	1.3	0.2	1.4	0.2
	1117	68.3	78.5	18.0	1.7	0.3	1.1	0.4	53.7	12.3	1.1	0.2	0.7	0.3
	Mean	51.5	71.0	24.6	1.8	0.3	2.0	0.3	36.7	12.7	0.9	0.2	1.0	0.2
	S.D.	21.0	5.3	5.3	0.4	0.0	0.6	0.1	15.7	6.0	0.3	0.1	0.5	0.1
500	4113	33.1	72.5	15.3	10.1	0.2	1.9	0.1	24.0	5.1	3.3	0.1	0.6	0.0
	4114	38.3	81.1	16.0	1.3	0.1	1.3	0.3	31.1	6.1	0.5	0.0	0.5	0.1
	4115	37.8	75.4	20.0	2.7	0.2	1.4	0.3	28.5	7.5	1.0	0.1	0.5	0.1
	4116	35.9	78.1	19.1	1.5	0.1	1.0	0.2	28.1	6.9	0.5	0.1	0.4	0.1
	4117	47.1	70.3	24.3	2.8	0.3	1.8	0.4	33.1	11.5	1.3	0.1	0.9	0.2
	Mean	38.4	75.5	18.9	3.7	0.2	1.5	0.3	29.0	7.4	1.3	0.1	0.6	0.1
	S.D.	5.3	4.3	3.6	3.7	0.1	0.4	0.1	3.4	2.5	1.2	0.0	0.2	0.1

LUC: Large unstained cells

Appendix 6-7

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual hematology of male rats (End of recovery)

Dose mg/kg	Animal number	RBC ×10 ⁴ /μL	Hb g/dL	Ht %	MCV fL	MCH pg	MCHC g/dL	Reticu- locyte %	Plate- let ×10 ⁴ /μL	PT s	APTT s	Fibri- nogen mg/dL
0	1008	946	16.8	46.2	48.9	17.8	36.4	2.0	116.2	16.2	22.6	319
	1009	970	16.5	47.8	49.3	17.0	34.4	1.7	98.6	21.9	27.4	312
	1010	905	16.0	44.7	49.4	17.7	35.7	2.1	94.9	13.8	23.5	280
	1011	954	16.6	46.6	48.9	17.4	35.5	1.7	90.1	18.3	23.4	275
	1012	951	16.4	47.1	49.5	17.3	34.9	1.3	93.8	18.0	23.6	296
	Mean	945	16.5	46.5	49.2	17.4	35.4	1.8	98.7	17.6	24.1	296
	S.D.	24	0.3	1.2	0.3	0.3	0.8	0.3	10.2	3.0	1.9	19
500	4008	997	17.0	48.6	48.7	17.0	35.0	1.1	97.4	19.3	21.6	389
	4009	944	16.6	46.6	49.4	17.6	35.6	1.4	102.6	17.5	22.4	300
	4010	943	16.1	45.3	48.1	17.1	35.5	2.3	104.2	18.6	23.6	380
	4011	921	16.1	45.2	49.0	17.5	35.7	1.6	86.5	19.1	20.7	330
	4012	949	16.8	47.3	49.8	17.7	35.5	1.5	102.2	22.2	23.1	307
	Mean	951	16.5	46.6	49.0	17.4	35.5	1.6	98.6	19.3	22.3	341
	S.D.	28	0.4	1.4	0.7	0.3	0.3	0.4	7.2	1.7	1.2	41

Appendix 6-8

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual hematology of male rats (End of recovery)

Dose mg/kg	Animal number	WBC $\times 10^2/\mu\text{L}$	Differential leukocyte counts (%)						Differential leukocyte counts ($\times 10^2/\mu\text{L}$)					
			Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	1008	96.4	72.1	23.1	1.7	0.4	2.3	0.4	69.5	22.3	1.6	0.4	2.2	0.4
	1009	124.4	70.6	24.7	0.8	0.6	2.8	0.5	87.8	30.8	1.0	0.7	3.5	0.6
	1010	75.1	73.7	21.4	1.4	0.4	2.6	0.4	55.3	16.1	1.1	0.3	2.0	0.3
	1011	72.3	71.0	22.5	2.5	0.4	3.0	0.7	51.3	16.3	1.8	0.3	2.2	0.5
	1012	45.9	70.9	24.1	1.9	0.2	2.6	0.3	32.6	11.1	0.9	0.1	1.2	0.1
	Mean	82.8	71.7	23.2	1.7	0.4	2.7	0.5	59.3	19.3	1.3	0.4	2.2	0.4
500	S.D.	29.4	1.3	1.3	0.6	0.1	0.3	0.2	20.7	7.5	0.4	0.2	0.8	0.2
	4008	92.2	83.5	13.1	1.0	0.3	1.6	0.5	76.9	12.1	0.9	0.3	1.5	0.5
	4009	69.1	78.0	15.9	2.3	0.4	2.6	0.8	53.9	11.0	1.6	0.3	1.8	0.5
	4010	43.0	78.0	17.8	0.9	0.3	2.7	0.4	33.5	7.6	0.4	0.1	1.2	0.2
	4011	91.5	64.6	31.2	1.5	0.3	2.1	0.4	59.1	28.5	1.3	0.3	1.9	0.3
	4012	63.4	72.2	23.9	1.0	0.2	2.2	0.5	45.7	15.2	0.6	0.1	1.4	0.3
	Mean	71.8	75.3	20.4	1.3	0.3	2.2	0.5	53.8	14.9	1.0	0.2	1.6	0.4
	S.D.	20.7	7.2	7.2	0.6	0.1	0.4	0.2	16.1	8.1	0.5	0.1	0.3	0.1

LUC: Large unstained cells

Appendix 6-9

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual hematology of female rats (End of recovery)

Dose mg/kg	Animal number	RBC ×10 ⁶ /μL	Hb g/dL	Ht %	MCV fL	MCH pg	MCHC g/dL	Reticu- locyte %	Plate- let ×10 ⁹ /μL	PT s	APTT s	Fibri- nogen mg/dL
0	1118	878	16.3	45.0	51.2	18.6	36.3	2.0	118.6	14.2	19.5	210
	1119	816	15.8	43.0	52.6	19.4	36.9	2.3	107.0	12.1	19.7	221
	1120	854	14.3	39.6	46.4	16.7	36.0	1.4	114.8	11.8	15.0	174
	1121	890	16.0	43.6	49.0	17.9	36.6	1.1	121.4	12.0	20.1	241
	1122	887	16.5	44.7	50.4	18.6	37.0	1.5	122.6	12.8	21.6	192
	Mean	865	15.8	43.2	49.9	18.2	36.6	1.7	116.9	12.6	19.2	208
	S.D.	31	0.9	2.2	2.4	1.0	0.4	0.5	6.3	1.0	2.5	26
500	4118	873	16.1	44.1	50.5	18.5	36.6	2.5	126.3	12.0	19.1	248
	4119	846	16.2	45.4	53.6	19.2	35.8	2.1	116.6	12.4	18.0	246
	4120	877	15.8	43.8	50.0	18.0	36.0	1.8	136.7	12.2	19.6	238
	4121	846	15.4	41.8	49.5	18.2	36.8	2.2	132.6	12.7	21.4	263
	4122	908	16.8	46.5	51.1	18.5	36.2	1.4	104.1	13.7	19.2	212
	Mean	870	16.1	44.3	50.9	18.5	36.3	2.0	123.3	12.6	19.5	241
	S.D.	26	0.5	1.8	1.6	0.5	0.4	0.4	13.1	0.7	1.2	19

Appendix 6-10

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual hematology of female rats (End of recovery)

Dose mg/kg	Animal number	WBC $\times 10^2/\mu\text{L}$	Differential leukocyte counts (%)						Differential leukocyte counts ($\times 10^2/\mu\text{L}$)					
			Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	1118	82.4	79.7	15.1	2.3	0.3	1.9	0.7	65.6	12.4	1.9	0.2	1.6	0.5
	1119	45.1	83.6	11.8	2.0	0.3	1.6	0.7	37.7	5.3	0.9	0.1	0.7	0.3
	1120	73.0	81.2	14.9	1.5	0.3	1.3	0.8	59.3	10.9	1.1	0.2	0.9	0.6
	1121	53.8	80.1	16.1	1.4	0.2	1.8	0.4	43.0	8.7	0.8	0.1	0.9	0.2
	1122	90.8	71.8	24.3	1.6	0.2	1.6	0.5	65.2	22.0	1.5	0.2	1.5	0.4
	Mean	69.0	79.3	16.4	1.8	0.3	1.6	0.6	54.2	11.9	1.2	0.2	1.1	0.4
500	S.D.	19.2	4.4	4.7	0.4	0.1	0.2	0.2	13.0	6.3	0.5	0.1	0.4	0.2
	4118	54.2	70.2	25.3	1.4	0.2	2.2	0.7	38.0	13.7	0.8	0.1	1.2	0.4
	4119	56.3	84.2	12.2	0.6	0.4	1.7	0.8	47.5	6.9	0.4	0.2	1.0	0.4
	4120	52.4	81.4	16.0	0.7	0.2	1.2	0.5	42.7	8.4	0.4	0.1	0.6	0.3
	4121	36.1	79.3	17.7	1.2	0.2	1.0	0.6	28.6	6.4	0.4	0.1	0.4	0.2
	4122	67.4	69.5	24.6	3.2	0.1	2.2	0.5	46.8	16.5	2.2	0.1	1.5	0.3
	Mean	53.3	76.9	19.2	1.4	0.2	1.7	0.6	40.7	10.4	0.8	0.1	0.9	0.3
	S.D.	11.2	6.7	5.7	1.0	0.1	0.6	0.1	7.8	4.5	0.8	0.0	0.4	0.1

LUC: Large unstained cells

Appendix 7-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual blood chemistry of male rats (End of administration)

Dose mg/kg	Animal number	AST (GOT) IU/L	ALT (GPT) IU/L	LDH IU/L	γ -GTP IU/L	ALP IU/L	TBA μ mol/L	T.cho mg/dL	TG mg/dL	PL mg/dL	T.bili- rubin mg/dL	Glucose mg/dL
0	1001	64	33	46	1	428	5.7	47	27	76	0.1	105
	1002	65	34	51	1	309	8.7	45	45	77	0.1	155
	1003	72	32	35	1	451	7.3	52	28	84	0.1	133
	1004	60	28	34	1	354	4.2	44	49	75	0.1	145
	1005	63	27	45	0	273	8.1	70	33	105	0.1	128
	Mean	65	31	42	1	363	6.8	52	36	83	0.1	133
	S.D.	4	3	7	0	76	1.8	11	10	13	0.0	19
20	2001	62	25	50	1	441	9.0	45	48	89	0.1	126
	2002	68	53	70	1	291	13.5	51	23	82	0.1	152
	2003	74	31	59	1	416	9.8	41	37	75	0.1	116
	2004	68	27	47	1	458	15.9	46	11	70	0.1	142
	2005	69	27	66	1	328	10.4	62	50	98	0.1	137
	Mean	68	33	58	1	387	11.7	49	34	83	0.1	135
	S.D.	4	12	10	0	73	2.9	8	17	11	0.0	14
100	3001	63	25	54	0	439	9.2	64	63	103	0.1	134
	3002	56	28	42	1	420	9.8	47	27	77	0.1	123
	3003	55	25	36	0	339	4.0	40	39	67	0.0	173
	3004	61	27	45	1	429	6.4	40	17	67	0.1	129
	3005	72	35	51	1	279	25.8	50	19	79	0.1	136
	Mean	61	28	46	1	381	11.0	48	33	79	0.1	139
	S.D.	7	4	7	1	70	8.6	10	19	15	0.0	20
500	4001	54	25	47	1	343	6.6	63	37	94	0.1	117
	4002	70	27	56	1	386	10.6	52	19	81	0.1	126
	4003	50	20	43	1	405	3.5	36	22	60	0.1	125
	4004	55	21	40	1	306	3.2	44	31	75	0.1	156
	4005	63	25	48	1	372	4.0	55	57	91	0.1	119
	Mean	58	24	47	1	362	5.6	50	33	80	0.1	129
	S.D.	8	3	6	0	39	3.1	10	15	14	0.0	16

Appendix 7-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual blood chemistry of male rats (End of administration)

Dose mg/kg	Animal number	BUN mg/dL	Crea- tinine mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	Albumin g/dL	A/G
0	1001	15	0.27	142	4.5	103	9.1	6.0	5.4	2.8	1.08
	1002	16	0.24	143	4.4	107	9.8	5.7	5.5	3.0	1.20
	1003	17	0.25	146	4.3	109	8.9	5.1	5.5	3.1	1.29
	1004	15	0.29	144	4.8	108	9.3	5.8	5.6	2.9	1.07
	1005	15	0.26	143	4.0	106	9.4	5.5	5.6	3.1	1.24
	Mean	16	0.26	144	4.4	107	9.3	5.6	5.5	3.0	1.18
	S.D.	1	0.02	2	0.3	2	0.3	0.3	0.1	0.1	0.10
20	2001	14	0.28	143	4.4	105	9.3	5.3	5.3	3.0	1.30
	2002	18	0.25	143	4.6	105	9.2	5.8	5.5	2.9	1.12
	2003	13	0.25	146	4.7	111	8.9	5.9	5.4	3.0	1.25
	2004	15	0.23	144	4.6	106	9.6	5.8	5.8	3.1	1.15
	2005	13	0.25	145	4.1	107	9.9	6.1	5.9	3.3	1.27
	Mean	15	0.25	144	4.5	107	9.4	5.8	5.6	3.1	1.22
	S.D.	2	0.02	1	0.2	2	0.4	0.3	0.3	0.2	0.08
100	3001	14	0.26	143	4.4	105	9.5	5.7	5.9	3.1	1.11
	3002	14	0.27	144	4.6	106	9.3	6.0	5.9	3.1	1.11
	3003	20	0.26	143	4.7	105	9.3	6.1	5.5	2.8	1.04
	3004	17	0.23	145	4.6	108	9.5	6.1	5.8	3.1	1.15
	3005	19	0.24	142	4.6	107	9.7	6.7	5.7	3.0	1.11
	Mean	17	0.25	143	4.6	106	9.5	6.1	5.8	3.0	1.10
	S.D.	3	0.02	1	0.1	1	0.2	0.4	0.2	0.1	0.04
500	4001	15	0.23	144	4.6	104	9.6	5.8	5.6	3.0	1.15
	4002	14	0.22	143	4.9	103	9.4	5.8	5.4	2.9	1.16
	4003	19	0.26	143	4.7	105	10.1	5.9	6.1	3.2	1.10
	4004	18	0.24	144	4.6	105	9.7	6.1	5.7	3.1	1.19
	4005	21	0.32	145	4.8	106	9.6	6.2	6.0	3.2	1.14
	Mean	17	0.25	144	4.7	105	9.7	6.0	5.8	3.1	1.15
	S.D.	3	0.04	1	0.1	1	0.3	0.2	0.3	0.1	0.03

Appendix 7-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual blood chemistry of female rats (Lactation day 5)

Dose mg/kg	Animal number	AST (GOT) IU/L	ALT (GPT) IU/L	LDH IU/L	γ -GTP IU/L	ALP IU/L	TBA μ mol/L	T.cho mg/dL	TG mg/dL	PL mg/dL	T.bili- rubin mg/dL	Glucose mg/dL
0	1101	89	48	64	1	192	9.2	57	56	117	0.1	111
	1103	67	39	45	1	172	23.0	66	59	127	0.1	101
	1104	74	39	40	1	212	9.3	46	38	96	0.1	124
	1108	76	43	50	1	146	9.0	51	42	104	0.1	121
	1110	111	53	37	1	221	19.4	59	51	112	0.1	114
	Mean	83	44	47	1	189	14.0	56	49	111	0.1	114
	S.D.	17	6	11	0	30	6.7	8	9	12	0.0	9
20	2102	73	45	39	1	237	7.7	55	46	109	0.1	113
	2103	91	44	35	1	197	9.1	46	69	103	0.1	127
	2106	139	101	66	2	499	128.5	79	60	149	0.1	112
	2108	55	33	33	1	207	7.2	69	48	130	0.1	115
	2109a)	49Z	39Z	34Z	1Z	438Z	58.6Z	66Z	59Z	137Z	0.1Z	165Z
	2111	66	41	31	1	141	32.0	47	29	90	0.1	120
	Mean	85	53	41	1	256	36.9	59	50	116	0.1	117
100	S.D.	33	27	14	0	140	52.3	14	15	23	0.0	6
	3102	157	80	79	1	240	33.7	46	61	113	0.1	115
	3104	85	43	58	1	270	15.2	56	30	112	0.1	115
	3106	60	40	31	1	219	157.1	48	45	104	0.1	125
	3107	78	44	29	0	233	9.7	84	77	153	0.1	110
	3111b)	59Z	30Z	54Z	1Z	218Z	25.9Z	64Z	58Z	130Z	0.1Z	153Z
	3112	87	70	64	1	166	38.0	45	26	96	0.1	117
500	Mean	93	55	52	1	226	50.7	56	48	116	0.1	116
	S.D.	37	18	22	0	38	60.6	16	21	22	0.0	5
	4101	75	50	43	1	374	12.4	62	53	116	0.0	105
	4102	80	36	51	1	153	15.0	49	24	98	0.1	100
	4103	68	49	46	1	221	9.2	52	54	111	0.1	111
	4104	77	37	76	1	372	12.4	60	43	129	0.1	116
	4111	60	35	33	1	197	15.8	58	86	122	0.1	99
500	Mean	72	41	50	1	263	13.0	56	52	115	0.1	106
	S.D.	8	7	16	0	103	2.6	5	23	12	0.0	7

a): Non-pregnant

b): Not copulated

Z: Data was excluded from statistical analysis.

Appendix 7-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual blood chemistry of female rats (Lactation day 5)

Dose mg/kg	Animal number	BUN mg/dL	Crea- tinine mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	Albumin g/dL	A/G
0	1101	18	0.36	142	3.5	108	9.9	6.1	6.1	3.4	1.26
	1103	16	0.22	142	4.2	108	10.1	6.1	6.1	3.5	1.35
	1104	14	0.26	141	4.5	107	10.2	6.3	5.7	3.2	1.28
	1108	14	0.22	141	4.3	108	9.9	6.1	5.7	3.3	1.38
	1110	15	0.28	143	4.6	108	9.8	6.4	5.6	3.1	1.24
	Mean	15	0.27	142	4.2	108	10.0	6.2	5.8	3.3	1.30
	S.D.	2	0.06	1	0.4	0	0.2	0.1	0.2	0.2	0.06
20	2102	21	0.26	140	4.2	103	10.1	6.7	6.0	3.3	1.22
	2103	17	0.32	140	4.4	105	9.8	6.0	5.9	3.2	1.19
	2106	17	0.23	141	5.1	103	11.1	7.2	6.7	3.7	1.23
	2108	16	0.21	140	4.5	107	10.3	7.3	5.8	3.2	1.23
	2109a)	17Z	0.22Z	141Z	3.5Z	107Z	10.2Z	4.7Z	6.3Z	3.7Z	1.42Z
	2111	15	0.21	142	4.2	109	10.6	6.6	5.7	3.3	1.38
	Mean	17	0.25	141	4.5	105	10.4	6.8	6.0	3.3	1.25
	S.D.	2	0.05	1	0.4	3	0.5	0.5	0.4	0.2	0.07
100	3102	18	0.30	142	4.3	110	9.9	6.4	6.0	3.3	1.22
	3104	17	0.27	142	4.3	109	10.2	6.5	6.1	3.4	1.26
	3106	18	0.26	140	4.3	104	10.3	6.2	6.1	3.5	1.35
	3107	16	0.23	142	4.1	108	10.5	7.0	5.7	3.3	1.38
	3111b)	19Z	0.26Z	139Z	4.1Z	104Z	10.3Z	5.0Z	6.6Z	3.7Z	1.28Z
	3112	15	0.25	141	4.7	107	10.1	6.6	5.7	3.3	1.38
	Mean	17	0.26	141	4.3	108	10.2	6.5	5.9	3.4	1.32
	S.D.	1	0.03	1	0.2	2	0.2	0.3	0.2	0.1	0.07
500	4101	19	0.23	142	4.8	107	10.0	6.9	5.8	3.2	1.23
	4102	12	0.21	142	4.6	107	10.2	6.2	5.7	3.2	1.28
	4103	16	0.24	139	4.4	104	9.8	6.6	5.8	3.2	1.23
	4104	17	0.21	141	4.3	105	10.6	7.6	6.2	3.6	1.38
	4111	14	0.22	139	4.4	106	10.5	6.0	6.0	3.3	1.22
	Mean	16	0.22	141	4.5	106	10.2	6.7	5.9	3.3	1.27
	S.D.	3	0.01	2	0.2	1	0.3	0.6	0.2	0.2	0.07

a): Non-pregnant

b): Not copulated

Z: Data was excluded from statistical analysis.

Appendix 7-5

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual blood chemistry of female rats (Satellite group, End of administration)

Dose mg/kg	Animal number	AST (GOT) IU/L	ALT (GPT) IU/L	LDH IU/L	γ -GTP IU/L	ALP IU/L	TBA μ mol/L	T.cho mg/dL	TG mg/dL	PL mg/dL	T.bili- rubin mg/dL	Glucose mg/dL
0	1113	69	32	48	1	212	8.3	46	16	93	0.1	125
	1114	79	52	55	1	180	14.8	59	27	120	0.1	139
	1115	55	19	34	1	175	9.1	72	17	135	0.1	152
	1116	54	28	39	1	271	12.7	67	39	127	0.1	129
	1117	67	35	37	2	225	10.2	37	9	75	0.1	126
	Mean	65	33	43	1	213	11.0	56	22	110	0.1	134
	S.D.	10	12	9	0	39	2.7	15	12	25	0.0	11
500	4113	62	27	51	1	137	6.2	69	38	134	0.1	95
	4114	56	27	37	1	200	13.6	63	16	123	0.1	125
	4115	64	26	53	1	150	5.9	60	14	108	0.1	111
	4116	64	27	48	1	213	9.7	52	11	101	0.1	93
	4117	63	27	33	1	147	9.5	73	27	131	0.0	107
	Mean	62	27	44	1	169	9.0	63	21	119	0.1	106
	S.D.	3	0	9	0	35	3.1	8	11	14	0.0	13

Appendix 7-6

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual blood chemistry of female rats (Satellite group, End of administration)

Dose mg/kg	Animal number	BUN mg/dL	Crea- tinine mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	Albumin g/dL	A/G
0	1113	17	0.30	142	4.4	107	9.3	3.6	5.6	3.2	1.33
	1114	18	0.32	143	4.1	107	10.1	3.3	6.4	3.7	1.37
	1115	14	0.26	145	4.0	112	9.9	3.7	6.3	3.7	1.42
	1116	16	0.26	143	4.0	109	9.5	3.7	6.2	3.6	1.38
	1117	18	0.29	142	4.4	110	9.4	3.6	6.1	3.3	1.18
	Mean	17	0.29	143	4.2	109	9.6	3.6	6.1	3.5	1.34
	S.D.	2	0.03	1	0.2	2	0.3	0.2	0.3	0.2	0.09
500	4113	19	0.30	141	4.4	105	9.9	4.3	6.4	3.6	1.29
	4114	17	0.31	142	3.8	108	9.5	2.7	6.4	3.7	1.37
	4115	17	0.32	142	4.5	106	9.9	5.0	6.4	3.4	1.13
	4116	17	0.28	142	4.5	108	9.7	4.9	6.2	3.5	1.30
	4117	15	0.27	141	4.4	107	10.0	5.7	6.3	3.3	1.10
	Mean	17	0.30	142	4.3	107	9.8	4.5	6.3	3.5	1.24
	S.D.	1	0.02	1	0.3	1	0.2	1.1	0.1	0.2	0.12

Appendix 7-7

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual blood chemistry of male rats (End of recovery)

Dose mg/kg	Animal number	AST (GOT) IU/L	ALT (GPT) IU/L	LDH IU/L	γ -GTP IU/L	ALP IU/L	TBA μ mol/L	T.cho mg/dL	TG mg/dL	PL mg/dL	T.bili- rubin mg/dL	Glucose mg/dL
0	1008	61	28	47	1	334	12.0	57	51	96	0.1	118
	1009	75	36	49	1	365	8.4	46	30	76	0.1	110
	1010	55	34	37	1	313	8.1	60	57	101	0.1	120
	1011	61	33	43	1	324	22.3	45	13	73	0.1	131
	1012	61	29	47	1	339	49.5	43	11	71	0.1	131
	Mean	63	32	45	1	335	20.1	50	32	83	0.1	122
	S.D.	7	3	5	0	20	17.4	8	21	14	0.0	9
500	4008	57	26	50	1	327	8.5	64	38	103	0.1	133
	4009	68	35	52	1	352	17.7	44	32	79	0.1	119
	4010	51	54	36	1	283	14.9	47	32	80	0.1	128
	4011	75	41	67	1	380	10.8	48	62	93	0.1	156
	4012	60	31	42	1	379	29.4	50	28	86	0.1	120
	Mean	62	37	49	1	344	16.3	51	38	88	0.1	131
	S.D.	9	11	12	0	41	8.2	8	14	10	0.0	15

Appendix 7-8

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual blood chemistry of male rats (End of recovery)

Dose mg/kg	Animal number	BUN mg/dL	Crea- tinine mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	Albumin g/dL	A/G
0	1008	14	0.23	140	4.2	101	9.3	6.6	5.7	3.0	1.11
	1009	17	0.25	142	4.4	107	9.4	6.1	5.7	2.9	1.04
	1010	14	0.17	143	4.2	107	9.6	6.0	5.8	3.0	1.07
	1011	16	0.25	143	4.4	107	9.4	5.2	5.6	3.0	1.15
	1012	19	0.23	143	4.6	106	9.3	5.1	5.9	3.1	1.11
	Mean	16	0.23	142	4.4	106	9.4	5.8	5.7	3.0	1.10
	S.D.	2	0.03	1	0.2	3	0.1	0.6	0.1	0.1	0.04
500	4008	13	0.20	143	4.5	104	9.3	6.4	5.5	3.0	1.20
	4009	17	0.24	143	4.7	106	9.4	5.8	5.9	3.0	1.03
	4010	15	0.22	144	4.7	105	9.5	6.2	6.1	3.1	1.03
	4011	14	0.22	144	4.3	107	9.6	5.0	5.8	3.1	1.15
	4012	17	0.25	144	4.5	108	9.3	5.7	5.5	3.1	1.29
	Mean	15	0.23	144	4.5	106	9.4	5.8	5.8	3.1	1.14
	S.D.	2	0.02	1	0.2	2	0.1	0.5	0.3	0.1	0.11

Appendix 7-9

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual blood chemistry of female rats (End of recovery)

Dose mg/kg	Animal number	AST (GOT) IU/L	ALT (GPT) IU/L	LDH IU/L	γ -GTP IU/L	ALP IU/L	TBA μ mol/L	T.cho mg/dL	TG mg/dL	PL mg/dL	T.bili- rubin mg/dL	Glucose mg/dL
0	1118	61	26	35	2	201	13.8	45	11	85	0.1	109
	1119	69	28	34	2	216	7.7	71	15	131	0.1	131
	1120	62	26	41	1	229	5.0	57	11	102	0.1	133
	1121	64	30	36	1	97	8.0	52	15	96	0.1	108
	1122	62	24	57	1	128	10.5	49	13	106	0.1	125
	Mean	64	27	41	1	174	9.0	55	13	104	0.1	121
	S.D.	3	2	10	1	58	3.3	10	2	17	0.0	12
500	4118	60	26	29	1	143	8.7	73	14	137	0.1	122
	4119	68	25	33	1	225	24.6	84	35	166	0.1	135
	4120	54	33	38	2	226	5.1	72	12	125	0.1	137
	4121	63	37	39	2	195	8.1	78	15	136	0.1	148
	4122	66	22	39	1	206	8.1	61	15	120	0.1	111
	Mean	62	29	36	1	199	10.9	74	18	137	0.1	131
	S.D.	5	6	4	1	34	7.8	9	9	18	0.0	14

Appendix 7-10

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual blood chemistry of female rats (End of recovery)

Dose mg/kg	Animal number	BUN mg/dL	Crea- tinine mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	Albumin g/dL	A/G
0	1118	15	0.31	142	4.4	107	9.4	4.2	5.8	3.3	1.32
	1119	17	0.34	144	3.6	108	9.8	3.8	6.2	3.5	1.30
	1120	20	0.23	142	4.7	109	9.9	5.0	5.8	3.4	1.42
	1121	18	0.33	144	3.9	111	10.2	5.0	6.0	3.7	1.61
	1122	23	0.37	142	4.3	109	9.7	5.1	6.2	3.6	1.38
	Mean	19	0.32	143	4.2	109	9.8	4.6	6.0	3.5	1.41
	S.D.	3	0.05	1	0.4	1	0.3	0.6	0.2	0.2	0.12
500	4118	17	0.27	141	4.3	109	9.8	3.9	6.5	3.6	1.24
	4119	16	0.32	141	3.9	108	9.4	3.7	6.1	3.6	1.44
	4120	13	0.25	143	4.1	109	10.3	5.1	6.7	3.9	1.39
	4121	17	0.36	142	3.9	107	9.9	4.5	6.5	3.6	1.24
	4122	17	0.29	142	4.7	107	9.8	5.9	5.6	3.0	1.15
	Mean	16	0.30	142	4.2	108	9.8	4.6	6.3	3.5	1.29
	S.D.	2	0.04	1	0.3	1	0.3	0.9	0.4	0.3	0.12

Appendix 8-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of male rats (End of administration)

Dose (mg/kg): 0

	Animal number	Body weight g	Brain	Pituitary	Thyroid (R)	Thyroid (L)	Thyroid (R+L)	Thymus	Heart
			g(g/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	g(g/100g BW)
Absolute	1001	503	2.15	13.6	12.8	13.8	26.6	295	1.67
	1002	454	1.97	13.5	12.5	11.2	23.7	319	1.43
	1003	384	2.05	9.6	8.5	10.0	18.5	225	1.23
	1004	516	2.17	14.4	10.5	8.7	19.2	205	1.61
	1005	473	2.08	14.3	12.7	11.1	23.8	210	1.63
	1006	478	2.07	12.3	14.5	14.8	29.3	503	1.40
	1007	527	2.03	12.8	8.4	14.0	22.4	511	1.51
	Mean	476	2.07	12.9	11.4	11.9	23.4	324	1.50
Relative	S.D.	48	0.07	1.6	2.3	2.3	3.8	132	0.16
	1001		0.43	2.7	2.5	2.7	5.3	59	0.33
	1002		0.43	3.0	2.8	2.5	5.2	70	0.31
	1003		0.53	2.5	2.2	2.6	4.8	59	0.32
	1004		0.42	2.8	2.0	1.7	3.7	40	0.31
	1005		0.44	3.0	2.7	2.3	5.0	44	0.34
	1006		0.43	2.6	3.0	3.1	6.1	105	0.29
	1007		0.39	2.4	1.6	2.7	4.3	97	0.29
	Mean		0.44	2.7	2.4	2.5	4.9	68	0.31
	S.D.		0.04	0.2	0.5	0.4	0.8	25	0.02

Appendix 8-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of male rats (End of administration)

Dose (mg/kg): 0

	Animal number	Liver	Spleen	Kidney (R)	Kidney (L)	Kidney (R+L)	Adrenal (R)	Adrenal (L)	Adrenal (R+L)
		g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)
Absolute	1001	12.31	0.91	1.69	1.80	3.49	31	35	66
	1002	12.66	0.71	1.54	1.53	3.07	38	37	75
	1003	9.27	0.67	1.47	1.31	2.78	21	21	42
	1004	13.44	0.57	1.65	1.67	3.32	19	21	40
	1005	11.57	0.88	1.43	1.38	2.81	34	38	72
	1006	12.59	0.78	1.71	1.74	3.45	34	38	72
	1007	14.82	0.92	1.88	1.89	3.77	31	30	61
	Mean	12.38	0.78	1.62	1.62	3.24	30	31	61
Relative	S.D.	1.71	0.13	0.16	0.22	0.37	7	8	15
	1001	2.45	0.18	0.34	0.36	0.69	6	7	13
	1002	2.79	0.16	0.34	0.34	0.68	8	8	17
	1003	2.41	0.17	0.38	0.34	0.72	5	5	11
	1004	2.60	0.11	0.32	0.32	0.64	4	4	8
	1005	2.45	0.19	0.30	0.29	0.59	7	8	15
	1006	2.63	0.16	0.36	0.36	0.72	7	8	15
	1007	2.81	0.17	0.36	0.36	0.72	6	6	12
	Mean	2.59	0.16	0.34	0.34	0.68	6	7	13
	S.D.	0.16	0.03	0.03	0.03	0.05	1	2	3

Appendix 8-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of male rats (End of administration)

Dose (mg/kg): 0

	Animal number	Seminal vesicle g(g/100g BW)	Prostate g(g/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)
Absolute	1001	2.11	1.29	1.73	1.69	3.42	749	921	1670
	1002	1.82	1.43	1.25	1.26	2.51	596	558	1154
	1003	1.90	1.42	1.73	1.70	3.43	708	681	1389
	1004	1.67	1.25	1.52	1.40	2.92	590	603	1193
	1005	1.53	1.33	1.55	1.54	3.09	607	600	1207
	1006	1.72	1.06	1.65	1.64	3.29	764	648	1412
	1007	1.76	1.19	1.55	1.53	3.08	677	630	1307
	Mean	1.79	1.28	1.57	1.54	3.11	670	663	1333
Relative	S.D.	0.18	0.13	0.16	0.16	0.32	74	120	178
	1001	0.42	0.26	0.34	0.34	0.68	149	183	332
	1002	0.40	0.31	0.28	0.28	0.55	131	123	254
	1003	0.49	0.37	0.45	0.44	0.89	184	177	362
	1004	0.32	0.24	0.29	0.27	0.57	114	117	231
	1005	0.32	0.28	0.33	0.33	0.65	128	127	255
	1006	0.36	0.22	0.35	0.34	0.69	160	136	295
	1007	0.33	0.23	0.29	0.29	0.58	128	120	248
	Mean	0.38	0.27	0.33	0.33	0.66	142	140	282
	S.D.	0.06	0.05	0.06	0.06	0.12	24	28	49

Appendix 8-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of male rats (End of administration)

Dose (mg/kg): 20

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)
Absolute	2001	467	2.07	12.1	12.9	10.1	23.0	274	1.33
	2002	533	2.19	14.7	13.0	12.9	25.9	297	1.42
	2003	474	2.17	12.3	11.8	7.6	19.4	235	1.20
	2004	541	2.21	14.0	13.6	12.7	26.3	335	1.39
	2005	519	2.06	14.8	12.6	14.4	27.0	301	1.69
	2006	478	2.17	12.2	12.0	11.5	23.5	254	1.30
	2007	424	2.05	13.4	7.5	8.7	16.2	308	1.36
	2008	490	2.24	11.9	10.9	15.1	26.0	371	1.32
	2009	425	2.08	11.7	8.2	11.0	19.2	255	1.42
	2010	470	2.21	13.6	13.1	13.4	26.5	301	1.72
	2011	468	2.10	12.9	7.7	11.7	19.4	249	1.57
	2012	441	2.16	13.5	13.1	10.8	23.9	279	1.54
	Mean	478	2.14	13.1	11.4	11.7	23.0	288	1.44
	S.D.	38	0.07	1.1	2.3	2.2	3.6	39	0.16
Relative	2001		0.44	2.6	2.8	2.2	4.9	59	0.28
	2002		0.41	2.8	2.4	2.4	4.9	56	0.27
	2003		0.46	2.6	2.5	1.6	4.1	50	0.25
	2004		0.41	2.6	2.5	2.3	4.9	62	0.26
	2005		0.40	2.9	2.4	2.8	5.2	58	0.33
	2006		0.45	2.6	2.5	2.4	4.9	53	0.27
	2007		0.48	3.2	1.8	2.1	3.8	73	0.32
	2008		0.46	2.4	2.2	3.1	5.3	76	0.27
	2009		0.49	2.8	1.9	2.6	4.5	60	0.33
	2010		0.47	2.9	2.8	2.9	5.6	64	0.37
	2011		0.45	2.8	1.6	2.5	4.1	53	0.34
	2012		0.49	3.1	3.0	2.4	5.4	63	0.35
	Mean		0.45	2.8	2.4	2.4	4.8	61	0.30
	S.D.		0.03	0.2	0.4	0.4	0.6	8	0.04

Appendix 8-5

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of male rats (End of administration)

Dose (mg/kg): 20

	Animal number	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)
Absolute	2001	11.85	0.73	1.50	1.46	2.96	27	31	58
	2002	14.88	0.88	1.96	1.92	3.88	34	36	70
	2003	10.83	0.81	1.56	1.60	3.16	20	22	42
	2004	13.95	0.88	1.86	1.73	3.59	30	33	63
	2005	13.93	1.08	1.77	1.71	3.48	28	29	57
	2006	11.66	0.62	1.53	1.49	3.02	24	28	52
	2007	10.04	0.66	1.54	1.46	3.00	31	32	63
	2008	12.33	0.74	1.78	1.77	3.55	30	33	63
	2009	10.40	0.66	1.51	1.54	3.05	37	41	78
	2010	10.76	0.76	1.53	1.50	3.03	40	40	80
	2011	12.98	0.73	1.73	1.66	3.39	30	34	64
	2012	10.04	0.63	1.56	1.56	3.12	29	31	60
	Mean	11.97	0.77	1.65	1.62	3.27	30	33	63
	S.D.	1.66	0.13	0.16	0.14	0.30	5	5	10
Relative	2001	2.54	0.16	0.32	0.31	0.63	6	7	12
	2002	2.79	0.17	0.37	0.36	0.73	6	7	13
	2003	2.28	0.17	0.33	0.34	0.67	4	5	9
	2004	2.58	0.16	0.34	0.32	0.66	6	6	12
	2005	2.68	0.21	0.34	0.33	0.67	5	6	11
	2006	2.44	0.13	0.32	0.31	0.63	5	6	11
	2007	2.37	0.16	0.36	0.34	0.71	7	8	15
	2008	2.52	0.15	0.36	0.36	0.72	6	7	13
	2009	2.45	0.16	0.36	0.36	0.72	9	10	18
	2010	2.29	0.16	0.33	0.32	0.64	9	9	17
	2011	2.77	0.16	0.37	0.35	0.72	6	7	14
	2012	2.28	0.14	0.35	0.35	0.71	7	7	14
	Mean	2.50	0.16	0.35	0.34	0.68	6	7	13
	S.D.	0.18	0.02	0.02	0.02	0.04	1	1	3

Appendix 8-6

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of male rats (End of administration)

Dose (mg/kg): 20

	Animal number	Seminal vesicle g(g/100g BW)	Prostate g(g/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)
Absolute	2001	2.13	1.33	1.73	1.64	3.37	670	609	1279
	2002	2.47	1.26	1.85	1.84	3.69	669	616	1285
	2003	1.76	0.91	1.58	1.59	3.17	706	659	1365
	2004	2.06	1.48	1.68	1.67	3.35	668	634	1302
	2005	1.56	0.99	1.60	1.63	3.23	662	641	1303
	2006	1.83	1.58	1.54	1.54	3.08	622	596	1218
	2007	1.52	1.26	1.84	1.79	3.63	768	735	1503
	2008	1.41	1.32	1.71	1.68	3.39	629	638	1267
	2009	1.40	1.03	1.51	1.45	2.96	553	501	1054
	2010	1.65	1.24	1.81	1.78	3.59	705	692	1397
	2011	1.84	1.36	1.47	1.42	2.89	633	621	1254
	2012	1.69	1.34	1.52	1.52	3.04	556	574	1130
	Mean	1.78	1.26	1.65	1.63	3.28	653	626	1280
	S.D.	0.32	0.20	0.14	0.13	0.27	61	58	117
Relative	2001	0.46	0.28	0.37	0.35	0.72	143	130	274
	2002	0.46	0.24	0.35	0.35	0.69	126	116	241
	2003	0.37	0.19	0.33	0.34	0.67	149	139	288
	2004	0.38	0.27	0.31	0.31	0.62	123	117	241
	2005	0.30	0.19	0.31	0.31	0.62	128	124	251
	2006	0.38	0.33	0.32	0.32	0.64	130	125	255
	2007	0.36	0.30	0.43	0.42	0.86	181	173	354
	2008	0.29	0.27	0.35	0.34	0.69	128	130	259
	2009	0.33	0.24	0.36	0.34	0.70	130	118	248
	2010	0.35	0.26	0.39	0.38	0.76	150	147	297
	2011	0.39	0.29	0.31	0.30	0.62	135	133	268
	2012	0.38	0.30	0.34	0.34	0.69	126	130	256
	Mean	0.37	0.26	0.35	0.34	0.69	137	132	269
	S.D.	0.05	0.04	0.04	0.03	0.07	16	16	32

Appendix 8-7

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of male rats (End of administration)

Dose (mg/kg): 100

	Animal number	Body weight g	Brain	Pituitary	Thyroid (R)	Thyroid (L)	Thyroid (R+L)	Thymus	Heart
			g(g/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	g(g/100g BW)
Absolute	3001	450	2.08	13.4	9.7	9.2	18.9	300	1.27
	3002	489	2.18	12.7	11.7	13.9	25.6	288	1.33
	3003	453	2.12	10.5	7.1	7.1	14.2	227	1.20
	3004	437	1.99	11.6	11.3	12.1	23.4	296	1.28
	3005	481	2.12	15.0	14.9	12.2	27.1	276	1.44
	3006	462	2.11	11.9	12.9	10.7	23.6	282	1.30
	3007	512	2.17	13.4	7.8	10.5	18.3	207	1.39
	3008	486	2.02	11.7	10.7	11.7	22.4	324	1.30
	3009	487	2.05	12.9	11.4	8.5	19.9	249	1.35
	3010	433	2.11	10.6	14.3	9.3	23.6	351	1.30
	3011	443	2.07	13.0	10.0	7.4	17.4	351	1.29
	3012	455	2.08	11.3	13.8	12.3	26.1	265	1.32
	Mean	466	2.09	12.3	11.3	10.4	21.7	285	1.31
	S.D.	25	0.06	1.3	2.4	2.1	4.0	45	0.06
Relative	3001		0.46	3.0	2.2	2.0	4.2	67	0.28
	3002		0.45	2.6	2.4	2.8	5.2	59	0.27
	3003		0.47	2.3	1.6	1.6	3.1	50	0.26
	3004		0.46	2.7	2.6	2.8	5.4	68	0.29
	3005		0.44	3.1	3.1	2.5	5.6	57	0.30
	3006		0.46	2.6	2.8	2.3	5.1	61	0.28
	3007		0.42	2.6	1.5	2.1	3.6	40	0.27
	3008		0.42	2.4	2.2	2.4	4.6	67	0.27
	3009		0.42	2.6	2.3	1.7	4.1	51	0.28
	3010		0.49	2.4	3.3	2.1	5.5	81	0.30
	3011		0.47	2.9	2.3	1.7	3.9	79	0.29
	3012		0.46	2.5	3.0	2.7	5.7	58	0.29
	Mean		0.45	2.6	2.4	2.2	4.7	62	0.28
	S.D.		0.02	0.2	0.6	0.4	0.9	12	0.01

Appendix 8-8

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of male rats (End of administration)

Dose (mg/kg): 100

	Animal number	Liver	Spleen	Kidney (R)	Kidney (L)	Kidney (R+L)	Adrenal (R)	Adrenal (L)	Adrenal (R+L)
		g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)
Absolute	3001	12.23	0.80	1.87	1.75	3.62	26	27	53
	3002	13.19	0.77	2.04	1.96	4.00	33	34	67
	3003	13.05	0.94	1.76	1.66	3.42	22	25	47
	3004	11.88	0.65	1.64	1.59	3.23	29	31	60
	3005	12.96	0.99	1.71	1.60	3.31	44	49	93
	3006	11.27	0.60	1.77	1.71	3.48	28	28	56
	3007	15.46	0.87	2.09	2.06	4.15	29	30	59
	3008	13.11	0.74	1.61	1.61	3.22	32	36	68
	3009	12.95	0.67	2.09	2.01	4.10	36	38	74
	3010	10.73	0.83	1.54	1.59	3.13	25	27	52
	3011	12.08	0.76	2.04	2.02	4.06	34	40	74
	3012	12.13	0.66	1.70	1.69	3.39	33	35	68
	Mean	12.59	0.77	1.82	1.77	3.59	31	33	64
	S.D.	1.19	0.12	0.20	0.19	0.38	6	7	13
Relative	3001	2.72	0.18	0.42	0.39	0.80	6	6	12
	3002	2.70	0.16	0.42	0.40	0.82	7	7	14
	3003	2.88	0.21	0.39	0.37	0.75	5	6	10
	3004	2.72	0.15	0.38	0.36	0.74	7	7	14
	3005	2.69	0.21	0.36	0.33	0.69	9	10	19
	3006	2.44	0.13	0.38	0.37	0.75	6	6	12
	3007	3.02	0.17	0.41	0.40	0.81	6	6	12
	3008	2.70	0.15	0.33	0.33	0.66	7	7	14
	3009	2.66	0.14	0.43	0.41	0.84	7	8	15
	3010	2.48	0.19	0.36	0.37	0.72	6	6	12
	3011	2.73	0.17	0.46	0.46	0.92	8	9	17
	3012	2.67	0.15	0.37	0.37	0.75	7	8	15
	Mean	2.70	0.17	0.39	0.38	0.77	7	7	14
	S.D.	0.15	0.03	0.04	0.04	0.07	1	1	2

Appendix 8-9

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of male rats (End of administration)

Dose (mg/kg): 100

	Animal number	Seminal vesicle g(g/100g BW)	Prostate g(g/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)
Absolute	3001	1.78	1.48	1.66	1.70	3.36	655	669	1324
	3002	1.99	1.38	1.56	1.57	3.13	684	646	1330
	3003	1.44	1.19	1.63	1.65	3.28	605	638	1243
	3004	1.68	1.25	1.66	1.61	3.27	635	580	1215
	3005	1.97	1.53	1.51	1.50	3.01	660	659	1319
	3006	1.68	1.44	1.73	1.69	3.42	637	646	1283
	3007	2.01	1.38	1.71	1.63	3.34	621	677	1298
	3008	1.59	1.64	1.69	1.62	3.31	668	624	1292
	3009	1.76	1.27	1.68	1.60	3.28	661	630	1291
	3010	1.93	1.18	1.89	1.89	3.78	686	708	1394
	3011	1.61	0.97	1.76	1.73	3.49	689	677	1366
	3012	2.17	1.47	1.58	1.60	3.18	672	701	1373
	Mean	1.80	1.35	1.67	1.65	3.32	656	655	1311
	S.D.	0.21	0.18	0.10	0.10	0.19	27	35	52
Relative	3001	0.40	0.33	0.37	0.38	0.75	146	149	294
	3002	0.41	0.28	0.32	0.32	0.64	140	132	272
	3003	0.32	0.26	0.36	0.36	0.72	134	141	274
	3004	0.38	0.29	0.38	0.37	0.75	145	133	278
	3005	0.41	0.32	0.31	0.31	0.63	137	137	274
	3006	0.36	0.31	0.37	0.37	0.74	138	140	278
	3007	0.39	0.27	0.33	0.32	0.65	121	132	254
	3008	0.33	0.34	0.35	0.33	0.68	137	128	266
	3009	0.36	0.26	0.34	0.33	0.67	136	129	265
	3010	0.45	0.27	0.44	0.44	0.87	158	164	322
	3011	0.36	0.22	0.40	0.39	0.79	156	153	308
	3012	0.48	0.32	0.35	0.35	0.70	148	154	302
	Mean	0.39	0.29	0.36	0.36	0.72	141	141	282
	S.D.	0.05	0.04	0.04	0.04	0.07	10	12	20

Appendix 8-10

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of male rats (End of administration)

Dose (mg/kg): 500

	Animal number	Body weight g	Brain	Pituitary	Thyroid (R)	Thyroid (L)	Thyroid (R+L)	Thymus	Heart
			g(g/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	g(g/100g BW)
Absolute	4001	486	2.12	12.8	10.8	11.6	22.4	257	1.45
	4002	473	2.12	14.4	9.6	9.3	18.9	261	1.30
	4003	479	2.02	13.4	11.4	15.9	27.3	308	1.34
	4004	487	2.04	12.3	10.2	13.3	23.5	378	1.57
	4005	404	2.07	10.6	8.1	7.6	15.7	174	1.23
	4006	491	2.08	12.6	10.0	11.4	21.4	248	1.49
	4007	513	2.04	12.8	13.8	13.7	27.5	254	1.49
	Mean	476	2.07	12.7	10.6	11.8	22.4	269	1.41
Relative	S.D.	34	0.04	1.2	1.8	2.8	4.3	62	0.12
	4001		0.44	2.6	2.2	2.4	4.6	53	0.30
	4002		0.45	3.0	2.0	2.0	4.0	55	0.27
	4003		0.42	2.8	2.4	3.3	5.7	64	0.28
	4004		0.42	2.5	2.1	2.7	4.8	78	0.32
	4005		0.51	2.6	2.0	1.9	3.9	43	0.30
	4006		0.42	2.6	2.0	2.3	4.4	51	0.30
	4007		0.40	2.5	2.7	2.7	5.4	50	0.29
	Mean		0.44	2.7	2.2	2.5	4.7	56	0.29
	S.D.		0.04	0.2	0.3	0.5	0.7	11	0.02

Appendix 8-11

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of male rats (End of administration)

Dose (mg/kg): 500

	Animal number	Liver	Spleen	Kidney (R)	Kidney (L)	Kidney (R+L)	Adrenal (R)	Adrenal (L)	Adrenal (R+L)
		g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)
Absolute	4001	14.04	0.79	1.85	1.78	3.63	36	39	75
	4002	13.69	0.69	1.98	1.97	3.95	32	32	64
	4003	13.60	0.90	2.04	1.92	3.96	40	40	80
	4004	15.94	0.74	1.90	2.12	4.02	38	39	77
	4005	12.01	0.54	1.65	1.52	3.17	29	27	56
	4006	15.45	0.83	1.80	1.71	3.51	31	37	68
	4007	14.51	0.80	2.20	2.02	4.22	28	33	61
	Mean	14.18	0.76	1.92	1.86	3.78	33	35	69
Relative	S.D.	1.30	0.12	0.18	0.21	0.36	5	5	9
	4001	2.89	0.16	0.38	0.37	0.75	7	8	15
	4002	2.89	0.15	0.42	0.42	0.84	7	7	14
	4003	2.84	0.19	0.43	0.40	0.83	8	8	17
	4004	3.27	0.15	0.39	0.44	0.83	8	8	16
	4005	2.97	0.13	0.41	0.38	0.78	7	7	14
	4006	3.15	0.17	0.37	0.35	0.71	6	8	14
	4007	2.83	0.16	0.43	0.39	0.82	5	6	12
	Mean	2.98	0.16	0.40	0.39	0.79	7	7	15
	S.D.	0.17	0.02	0.02	0.03	0.05	1	1	2

Appendix 8-12

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of male rats (End of administration)

Dose (mg/kg): 500

	Animal number	Seminal vesicle g(g/100g BW)	Prostate g(g/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)
Absolute	4001	2.32	1.50	1.62	1.59	3.21	684	642	1326
	4002	2.15	1.54	1.57	1.55	3.12	675	663	1338
	4003	1.55	1.31	1.61	1.57	3.18	684	668	1352
	4004	1.67	1.13	1.42	1.40	2.82	663	645	1308
	4005	2.12	1.31	1.68	1.67	3.35	629	607	1236
	4006	1.64	1.40	1.72	1.71	3.43	737	739	1476
	4007	1.90	1.23	1.44	1.46	2.90	630	634	1264
	Mean	1.91	1.35	1.58	1.56	3.14	672	657	1329
Relative	S.D.	0.30	0.15	0.11	0.11	0.22	37	41	77
	4001	0.48	0.31	0.33	0.33	0.66	141	132	273
	4002	0.45	0.33	0.33	0.33	0.66	143	140	283
	4003	0.32	0.27	0.34	0.33	0.66	143	139	282
	4004	0.34	0.23	0.29	0.29	0.58	136	132	269
	4005	0.52	0.32	0.42	0.41	0.83	156	150	306
	4006	0.33	0.29	0.35	0.35	0.70	150	151	301
	4007	0.37	0.24	0.28	0.28	0.57	123	124	246
	Mean	0.40	0.28	0.33	0.33	0.67	142	138	280
	S.D.	0.08	0.04	0.05	0.04	0.09	10	10	20

Appendix 8-13

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of female rats (Lactation day 5)

Dose (mg/kg): 0

	Animal number	Body weight g	Brain	Pituitary	Thyroid (R)	Thyroid (L)	Thyroid (R+L)	Thymus	Heart
			g(g/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	g(g/100g BW)
Absolute	1101	317	2.01	18.3	7.5	7.6	15.1	219	0.98
	1102	284	1.98	12.3	7.6	5.9	13.5	345	0.94
	1103	320	1.99	17.9	9.9	7.3	17.2	271	1.04
	1104	284	1.90	18.6	9.0	9.6	18.6	125	0.96
	1105	278	1.99	15.9	7.4	7.8	15.2	157	1.07
	1106	304	2.11	18.4	11.3	6.8	18.1	320	1.04
	1107	297	2.09	16.0	9.3	8.1	17.4	154	1.02
	1108	286	1.91	18.8	7.6	7.8	15.4	217	1.03
	1109	323	2.02	16.0	6.4	7.1	13.5	204	1.03
	1110	349	1.83	22.1	10.0	7.4	17.4	192	1.08
	1111	305	1.90	18.8	10.8	9.0	19.8	276	1.01
	1112	292	1.95	16.5	7.4	8.9	16.3	171	1.14
	Mean	303	1.97	17.5	8.7	7.8	16.5	221	1.03
	S.D.	21	0.08	2.4	1.6	1.0	2.0	69	0.05
Relative	1101		0.63	5.8	2.4	2.4	4.8	69	0.31
	1102		0.70	4.3	2.7	2.1	4.8	121	0.33
	1103		0.62	5.6	3.1	2.3	5.4	85	0.33
	1104		0.67	6.5	3.2	3.4	6.5	44	0.34
	1105		0.72	5.7	2.7	2.8	5.5	56	0.38
	1106		0.69	6.1	3.7	2.2	6.0	105	0.34
	1107		0.70	5.4	3.1	2.7	5.9	52	0.34
	1108		0.67	6.6	2.7	2.7	5.4	76	0.36
	1109		0.63	5.0	2.0	2.2	4.2	63	0.32
	1110		0.52	6.3	2.9	2.1	5.0	55	0.31
	1111		0.62	6.2	3.5	3.0	6.5	90	0.33
	1112		0.67	5.7	2.5	3.0	5.6	59	0.39
	Mean		0.65	5.8	2.9	2.6	5.5	73	0.34
	S.D.		0.05	0.7	0.5	0.4	0.7	23	0.03

Appendix 8-14

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of female rats (Lactation day 5)

Dose (mg/kg): 0

	Animal number	Liver	Spleen	Kidney (R)	Kidney (L)	Kidney (R+L)	Adrenal (R)	Adrenal (L)	Adrenal (R+L)
		g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)
Absolute	1101	10.02	0.58	0.93	0.94	1.87	32	34	66
	1102	8.66	0.55	1.07	1.00	2.07	38	39	77
	1103	10.21	0.69	1.03	1.05	2.08	40	45	85
	1104	8.92	0.64	0.99	0.97	1.96	40	48	88
	1105	9.17	0.72	0.97	1.03	2.00	42	48	90
	1106	10.32	0.71	1.01	0.99	2.00	33	35	68
	1107	10.51	0.67	1.31	1.22	2.53	42	47	89
	1108	9.33	0.75	1.16	1.14	2.30	40	37	77
	1109	9.05	0.71	1.13	1.06	2.19	33	40	73
	1110	11.24	0.67	1.13	1.17	2.30	44	51	95
	1111	9.59	0.63	1.14	1.11	2.25	31	33	64
	1112	9.15	0.71	1.07	1.08	2.15	33	37	70
	Mean	9.68	0.67	1.08	1.06	2.14	37	41	79
	S.D.	0.78	0.06	0.10	0.08	0.18	5	6	11
Relative	1101	3.16	0.18	0.29	0.30	0.59	10	11	21
	1102	3.05	0.19	0.38	0.35	0.73	13	14	27
	1103	3.19	0.22	0.32	0.33	0.65	13	14	27
	1104	3.14	0.23	0.35	0.34	0.69	14	17	31
	1105	3.30	0.26	0.35	0.37	0.72	15	17	32
	1106	3.39	0.23	0.33	0.33	0.66	11	12	22
	1107	3.54	0.23	0.44	0.41	0.85	14	16	30
	1108	3.26	0.26	0.41	0.40	0.80	14	13	27
	1109	2.80	0.22	0.35	0.33	0.68	10	12	23
	1110	3.22	0.19	0.32	0.34	0.66	13	15	27
	1111	3.14	0.21	0.37	0.36	0.74	10	11	21
	1112	3.13	0.24	0.37	0.37	0.74	11	13	24
	Mean	3.19	0.22	0.36	0.35	0.71	12	14	26
	S.D.	0.18	0.03	0.04	0.03	0.07	2	2	4

Appendix 8-15

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of female rats (Lactation day 5)

Dose (mg/kg): 0

	Animal number	Ovary (R)	Ovary (L)	Ovary (R+L)	Uterus
		mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)
Absolute	1101	50.6	52.5	103.1	703
	1102	52.8	47.5	100.3	640
	1103	50.7	60.0	110.7	710
	1104	54.7	54.7	109.4	792
	1105	58.7	49.8	108.5	599
	1106	52.5	46.3	98.8	631
	1107	56.8	61.8	118.6	793
	1108	55.6	46.9	102.5	841
	1109	47.6	42.0	89.6	745
	1110	66.4	56.9	123.3	731
	1111	52.7	44.8	97.5	854
	1112	65.7	68.8	134.5	950
Mean		55.4	52.7	108.1	749
S.D.		5.8	8.0	12.5	103
Relative	1101	16.0	16.6	32.5	222
	1102	18.6	16.7	35.3	225
	1103	15.8	18.8	34.6	222
	1104	19.3	19.3	38.5	279
	1105	21.1	17.9	39.0	215
	1106	17.3	15.2	32.5	208
	1107	19.1	20.8	39.9	267
	1108	19.4	16.4	35.8	294
	1109	14.7	13.0	27.7	231
	1110	19.0	16.3	35.3	209
	1111	17.3	14.7	32.0	280
	1112	22.5	23.6	46.1	325
Mean		18.3	17.4	35.8	248
S.D.		2.2	2.9	4.7	39

Appendix 8-16

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of female rats (Lactation day 5)

Dose (mg/kg): 20

	Animal number	Body weight g	Brain	Pituitary	Thyroid (R)	Thyroid (L)	Thyroid (R+L)	Thymus	Heart
			g(g/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	g(g/100g BW)
Absolute	2101	283	1.87	18.1	7.1	6.9	14.0	209	1.11
	2102	298	1.85	21.3	9.6	7.6	17.2	183	1.11
	2103	293	1.97	14.0	7.4	6.3	13.7	228	1.09
	2104	288	1.97	20.8	6.9	7.4	14.3	385	0.92
	2105	279	1.92	14.8	6.9	8.3	15.2	267	0.92
	2106	319	1.94	17.4	8.6	9.9	18.5	220	1.05
	2107	305	1.93	21.1	9.9	9.8	19.7	114	0.98
	2108	306	1.90	15.9	6.8	5.4	12.2	238	0.98
	2109a)	311Z	1.90Z	18.7Z	7.7Z	6.5Z	14.2Z	471Z	1.00Z
	2110	286	1.86	21.9	7.2	6.1	13.3	168	0.92
	2111	285	1.88	22.9	8.5	8.5	17.0	339	1.00
	2112	317	1.95	15.7	7.4	7.7	15.1	174	1.06
	Mean	296	1.91	18.5	7.8	7.6	15.5	230	1.01
	S.D.	14	0.04	3.2	1.1	1.4	2.3	78	0.08
Relative	2101		0.66	6.4	2.5	2.4	4.9	74	0.39
	2102		0.62	7.1	3.2	2.6	5.8	61	0.37
	2103		0.67	4.8	2.5	2.2	4.7	78	0.37
	2104		0.68	7.2	2.4	2.6	5.0	134	0.32
	2105		0.69	5.3	2.5	3.0	5.4	96	0.33
	2106		0.61	5.5	2.7	3.1	5.8	69	0.33
	2107		0.63	6.9	3.2	3.2	6.5	37	0.32
	2108		0.62	5.2	2.2	1.8	4.0	78	0.32
	2109a)		0.61Z	6.0Z	2.5Z	2.1Z	4.6Z	151Z	0.32Z
	2110		0.65	7.7	2.5	2.1	4.7	59	0.32
	2111		0.66	8.0	3.0	3.0	6.0	119	0.35
	2112		0.62	5.0	2.3	2.4	4.8	55	0.33
	Mean		0.65	6.3	2.6	2.6	5.2	78	0.34
	S.D.		0.03	1.2	0.3	0.5	0.7	28	0.03

a): Non-pregnant

Z: Data was excluded from statistical analysis.

Appendix 8-17

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of female rats (Lactation day 5)

Dose (mg/kg): 20

	Animal number	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)
Absolute	2101	9.58	0.78	1.09	1.06	2.15	48	45	93
	2102	9.81	0.67	5.72	1.20	6.92	37	39	76
	2103	9.95	0.79	0.99	1.01	2.00	41	46	87
	2104	9.35	0.64	1.05	1.01	2.06	34	39	73
	2105	8.24	0.69	1.01	0.96	1.97	34	33	67
	2106	10.09	0.81	1.18	1.18	2.36	39	44	83
	2107	11.12	0.61	1.08	1.10	2.18	40	45	85
	2108	10.18	0.64	1.09	1.06	2.15	36	40	76
	2109a)	11.38Z	0.67Z	1.14Z	1.08Z	2.22Z	35Z	38Z	73Z
	2110	10.24	0.62	1.07	1.01	2.08	34	36	70
	2111	9.18	0.64	1.04	1.02	2.06	38	38	76
	2112	10.31	0.71	1.18	1.11	2.29	38	40	78
	Mean	9.82	0.69	1.50	1.07	2.57	38	40	79
	S.D.	0.74	0.07	1.40	0.08	1.45	4	4	8
Relative	2101	3.39	0.28	0.39	0.37	0.76	17	16	33
	2102	3.29	0.22	1.92	0.40	2.32	12	13	26
	2103	3.40	0.27	0.34	0.34	0.68	14	16	30
	2104	3.25	0.22	0.36	0.35	0.72	12	14	25
	2105	2.95	0.25	0.36	0.34	0.71	12	12	24
	2106	3.16	0.25	0.37	0.37	0.74	12	14	26
	2107	3.65	0.20	0.35	0.36	0.71	13	15	28
	2108	3.33	0.21	0.36	0.35	0.70	12	13	25
	2109a)	3.66Z	0.22Z	0.37Z	0.35Z	0.71Z	11Z	12Z	23Z
	2110	3.58	0.22	0.37	0.35	0.73	12	13	24
	2111	3.22	0.22	0.36	0.36	0.72	13	13	27
	2112	3.25	0.22	0.37	0.35	0.72	12	13	25
	Mean	3.32	0.23	0.50	0.36	0.86	13	14	27
	S.D.	0.19	0.03	0.47	0.02	0.48	2	1	3

a): Non-pregnant

Z: Data was excluded from statistical analysis.

Appendix 8-18

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of female rats (Lactation day 5)

Dose (mg/kg): 20

	Animal number	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	2101	46.9	64.2	111.1	625
	2102	60.4	47.3	107.7	555
	2103	46.7	58.3	105.0	659
	2104	58.1	64.3	122.4	742
	2105	50.2	29.4	79.6	585
	2106	59.4	53.9	113.3	880
	2107	50.0	48.5	98.5	584
	2108	42.8	50.3	93.1	792
	2109a)	39.8Z	45.6Z	85.4Z	738Z
	2110	52.6	40.7	93.3	658
	2111	48.3	50.1	98.4	711
	2112	71.1	50.8	121.9	758
	Mean	53.3	50.7	104.0	686
	S.D.	8.2	10.0	13.0	100
Relative	2101	16.6	22.7	39.3	221
	2102	20.3	15.9	36.1	186
	2103	15.9	19.9	35.8	225
	2104	20.2	22.3	42.5	258
	2105	18.0	10.5	28.5	210
	2106	18.6	16.9	35.5	276
	2107	16.4	15.9	32.3	191
	2108	14.0	16.4	30.4	259
	2109a)	12.8Z	14.7Z	27.5Z	237Z
	2110	18.4	14.2	32.6	230
	2111	16.9	17.6	34.5	249
	2112	22.4	16.0	38.5	239
	Mean	18.0	17.1	35.1	231
	S.D.	2.4	3.5	4.1	29

a): Non-pregnant

Z: Data was excluded from statistical analysis.

Appendix 8-19

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of female rats (Lactation day 5)

Dose (mg/kg): 100

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)
Absolute	3101	292	1.89	20.2	9.8	6.5	16.3	204	1.02
	3102	296	1.94	20.0	10.1	8.2	18.3	359	0.99
	3103	270	1.99	14.0	6.2	6.4	12.6	172	0.95
	3104	279	1.95	18.3	7.0	5.0	12.0	243	0.90
	3105	304	1.90	15.5	8.1	7.8	15.9	205	0.98
	3106	311	1.98	18.4	9.5	8.6	18.1	253	1.04
	3107	300	1.92	16.4	8.3	6.7	15.0	224	1.03
	3108	310	1.91	21.6	6.9	6.9	13.8	329	1.11
	3109	271	1.90	15.6	10.0	8.7	18.7	246	0.97
	3110	309	2.00	19.1	7.5	5.7	13.2	199	1.06
	3111a)	285Z	1.83Z	14.5Z	6.9Z	6.4Z	13.3Z	335Z	1.00Z
	3112	283	1.83	16.4	6.8	7.5	14.3	275	1.00
	Mean	293	1.93	17.8	8.2	7.1	15.3	246	1.00
	S.D.	15	0.05	2.4	1.4	1.2	2.4	57	0.06
Relative	3101		0.65	6.9	3.4	2.2	5.6	70	0.35
	3102		0.66	6.8	3.4	2.8	6.2	121	0.33
	3103		0.74	5.2	2.3	2.4	4.7	64	0.35
	3104		0.70	6.6	2.5	1.8	4.3	87	0.32
	3105		0.63	5.1	2.7	2.6	5.2	67	0.32
	3106		0.64	5.9	3.1	2.8	5.8	81	0.33
	3107		0.64	5.5	2.8	2.2	5.0	75	0.34
	3108		0.62	7.0	2.2	2.2	4.5	106	0.36
	3109		0.70	5.8	3.7	3.2	6.9	91	0.36
	3110		0.65	6.2	2.4	1.8	4.3	64	0.34
	3111a)		0.64Z	5.1Z	2.4Z	2.2Z	4.7Z	118Z	0.35Z
	3112		0.65	5.8	2.4	2.7	5.1	97	0.35
	Mean		0.66	6.1	2.8	2.4	5.2	84	0.34
	S.D.		0.04	0.7	0.5	0.4	0.8	19	0.01

a): Not copulated

Z: Data was excluded from statistical analysis.

Appendix 8-20

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of female rats (Lactation day 5)

Dose (mg/kg): 100

	Animal number	Liver	Spleen	Kidney (R)	Kidney (L)	Kidney (R+L)	Adrenal (R)	Adrenal (L)	Adrenal (R+L)
		g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)
Absolute	3101	10.17	0.71	1.17	1.08	2.25	45	51	96
	3102	10.01	0.66	0.95	0.91	1.86	40	42	82
	3103	9.43	0.57	1.12	1.02	2.14	44	46	90
	3104	8.87	0.55	1.05	0.99	2.04	37	38	75
	3105	9.93	0.63	1.14	1.08	2.22	35	36	71
	3106	11.35	0.82	1.07	1.12	2.19	49	48	97
	3107	9.84	0.62	1.05	1.10	2.15	38	39	77
	3108	10.26	0.67	1.12	1.11	2.23	42	48	90
	3109	9.47	0.73	1.18	1.16	2.34	43	47	90
	3110	9.82	0.72	1.09	1.16	2.25	42	48	90
	3111a)	7.48Z	0.43Z	0.87Z	0.88Z	1.75Z	21Z	25Z	46Z
	3112	9.13	0.73	1.04	1.05	2.09	36	37	73
	Mean	9.84	0.67	1.09	1.07	2.16	41	44	85
	S.D.	0.66	0.08	0.07	0.08	0.13	4	5	9
Relative	3101	3.48	0.24	0.40	0.37	0.77	15	17	33
	3102	3.38	0.22	0.32	0.31	0.63	14	14	28
	3103	3.49	0.21	0.41	0.38	0.79	16	17	33
	3104	3.18	0.20	0.38	0.35	0.73	13	14	27
	3105	3.27	0.21	0.38	0.36	0.73	12	12	23
	3106	3.65	0.26	0.34	0.36	0.70	16	15	31
	3107	3.28	0.21	0.35	0.37	0.72	13	13	26
	3108	3.31	0.22	0.36	0.36	0.72	14	15	29
	3109	3.49	0.27	0.44	0.43	0.86	16	17	33
	3110	3.18	0.23	0.35	0.38	0.73	14	16	29
	3111a)	2.62Z	0.15Z	0.31Z	0.31Z	0.61Z	7Z	9Z	16Z
	3112	3.23	0.26	0.37	0.37	0.74	13	13	26
	Mean	3.36	0.23	0.37	0.37	0.74	14	15	29
	S.D.	0.15	0.02	0.03	0.03	0.06	1	2	3

a): Not copulated

Z: Data was excluded from statistical analysis.

Appendix 8-21

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of female rats (Lactation day 5)

Dose (mg/kg): 100

	Animal number	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	3101	70.7	57.8	128.5	713
	3102	48.1	39.2	87.3	683
	3103	61.3	56.2	117.5	861
	3104	59.6	46.3	105.9	723
	3105	58.0	56.4	114.4	825
	3106	59.5	61.7	121.2	940
	3107	55.5	44.7	100.2	611
	3108	48.2	71.0	119.2	790
	3109	58.8	46.8	105.6	834
	3110	59.1	49.0	108.1	963
	3111a)	44.0Z	36.8Z	80.8Z	418Z
	3112	49.8	57.9	107.7	867
	Mean	57.1	53.4	110.5	801
	S.D.	6.6	9.1	11.3	109
Relative	3101	24.2	19.8	44.0	244
	3102	16.3	13.2	29.5	231
	3103	22.7	20.8	43.5	319
	3104	21.4	16.6	38.0	259
	3105	19.1	18.6	37.6	271
	3106	19.1	19.8	39.0	302
	3107	18.5	14.9	33.4	204
	3108	15.5	22.9	38.5	255
	3109	21.7	17.3	39.0	308
	3110	19.1	15.9	35.0	312
	3111a)	15.4Z	12.9Z	28.4Z	147Z
	3112	17.6	20.5	38.1	306
	Mean	19.6	18.2	37.8	274
	S.D.	2.7	2.9	4.1	38

a): Not copulated

Z: Data was excluded from statistical analysis.

Appendix 8-22

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of female rats (Lactation day 5)

Dose (mg/kg): 500

	Animal number	Body weight g	Brain	Pituitary	Thyroid (R)	Thyroid (L)	Thyroid (R+L)	Thymus	Heart
			g(g/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	g(g/100g BW)
Absolute	4101	266	1.89	16.9	6.9	6.8	13.7	153	0.90
	4102	311	1.99	23.2	9.6	8.0	17.6	226	1.12
	4103	288	1.92	18.8	6.6	5.4	12.0	253	0.90
	4104	284	1.87	17.4	8.3	8.1	16.4	173	0.98
	4105	286	1.98	14.4	7.9	9.1	17.0	227	0.90
	4106	288	1.90	18.8	6.2	4.3	10.5	281	0.93
	4107	284	2.00	18.9	8.7	8.6	17.3	205	0.97
	4108	304	1.93	19.8	9.8	10.6	20.4	199	1.20
	4109	315	1.85	17.2	9.5	7.4	16.9	192	0.98
	4110	274	1.86	15.2	10.7	6.6	17.3	70	0.89
	4111	270	1.88	16.4	6.3	6.4	12.7	187	0.93
	4112	293	1.89	17.9	9.2	7.5	16.7	210	0.96
	Mean	289	1.91	17.9	8.3	7.4	15.7	198	0.97
	S.D.	15	0.05	2.3	1.5	1.7	2.8	53	0.10
Relative	4101		0.71	6.4	2.6	2.6	5.2	58	0.34
	4102		0.64	7.5	3.1	2.6	5.7	73	0.36
	4103		0.67	6.5	2.3	1.9	4.2	88	0.31
	4104		0.66	6.1	2.9	2.9	5.8	61	0.35
	4105		0.69	5.0	2.8	3.2	5.9	79	0.31
	4106		0.66	6.5	2.2	1.5	3.6	98	0.32
	4107		0.70	6.7	3.1	3.0	6.1	72	0.34
	4108		0.63	6.5	3.2	3.5	6.7	65	0.39
	4109		0.59	5.5	3.0	2.3	5.4	61	0.31
	4110		0.68	5.5	3.9	2.4	6.3	26	0.32
	4111		0.70	6.1	2.3	2.4	4.7	69	0.34
	4112		0.65	6.1	3.1	2.6	5.7	72	0.33
	Mean		0.67	6.2	2.9	2.6	5.4	69	0.34
	S.D.		0.03	0.7	0.5	0.5	0.9	18	0.02

Appendix 8-23

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of female rats (Lactation day 5)

Dose (mg/kg): 500

	Animal number	Liver	Spleen	Kidney (R)	Kidney (L)	Kidney (R+L)	Adrenal (R)	Adrenal (L)	Adrenal (R+L)
		g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)
Absolute	4101	9.73	0.50	0.86	1.00	1.86	31	39	70
	4102	10.77	0.77	1.18	1.18	2.36	45	52	97
	4103	10.84	0.70	1.18	1.24	2.42	38	37	75
	4104	10.33	0.64	1.12	1.15	2.27	35	38	73
	4105	9.92	0.63	0.97	0.89	1.86	28	32	60
	4106	10.59	0.71	1.09	1.05	2.14	33	35	68
	4107	10.31	0.60	1.17	1.14	2.31	46	49	95
	4108	10.25	0.66	1.12	1.17	2.29	37	36	73
	4109	10.98	0.83	1.08	1.06	2.14	39	39	78
	4110	11.08	0.69	1.07	1.08	2.15	42	43	85
	4111	8.80	0.58	0.95	0.99	1.94	39	44	83
	4112	9.26	0.61	1.16	1.07	2.23	34	36	70
	Mean	10.24	0.66	1.08	1.09	2.16	37	40	77
	S.D.	0.70	0.09	0.10	0.10	0.19	5	6	11
Relative	4101	3.66	0.19	0.32	0.38	0.70	12	15	26
	4102	3.46	0.25	0.38	0.38	0.76	14	17	31
	4103	3.76	0.24	0.41	0.43	0.84	13	13	26
	4104	3.64	0.23	0.39	0.40	0.80	12	13	26
	4105	3.47	0.22	0.34	0.31	0.65	10	11	21
	4106	3.68	0.25	0.38	0.36	0.74	11	12	24
	4107	3.63	0.21	0.41	0.40	0.81	16	17	33
	4108	3.37	0.22	0.37	0.38	0.75	12	12	24
	4109	3.49	0.26	0.34	0.34	0.68	12	12	25
	4110	4.04	0.25	0.39	0.39	0.78	15	16	31
	4111	3.26	0.21	0.35	0.37	0.72	14	16	31
	4112	3.16	0.21	0.40	0.37	0.76	12	12	24
	Mean	3.55	0.23	0.37	0.38	0.75	13	14	27
	S.D.	0.24	0.02	0.03	0.03	0.06	2	2	4

Appendix 8-24

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of female rats (Lactation day 5)

Dose (mg/kg): 500

	Animal number	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	4101	51.2	62.2	113.4	696
	4102	64.9	48.6	113.5	824
	4103	71.0	56.1	127.1	822
	4104	45.6	58.4	104.0	783
	4105	47.8	41.3	89.1	523
	4106	52.6	69.1	121.7	705
	4107	57.4	47.8	105.2	848
	4108	52.9	53.0	105.9	695
	4109	62.9	47.3	110.2	805
	4110	59.3	60.0	119.3	600
	4111	36.7	38.1	74.8	673
	4112	55.9	38.6	94.5	716
	Mean	54.9	51.7	106.6	724
	S.D.	9.2	9.8	14.7	98
Relative	4101	19.2	23.4	42.6	262
	4102	20.9	15.6	36.5	265
	4103	24.7	19.5	44.1	285
	4104	16.1	20.6	36.6	276
	4105	16.7	14.4	31.2	183
	4106	18.3	24.0	42.3	245
	4107	20.2	16.8	37.0	299
	4108	17.4	17.4	34.8	229
	4109	20.0	15.0	35.0	256
	4110	21.6	21.9	43.5	219
	4111	13.6	14.1	27.7	249
	4112	19.1	13.2	32.3	244
	Mean	19.0	18.0	37.0	251
	S.D.	2.9	3.8	5.3	31

Appendix 8-25

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of female rats (Satellite group, End of administration)

Dose (mg/kg): 0

	Animal number	Body weight g	Brain	Pituitary	Thyroid (R)	Thyroid (L)	Thyroid (R+L)	Thymus	Heart
			g(g/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	g(g/100g BW)
Absolute	1113	257	1.89	16.3	9.0	6.6	15.6	245	0.83
	1114	276	1.95	14.4	8.0	7.0	15.0	311	0.90
	1115	275	1.91	18.4	6.3	7.5	13.8	312	0.83
	1116	283	1.89	16.4	6.9	6.2	13.1	363	0.94
	1117	257	1.97	15.3	11.1	9.6	20.7	348	0.86
	Mean	270	1.92	16.2	8.3	7.4	15.6	316	0.87
	S.D.	12	0.04	1.5	1.9	1.3	3.0	46	0.05
Relative	1113		0.74	6.3	3.5	2.6	6.1	95	0.32
	1114		0.71	5.2	2.9	2.5	5.4	113	0.33
	1115		0.69	6.7	2.3	2.7	5.0	113	0.30
	1116		0.67	5.8	2.4	2.2	4.6	128	0.33
	1117		0.77	6.0	4.3	3.7	8.1	135	0.33
	Mean		0.72	6.0	3.1	2.7	5.8	117	0.32
	S.D.		0.04	0.6	0.8	0.6	1.4	15	0.01

Appendix 8-26

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of female rats (Satellite group, End of administration)

Dose (mg/kg): 0

	Animal number	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)
Absolute	1113	6.00	0.39	0.90	0.85	1.75	36	40	76
	1114	6.89	0.61	0.92	0.90	1.82	29	36	65
	1115	7.12	0.48	0.91	0.89	1.80	32	35	67
	1116	7.58	0.58	0.94	0.99	1.93	32	30	62
	1117	6.08	0.59	0.99	0.93	1.92	33	34	67
	Mean	6.73	0.53	0.93	0.91	1.84	32	35	67
	S.D.	0.68	0.09	0.04	0.05	0.08	3	4	5
Relative	1113	2.33	0.15	0.35	0.33	0.68	14	16	30
	1114	2.50	0.22	0.33	0.33	0.66	11	13	24
	1115	2.59	0.17	0.33	0.32	0.65	12	13	24
	1116	2.68	0.20	0.33	0.35	0.68	11	11	22
	1117	2.37	0.23	0.39	0.36	0.75	13	13	26
	Mean	2.49	0.19	0.35	0.34	0.68	12	13	25
	S.D.	0.15	0.03	0.03	0.02	0.04	1	2	3

Appendix 8-27

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of female rats (Satellite group, End of administration)

Dose (mg/kg): 0

	Animal number	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	1113	39.7	40.6	80.3	762
	1114	43.0	46.6	89.6	806
	1115	49.4	51.3	100.7	623
	1116	38.3	35.9	74.2	598
	1117	51.1	51.4	102.5	530
	Mean	44.3	45.2	89.5	664
	S.D.	5.7	6.8	12.4	116
Relative	1113	15.4	15.8	31.2	296
	1114	15.6	16.9	32.5	292
	1115	18.0	18.7	36.6	227
	1116	13.5	12.7	26.2	211
	1117	19.9	20.0	39.9	206
	Mean	16.5	16.8	33.3	246
	S.D.	2.5	2.8	5.2	44

Appendix 8-28

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of female rats (Satellite group, End of administration)

Dose (mg/kg): 500

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)
Absolute	4113	255	1.92	17.7	10.6	8.8	19.4	263	0.84
	4114	244	1.94	18.5	8.8	5.3	14.1	239	0.98
	4115	289	2.03	15.8	7.1	5.0	12.1	361	0.90
	4116	245	1.98	14.4	9.8	7.2	17.0	287	0.86
	4117	251	1.92	15.1	7.3	6.5	13.8	280	0.80
	Mean	257	1.96	16.3	8.7	6.6	15.3	286	0.88
	S.D.	19	0.05	1.7	1.5	1.5	2.9	46	0.07
Relative	4113		0.75	6.9	4.2	3.5	7.6	103	0.33
	4114		0.80	7.6	3.6	2.2	5.8	98	0.40
	4115		0.70	5.5	2.5	1.7	4.2	125	0.31
	4116		0.81	5.9	4.0	2.9	6.9	117	0.35
	4117		0.76	6.0	2.9	2.6	5.5	112	0.32
	Mean		0.76	6.4	3.4	2.6	6.0	111	0.34
	S.D.		0.04	0.9	0.7	0.7	1.3	11	0.04

Appendix 8-29

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of female rats (Satellite group, End of administration)

Dose (mg/kg): 500

	Animal number	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)
Absolute	4113	7.75	0.47	0.98	0.90	1.88	40	46	86
	4114	6.75	0.40	0.79	0.85	1.64	38	43	81
	4115	8.19	0.54	1.09	1.07	2.16	35	42	77
	4116	6.89	0.44	0.93	0.95	1.88	46	54	100
	4117	7.33	0.44	0.94	0.89	1.83	36	38	74
	Mean	7.38	0.46	0.95	0.93	1.88	39	45	84
	S.D.	0.60	0.05	0.11	0.08	0.19	4	6	10
Relative	4113	3.04	0.18	0.38	0.35	0.74	16	18	34
	4114	2.77	0.16	0.32	0.35	0.67	16	18	33
	4115	2.83	0.19	0.38	0.37	0.75	12	15	27
	4116	2.81	0.18	0.38	0.39	0.77	19	22	41
	4117	2.92	0.18	0.37	0.35	0.73	14	15	29
	Mean	2.87	0.18	0.37	0.36	0.73	15	18	33
	S.D.	0.11	0.01	0.03	0.02	0.04	3	3	5

Appendix 8-30

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of female rats (Satellite group, End of administration)

Dose (mg/kg): 500

	Animal number	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	4113	32.7	41.0	73.7	521
	4114	40.3	42.9	83.2	484
	4115	54.3	61.9	116.2	433
	4116	50.7	48.8	99.5	411
	4117	45.5	41.4	86.9	482
	Mean	44.7	47.2	91.9	466
	S.D.	8.5	8.8	16.4	44
Relative	4113	12.8	16.1	28.9	204
	4114	16.5	17.6	34.1	198
	4115	18.8	21.4	40.2	150
	4116	20.7	19.9	40.6	168
	4117	18.1	16.5	34.6	192
	Mean	17.4	18.3	35.7	182
	S.D.	3.0	2.3	4.9	23

Appendix 8-31

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of male rats (End of recovery)

Dose (mg/kg): 0

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)
Absolute	1008	481	2.15	13.4	12.5	9.8	22.3	288	1.34
	1009	442	2.14	12.3	9.6	9.0	18.6	241	1.30
	1010	490	2.11	12.7	13.4	15.1	28.5	249	1.57
	1011	492	2.21	12.1	9.8	9.0	18.8	223	1.53
	1012	486	2.06	12.0	10.9	11.5	22.4	272	1.53
	Mean	478	2.13	12.5	11.2	10.9	22.1	255	1.45
	S.D.	21	0.06	0.6	1.7	2.6	4.0	26	0.12
Relative	1008		0.45	2.8	2.6	2.0	4.6	60	0.28
	1009		0.48	2.8	2.2	2.0	4.2	55	0.29
	1010		0.43	2.6	2.7	3.1	5.8	51	0.32
	1011		0.45	2.5	2.0	1.8	3.8	45	0.31
	1012		0.42	2.5	2.2	2.4	4.6	56	0.31
	Mean		0.45	2.6	2.3	2.3	4.6	53	0.30
	S.D.		0.02	0.2	0.3	0.5	0.7	6	0.02

Appendix 8-32

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of male rats (End of recovery)

Dose (mg/kg): 0

	Animal number	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)
Absolute	1008	11.66	0.85	1.72	1.70	3.42	40	39	79
	1009	10.76	0.84	1.53	1.61	3.14	26	26	52
	1010	14.64	0.76	1.73	1.86	3.59	29	37	66
	1011	11.26	0.67	1.52	1.60	3.12	28	31	59
	1012	11.65	0.85	1.61	1.57	3.18	31	34	65
	Mean	11.99	0.79	1.62	1.67	3.29	31	33	64
	S.D.	1.52	0.08	0.10	0.12	0.21	5	5	10
Relative	1008	2.42	0.18	0.36	0.35	0.71	8	8	16
	1009	2.43	0.19	0.35	0.36	0.71	6	6	12
	1010	2.99	0.16	0.35	0.38	0.73	6	8	13
	1011	2.29	0.14	0.31	0.33	0.63	6	6	12
	1012	2.40	0.17	0.33	0.32	0.65	6	7	13
	Mean	2.51	0.17	0.34	0.35	0.69	6	7	13
	S.D.	0.28	0.02	0.02	0.02	0.04	1	1	2

Appendix 8-33

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of male rats (End of recovery)

Dose (mg/kg): 0

	Animal number	Seminal vesicle g(g/100g BW)	Prostate g(g/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)
Absolute	1008	1.89	1.45	1.72	1.67	3.39	702	672	1374
	1009	1.83	1.17	1.59	1.62	3.21	647	640	1287
	1010	1.57	1.48	1.85	1.92	3.77	782	753	1535
	1011	1.58	1.48	1.63	1.66	3.29	629	619	1248
	1012	2.05	1.37	1.89	1.89	3.78	757	700	1457
	Mean	1.78	1.39	1.74	1.75	3.49	703	677	1380
	S.D.	0.21	0.13	0.13	0.14	0.27	67	53	118
Relative	1008	0.39	0.30	0.36	0.35	0.70	146	140	286
	1009	0.41	0.26	0.36	0.37	0.73	146	145	291
	1010	0.32	0.30	0.38	0.39	0.77	160	154	313
	1011	0.32	0.30	0.33	0.34	0.67	128	126	254
	1012	0.42	0.28	0.39	0.39	0.78	156	144	300
	Mean	0.37	0.29	0.36	0.37	0.73	147	142	289
	S.D.	0.05	0.02	0.02	0.02	0.05	12	10	22

Appendix 8-34

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of male rats (End of recovery)

Dose (mg/kg): 500

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)
Absolute	4008	467	2.05	12.8	10.7	10.4	21.1	163	1.49
	4009	479	2.10	13.8	9.8	9.9	19.7	217	1.64
	4010	555	2.22	14.8	10.3	15.7	26.0	217	1.48
	4011	479	2.02	11.4	11.8	11.6	23.4	199	1.29
	4012	436	2.05	13.6	9.6	10.4	20.0	138	1.22
	Mean	483	2.09	13.3	10.4	11.6	22.0	187	1.42
	S.D.	44	0.08	1.3	0.9	2.4	2.6	35	0.17
Relative	4008		0.44	2.7	2.3	2.2	4.5	35	0.32
	4009		0.44	2.9	2.0	2.1	4.1	45	0.34
	4010		0.40	2.7	1.9	2.8	4.7	39	0.27
	4011		0.42	2.4	2.5	2.4	4.9	42	0.27
	4012		0.47	3.1	2.2	2.4	4.6	32	0.28
	Mean		0.43	2.8	2.2	2.4	4.6	39	0.30
	S.D.		0.03	0.3	0.2	0.3	0.3	5	0.03

Appendix 8-35

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of male rats (End of recovery)

Dose (mg/kg): 500

	Animal number	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)
Absolute	4008	13.02	0.59	1.78	1.82	3.60	29	32	61
	4009	11.77	0.55	1.54	1.53	3.07	30	31	61
	4010	16.06	0.77	1.88	1.99	3.87	30	31	61
	4011	13.53	0.73	1.75	1.67	3.42	31	33	64
	4012	11.23	0.71	1.51	1.44	2.95	26	30	56
	Mean	13.12	0.67	1.69	1.69	3.38	29	31	61
	S.D.	1.89	0.09	0.16	0.22	0.38	2	1	3
Relative	4008	2.79	0.13	0.38	0.39	0.77	6	7	13
	4009	2.46	0.11	0.32	0.32	0.64	6	6	13
	4010	2.89	0.14	0.34	0.36	0.70	5	6	11
	4011	2.82	0.15	0.37	0.35	0.71	6	7	13
	4012	2.58	0.16	0.35	0.33	0.68	6	7	13
	Mean	2.71	0.14	0.35	0.35	0.70	6	7	13
	S.D.	0.18	0.02	0.02	0.03	0.05	0	1	1

Appendix 8-36

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of male rats (End of recovery)

Dose (mg/kg): 500

	Animal number	Seminal vesicle g(g/100g BW)	Prostate g(g/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)
Absolute	4008	1.71	1.17	1.46	1.45	2.91	594	578	1172
	4009	1.69	1.51	1.75	1.75	3.50	665	611	1276
	4010	2.16	1.46	1.69	1.64	3.33	672	692	1364
	4011	1.68	1.36	1.46	1.41	2.87	690	652	1342
	4012	2.03	0.94	1.57	1.60	3.17	672	656	1328
	Mean	1.85	1.29	1.59	1.57	3.16	659	638	1296
	S.D.	0.23	0.23	0.13	0.14	0.27	37	44	77
Relative	4008	0.37	0.25	0.31	0.31	0.62	127	124	251
	4009	0.35	0.32	0.37	0.37	0.73	139	128	266
	4010	0.39	0.26	0.30	0.30	0.60	121	125	246
	4011	0.35	0.28	0.30	0.29	0.60	144	136	280
	4012	0.47	0.22	0.36	0.37	0.73	154	150	305
	Mean	0.39	0.27	0.33	0.33	0.66	137	133	270
	S.D.	0.05	0.04	0.03	0.04	0.07	13	11	24

Appendix 8-37

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of female rats (End of recovery)

Dose (mg/kg): 0

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)
Absolute	1118	289	2.06	15.5	10.1	8.4	18.5	403	0.94
	1119	281	2.02	17.0	7.9	6.8	14.7	211	0.90
	1120	282	1.86	14.1	6.7	5.7	12.4	230	0.82
	1121	284	1.87	21.1	7.2	5.5	12.7	189	0.82
	1122	286	1.89	16.0	7.5	8.8	16.3	261	0.85
	Mean	284	1.94	16.7	7.9	7.0	14.9	259	0.87
	S.D.	3	0.09	2.7	1.3	1.5	2.6	85	0.05
Relative	1118		0.71	5.4	3.5	2.9	6.4	139	0.33
	1119		0.72	6.0	2.8	2.4	5.2	75	0.32
	1120		0.66	5.0	2.4	2.0	4.4	82	0.29
	1121		0.66	7.4	2.5	1.9	4.5	67	0.29
	1122		0.66	5.6	2.6	3.1	5.7	91	0.30
	Mean		0.68	5.9	2.8	2.5	5.2	91	0.31
	S.D.		0.03	0.9	0.4	0.5	0.8	28	0.02

Appendix 8-38

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of female rats (End of recovery)

Dose (mg/kg): 0

	Animal number	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)
Absolute	1118	6.72	0.76	0.97	0.99	1.96	32	35	67
	1119	7.13	0.47	0.86	0.86	1.72	37	39	76
	1120	6.74	0.49	0.97	0.98	1.95	25	27	52
	1121	6.96	0.50	0.88	0.88	1.76	36	36	72
	1122	6.43	0.46	0.92	0.90	1.82	31	30	61
	Mean	6.80	0.54	0.92	0.92	1.84	32	33	66
	S.D.	0.27	0.13	0.05	0.06	0.11	5	5	9
Relative	1118	2.33	0.26	0.34	0.34	0.68	11	12	23
	1119	2.54	0.17	0.31	0.31	0.61	13	14	27
	1120	2.39	0.17	0.34	0.35	0.69	9	10	18
	1121	2.45	0.18	0.31	0.31	0.62	13	13	25
	1122	2.25	0.16	0.32	0.31	0.64	11	10	21
	Mean	2.39	0.19	0.32	0.32	0.65	11	12	23
	S.D.	0.11	0.04	0.02	0.02	0.04	2	2	3

Appendix 8-39

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of female rats (End of recovery)

Dose (mg/kg): 0

	Animal number	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	1118	48.2	49.5	97.7	633
	1119	40.3	45.4	85.7	545
	1120	42.8	40.6	83.4	411
	1121	49.8	49.4	99.2	438
	1122	38.6	42.4	81.0	368
	Mean	43.9	45.5	89.4	479
	S.D.	4.9	4.0	8.4	108
Relative	1118	16.7	17.1	33.8	219
	1119	14.3	16.2	30.5	194
	1120	15.2	14.4	29.6	146
	1121	17.5	17.4	34.9	154
	1122	13.5	14.8	28.3	129
	Mean	15.4	16.0	31.4	168
	S.D.	1.7	1.3	2.8	37

Appendix 8-40

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of female rats (End of recovery)

Dose (mg/kg): 500

	Animal number	Body weight g	Brain	Pituitary	Thyroid (R)	Thyroid (L)	Thyroid (R+L)	Thymus	Heart
			g(g/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	g(g/100g BW)
Absolute	4118	284	2.00	18.3	10.6	7.6	18.2	252	0.97
	4119	305	1.90	23.1	11.1	8.6	19.7	238	1.03
	4120	264	1.81	15.2	5.3	5.3	10.6	193	0.85
	4121	286	1.93	16.7	5.0	7.1	12.1	230	0.87
	4122	264	1.84	12.7	7.7	8.4	16.1	237	0.89
	Mean	281	1.90	17.2	7.9	7.4	15.3	230	0.92
	S.D.	17	0.08	3.9	2.9	1.3	3.9	22	0.08
Relative	4118		0.70	6.4	3.7	2.7	6.4	89	0.34
	4119		0.62	7.6	3.6	2.8	6.5	78	0.34
	4120		0.69	5.8	2.0	2.0	4.0	73	0.32
	4121		0.67	5.8	1.7	2.5	4.2	80	0.30
	4122		0.70	4.8	2.9	3.2	6.1	90	0.34
	Mean		0.68	6.1	2.8	2.6	5.4	82	0.33
	S.D.		0.03	1.0	0.9	0.4	1.2	7	0.02

Appendix 8-41

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of female rats (End of recovery)

Dose (mg/kg): 500

	Animal number	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)
Absolute	4118	7.61	0.52	0.95	1.08	2.03	35	38	73
	4119	8.30	0.61	0.99	1.01	2.00	40	45	85
	4120	7.13	0.55	0.90	0.90	1.80	28	31	59
	4121	7.59	0.52	1.05	0.97	2.02	40	41	81
	4122	6.60	0.53	0.90	0.87	1.77	39	41	80
	Mean	7.45	0.55	0.96	0.97	1.92	36	39	76
	S.D.	0.63	0.04	0.06	0.08	0.13	5	5	10
Relative	4118	2.68	0.18	0.33	0.38	0.71	12	13	26
	4119	2.72	0.20	0.32	0.33	0.66	13	15	28
	4120	2.70	0.21	0.34	0.34	0.68	11	12	22
	4121	2.65	0.18	0.37	0.34	0.71	14	14	28
	4122	2.50	0.20	0.34	0.33	0.67	15	16	30
	Mean	2.65	0.19	0.34	0.34	0.69	13	14	27
	S.D.	0.09	0.01	0.02	0.02	0.02	2	2	3

Appendix 8-42

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual organ weight of female rats (End of recovery)

Dose (mg/kg): 500

	Animal number	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	4118	36.7	39.6	76.3	756
	4119	35.8	28.1	63.9	735
	4120	56.6	56.2	112.8	789
	4121	43.8	57.2	101.0	520
	4122	49.7	45.4	95.1	510
	Mean	44.5	45.3	89.8	662
	S.D.	8.8	12.1	19.6	136
Relative	4118	12.9	13.9	26.9	266
	4119	11.7	9.2	21.0	241
	4120	21.4	21.3	42.7	299
	4121	15.3	20.0	35.3	182
	4122	18.8	17.2	36.0	193
	Mean	16.0	16.3	32.4	236
	S.D.	4.0	4.9	8.5	49

Appendix 9-1(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 1001 Male 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

Epididymis Focus, white: 2 present, bilateral
cauda, 5x5mm, 5x5mm

Other tissues Not remarkable

Histopathology:

Epididymis Granuloma, spermatic: mild, bilateral

Kidney Regeneration, tubular: minimal
proximal
Eosinophilic body, tubular cell: minimal
proximal

Prostate Cell infiltration: minimal, mononuclear
ventral

Spleen Hematopoiesis, extramedullary: 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), Parathyroid, Pancreas
Pituitary, Salivary gland, submandibular, Sciatic nerve, Stomach
Skeletal muscle, femoral, Seminal vesicle(Coagulating gland)
Spinal cord, thoracic, Testis, Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-2(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 1002 Male 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Microgranuloma: minimal

Lung(bronchus) Aggregation, foamy cell: minimal

Prostate Cell infiltration: minimal, mononuclear
ventral and dorsolateral

Spleen Hematopoiesis, extramedullary: 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, Kidney
Lymph node, mesenteric, Lymph node, submandibular, Parathyroid, Pancreas
Pituitary, Salivary gland, submandibular, Sciatic nerve, Stomach
Skeletal muscle, femoral, Seminal vesicle(Coagulating gland)
Spinal cord, thoracic, Testis, Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-3(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 1003 Male 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Necrosis,focal: minimal
Microgranuloma: minimal

Prostate Cell infiltration: minimal, mononuclear
ventral

Spleen Hematopoiesis,extramedullary: 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, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Parathyroid
Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve, Stomach
Skeletal muscle,femoral, Seminal vesicle(Coagulating gland)
Spinal cord,thoracic, Testis, Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-4(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 1004 Male 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

Kidney Regeneration, tubular: minimal
proximal

Liver Microgranuloma: minimal

Prostate Cell infiltration: minimal, inflammatory
dorsolateral

Spleen Hematopoiesis, extramedullary: 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, Lung(bronchus), Parathyroid, Pancreas, Pituitary
Salivary gland, submandibular, Sciatic nerve, Stomach, Skeletal muscle, femoral
Seminal vesicle(Coagulating gland), Spinal cord, thoracic, Testis, Thymus
Trachea, Thyroid, Urinary bladder

Appendix 9-5(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 1005 Male 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

Heart Cell infiltration: minimal, mononuclear

Liver Microgranuloma: minimal

Lung(bronchus) Aggregation, foamy cell: minimal

Prostate Cell infiltration: minimal, mononuclear
ventral

Spleen Hematopoiesis, extramedullary: 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, Parathyroid, Pancreas
Pituitary, Salivary gland, submandibular, Sciatic nerve, Stomach
Skeletal muscle, femoral, Seminal vesicle(Coagulating gland)
Spinal cord, thoracic, Testis, Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-6(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 1006 Male 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-7(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 1007 Male 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

Stomach Focus, dark red, glandular stomach: 1 present
 1x1mm

Other tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-8(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 1008 Male 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Kidney Regeneration, tubular: minimal
 proximal
 Eosinophilic body, tubular cell: minimal
 proximal

Following tissues : Not remarkable

Stomach, Thymus

Appendix 9-9(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 1009 Male 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Kidney Regeneration,tubular: minimal
 proximal

Following tissues : Not remarkable

Stomach, Thymus

Appendix 9-10(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 1010 Male 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Kidney Regeneration, tubular: minimal
proximal

Stomach Hyperplasia, squamous, limiting ridge: minimal

Following tissues : Not remarkable

Thymus

Appendix 9-11(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 1011 Male 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Kidney Regeneration, tubular: minimal
proximal

Following tissues : Not remarkable

Stomach, Thymus

Appendix 9-12(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 1012 Male 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Kidney, Stomach, Thymus

Appendix 9-13(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 2001 Male 20 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

Kidney Regeneration, tubular: minimal
proximal
Eosinophilic body, tubular cell: minimal
proximal

Following tissues : Not remarkable

Stomach

Appendix 9-14(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 2002 Male 20 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

Kidney Regeneration, tubular: minimal
proximal

Following tissues : Not remarkable

Stomach

Appendix 9-15(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 2003 Male 20 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Kidney, Stomach

Appendix 9-16(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 2004 Male 20 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Kidney, Stomach

Appendix 9-17(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 2005 Male 20 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

Kidney Eosinophilic body, tubular cell: minimal
proximal

Following tissues : Not remarkable

Stomach

Appendix 9-18(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 2006 Male 20 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-19(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 2007 Male 20 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-20(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 2008 Male 20 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-21(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 2009 Male 20 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-22(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 2010 Male 20 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-23(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 2011 Male 20 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-24(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 2012 Male 20 mg/kg Day 43 End of administration period (D42)

Gross pathology:

Stomach Focus, dark red, glandular stomach: 1 present
1x1mm

Other tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-25(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 3001 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

Kidney Regeneration, tubular: mild
proximal
Eosinophilic body, tubular cell: mild
proximal

Following tissues : Not remarkable

Stomach

Appendix 9-26(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 3002 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

Kidney Regeneration, tubular: mild
proximal
Eosinophilic body, tubular cell: mild
proximal

Following tissues : Not remarkable

Stomach

Appendix 9-27(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 3003 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

Kidney
Regeneration, tubular: mild
proximal
Eosinophilic body, tubular cell: mild
proximal
Urinary cast, granular: minimal

Following tissues : Not remarkable

Stomach

Appendix 9-28(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 3004 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

Kidney Regeneration, tubular: mild
 proximal
 Eosinophilic body, tubular cell: mild
 proximal
 Urinary cast, granular: minimal

Following tissues : Not remarkable

Stomach

Appendix 9-29(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 3005 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

Stomach Thickening, limiting ridge

Other tissues Not remarkable

Histopathology:

Kidney Regeneration, tubular: minimal
proximal
Eosinophilic body, tubular cell: minimal
proximal

Following tissues : Not remarkable

Stomach

Appendix 9-30(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 3006 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

Intestine, ileum(Peyer's patch)	Diverticulum: 1 present 2x2x10mm, 20cm above cecum
Stomach	Focus, dark red, glandular stomach: 1 present 3x3mm
Other tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-31(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 3007 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-32(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 3008 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-33(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 3009 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-34(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 3010 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-35(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 3011 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

Kidney	Regeneration, tubular: mild proximal Eosinophilic body, tubular cell: mild proximal
Liver	Microgranuloma: minimal
Prostate	Cell infiltration: mild, mononuclear 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, Lymph node, mesenteric
Lymph node, submandibular, Lung(bronchus), Parathyroid, Pancreas, Pituitary
Salivary gland, submandibular, Sciatic nerve, Spleen, Stomach
Skeletal muscle, femoral, Seminal vesicle(Coagulating gland)
Spinal cord, thoracic, Testis, Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-36(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 3012 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-37(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4001 Male 500 mg/kg Day 43 End of administration period (D42)

Gross pathology:

Stomach Thickening, limiting ridge

Other tissues Not remarkable

Histopathology:

Intestine, cecum Cell infiltration: mild, mucosal

Kidney Dilatation, tubular: minimal
Regeneration, tubular: minimal
proximal
Eosinophilic body, tubular cell: moderate
proximal

Liver Microgranuloma: minimal

Prostate Cell infiltration: minimal, mononuclear
ventral

Spleen Hematopoiesis, extramedullary: minimal

Stomach Hyperplasia, squamous, limiting ridge: 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, colon, Intestine, rectum, Lymph node, mesenteric
Lymph node, submandibular, Lung(bronchus), Parathyroid, Pancreas, Pituitary
Salivary gland, submandibular, Sciatic nerve, Skeletal muscle, femoral
Seminal vesicle(Coagulating gland), Spinal cord, thoracic, Testis, Thymus
Trachea, Thyroid, Urinary bladder

Appendix 9-38(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4002 Male 500 mg/kg Day 43 End of administration period (D42)

Gross pathology:

Stomach Thickening, limiting ridge

Other tissues Not remarkable

Histopathology:

Heart Cell infiltration: minimal, mononuclear

Kidney Regeneration, tubular: mild
proximal
Eosinophilic body, tubular cell: moderate
proximal
Necrosis/Desquamation, tubular cell: minimal
proximal

Prostate Cell infiltration: minimal, inflammatory
ventral and dorsolateral

Spleen Hematopoiesis, extramedullary: minimal

Stomach Hyperplasia, squamous, limiting ridge: 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, Lymph node, mesenteric
Lymph node, submandibular, Liver, Lung(bronchus), Parathyroid, Pancreas
Pituitary, Salivary gland, submandibular, Sciatic nerve, Skeletal muscle, femoral
Seminal vesicle(Coagulating gland), Spinal cord, thoracic, Testis, Thymus
Trachea, Thyroid, Urinary bladder

Appendix 9-39(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4003 Male 500 mg/kg Day 43 End of administration period (D42)

Gross pathology:

Stomach Thickening, limiting ridge

Other tissues Not remarkable

Histopathology:

Kidney Regeneration, tubular: mild
proximal
Eosinophilic body, tubular cell: mild
proximal

Pancreas Cell infiltration: minimal, lymphocytic
interstitial

Prostate Cell infiltration: mild, mononuclear
ventral

Spleen Hematopoiesis, extramedullary: minimal

Stomach Hyperplasia, squamous, limiting ridge: minimal

Testis Atrophy, seminiferous tubular: minimal, 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, Lymph node, mesenteric
Lymph node, submandibular, Liver, Lung(bronchus), Parathyroid, Pituitary
Salivary gland, submandibular, Sciatic nerve, Skeletal muscle, femoral
Seminal vesicle(Coagulating gland), Spinal cord, thoracic, Thymus, Trachea
Thyroid, Urinary bladder

Appendix 9-40(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4004 Male 500 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

Kidney	Dilatation,tubular: minimal Regeneration,tubular: mild proximal Eosinophilic body,tubular cell: mild proximal
Liver	Microgranuloma: minimal
Prostate	Cell infiltration: minimal, inflammatory dorsolateral
Spleen	Hematopoiesis,extramedullary: minimal
Stomach	Hyperplasia,squamous,limiting ridge: 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, Lung(bronchus), Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Sciatic nerve, Skeletal muscle,femoral
Seminal vesicle(Coagulating gland), Spinal cord,thoracic, Testis, Thymus
Trachea, Thyroid, Urinary bladder

Appendix 9-41(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4005 Male 500 mg/kg Day 43 End of administration period (D42)

Gross pathology:

Stomach Thickening, limiting ridge

Other tissues Not remarkable

Histopathology:

Kidney Regeneration, tubular: mild
proximal
Eosinophilic body, tubular cell: mild
proximal
Urinary cast, granular: mild
Necrosis/Desquamation, tubular cell: minimal
proximal

Liver Microgranuloma: minimal

Stomach Hyperplasia, squamous, limiting ridge: 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, Lung(bronchus), Parathyroid, Pancreas, Pituitary
Prostate, Salivary gland, submandibular, Sciatic nerve, Spleen
Skeletal muscle, femoral, Seminal vesicle(Coagulating gland)
Spinal cord, thoracic, Testis, Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-42(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4006 Male 500 mg/kg Day 43 End of administration period (D42)

Gross pathology:

Stomach Thickening, limiting ridge

Other tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-43(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4007 Male 500 mg/kg Day 43 End of administration period (D42)

Gross pathology:

Stomach Thickening, limiting ridge

Other tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-44(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4008 Male 500 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Kidney Regeneration, tubular: mild
 proximal
 Eosinophilic body, tubular cell: minimal
 proximal
 Urinary cast, granular: minimal

Following tissues : Not remarkable

Stomach, Thymus

Appendix 9-45(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4009 Male 500 mg/kg Day 57 End of recovery period

Gross pathology:

Stomach Focus, dark red, glandular stomach: 2 present
1x1mm, 1x1mm

Other tissues Not remarkable

Histopathology:

Kidney Regeneration, tubular: mild
proximal
Eosinophilic body, tubular cell: minimal
proximal

Stomach Erosion, glandular stomach: minimal

Following tissues : Not remarkable

Thymus

Appendix 9-46(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4010 Male 500 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Kidney Regeneration, tubular: mild
proximal

Stomach Hyperplasia, squamous, limiting ridge: minimal

Following tissues : Not remarkable

Thymus

Appendix 9-47(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4011 Male 500 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Kidney Regeneration, tubular: mild
proximal
Eosinophilic body, tubular cell: minimal
proximal

Following tissues : Not remarkable

Stomach, Thymus

Appendix 9-48(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4012 Male 500 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Kidney Regeneration, tubular: mild
 proximal
 Eosinophilic body, tubular cell: minimal
 proximal
 Urinary cast, granular: minimal

Following tissues : Not remarkable

Stomach, Thymus

Appendix 9-49(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 1101 Female 0 mg/kg Day 44 End of administration period (L4)

Gross pathology:

Stomach Focus, dark red, glandular stomach: 2 present
1x1mm, 2x2mm

Other tissues Not remarkable

Histopathology:

Spleen Hematopoiesis, extramedullary: mild

Stomach Erosion, 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), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland, submandibular, Sciatic nerve
Skeletal muscle, femoral, Spinal cord, thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-50(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 1102 Female 0 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-51(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 1103 Female 0 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

Kidney Regeneration, tubular: minimal
proximal

Liver Microgranuloma: minimal

Spleen Hematopoiesis, extramedullary: mild

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, Lung(bronchus), Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland, submandibular, Sciatic nerve, Stomach
Skeletal muscle, femoral, Spinal cord, thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-52(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 1104 Female 0 mg/kg Day 42 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Microgranuloma: minimal

Spleen Hematopoiesis, extramedullary: mild

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, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland, submandibular, Sciatic nerve
Stomach, Skeletal muscle, femoral, Spinal cord, thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-53(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 1105 Female 0 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-54(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 1106 Female 0 mg/kg Day 45 End of administration period (L4)

Gross pathology:

Stomach Focus, dark red, glandular stomach: 1 present
1x1mm

Other tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-55(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 1107 Female 0 mg/kg Day 46 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Animal No. 1108 Female 0 mg/kg Day 42 End of administration period (L4)

All tissues Not remarkable

Liver Microgranuloma: minimal

Spleen Hematopoiesis, extramedullary: mild

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, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-57(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 1109 Female 0 mg/kg Day 45 End of administration period (L4)

Gross pathology:

Stomach Focus, dark red, glandular stomach: 1 present
1x1mm

Other tissues Not remarkable

Histopathology:

No tissues examined

Animal No. 1110 Female 0 mg/kg Day 43 End of administration period (L4)

All tissues Not remarkable

Liver Microgranuloma: minimal

Spleen Hematopoiesis,extramedullary: mild

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, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-59(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 1111 Female 0 mg/kg Day 47 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-60(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 1112 Female 0 mg/kg Day 45 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-61(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 1113 Female 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Microgranuloma: 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, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea
Thyroid, Urinary bladder, Uterus, Vagina

Animal No. 1114 Female 0 mg/kg Day 43 End of administration period (D42)

All tissues Not remarkable

Liver Microgranuloma: minimal

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, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea
Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-63(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 1115 Female 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Microgranuloma: minimal

Spleen Hematopoiesis,extramedullary: 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, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-64(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 1116 Female 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Microgranuloma: minimal

Spleen Hematopoiesis,extramedullary: 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, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Animal No. 1117 Female 0 mg/kg Day 43 End of administration period (D42)

All tissues Not remarkable

Liver Microgranuloma: minimal

Lung(bronchus)	Aggregation,foamy cell: minimal
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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, Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Sciatic nerve, Spleen, Stomach
Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Animal No. 1118 Female 0 mg/kg Day 57 End of recovery period

All tissues Not remarkable

Following tissues : Not remarkable

Stomach, Uterus

Appendix 9-67(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 1119 Female 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Stomach, Uterus

Appendix 9-68(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 1120 Female 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Stomach, Uterus

Appendix 9-69(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 1121 Female 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Stomach, Uterus

Appendix 9-70(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 1122 Female 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Stomach, Uterus

Appendix 9-71(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 2101 Female 20 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-72(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 2102 Female 20 mg/kg Day 43 End of administration period (L4)

Gross pathology:

Kidney	Nodule: 1 present, right 20x20x15mm
Stomach	Focus, dark red, glandular stomach: 1 present 1x1mm
Other tissues	Not remarkable

Histopathology:

Stomach	Erosion, glandular stomach: minimal
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Appendix 9-73(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 2103 Female 20 mg/kg Day 42 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Stomach

Appendix 9-74(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 2104 Female 20 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-75(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 2105 Female 20 mg/kg Day 45 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-76(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 2106 Female 20 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Stomach

Appendix 9-77(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 2107 Female 20 mg/kg Day 46 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-78(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 2108 Female 20 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Stomach

Appendix 9-79(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 2109 Female 20 mg/kg Day 41 Undelivered

Gross pathology:

All tissues Not remarkable

Histopathology:

Spleen Hematopoiesis, extramedullary: 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), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland, submandibular, Sciatic nerve
Stomach, Skeletal muscle, femoral, Spinal cord, thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-80(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 2110 Female 20 mg/kg Day 45 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-81(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 2111 Female 20 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Stomach

Appendix 9-82(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 2112 Female 20 mg/kg Day 45 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-83(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 3101 Female 100 mg/kg Day 45 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-84(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 3102 Female 100 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Stomach

Appendix 9-85(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 3103 Female 100 mg/kg Day 45 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-86(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 3104 Female 100 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Stomach

Appendix 9-87(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 3105 Female 100 mg/kg Day 44 End of administration period (L4)

Gross pathology:

Stomach Focus, dark red, glandular stomach: 1 present
2x2mm

Other tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-88(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 3106 Female 100 mg/kg Day 42 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

Stomach Erosion, glandular stomach: minimal

Appendix 9-89(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 3107 Female 100 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Stomach

Animal No. 3108 Female 100 mg/kg Day 44 End of administration period (L4)

All tissues Not remarkable

No tissues examined

Appendix 9-91(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 3109 Female 100 mg/kg Day 45 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-92(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 3110 Female 100 mg/kg Day 45 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Animal No. 3111 Female 100 mg/kg Day 54 Not copulated

All tissues Not remarkable

Liver	Microgranuloma: minimal
Lung(bronchus)	Aggregation,foamy cell: minimal
Spleen	Hematopoiesis,extramedullary: minimal

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, Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland, submandibular, Sciatic nerve, Stomach
Skeletal muscle, femoral, Spinal cord, thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-94(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 3112 Female 100 mg/kg Day 42 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Stomach

Appendix 9-95(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4101 Female 500 mg/kg Day 43 End of administration period (L4)

Gross pathology:

Spleen	Small: mild partical
Other tissues	Not remarkable

Histopathology:

Lung(bronchus)	Aggregation,foamy cell: minimal
Spleen	Hematopoiesis,extramedullary: minimal No finding correlating with necropsy data

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, Ovary, Parathyroid
Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve, Stomach
Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-96(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4102 Female 500 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

Kidney Regeneration, tubular: minimal
proximal

Spleen Hematopoiesis, extramedullary: mild

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), Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland, submandibular, Sciatic nerve, Stomach
Skeletal muscle, femoral, Spinal cord, thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-97(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4103 Female 500 mg/kg Day 42 End of administration period (L4)

Gross pathology:

Stomach Focus, dark red, glandular stomach: 1 present
1x2mm

Other tissues Not remarkable

Histopathology:

Liver Microgranuloma: minimal

Spleen Hematopoiesis, extramedullary: mild

Stomach Erosion, 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, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland, submandibular, Sciatic nerve.
Skeletal muscle, femoral, Spinal cord, thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Animal No. 4104 Female 500 mg/kg Day 43 End of administration period (L4)

All tissues Not remarkable

Liver Microgranuloma: minimal

Spleen Hematopoiesis,extramedullary: mild

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, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland, submandibular, Sciatic nerve
Stomach, Skeletal muscle, femoral, Spinal cord, thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-99(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4105 Female 500 mg/kg Day 46 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-100(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4106 Female 500 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-101(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4107 Female 500 mg/kg Day 45 End of administration period (L4)

Gross pathology:

Stomach Focus, dark red, glandular stomach: 2 present
1x1mm, 1x1mm

Other tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-102(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4108 Female 500 mg/kg Day 46 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-103(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4109 Female 500 mg/kg Day 44 End of administration period (L4)

Gross pathology:

Stomach Focus, dark red, glandular stomach: 4 present
1x1mm, 1x1mm, 1x2mm, 1x2mm

Other tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-104(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4110 Female 500 mg/kg Day 46 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-105(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4111 Female 500 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

Spleen Hematopoiesis,extramedullary: mild

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), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-106(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4112 Female 500 mg/kg Day 44 End of administration period (L4)

Gross pathology:

Stomach Focus, dark red, glandular stomach: many
1x1mm

Other tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-107(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4113 Female 500 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Microgranuloma: 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, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea
Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-108(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4114 Female 500 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

Eye Dysplasia,retinal: minimal

Liver Microgranuloma: minimal

Stomach Hyperplasia,squamous,limiting ridge: 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, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Spleen, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-109(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4115 Female 500 mg/kg Day 43 End of administration period (D42)

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), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea
Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-110(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4116 Female 500 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Microgranuloma: minimal

Stomach Hyperplasia, squamous, limiting ridge: 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, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland, submandibular, Sciatic nerve
Spleen, Skeletal muscle, femoral, Spinal cord, thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-111(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4117 Female 500 mg/kg Day 43 End of administration period (D42)

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), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland, submandibular, Sciatic nerve
Spleen, Stomach, Skeletal muscle, femoral, Spinal cord, thoracic, Thymus, Trachea
Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-112(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4118 Female 500 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Stomach, Uterus

Appendix 9-113(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4119 Female 500 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Stomach, Uterus

Appendix 9-114(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4120 Female 500 mg/kg Day 57 End of recovery period

Gross pathology:

Stomach Focus, dark red, glandular stomach: 1 present
1x1mm

Other tissues Not remarkable

Histopathology:

Stomach Erosion, glandular stomach: minimal

Following tissues : Not remarkable

Uterus

Appendix 9-115(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4121 Female 500 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Stomach, Uterus

Appendix 9-116(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol, 2-butyl-2-ethyl by oral administration in rats

Individual gross and histopathological findings

Animal No. 4122 Female 500 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Stomach, Uterus

Appendix 10-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual estrous cycle in female rats during the pre-mating period

Dose (mg/kg): 0

Animal number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)	Count of estrus	Mean duration of cycles
1101	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0
1102	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0
1103	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0
1104	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0
1105	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0
1106	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0
1107	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0
1108	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0
1109	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0
1110	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0
1111	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0
1112	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0
Mean																3.7	4.0
S.D.																0.5	0.0

P: Proestrus E: Estrus M: Metestrus D: Diestrus
a): Day of sampling

Appendix 10-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual estrous cycle in female rats during the pre-mating period

Dose (mg/kg): 20

Animal number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)	Count of estrus	Mean duration of cycles
2101	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0
2102	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0
2103	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0
2104	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0
2105	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0
2106	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0
2107	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0
2108	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0
2109	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0
2110	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0
2111	P	E	M	D	D	P	E	M	D	D	P	E	M	D	P	3	5.0
2112	E	M	D	P	E	M	D	D	P	E	M	D	P	E	M	4	4.3
Mean																3.8	4.1
S.D.																0.5	0.3

P: Proestrus E: Estrus M: Metestrus D: Diestrus
a): Day of sampling

Appendix 10-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual estrous cycle in female rats during the pre-mating period

Dose (mg/kg): 100

Animal number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)	Count of estrus	Mean duration of cycles
3101	E	M	D	P	E	M	D	P	E	M	D	D	P	E	M	4	4.3
3102	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0
3103	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0
3104	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0
3105	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0
3106	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0
3107	E	M	D	D	P	E	M	D	D	P	E	M	D	D	P	3	5.0
3108	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0
3109	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0
3110	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0
3111	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0
3112	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0
Mean																3.8	4.1
S.D.																0.4	0.3

P: Proestrus E: Estrus M: Metestrus D: Diestrus
a): Day of sampling

Appendix 10-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual estrous cycle in female rats during the pre-mating period

Dose (mg/kg): 500

Animal number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)	Count of estrus	Mean duration of cycles
4101	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0
4102	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0
4103	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0
4104	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0
4105	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0
4106	M	D	P	E	M	D	P	E	M	D	D	P	E	M	D	3	4.5
4107	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0
4108	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0
4109	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0
4110	P	E	M	D	P	E	M	D	P	E	M	D	P	E	E	4	4.0
4111	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0
4112	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0
Mean																3.6	4.0
S.D.																0.5	0.1

P: Proestrus E: Estrus M: Metestrus D: Diestrus
a): Day of sampling

Appendix 11-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual mating and fertility of animals

Dose (mg/kg): 0

Pairing number		Copulated or not copulated	Days until copulation	Pregnant or non-pregnant
Male	Female			
1001	1101	C	2	P
1002	1102	C	2	P
1003	1103	C	1	P
1004	1104	C	1	P
1005	1105	C	2	P
1006	1106	C	3	P
1007	1107	C	4	P
1008	1108	C	1	P
1009	1109	C	3	P
1010	1110	C	1	P
1011	1111	C	6	P
1012	1112	C	4	P

C: Copulated P: Pregnant

Appendix 11-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual mating and fertility of animals

Dose (mg/kg): 20

Pairing number		Copulated or not copulated	Days until copulation	Pregnant or non-pregnant
Male	Female			
2001	2101	C	2	P
2002	2102	C	1	P
2003	2103	C	1	P
2004	2104	C	2	P
2005	2105	C	3	P
2006	2106	C	2	P
2007	2107	C	4	P
2008	2108	C	2	P
2009	2109	C	1	NP
2010	2110	C	3	P
2011	2111	C	1	P
2012	2112	C	3	P

C: Copulated P: Pregnant NP: Non-pregnant

Appendix 11-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual mating and fertility of animals

Dose (mg/kg): 100

Pairing number Male	Female	Copulated or not copulated	Days until copulation	Pregnant or non-pregnant
3001	3101	C	3	P
3002	3102	C	2	P
3003	3103	C	4	P
3004	3104	C	3	P
3005	3105	C	2	P
3006	3106	C	1	P
3007	3107	C	1	P
3008	3108	C	2	P
3009	3109	C	3	P
3010	3110	C	4	P
3011	3111	NC	-	-
3012	3112	C	1	P

C: Copulated NC: Not copulated P: Pregnant

Appendix 11-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual mating and fertility of animals

Dose (mg/kg): 500

Pairing number Male	Female	Copulated or not copulated	Days until copulation	Pregnant or non-pregnant
4001	4101	C	1	P
4002	4102	C	1	P
4003	4103	C	1	P
4004	4104	C	2	P
4005	4105	C	3	P
4006	4106	C	2	P
4007	4107	C	4	P
4008	4108	C	4	P
4009	4109	C	3	P
4010	4110	C	4	P
4011	4111	C	1	P
4012	4112	C	2	P

C: Copulated

P: Pregnant

Appendix 12-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Delivery data on dams

Dose (mg/kg): 0

Dam number	Gestation length in days	No. of corpora lutea	No. of implantation sites	Implantation index % a)	No. of stillborns (%)b)	No. of liveborns	External c) abnormalities(%)d)	Live birth index % e)
1101	22	15	15	100.0	0(0.0)	14	0(0.0)	93.3
1102	22	19	12	63.2	0(0.0)	6	0(0.0)	50.0
1103	22	14	13	92.9	0(0.0)	12	0(0.0)	92.3
1104	21	17	14	82.4	0(0.0)	14	0(0.0)	100.0
1105	22	17	15	88.2	0(0.0)	14	0(0.0)	93.3
1106	22	14	11	78.6	0(0.0)	10	0(0.0)	90.9
1107	22	20	20	100.0	1(5.3)	18	0(0.0)	90.0
1108	21	19	17	89.5	1(5.9)	16	0(0.0)	94.1
1109	22	15	15	100.0	0(0.0)	15	0(0.0)	100.0
1110	22	16	16	100.0	0(0.0)	14	0(0.0)	87.5
1111	21	15	15	100.0	0(0.0)	13	0(0.0)	86.7
1112	21	21	19	90.5	0(0.0)	18	0(0.0)	94.7
Total		202	182		2	164	0	
Mean	21.7	16.8	15.2	90.4	(0.9)	13.7	(0.0)	89.4
S.D.	0.5	2.4	2.6	11.3	(2.2)	3.3	(0.0)	13.1

a): (No. of implantation sites / No. of corpora lutea) × 100

b): (No. of stillborns / No. of liveborns and stillborns) × 100

c): No. of delivered pups with external abnormalities

d): (No. of delivered pups with external abnormalities / No. of liveborns and stillborns) × 100

e): (No. of liveborns / No. of implantation sites) × 100

Appendix 12-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Delivery data on dams

Dose (mg/kg): 20

Dam number	Gestation length in days	No. of corpora lutea	No. of implantation sites	Implantation index % a)	No. of stillborns (%)b)	No. of liveborns	External abnormalities(%)c)d)	Live birth index % e)
2101	22	17	16	94.1	0(0.0)	16	0(0.0)	100.0
2102	22	15	13	86.7	0(0.0)	13	0(0.0)	100.0
2103	21	15	15	100.0	0(0.0)	14	0(0.0)	93.3
2104	22	16	16	100.0	0(0.0)	16	0(0.0)	100.0
2105	22	12	10	83.3	0(0.0)	10	0(0.0)	100.0
2106	21	18	17	94.4	0(0.0)	17	0(0.0)	100.0
2107	22	16	16	100.0	1(6.3)	15	0(0.0)	93.8
2108	21	14	14	100.0	0(0.0)	13	0(0.0)	92.9
2109	Non-pregnant							
2110	22	13	13	100.0	0(0.0)	12	0(0.0)	92.3
2111	22	15	14	93.3	0(0.0)	10	0(0.0)	71.4
2112	22	17	16	94.1	0(0.0)	16	0(0.0)	100.0
Total		168	160		1	152	0	
Mean	21.7	15.3	14.5	95.1	(0.6)	13.8	(0.0)	94.9
S.D.	0.5	1.8	2.0	5.8	(1.9)	2.4	(0.0)	8.5

a): (No. of implantation sites / No. of corpora lutea) × 100

b): (No. of stillborns / No. of liveborns and stillborns) × 100

c): No. of delivered pups with external abnormalities

d): (No. of delivered pups with external abnormalities / No. of liveborns and stillborns) × 100

e): (No. of liveborns / No. of implantation sites) × 100

Appendix 12-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Delivery data on dams

Dose (mg/kg): 100

Dam number	Gestation length in days	No. of corpora lutea	No. of implantation sites	Implantation index % a)	No. of stillborns (%)b)	No. of liveborns	External c) abnormalities(%)d)	Live birth index % e)
3101	22	19	18	94.7	0(0.0)	17	0(0.0)	94.4
3102	22	15	13	86.7	0(0.0)	13	0(0.0)	100.0
3103	21	16	16	100.0	0(0.0)	16	0(0.0)	100.0
3104	21	19	15	78.9	0(0.0)	13	0(0.0)	86.7
3105	22	16	16	100.0	0(0.0)	16	0(0.0)	100.0
3106	21	15	15	100.0	0(0.0)	12	0(0.0)	80.0
3107	22	15	13	86.7	0(0.0)	13	0(0.0)	100.0
3108	22	17	16	94.1	0(0.0)	13	0(0.0)	81.3
3109	22	14	14	100.0	0(0.0)	12	0(0.0)	85.7
3110	21	17	14	82.4	0(0.0)	13	0(0.0)	92.9
3111	Not copulated							
3112	21	16	16	100.0	0(0.0)	13	0(0.0)	81.3
Total		179	166		0	151	0	
Mean	21.5	16.3	15.1	93.0	(0.0)	13.7	(0.0)	91.1
S.D.	0.5	1.6	1.5	8.0	(0.0)	1.7	(0.0)	8.3

a): (No. of implantation sites / No. of corpora lutea) × 100

b): (No. of stillborns / No. of liveborns and stillborns) × 100

c): No. of delivered pups with external abnormalities

d): (No. of delivered pups with external abnormalities / No. of liveborns and stillborns) × 100

e): (No. of liveborns / No. of implantation sites) × 100

Appendix 12-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Delivery data on dams

Dose (mg/kg): 500

Dam number	Gestation length in days	No. of corpora lutea	No. of implantation sites	Implantation index % a)	No. of stillborns (%)b)	No. of liveborns	External abnormalities(%)d)	Live birth index % e)
4101	22	14	14	100.0	0(0.0)	14	0(0.0)	100.0
4102	22	16	15	93.8	1(6.7)	14	0(0.0)	93.3
4103	21	18	18	100.0	0(0.0)	17	0(0.0)	94.4
4104	21	18	18	100.0	0(0.0)	17	0(0.0)	94.4
4105	23	14	13	92.9	0(0.0)	5	0(0.0)	38.5
4106	22	17	15	88.2	0(0.0)	14	0(0.0)	93.3
4107	21	15	15	100.0	0(0.0)	14	0(0.0)	93.3
4108	22	15	15	100.0	0(0.0)	13	0(0.0)	86.7
4109	21	17	15	88.2	0(0.0)	15	0(0.0)	100.0
4110	22	15	15	100.0	0(0.0)	15	0(0.0)	100.0
4111	22	13	13	100.0	0(0.0)	13	0(0.0)	100.0
4112	22	18	13	72.2	0(0.0)	12	0(0.0)	92.3
Total		190	179		1	163	0	
Mean	21.8	15.8	14.9	94.6	(0.6)	13.6	(0.0)	90.5
S.D.	0.6	1.7	1.7	8.5	(1.9)	3.1	(0.0)	16.9

a): (No. of implantation sites / No. of corpora lutea) × 100

b): (No. of stillborns / No. of liveborns and stillborns) × 100

c): No. of delivered pups with external abnormalities

d): (No. of delivered pups with external abnormalities / No. of liveborns and stillborns) × 100

e): (No. of liveborns / No. of implantation sites) × 100

Appendix 13-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual viability index of pups

Dose (mg/kg): 0

Dam number	No. of live pups		Viability index on postnatal day 4 % a)
	Day 0	Day 4	
1101	14	14	100.0
1102	6	6	100.0
1103	12	12	100.0
1104	14	14	100.0
1105	14	14	100.0
1106	10	10	100.0
1107	18	17	94.4
1108	16	14	87.5
1109	15	15	100.0
1110	14	14	100.0
1111	13	12	92.3
1112	18	18	100.0
Total	164	160	
Mean	13.7	13.3	97.9
S.D.	3.3	3.1	4.2

a): (No. of live pups on postnatal day 4 / No. of liveborns) $\times$ 100

Appendix 13-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual viability index of pups

Dose (mg/kg): 20

Dam number	No. of live pups		Viability index on postnatal day 4 % a)
	Day 0	Day 4	
2101	16	16	100.0
2102	13	13	100.0
2103	14	13	92.9
2104	16	16	100.0
2105	10	10	100.0
2106	17	15	88.2
2107	15	15	100.0
2108	13	13	100.0
2109	Non-pregnant		
2110	12	12	100.0
2111	10	10	100.0
2112	16	16	100.0
Total	152	149	
Mean	13.8	13.5	98.3
S.D.	2.4	2.3	4.0

a): (No. of live pups on postnatal day 4 / No. of liveborns) × 100

Appendix 13-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual viability index of pups

Dose (mg/kg): 100

Dam number	No. of live pups		Viability index on postnatal day 4 % a)
	Day 0	Day 4	
3101	17	16	94.1
3102	13	13	100.0
3103	16	16	100.0
3104	13	13	100.0
3105	16	16	100.0
3106	12	11	91.7
3107	13	13	100.0
3108	13	13	100.0
3109	12	12	100.0
3110	13	13	100.0
3111	Not copulated		
3112	13	13	100.0
Total	151	149	
Mean	13.7	13.5	98.7
S.D.	1.7	1.7	2.9

a): (No. of live pups on postnatal day 4 / No. of liveborns) $\times$ 100

Appendix 13-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual viability index of pups

Dose (mg/kg): 500

Dam number	No. of live pups		Viability index on postnatal day 4 % a)
	Day 0	Day 4	
4101	14	14	100.0
4102	14	14	100.0
4103	17	17	100.0
4104	17	16	94.1
4105	5	5	100.0
4106	14	14	100.0
4107	14	14	100.0
4108	13	12	92.3
4109	15	15	100.0
4110	15	15	100.0
4111	13	13	100.0
4112	12	12	100.0
Total	163	161	
Mean	13.6	13.4	98.9
S.D.	3.1	3.0	2.7

a): (No. of live pups on postnatal day 4 / No. of liveborns) $\times$ 100

Appendix 14-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual sex ratio of pups

Dose (mg/kg): 0

Dam number	Liveborns		Sex ratio of liveborns at birth a)	Postnatal day 4		Sex ratio of live pups on day 4 b)
	No. of males	No. of females		No. of males	No. of females	
1101	6	8	0.43	6	8	0.43
1102	4	2	0.67	4	2	0.67
1103	9	3	0.75	9	3	0.75
1104	7	7	0.50	7	7	0.50
1105	9	5	0.64	9	5	0.64
1106	2	8	0.20	2	8	0.20
1107	7	11	0.39	7	10	0.41
1108	9	7	0.56	8	6	0.57
1109	7	8	0.47	7	8	0.47
1110	8	6	0.57	8	6	0.57
1111	0	13	0.00	0	12	0.00
1112	7	11	0.39	7	11	0.39
Total	75	89		74	86	
Mean	6.3	7.4	0.46	6.2	7.2	0.47
S.D.	2.9	3.2	0.21	2.8	3.0	0.21

a): No. of liveborn males / No. of liveborns

b): No. of live males on day 4 / No. of live pups on day 4

Appendix 14-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual sex ratio of pups

Dose (mg/kg): 20

Dam number	Liveborns		Sex ratio of liveborns at birth a)	Postnatal day 4		Sex ratio of live pups on day 4 b)
	No. of males	No. of females		No. of males	No. of females	
2101	6	10	0.38	6	10	0.38
2102	8	5	0.62	8	5	0.62
2103	8	6	0.57	7	6	0.54
2104	5	11	0.31	5	11	0.31
2105	3	7	0.30	3	7	0.30
2106	4	13	0.24	3	12	0.20
2107	6	9	0.40	6	9	0.40
2108	7	6	0.54	7	6	0.54
2109	Non-pregnant					
2110	7	5	0.58	7	5	0.58
2111	2	8	0.20	2	8	0.20
2112	8	8	0.50	8	8	0.50
Total	64	88		62	87	
Mean	5.8	8.0	0.42	5.6	7.9	0.42
S.D.	2.1	2.6	0.15	2.1	2.4	0.15

a): No. of liveborn males / No. of liveborns

b): No. of live males on day 4 / No. of live pups on day 4

Appendix 14-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual sex ratio of pups

Dose (mg/kg): 100

Dam number	Liveborns		Sex ratio of liveborns at birth a)	Postnatal day 4		Sex ratio of live pups on day 4 b)
	No. of males	No. of females		No. of males	No. of females	
3101	11	6	0.65	11	5	0.69
3102	6	7	0.46	6	7	0.46
3103	4	12	0.25	4	12	0.25
3104	8	5	0.62	8	5	0.62
3105	6	10	0.38	6	10	0.38
3106	6	6	0.50	6	5	0.55
3107	6	7	0.46	6	7	0.46
3108	7	6	0.54	7	6	0.54
3109	6	6	0.50	6	6	0.50
3110	8	5	0.62	8	5	0.62
3111	Not copulated					
3112	6	7	0.46	6	7	0.46
Total	74	77		74	75	
Mean	6.7	7.0	0.49	6.7	6.8	0.50
S.D.	1.8	2.1	0.12	1.8	2.3	0.12

a): No. of liveborn males / No. of liveborns

b): No. of live males on day 4 / No. of live pups on day 4

Appendix 14-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual sex ratio of pups

Dose (mg/kg): 500

Dam number	Liveborns		Sex ratio of liveborns at birth a)	Postnatal day 4		Sex ratio of live pups on day 4 b)
	No. of males	No. of females		No. of males	No. of females	
4101	3	11	0.21	3	11	0.21
4102	8	6	0.57	8	6	0.57
4103	9	8	0.53	9	8	0.53
4104	10	7	0.59	9	7	0.56
4105	3	2	0.60	3	2	0.60
4106	7	7	0.50	7	7	0.50
4107	7	7	0.50	7	7	0.50
4108	8	5	0.62	7	5	0.58
4109	8	7	0.53	8	7	0.53
4110	11	4	0.73	11	4	0.73
4111	8	5	0.62	8	5	0.62
4112	8	4	0.67	8	4	0.67
Total	90	73		88	73	
Mean	7.5	6.1	0.56	7.3	6.1	0.55
S.D.	2.4	2.3	0.13	2.3	2.3	0.13

a): No. of liveborn males / No. of liveborns

b): No. of live males on day 4 / No. of live pups on day 4

Appendix 15-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual body weight of pups

Dose (mg/kg): 0

Dam number	Male			Female		
	0	4a)	Gain	0	4a)	Gain
1101	7.5	11.1	3.6	6.7	10.2	3.5
1102	7.3	14.0	6.7	6.7	13.0	6.3
1103	7.1	10.0	2.9	7.2	9.5	2.3
1104	6.1	9.6	3.5	5.8	9.4	3.6
1105	6.4	10.1	3.7	6.1	9.9	3.8
1106	6.8	10.7	3.9	6.4	10.4	4.0
1107	6.4	9.0	2.6	6.1	8.6	2.5
1108	5.7	8.9	3.2	5.4	8.4	3.0
1109	6.5	9.9	3.4	5.9	9.3	3.4
1110	6.9	11.4	4.5	6.6	10.7	4.1
1111	b)			6.1	8.7	2.6
1112	5.8	8.5	2.7	5.4	7.9	2.5
Mean	6.6	10.3	3.7	6.2	9.7	3.5
S.D.	0.6	1.5	1.1	0.5	1.4	1.1

Unit: g

a): Postnatal day

b): No male pups were born.

Appendix 15-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual body weight of pups

Dose (mg/kg): 20

Dam number	Male			Female		
	0	4a)	Gain	0	4a)	Gain
2101	6.1	8.2	2.1	6.0	8.0	2.0
2102	6.5	9.9	3.4	6.1	9.3	3.2
2103	6.4	9.7	3.3	5.9	9.0	3.1
2104	6.0	9.4	3.4	6.0	9.3	3.3
2105	7.2	11.2	4.0	6.6	10.5	3.9
2106	5.8	8.5	2.7	5.7	8.3	2.6
2107	6.6	10.2	3.6	6.1	9.6	3.5
2108	6.1	8.7	2.6	5.9	8.0	2.1
2109	Non-pregnant					
2110	7.0	11.5	4.5	6.5	11.1	4.6
2111	7.0	10.3	3.3	6.8	10.1	3.3
2112	7.0	9.7	2.7	6.4	9.1	2.7
Mean	6.5	9.8	3.2	6.2	9.3	3.1
S.D.	0.5	1.0	0.7	0.3	1.0	0.8

Unit: g

a): Postnatal day

Appendix 15-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual body weight of pups

Dose (mg/kg): 100

Dam number	Male			Female		
	0	4a)	Gain	0	4a)	Gain
3101	6.2	8.6	2.4	5.7	8.0	2.3
3102	6.6	10.3	3.7	6.1	10.0	3.9
3103	6.1	9.4	3.3	5.8	8.5	2.7
3104	5.9	8.7	2.8	5.6	8.2	2.6
3105	6.6	10.5	3.9	6.2	9.4	3.2
3106	6.4	9.8	3.4	5.9	9.3	3.4
3107	7.1	10.4	3.3	6.7	10.6	3.9
3108	7.0	11.8	4.8	6.7	10.8	4.1
3109	6.9	10.5	3.6	6.4	9.9	3.5
3110	6.3	10.3	4.0	6.1	9.6	3.5
3111	Not copulated					
3112	6.6	9.6	3.0	6.1	8.9	2.8
Mean	6.5	10.0	3.5	6.1	9.4	3.3
S.D.	0.4	0.9	0.6	0.4	0.9	0.6

Unit: g

a): Postnatal day

Appendix 15-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual body weight of pups

Dose (mg/kg): 500

Dam number	Male			Female		
	0	4a)	Gain	0	4a)	Gain
4101	7.5	11.1	3.6	6.9	10.3	3.4
4102	7.2	9.9	2.7	7.0	9.4	2.4
4103	5.9	7.7	1.8	5.4	7.2	1.8
4104	5.5	7.6	2.1	5.3	7.4	2.1
4105	6.9	12.1	5.2	7.9	14.1	6.2
4106	6.7	10.1	3.4	6.3	9.4	3.1
4107	6.4	9.2	2.8	5.8	8.4	2.6
4108	6.9	11.4	4.5	6.2	10.0	3.8
4109	6.0	8.7	2.7	5.6	8.0	2.4
4110	6.4	7.0	0.6	5.8	6.6	0.8
4111	6.5	10.6	4.1	6.1	9.9	3.8
4112	6.7	10.6	3.9	6.5	10.3	3.8
Mean	6.6	9.7	3.1	6.2	9.3	3.0
S.D.	0.6	1.6	1.3	0.8	2.0	1.4

Unit: g

a): Postnatal day

Appendix 16-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual externally for gross abnormalities in pups on postnatal day 4

Dose (mg/kg): 0

Dam number	No. of pups examined				Findings
	Total (Male + Female)				
1101	14	(	6	+ 8)	NAF
1102	6	(	4	+ 2)	NAF
1103	12	(	9	+ 3)	NAF
1104	14	(	7	+ 7)	NAF
1105	14	(	9	+ 5)	NAF
1106	10	(	2	+ 8)	NAF
1107	17	(	7	+ 10)	NAF
1108	14	(	8	+ 6)	NAF
1109	15	(	7	+ 8)	NAF
1110	14	(	8	+ 6)	NAF
1111	12	(	0	+ 12)	NAF
1112	18	(	7	+ 11)	NAF

NAF: No abnormal findings

Appendix 16-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual externally for gross abnormalities in pups on postnatal day 4

Dose (mg/kg): 20

Dam number	No. of pups examined				Findings
	Total (Male + Female)				
2101	16	(	6	+ 10)	NAF
2102	13	(	8	+ 5)	NAF
2103	13	(	7	+ 6)	NAF
2104	16	(	5	+ 11)	NAF
2105	10	(	3	+ 7)	NAF
2106	15	(	3	+ 12)	NAF
2107	15	(	6	+ 9)	NAF
2108	13	(	7	+ 6)	NAF
2109	Non-pregnant				
2110	12	(	7	+ 5)	NAF
2111	10	(	2	+ 8)	NAF
2112	16	(	8	+ 8)	NAF

NAF: No abnormal findings

Appendix 16-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual externally for gross abnormalities in pups on postnatal day 4

Dose (mg/kg): 100

Dam number	No. of pups examined Total (Male + Female)				Findings
3101	16	(	11	+ 5)	NAF
3102	13	(	6	+ 7)	NAF
3103	16	(	4	+ 12)	NAF
3104	13	(	8	+ 5)	NAF
3105	16	(	6	+ 10)	NAF
3106	11	(	6	+ 5)	NAF
3107	13	(	6	+ 7)	NAF
3108	13	(	7	+ 6)	NAF
3109	12	(	6	+ 6)	NAF
3110	13	(	8	+ 5)	NAF
3111	Not copulated				
3112	13	(	6	+ 7)	NAF

NAF: No abnormal findings

Appendix 16-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 1,3-Propanediol,2-butyl-2-ethyl by oral administration in rats

Individual externally for gross abnormalities in pups on postnatal day 4

Dose (mg/kg): 500

Dam number	No. of pups examined					Findings
	Total	(	Male	+	Female)	
4101	14	(	3	+	11)	NAF
4102	14	(	8	+	6)	NAF
4103	17	(	9	+	8)	NAF
4104	16	(	9	+	7)	NAF
4105	5	(	3	+	2)	NAF
4106	14	(	7	+	7)	NAF
4107	14	(	7	+	7)	NAF
4108	12	(	7	+	5)	NAF
4109	15	(	8	+	7)	NAF
4110	15	(	11	+	4)	NAF
4111	13	(	8	+	5)	NAF
4112	12	(	8	+	4)	NAF

NAF: No abnormal findings