試験番号:R-15-003

最終報告書

酢酸ヘキシルのラットを用いる
反復投与毒性・生殖発生毒性併合試験

厚生労働省医薬・生活衛生局審査管理課 化学物質安全対策室 委託

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試験番号	R-15-003
被験物質	酢酸ヘキシル
試験項目	反復投与毒性・生殖発生毒性併合試験
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試験終了日	試験責任者の押印日
試資料保管場所	秦野研究所資料保存施設
被験物質保管場所	秦野研究所資料保存施設
保管期間	試験終了後 10 年間 その後の保管については試験委託者と協議する。
運営管理者	一般財団法人食品薬品安全センター 秦野研究所 所長 [redacted]

本試験は、「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 日付け、薬食発 0331 第 7 号厚生労働省医薬食品局長、平成 23・03・29 製局第 5 号経済産業省製造産業局長、環保企発第 110331009 号環境省総合環境政策局長通知)に準拠し、「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 日付け、薬食発 0331 第 8 号厚生労働省医薬食品局長、平成 23・03・29 製局第 6 号経済産業省製造産業局長、環保企発第 110331010 号環境省総合環境政策局長通知)を遵守して実施した。

2016 年 2 月 29 日　　試験責任者 [redacted]

試験従事者

試験責任者	[redacted]
試験担当主任者	
試験担当者 投与観察	
動物飼育管理 (検疫を含む)	
血液学的検査 (採血を含む) 血液生化学的検査 尿検査 病理学検査	
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要約

酢酸ヘキシルの反復投与毒性・生殖発生毒性併合試験を化審法ガイドラインに従って実施した。被験物質をトウモロコシ油(媒体)に溶解して、0、100、300ならびに1000 mg/kgの用量で、各群とも雌雄各12匹のCrl:CD(SD)ラットに強制経口投与した。雄は42日間投与した後に剖検し、雌は交配前14日間および交配期間、妊娠期間を通して哺育4日まで41～49日間投与し、出生児は哺育4日、母動物は哺育5日に剖検した。また、0および1000 mg/kgの用量に非交配(サテライト)群(10匹/群)を設け、42日間投与した後に半数の5例を剖検した。回復性を確認するために、雄の0および1000 mg/kg群の各5例、雌の非交配群の各5例は42日間投与した後、14日間飼育して剖検した。

1. 反復投与毒性学的所見および回復群における所見

1000 mg/kg 投与群の雄および交配雌に被験物質の刺激性に起因すると考えられる投与後の一過性の流涎が観察された。

14日間の回復期間終了後、遅発毒性と考えられる変化はみられなかった。

2. 生殖発生毒性学的所見および出生児所見

1000 mg/kg 投与群では分娩率[(産児数/着床痕数)×100, %]および生児出産率[(出産生児数/着床痕数)×100, %]の低下が認められた。

3. 無毒性量

反復投与毒性学的所見においては1000 mg/kg投与群で被験物質の刺激性に起因すると考えられた一過性の流涎が観察されたのみであったことから、本試験条件下における酢酸ヘキシルの親動物に対する一般毒性学的無毒性量は雌雄ともに 1000 mg/kg/day、生殖発生毒性および次世代児に対する無毒性量は1000 mg/kg 投与群で分娩率および生児出産率の低下が認められたことから300 mg/kg/dayと考えられた。

試験目的

本試験は、ラットに酢酸ヘキシル(HA)を一定期間反復投与した時に現れる反復投与毒性および回復性、ならびに生殖発生毒性および新生児の発育に及ぼす影響を明らかにすることを目的とした。

試験ガイドラインとGLP

本試験は、「新規化学物質等に係る試験の方法について:以下、化審法ガイドライン」(平成23年3月31日付け、薬食発0331第7号厚生労働省医薬食品局長、平成23・03・29製局第5号経済産業省製造産業局長、環保企発第110331009号環境省総合環境政策局長通知)に準拠し、「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日付け、薬食発0331第8号厚生労働省医薬食品局長、平成23・03・29製局第6号経済産業省製造産業局長、環保企発第110331010号環境省総合環境政策局長通知)を遵守して実施した。

動物愛護

全ての実験操作は、「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、平成26年5月30日 一部改正)、「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、平成25年8月30日 一部改正)および「厚生労働省の所管する実施機関における動物実験等の実施に関する基本指針」(平成27年2月20日、科発0220第1号)を遵守し、「一般財団法人食品薬品安全センター 動物実験に関する指針(機関内規程)」(平成2年10月1日、平成27年4月20日改定)に基づいて実施した。本試験における動物実験計画は、秦野研究所動物実験委員会の審査を受け、承認されている(動物実験承認番号:1150202A)。なお、承認された動物実験計画からの変更はなかった。

材料と方法

1. 被験物質

1) 名称	酢酸ヘキシル
2) 英名	Hexyl acetate
3) 別名	Acetic acid hexyl ester
4) 略称	HA
5) CAS番号	142-92-7
6) 分子式	$C_8H_{16}O_2$
7) 分子量	144.21

8) 物理化学的性質　外観・性状:無色透明な液体、果香

融点:情報なし

沸点:169℃

蒸気圧:176Pa/25℃

引火点:62℃

比重:0.8745

屈折率:1.4091

溶解度:水に不溶、エーテル、アルコール、プロピレングリコールに易溶

9) 構造式

10) ロット番号　NWQZH(Annex A)

11) 純度　99.5%(GC)

12) 不純物　情報なし

13) 安定性

実験開始前(2015年9月16日)、実験終了後(2016年1月5日)に秦野研究所にて性状の確認および赤外吸収スペクトルを測定し、色調や性状、スペクトルに変化がないことを確認した(Annex B)。

14)取り扱い上の注意　引火性あり

15)保管条件　冷蔵(実測値3～7℃)、遮光、密閉

16)購入元　東京化成工業株式会社(被験物質入手:2015年8月19日)

17)被験物質の保管　秦野研究所資料保存施設に5gを保管した。

2. 動物および飼育方法

日本チャールス・リバー厚木飼育センターより8週齢のSprague-Dawley(SD)系〔Crl:CD(SD)、SPF〕ラットの雄55匹、雌83匹を購入し、6号室に収容した。入荷日も含めて15日間、検疫と飼育環境への馴化のため飼育した。その間毎日、動物の一般状態を観察し、入荷日(検疫1日)および検疫終了日に体重を測定した。検疫・馴化期間中は動物の尾にフェルトペンで馴化番号を記し、飼育ケージに試験番号、性別および馴化番号を記入した動物カードを掛けて識別した。また、雌動物については、検疫3日から毎日、性周期を観察した。入荷動物の入荷時および検疫終了時の体重は下記の通りであった。

動物入荷日　:2015年9月14日

入荷時体重　:雄252.9～294.5 g、雌176.5～209.9 g

検疫終了日　:2015年9月28日

検疫終了時体重　:雄356.3～460.1 g、雌201.3～268.2 g

検疫・馴化の結果、入荷した動物において、検疫期間中の一般状態および体重推移に異常は認められなかった。詳細な症状観察では雄1匹(馴化番号M00014)の背部に痂皮がみられた。雄動物では一般状態に異常が観察された1匹、雌動物では規則的な4または5日の性周期の回帰が認められない7

匹を除外し、体重別層化無作為抽出法により群分けを行った。群分けした動物には一連の動物番号を割り当て、フェルトペンで尾に動物番号を標識し、色彩の異なった動物カードに試験番号、性別および動物番号を記入して飼育ケージに掛けた。群分けから除外した雄動物 7 匹、雌動物 15 匹は全て余剰動物とし、他目的に転用した。

動物は許容温度 21.0～25.0℃、許容湿度 40.0～75.0%、換気設定約 15 回/時間、明暗サイクル 12 時間(7 時～19 時)点灯、12 時間(19 時～7 時)消灯に設定された飼育室内で、金属製金網床ケージ[220w×270d×190h mm、金属製休息板 130w×150d mm 付、交配期間(2 週間)は雄動物ケージ内の金属製休息板は使用せず]に1匹ずつ(交配時は2匹)収容し、固型飼料(CE-2、日本クレア)と水道水(秦野市水道局給水)を自由に摂取させて飼育した。ただし、未分娩例および未交尾例を除いて解剖前に絶食させた。雌動物は分娩例全例について、妊娠 18 日から哺育 4 日までラット用プラスチック製繁殖ケージ(350w×400d×180h mm)に1匹ずつ収容し、床敷として紙パルプ製チップ(ペパークリーン、日本エスエルシー)を適宜供給した。飼育期間中の動物室の温度は 22.0～24.5℃、湿度は 51.5～74.0%であった。また、供給した飼料、飲料水および床敷の分析結果は、いずれも標準操作手順書に記載の許容範囲内であることを確認した。

3. 投与検体

1)調製

被験物質を秤量し、媒体(トウモロコシ油、製造元:ナカライテスク、製造番号:V3A0313)を加え撹拌混和させ、250 mg/mL 液を調製した。さらに、250 mg/mL 液を媒体によって希釈し、75.0 ならびに 25.0 mg/mL 液を段階的に調製した。調製した検体は冷蔵、遮光、密閉下(実測値 3～7℃)で保管し、安定性の保証期間内に使用した。

2)安定性試験

投与に先立ち、25 および 250 mg/mL 濃度の投与検体について、冷蔵、遮光条件下における 8 日間の安定性を確認した後、本試験の動物実験を開始した(安定性試験開始日 2015 年 9 月 17 日、8 日目:2015 年 9 月 25 日、Annex C)。

3)含量の測定

本試験の初回調製検体(調製日:2015 年 9 月 28 日)について、25.0、75.0 および 250 mg/mL の投与検体の含量を測定した。その結果、平均含量は調製濃度の 99.1～104.5%であり、各測定値のばらつきは平均値の 98.8～101.1%で規定範囲内にあった(Annex D)。

投与検体中の被験物質濃度は以下の方法で測定した。

25.0、75.0、250 mg/mL の投与検体 1 mL を正確にとり、2-プロパノール(以下 2-PrOH)を加えて適宜希釈して試料溶液(約 10 μg/mL あるいは約 15 μg/mL)を調製した。試料溶液の調製は投与検体の採取から n=3 とした。試料溶液および標準溶液を以下に示す測定条件でガスクロマトグラフィーにより測定し、標準溶液から作成した検量線を用いて投与検体中の HA 濃度を算出した。

試験条件

検出器	水素炎イオン化検出器(FID)
カラム	DB-5(内径 0.32 mm、長さ 30 m、膜厚 0.25 μm)、J&W Scientific
キャリアガス	ヘリウム(He、100 kPa)
カラム温度	50℃(1min)、15℃/min、140℃(30℃/min、300℃、4min)*
	*:媒体を含む試料溶液を測定する場合のみ実施
注入口温度	280℃
検出器温度	300℃
注入量	2 μL
注入方式	スプリットレス(サンプリング時間 0.5 分)
オートインジェクタ洗浄溶媒	2-PrOH

システム適合性

測定開始前に 2-PrOH を 1 回測定し、クロマトグラム上の測定対象物質の保持時間付近に妨害ピークがないことを確認した。また、測定開始前および測定終了後に標準溶液(St 3)を 1 回ずつ測定し、測定開始前に対する測定終了後の保持時間およびピーク面積の変動を確認した。変動の許容基準は保持時間の差が±0.5 分以内、ピーク面積が±5.0%以内(測定開始前に対する測定終了後の偏差%)を目安とした。

4. 投与量の設定および投与方法

本試験の投与量は、食品薬品安全センターにおいて GLP 基準で実施された「ヘキシルアセテートのラットを用いる 90 日間反復経口投与試験」(試験番号 C-13-006) [1]の結果をもとに設定した。すなわち、0(媒体、トウモロコシ油)、100、300 および 1000 mg/kg のヘキシルアセテート(酢酸ヘキシル、HA)を各群雌雄各 10 匹の 5 週齢の SD 系ラットに 90 日間、反復強制経口投与した結果、雄の 1000 mg/kg 投与群において被験物質投与による変化と考えられた尿潜血反応と血漿中無機リン濃度の増加がみられたが、雌雄ともに一般状態、体重、摂餌量、眼科学的検査、血液学的検査および病理学的検査結果に被験物質投与による毒性変化は認められなかった。したがって、1000 mg/kg の HA は被験物質の雌雄動物に対する一般毒性学的変化、さらに生殖毒性への影響も評価ができると考えられることから、1000 mg/kg を本試験における高用量群の投与量に設定し、以下、公比 3 で減じて、300 mg/kg を中用量、100 mg/kg を低用量に設定した。投与経路は化審法ガイドラインに拠り、ラット用胃管による強制経口投与とした。

本試験では、雄動物は交配前 14 日間、交配期間(最長 14 日間)を通して剖検前日まで(総投与回数 42 回)、雌動物は交配前 14 日間、交配期間、妊娠期間を通して分娩後の哺育 4 日まで、非妊娠雌の反復毒性を評価するために設定した非交配(サテライト)群では投与 42 日まで、経口的に 1 日 1 回、1 週 7 回、9 時 05 分～11 時 53 分に投与した。また、交尾は確認されたが分娩しなかった雌は剖検前日(妊娠 25 日相当日)まで、交尾が確認されなかった雌は剖検前日(投与 52 日)まで、分娩状態不良と判断した

雌は剖検前日(妊娠 22 日)まで投与した。投与容量は 4 mL/kg とし、雌雄ともに最新の測定日の体重を基準に投与液量を算出した。なお、対照群には媒体であるトウモロコシ油を同様に投与した。

本試験開始時の群構成および動物番号を次に示した。

群	投与物質	投与量 (mg/kg)	濃度 (mg/mL)	投与容量 (mL/kg)	動物番号	
					雄	雌
対照群	トウモロコシ油(媒体)	0	0	4	M01001～M01012*	F01001～F01012
低用量群	HA	100	25	4	M02013～M02024	F02013～F02024
中用量群	HA	300	75	4	M03025**～M03036	F03025～F03036
高用量群	HA	1000	250	4	M04037～M04048*	F04037～F04048
対照群[非交配(サテライト)群]	トウモロコシ油(媒体)	0	0	4	-	F05049～F05058*
高用量群[非交配(サテライト)群]	HA	1000	250	4	-	F06059～F06068*

* 雄の対照群および高用量群、雌の非交配群の動物番号の大きい各 5 例は回復観察に供した。
** 雄の中用量群の 1 例(動物番号 M03025)は投与 11 日に死亡したため、機能検査、尿検査、採血、血液学的検査、血液生化学的検査および病理組織学的検査の対象動物から除外した。

5. 検査法

1)親動物(F0)

①一般状態の観察

全例について、飼育期間中は毎日 1 回、投与期間中は投与前後の毎日 2 回観察した。

②回復および遅発毒性の観察

雄動物は対照群および高用量群のうち動物番号の大きい各 5 例を、雌動物は非交配(サテライト)群の動物番号の大きい各 5 例を最終投与翌日(回復 1 日)から 14 日間、毎日 1 回、前項に示した方法で、一般状態を観察した。

③詳細な症状観察

雌雄動物は検疫終了日、投与 8、15、23、29、35 および 42 日(分娩例は哺育 0 日から 4 日の間に 1 回)、回復期間中は回復 7 および 14 日にも、スコアリング法による詳細な症状観察を行った。なお、交尾確認までに日数を要した 100 mg/kg 投与群の 1 例、交尾が確認されなかった対照群および 1000 mg/kg 投与群の各 1 例は投与 49 日にも観察した。観察は、いずれも 13 時 10 分～15 時 02 分の間に行った。まず、ケージ越しでの観察を行い、ケージから取り出す際に外表を観察し、作業台上での観察を行った。作業台上では、体位、姿勢、探索行動、立毛、眼裂、振戦、痙攣、呼吸数、歩行、常同行動、奇妙な行動、挙尾反応、身づくろい、発声、排尿、排便、接触に対する反応、撤去反射、耳介反射を観察した。

④機能検査

握力測定および自発運動測定は、雄は投与 39 日に、雌は投与 41 日に検査した。また、投与 42 日(同居翌日に交尾が確認され、妊娠 21 日に分娩した雌 4 例は投与 39 日)の詳細な症状観察に引き続き、

雌雄ともに刺激に対する感覚運動反応を検査した。対象動物は雄および非交配(サテライト)群は各群の動物番号の若い5例とし、分娩雌は投与期間が近接し、可能な限り分娩から日数が経過した各群5例とした。

(1)刺激に対する感覚運動反応

プライエル反応、瞳孔反射、視覚定位、驚愕反応、後肢引込み反射、眼瞼(瞬目)反射、正向反射の有無を検査した。

(2)握力測定

ラット・マウス用握力測定装置(Model MK-380CM/R、室町機械)を用いて握力を測定した。各動物の前肢および後肢の握力をそれぞれ5回測定し、握力値の平均値を求めた。

(3)自発運動測定

自発運動量測定装置(SUPER-MEX、室町機械)を用いて、20分間の自発運動量(区画移動数および立ち上がり回数)を計測し、計測値は5分毎に集計した。試験対象動物は、検査直前に別室の装置設置場所(行動観察室2)に運搬し、速やかに自発運動測定を開始した。

⑤体重測定

雄および雌動物の非交配(サテライト)群は、投与1(投与開始日)、4、7、14、21、28、35、42日、回復1、7、14日および剖検日に測定した。雌動物は投与1、4、7、14日、妊娠0、7、14、20日、哺育0、4日および剖検日に測定した。交尾が確認されなかった雌では投与21、28、35、42、49日にも測定した。分娩が確認されなかった動物では妊娠26日相当日にも測定した。

⑥摂餌量測定

雄および雌動物の非交配(サテライト)群は、投与1～2、7～8、14～15、29～30、35～36、41～42日、回復6～7、12～13日に測定し、非交配(サテライト)群のみ投与21～22日にも測定した。雌動物は投与1～2、7～8、14～15日、妊娠0～1、7～8、14～15、20～21日および哺育3～4日、さらに交尾が確認されなかった雌では投与29～30、35～36、41～42、48～49日にも測定した。

⑦尿検査

雄動物および雌動物の非交配(サテライト)群を検査対象とし、投与37日の検査では各群動物番号の若い5例、また、回復13日における検査では回復例全例を検査した。

投与37日の検査では当日の投与後に、回復13日の検査では一般状態の観察終了後に動物を代謝ケージに収容し、以下の項目について検査した。ただし、色調・濁度、試験紙による検査および尿沈渣は、採尿開始後約4～8時間の時点で採取した蓄尿で、その他の項目は約24時間の蓄尿で行った。

項目	測定法	使用機器
色調・濁度	視診	
pH・潜血・蛋白・糖・ケトン体	試験紙法	オーションイレブン AE-4020(アークレイ)
ウロビリノーゲン・ビリルビン	同上	同上
沈渣	鏡検	光学顕微鏡
尿量	計量	メスシリンダー等
比重	屈折法	デジタル臨床屈折計 SU-202(エルマ販売)
ナトリウムイオン濃度	イオン電極法	全自動分析装置 JCA-BM6010(日本電子)
カリウムイオン濃度	同上	同上
塩素イオン濃度	同上	同上

⑧性周期観察

全例の雌について、検疫 3 日から性周期を観察し、群分け後、投与開始以降も引き続き非交配(サテライト)群を除く全例の腟スメア標本を作製し、各動物の同居後、交尾が確認されるまで性周期を観察した。また、群毎の平均発情回帰日数(個体毎の発情期から発情期までの日数の平均)および投与開始後に 4 あるいは 5 日間隔の性周期がそれ以外の性周期に変化した動物の頻度を群毎に算出した。なお、規則的に 4～5 日の間隔で性周期が回帰している動物は正常と判断した。

⑨交配

投与 15 日の 16 時 05 分より、同群内の雌雄を 1 対 1 で同居させた。300 mg/kg 投与群の雌 1 例(動物番号 F03025)は交配相手雄(動物番号 M03025)が死亡したことから、投与 17 日の 15 時 36 分より、交尾が確認された同群内の雄(動物番号 M03026)と同居させた。翌朝より毎朝、腟栓を確認し、同居中の雌の腟垢標本を作製して鏡検した。腟内に腟栓あるいは腟垢標本中に精子が確認された動物を交尾成立動物とし、この日を妊娠 0 日と起算して同居を解消し、個別に飼育した。交配結果および妊娠の成否により、同居開始日から交尾確認日までの日数およびその間に回帰した発情期の回数、交尾率〔(交尾動物数/交配に用いた動物数)×100, %〕、妊娠率〔(妊娠動物数/交尾した雌動物数)×100, %〕を算出した。

⑩妊娠・分娩・哺育状態の観察

交尾が確認された全例を自然分娩させた。分娩の確認は、妊娠 21 日相当日から分娩が確認されるまで毎日行った。午前と午後に観察し、15 時までに分娩が完了した例について、その日を哺育 0 日(分娩日)とした。分娩状態については直接観察可能な動物について行い、直接観察できなかった動物についても、分娩後の一般状態および産児の状態から異常の有無を判断した。分娩後は、哺育 1～4 日の間に哺育状態を毎日観察した。分娩した全例の妊娠期間(妊娠 0 日から分娩日までの日数)を求め、各群の出産率〔(生児出産雌数/妊娠動物数)×100, %〕を算出した。哺育5日の剖検時に卵巣については実体顕微鏡下で妊娠黄体数を、子宮については着床数を数え、着床率〔(着床数/妊娠黄体数)×100, %〕を算出した。

⑪採血

雄の投与終了時剖検では、各群の動物番号の若い 5 例、回復 15 日における剖検では回復例全例で採血を行った。また、雌の投与終了時剖検では、分娩例について投与期間が近接している各群 5 例、非交配(サテライト)群の投与終了時剖検では各群動物番号の若い5例、回復15日における剖検では回復例全例で採血を行った。いずれも解剖前 18～24 時間絶食させた後、腹部後大静脈から以下の 1)、2)、3)の順に注射筒を換えて採血した。

1) 血液学的検査用:抗凝固剤 EDTA-2K
2) 血液学的検査用:抗凝固剤 クエン酸ナトリウム
3) 血液生化学的検査用:抗凝固剤 ヘパリン

⑫血液学的検査

採血対象動物について以下の項目を検査した。抗凝固剤としてクエン酸ナトリウムを用いて採取した血液から血漿を分離して、プロトロンビン時間および活性化部分トロンボプラスチン時間を測定し、その他の項目は抗凝固剤として EDTA-2K を用いて採取した血液で測定した。

項目	測定法	使用機器
赤血球数(RBC)	電気抵抗検出法	血液自動分析装置 XT-2000iV(ｼｽﾒｯｸｽ)
白血球数(WBC)	半導体レーザを用いた フローサイトメトリー法	同上
白血球分類	同上	同上
網状赤血球比率(RET%)	同上	同上
血色素量(HGB)	SLS ヘモグロビン法	同上
平均赤血球容積(MCV)	計算(HCT×1000/RBC)	同上
血小板数(PLT)	電気抵抗検出法	同上
ヘマトクリット値(HCT)	同上	同上
平均赤血球血色素量(MCH)	計算(HGB×1000/RBC)	同上
平均赤血球血色素濃度(MCHC)	計算(HGB×100/HCT)	同上
活性化部分ﾄﾛﾝﾎﾞﾌﾟﾗｽﾁﾝ時間(APTT)	光散乱検出法	全自動血液凝固測定装置 CA-650(ｼｽﾒｯｸｽ)
ﾌﾟﾛﾄﾛﾝﾋﾞﾝ時間(PT)	同上	同上

⑬血液生化学的検査

採血対象動物について以下の項目を検査した。抗凝固剤としてヘパリンを用いて採取した血液から血漿を分離して測定した。なお、得られた血漿の一部は甲状腺機能に関するホルモン(T3、T4 および TSH)測定用として凍結保存(-70℃以下)したが、甲状腺の病理学検査およびその他全ての検査項目の結果から、本被験物質は甲状腺機能に影響を及ぼさないと判断されたため、甲状腺ホルモン測定は実施しなかった。

項目	測定法	使用機器
総蛋白濃度(TP)	ﾋﾞｳﾚｯﾄ法	自動分析装置 JCA-BM6010(日本電子)
ｱﾙﾌﾞﾐﾝ濃度(rALB)	BCG 法	同上
ｸﾞﾙｺｰｽ濃度(Glc)	ﾍｷｿｷﾅｰｾﾞ・G-6-PDH 法	同上
総ｺﾚｽﾃﾛｰﾙ濃度(TC)	ｺﾚｽﾃﾛｰﾙｵｷｼﾀﾞｰｾﾞ・HMMPS 法	同上
ﾄﾘｸﾞﾘｾﾗｲﾄﾞ濃度(TG)	GPO・HMMPS 法、ｸﾞﾘｾﾘﾝ消去法	同上
ﾘﾝ脂質濃度(PL)	ｺﾘﾝｵｷｼﾀﾞｰｾﾞ・DAOS 法	同上
尿素窒素濃度(BUN)	ｳﾚｱｰｾﾞ・GℓDH 法,ｱﾝﾓﾆｱ消去法	同上
ｸﾚｱﾁﾆﾝ濃度(cre)	ｸﾚｱﾁﾆﾅｰｾﾞ・HMMPS 法	同上
γ-ｸﾞﾙﾀﾐﾙﾄﾗﾝｽﾍﾟﾌﾟﾁﾀﾞｰｾﾞ活性 (γ-GTP)	IFCC 法	同上
ｱﾙｶﾘﾌｫｽﾌｧﾀｰｾﾞ活性(ALP)	GSCC 法	同上
ｱｽﾊﾟﾗｷﾞﾝ酸ｱﾐﾉﾄﾗﾝｽﾌｪﾗｰｾﾞ活性 (AST)	IFCC 法	同上
ｱﾗﾆﾝｱﾐﾉﾄﾗﾝｽﾌｪﾗｰｾﾞ活性(ALT)	IFCC 法	同上
乳酸脱水素酵素活性(LDH)	JSCC 標準化対応法	同上
ｶﾙｼｳﾑ濃度(Ca)	OCPC 法	同上
総ﾋﾞﾘﾙﾋﾞﾝ濃度(tbil)	酵素法	同上
無機ﾘﾝ濃度(IP)	ﾓﾘﾌﾞﾃﾞﾝ酸直接法	同上
胆汁酸濃度(TBA)	酵素サイクリング法	同上
A/G 比	計算(rALB/(TP- rALB))	同上
ﾅﾄﾘｳﾑｲｵﾝ濃度(Na)	ｲｵﾝ電極法	同上
ｶﾘｳﾑｲｵﾝ濃度(K)	同上	同上
塩素ｲｵﾝ濃度(Cl)	同上	同上

⑭剖検および器官重量

雄動物および雌動物の非交配(サテライト)群の投与終了時剖検例は投与 42 日の翌日に、雌動物の分娩例は哺育 4 日の翌日に、交尾はしたが分娩しなかった雌(100 mg/kg 投与群の 2 例:動物番号 F02013 および F02024)は妊娠 26 日相当日に、交尾が確認されなかった雌(0 mg/kg 投与群の 1 例:動物番号 F01003 および 1000 mg/kg 投与群の 1 例:動物番号 F04041)は投与 52 日の翌日に、雄動物および非交配(サテライト)群の回復観察例は回復 15 日に、死亡動物(300 mg/kg 投与群の 1 例:動物番号 M03025)は死亡確認日に、それぞれ剖検した。なお、分娩状態不良と判断した雌(300 mg/kg 投与群の 1 例:動物番号 F03032)は妊娠 23 日に剖検した。

血液学的検査、血液生化学的検査を実施する動物はペントバルビタールナトリウム麻酔下で採血し、これ以外の動物はペントバルビタールナトリウム麻酔下で放血致死させた。

なお、死亡動物を除く全例について、脳、甲状腺および上皮小体、胸腺、心臓、肝臓、腎臓、脾臓、副腎、精巣、精巣上体、前立腺(腹側葉)および精嚢(凝固腺を含む)、卵巣、子宮の重量を測定した。

また、全例の脳、脊髄、下垂体、眼球(ハーダー腺)、顎下腺および舌下腺、気管、甲状腺および上皮小体、胸腺、心臓、肺および気管支、肝臓、腎臓、脾臓、膵臓、副腎、胃、十二指腸、空腸、回腸、盲腸、結腸、直腸、下顎リンパ節、腸間膜リンパ節、精巣、精巣上体、前立腺(腹側葉)、精嚢および凝固腺、卵巣、子宮、腟、膀胱、大腿骨および大腿骨骨髄、骨格筋、坐骨神経および病変部(皮膚)を採取し、保存した。肺および気管支は 15 cm 水柱以下の圧力で、気管内に 10%中性緩衝ホルマリン溶液 5 mL 以下を注入し固定してから摘出して同固定液に保存した。精巣および精巣上体はブアン液に固定(長期保存は 10%中性緩衝ホルマリン溶液)し、その他は 10%中性緩衝ホルマリン溶液に固定した。なお、死亡例、未分娩例および未交尾例の器官重量値は評価対象から除外した。

⑮病理組織学的検査

剖検した動物のうち、雄および非交配(サテライト)群の投与終了時剖検では動物番号の若い 5 例ならびに高用量群の動物番号が若い 5 例、雌の投与終了時剖検では分娩例について投与期間が近接している対照群ならびに高用量群の 5 例について、病理組織学的検査対象器官(保存した器官・組織)のヘマトキシリン・エオジン(HE)標本を作製し、病理組織学的検査を実施した。死亡動物についても同様に病理組織学的検査を実施した。また、剖検時に肉眼的変化がみられた器官(胸腺、肺、肝臓、腎臓、脾臓、胃、精巣上体、子宮、膀胱)についても検査した。

回復群については肉眼的変化がみられた精巣上体について、病理組織学的検査を実施した。

2)出生児(F_1)

①出生児の観察

哺育 0 日に生存児数および死亡児数を雌雄別に数えて、性別および外表奇形の有無を観察し、分娩率[(産児数/着床痕数)×100, %]、生児出産率[(出産生児数/着床痕数)×100, %]、出産率[(生児出産雌数/妊娠動物数)×100, %]および出生率[(出産生児数/産児数)×100, %]を算出した。また、哺育 0～4 日まで、毎日、一般状態を観察し、生存児数と死亡児数を雌雄別に数え、新生児生存率[(哺育 4 日の生児数/哺育 0 日の生児数)×100, %]を算出した。生存児については、哺育 0 および 4 日に個別の

体重を測定し、腹ごとに雌雄別の平均体重を算出するとともに、哺育 0 日および 4 日における性比[(雄生児数/総生児数)×100, %]を算出した。

②剖検

死亡児は肉眼による異常(口蓋を含む)の有無を観察して剖検し、10%中性緩衝ホルマリン溶液に固定して保存した。生存児は哺育 4 日に肉眼による異常(口蓋を含む)の有無を観察してセボフルラン吸入麻酔下に放血致死させて剖検し、内部器官の異常の有無を観察した。

6. データの解析法

性周期の変化した動物の頻度、交尾率、受胎率については Fisher の直接確率検定を行った(有意水準:5%)。

HA 投与群の病理組織学検査所見のうち、グレード分けした病理組織所見は、Mann-Whitney の U 検定により、また陽性グレードの合計値は Fisher の直接確率の片側検定により、HA 投与群と対照群との間の有意差検定を行った(有意水準:5%)。

その他のデータは、個体ごとに得られた値あるいは litter ごとの平均値を 1 標本とし、非交配(サテライト)群内あるいはその他の群内で比較した。その際、解析の対象が 2 群の場合には、まず F 検定を行い、有意差が認められなければ Student's - t 検定を行った。F 検定において有意差が認められた場合は、Aspin-Welch 検定を行った。解析の対象が 3 群以上の場合は、先ず、Bartlett の方法により各群の分散の一様性について検定を行った。分散が一様である場合には、一元配置型の分散分析を行い、群間に有意性が認められる場合は、Dunnett 法により多重比較を行った。一方、いずれかの群で分散が 0 となる場合および分散が一様でない場合には、Kruskal-Wallis の順位検定を行い、群間に有意性が認められる場合には、Dunnett 型の検定法により多重比較を行った(有意水準:5%)。

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

2015 年 11 月 12 日、11:00 から受変電設備の定期点検のために停電した。これに伴い動物飼育室内の照明が消え、空調が停止した。照明は14:28に、空調は14:39に再開した。停電時の動物飼育室内の温湿度に異常はなく、いずれの動物の一般状態にも変化は認められなかったことから、試験への影響はないと判断した。

その他、「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」はなかった。

試験成績

1. 親動物

1)一般状態(Table 1-1～Table 4, Appendix 1-1-1～Appendix 4-4)

投与 11 日の投与前に 300 mg/kg 投与群の雄 1 例の死亡を発見した。死亡する前日までに一般状態に異常はみられなかった。

1000 mg/kg 投与群において、投与後の一過性の流涎が投与 20 日に雄 2 例で、投与 34、35、37 日に雄 1 例で、投与 48 日に 1 例(未交尾例)で観察された。

雌の 1000 mg/kg 投与群の 1 例(未交尾例)では、投与 15 日に赤色尿が観察された。

雄の 100 mg/kg 投与群の 1 例では投与 25～30 日に後頚部の痂皮形成が観察され、投与 31 日以降は脱毛に移行したが、投与 39 日に再び同部位に痂皮形成がみられ、剖検時まで継続して観察された。また、1000 mg/kg 投与群の 1 例では、投与 37 日に両側前肢に痂皮形成がみられ、剖検時まで継続して観察された。雌の 1000 mg/kg 投与群の 1 例では、妊娠 7～11 日に後頚部に痂皮形成が観察され、妊娠 12 日以降は脱毛に移行し、妊娠 17 日に回復した。

その他、雌雄ともに一般状態の変化は観察されなかった。

回復期間中の 1000 mg/kg 投与群において、雄の 1 例では回復 10～12 日に後頚部の痂皮形成が観察され、その後は脱毛に移行した。

2)詳細な症状観察(Table 5～Table 6-2, Appendix 5-1-1～Appendix 6-2-2)

一般状態観察にて痂皮形成あるいは脱毛が認められた例において、同所見が雄では投与 29、35、42 日、回復 14 日に観察された。同様に、雌では投与 29 日に痂皮形成が観察された。その他の観察項目にはいずれの観察日にも異常は認められず、排尿数および排便数も対照群と比較して差はなかった。

3)体重(Table 7-1～Table 10, Appendix 7-1-1～Appendix 10-4)

雄の HA 投与群の体重は投与期間を通して対照群と同様に推移し、対照群と HA 投与群との間に有意差は認められなかった。

生殖能を評価した交配雌、反復投与毒性を評価した非交配雌ともに HA 投与群の体重は、対照群と同様に推移し、対照群と HA 投与群との間に有意差は認められなかった。

回復期間中の体重推移は雌雄ともに対照群と 1000 mg/kg 投与群との間に有意差は認められなかった。

4)摂餌量(Table 11-1～Table 14, Appendix 11-1-1～Appendix 14-4)

雄の HA 投与群の摂餌量は投与期間を通して対照群と同様に推移し、対照群と HA 投与群との間に有意差は認められなかった。

交配雌、非交配雌ともに HA 投与群の摂餌量は、対照群と同様に推移し、対照群と HA 投与群との間に有意差は認められなかった。

回復期間中の摂餌量は雌雄ともに対照群と 1000 mg/kg 投与群との間に有意差は認められなかった。

5)機能検査

①刺激に対する感覚運動反応(Table 15～Table 16, Appendix 15-1～Appendix 16-2-2)

プライエル反応、瞳孔反射、視覚定位、驚愕反応、後肢引込み反射、眼瞼反射、正向反射の検査では、雄、分娩雌および非交配雌いずれの群の検査対象動物においても異常は認められなかった。

②握力測定(Table 17～Table 19, Appendix 17-1～Appendix 19-2)

雄、分娩雌および非交配雌の前肢、後肢の握力には、対照群と HA 投与群との間に有意差は認められなかった。

③自発運動量測定(Table 20～Table 22, Appendix 20-1～Appendix 22-2)

雄、分娩雌および非交配雌の区画移動数および立ち上がり回数には、対照群と HA 投与群との間に有意差は認められなかった。

6)尿検査(Table 23-1～Table 24-4, Appendix 23-1-1～Appendix 24-4-2)

①投与期間終了時

雌雄ともに対照群と 1000 mg/kg 投与群との間に有意差は認められなかった。

②回復期間終了時

雄の 1000 mg/kg 投与群において、塩素イオン排泄量が有意($P<0.05$)な低値を示した。

雌の 1000 mg/kg 投与群において、塩素イオン濃度が有意($P<0.05$)な高値を示した。

7)血液学的検査(Table 25-1～Table 26-3, Appendix 25-1-1～Appendix 26-3-2)

①投与期間終了時

雄では、1000 mg/kg 投与群の好酸球比率が有意($P<0.05$)に低下した。

分娩雌では、対照群と HA 投与群との間に有意差は認められなかった。

非交配雌では、対照群と 1000 mg/kg 投与群との間に有意差は認められなかった。

②回復期間終了時

雄では、対照群と 1000 mg/kg 投与群との間に有意差は認められなかった。

雌では、1000 mg/kg 投与群の好酸球比率が有意($P<0.05$)に低下した。

8)血液生化学的検査(Table 27-1～Table 28-3, Appendix 27-1-1～Appendix 28-3-2)

①投与期間終了時

雄では、対照群と HA 投与群との間に有意差は認められなかった。

分娩雌では、塩素イオン濃度が 1000 mg/kg 投与群で有意($P<0.01$)な低値を示した。

非交配雌では、γ-グルタミルトランスペプチダーゼ活性が有意($P<0.01$)な低値を示した。

②回復期間終了時

雌雄ともに、対照群と 1000 mg/kg 投与群との間に有意差は認められなかった。

9)器官重量(Table 29-1～Table 30-3, Appendix 29-1-1～Appendix 30-3-2)

①投与期間終了時

雄では、対照群と HA 投与群との間に有意差は認められなかった。

分娩雌では、1000 mg/kg 投与群の右卵巣が実重量、相対重量ともに有意($P<0.01$)に減少した。

非交配雌では、脾臓の実重量(P<0.01)および相対重量(P<0.05)が有意に増加した。

②回復期間終了時

雄では、1000 mg/kg 投与群において左精巣上体および精嚢の実重量が有意(P<0.05)に増加した。

雌では、1000 mg/kg 投与群において脾臓の相対重量が有意(P<0.05)に減少し、右副腎の相対重量が有意(P<0.05)に増加した。

10)剖検所見(Table 31-1～Table 32-3, Appendix 31-1～Appendix 32-3)

①雄の投与期間終了時屠殺例

100 mg/kg 投与群において肝臓の横隔膜結節が 1 例、後頚部の痂皮が 1 例、300 mg/kg 投与群において胸腺の小型が 1 例、精巣上体尾部(両側)の黄色結節が 1 例、1000 mg/kg 投与群において両前肢の痂皮が 1 例に観察された。

②雄の回復期間終了時屠殺例

対照群において精巣上体尾部(右側)の黄白色結節が 1 例、1000 mg/kg 投与群において後頚部の脱毛が 1 例に観察された。

③雌の投与期間終了時屠殺例

哺育 5 日剖検例では、対照群において腺胃粘膜に暗赤色点が 1 例、100 mg/kg 投与群において腺胃粘膜に暗色物付着が 1 例、300 mg/kg 投与群において腺胃粘膜に暗色点および陥凹部が 1 例、別の 1 例では腺胃粘膜の赤色点、肝臓(外側左葉)の白色点、脾臓に副脾が観察された。

④非交配(サテライト)群の投与期間終了時屠殺例

剖検の結果、異常所見は認められなかった。

⑤非交配(サテライト)群の回復期間終了時屠殺例

剖検の結果、異常所見は認められなかった。

⑥雄の死亡例

投与 11 日に死亡した 300 mg/kg 投与群の 1 例では、胸腺に暗赤色点の散在がみられ、肺は暗赤色調で暗色斑の散在が認められ、肝臓および腎臓は大型であった。

⑦雌の未分娩例および未交尾例

妊娠 23 日に剖検した 300 mg/kg 投与群の 1 例では、肺(右後葉)に暗色斑が認められた。右子宮角は赤色内容液の貯留および暗色化がみられ、左子宮角は黄色内容液が貯留し、子宮内には 2 匹(右側:雌 1 匹、左側:雄 1 匹)の生存胎児が認められ、胎児および胎盤に異常は認められなかった。

妊娠 26 日に剖検した 100 mg/kg 投与群の 2 例の未分娩例に異常はみられなかった。

1000 mg/kg 投与群の未交尾例では、右腎臓に白色の隆起部が認められ、膀胱の壁が肥厚していた。

対照群の未交尾例では、異常所見は認められなかった。

11)病理組織学的検査(Table 33-1～Table 34-2, Appendix 33-1～Appendix 34-2)

①雄の投与期間終了時屠殺例

対照群および 1000 mg/kg 投与群の両群の心臓、肺、肝臓、脾臓、腎臓、前立腺に病理組織学的変化が観察されたが、両群間に程度および頻度の差はなかった。1000 mg/kg 投与群の甲状腺に鰓後体が

2 例に観察されたが対照群と比較して頻度の差はなかった。その他、対照群では胃の境界縁粘膜下織血管周囲に限局性のリンパ球浸潤が 1 例、精巣に精細管の変性が 1 例、それぞれ観察された。

剖検時に肉眼的変化がみられた 100 mg/kg 投与群の肝臓では肝横隔膜結節が、300 mg/kg 投与群の精巣上体では精子肉芽腫が観察され、同群の胸腺では病理組織学的変化は認められなかった。

その他の観察組織・器官には病理組織学的変化は認められなかった。

②雄の回復期間終了時屠殺例

剖検時に、精巣上体に肉眼的変化が認められた対照群の 1 例では、精子肉芽腫が観察された。

③雌の投与期間終了時屠殺例(哺育 5 日剖検)

対照群および 1000 mg/kg 投与群の両群の甲状腺、胸腺、心臓、肝臓、脾臓、腎臓に病理組織学的変化が観察されたが、両群間に程度および頻度の差はなかった。1000 mg/kg 投与群では膵臓間質にリンパ球浸潤が 1 例、腺胃の胃底腺の拡張が 1 例観察されたが、いずれも限局性でごく軽度な所見であった。その他、対照群の肺では、肺胞に限局性の泡沫細胞の集簇が 2 例、動脈周囲に単核細胞浸潤が 1 例に観察された。

剖検時に胃に肉眼的変化が認められた対照群および 300 mg/kg 投与群の各 1 例では、腺胃に限局性のびらんが認められた。また、肝臓、脾臓および胃に肉眼的変化が観察された 300 mg/kg 投与群の 1 例では、肝臓では限局性の壊死巣と小肉芽腫が、胃では腺胃に限局性のびらんが観察された。脾臓では、髄外造血および褐色色素の沈着が他動物と同程度に観察されたのみであった。なお、胃に肉眼的変化が認められた 100 mg/kg 投与群の 1 例では病理組織学的な変化はなかった。

その他の観察組織・器官には病理組織学的変化は認められなかった。

④非交配(サテライト)群の投与期間終了時屠殺例

対照群および 1000 mg/kg 投与群の両群の胸腺、肝臓、膵臓、脾臓、腎臓、ハーダー腺に病理組織学的変化が観察されたが、両群間の程度および頻度に差はなかった。

1000 mg/kg 投与群の舌下腺では間質にリンパ球浸潤が 1 例に、心臓では心筋の変性/線維化が 1 例に観察されたが、いずれも軽微な変化であった。

その他、対照群の顎下腺では間質にリンパ球浸潤、甲状腺に鰓後体、肺に限局性の泡沫細胞の集簇が各 1 例観察された。

その他の観察組織・器官には病理組織学的変化は認められなかった。

⑤雄の死亡例

両側の精巣に精細管の変性および両側の精巣上体の管腔内に細胞残屑が観察された。脾臓では髄外造血および褐色色素の沈着が観察されたが他の雄動物と同程度の変化であった。また、死後変化によるうっ血が、下垂体、胸腺、肺、肝臓に観察された。なお、一部の組織は死後変化による自己融解により観察不能であった。病理組織学的観察からは死因と考えられる変化は認められなかった。

⑥雌の未分娩例および未交尾例

妊娠 23 日に剖検した 300 mg/kg 投与群の 1 例の肺では、肺胞に限局性の泡沫細胞の集簇が認められたが、ごく軽度な変化であった。

未交尾動物で剖検時に腎臓と膀胱に肉眼的変化が認められた 1000 mg/kg の 1 例では、片側の腎臓に好塩基性尿細管、間質および管腔に炎症細胞浸潤が顕著に観察され、腎盂および乳頭部の移行上皮の過形成が認められた。また、膀胱の移行上皮でもびまん性に過形成が認められ、粘膜上皮および粘膜下織に好中球浸潤が観察された。

2. 生殖能力

1) 性周期および交配成績(Table 35～Table 36, Appendix 35-1～Appendix 36-4)

性周期には、HA 投与の影響を示唆する変化はみられなかった。4 あるいは 5 日間隔の性周期が投与開始後にそれ以外の性周期に変化した動物は、100 mg/kg 投与群および 1000 mg/kg 投与群に各 1 例認められたが、その頻度には対照群と HA 投与群との間に有意差はなかった。2 週間の交配期間中に交尾が確認されなかった動物は、対照群および 1000 mg/kg 群で各 1 組みられたが、その他の動物では交尾が確認され、交尾までの日数およびその間の発情回数に、対照群と HA 投与群との間に有意差は認められなかった。また、100 mg/kg 投与群の 2 例(動物番号 F02013 および F02024)は、交尾は確認されたが妊娠していなかった。それ以外の動物は妊娠が確認され、交尾率および妊娠率(受胎率)には、対照群と HA 投与群との間に有意差は認められなかった。

2) 出産率および妊娠期間(Table 37, Appendix 37-1～Appendix 37-4)

出産率および妊娠期間には対照群と HA 投与群との間に差は認められなかった。

3) 分娩および哺育状態(Table 37, Appendix 37-1～Appendix 37-4)

100 mg/kg 投与群の 2 例(動物番号 F02013 および F02024)は妊娠 25 日までに分娩が確認されなかった。剖検の結果、着床痕および妊娠黄体は認められず、不妊と判断した。300 mg/kg 投与群の 1 例(動物番号 F03032)は妊娠 23 日に出血がみられたが、出生児が観察されなかったため、分娩状態不良と判断し、妊娠 23 日に搬出した(前述)。剖検の結果、妊娠黄体数 14 および着床数 2 が認められた。その他の動物の分娩状態および哺育状態に異常は認められなかった。

4) 黄体数、着床数および着床率(Table 37, Appendix 37)

黄体数、着床数および着床率には、対照群と HA 投与群との間に有意差は認められなかった。

3. 出生児

1) 生存(Table 37, Appendix 37-1～Appendix 37-4)

1000 mg/kg 投与群では対照群と比較して産児数および出産生児数が減少傾向を示し、分娩率($P<0.05$)および生児出産率($P<0.01$)が有意に低下した。その他、出生率、哺育 0 日および哺育 4 日の性比、新生児生存率に HA 投与の影響は認められなかった。また、哺育 0 日に産児の外表奇形は観察されなかった。

2) 体重(Table 38, Appendix 38-1～Appendix 38-4)

哺育 0 および 4 日における出生児の体重には、対照群と HA 投与群との間に有意差は認められなかった。

3)出生児観察(Table 39～Table 40, Appendix 39-1～Appendix 39-4)

死亡児は対照群を含む各投与群に認められたが、剖検が可能であった死亡児には外表奇形は観察されず、内部器官に異常は認められなかった。

哺育4日の出生児剖検の結果、対照群、HA投与群ともに異常は認められなかった。

考察

酢酸ヘキシルを雌雄ラットに強制経口投与し、反復投与毒性および回復性、ならびに生殖発生毒性および新生児の発育に及ぼす影響について検討した。

1. 反復投与毒性学的所見

投与11日に300 mg/kg投与群の雄1例が死亡した。しかし、一般状態、剖検所見、病理組織学的検査の結果から死因は特定できなかった。死亡動物はこの1例のみであり、雄性生殖器官に観察された変化も他動物にみられていないことから、被験物質投与とは関連のない変化と考えられた。

1000 mg/kg 投与群の雌雄では投与後に流涎が散見された。しかし、一過性の変化であり、詳細な一般状態観察においても神経毒性を示唆する変化は観察されていないことから、被験物質の刺激性に起因した変化であると考えられた。

1000 mg/kg投与群の雌1例(未交尾例)では投与15日に赤色尿が観察され、病理組織学的検査の結果から上行性の腎盂腎炎が疑われた。同被験物質を用いた90日間反復経口投与試験[1)]においては1000 mg/kg 投与群の雄に尿潜血反応が認められたが、本試験の尿検査では同様の変化は認められていない。また、この動物の泌尿器系で観察された病理組織学変化は片側性であり、他の動物には同様の病理組織学的変化は認められていないことから、被験物質投与とは関連のない偶発的な変化であり、本条件下ではHA投与により尿潜血反応を含む泌尿器系への影響はないと判断した。

分娩雌の1000 mg/kg投与群では血漿中塩素イオン濃度が僅かに低値を示した。同様の変化は90日間反復経口投与試験[1)]においても観察されているが、本試験の雄および非交配雌には認められていない。分娩雌の血漿中塩素イオン濃度は本施設で実施した同種試験の背景値[2)](Mean±2SD:105.6±4.8、最小値～最大値:101.9～108.5)よりも僅かに高い数値を示したが、その変動の程度から毒性学的意義は低いと考えられ、被験物質投与による変化ではないと判断した。

非交配雌の1000 mg/kg投与群では脾臓重量の増加が認められた。同群の一般状態、剖検、血液学検査から造血能に影響を及ぼす変化は認められず、病理組織学的観察の結果からも、対照群と比較して顕著な差はなかったことから、偶発的な変化であり被験物質投与の影響ではないと考えられた。

分娩雌の1000 mg/kg投与群では片側のみ卵巣重量の減少がみられた。同群の黄体数および着床数に左右差はなく、対照群の黄体数および着床数とも差がみられていないこと、卵巣の病理組織学的観察においても重量減少を示唆する変化がなかったことから、偶発的な変化であると判断した。

その他、1000 mg/kg 投与群の雄において白血球分類比の変動が認められたが、用量依存的な変化ではないことから、被験物質投与の影響ではないと判断した。また、同群の非交配雌ではγ-グルタミルト

ランスペプチダーゼ活性が低値を示したが、僅かな変化であり、病理組織学的にも肝障害を示唆する変化が観察されていないことから被験物質投与による影響ではないと判断した。

なお、90 日間反復経口投与試験[1)]の 1000 mg/kg 投与群の雄において無機リン濃度の増加が認められたが、本試験では認められなかった。

2. 回復群における所見

14 日間の回復期間終了後、1000 mg/kg 投与群において雄は尿中の塩素イオン排泄量が低値を示し、雌は塩素イオン濃度が高値を示した。しかし、投与終了時には同様の変化はみられていない。雄の尿中電解質濃度に対照群との差はみられていないことから、塩素イオン排泄量の低値は対照群の尿量が多いことに起因した変化であると考えられた。また、雌の塩素イオン濃度は背景値[2)] (Mean±2SD:131.4±27.0、最小値～最大値:119.9～154.4)よりも僅かに高い数値を示したが、他の電解質濃度には差はなかったことから総合的に判断し、これらの変化は遅発毒性を示唆する変化ではないと考えられた。また、同群の雌では好酸球比率の低下が認められたが、背景値[2)] (Mean±2SD:2.1±1.0、最小値～最大値:1.4～2.6)の範囲内であったことから、遅発毒性を示唆する変化ではないと考えられた。

1000 mg/kg 投与群の雌では脾臓重量の減少が認められた。血液学および血液生化学的検査において貧血を示唆する変化は認められず、剖検においても異常は認められなかったことから、偶発的な変化であり遅発毒性を示唆する変化ではないと判断した。その他、同群の雄では左精巣および精嚢の実重量の増加が認められ、雌では右副腎の増加が認められた。剖検において異常は認められなかったこと、投与期間中に同様の変化がみられなかったことから、偶発的な変化であり遅発毒性を示唆する変化ではないと判断した。

3. 生殖発生毒性学的所見および出生児所見

1000 mg/kg 投与群では産児数および出産生児数が減少傾向を示し、分娩率および生児出産率が低下した。しかし、黄体数と着床数には対照群と差はなく、出産日の死亡児数の増加も認められなかった。また、哺育期間中の死亡児数は対照群と比較して差は認められず、新生児体重および生存率にも影響はみられなかった。したがって、HA は排卵、着床には影響はなく、着床後の胚・胎児生存性を低下させると考えられた。

1000 mg/kg 群の1組で交尾が確認されなかったが、対照群でも未交尾動物は1例に認められている。また、100 mg/kg 投与群では 2 例に不妊が確認されたが、300 mg/kg 投与群および 1000 mg/kg 投与群では不妊動物は認められていない。したがって、交尾率および妊娠率(受胎率)には被験物質投与による影響はないと判断した。

4. 無毒性量

反復投与毒性学的所見においては 1000 mg/kg 投与群で被験物質の刺激性に起因すると考えられた一過性の流涎が観察されたのみであったことから、本試験条件下における酢酸ヘキシルの親動物に対

する一般毒性学的無毒性量は雌雄ともに 1000 mg/kg/day、生殖発生毒性および次世代児に対する無毒性量は 1000 mg/kg 投与群で分娩率および生児出産率の低下が認められたことから 300 mg/kg/day と考えられた。

参考文献

1) 「ヘキシルアセテートのラットを用いる 90 日間反復経口投与試験」(試験番号 C-13-006)

2) [redacted]「ラットを用いる反復経口投与毒性・生殖発生毒性併合試験の背景データ:媒体対照群の比較」 秦野研究所年報第 37 巻、2015、p8-25

Annex A

試験成績書

2015年08月19日

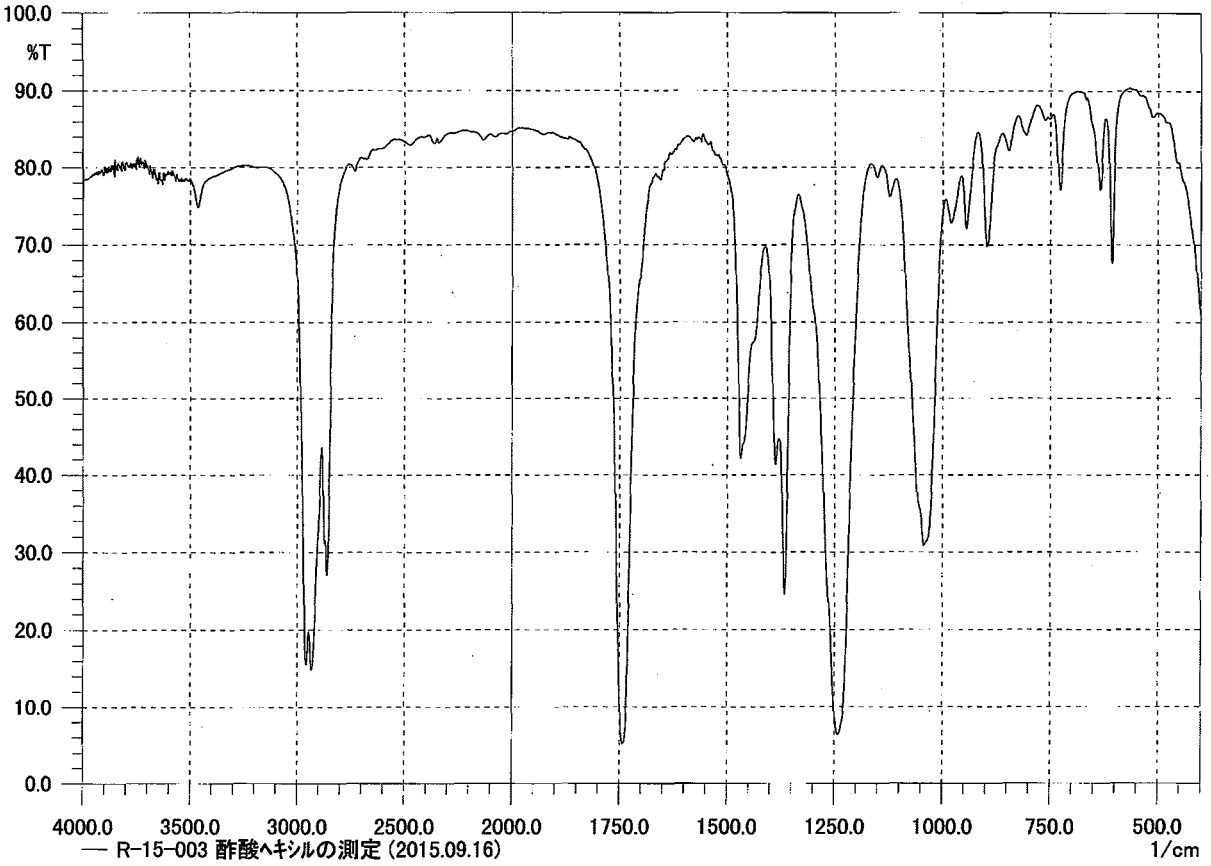
東京化成工業株式会社　品質保証[redacted]
〒103-0023
東京都中央区日本橋本町4丁目10[redacted]
TEL: 03(5640)8860　FAX: 03(564[redacted]

製品名：Hexyl Acetate				[redacted]
製品コード：A0032 CAS番号：142-92-7	等級：GR	製品ロット：NWQZH	判定：合格	

項目	結果	規格値
純度(GC)	99.5 %	99.0 %以上
比重 (20/20)	0.8745	0.8720 ～ 0.8760
屈折率 n20/D	1.4091	1.4070 ～ 1.4100

製品ラベルに記載された弊社のロット番号は、半角のアルファベットと数字の組み合わせで4桁又は5桁です。
それ以降は、社内管理用の記号となります。

Annex B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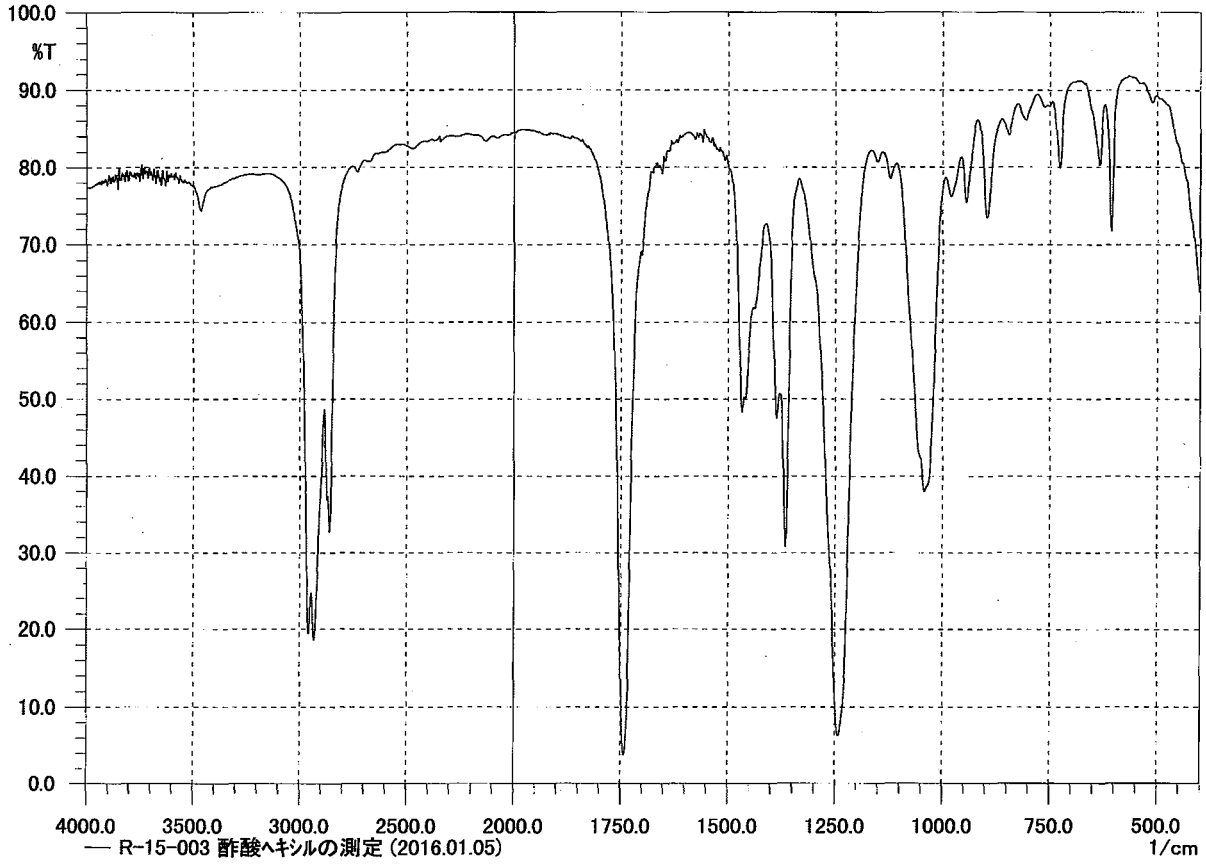
0.0
4000.0
3500.0
3000.0
2500.0
2000.0
1750.0
1500.0
1250.0
1000.0
750.0
500.0
1/cm
— R-15-003 酢酸ヘキシルの測定 (2015.09.16)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4000.0
3500.0
3000.0
2500.0
2000.0
1750.0
1500.0
1250.0
1000.0
750.0
500.0
1/cm
— R-15-003 酢酸ヘキシルの測定 (2016.01.05)

Annex C

安定性試験結果

SOP/CHE/001

被験物質:酢酸ヘキシル
ロット番号:NWQZH
媒　　体:トウモロコシ油

試験番号　:R-15-003

調製年月日　:2015年9月17日
測定年月日 A :2015年9月17日(調製直後)
B :2015年9月25日(保管後8日)
保管条件　:冷蔵、遮光

調製濃度 (mg/mL)	A				B				
	試料番号	測定濃度 (mg/mL)	含量[a] (%)	ばらつき[b] (%)	試料番号	測定濃度 (mg/mL)	含量[a] (%)	ばらつき[b] (%)	残存率[c] (%)
25.0	1	26.2	104.8	101.2	7	25.7	102.8	101.2	99.2
	2	26.0	104.0	100.4	8	25.4	101.6	100.0	98.1
	3	25.6	102.4	98.8	9	25.2	100.8	99.2	97.3
	平均	25.9	103.7		平均	25.4	101.7		98.2
250	4	253	101.2	100.0	10	250	100.0	100.0	98.8
	5	252	100.8	99.6	11	251	100.4	100.4	99.2
	6	253	101.2	100.0	12	248	99.2	99.2	98.0
	平均	253	101.1		平均	250	99.9		98.7

a):各測定時の測定濃度／調製濃度×100　b):各測定時の測定濃度／各測定時の平均測定濃度×100　c):各測定時の測定濃度／初回の平均測定濃度×100

安定性の判定基準(溶液検体)

各試料採取時点の平均含量がそれぞれ調製濃度の90.0～110.0%、また、各測定濃度のばらつきがそれぞれ平均値の90.0～110.0%以内であり、かつ、初回の平均測定濃度に対する保管期間後の測定農度の比(残存率)の平均値が90.0%以上を示す期間とする

Annex D

SOP/CHE/001

試験番号　：R-15-003

含　量　試　験　結　果

被験物質：酢酸ヘキシル
ロット番号：NWQZH
媒　　体：トウモロコシ油

調製年月日：2015年9月28日
測定年月日：2015年9月28日

試料番号	調製濃度(A) (mg/mL)	測定濃度(B) (mg/mL)	平均測定濃度(C) (mg/mL)	含量 B/A×100 (%)	平均含量 (%)	ばらつき B/C×100 (%)
13	25.0	26.4	26.1	105.6	104.5	101.1
14		26.1		104.4		100.0
15		25.9		103.6		99.2
16	75.0	77.3	77.8	103.1	103.7	99.4
17		77.4		103.2		99.5
18		78.6		104.8		101.0
19	250	245	248	98.0	99.1	98.8
20		249		99.6		100.4
21		249		99.6		100.4

含量の判定基準(溶液検体)

平均含量が調製濃度の90.0～110.0%、各測定濃度のばらつきが平均値の90.0～110.0%以内とする

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 1-1. General conditions of male rats

Group	Number of males and general conditions	Days of administration																																																	
		1		2		3		4		5		6		7		8		9		10		11		12		13		14		15		16		17		18		19		20		21		22		23		24		25	
		Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Control (vehicle: corn oil)	Number of males	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	General appearance, No abnormality	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
HA 100 mg/kg	Number of males	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	General appearance, No abnormality	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	11	11
	Skin, Crust formation	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
HA 300 mg/kg	Number of males	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
	General appearance, No abnormality	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
	General appearance, Death	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
HA 1000 mg/kg	Number of males	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	General appearance, No abnormality	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	10	12	12	12	12	12	12	12	12	12	12
	Mouth, Salivation	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0

Pre: Before administration, Post: after administration.

Group	Number of males and general conditions	Days of administration																																	
		26		27		28		29		30		31		32		33		34		35		36		37		38		39		40		41		42		43
		Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre
Control (vehicle: corn oil)	Number of males	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	7
	General appearance, No abnormality	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	7
HA 100 mg/kg	Number of males	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	General appearance, No abnormality	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
	Skin, Crust formation	1	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1
	Fur, Hair, Coat, Loss of fur	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
HA 300 mg/kg	Number of males	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
	General appearance, No abnormality	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
HA 1000 mg/kg	Number of males	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	7
	General appearance, No abnormality	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	11	12	11	12	12	11	10	11	11	11	11	11	11	11	11	11	11	6
	Skin, Crust formation	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1
	Mouth, Salivation	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0

Pre: Before administration, Post: after administration.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 1-2. General conditions of male rats at the recovery period

Group	Number of males and general conditions	Days of recovery														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Control (vehicle: corn oil)	Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	General appearance, No abnormality	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
HA 1000 mg/kg	Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	General appearance, No abnormality	5	5	5	5	5	5	5	5	5	4	4	4	4	4	4
	Skin, Crust formation	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0
	Fur, Hair, Coat, Loss of fur	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 2-1. General conditions of female rats

Group	Number of females and general conditions	Days of administration																											
		1		2		3		4		5		6		7		8		9		10		11		12		13		14	
		Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Control (vehicle: corn oil)	Number of females	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	General appearance, No abnormality	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
HA 100 mg/kg	Number of females	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	General appearance, No abnormality	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
HA 300 mg/kg	Number of females	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	General appearance, No abnormality	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
HA 1000 mg/kg	Number of females	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	General appearance, No abnormality	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12

Pre: Before administration, Post: after administration.

Group	Number of females and general conditions	Days of administration																											
		15		16		17		18		19		20		21		22		23		24		25		26		27		28	
		Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Control (vehicle: corn oil)	Number of females	12	12	11	11	9	9	4	4	2	2	2	2	2	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	General appearance, No abnormality	12	12	11	11	9	9	4	4	2	2	2	2	2	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1
HA 100 mg/kg	Number of females	12	12	10	10	7	7	7	7	2	2	2	2	2	2	2	2	1	1	1	1	1	1	1	1	1	1	1	1
	General appearance, No abnormality	12	12	10	10	7	7	7	7	2	2	2	2	2	2	2	2	1	1	1	1	1	1	1	1	1	1	1	1
HA 300 mg/kg	Number of females	12	12	8	8	8	8	3	3	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	General appearance, No abnormality	12	12	8	8	8	8	3	3	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
HA 1000 mg/kg	Number of females	12	12	8	8	7	7	3	3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	General appearance, No abnormality	11	12	8	8	7	7	3	3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	Excretion, Reddish urine	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Pre: Before administration, Post: after administration.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 2-2. General conditions of female rats, satellite group

Group	Number of females and general conditions	Days of administration																																																	
		1		2		3		4		5		6		7		8		9		10		11		12		13		14		15		16		17		18		19		20		21		22		23		24		25	
		Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Control (vehicle: corn oil)	Number of females	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	General appearance, No abnormality	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
HA 1000 mg/kg	Number of females	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	General appearance, No abnormality	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10

Pre: Before administration, Post: after administration.

Group	Number of females and general conditions	Days of administration																																	
		26		27		28		29		30		31		32		33		34		35		36		37		38		39		40		41		42		43
		Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre
Control (vehicle: corn oil)	Number of females	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5
	General appearance, No abnormality	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5
HA 1000 mg/kg	Number of females	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5
	General appearance, No abnormality	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5

Pre: Before administration, Post: after administration.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 2-3. General conditions of female rats at the recovery period

Group	Number of females and general conditions	Days of recovery														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Control (vehicle: corn oil)	Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	General appearance, No abnormality	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
HA 1000 mg/kg	Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	General appearance, No abnormality	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 3. General conditions in dams during pregnancy

Group	Number of dams and general conditions	Days of pregnancy																											
		0		1		2		3		4		5		6		7		8		9		10		11		12		13	
		Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Control (vehicle: corn oil)	Number of dams	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
	General appearance, No abnormality	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
HA 100 mg/kg	Number of dams	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	General appearance, No abnormality	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
HA 300 mg/kg	Number of dams	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	General appearance, No abnormality	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
HA 1000 mg/kg	Number of dams	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
	General appearance, No abnormality	11	11	11	11	11	11	11	11	11	11	11	11	11	11	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	Skin, Crust formation	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	0	0	0	0
	Fur, Hair, Coat, Loss of fur	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1

Pre: Before administration, Post: after administration.

Table 3 (continued). General conditions in dams during pregnancy

Group	Number of dams and general conditions	Days of pregnancy																	
		14		15		16		17		18		19		20		21		22	
		Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Control (vehicle: corn oil)	Number of dams	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	2	2
	General appearance, No abnormality	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	2	2
HA 100 mg/kg	Number of dams	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	1	1
	General appearance, No abnormality	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	1	1
HA 300 mg/kg	Number of dams	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	1	1
	General appearance, No abnormality	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	1	1
HA 1000 mg/kg	Number of dams	11	11	11	11	11	11	11	11	11	11	11	11	11	11	10	10	3	3
	General appearance, No abnormality	10	10	10	10	10	10	11	11	11	11	11	11	11	11	10	10	3	3
	Fur, Hair, Coat, Loss of fur	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0

Pre: Before administration, Post: after administration.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 4. General conditions in dams during lactation

Group	Number of dams and general conditions	Days of lactation										
		0		1		2		3		4		5
		Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre
Control (vehicle: corn oil)	Number of dams	8	8	11	11	11	11	11	11	11	11	11
	General appearance, No abnormality	8	8	11	11	11	11	11	11	11	11	11
HA 100 mg/kg	Number of dams	7	7	10	10	10	10	10	10	10	10	10
	General appearance, No abnormality	7	7	10	10	10	10	10	10	10	10	10
HA 300 mg/kg	Number of dams	10	10	11	11	11	11	11	11	11	11	11
	General appearance, No abnormality	10	10	11	11	11	11	11	11	11	11	11
HA 1000 mg/kg	Number of dams	5	5	11	11	11	11	11	11	11	11	11
	General appearance, No abnormality	5	5	11	11	11	11	11	11	11	11	11

Pre: Before administration, Post: after administration.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 5. Detailed clinical observations of male rats

Findings	Group	Initial number of animals	Pre-treatment	Days of treatment						Days of recovery [a]	
				8	15	23	29	35	42	7	14
[Fur]	Control (vehicle: corn oil)	12	0 [b]	0	0	0	0	0	0	0	0
Crust formation/Loss of fur	HA 100 mg/kg	12	0	0	0	0	1	1	1		
	HA 300 mg/kg	12	0	0	0 (11)	0 (11)	0 (11)	0 (11)	0 (11)		
	HA 1000 mg/kg	12	0	0	0	0	0	0	1	0	1
[Urination]	Control (vehicle: corn oil)	12	5 [c]	3	3	4	4	10	3	3	0
(frequency/30sec)	HA 100 mg/kg	12	2	1	0	1	2	2	2		
	HA 300 mg/kg	12	4	0	1 (11)	1 (11)	2 (11)	3 (11)	2 (11)		
	HA 1000 mg/kg	12	6	1	3	2	4	6	5	1	0
[Defecation]	Control (vehicle: corn oil)	12	1 [c]	0	0	0	0	1	0	0	0
(frequency/30sec)	HA 100 mg/kg	12	1	1	0	0	0	1	0		
	HA 300 mg/kg	12	0	0	0 (11)	0 (11)	0 (11)	0 (11)	0 (11)		
	HA 1000 mg/kg	12	0	0	0	0	0	0	0	0	0

[a] The recovery test was performed in 5 animals for each of the 0 and 1000 mg/kg groups.
[b] Values represent number of animals with the findings.
[c] Values represent total score of each group.
Figures in parenthese indicate number of animals.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 6-1. Detailed clinical observations of female rats

Findings	Group	Initial number of animals	Pre-treatment	Days of treatment							The lactation period
				8	15	23	29	35	42	49	
[Fur] Crust formation	Control (vehicle: corn oil)	12	0 [a]	0	0	0	0	0	0 (2)	0 (1)	0 (11)
	HA 100 mg/kg	12	0	0	0	0	0	0	0 (2)	0 (1)	0 (10)
	HA 300 mg/kg	12	0	0	0	0	0	0	0 (0)	0 (0)	0 (11)
	HA 1000 mg/kg	12	0	0	0	0	1	0	0 (1)	0 (1)	0 (11)
[Urination] (frequency/30sec)	Control (vehicle: corn oil)	12	2 [b]	0	0	0	0	0	0 (2)	0 (1)	0 (11)
	HA 100 mg/kg	12	1	1	0	1	1	0	0 (2)	0 (1)	0 (10)
	HA 300 mg/kg	12	1	0	0	0	0	0	0 (0)	0 (0)	0 (11)
	HA 1000 mg/kg	12	1	0	0	1	0	1	0 (1)	0 (1)	0 (11)
[Defecation] (frequency/30sec)	Control (vehicle: corn oil)	12	0 [b]	0	0	0	0	0	0 (2)	0 (1)	0 (11)
	HA 100 mg/kg	12	0	0	0	0	0	0	0 (2)	0 (1)	0 (10)
	HA 300 mg/kg	12	0	0	0	0	0	0	0 (0)	0 (0)	0 (11)
	HA 1000 mg/kg	12	0	0	0	0	0	0	0 (1)	0 (1)	0 (11)

[a] Values represent number of animals with the findings.
[b] Values represent total score of each group.
Figures in parenthese indicate number of animals.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 6-2. Detailed clinical observations of female rats, satellite group

Findings	Group	Initial number of animals	Pre-treatment	Days of treatment						Days of recovery [a]	
				8	15	23	29	35	42	7	14
[Urination] (frequency/30sec)	Control (vehicle: corn oil)	10	0 [b]	1	0	0	0	0	0	0	0
	HA 1000 mg/kg	10	0	0	1	0	1	0	0	0	0
[Defecation] (frequency/30sec)	Control (vehicle: corn oil)	10	0 [b]	0	0	0	0	0	0	0	0
	HA 1000 mg/kg	10	0	0	0	0	0	0	0	0	0

[a] The recovery test was performed in 5 animals for each of the 0 and 1000 mg/kg groups.
[b] Values represent total score of each group.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 7-1. Body weights of male rats

Group	Control (vehicle: corn oil)	HA 100 mg/kg	HA 300 mg/kg	HA 1000 mg/kg
Number of males	12	12	12	12
Days of administration				
1	401.7 ± 17.6	401.4 ± 19.7	400.8 ± 17.2	402.0 ± 19.9
4	414.2 ± 19.6	415.9 ± 24.3	415.1 ± 22.3	416.7 ± 22.8
7	424.8 ± 21.4	427.3 ± 29.5	426.4 ± 27.5	430.3 ± 24.0
14	445.3 ± 22.5	448.0 ± 33.2	453.0 ± 31.3 (11)	457.3 ± 30.7
21	465.7 ± 25.5	465.2 ± 34.5	472.4 ± 34.3 (11)	479.7 ± 36.5
28	491.3 ± 27.8	484.9 ± 37.8	497.4 ± 36.5 (11)	505.0 ± 41.3
35	509.3 ± 30.2	506.7 ± 42.4	517.5 ± 40.4 (11)	527.0 ± 46.8
42	521.4 ± 35.7	518.8 ± 43.0	527.3 ± 44.7 (11)	540.4 ± 50.9

Each value shows mean (g) ± S.D.

Significantly different from the control group (*: P<0.05, **: P<0.01).

Figures in parentheses indicate number of males.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 7-2. Body weights of male rats at the recovery period

Group		Control (vehicle: corn oil)	HA 1000 mg/kg
Number of males		5	5
Days of recovery			
	1	520.7 ± 12.5	543.6 ± 46.9
	7	536.9 ± 15.0	563.5 ± 47.8
	14	550.5 ± 15.5	573.2 ± 44.3

Each value shows mean (g) ± S.D.

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 8-1. Body weights of female rats

Group	Control (vehicle: corn oil)	HA 100 mg/kg	HA 300 mg/kg	HA 1000 mg/kg
Number of females	12	12	12	12
Days of administration				
1	242.3 ± 10.3	234.5 ± 9.7	236.6 ± 9.3	238.5 ± 12.8
4	248.2 ± 13.1	241.3 ± 12.4	240.1 ± 12.6	244.7 ± 12.8
7	251.3 ± 11.6	244.4 ± 14.7	245.1 ± 10.4	249.3 ± 14.5
14	259.7 ± 13.8	254.8 ± 14.2	252.6 ± 13.2	256.0 ± 17.8

Each value shows mean (g) ± S.D.

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 8-2. Body weights of female rats, satellite group

Group	Control (vehicle: corn oil)	HA 1000 mg/kg
Number of females	10	10
Days of administration		
1	240.4 ± 13.8	240.3 ± 13.6
4	247.3 ± 13.3	249.4 ± 13.0
7	252.2 ± 11.7	256.6 ± 13.9
14	265.3 ± 15.9	267.3 ± 18.7
21	273.4 ± 18.0	272.9 ± 16.7
28	278.5 ± 17.5	282.7 ± 18.1
35	284.9 ± 17.9	294.1 ± 20.2
42	290.3 ± 18.6	300.9 ± 22.3

Each value shows mean (g) ± S.D.

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 8-3. Body weights of female rats at the recovery period

Group	Control (vehicle: corn oil)	HA 1000 mg/kg
Number of females	5	5
Days of recovery		
1	288.1 ± 25.0	288.4 ± 11.2
7	293.1 ± 24.2	294.2 ± 11.6
14	297.8 ± 29.9	301.8 ± 13.2

Each value shows mean (g) ± S.D.

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 9. Body weights of dams during pregnancy

Group	Control (vehicle: corn oil)	HA 100 mg/kg	HA 300 mg/kg	HA 1000 mg/kg
Number of dams	11	10	12	11
Days of pregnancy				
0	271.5 ± 12.8	260.9 ± 15.3	264.9 ± 13.9	262.9 ± 15.2
7	306.3 ± 17.1	300.0 ± 15.2	300.2 ± 17.5	301.8 ± 17.6
14	342.3 ± 19.8	337.2 ± 18.5	334.7 ± 22.7	335.3 ± 20.7
20	423.1 ± 24.4	419.0 ± 25.2	412.4 ± 33.9	408.3 ± 29.1

Each value shows mean ± S.D. (g).

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 10. Body weights of dams during lactation

Group	Control (vehicle: corn oil)	HA 100 mg/kg	HA 300 mg/kg	HA 1000 mg/kg
Number of dams	11	10	11	11
Days of lactation				
0	327.2 ± 20.2	323.4 ± 24.9	319.9 ± 27.8	333.8 ± 19.9
4	335.1 ± 17.9	335.6 ± 17.6	333.6 ± 25.6	337.1 ± 22.3

Each value shows mean ± S.D. (g).

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 11-1. Food consumption of male rats

Group	Control (vehicle: corn oil)	HA 100 mg/kg	HA 300 mg/kg	HA 1000 mg/kg
Number of males	12	12	12	12
Days of administration				
1	26.6 ± 4.0	27.4 ± 3.0	27.5 ± 3.1	27.0 ± 3.9
7	25.7 ± 3.0	26.9 ± 3.0	25.9 ± 3.6	26.1 ± 3.3
14	24.1 ± 2.6	23.9 ± 2.1	25.1 ± 4.3 (11)	24.7 ± 2.6
29	24.6 ± 3.0	25.2 ± 2.8	25.0 ± 3.2 (11)	25.5 ± 3.4
35	22.8 ± 4.8	23.1 ± 1.9	23.5 ± 3.9 (11)	23.5 ± 3.0
41	25.0 ± 3.5	25.5 ± 3.6	24.4 ± 3.5 (11)	25.1 ± 4.3

Each value shows mean (g) ± S.D.

Significantly different from the control group (*: P<0.05, **: P<0.01).

Figures in parentheses indicate number of males.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 11-2. Food consumption of male rats at the recovery period

Group	Control (vehicle: corn oil)	HA 1000 mg/kg
Number of males	5	5
Days of recovery		
6	31.2 ± 3.2	32.7 ± 5.1
12	30.9 ± 3.0	33.5 ± 2.9

Each value shows mean (g) ± S.D.

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 12-1. Food consumption of female rats

Group	Control (vehicle: corn oil)	HA 100 mg/kg	HA 300 mg/kg	HA 1000 mg/kg
Number of females	12	12	12	12
Days of administration				
1	16.9 ± 3.3	18.2 ± 2.7	18.0 ± 2.9	17.1 ± 3.9
7	16.4 ± 2.8	16.8 ± 2.6	16.6 ± 3.6	17.0 ± 3.9
14	17.7 ± 3.6	15.3 ± 3.8	16.9 ± 2.2	17.1 ± 2.8

Each value shows mean (g) ± S.D.

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 12-2. Food consumption of female rats, satellite group

Group	Control (vehicle: corn oil)	HA 1000 mg/kg
Number of females	10	10
Days of administration		
1	19.9 ± 1.9	19.7 ± 2.7
7	17.9 ± 3.1	17.8 ± 2.9
14	17.4 ± 1.8	17.9 ± 2.9
21	18.6 ± 1.6	18.8 ± 1.7
29	17.9 ± 2.0	18.7 ± 1.8
35	14.4 ± 3.3	16.9 ± 2.3
41	16.1 ± 3.7	18.5 ± 2.5

Each value shows mean (g) ± S.D.

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 12-3. Food consumption of female rats at the recovery period

Group		Control (vehicle: corn oil)	HA 1000 mg/kg
Number of females		5	5
Days of recovery			
	6	20.2 ± 2.5	19.0 ± 2.7
	12	21.4 ± 1.8	20.8 ± 2.4

Each value shows mean (g) ± S.D.

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 13. Food consumption in dams during pregnancy

Group	Control (vehicle: corn oil)	HA 100 mg/kg	HA 300 mg/kg	HA 1000 mg/kg
Number of dams	11	10	12	11
Days of pregnancy				
0	17.9 ± 1.9	18.8 ± 1.6	18.2 ± 2.1	17.0 ± 4.0
7	24.0 ± 4.4	23.5 ± 2.6	23.1 ± 3.1	23.2 ± 2.5
14	24.1 ± 2.5	22.8 ± 2.5	22.4 ± 3.4	23.4 ± 3.8
20	21.2 ± 2.1	22.7 ± 3.1	22.0 ± 4.3	21.9 ± 3.6

Each value shows mean ± S.D. (g).

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 14. Food consumption in dams during lactation

Group	Control (vehicle: corn oil)	HA 100 mg/kg	HA 300 mg/kg	HA 1000 mg/kg
Number of dams	11	10	11	11
Days of lactation				
3	39.1 ± 5.8	39.6 ± 7.0	39.6 ± 8.6	37.0 ± 8.8

Each value shows mean ± S.D. (g).

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 15. Functional findings of male rats at the end of the dosing period

Group	Control (vehicle: corn oil)	HA 100 mg/kg	HA 300 mg/kg	HA 1000 mg/kg
Number of animals	5	5	5	5
Righting reflex	100	100	100	100
Visual placing	100	100	100	100
Pupillary reflex	100	100	100	100
Startle reaction	100	100	100	100
Preyer's reaction	100	100	100	100
Withdrawal reflex	100	100	100	100
Eyelid reflex	100	100	100	100

Values represent % of animals showing normal responses.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 16. Functional findings of female rats at the end of the dosing period

Group	Control (vehicle: corn oil)	HA 100 mg/kg	HA 300 mg/kg	HA 1000 mg/kg
Female, dam				
Number of animals	5	5	5	5
Righting reflex	100	100	100	100
Visual placing	100	100	100	100
Pupillary reflex	100	100	100	100
Startle reaction	100	100	100	100
Preyer's reaction	100	100	100	100
Withdrawal reflex	100	100	100	100
Eyelid reflex	100	100	100	100
Female, satellite groups				
Number of animals	5			5
Righting reflex	100			100
Visual placing	100			100
Pupillary reflex	100			100
Startle reaction	100			100
Preyer's reaction	100			100
Withdrawal reflex	100			100
Eyelid reflex	100			100

Values represent % of animals showing normal responses.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 17. Assessment of grip strength of male rats

Group	Control (vehicle: corn oil)	HA 100 mg/kg	HA 300 mg/kg	HA 1000 mg/kg
Number of males	5	5	5	5
Administration period				
Forelimb	0.922 ± 0.148	0.852 ± 0.147	0.953 ± 0.265	0.956 ± 0.230
Hindlimb	0.481 ± 0.062	0.420 ± 0.056	0.452 ± 0.083	0.505 ± 0.145

Each value shows mean (kg) ±S.D.

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 18. Assessment of grip strength of female rats

Group	Control (vehicle: corn oil)	HA 100 mg/kg	HA 300 mg/kg	HA 1000 mg/kg
Number of females	5	5	5	5
Administration period				
Forelimb	0.810 ± 0.135	0.823 ± 0.068	0.892 ± 0.117	0.898 ± 0.094
Hindlimb	0.447 ± 0.114	0.461 ± 0.121	0.493 ± 0.050	0.502 ± 0.076

Each value shows mean (kg) ±S.D.

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 19. Assessment of grip strength of female rats, satellite group

Group	Control (vehicle: corn oil)	HA 1000 mg/kg
Number of females	5	5
Administration period		
Forelimb	0.681 ± 0.214	0.891 ± 0.054
Hindlimb	0.413 ± 0.017	0.465 ± 0.088

Each value shows mean (kg) ±S.D.

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 20. Motor activity of male rats

Group	Control (vehicle: corn oil)	HA 100 mg/kg	HA 300 mg/kg	HA 1000 mg/kg
Number of males	5	5	5	5
Administration period				
Ambulation (counts)				
5min	1309 ± 289	1258 ± 143	1217 ± 101	1117 ± 170
10min	1213 ± 405	1046 ± 130	1027 ± 176	937 ± 242
15min	966 ± 379	848 ± 198	1054 ± 94	775 ± 282
20min	895 ± 183	693 ± 239	810 ± 231	539 ± 311
Total	4383 ± 1174	3844 ± 560	4108 ± 555	3368 ± 889
Rearing (counts)				
5min	27 ± 2	26 ± 4	31 ± 9	30 ± 5
10min	20 ± 6	18 ± 7	22 ± 12	21 ± 12
15min	15 ± 5	11 ± 8	17 ± 5	14 ± 9
20min	11 ± 8	9 ± 9	9 ± 5	8 ± 6
Total	72 ± 7	65 ± 18	79 ± 25	73 ± 25

Each value shows mean±S.D.

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 21. Motor activity of female rats

Group	Control (vehicle: corn oil)	HA 100 mg/kg	HA 300 mg/kg	HA 1000 mg/kg
Number of females	5	5	5	5
Administration period				
Ambulation (counts)				
5min	1309 ± 182	1122 ± 88	1073 ± 189	1165 ± 156
10min	928 ± 250	975 ± 105	777 ± 145	918 ± 250
15min	1001 ± 289	879 ± 169	564 ± 285	660 ± 243
20min	760 ± 301	767 ± 166	417 ± 231	649 ± 168
Total	3997 ± 928	3744 ± 439	2831 ± 620	3392 ± 671
Rearing (counts)				
5min	34 ± 8	31 ± 7	26 ± 8	31 ± 5
10min	13 ± 9	24 ± 8	13 ± 7	16 ± 6
15min	12 ± 15	14 ± 7	6 ± 7	8 ± 8
20min	9 ± 6	10 ± 6	3 ± 3	7 ± 5
Total	68 ± 20	80 ± 24	47 ± 14	62 ± 6

Each value shows mean±S.D.

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 22. Motor activity of female rats, satellite group

Group	Control (vehicle: corn oil)	HA 1000 mg/kg
Number of females	5	5
Administration period		
Ambulation (counts)		
5min	1264 ± 310	1278 ± 49
10min	1178 ± 311	1205 ± 152
15min	1086 ± 263	1252 ± 129
20min	985 ± 259	1135 ± 209
Total	4513 ± 1118	4871 ± 431
Rearing (counts)		
5min	37 ± 8	36 ± 9
10min	34 ± 12	31 ± 8
15min	29 ± 16	40 ± 20
20min	23 ± 13	32 ± 19
Total	122 ± 40	138 ± 38

Each value shows mean±S.D.

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 23-1. Urinalysis in male rats

Group	Control (vehicle: corn oil)	HA 100 mg/kg	HA 300 mg/kg	HA 1000 mg/kg
Number of males	5	5	5	5
pH				
≦5.0	0	0	0	0
5.5	0	0	0	0
6.0	0	0	0	0
6.5	1	1	1	1
7.0	2	2	0	2
7.5	0	1	1	1
8.0	1	1	2	1
8.5	0	0	1	0
≧9.0	1	0	0	0
Protein				
- (negative)	0	0	0	0
±(10 ≦ and < 30 mg/dL)	0	0	1	2
+ (30 ≦ and < 100 mg/dL)	2	1	3	1
2+ (100 ≦ and < 300 mg/dL)	3	4	1	2
3+ (300 ≦ and < 600 mg/dL)	0	0	0	0
4+ (600 mg/dL ≦)	0	0	0	0
Glucose				
- (negative)	5	5	5	5
±(30 ≦ and < 70 mg/dL)	0	0	0	0
+ (70 ≦ and < 150 mg/dL)	0	0	0	0
2+ (150 ≦ and < 300 mg/dL)	0	0	0	0
3+ (300 ≦ and < 1,000 mg/dL)	0	0	0	0
4+ (1,000 mg/dL ≦)	0	0	0	0
Ketone				
- (negative)	0	0	1	1
±(5 ≦ and < 10 mg/dL)	1	0	0	1
+ (10 ≦ and < 40 mg/dL)	4	5	4	3
2+ (40 ≦ and < 80 mg/dL)	0	0	0	0
3+ (80 ≦ and < 150 mg/dL)	0	0	0	0
4+ (150 mg/dL ≦)	0	0	0	0
Bilirubin				
- (negative)	5	5	5	5
+ (0.5 ≦ and < 2.0 mg/dL)	0	0	0	0
2+ (2.0 ≦ and < 6.0 mg/dL)	0	0	0	0
3+ (6.0 ≦ and < 10.0 mg/dL)	0	0	0	0
4+ (10.0 mg/dL ≦)	0	0	0	0
Occult blood				
- (negative)	5	5	5	5
±(0.03 ≦ and <0.06 mg/dL)	0	0	0	0
+ (0.06 ≦ and <0.20 mg/dL)	0	0	0	0
2+ (0.20 ≦ and <1.00 mg/dL)	0	0	0	0
3+ (1.00 mg/dL ≦)	0	0	0	0
Urobilinogen				
±(normal)	1	1	4	4
+ (2.0 ≦ and < 4.0 mg/dL)	4	2	1	1
2+ (4.0 ≦ and < 8.0 mg/dL)	0	2	0	0
3+ (8.0 ≦ and < 12.0 mg/dL)	0	0	0	0
4+ (12.0 mg/dL ≦)	0	0	0	0

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 23-1 (continued). Urinalysis in male rats

Group	Control (vehicle: corn oil)	HA 100 mg/kg	HA 300 mg/kg	HA 1000 mg/kg
Number of males	5	5	5	5
Color				
light yellow	3	3	5	4
yellow	2	2	0	1
yellowish brown	0	0	0	0
brown	0	0	0	0
bloody	0	0	0	0
Turbidity				
- (negative)	5	5	5	5
±(trace)	0	0	0	0
+ (slight)	0	0	0	0
2+ (moderate)	0	0	0	0
3+ (marked)	0	0	0	0
Red Blood cells				
- (not observed)	5	5	5	5
±(1-9/3 visual field)	0	0	0	0
+ (10-99/3 visual field)	0	0	0	0
2+ (100-299/3 visual field)	0	0	0	0
3+ (≧300/3 visual field)	0	0	0	0
White Blood cells				
- (not observed)	5	5	5	5
±(1-9/3 visual field)	0	0	0	0
+ (10-99/3 visual field)	0	0	0	0
2+ (100-299/3 visual field)	0	0	0	0
3+ (≧300/3 visual field)	0	0	0	0
Casts				
- (not observed)	5	5	5	5
±(1-9/3 visual field)	0	0	0	0
+ (10-99/3 visual field)	0	0	0	0
2+ (100-299/3 visual field)	0	0	0	0
3+ (≧300/3 visual field)	0	0	0	0
Cristals				
- (not observed)	0	0	1	1
±(a few)	5	5	4	4
+ (abundant)	0	0	0	0
Epithelial cells				
- (not observed)	5	5	5	5
±(a few)	0	0	0	0
+ (abundant)	0	0	0	0

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 23-2. Urinalysis in male rats

Group	Control (vehicle: corn oil)			HA 100 mg/kg			HA 300 mg/kg			HA 1000 mg/kg		
Number of males	5			5			5			5		
Urine volume (mL/24hr)	15.7	±	9.6	15.1	±	5.3	19.8	±	19.0	19.5	±	14.1
Specific gravity	1.059	±	0.019	1.062	±	0.015	1.060	±	0.025	1.057	±	0.021
Electrolyte, density												
Na(mEq/L)	116.6	±	41.5	120.2	±	29.5	111.7	±	48.2	113.5	±	44.4
K(mEq/L)	268.61	±	93.37	290.83	±	74.51	263.83	±	113.56	262.31	±	107.29
Cl(mEq/L)	156.3	±	55.2	166.1	±	46.1	149.4	±	70.2	159.1	±	60.9
Electrolyte, gross volume												
Na(mEq/24hr)	1.58	±	0.34	1.70	±	0.17	1.61	±	0.53	1.79	±	0.29
K(mEq/24hr)	3.56	±	0.46	4.10	±	0.16	3.57	±	0.56	4.03	±	0.42
Cl(mEq/24hr)	2.09	±	0.37	2.33	±	0.16	2.06	±	0.61	2.47	±	0.25

Each value shows mean ± S.D.

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 23-3. Urinalysis in male rats of the recovery period

Group	Control (vehicle: corn oil)	HA 1000 mg/kg
Number of males	5	5
pH		
≦5.0	0	0
5.5	0	0
6.0	0	0
6.5	0	0
7.0	0	2
7.5	1	1
8.0	2	2
8.5	2	0
≧9.0	0	0
Protein		
- (negative)	0	0
±(10 ≦ and < 30 mg/dL)	2	0
+ (30 ≦ and < 100 mg/dL)	3	5
2+ (100 ≦ and < 300 mg/dL)	0	0
3+ (300 ≦ and < 600 mg/dL)	0	0
4+ (600 mg/dL ≦)	0	0
Glucose		
- (negative)	5	5
±(30 ≦ and < 70 mg/dL)	0	0
+ (70 ≦ and < 150 mg/dL)	0	0
2+ (150 ≦ and < 300 mg/dL)	0	0
3+ (300 ≦ and < 1,000 mg/dL)	0	0
4+ (1,000 mg/dL ≦)	0	0
Ketone		
- (negative)	4	1
±(5 ≦ and < 10 mg/dL)	1	3
+ (10 ≦ and < 40 mg/dL)	0	1
2+ (40 ≦ and < 80 mg/dL)	0	0
3+ (80 ≦ and < 150 mg/dL)	0	0
4+ (150 mg/dL ≦)	0	0
Bilirubin		
- (negative)	5	5
+ (0.5 ≦ and < 2.0 mg/dL)	0	0
2+ (2.0 ≦ and < 6.0 mg/dL)	0	0
3+ (6.0 ≦ and < 10.0 mg/dL)	0	0
4+ (10.0 mg/dL ≦)	0	0
Occult blood		
- (negative)	5	5
±(0.03 ≦ and <0.06 mg/dL)	0	0
+ (0.06 ≦ and <0.20 mg/dL)	0	0
2+ (0.20 ≦ and <1.00 mg/dL)	0	0
3+ (1.00 mg/dL ≦)	0	0
Urobilinogen		
±(normal)	5	4
+ (2.0 ≦ and < 4.0 mg/dL)	0	1
2+ (4.0 ≦ and < 8.0 mg/dL)	0	0
3+ (8.0 ≦ and < 12.0 mg/dL)	0	0
4+ (12.0 mg/dL ≦)	0	0

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 23-3 (continued). Urinalysis in male rats of the recovery period

Group	Control (vehicle: corn oil)	HA 1000 mg/kg
Number of males	5	5
Color		
light yellow	5	5
yellow	0	0
yellowish brown	0	0
brown	0	0
bloody	0	0
Turbidity		
- (negative)	4	5
±(trace)	0	0
+ (slight)	1	0
2+ (moderate)	0	0
3+ (marked)	0	0
Red Blood cells		
- (not observed)	5	5
±(1-9/3 visual field)	0	0
+ (10-99/3 visual field)	0	0
2+ (100-299/3 visual field)	0	0
3+ (≧300/3 visual field)	0	0
White Blood cells		
- (not observed)	5	5
±(1-9/3 visual field)	0	0
+ (10-99/3 visual field)	0	0
2+ (100-299/3 visual field)	0	0
3+ (≧300/3 visual field)	0	0
Casts		
- (not observed)	5	5
±(1-9/3 visual field)	0	0
+ (10-99/3 visual field)	0	0
2+ (100-299/3 visual field)	0	0
3+ (≧300/3 visual field)	0	0
Cristals		
- (not observed)	1	0
±(a few)	4	5
+ (abundant)	0	0
Epithelial cells		
- (not observed)	5	5
±(a few)	0	0
+ (abundant)	0	0

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 23-4. Urinalysis in male rats of the recovery period

Group	Control (vehicle: corn oil)			HA 1000 mg/kg		
Number of males	5			5		
Urine volume (mL/24hr)	27.3	±	6.9	18.8	±	5.0
Specific gravity	1.045	±	0.013	1.061	±	0.017
Electrolyte, density						
Na(mEq/L)	97.4	±	19.1	123.5	±	26.1
K(mEq/L)	206.41	±	53.56	282.11	±	84.59
Cl(mEq/L)	136.5	±	30.0	168.7	±	47.5
Electrolyte, gross volume						
Na(mEq/24hr)	2.57	±	0.47	2.22	±	0.24
K(mEq/24hr)	5.37	±	0.64	4.97	±	0.38
Cl(mEq/24hr)	3.58	±	0.51	2.99	±	0.22 *

Each value shows mean ± S.D.

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 24-1. Urinalysis in female rats, satellite group

Group	Control (vehicle: corn oil)	HA 1000 mg/kg
Number of females	5	5
pH		
≦5.0	0	0
5.5	0	0
6.0	0	0
6.5	4	3
7.0	1	2
7.5	0	0
8.0	0	0
8.5	0	0
≧9.0	0	0
Protein		
- (negative)	0	2
±(10 ≦ and < 30 mg/dL)	1	1
+ (30 ≦ and < 100 mg/dL)	3	0
2+ (100 ≦ and < 300 mg/dL)	1	2
3+ (300 ≦ and < 600 mg/dL)	0	0
4+ (600 mg/dL ≦)	0	0
Glucose		
- (negative)	5	5
±(30 ≦ and < 70 mg/dL)	0	0
+ (70 ≦ and < 150 mg/dL)	0	0
2+ (150 ≦ and < 300 mg/dL)	0	0
3+ (300 ≦ and < 1,000 mg/dL)	0	0
4+ (1,000 mg/dL ≦)	0	0
Ketone		
- (negative)	0	2
±(5 ≦ and < 10 mg/dL)	4	1
+ (10 ≦ and < 40 mg/dL)	1	2
2+ (40 ≦ and < 80 mg/dL)	0	0
3+ (80 ≦ and < 150 mg/dL)	0	0
4+ (150 mg/dL ≦)	0	0
Bilirubin		
- (negative)	4	4
+ (0.5 ≦ and < 2.0 mg/dL)	1	1
2+ (2.0 ≦ and < 6.0 mg/dL)	0	0
3+ (6.0 ≦ and < 10.0 mg/dL)	0	0
4+ (10.0 mg/dL ≦)	0	0
Occult blood		
- (negative)	5	5
±(0.03 ≦ and <0.06 mg/dL)	0	0
+ (0.06 ≦ and <0.20 mg/dL)	0	0
2+ (0.20 ≦ and <1.00 mg/dL)	0	0
3+ (1.00 mg/dL ≦)	0	0
Urobilinogen		
±(normal)	2	3
+ (2.0 ≦ and < 4.0 mg/dL)	3	2
2+ (4.0 ≦ and < 8.0 mg/dL)	0	0
3+ (8.0 ≦ and < 12.0 mg/dL)	0	0
4+ (12.0 mg/dL ≦)	0	0

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 24-1 (continued). Urinalysis in female rats, satellite group

Group	Control (vehicle: corn oil)	HA 1000 mg/kg
Number of females	5	5
Color		
light yellow	4	3
yellow	1	2
yellowish brown	0	0
brown	0	0
bloody	0	0
Turbidity		
- (negative)	5	5
±(trace)	0	0
+ (slight)	0	0
2+ (moderate)	0	0
3+ (marked)	0	0
Red Blood cells		
- (not observed)	5	5
±(1-9/3 visual field)	0	0
+ (10-99/3 visual field)	0	0
2+ (100-299/3 visual field)	0	0
3+ (≧300/3 visual field)	0	0
White Blood cells		
- (not observed)	5	5
±(1-9/3 visual field)	0	0
+ (10-99/3 visual field)	0	0
2+ (100-299/3 visual field)	0	0
3+ (≧300/3 visual field)	0	0
Casts		
- (not observed)	5	5
±(1-9/3 visual field)	0	0
+ (10-99/3 visual field)	0	0
2+ (100-299/3 visual field)	0	0
3+ (≧300/3 visual field)	0	0
Cristals		
- (not observed)	3	3
±(a few)	2	2
+ (abundant)	0	0
Epithelial cells		
- (not observed)	5	5
±(a few)	0	0
+ (abundant)	0	0

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 24-2. Urinalysis in female rats, satellite group

Group	Control (vehicle: corn oil)			HA 1000 mg/kg		
Number of females	5			5		
Urine volume (mL/24hr)	11.5	±	5.9	14.0	±	7.7
Specific gravity	1.055	±	0.023	1.057	±	0.025
Electrolyte, density						
Na(mEq/L)	104.6	±	56.7	101.8	±	34.5
K(mEq/L)	253.59	±	122.62	252.62	±	105.54
Cl(mEq/L)	152.2	±	83.0	159.1	±	68.9
Electrolyte, gross volume						
Na(mEq/24hr)	1.09	±	0.56	1.24	±	0.41
K(mEq/24hr)	2.56	±	1.00	2.96	±	0.74
Cl(mEq/24hr)	1.57	±	0.78	1.85	±	0.49

Each value shows mean ± S.D.

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 24-3. Urinalysis in female rats of the recovery period

Group	Control (vehicle: corn oil)	HA 1000 mg/kg
Number of females	5	5
pH		
≦5.0	0	0
5.5	0	0
6.0	0	0
6.5	2	1
7.0	3	3
7.5	0	1
8.0	0	0
8.5	0	0
≧9.0	0	0
Protein		
- (negative)	3	2
±(10 ≦ and < 30 mg/dL)	2	1
+ (30 ≦ and < 100 mg/dL)	0	2
2+ (100 ≦ and < 300 mg/dL)	0	0
3+ (300 ≦ and < 600 mg/dL)	0	0
4+ (600 mg/dL ≦)	0	0
Glucose		
- (negative)	5	5
±(30 ≦ and < 70 mg/dL)	0	0
+ (70 ≦ and < 150 mg/dL)	0	0
2+ (150 ≦ and < 300 mg/dL)	0	0
3+ (300 ≦ and < 1,000 mg/dL)	0	0
4+ (1,000 mg/dL ≦)	0	0
Ketone		
- (negative)	5	5
±(5 ≦ and < 10 mg/dL)	0	0
+ (10 ≦ and < 40 mg/dL)	0	0
2+ (40 ≦ and < 80 mg/dL)	0	0
3+ (80 ≦ and < 150 mg/dL)	0	0
4+ (150 mg/dL ≦)	0	0
Bilirubin		
- (negative)	5	5
+ (0.5 ≦ and < 2.0 mg/dL)	0	0
2+ (2.0 ≦ and < 6.0 mg/dL)	0	0
3+ (6.0 ≦ and < 10.0 mg/dL)	0	0
4+ (10.0 mg/dL ≦)	0	0
Occult blood		
- (negative)	5	5
±(0.03 ≦ and <0.06 mg/dL)	0	0
+ (0.06 ≦ and <0.20 mg/dL)	0	0
2+ (0.20 ≦ and <1.00 mg/dL)	0	0
3+ (1.00 mg/dL ≦)	0	0
Urobilinogen		
±(normal)	5	5
+ (2.0 ≦ and < 4.0 mg/dL)	0	0
2+ (4.0 ≦ and < 8.0 mg/dL)	0	0
3+ (8.0 ≦ and < 12.0 mg/dL)	0	0
4+ (12.0 mg/dL ≦)	0	0

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 24-3 (continued). Urinalysis in female rats of the recovery period

Group	Control (vehicle: corn oil)	HA 1000 mg/kg
Number of females	5	5
Color		
light yellow	5	5
yellow	0	0
yellowish brown	0	0
brown	0	0
bloody	0	0
Turbidity		
- (negative)	5	5
±(trace)	0	0
+ (slight)	0	0
2+ (moderate)	0	0
3+ (marked)	0	0
Red Blood cells		
- (not observed)	5	5
±(1-9/3 visual field)	0	0
+ (10-99/3 visual field)	0	0
2+ (100-299/3 visual field)	0	0
3+ (≧300/3 visual field)	0	0
White Blood cells		
- (not observed)	5	5
±(1-9/3 visual field)	0	0
+ (10-99/3 visual field)	0	0
2+ (100-299/3 visual field)	0	0
3+ (≧300/3 visual field)	0	0
Casts		
- (not observed)	5	5
±(1-9/3 visual field)	0	0
+ (10-99/3 visual field)	0	0
2+ (100-299/3 visual field)	0	0
3+ (≧300/3 visual field)	0	0
Cristals		
- (not observed)	3	1
±(a few)	2	4
+ (abundant)	0	0
Epithelial cells		
- (not observed)	5	5
±(a few)	0	0
+ (abundant)	0	0

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 24-4. Urinalysis in female rats of the recovery period

Group	Control (vehicle: corn oil)			HA 1000 mg/kg		
Number of females	5			5		
Urine volume (mL/24hr)	17.2	±	8.2	16.5	±	4.3
Specific gravity	1.044	±	0.010	1.051	±	0.010
Electrolyte, density						
Na(mEq/L)	98.1	±	21.5	127.4	±	30.8
K(mEq/L)	181.54	±	34.56	234.18	±	49.06
Cl(mEq/L)	114.4	±	20.6	163.4	±	39.1 *
Electrolyte, gross volume						
Na(mEq/24hr)	1.59	±	0.52	2.03	±	0.37
K(mEq/24hr)	2.92	±	0.90	3.75	±	0.68
Cl(mEq/24hr)	1.86	±	0.62	2.60	±	0.44

Each value shows mean ± S.D.

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 25-1. Hematological findings of male rats at the end of the dosing period

Group		Control (vehicle: corn oil)	HA 100 mg/kg	HA 300 mg/kg	HA 1000 mg/kg
Number of males		5	5	5	5
RBC	10000/μL	798 ± 56	787 ± 38	814 ± 15	789 ± 36
HGB	g/dL	14.7 ± 1.1	14.4 ± 0.7	14.7 ± 0.4	14.2 ± 0.4
Hematocrit	%	43.2 ± 2.7	42.5 ± 2.0	42.8 ± 1.5	42.1 ± 0.8
MCV	fL	54.1 ± 2.4	54.0 ± 2.7	52.5 ± 1.9	53.4 ± 2.2
MCH	pg	18.5 ± 0.9	18.2 ± 0.7	18.0 ± 0.5	18.0 ± 0.4
MCHC	g/dL	34.1 ± 0.5	33.8 ± 0.8	34.3 ± 0.5	33.8 ± 0.8
Platelet	10000/μL	88.7 ± 12.1	93.3 ± 5.9	98.7 ± 8.5	95.8 ± 8.3
PT	sec.	16.6 ± 2.3	20.2 ± 5.4	18.1 ± 2.6	17.2 ± 2.9
APTT	sec.	18.9 ± 1.5	23.5 ± 5.9	20.9 ± 1.7	20.1 ± 2.3
WBC	100/μL	68.5 ± 19.3	90.1 ± 36.8	78.5 ± 15.1	90.6 ± 14.1
Neutrophil	%	18.5 ± 5.4	23.7 ± 11.6	20.0 ± 3.2	19.6 ± 4.0
Eosinophil	%	2.4 ± 0.8	1.4 ± 0.5	1.9 ± 0.7	1.3 ± 0.3 *
Basophil	%	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.1
Monocyte	%	4.9 ± 0.9	3.6 ± 1.3	4.8 ± 1.2	4.7 ± 1.0
Lymphocyte	%	74.2 ± 6.4	71.2 ± 10.4	73.3 ± 4.6	74.4 ± 3.5
Reticulocyte	%	3.17 ± 0.32	3.10 ± 0.54	3.19 ± 0.60	2.89 ± 0.62

Each value shows mean ± S.D.

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 25-2. Hematological findings of male rats at the end of the recovery period

Group		Control (vehicle: corn oil)	HA 1000 mg/kg
Number of males		5	5
RBC	10000/μL	770 ± 27	768 ± 23
HGB	g/dL	13.5 ± 0.8	13.7 ± 0.4
Hematocrit	%	40.2 ± 2.3	40.7 ± 0.9
MCV	fL	52.2 ± 1.5	53.0 ± 1.8
MCH	pg	17.6 ± 0.5	17.9 ± 0.6
MCHC	g/dL	33.6 ± 0.2	33.7 ± 0.4
Platelet	10000/μL	97.7 ± 14.6	101.4 ± 12.6
PT	sec.	15.2 ± 2.1	14.8 ± 1.2
APTT	sec.	17.0 ± 3.5	16.7 ± 1.4
WBC	100/μL	88.1 ± 25.3	79.9 ± 26.0
Neutrophil	%	14.7 ± 7.8	16.4 ± 4.3
Eosinophil	%	1.4 ± 0.4	1.7 ± 1.2
Basophil	%	0.0 ± 0.0	0.0 ± 0.1
Monocyte	%	3.2 ± 1.0	4.4 ± 0.9
Lymphocyte	%	80.7 ± 8.4	77.4 ± 5.7
Reticulocyte	%	3.57 ± 0.36	3.47 ± 0.50

Each value shows mean ± S.D.

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 26-1. Hematological findings of female rats at the end of the dosing period

Group		Control (vehicle: corn oil)	HA 100 mg/kg	HA 300 mg/kg	HA 1000 mg/kg
Number of females		5	5	5	5
RBC	10000/μL	617 ± 22	632 ± 48	619 ± 25	657 ± 31
HGB	g/dL	12.3 ± 0.5	12.2 ± 0.7	12.2 ± 0.6	12.7 ± 0.6
Hematocrit	%	37.4 ± 1.8	37.4 ± 2.2	37.5 ± 1.8	38.4 ± 1.5
MCV	fL	60.6 ± 3.1	59.2 ± 2.1	60.5 ± 3.8	58.5 ± 1.0
MCH	pg	19.9 ± 0.7	19.3 ± 0.5	19.7 ± 0.9	19.3 ± 0.2
MCHC	g/dL	32.9 ± 0.7	32.6 ± 0.5	32.6 ± 0.6	33.0 ± 0.5
Platelet	10000/μL	106.5 ± 10.1	98.5 ± 7.5	98.0 ± 7.5	111.1 ± 22.8
PT	sec.	13.5 ± 0.6	13.6 ± 1.0	13.3 ± 0.6	13.1 ± 0.5
APTT	sec.	14.6 ± 0.5	14.9 ± 1.1	16.2 ± 1.6	15.2 ± 2.2
WBC	100/μL	92.5 ± 15.6	100.6 ± 32.1	77.7 ± 18.8	103.2 ± 21.8
Neutrophil	%	27.0 ± 5.4	35.4 ± 6.8	36.5 ± 14.9	37.3 ± 8.1
Eosinophil	%	0.8 ± 0.4	0.9 ± 0.5	0.9 ± 0.4	0.6 ± 0.3
Basophil	%	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
Monocyte	%	3.2 ± 1.2	3.3 ± 0.6	4.9 ± 0.6	4.4 ± 1.5
Lymphocyte	%	68.9 ± 5.5	60.4 ± 6.7	57.7 ± 15.4	57.7 ± 9.6
Reticulocyte	%	8.43 ± 0.84	7.94 ± 1.47	7.76 ± 1.36	7.27 ± 1.34

Each value shows mean ± S.D.

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 26-2. Hematological findings of female rats at the end of the dosing period, satellite group

Group		Control (vehicle: corn oil)	HA 1000 mg/kg
Number of females		5	5
RBC	10000/μL	694 ± 15	668 ± 32
HGB	g/dL	13.2 ± 0.5	12.7 ± 0.4
Hematocrit	%	39.1 ± 0.8	38.0 ± 1.4
MCV	fL	56.4 ± 0.5	56.9 ± 1.6
MCH	pg	19.0 ± 0.3	19.0 ± 0.7
MCHC	g/dL	33.8 ± 0.6	33.4 ± 0.6
Platelet	10000/μL	93.3 ± 2.0	84.7 ± 13.4
PT	sec.	12.4 ± 0.6	12.9 ± 0.6
APTT	sec.	14.9 ± 2.1	15.1 ± 3.3
WBC	100/μL	59.7 ± 14.5	52.0 ± 20.8
Neutrophil	%	12.9 ± 5.2	15.2 ± 5.2
Eosinophil	%	1.7 ± 0.4	1.9 ± 0.7
Basophil	%	0.0 ± 0.0	0.0 ± 0.0
Monocyte	%	3.1 ± 0.9	2.9 ± 1.2
Lymphocyte	%	82.3 ± 6.1	80.0 ± 5.3
Reticulocyte	%	3.43 ± 0.44	3.66 ± 0.37

Each value shows mean ± S.D.

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 26-3. Hematological findings of female rats at the end of the recovery period

Group		Control (vehicle: corn oil)	HA 1000 mg/kg	
Number of females		5	5	
RBC	10000/μL	747 ± 37	723 ± 19	
HGB	g/dL	13.7 ± 0.4	13.3 ± 0.4	
Hematocrit	%	39.9 ± 1.4	39.5 ± 1.0	
MCV	fL	53.6 ± 2.0	54.7 ± 1.2	
MCH	pg	18.3 ± 0.6	18.5 ± 0.4	
MCHC	g/dL	34.2 ± 0.3	33.8 ± 0.6	
Platelet	10000/μL	96.2 ± 8.0	95.4 ± 5.8	
PT	sec.	12.9 ± 0.3	12.9 ± 0.3	
APTT	sec.	14.9 ± 0.6	15.6 ± 1.3	
WBC	100/μL	41.0 ± 8.9	34.3 ± 7.2	
Neutrophil	%	16.8 ± 3.0	19.3 ± 2.7	
Eosinophil	%	2.8 ± 0.4	2.1 ± 0.4	*
Basophil	%	0.0 ± 0.0	0.0 ± 0.0	
Monocyte	%	2.9 ± 0.4	3.0 ± 0.3	
Lymphocyte	%	77.5 ± 3.4	75.6 ± 2.8	
Reticulocyte	%	3.16 ± 1.06	3.30 ± 0.83	

Each value shows mean ± S.D.

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 27-1. Biochemical findings of male rats at the end of the dosing period

Group		Control (vehicle: corn oil)	HA 100 mg/kg	HA 300 mg/kg	HA 1000 mg/kg
Number of males		5	5	5	5
Total protein	g/dL	4.7 ± 0.1	4.8 ± 0.4	4.6 ± 0.3	4.8 ± 0.4
Albumin	g/dL	3.2 ± 0.1	3.2 ± 0.2	3.1 ± 0.3	3.2 ± 0.2
A/G		2.25 ± 0.21	1.95 ± 0.33	2.02 ± 0.17	1.99 ± 0.16
Glucose	mg/dL	125 ± 19	126 ± 7	138 ± 10	117 ± 5
Total cholesterol	mg/dL	43 ± 5	45 ± 9	47 ± 9	51 ± 11
Triglyceride	mg/dL	41 ± 10	41 ± 22	38 ± 18	41 ± 10
Phospholipid	mg/dL	78 ± 9	82 ± 16	81 ± 13	84 ± 15
AST	U/L	52 ± 6	47 ± 4	53 ± 4	52 ± 6
ALT	U/L	24 ± 4	24 ± 2	26 ± 1	23 ± 2
γ-GTP	U/L	0 ± 0	0 ± 0	0 ± 0	0 ± 0
LDH	U/L	77 ± 15	151 ± 101	183 ± 83	157 ± 96
Bile acid	μmol/L	9.5 ± 2.6	7.2 ± 3.6	13.2 ± 9.4	14.8 ± 9.9
BUN	mg/dL	12.2 ± 1.9	13.4 ± 3.9	12.8 ± 0.8	12.1 ± 2.0
Creatinine	mg/dL	0.22 ± 0.04	0.26 ± 0.05	0.27 ± 0.03	0.27 ± 0.03
Total bilirubin	mg/dL	0.08 ± 0.01	0.07 ± 0.02	0.08 ± 0.01	0.07 ± 0.01
ALP	U/L	616 ± 138	491 ± 124	534 ± 35	531 ± 100
Inorganic phosphorus	mg/dL	5.4 ± 0.2	5.4 ± 0.3	5.5 ± 0.7	5.4 ± 0.2
Ca	mg/dL	8.2 ± 0.1	8.4 ± 0.3	8.2 ± 0.4	8.3 ± 0.3
Na	mEq/L	146.4 ± 1.4	146.0 ± 1.3	145.9 ± 0.9	146.3 ± 1.2
K	mEq/L	3.76 ± 0.17	3.88 ± 0.25	3.75 ± 0.14	3.75 ± 0.22
Cl	mEq/L	112.8 ± 1.3	112.6 ± 0.8	112.3 ± 1.5	112.6 ± 1.2

Each value shows mean ± S.D.

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 27-2. Biochemical findings of male rats at the end of the recovery period

Group		Control (vehicle: corn oil)	HA 1000 mg/kg
Number of males		5	5
Total protein	g/dL	5.4 ± 0.3	5.5 ± 0.3
Albumin	g/dL	3.5 ± 0.2	3.5 ± 0.2
A/G		1.86 ± 0.12	1.74 ± 0.11
Glucose	mg/dL	141 ± 14	140 ± 13
Total cholesterol	mg/dL	50 ± 11	58 ± 10
Triglyceride	mg/dL	47 ± 31	31 ± 10
Phospholipid	mg/dL	78 ± 11	84 ± 12
AST	U/L	57 ± 8	62 ± 9
ALT	U/L	25 ± 3	33 ± 14
γ-GTP	U/L	0 ± 0	0 ± 0
LDH	U/L	102 ± 46	108 ± 40
Bile acid	μmol/L	15.1 ± 10.6	11.0 ± 3.5
BUN	mg/dL	15.3 ± 1.6	14.1 ± 1.5
Creatinine	mg/dL	0.31 ± 0.04	0.32 ± 0.03
Total bilirubin	mg/dL	0.06 ± 0.01	0.06 ± 0.01
ALP	U/L	390 ± 49	443 ± 68
Inorganic phosphorus	mg/dL	5.9 ± 0.8	5.8 ± 0.6
Ca	mg/dL	9.0 ± 0.3	9.0 ± 0.3
Na	mEq/L	144.0 ± 1.2	144.3 ± 1.4
K	mEq/L	3.68 ± 0.21	3.60 ± 0.24
Cl	mEq/L	111.2 ± 2.0	111.2 ± 1.6

Each value shows mean ± S.D.

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 28-1. Biochemical findings of female rats at the end of the dosing period

Group		Control (vehicle: corn oil)	HA 100 mg/kg	HA 300 mg/kg	HA 1000 mg/kg
Number of females		5	5	5	5
Total protein	g/dL	5.4 ± 0.2	5.5 ± 0.3	5.6 ± 0.1	5.7 ± 0.2
Albumin	g/dL	3.7 ± 0.1	3.7 ± 0.2	3.8 ± 0.1	3.9 ± 0.1
A/G		2.17 ± 0.15	2.07 ± 0.11	2.13 ± 0.20	2.25 ± 0.15
Glucose	mg/dL	122 ± 6	124 ± 9	116 ± 8	121 ± 14
Total cholesterol	mg/dL	46 ± 7	48 ± 8	43 ± 6	53 ± 2
Triglyceride	mg/dL	26 ± 13	31 ± 12	23 ± 9	29 ± 12
Phospholipid	mg/dL	89 ± 10	93 ± 11	87 ± 10	101 ± 9
AST	U/L	65 ± 6	103 ± 48	92 ± 31	83 ± 25
ALT	U/L	35 ± 3	44 ± 7	44 ± 9	38 ± 6
γ-GTP	U/L	0 ± 0	0 ± 0	0 ± 0	0 ± 0
LDH	U/L	75 ± 27	117 ± 54	176 ± 70	120 ± 47
Bile acid	μmol/L	21.6 ± 21.2	11.0 ± 2.6	10.7 ± 3.9	9.1 ± 2.0
BUN	mg/dL	11.6 ± 1.2	13.4 ± 1.4	12.3 ± 1.8	12.8 ± 2.3
Creatinine	mg/dL	0.32 ± 0.02	0.35 ± 0.06	0.34 ± 0.03	0.37 ± 0.05
Total bilirubin	mg/dL	0.06 ± 0.01	0.06 ± 0.01	0.05 ± 0.02	0.07 ± 0.01
ALP	U/L	250 ± 74	246 ± 61	263 ± 46	277 ± 184
Inorganic phosphorus	mg/dL	6.0 ± 1.2	5.7 ± 0.5	6.0 ± 0.4	6.4 ± 0.4
Ca	mg/dL	9.0 ± 0.2	9.1 ± 0.4	9.2 ± 0.1	9.4 ± 0.4
Na	mEq/L	142.9 ± 1.3	143.2 ± 1.0	143.6 ± 1.1	142.6 ± 0.8
K	mEq/L	3.68 ± 0.20	3.62 ± 0.33	3.51 ± 0.22	3.55 ± 0.34
Cl	mEq/L	112.0 ± 2.0	111.4 ± 0.8	110.5 ± 1.4	108.6 ± 1.5 **

Each value shows mean ± S.D.

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 28-2. Biochemical findings of female rats at the end of the dosing period, satellite group

Group		Control (vehicle: corn oil)	HA 1000 mg/kg
Number of females		5	5
Total protein	g/dL	4.9 ± 0.2	4.8 ± 0.2
Albumin	g/dL	3.5 ± 0.2	3.3 ± 0.2
A/G		2.48 ± 0.21	2.23 ± 0.19
Glucose	mg/dL	104 ± 13	102 ± 11
Total cholesterol	mg/dL	54 ± 7	53 ± 13
Triglyceride	mg/dL	18 ± 9	12 ± 6
Phospholipid	mg/dL	105 ± 14	98 ± 20
AST	U/L	54 ± 16	57 ± 6
ALT	U/L	21 ± 7	21 ± 2
γ-GTP	U/L	1 ± 0	0 ± 0 **
LDH	U/L	58 ± 25	74 ± 25
Bile acid	μmol/L	11.8 ± 4.0	11.9 ± 6.5
BUN	mg/dL	13.6 ± 2.1	16.4 ± 2.0
Creatinine	mg/dL	0.40 ± 0.03	0.42 ± 0.05
Total bilirubin	mg/dL	0.09 ± 0.02	0.09 ± 0.01
ALP	U/L	267 ± 77	282 ± 74
Inorganic phosphorus	mg/dL	4.0 ± 0.4	4.3 ± 0.2
Ca	mg/dL	7.8 ± 0.4	8.0 ± 0.1
Na	mEq/L	145.3 ± 0.9	145.6 ± 0.5
K	mEq/L	3.52 ± 0.18	3.65 ± 0.16
Cl	mEq/L	113.8 ± 0.9	113.4 ± 1.2

Each value shows mean ± S.D.

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 28-3. Biochemical findings of female rats at the end of the recovery period

Group		Control (vehicle: corn oil)	HA 1000 mg/kg
Number of females		5	5
Total protein	g/dL	5.7 ± 0.4	5.9 ± 0.4
Albumin	g/dL	3.9 ± 0.4	4.1 ± 0.4
A/G		2.25 ± 0.41	2.24 ± 0.25
Glucose	mg/dL	115 ± 16	130 ± 14
Total cholesterol	mg/dL	74 ± 14	61 ± 10
Triglyceride	mg/dL	23 ± 17	23 ± 13
Phospholipid	mg/dL	127 ± 21	115 ± 17
AST	U/L	68 ± 17	61 ± 5
ALT	U/L	26 ± 8	27 ± 7
γ-GTP	U/L	0 ± 0	0 ± 0
LDH	U/L	81 ± 34	85 ± 47
Bile acid	μmol/L	11.6 ± 4.0	9.0 ± 0.8
BUN	mg/dL	20.1 ± 2.9	19.6 ± 2.1
Creatinine	mg/dL	0.46 ± 0.07	0.46 ± 0.05
Total bilirubin	mg/dL	0.08 ± 0.01	0.07 ± 0.01
ALP	U/L	201 ± 39	207 ± 33
Inorganic phosphorus	mg/dL	4.2 ± 0.6	3.6 ± 0.4
Ca	mg/dL	8.8 ± 0.5	9.0 ± 0.4
Na	mEq/L	144.2 ± 0.8	144.0 ± 0.3
K	mEq/L	3.44 ± 0.19	3.23 ± 0.16
Cl	mEq/L	112.4 ± 0.8	113.0 ± 1.0

Each value shows mean ± S.D.

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 29-1. Organ weights of male rats at the end of the dosing period

Group		Control (vehicle: corn oil)	HA 100 mg/kg	HA 300 mg/kg	HA 1000 mg/kg
Number of males		7	12	11	7
Body weight	(g)	496.2 ± 45.3	492.8 ± 41.5	503.5 ± 43.3	511.1 ± 53.4
Brain	(mg)	2073.7 ± 50.4	2027.4 ± 95.4	2051.4 ± 85.8	2081.6 ± 87.6
	(mg/g)	4.205 ± 0.339	4.136 ± 0.333	4.097 ± 0.323	4.101 ± 0.351
Thymus	(mg)	269.5 ± 67.3	279.0 ± 44.5	261.8 ± 81.6	342.7 ± 81.4
	(mg/g)	0.546 ± 0.145	0.568 ± 0.090	0.516 ± 0.135	0.666 ± 0.114
Heart	(mg)	1464.1 ± 93.1	1422.5 ± 150.4	1537.3 ± 110.2	1483.8 ± 230.7
	(mg/g)	2.963 ± 0.209	2.890 ± 0.242	3.062 ± 0.196	2.892 ± 0.213
Liver	(mg)	13368.3 ± 1882.6	13539.6 ± 1788.7	13922.0 ± 2212.9	13818.3 ± 2217.8
	(mg/g)	26.892 ± 2.028	27.441 ± 2.470	27.533 ± 2.667	26.913 ± 1.710
Kidney (R)	(mg)	1626.8 ± 139.9	1642.0 ± 159.1	1718.1 ± 151.7	1638.2 ± 208.3
	(mg/g)	3.284 ± 0.171	3.338 ± 0.267	3.427 ± 0.342	3.210 ± 0.301
Kidney (L)	(mg)	1628.2 ± 169.7	1635.3 ± 154.1	1711.4 ± 148.0	1633.2 ± 174.2
	(mg/g)	3.281 ± 0.164	3.323 ± 0.229	3.412 ± 0.310	3.200 ± 0.194
Kidneys	(mg)	3255.0 ± 308.9	3277.3 ± 309.5	3429.5 ± 295.1	3271.4 ± 378.9
	(mg/g)	6.564 ± 0.328	6.660 ± 0.486	6.839 ± 0.643	6.410 ± 0.491
Spleen	(mg)	805.5 ± 108.5	754.7 ± 168.3	753.8 ± 109.5	797.6 ± 117.5
	(mg/g)	1.627 ± 0.196	1.530 ± 0.303	1.497 ± 0.168	1.559 ± 0.120
Testis (R)	(mg)	1706.0 ± 120.3	1712.8 ± 171.4	1741.6 ± 151.3	1701.8 ± 97.0
	(mg/g)	3.477 ± 0.528	3.490 ± 0.390	3.481 ± 0.423	3.362 ± 0.409
Testis (L)	(mg)	1704.5 ± 119.6	1701.2 ± 167.9	1735.5 ± 136.8	1702.1 ± 103.7
	(mg/g)	3.472 ± 0.511	3.469 ± 0.399	3.468 ± 0.390	3.358 ± 0.363
Testes	(mg)	3410.5 ± 236.7	3414.0 ± 335.3	3477.1 ± 284.8	3403.9 ± 197.0
	(mg/g)	6.949 ± 1.036	6.959 ± 0.784	6.949 ± 0.809	6.719 ± 0.769
Epididymis (R)	(mg)	625.3 ± 58.6	623.9 ± 59.9	631.3 ± 56.9	622.9 ± 52.5
	(mg/g)	1.272 ± 0.188	1.273 ± 0.150	1.257 ± 0.105	1.228 ± 0.140
Epididymis (L)	(mg)	615.4 ± 58.3	617.9 ± 54.9	617.6 ± 52.6	623.2 ± 33.4
	(mg/g)	1.250 ± 0.172	1.260 ± 0.126	1.231 ± 0.111	1.227 ± 0.103
Epididymides	(mg)	1240.7 ± 115.0	1241.8 ± 112.5	1248.8 ± 105.6	1246.0 ± 82.3
	(mg/g)	2.522 ± 0.358	2.533 ± 0.273	2.488 ± 0.208	2.455 ± 0.239

Each value shows mean ± S.D.
Significantly different from the control group (*: P<0.05, **: P<0.01).

Group		Control (vehicle: corn oil)	HA 100 mg/kg	HA 300 mg/kg	HA 1000 mg/kg
Number of males		7	12	11	7
Body weight	(g)	496.2 ± 45.3	492.8 ± 41.5	503.5 ± 43.3	511.1 ± 53.4
Prostate, ventral	(mg)	619.5 ± 84.5	681.4 ± 165.6	672.9 ± 179.5	671.4 ± 105.0
	(mg/g)	1.255 ± 0.196	1.401 ± 0.384	1.338 ± 0.348	1.341 ± 0.320
Seminal vesicles	(mg)	1625.7 ± 353.8	1729.3 ± 243.1	1827.1 ± 184.0	1815.7 ± 159.4
	(mg/g)	3.289 ± 0.767	3.529 ± 0.543	3.655 ± 0.501	3.568 ± 0.310
Thyroid gland	(mg)	24.8 ± 4.3	23.7 ± 5.4	25.2 ± 4.3	27.1 ± 5.2
	(mg/g)	0.051 ± 0.012	0.048 ± 0.009	0.051 ± 0.010	0.053 ± 0.010
Adrenal gland (R)	(mg)	25.2 ± 4.1	26.3 ± 3.2	28.2 ± 5.8	28.3 ± 3.0
	(mg/g)	0.051 ± 0.010	0.054 ± 0.007	0.056 ± 0.012	0.056 ± 0.006
Adrenal gland (L)	(mg)	25.9 ± 4.7	28.7 ± 4.9	29.7 ± 5.1	30.0 ± 1.9
	(mg/g)	0.053 ± 0.012	0.059 ± 0.011	0.059 ± 0.010	0.059 ± 0.006
Adrenal glands	(mg)	51.1 ± 8.3	55.0 ± 7.9	57.8 ± 10.7	58.3 ± 4.7
	(mg/g)	0.104 ± 0.021	0.112 ± 0.018	0.115 ± 0.022	0.115 ± 0.012

Each value shows mean ± S.D.
Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 29-2. Organ weights of male rats at the end of the recovery period

Group		Control (vehicle: corn oil)			HA 1000 mg/kg			
Number of males		5			5			
Body weight	(g)	520.8	±	9.2	546.0	±	41.8	
Brain	(mg)	2091.1	±	88.3	2098.6	±	70.3	
	(mg/g)	4.016	±	0.191	3.867	±	0.395	
Thymus	(mg)	260.7	±	48.2	247.4	±	51.4	
	(mg/g)	0.499	±	0.084	0.451	±	0.073	
Heart	(mg)	1500.1	±	53.9	1568.6	±	97.2	
	(mg/g)	2.882	±	0.148	2.880	±	0.185	
Liver	(mg)	13630.5	±	979.0	14270.3	±	2205.8	
	(mg/g)	26.178	±	1.934	26.059	±	2.691	
Kidney (R)	(mg)	1661.3	±	108.0	1783.8	±	110.9	
	(mg/g)	3.188	±	0.164	3.272	±	0.153	
Kidney (L)	(mg)	1643.7	±	77.9	1769.6	±	151.9	
	(mg/g)	3.156	±	0.125	3.243	±	0.173	
Kidneys	(mg)	3305.0	±	183.3	3553.4	±	259.2	
	(mg/g)	6.344	±	0.280	6.515	±	0.307	
Spleen	(mg)	783.9	±	69.8	766.0	±	69.7	
	(mg/g)	1.506	±	0.146	1.405	±	0.094	
Testis (R)	(mg)	1711.2	±	186.2	1849.0	±	73.3	
	(mg/g)	3.289	±	0.388	3.399	±	0.237	
Testis (L)	(mg)	1689.3	±	186.0	1875.2	±	113.2	
	(mg/g)	3.247	±	0.391	3.444	±	0.233	
Testes	(mg)	3400.5	±	369.4	3724.2	±	181.8	
	(mg/g)	6.536	±	0.775	6.843	±	0.458	
Epididymis (R)	(mg)	684.5	±	44.9	733.7	±	40.9	
	(mg/g)	1.315	±	0.095	1.347	±	0.083	
Epididymis (L)	(mg)	652.4	±	38.2	700.1	±	18.3	*
	(mg/g)	1.253	±	0.084	1.287	±	0.071	
Epididymides	(mg)	1336.9	±	82.3	1433.8	±	54.6	
	(mg/g)	2.568	±	0.177	2.634	±	0.143	

Each value shows mean ± S.D.
Significantly different from the control group (*: P<0.05, **: P<0.01).

Group		Control (vehicle: corn oil)			HA 1000 mg/kg			
Number of males		5			5			
Body weight	(g)	520.8	±	9.2	546.0	±	41.8	
Prostate, ventral	(mg)	596.5	±	87.1	580.2	±	78.7	
	(mg/g)	1.145	±	0.168	1.071	±	0.197	
Seminal vesicles	(mg)	1675.2	±	156.9	1910.7	±	130.9	*
	(mg/g)	3.215	±	0.281	3.524	±	0.442	
Thyroid gland	(mg)	28.0	±	5.9	26.5	±	5.5	
	(mg/g)	0.054	±	0.011	0.049	±	0.009	
Adrenal gland (R)	(mg)	26.1	±	3.8	29.6	±	3.9	
	(mg/g)	0.050	±	0.007	0.054	±	0.007	
Adrenal gland (L)	(mg)	27.3	±	3.8	30.1	±	2.6	
	(mg/g)	0.052	±	0.008	0.056	±	0.006	
Adrenal glands	(mg)	53.4	±	7.5	59.6	±	5.9	
	(mg/g)	0.103	±	0.015	0.110	±	0.012	

Each value shows mean ± S.D.
Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 30-1. Organ weights of female rats at the end of the dosing period

Group		Control (vehicle: corn oil)	HA 100 mg/kg	HA 300 mg/kg	HA 1000 mg/kg
Number of females		11	10	11	11
Body weight	(g)	303.4 ± 18.9	299.7 ± 18.3	299.6 ± 23.4	302.1 ± 20.8
Brain	(mg)	1877.8 ± 68.3	1922.8 ± 58.2	1873.0 ± 85.2	1881.8 ± 67.9
	(mg/g)	6.211 ± 0.431	6.436 ± 0.396	6.276 ± 0.423	6.257 ± 0.523
Thymus	(mg)	238.5 ± 49.9	206.2 ± 46.6	228.5 ± 97.7	236.3 ± 62.0
	(mg/g)	0.785 ± 0.154	0.691 ± 0.169	0.761 ± 0.317	0.784 ± 0.212
Heart	(mg)	1001.3 ± 74.7	1029.0 ± 89.8	970.9 ± 64.6	982.6 ± 72.4
	(mg/g)	3.305 ± 0.226	3.442 ± 0.322	3.248 ± 0.200	3.260 ± 0.258
Liver	(mg)	9890.5 ± 773.5	10171.0 ± 779.0	9941.8 ± 714.4	9610.1 ± 729.3
	(mg/g)	32.621 ± 1.967	33.958 ± 1.918	33.233 ± 1.707	31.887 ± 2.626
Kidney (R)	(mg)	1013.4 ± 72.6	1011.0 ± 93.0	1006.8 ± 107.5	971.2 ± 50.2
	(mg/g)	3.343 ± 0.178	3.372 ± 0.212	3.359 ± 0.221	3.227 ± 0.255
Kidney (L)	(mg)	995.8 ± 73.2	992.8 ± 100.8	1000.1 ± 112.5	951.5 ± 58.1
	(mg/g)	3.284 ± 0.175	3.312 ± 0.260	3.336 ± 0.228	3.164 ± 0.301
Kidneys	(mg)	2009.3 ± 144.4	2003.8 ± 189.0	2006.9 ± 216.6	1922.7 ± 99.5
	(mg/g)	6.627 ± 0.348	6.684 ± 0.453	6.695 ± 0.430	6.391 ± 0.538
Spleen	(mg)	659.7 ± 86.1	722.1 ± 103.3	671.9 ± 80.7	626.5 ± 69.9
	(mg/g)	2.183 ± 0.321	2.406 ± 0.280	2.250 ± 0.285	2.076 ± 0.205
Ovary (R)	(mg)	55.4 ± 7.6	58.9 ± 5.2	58.3 ± 6.6	46.0 ± 4.8 **
	(mg/g)	0.183 ± 0.028	0.197 ± 0.023	0.195 ± 0.021	0.153 ± 0.018 **
Ovary (L)	(mg)	52.1 ± 7.7	52.1 ± 9.7	54.9 ± 6.3	52.2 ± 6.2
	(mg/g)	0.173 ± 0.029	0.173 ± 0.026	0.184 ± 0.025	0.173 ± 0.021
Ovaries	(mg)	107.5 ± 10.2	110.9 ± 11.5	113.2 ± 9.7	98.3 ± 5.7
	(mg/g)	0.356 ± 0.042	0.370 ± 0.030	0.379 ± 0.037	0.326 ± 0.023
Uterus	(mg)	644.6 ± 76.4	648.0 ± 110.7	639.2 ± 106.5	575.1 ± 77.0
	(mg/g)	2.130 ± 0.267	2.166 ± 0.377	2.137 ± 0.345	1.915 ± 0.309
Thyroid gland	(mg)	19.8 ± 3.6	19.8 ± 3.7	20.4 ± 4.8	18.4 ± 3.7
	(mg/g)	0.066 ± 0.013	0.066 ± 0.013	0.068 ± 0.018	0.061 ± 0.010
Adrenal gland (R)	(mg)	34.5 ± 2.3	37.2 ± 6.5	34.5 ± 6.5	36.3 ± 6.4
	(mg/g)	0.114 ± 0.010	0.125 ± 0.022	0.115 ± 0.023	0.121 ± 0.024
Adrenal gland (L)	(mg)	36.9 ± 4.9	39.9 ± 6.9	36.8 ± 7.1	38.9 ± 7.2
	(mg/g)	0.122 ± 0.016	0.133 ± 0.023	0.123 ± 0.025	0.129 ± 0.026
Adrenal glands	(mg)	71.3 ± 7.0	77.1 ± 13.2	71.3 ± 13.5	75.2 ± 13.4
	(mg/g)	0.236 ± 0.025	0.258 ± 0.045	0.239 ± 0.048	0.250 ± 0.049

Each value shows mean ± S.D.
Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 30-2. Organ weights of female rats at the end of the dosing period, satellite group

Group		Control (vehicle: corn oil)			HA 1000 mg/kg			
Number of females		5			5			
Body weight	(g)	277.8	±	14.0	293.9	±	20.5	
Brain	(mg)	1874.1	±	78.7	1888.6	±	48.1	
	(mg/g)	6.751	±	0.196	6.461	±	0.631	
Thymus	(mg)	297.4	±	67.7	325.0	±	107.4	
	(mg/g)	1.069	±	0.224	1.097	±	0.331	
Heart	(mg)	914.9	±	61.4	947.4	±	128.8	
	(mg/g)	3.295	±	0.170	3.221	±	0.334	
Liver	(mg)	7055.6	±	808.3	7672.2	±	303.8	
	(mg/g)	25.347	±	1.745	26.202	±	1.963	
Kidney (R)	(mg)	884.0	±	100.8	960.4	±	105.5	
	(mg/g)	3.186	±	0.362	3.302	±	0.623	
Kidney (L)	(mg)	909.5	±	120.4	959.1	±	97.7	
	(mg/g)	3.273	±	0.363	3.296	±	0.595	
Kidneys	(mg)	1793.5	±	215.3	1919.5	±	202.4	
	(mg/g)	6.459	±	0.698	6.598	±	1.216	
Spleen	(mg)	478.1	±	41.5	604.6	±	65.3	**
	(mg/g)	1.727	±	0.197	2.060	±	0.207	*
Ovary (R)	(mg)	39.1	±	6.1	49.1	±	9.3	
	(mg/g)	0.140	±	0.015	0.167	±	0.033	
Ovary (L)	(mg)	39.8	±	3.7	47.4	±	8.7	
	(mg/g)	0.144	±	0.016	0.162	±	0.031	
Ovaries	(mg)	78.9	±	6.3	96.6	±	17.1	
	(mg/g)	0.284	±	0.011	0.330	±	0.061	
Uterus	(mg)	598.6	±	126.3	730.7	±	274.3	
	(mg/g)	2.149	±	0.403	2.486	±	0.945	
Thyroid gland	(mg)	21.0	±	3.9	16.9	±	3.2	
	(mg/g)	0.075	±	0.011	0.058	±	0.013	
Adrenal gland (R)	(mg)	29.2	±	3.1	32.7	±	4.1	
	(mg/g)	0.105	±	0.010	0.112	±	0.017	
Adrenal gland (L)	(mg)	31.3	±	2.5	33.7	±	5.6	
	(mg/g)	0.113	±	0.010	0.115	±	0.022	
Adrenal glands	(mg)	60.6	±	5.4	66.4	±	9.6	
	(mg/g)	0.218	±	0.018	0.227	±	0.038	

Each value shows mean ± S.D.
Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 30-3. Organ weights of female rats at the end of the recovery period

Group		Control (vehicle: corn oil)			HA 1000 mg/kg			
Number of females		5			5			
Body weight	(g)	278.9	±	25.1	281.8	±	11.4	
Brain	(mg)	1906.9	±	51.7	1892.3	±	78.3	
	(mg/g)	6.883	±	0.659	6.718	±	0.251	
Thymus	(mg)	300.5	±	46.3	273.3	±	33.1	
	(mg/g)	1.076	±	0.119	0.972	±	0.134	
Heart	(mg)	900.1	±	73.6	858.5	±	66.8	
	(mg/g)	3.233	±	0.169	3.044	±	0.158	
Liver	(mg)	6919.6	±	982.1	7169.1	±	395.1	
	(mg/g)	24.714	±	1.484	25.429	±	0.636	
Kidney (R)	(mg)	862.0	±	53.2	869.6	±	75.1	
	(mg/g)	3.103	±	0.221	3.090	±	0.296	
Kidney (L)	(mg)	848.6	±	65.6	870.8	±	78.5	
	(mg/g)	3.057	±	0.291	3.093	±	0.289	
Kidneys	(mg)	1710.6	±	115.9	1740.4	±	152.9	
	(mg/g)	6.160	±	0.507	6.182	±	0.583	
Spleen	(mg)	579.2	±	82.1	481.1	±	64.6	
	(mg/g)	2.075	±	0.220	1.704	±	0.196	*
Ovary (R)	(mg)	41.1	±	6.9	47.9	±	10.1	
	(mg/g)	0.147	±	0.019	0.169	±	0.030	
Ovary (L)	(mg)	42.0	±	4.6	46.2	±	7.7	
	(mg/g)	0.150	±	0.005	0.163	±	0.024	
Ovaries	(mg)	83.2	±	10.6	94.1	±	15.2	
	(mg/g)	0.298	±	0.022	0.333	±	0.042	
Uterus	(mg)	519.7	±	68.4	491.3	±	48.7	
	(mg/g)	1.867	±	0.206	1.750	±	0.235	
Thyroid gland	(mg)	21.1	±	4.1	19.7	±	1.7	
	(mg/g)	0.077	±	0.020	0.070	±	0.006	
Adrenal gland (R)	(mg)	30.5	±	3.1	35.3	±	3.5	
	(mg/g)	0.109	±	0.008	0.126	±	0.013	*
Adrenal gland (L)	(mg)	33.3	±	4.4	36.7	±	5.1	
	(mg/g)	0.119	±	0.010	0.130	±	0.018	
Adrenal glands	(mg)	63.7	±	6.4	72.0	±	8.6	
	(mg/g)	0.229	±	0.010	0.256	±	0.031	

Each value shows mean ± S.D.

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 31-1. Macroscopic findings of male rats at the end of the dosing period

Group	HA		HA		HA		HA	
Dose (mg/kg)	0		100		300		1000	
Findings / Grade	-	P	-	P	-	P	-	P
Epididymis								
Nodule	7	0	12	0	10	1	7	0
Liver								
Diaphragmatic nodule	7	0	11	1	11	0	7	0
Skin								
Crust	7	0	11	1	11	0	6	1
Thymus								
Small	7	0	12	0	10	1	7	0

Notes) - : No abnormal changes P : Non-graded change
Numerals represent the number of animals.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 31-2. Macroscopic findings of male rats at the end of the recovery period

Group	HA		HA	
Dose(mg/kg)	0		1000	
Findings / Grade	-	P	-	P
Epididymis				
Nodule	4	1	5	0
Skin				
Alopecia	5	0	4	1

Notes) - : No abnormal changes P : Non-graded change
Numerals represent the number of animals.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 32-1. Macroscopic findings of female rats at the end of the dosing period

Group	HA		HA		HA		HA	
Dose (mg/kg)	0		100		300		1000	
Findings / Grade	-	P	-	P	-	P	-	P
Liver								
Whitish spot	11	0	10	0	10	1	11	0
Spleen								
Accessory spleen	11	0	10	0	10	1	11	0
Stomach								
Attachment, black content, mucosa	11	0	9	1	11	0	11	0
Dark colored spot	11	0	10	0	10	1	11	0
Dark reddish spot	10	1	10	0	11	0	11	0
Recessed area	11	0	10	0	10	1	11	0
Reddish spot	11	0	10	0	10	1	11	0

Notes) - : No abnormal changes P : Non-graded change

Numerals represent the number of animals.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 32-2. Macroscopic findings of female rats at the end of the dosing period, satellite group

	Group	HA		HA	
	Dose(mg/kg)	0		1000	
Findings	Grade	-	P	-	P
All organs and tissues					
		5		5	

Notes) - : No abnormal changes P : Non-graded change
Numerals represent the number of animals.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 32-3. Macroscopic findings of female rats at the end of the recovery period

	Group	HA		HA	
	Dose(mg/kg)	0		1000	
Findings	Grade	-	P	-	P
All organs and tissues					
		5		5	

Notes) - : No abnormal changes P : Non-graded change
Numerals represent the number of animals.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 33-1. Histopathological findings of male rats at the end of the dosing period [H.E. staining]

Group	HA							HA						
Dose (mg/kg)	0							1000						
Findings / Grade	-	±	+	2+	3+	P	NE	-	±	+	2+	3+	P	NE
Brain	5							5						
Spinal cord	5							5						
Pituitary gland	5							5						
Submandibular gland	5							5						
Sublingual gland	5							5						
Lymph node, submandibular	5							5						
Thyroid gland														
Ultimobranchial body	5					0		3					2	
Parathyroid gland	5							5						
Thymus	5							5						
Heart														
Degeneration/fibrosis, myocardial	4	1	0	0	0			3	2	0	0	0		
Trachea	5							5						

Notes) - : No abnormal changes ±: Very slight + : Slight 2+: Moderate 3+: Marked
P : Non-graded change NE: Not examined
Numerals represent the number of animals.
Not significantly different from control.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 33-1 (continued). Histopathological findings of male rats at the end of the dosing period [H.E. staining]

Group	HA							HA						
Dose (mg/kg)	0							1000						
Findings / Grade	-	±	+	2+	3+	P	NE	-	±	+	2+	3+	P	NE
Lung														
Accumulation, foam cell	4	1	0	0	0			4	1	0	0	0		
Metaplasia, osseous	3					2		5					0	
Microgranuloma	4	1	0	0	0			4	1	0	0	0		
Bronchus	5							5						
Liver														
Fatty change, hepatocyte	3	2	0	0	0			5	0	0	0	0		
Fibrosis, focal	5	0	0	0	0			4	1	0	0	0		
Hematopoiesis, extramedullary	4	1	0	0	0			4	1	0	0	0		
Microgranuloma	1	4	0	0	0			1	4	0	0	0		
Pancreas	5							5						
Stomach														
Cellular infiltration, lymphocyte	4	1	0	0	0			5	0	0	0	0		
Duodenum	5							5						
Jejunum	5							5						

Notes) - : No abnormal changes ±: Very slight + : Slight 2+: Moderate 3+: Marked
P : Non-graded change NE: Not examined
Numerals represent the number of animals.
Not significantly different from control.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 33-1 (continued). Histopathological findings of male rats at the end of the dosing period [H.E. staining]

Group	HA							HA						
Dose(mg/kg)	0							1000						
Findings / Grade	-	±	+	2+	3+	P	NE	-	±	+	2+	3+	P	NE
Ileum	5							5						
Cecum	5							5						
Colon	5							5						
Rectum	5							5						
Lymph node, mesenteric	5							5						
Spleen														
Deposit, pigment, brown	0	4	1	0	0			0	4	1	0	0		
Hematopoiesis, extramedullary	0	4	1	0	0			0	3	2	0	0		
Kidney														
Basophilic tubule, cortex	2	2	1	0	0			1	4	0	0	0		
Cellular infiltration, lymphocyte	3	1	1	0	0			3	2	0	0	0		
Dilatation, lumen	5	0	0	0	0			4	1	0	0	0		
Eosinophilic body	5	0	0	0	0			4	1	0	0	0		
Mineralization	4	1	0	0	0			4	1	0	0	0		
Urinary bladder	5							5						

Notes) - : No abnormal changes ±: Very slight + : Slight 2+: Moderate 3+: Marked
P : Non-graded change NE: Not examined
Numerals represent the number of animals.
Not significantly different from control.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 33-1 (continued). Histopathological findings of male rats at the end of the dosing period [H.E. staining]

Group	HA							HA						
Dose (mg/kg)	0							1000						
Findings / Grade	-	±	+	2+	3+	P	NE	-	±	+	2+	3+	P	NE
Adrenal gland	5							5						
Testis														
Degeneration, seminiferous tubule	4	1	0	0	0			5	0	0	0	0		
Epididymis	5							5						
Prostate														
Cellular infiltration, lymphocyte	4	1	0	0	0			3	2	0	0	0		
Seminal vesicle	5							5						
Coagulating gland	5							5						
Eyeball	5							5						
Harderian gland	5							5						
Sciatic nerve	5							5						
Skeletal muscle	5							5						
Femur	5							5						
Marrow, femur	5							5						

Notes) - : No abnormal changes ±: Very slight + : Slight 2+: Moderate 3+: Marked
P : Non-graded change NE: Not examined
Numerals represent the number of animals.
Not significantly different from control.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 33-2. Histopathological findings of male rats at the end of the recovery period [H.E. staining]

	Group	HA							HA						
	Dose (mg/kg)	0							1000						
Findings	Grade	-	±	+	2+	3+	P	NE	-	±	+	2+	3+	P	NE
Epididymis															
Granuloma, spermatic		0					1								

Notes) - : No abnormal changes ±: Very slight + : Slight 2+: Moderate 3+: Marked
P : Non-graded change NE: Not examined
Numerals represent the number of animals.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 34-1. Histopathological findings of female rats at the end of the dosing period [H.E. staining]

Group	HA							HA						
Dose (mg/kg)	0							1000						
Findings / Grade	-	±	+	2+	3+	P	NE	-	±	+	2+	3+	P	NE
Brain	5							5						
Spinal cord	5							5						
Pituitary gland	5							5						
Submandibular gland	5							5						
Sublingual gland	5							5						
Lymph node, submandibular	5							5						
Thyroid gland														
Ultimobranchial body	2					3		3					2	
Parathyroid gland	5							5						
Thymus														
Hyperplasia, epithelial tubule/cord	2	3	0	0	0			3	2	0	0	0		
Heart														
Degeneration/fibrosis, myocardial	4	1	0	0	0			4	1	0	0	0		
Trachea	5							5						

Notes) - : No abnormal changes ±: Very slight + : Slight 2+: Moderate 3+: Marked
P : Non-graded change NE: Not examined
Numerals represent the number of animals.
Not significantly different from control.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 34-1 (continued). Histopathological findings of female rats at the end of the dosing period [H.E. staining]

Group	HA							HA						
Dose (mg/kg)	0							1000						
Findings / Grade	-	±	+	2+	3+	P	NE	-	±	+	2+	3+	P	NE
Lung														
Accumulation, foam cell	3	2	0	0	0			5	0	0	0	0		
Cellular infiltration, mononuclear cell	4	0	1	0	0			5	0	0	0	0		
Bronchus	5							5						
Liver														
Cellular infiltration, mononuclear cell	4	1	0	0	0			4	1	0	0	0		
Fatty change, hepatocyte	3	2	0	0	0			4	1	0	0	0		
Microgranuloma	5	0	0	0	0			3	2	0	0	0		
Pancreas														
Cellular infiltration, lymphocyte	5	0	0	0	0			4	1	0	0	0		
Stomach														
Dilatation, fundic gland	5	0	0	0	0			4	1	0	0	0		
Duodenum	5							5						
Jejunum	5							5						
Ileum	5							5						

Notes) - : No abnormal changes ±: Very slight + : Slight 2+: Moderate 3+: Marked
P : Non-graded change NE: Not examined
Numerals represent the number of animals.
Not significantly different from control.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 34-1 (continued). Histopathological findings of female rats at the end of the dosing period [H.E. staining]

Group	HA							HA						
Dose (mg/kg)	0							1000						
Findings / Grade	-	±	+	2+	3+	P	NE	-	±	+	2+	3+	P	NE
Cecum	5							5						
Colon	5							5						
Rectum	5							5						
Lymph node, mesenteric	5							5						
Spleen														
Deposit, pigment, brown	0	1	4	0	0			0	3	2	0	0		
Hematopoiesis, extramedullary	0	0	2	3	0			0	1	2	2	0		
Kidney														
Basophilic tubule, cortex	4	1	0	0	0			5	0	0	0	0		
Cellular infiltration, lymphocyte	5	0	0	0	0			4	1	0	0	0		
Mineralization	4	1	0	0	0			3	2	0	0	0		
Urinary bladder	5							5						
Adrenal gland	5							5						
Ovary	5							5						
Uterus	5							5						

Notes) - : No abnormal changes ±: Very slight + : Slight 2+: Moderate 3+: Marked
P : Non-graded change NE: Not examined
Numerals represent the number of animals.
Not significantly different from control.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 34-1 (continued). Histopathological findings of female rats at the end of the dosing period [H.E. staining]

	Group	HA							HA						
	Dose (mg/kg)	0							1000						
Findings	Grade	-	±	+	2+	3+	P	NE	-	±	+	2+	3+	P	NE
Vagina		5							5						
Eyeball		5							5						
Harderian gland		5							5						
Sciatic nerve		5							5						
Skeletal muscle		5							5						
Femur		5							5						
Marrow, femur		5							5						

Notes) - : No abnormal changes ±: Very slight + : Slight 2+: Moderate 3+: Marked
P : Non-graded change NE: Not examined
Numerals represent the number of animals.
Not significantly different from control.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 34-2. Histopathological findings of female rats at the end of the dosing period, satellite group [H.E. staining]

Group	HA							HA						
Dose (mg/kg)	0							1000						
Findings / Grade	-	±	+	2+	3+	P	NE	-	±	+	2+	3+	P	NE
Brain	5							5						
Spinal cord	5							5						
Pituitary gland	5							5						
Submandibular gland														
Cellular infiltration, lymphocyte	4	1	0	0	0			5	0	0	0	0		
Sublingual gland														
Cellular infiltration, lymphocyte	5	0	0	0	0			4	1	0	0	0		
Lymph node, submandibular	5							5						
Thyroid gland														
Ultimobranchial body	4					1		5					0	
Parathyroid gland	5							5						
Thymus														
Hyperplasia, epithelial tubule/cord	3	2	0	0	0			2	3	0	0	0		
Heart														
Degeneration/fibrosis, myocardial	5	0	0	0	0			4	1	0	0	0		
Trachea	5							5						

Notes) - : No abnormal changes ±: Very slight + : Slight 2+: Moderate 3+: Marked
P : Non-graded change NE: Not examined
Numerals represent the number of animals.
Not significantly different from control.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 34-2 (continued). Histopathological findings of female rats at the end of the dosing period, satellite group [H.E. staining]

Group	HA							HA						
Dose (mg/kg)	0							1000						
Findings / Grade	-	±	+	2+	3+	P	NE	-	±	+	2+	3+	P	NE
Lung														
Accumulation, foam cell	4	1	0	0	0			5	0	0	0	0		
Bronchus	5							5						
Liver														
Hematopoiesis, extramedullary	4	1	0	0	0			5	0	0	0	0		
Microgranuloma	2	3	0	0	0			3	2	0	0	0		
Pancreas														
Atrophy, acinar cell	4	1	0	0	0			4	1	0	0	0		
Cellular infiltration, lymphocyte	4	1	0	0	0			5	0	0	0	0		
Stomach	5							5						
Duodenum	5							5						
Jejunum	5							5						
Ileum	5							5						
Cecum	5							5						
Colon	5							5						

Notes) - : No abnormal changes ±: Very slight + : Slight 2+: Moderate 3+: Marked
P : Non-graded change NE: Not examined
Numerals represent the number of animals.
Not significantly different from control.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 34-2 (continued). Histopathological findings of female rats at the end of the dosing period, satellite group [H.E. staining]

Group	HA							HA						
Dose (mg/kg)	0							1000						
Findings / Grade	-	±	+	2+	3+	P	NE	-	±	+	2+	3+	P	NE
Rectum	5							5						
Lymph node, mesenteric	5							5						
Spleen														
Deposit, pigment, brown	0	1	4	0	0			0	1	4	0	0		
Hematopoiesis, extramedullary	0	4	1	0	0			0	1	4	0	0		
Kidney														
Basophilic tubule, cortex	2	3	0	0	0			3	2	0	0	0		
Cast, hyalin	4					1		5					0	
Mineralization	4	1	0	0	0			4	1	0	0	0		
Urinary bladder	5							5						
Adrenal gland	5							5						
Ovary	5							5						
Uterus	5							5						
Vagina	5							5						
Eyeball	5							5						

Notes) - : No abnormal changes ±: Very slight + : Slight 2+: Moderate 3+: Marked
P : Non-graded change NE: Not examined
Numerals represent the number of animals.
Not significantly different from control.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 34-2 (continued). Histopathological findings of female rats at the end of the dosing period, satellite group [H.E. staining]

Group	HA							HA						
Dose(mg/kg)	0							1000						
Findings / Grade	-	±	+	2+	3+	P	NE	-	±	+	2+	3+	P	NE
Harderian gland														
Cellular infiltration, lymphocyte	4	1	0	0	0			4	1	0	0	0		
Sciatic nerve	5							5						
Skeletal muscle	5							5						
Femur	5							5						
Marrow, femur	5							5						

Notes) - : No abnormal changes ±: Very slight + : Slight 2+: Moderate 3+: Marked
P : Non-graded change NE: Not examined
Numerals represent the number of animals.
Not significantly different from control.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 35. Results of observations about estrous cycle

Group	Control (vehicle: corn oil)	HA 100 mg/kg	HA 300 mg/kg	HA 1000 mg/kg
Number of animals examined	12	12	12	12
Pre-treatment period				
Number of animals showing type of cycle				
4-day cycle	6	9	6	9
4/5-day cycle	1	2	1	0
5-day cycle	5	1	5	3
Mean length of estrous cycle in days; Mean±S.D. (N)	4.5 ± 0.5 (12)	4.2 ± 0.3 (12)	4.5 ± 0.5 (12)	4.3 ± 0.5 (12)
Treatment period				
Number of animals showing each type of cycle				
4-day cycle	8	8	8	8
4/5-day cycle	1	1	1	1
5-day cycle	3	2	3	2
irregular	0	1	0	1
Mean length of estrous cycle in days; Mean±S.D. (N)	4.3 ± 0.5 (12)	4.3 ± 0.4 (12)	4.3 ± 0.5 (12)	4.2 ± 0.4 (11)
Frequency of animals that show abnormal estrous cycles after the treatment	0 / 12	1 / 12	0 / 12	1 / 12
Mean times of vaginal estrus during mating period; Mean±S.D. (N)	1.1 ± 0.3 (11)	1.1 ± 0.3 (12)	1.0 ± 0.0 (12)	1.0 ± 0.0 (11)

Significantly different from the control group (*: $p<0.05$, **: $p<0.01$).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 36. Results of observations about reproductive performance

Group	Control (vehicle: corn oil)	HA 100 mg/kg	HA 300 mg/kg	HA 1000 mg/kg
Number of mated pairs [A]	12	12	12	12
Number of copulated pairs [B]	11	12	12	11
Copulation index [(B/A)×100,%]	91.7	100.0	100.0	91.7
Number of pregnant females [C]	11	10	12	11
Fertility index [(C/B)×100,%]	100.0	83.3	100.0	100.0
Pairing days until copulation ; Mean±S.D.(N)	3.2 ± 1.5 (11)	4.2 ± 3.6 (12)	2.5 ± 1.2 (12)	2.4 ± 1.2 (11)

Significantly different from the control group (*: $p<0.05$, **: $p<0.01$).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 37. Observation of offspring (F_1)

Group	Control (vehicle: corn oil)	HA 100 mg/kg	HA 300 mg/kg	HA 1000 mg/kg
Number of dams	11	10	11	11
Gestation length (days)				
Mean ± S.D. per dam	21.9 ± 0.5	21.8 ± 0.4	21.9 ± 0.3	21.6 ± 0.5
Number of corpora lutea				
Total	169	163	182	162
Mean ± S.D. per dam	15.4 ± 3.0	16.3 ± 1.9	15.2 ± 1.9 (12)	14.7 ± 1.8
Number of implantation scars				
Total	164	154	164	155
Mean ± S.D. per dam	14.9 ± 2.7	15.4 ± 3.4	13.7 ± 4.8 (12)	14.1 ± 2.2
Implantation index (%) [a]	97.4 ± 3.8	93.4 ± 15.7	89.0 ± 27.0 (12)	95.4 ± 7.5
Delivery index (dams,%) [b]	100.0	100.0	91.7	100.0
Number of offspring at birth				
Total	159	141	154	138
Mean ± S.D. per dam	14.5 ± 3.0	14.1 ± 3.1	14.0 ± 3.1	12.5 ± 2.5
Number of live offspring at birth				
Male	84	66	83	78
Female	74	75	70	59
Total	158	141	153	137
Mean ± S.D. per dam	14.4 ± 2.9	14.1 ± 3.1	13.9 ± 3.4	12.5 ± 2.5
Sex ratio [c]				
Mean ± S.D. per dam	0.54 ± 0.13	0.44 ± 0.18	0.54 ± 0.10	0.56 ± 0.12
Number of dead offspring				
Total	1	0	1	1
Mean ± S.D. per dam	0.1 ± 0.3	0.0 ± 0.0	0.1 ± 0.3	0.1 ± 0.3
Delivery index (offspring) [d]				
Mean% ± S.D. per dam	96.5 ± 4.2	92.1 ± 6.4	95.2 ± 5.4	88.4 ± 8.4 *
Birth index [e]				
Mean% ± S.D. per dam	96.0 ± 4.0	92.1 ± 6.4	93.9 ± 5.8	87.8 ± 7.7 **
Live birth index [f]				
Mean% ± S.D. per dam	99.5 ± 1.6	100.0 ± 0.0	98.7 ± 4.3	99.4 ± 2.1
Number of offspring on day 4				
Male	83	66	83	78
Female	74	75	70	59
Sex ratio [c]				
Mean ± S.D. per dam	0.54 ± 0.13	0.44 ± 0.18	0.54 ± 0.10	0.56 ± 0.12
Viability index [g]				
Mean% ± S.D. per dam	99.5 ± 1.7	100.0 ± 0.0	100.0 ± 0.0	100.0 ± 0.0
Number of external abnormalities [h]	0	0	0	0
Mean% ± S.D. per dam	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0

Significantly different from the control group (*: P<0.05, **: P<0.01).

a): (Number of implantation scars/Number of corpora lutea)×100.

b): (Number of dams with live offspring/number of pregnant dams)×100.

c): Number of male offspring/(number of male offspring + number of female offspring).

d): (Number of offspring at birth/Number of implantation scars)×100.

e): (Number of live offspring at birth/number of implantation scars)×100.

f): (Number of live offspring at birth/number of offspring at birth)×100.

g): (Number of live offspring 4 days after birth/number of live offspring at birth)×100.

h): Number of external abnormalities in live offspring at birth.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 38. Body weights of offspring (F_1) before weaning

Group	Control (vehicle: corn oil)	HA 100 mg/kg	HA 300 mg/kg	HA 1000 mg/kg
Number of dams	11	9	11	11
Male				
Days after birth				
0	6.6 ± 0.6	6.4 ± 0.4	6.8 ± 0.5	6.6 ± 0.6
4	10.6 ± 1.5	10.5 ± 0.6	11.1 ± 1.5	11.2 ± 1.5
Number of dams	11	10	11	11
Female				
Days after birth				
0	6.3 ± 0.5	6.3 ± 0.4	6.4 ± 0.5	6.3 ± 0.6
4	10.3 ± 1.3	10.5 ± 1.2	10.5 ± 1.3	10.9 ± 1.7

Each value shows mean ± S.D. per dam. (g).

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 39. General conditions in offspring (F_1) before weaning

Group	Number of offspring and general conditions	Days after birth				
		0	1	2	3	4
Control (vehicle: corn oil)	Number of offspring	158	158	157	157	157
	General appearance, No abnormality	158	157	157	157	157
	General appearance, Death		1			
HA 100 mg/kg	Number of offspring	141	141	141	141	141
	General appearance, No abnormality	141	141	141	141	141
HA 300 mg/kg	Number of offspring	153	153	153	153	153
	General appearance, No abnormality	153	153	153	153	153
HA 1000 mg/kg	Number of offspring	137	137	137	137	137
	General appearance, No abnormality	137	137	137	137	137

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Table 40. Morphological observations of offspring (F_1)

Group	Control (vehicle: corn oil)	HA 100 mg/kg	HA 300 mg/kg	HA 1000 mg/kg
Dead offspring				
Number of dead offspring	2	0	1	1
Number of missing offspring	0	0	0	0
Number of dead offspring examined [a)]	2 (1)	0 (0)	1 (0)	1 (0)
Number of dead offspring with external changes	0	0	0	0
Number of dead offspring with visceral changes	0	0	0	0
Live offspring				
Number of live offspring examined (postnatal day 0)	158	141	153	137
Number of live offsping with external changes	0	0	0	0
Number of live offspring examined (postnatal day 4)	157	141	153	137
Number of live offspring with external changes	0	0	0	0
Number of live offspring with visceral changes	0	0	0	0

Significantly different from the control group (*: $p<0.05$, **: $p<0.01$).
a) Parenthesis indicates the number of offspring not examined bacause of their autolysis.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 1-1-1. General conditions of male rats

Control (vehicle: corn oil)

Male No.	Days of administration																																																	
	1		2		3		4		5		6		7		8		9		10		11		12		13		14		15		16		17		18		19		20		21		22		23		24		25	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
M01001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M01002	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M01003	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M01004	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M01005	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M01006	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M01007	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M01008	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M01009	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M01010	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M01011	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M01012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Number of males	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
-	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12

Pre: Before administration, Post: after administration.

-: General appearance, No abnormality.

Control (vehicle: corn oil)

Male No.	Days of administration																																																	
	26		27		28		29		30		31		32		33		34		35		36		37		38		39		40		41		42		43	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	
M01001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
M01002	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
M01003	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
M01004	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
M01005	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
M01006	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
M01007	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
M01008	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
M01009	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
M01010	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
M01011	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
M01012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
Number of males	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	7	
-	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	7	

Pre: Before administration, Post: after administration.

-: General appearance, No abnormality.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 1-1-2. General conditions of male rats

HA 100 mg/kg

Male No.	Days of administration																																																	
	1		2		3		4		5		6		7		8		9		10		11		12		13		14		15		16		17		18		19		20		21		22		23		24		25	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
M02013	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M02014	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M02015	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M02016	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M02017	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M02018	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M02019	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M02020	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M02021	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M02022	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M02023	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	a	a
M02024	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Number of males	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
-	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	11	11
a	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1

Pre: Before administration, Post: after administration.
-: General appearance, No abnormality.
a: Skin, Crust formation.

HA 100 mg/kg

Male No.	Days of administration																																		
	26		27		28		29		30		31		32		33		34		35		36		37		38		39		40		41		42		43
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre
M02013	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M02014	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M02015	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M02016	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M02017	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M02018	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M02019	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M02020	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M02021	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M02022	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M02023	a	a	a	a	a	a	a	a	a	a	b	b	b	b	b	b	b	b	b	b	b	b	b	b	b	b	a,b	a,b	a,b	a,b	a,b	a,b	a,b	a,b	a,b
M02024	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Number of males	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
-	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
a	1	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1
b	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

Pre: Before administration, Post: after administration.
-: General appearance, No abnormality.
a: Skin, Crust formation.
b: Fur, Hair, Coat, Loss of fur.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 1-1-3. General conditions of male rats

HA 300 mg/kg

Male No.	Days of administration																																																	
	1		2		3		4		5		6		7		8		9		10		11		12		13		14		15		16		17		18		19		20		21		22		23		24		25	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
M03025	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	c																													
M03026	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M03027	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M03028	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M03029	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M03030	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M03031	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M03032	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M03033	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M03034	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M03035	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M03036	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Number of males	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
-	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
c	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Pre: Before administration, Post: after administration.

-: General appearance, No abnormality.

c: General appearance, Death.

HA 300 mg/kg

Male No.	Days of administration																																			
	26		27		28		29		30		31		32		33		34		35		36		37		38		39		40		41		42		43	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre
M03026	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M03027	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M03028	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M03029	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M03030	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M03031	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M03032	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M03033	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M03034	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M03035	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M03036	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Number of males	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
-	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11

Pre: Before administration, Post: after administration.

-: General appearance, No abnormality.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 1-1-4. General conditions of male rats

HA 1000 mg/kg

Male No.	Days of administration																																																	
	1		2		3		4		5		6		7		8		9		10		11		12		13		14		15		16		17		18		19		20		21		22		23		24		25	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
M04037	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M04038	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M04039	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M04040	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M04041	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M04042	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M04043	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	-	-	-	-	-	-	-	-	-	-
M04044	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	-	-	-	-	-	-	-	-	-	-
M04045	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M04046	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M04047	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M04048	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Number of males	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
-	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	10	12	12	12	12	12	12	12	12	12	12
d	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0

Pre: Before administration, Post: after administration.
-: General appearance, No abnormality.
d: Mouth, Salivation.

HA 1000 mg/kg

Male No.	Days of administration																																																	
	26		27		28		29		30		31		32		33		34		35		36		37		38		39		40		41		42		43	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	
M04037	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
M04038	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
M04039	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
M04040	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
M04041	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	a	a	a	a	a	a	a	a	a	a	a	a	a	
M04042	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
M04043	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
M04044	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	-	d	-	-	-	d	-	-	-	-	-	-	-	-	-	-		
M04045	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
M04046	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
M04047	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
M04048	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
Number of males	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	7	
-	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	11	12	11	12	12	11	10	11	11	11	11	11	11	11	11	11	11	6	
a	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	
d	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	

Pre: Before administration, Post: after administration.
-: General appearance, No abnormality.
a: Skin, Crust formation.
d: Mouth, Salivation.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 1-2-1. General conditions of male rats at the recovery period

Control (vehicle: corn oil)

Male No.	Days of recovery														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
M01008	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M01009	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M01010	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M01011	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M01012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
-	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5

-: General appearance, No abnormality.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 1-2-2. General conditions of male rats at the recovery period

HA 1000 mg/kg

Male No.	Days of recovery														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
M04044	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M04045	-	-	-	-	-	-	-	-	-	a	a	a	b	b	b
M04046	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M04047	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
M04048	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
-	5	5	5	5	5	5	5	5	5	4	4	4	4	4	4
a	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0
b	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1

-: General appearance, No abnormality.

a: Skin, Crust formation.

b: Fur, Hair, Coat, Loss of fur.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 2-1-1. General conditions of female rats

Control (vehicle: corn oil)

Female No.	Days of administration																											
	1		2		3		4		5		6		7		8		9		10		11		12		13		14	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F01001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01002	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01003	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01004	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01005	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01006	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01007	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01008	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01009	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01010	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01011	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Number of females	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
-	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12

Control (vehicle: corn oil)

Female No.	Days of administration																											
	15		16		17		18		19		20		21		22		23		24		25		26		27		28	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F01001	-	-	-	-	-	-																						
F01002	-	-	-	-	-	-	-	-																				
F01003	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01004	-	-	-	-	-	-	-	-																				
F01005	-	-	-	-	-	-																						
F01006	-	-	-	-	-	-																						
F01007	-	-	-	-	-	-	-	-	-	-	-	-	-	-														
F01008	-	-	-	-	-	-																						
F01009	-	-	-	-																								
F01010	-	-																										
F01011	-	-	-	-																								
F01012	-	-	-	-	-	-																						
Number of females	12	12	11	11	9	9	4	4	2	2	2	2	2	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1
-	12	12	11	11	9	9	4	4	2	2	2	2	2	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1

Control (vehicle: corn oil)

Female No.	Days of administration																											
	29		30		31		32		33		34		35		36		37		38		39		40		41		42	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F01003	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-

Control (vehicle: corn oil)

Female No.	Days of administration																											
	43		44		45		46		47		48		49		50		51		52		53							
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre							
F01003	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-

Pre: Before administration, Post: after administration.

-: General appearance, No abnormality.

>: Excluded from analysis (not copulated)

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 2-1-2. General conditions of female rats

HA 100 mg/kg

Female No.	Days of administration																											
	1		2		3		4		5		6		7		8		9		10		11		12		13		14	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F02013	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F02014	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F02015	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F02016	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F02017	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F02018	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F02019	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F02020	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F02021	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F02022	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F02023	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F02024	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Number of females	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
-	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12

HA 100 mg/kg

Female No.	Days of administration																											
	15		16		17		18		19		20		21		22		23		24		25		26		27		28	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F02013	-	-																										
F02014	-	-	-	-	-	-	-	-																				
F02015	-	-	-	-	-	-	-	-																				
F02016	-	-	-	-																								
F02017	-	-	-	-	-	-	-	-																				
F02018	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-												
F02019	-	-	-	-																								
F02020	-	-	-	-	-	-	-	-																				
F02021	-	-	-	-	-	-	-	-																				
F02022	-	-																										
F02023	-	-	-	-																								
F02024	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Number of females	12	12	10	10	7	7	7	7	2	2	2	2	2	2	2	2	1	1	1	1	1	1	1	1	1	1	1	1
-	12	12	10	10	7	7	7	7	2	2	2	2	2	2	2	2	1	1	1	1	1	1	1	1	1	1	1	1

Pre: Before administration, Post: after administration.

-: General appearance, No abnormality.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 2-1-3. General conditions of female rats

HA 300 mg/kg

Female No.	Days of administration																											
	1		2		3		4		5		6		7		8		9		10		11		12		13		14	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F03025	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03026	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03027	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03028	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03029	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03030	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03031	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03032	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03033	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03034	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03035	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03036	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Number of females	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
-	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12

HA 300 mg/kg

Female No.	Days of administration									
	15		16		17		18		19	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F03025	-	-	-	-	-	-	-	-	-	-
F03026	-	-								
F03027	-	-	-	-	-	-	-	-		
F03028	-	-	-	-	-	-				
F03029	-	-	-	-	-	-				
F03030	-	-								
F03031	-	-	-	-	-	-	-	-		
F03032	-	-								
F03033	-	-	-	-	-	-				
F03034	-	-	-	-	-	-				
F03035	-	-	-	-	-	-				
F03036	-	-								
Number of females	12	12	8	8	8	8	3	3	1	1
-	12	12	8	8	8	8	3	3	1	1

Pre: Before administration, Post: after administration.

-: General appearance, No abnormality.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 2-1-4. General conditions of female rats

HA 1000 mg/kg

Female No.	Days of administration																											
	1		2		3		4		5		6		7		8		9		10		11		12		13		14	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F04037	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04038	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04039	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04040	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04041	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04042	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04043	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04044	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04045	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04046	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04047	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04048	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Number of females	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
-	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12

HA 1000 mg/kg

Female No.	Days of administration																											
	15		16		17		18		19		20		21		22		23		24		25		26		27		28	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F04037	-	-																										
F04038	-	-	-	-																								
F04039	-	-	-	-	-	-																						
F04040	-	-	-	-	-	-																						
F04041	c	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04042	-	-																										
F04043	-	-	-	-	-	-																						
F04044	-	-																										
F04045	-	-																										
F04046	-	-	-	-	-	-	-	-																				
F04047	-	-	-	-	-	-	-	-																				
F04048	-	-	-	-	-	-																						
Number of females	12	12	8	8	7	7	3	3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
-	11	12	8	8	7	7	3	3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
c	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

c: Excretion, Reddish urine.

HA 1000 mg/kg

Female No.	Days of administration																											
	29		30		31		32		33		34		35		36		37		38		39		40		41		42	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F04041	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-

HA 1000 mg/kg

Female No.	Days of administration																											
	43		44		45		46		47		48		49		50		51		52		53							
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre							
F04041	>	-	>	-	>	-	>	-	>	-	>	-	>	d	>	-	>	-	>	-	>	-	>	-	>	-	>	-

Pre: Before administration, Post: after administration.

d: Mouth, Salivation.

-: General appearance, No abnormality.

>: Excluded from analysis (not copulated)

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 2-2-1. General conditions of female rats, satellite group

Control (vehicle: corn oil)

Female No.	Days of administration																																																	
	1		2		3		4		5		6		7		8		9		10		11		12		13		14		15		16		17		18		19		20		21		22		23		24		25	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F05049	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F05050	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F05051	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F05052	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F05053	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F05054	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F05055	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F05056	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F05057	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F05058	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Number of females	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
-	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10

Pre: Before administration, Post: after administration.
-: General appearance, No abnormality.

Control (vehicle: corn oil)

Female No.	Days of administration																																	
	26		27		28		29		30		31		32		33		34		35		36		37		38		39		40		41		42		43
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre
F05049	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F05050	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F05051	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F05052	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F05053	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F05054	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
F05055	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
F05056	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
F05057	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
F05058	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Number of females	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5
-	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5

Pre: Before administration, Post: after administration.
-: General appearance, No abnormality.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 2-2-2. General conditions of female rats, satellite group

HA 1000 mg/kg

Female No.	Days of administration																																																	
	1		2		3		4		5		6		7		8		9		10		11		12		13		14		15		16		17		18		19		20		21		22		23		24		25	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F06059	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F06060	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F06061	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F06062	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F06063	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F06064	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F06065	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F06066	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F06067	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F06068	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Number of females	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
-	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10

Pre: Before administration, Post: after administration.

-: General appearance, No abnormality.

HA 1000 mg/kg

Female No.	Days of administration																																			
	26		27		28		29		30		31		32		33		34		35		36		37		38		39		40		41		42		43	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	
F06059	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
F06060	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
F06061	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
F06062	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
F06063	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
F06064	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
F06065	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
F06066	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
F06067	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
F06068	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
Number of females	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5	
-	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5	

Pre: Before administration, Post: after administration.

-: General appearance, No abnormality.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 2-3-1. General conditions of female rats at the recovery period

Control (vehicle: corn oil)

Female No.	Days of recovery														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
F05054	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F05055	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F05056	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F05057	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F05058	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
-	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5

-: General appearance, No abnormality.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 2-3-2. General conditions of female rats at the recovery period

HA 1000 mg/kg

Female No.	Days of recovery														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
F06064	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F06065	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F06066	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F06067	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F06068	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
-	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5

-: General appearance, No abnormality.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 3-1. General conditions in dams during pregnancy

Control (vehicle: corn oil)

Dam No.	Days of pregnancy																											
	0		1		2		3		4		5		6		7		8		9		10		11		12		13	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F01001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01002	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01004	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01005	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01006	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01007	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01008	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01009	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01010	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01011	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Number of dams	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
-	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11

Pre: Before administration, Post: after administration.

-: General appearance, No abnormality.

Control (vehicle: corn oil)

Dam No.	Days of pregnancy																	
	14		15		16		17		18		19		20		21		22	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F01001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
F01002	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
F01004	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
F01005	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01006	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
F01007	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
F01008	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
F01009	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01010	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
F01011	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
F01012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
Number of dams	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	2	2
-	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	2	2

Pre: Before administration, Post: after administration.

-: General appearance, No abnormality.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 3-2. General conditions in dams during pregnancy

HA 100 mg/kg

Dam No.	Days of pregnancy																													
	0		1		2		3		4		5		6		7		8		9		10		11		12		13	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F02013	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-
F02014		-		-		-		-		-		-		-		-		-		-		-		-		-		-
F02015		-		-		-		-		-		-		-		-		-		-		-		-		-		-
F02016		-		-		-		-		-		-		-		-		-		-		-		-		-		-
F02017		-		-		-		-		-		-		-		-		-		-		-		-		-		-
F02018		-		-		-		-		-		-		-		-		-		-		-		-		-		-
F02019		-		-		-		-		-		-		-		-		-		-		-		-		-		-
F02020		-		-		-		-		-		-		-		-		-		-		-		-		-		-
F02021		-		-		-		-		-		-		-		-		-		-		-		-		-		-
F02022		-		-		-		-		-		-		-		-		-		-		-		-		-		-
F02023		-		-		-		-		-		-		-		-		-		-		-		-		-		-
F02024	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-
Number of dams	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
-	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10

>: Excluded from analysis (not pregnant)

Pre: Before administration, Post: after administration.

-: General appearance, No abnormality.

HA 100 mg/kg

Dam No.	Days of pregnancy																										
	14		15		16		17		18		19		20		21		22		23		24		25		26
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre
F02013	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-
F02014		-		-		-		-		-		-		-		-												
F02015		-		-		-		-		-		-		-		-												
F02016		-		-		-		-		-		-		-		-												
F02017		-		-		-		-		-		-		-		-		-										
F02018		-		-		-		-		-		-		-		-												
F02019		-		-		-		-		-		-		-		-												
F02020		-		-		-		-		-		-		-		-												
F02021		-		-		-		-		-		-		-		-												
F02022		-		-		-		-		-		-		-		-												
F02023		-		-		-		-		-		-		-		-												
F02024	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-	>	-
Number of dams	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	1	1	0	0	0	0	0	0	0
-	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	1	1	0	0	0	0	0	0	0

>: Excluded from analysis (not pregnant)

Pre: Before administration, Post: after administration.

-: General appearance, No abnormality.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 3-3. General conditions in dams during pregnancy

HA 300 mg/kg

Dam No.	Days of pregnancy																											
	0		1		2		3		4		5		6		7		8		9		10		11		12		13	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F03025	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03026	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03027	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03028	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03029	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03030	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03031	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03032	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03033	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03034	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03035	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03036	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Number of dams	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
-	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12

Pre: Before administration, Post: after administration.

-: General appearance, No abnormality.

HA 300 mg/kg

Dam No.	Days of pregnancy																	
	14		15		16		17		18		19		20		21		22	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F03025	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
F03026	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
F03027	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
F03028	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
F03029	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
F03030	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
F03031	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
F03032	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03033	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
F03034	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
F03035	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
F03036	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
Number of dams	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	1	1
-	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	1	1

Pre: Before administration, Post: after administration.

-: General appearance, No abnormality.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 3-4. General conditions in dams during pregnancy

HA 1000 mg/kg

Dam No.	Days of pregnancy																											
	0		1		2		3		4		5		6		7		8		9		10		11		12		13	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F04037	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04038	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04039	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04040	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04042	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04043	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04044	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04045	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04046	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04047	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04048	-	-	-	-	-	-	-	-	-	-	-	-	-	-	a	a	a	a	a	a	a	a	a	a	b	b	b	b
Number of dams	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
-	11	11	11	11	11	11	11	11	11	11	11	11	11	11	10	10	10	10	10	10	10	10	10	10	10	10	10	10
a	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	0	0	0	0
b	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1

Pre: Before administration, Post: after administration.

-: General appearance, No abnormality.

a: Skin, Crust formation.

b: Fur, Hair, Coat, Loss of fur.

HA 1000 mg/kg

Dam No.	Days of pregnancy																	
	14		15		16		17		18		19		20		21		22	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F04037	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04038	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04039	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
F04040	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
F04042	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
F04043	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
F04044	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
F04045	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
F04046	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
F04047	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04048	b	b	b	b	b	b	-	-	-	-	-	-	-	-				
Number of dams	11	11	11	11	11	11	11	11	11	11	11	11	11	11	10	10	3	3
-	10	10	10	10	10	10	11	11	11	11	11	11	11	11	10	10	3	3
b	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0

Pre: Before administration, Post: after administration.

-: General appearance, No abnormality.

b: Fur, Hair, Coat, Loss of fur.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 4-1. General conditions in dams during lactation

Control (vehicle: corn oil)

Dam No.	Days of lactation										
	0		1		2		3		4		5
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre
F01001	-	-	-	-	-	-	-	-	-	-	-
F01002	-	-	-	-	-	-	-	-	-	-	-
F01004	-	-	-	-	-	-	-	-	-	-	-
F01005	#	#	-	-	-	-	-	-	-	-	-
F01006	-	-	-	-	-	-	-	-	-	-	-
F01007	-	-	-	-	-	-	-	-	-	-	-
F01008	#	#	-	-	-	-	-	-	-	-	-
F01009	-	-	-	-	-	-	-	-	-	-	-
F01010	#	#	-	-	-	-	-	-	-	-	-
F01011	-	-	-	-	-	-	-	-	-	-	-
F01012	-	-	-	-	-	-	-	-	-	-	-
Number of dams	8	8	11	11	11	11	11	11	11	11	11
-	8	8	11	11	11	11	11	11	11	11	11

#, Animal was administered to dosing formulation before delivery, and no abnormality was on day 0 of lactation.

Pre: Before administration, Post: after administration.

-: General appearance, No abnormality.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 4-2. General conditions in dams during lactation

HA 100 mg/kg

Dam No.	Days of lactation										
	0		1		2		3		4		5
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre
F02014	-	-	-	-	-	-	-	-	-	-	-
F02015	-	-	-	-	-	-	-	-	-	-	-
F02016	-	-	-	-	-	-	-	-	-	-	-
F02017	#	#	-	-	-	-	-	-	-	-	-
F02018	-	-	-	-	-	-	-	-	-	-	-
F02019	-	-	-	-	-	-	-	-	-	-	-
F02020	-	-	-	-	-	-	-	-	-	-	-
F02021	#	#	-	-	-	-	-	-	-	-	-
F02022	-	-	-	-	-	-	-	-	-	-	-
F02023	#	#	-	-	-	-	-	-	-	-	-
Number of dams	7	7	10	10	10	10	10	10	10	10	10
-	7	7	10	10	10	10	10	10	10	10	10

#, Animal was administered to dosing formulation before delivery, and no abnormality was on day 0 of lactation.

Pre: Before administration, Post: after administration.

-: General appearance, No abnormality.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 4-3. General conditions in dams during lactation

HA 300 mg/kg

Dam No.	Days of lactation										
	0		1		2		3		4		5
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre
F03025	-	-	-	-	-	-	-	-	-	-	-
F03026	-	-	-	-	-	-	-	-	-	-	-
F03027	-	-	-	-	-	-	-	-	-	-	-
F03028	-	-	-	-	-	-	-	-	-	-	-
F03029	-	-	-	-	-	-	-	-	-	-	-
F03030	#	#	-	-	-	-	-	-	-	-	-
F03031	-	-	-	-	-	-	-	-	-	-	-
F03033	-	-	-	-	-	-	-	-	-	-	-
F03034	-	-	-	-	-	-	-	-	-	-	-
F03035	-	-	-	-	-	-	-	-	-	-	-
F03036	-	-	-	-	-	-	-	-	-	-	-
Number of dams	10	10	11	11	11	11	11	11	11	11	11
-	10	10	11	11	11	11	11	11	11	11	11

#, Animal was administered to dosing formulation before delivery, and no abnormality was on day 0 of lactation.

Pre: Before administration, Post: after administration.

-: General appearance, No abnormality.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 4-4. General conditions in dams during lactation

HA 1000 mg/kg

Dam No.	Days of lactation										
	0		1		2		3		4		5
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre
F04037	#	#	-	-	-	-	-	-	-	-	-
F04038	#	#	-	-	-	-	-	-	-	-	-
F04039	#	#	-	-	-	-	-	-	-	-	-
F04040	-	-	-	-	-	-	-	-	-	-	-
F04042	#	#	-	-	-	-	-	-	-	-	-
F04043	-	-	-	-	-	-	-	-	-	-	-
F04044	-	-	-	-	-	-	-	-	-	-	-
F04045	#	#	-	-	-	-	-	-	-	-	-
F04046	-	-	-	-	-	-	-	-	-	-	-
F04047	#	#	-	-	-	-	-	-	-	-	-
F04048	-	-	-	-	-	-	-	-	-	-	-
Number of dams	5	5	11	11	11	11	11	11	11	11	11
-	5	5	11	11	11	11	11	11	11	11	11

#, Animal was administered to dosing formulation before delivery, and no abnormality was on day 0 of lactation.

Pre: Before administration, Post: after administration.

-: General appearance, No abnormality.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 5-1-1. Detailed clinical observations of male rats

Control (vehicle: corn oil)

Male No.	Observations made while handling [b]									Open-field observations [c]																	
	Fur									Urination									Defecation								
	Pre [a]	T8 [b]	T15	T23	T29	T35	T42	R7 [c]	R14	Pre	T8	T15	T23	T29	T35	T42	R7	R14	Pre	T8	T15	T23	T29	T35	T42	R7	R14
M01001	2	2	2	2	2	2	2			0	0	0	1	0	1	0			0	0	0	0	0	0	0		
M01002	2	2	2	2	2	2	2			0	1	0	0	0	0	0			1	0	0	0	0	1	0		
M01003	2	2	2	2	2	2	2			0	0	0	0	0	0	0			0	0	0	0	0	0	0		
M01004	2	2	2	2	2	2	2			0	0	0	0	0	1	0			0	0	0	0	0	0	0		
M01005	2	2	2	2	2	2	2			3	1	1	1	1	3	1			0	0	0	0	0	0	0		
M01006	2	2	2	2	2	2	2			0	0	0	0	0	1	0			0	0	0	0	0	0	0		
M01007	2	2	2	2	2	2	2			0	0	0	0	0	0	0			0	0	0	0	0	0	0		
M01008	2	2	2	2	2	2	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M01009	2	2	2	2	2	2	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M01010	2	2	2	2	2	2	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M01011	2	2	2	2	2	2	2	2	2	1	0	1	1	1	3	2	2	0	0	0	0	0	0	0	0	0	0
M01012	2	2	2	2	2	2	2	2	2	1	1	1	1	2	1	0	1	0	0	0	0	0	0	0	0	0	0
Total	1:0	1:0	1:0	1:0	1:0	1:0	1:0	1:0	1:0	5	3	3	4	4	10	3	3	0	1	0	0	0	0	1	0	0	0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(5)	(5)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(5)	(5)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(5)	(5)

[a] pre-treatment; [b] day 8 of treatment; [c] day 7 of recovery

Fur [2, normal; 1, crust formation/loss of fur]

Urination [frequency/30sec]

Defecation [frequency/30sec]

Except the above findings, there were no changes in all animals; a) Cage-side observation (posture in home-cage, locomoter activity in home-cage, vocalization, tremor, convulsion), b) Observations made while handling (behavior while removing from cage, handling behavir, heart beats, body temperature, lacrimation, exophthalmos, pupillary size, salivation), and c) Open-field observations (posture, exploration, piloerection, palpebral opening, tremor, convulsion, respiratory rate, gait, stereotypy, bizarre behavior, grooming, straub tail, vocalization, touch response, withdrawal reflex, pinna reflex).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 5-1-2. Detailed clinical observations of male rats

HA 100 mg/kg

Male No.	Observations made while handling [b]							Open-field observations [c]																		
	Fur							Urination							Defecation						
	Pre [a]	T8 [b]	T15	T23	T29	T35	T42	Pre	T8	T15	T23	T29	T35	T42	Pre	T8	T15	T23	T29	T35	T42
M02013	2	2	2	2	2	2	2	1	0	0	0	1	1	0	0	0	0	0	0	1	0
M02014	2	2	2	2	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M02015	2	2	2	2	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M02016	2	2	2	2	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M02017	2	2	2	2	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M02018	2	2	2	2	2	2	2	1	0	0	0	0	0	0	0	0	0	0	0	0	0
M02019	2	2	2	2	2	2	2	0	0	0	0	0	0	0	1	1	0	0	0	0	0
M02020	2	2	2	2	2	2	2	0	0	0	0	0	1	0	0	0	0	0	0	0	0
M02021	2	2	2	2	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M02022	2	2	2	2	2	2	2	0	0	0	0	1	0	1	0	0	0	0	0	0	0
M02023	2	2	2	2	1	1	1	0	0	0	1	0	0	1	0	0	0	0	0	0	0
M02024	2	2	2	2	2	2	2	0	1	0	0	0	0	0	0	0	0	0	0	0	0
Total score	1:0	1:0	1:0	1:0	1:1	1:1	1:1	2	1	0	1	2	2	2	1	1	0	0	0	1	0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)

[a] pre-treatment; [b] day 8 of treatment; [c] day 7 of recovery

Fur [2, normal; 1, crust formation/loss of fur]

Urination [frequency/30sec]

Defecation [frequency/30sec]

Except the above findings, there were no changes in all animals; a) Cage-side observation (posture in home-cage, locomoter activity in home-cage, vocalization, tremor, convulsion), b) Observations made while handling (behavior while removing from cage, handling behavir, heart beats, body temperature, lacrimation, exophthalmos, pupillary size, salivation), and c) Open-field observations (posture, exploration, piloerection, palpebral opening, tremor, convulsion, respiratory rate, gait, stereotypy, bizarre behavior, grooming, straub tail, vocalization, touch response, withdrawal reflex, pinna reflex).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 5-1-3. Detailed clinical observations of male rats

HA 300 mg/kg

Male No.	Observations made while handling [b]							Open-field observations [c]																	
	Fur							Urination							Defecation						
	Pre [a]	T8 [b]	T15	T23	T29	T35	T42	Pre	T8	T15	T23	T29	T35	T42	Pre	T8	T15	T23	T29	T35	T42
M03025	2	2						1	0						0	0					
M03026	2	2	2	2	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M03027	2	2	2	2	2	2	2	1	0	0	0	1	0	0	0	0	0	0	0	0	0
M03028	2	2	2	2	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M03029	2	2	2	2	2	2	2	0	0	0	0	0	1	0	0	0	0	0	0	0	0
M03030	2	2	2	2	2	2	2	0	0	0	0	0	1	1	0	0	0	0	0	0	0
M03031	2	2	2	2	2	2	2	0	0	1	0	0	0	0	0	0	0	0	0	0	0
M03032	2	2	2	2	2	2	2	1	0	0	0	1	0	0	0	0	0	0	0	0	0
M03033	2	2	2	2	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M03034	2	2	2	2	2	2	2	1	0	0	1	0	1	0	0	0	0	0	0	0	0
M03035	2	2	2	2	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M03036	2	2	2	2	2	2	2	0	0	0	0	0	0	1	0	0	0	0	0	0	0
Total score	1:0	1:0	1:0	1:0	1:0	1:0	1:0	4	0	1	1	2	3	2	0	0	0	0	0	0	0
(N)	(12)	(12)	(11)	(11)	(11)	(11)	(11)	(12)	(12)	(11)	(11)	(11)	(11)	(11)	(12)	(12)	(11)	(11)	(11)	(11)	(11)

[a] pre-treatment; [b] day 8 of treatment; [c] day 7 of recovery

Fur [2, normal; 1, crust formation/loss of fur]

Urination [frequency/30sec]

Defecation [frequency/30sec]

Except the above findings, there were no changes in all animals; a) Cage-side observation (posture in home-cage, locomoter activity in home-cage, vocalization, tremor, convulsion), b) Observations made while handling (behavior while removing from cage, handling behavir, heart beats, body temperature, lacrimation, exophthalmos, pupillary size, salivation), and c) Open-field observations (posture, exploration, piloerection, palpebral opening, tremor, convulsion, respiratory rate, gait, stereotypy, bizarre behavior, grooming, straub tail, vocalization, touch response, withdrawal reflex, pinna reflex).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 5-1-4. Detailed clinical observations of male rats

HA 1000 mg/kg

Male No.	Observations made while handling [b]									Open-field observations [c]																			
	Fur									Urination									Defecation										
	Pre [a]	T8 [b]	T15	T23	T29	T35	T42	R7 [c]	R14	Pre	T8	T15	T23	T29	T35	T42	R7	R14	Pre	T8	T15	T23	T29	T35	T42	R7	R14
M04037	2	2	2	2	2	2	2			2	1	1	1	1	1	2			0	0	0	0	0	0	0		
M04038	2	2	2	2	2	2	2			0	0	1	0	0	1	0			0	0	0	0	0	0	0		
M04039	2	2	2	2	2	2	2			0	0	0	0	0	0	0			0	0	0	0	0	0	0		
M04040	2	2	2	2	2	2	2			1	0	0	0	0	0	1			0	0	0	0	0	0	0		
M04041	2	2	2	2	2	2	1			1	0	1	0	0	1	0			0	0	0	0	0	0	0		
M04042	2	2	2	2	2	2	2			0	0	0	0	1	0	0			0	0	0	0	0	0	0		
M04043	2	2	2	2	2	2	2			1	0	0	0	1	1	1			0	0	0	0	0	0	0		
M04044	2	2	2	2	2	2	2	2	2	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
M04045	2	2	2	2	2	2	2	2	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M04046	2	2	2	2	2	2	2	2	2	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0
M04047	2	2	2	2	2	2	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M04048	2	2	2	2	2	2	2	2	2	1	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0
Total score	1:0	1:0	1:0	1:0	1:0	1:0	1:1	1:0	1:1	6	1	3	2	4	6	5	1	0	0	0	0	0	0	0	0	0	0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(5)	(5)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(5)	(5)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(5)	(5)

[a] pre-treatment; [b] day 8 of treatment; [c] day 7 of recovery

Fur [2, normal; 1, crust formation/loss of fur]

Urination [frequency/30sec]

Defecation [frequency/30sec]

Except the above findings, there were no changes in all animals; a) Cage-side observation (posture in home-cage, locomoter activity in home-cage, vocalization, tremor, convulsion), b) Observations made while handling (behavior while removing from cage, handling behavir, heart beats, body temperature, lacrimation, exophthalmos, pupillary size, salivation), and c) Open-field observations (posture, exploration, piloerection, palpebral opening, tremor, convulsion, respiratory rate, gait, stereotypy, bizarre behavior, grooming, straub tail, vocalization, touch response, withdrawal reflex, pinna reflex).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 6-1-1. Detailed clinical observations of female rats

Control (vehicle: corn oil)

Female No.	Observations made while handling [b]									Open-field observations [c]																	
	Fur									Urination									Defecation								
	Pre [a]	T8 [b]	T15	T23	T29	T35	T42	T49	L [c]	Pre	T8	T15	T23	T29	T35	T42	T49	L	Pre	T8	T15	T23	T29	T35	T42	T49	L
F01001	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F01002	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F01003	2	2	2	2	2	2	2	2		0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	
F01004	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F01005	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F01006	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F01007	2	2	2	2	2	2	2		2	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0		0
F01008	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F01009	2	2	2	2	2	2			2	1	0	0	0	0	0			0	0	0	0	0	0	0			0
F01010	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F01011	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F01012	2	2	2	2	2	2			2	1	0	0	0	0	0			0	0	0	0	0	0	0			0
Total score	1:0	1:0	1:0	1:0	1:0	1:0	1:0	1:0	1:0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(2)	(1)	(11)	(12)	(12)	(12)	(12)	(12)	(12)	(2)	(1)	(11)	(12)	(12)	(12)	(12)	(12)	(12)	(2)	(1)	(11)

[a] pre-treatment; [b] day 8 of treatment; [c] lactation period

Fur [2, normal; 1, crust formation]

Urination [frequency/30sec]

Defecation [frequency/30sec]

Except the above findings, there were no changes in all animals; a) Cage-side observation (posture in home-cage, locomoter activity in home-cage, vocalization, tremor, convulsion), b) Observations made while handling (behavior while removing from cage, handling behavir, heart beats, body temperature, skin/mucous membranes color, lacrimation, exophthalmos, pupillary size, salivation), and c) Open-field observations (posture, exploration, piloerection, palpebral opening, tremor, convulsion, respiratory rate, gait, stereotypy, bizarre behavior, grooming, straub tail, vocalization, touch response, withdrawal reflex, pinna reflex).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 6-1-2. Detailed clinical observations of female rats

HA 100 mg/kg

Female No.	Observations made while handling [b]									Open-field observations [c]																		
	Fur									Urination									Defecation									
	Pre [a]	T8 [b]	T15	T23	T29	T35	T42	T49	L [c]	Pre	T8	T15	T23	T29	T35	T42	T49	L	Pre	T8	T15	T23	T29	T35	T42	T49	L
F02013	2	2	2	2	2	2				0	0	0	0	0	0				0	0	0	0	0	0			
F02014	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F02015	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F02016	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F02017	2	2	2	2	2	2			2	0	0	0	1	0	0			0	0	0	0	0	0	0			0
F02018	2	2	2	2	2	2	2		2	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0		0
F02019	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F02020	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F02021	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F02022	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F02023	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F02024	2	2	2	2	2	2	2	2		1	1	0	0	1	0	0	0		0	0	0	0	0	0	0	0	
Total score	1:0	1:0	1:0	1:0	1:0	1:0	1:0	1:0	1:0	1	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(2)	(1)	(10)	(12)	(12)	(12)	(12)	(12)	(12)	(2)	(1)	(10)	(12)	(12)	(12)	(12)	(12)	(12)	(2)	(1)	(10)

[a] pre-treatment; [b] day 8 of treatment; [c] lactation period

Fur [2, normal; 1, crust formation]

Urination [frequency/30sec]

Defecation [frequency/30sec]

Except the above findings, there were no changes in all animals; a) Cage-side observation (posture in home-cage, locomoter activity in home-cage, vocalization, tremor, convulsion), b) Observations made while handling (behavior while removing from cage, handling behavir, heart beats, body temperature, skin/mucous membranes color, lacrimation, exophthalmos, pupillary size, salivation), and c) Open-field observations (posture, exploration, piloerection, palpebral opening, tremor, convulsion, respiratory rate, gait, stereotypy, bizarre behavior, grooming, straub tail, vocalization, touch response, withdrawal reflex, pinna reflex).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 6-1-3. Detailed clinical observations of female rats

HA 300 mg/kg

Female No.	Observations made while handling [b]									Open-field observations [c]																	
	Fur									Urination									Defecation								
	Pre [a]	T8 [b]	T15	T23	T29	T35	T42	T49	L [c]	Pre	T8	T15	T23	T29	T35	T42	T49	L	Pre	T8	T15	T23	T29	T35	T42	T49	L
F03025	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F03026	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F03027	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F03028	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F03029	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F03030	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F03031	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F03032	2	2	2	2	2	2				0	0	0	0	0	0				0	0	0	0	0	0			
F03033	2	2	2	2	2	2			2	1	0	0	0	0	0			0	0	0	0	0	0	0			0
F03034	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F03035	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F03036	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
Total score	1:0	1:0	1:0	1:0	1:0	1:0	1:0	1:0	1:0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(0)	(0)	(11)	(12)	(12)	(12)	(12)	(12)	(12)	(0)	(0)	(11)	(12)	(12)	(12)	(12)	(12)	(12)	(0)	(0)	(11)

[a] pre-treatment; [b] day 8 of treatment; [c] lactation period

Fur [2, normal; 1, crust formation]

Urination [frequency/30sec]

Defecation [frequency/30sec]

Except the above findings, there were no changes in all animals; a) Cage-side observation (posture in home-cage, locomoter activity in home-cage, vocalization, tremor, convulsion), b) Observations made while handling (behavior while removing from cage, handling behavir, heart beats, body temperature, skin/mucous membranes color, lacrimation, exophthalmos, pupillary size, salivation), and c) Open-field observations (posture, exploration, piloerection, palpebral opening, tremor, convulsion, respiratory rate, gait, stereotypy, bizarre behavior, grooming, straub tail, vocalization, touch response, withdrawal reflex, pinna reflex).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 6-1-4. Detailed clinical observations of female rats

HA 1000 mg/kg

Female No.	Observations made while handling [b)]									Open-field observations [c)]																		
	Fur									Urination									Defecation									
	Pre [a]	T8 [b]	T15	T23	T29	T35	T42	T49	L [c]	Pre	T8	T15	T23	T29	T35	T42	T49	L	Pre	T8	T15	T23	T29	T35	T42	T49	L
F04037	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F04038	2	2	2	2	2	2			2	1	0	0	0	0	0			0	0	0	0	0	0	0			0
F04039	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F04040	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F04041	2	2	2	2	2	2	2	2		0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	
F04042	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F04043	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F04044	2	2	2	2	2	2			2	0	0	0	0	0	1			0	0	0	0	0	0	0			0
F04045	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F04046	2	2	2	2	2	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F04047	2	2	2	2	2	2			2	0	0	0	1	0	0			0	0	0	0	0	0	0			0
F04048	2	2	2	2	1	2			2	0	0	0	0	0	0			0	0	0	0	0	0	0			0
Total score	1:0	1:0	1:0	1:0	1:1	1:0	1:0	1:0	1:0	1	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(1)	(1)	(11)	(12)	(12)	(12)	(12)	(12)	(12)	(1)	(1)	(11)	(12)	(12)	(12)	(12)	(12)	(12)	(1)	(1)	(11)

[a] pre-treatment; [b] day 8 of treatment; [c] lactation period

Fur [2, normal; 1, crust formation]

Urination [frequency/30sec]

Defecation [frequency/30sec]

Except the above findings, there were no changes in all animals; a) Cage-side observation (posture in home-cage, locomoter activity in home-cage, vocalization, tremor, convulsion), b) Observations made while handling (behavior while removing from cage, handling behavir, heart beats, body temperature, skin/mucous membranes color, lacrimation, exophthalmos, pupillary size, salivation), and c) Open-field observations (posture, exploration, piloerection, palpebral opening, tremor, convulsion, respiratory rate, gait, stereotypy, bizarre behavior, grooming, straub tail, vocalization, touch response, withdrawal reflex, pinna reflex).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 6-2-1. Detailed clinical observations of female rats, satellite group

Control (vehicle: corn oil)

Female No.	Open-field observations [c)]																	
	Urination									Defecation								
	Pre [a]	T8 [b]	T15	T23	T29	T35	T42	R7 [c]	R14	Pre	T8	T15	T23	T29	T35	T42	R7	R14
F05049	0	0	0	0	0	0	0			0	0	0	0	0	0	0		
F05050	0	0	0	0	0	0	0			0	0	0	0	0	0	0		
F05051	0	0	0	0	0	0	0			0	0	0	0	0	0	0		
F05052	0	0	0	0	0	0	0			0	0	0	0	0	0	0		
F05053	0	0	0	0	0	0	0			0	0	0	0	0	0	0		
F05054	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F05055	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F05056	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F05057	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F05058	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Total score	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
(N)	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(5)	(5)	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(5)	(5)

[a] pre-treatment; [b] day 8 of treatment; [c] day 7 of recovery

Urination [frequency/30sec]

Defecation [frequency/30sec]

Except the above findings, there were no changes in all animals; a) Cage-side observation (posture in home-cage, locomoter activity in home-cage, vocalization, tremor, convulsion), b) Observations made while handling (behavior while removing from cage, handling behavir, heart beats, body temperature, fur, skin/mucous membranes color, lacrimation, exophthalmos, pupillary size, salivation), and c) Open-field observations (posture, exploration, piloerection, palpebral opening, tremor, convulsion, respiratory rate, gait, stereotypy, bizarre behavior, grooming, straub tail, vocalization, touch response, withdrawal reflex, pinna reflex).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 6-2-2. Detailed clinical observations of female rats, satellite group

HA 1000 mg/kg

Female No.	Open-field observations [c)]																	
	Urination									Defecation								
	Pre [a]	T8 [b]	T15	T23	T29	T35	T42	R7 [c]	R14	Pre	T8	T15	T23	T29	T35	T42	R7	R14
F06059	0	0	0	0	0	0	0			0	0	0	0	0	0	0		
F06060	0	0	0	0	0	0	0			0	0	0	0	0	0	0		
F06061	0	0	0	0	0	0	0			0	0	0	0	0	0	0		
F06062	0	0	0	0	0	0	0			0	0	0	0	0	0	0		
F06063	0	0	0	0	0	0	0			0	0	0	0	0	0	0		
F06064	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
F06065	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F06066	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F06067	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F06068	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Total score	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
(N)	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(5)	(5)	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(5)	(5)

[a] pre-treatment; [b] day 8 of treatment; [c] day 7 of recovery

Urination [frequency/30sec]

Defecation [frequency/30sec]

Except the above findings, there were no changes in all animals; a) Cage-side observation (posture in home-cage, locomoter activity in home-cage, vocalization, tremor, convulsion), b) Observations made while handling (behavior while removing from cage, handling behavir, heart beats, body temperature, fur, skin/mucous membranes color, lacrimation, exophthalmos, pupillary size, salivation), and c) Open-field observations (posture, exploration, piloerection, palpebral opening, tremor, convulsion, respiratory rate, gait, stereotypy, bizarre behavior, grooming, straub tail, vocalization, touch response, withdrawal reflex, pinna reflex).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 7-1-1. Body weights of male rats (g)

Control (vehicle: corn oil)

Male No.	Days of administration							
	1	4	7	14	21	28	35	42
M01001	412.5	422.1	435.0	454.3	475.3	500.8	523.7	528.2
M01002	384.2	389.3	401.4	415.8	430.4	451.5	471.2	473.8
M01003	426.7	438.2	445.1	465.3	487.4	516.5	536.2	552.8
M01004	396.8	403.6	417.5	442.1	469.5	496.3	520.8	529.8
M01005	370.0	384.6	385.7	406.0	417.7	446.2	462.4	472.3
M01006	391.5	398.9	411.6	421.9	443.4	461.3	471.6	479.4
M01007	419.4	438.4	453.1	483.9	509.7	541.8	567.8	598.4
M01008	415.6	429.4	440.7	464.2	471.9	497.6	513.7	526.7
M01009	378.2	390.8	400.2	434.9	452.5	477.8	499.0	510.8
M01010	406.1	421.8	424.4	446.8	475.6	495.1	506.9	528.2
M01011	411.3	426.4	443.0	454.0	478.7	509.5	528.5	539.6
M01012	408.5	426.8	439.5	454.4	476.6	501.6	509.2	516.2
Number of males	12	12	12	12	12	12	12	12
Mean	401.7	414.2	424.8	445.3	465.7	491.3	509.3	521.4
S.D.	17.6	19.6	21.4	22.5	25.5	27.8	30.2	35.7

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 7-1-2. Body weights of male rats (g)

HA 100 mg/kg

Male No.	Days of administration							
	1	4	7	14	21	28	35	42
M02013	413.3	433.8	449.2	473.5	491.7	513.9	533.5	541.6
M02014	424.5	445.2	460.8	483.3	499.4	530.8	562.1	576.8
M02015	386.4	396.1	397.5	415.5	432.0	461.5	477.4	487.8
M02016	413.4	430.7	439.6	456.8	466.7	491.5	512.3	524.3
M02017	391.5	404.3	406.7	429.8	452.6	466.1	487.0	487.3
M02018	388.5	402.0	411.4	434.3	464.8	485.0	502.7	521.6
M02019	403.3	414.0	427.5	442.2	453.4	469.6	499.4	516.5
M02020	442.6	468.0	494.6	528.2	550.3	572.0	604.3	617.2
M02021	370.0	383.2	396.7	418.4	442.8	463.6	482.3	501.1
M02022	385.4	396.9	408.3	418.6	428.0	436.5	447.8	460.4
M02023	400.2	416.5	428.6	446.8	459.9	477.3	494.6	494.6
M02024	397.2	400.6	406.8	428.3	440.2	451.3	476.6	496.2
Number of males	12	12	12	12	12	12	12	12
Mean	401.4	415.9	427.3	448.0	465.2	484.9	506.7	518.8
S.D.	19.7	24.3	29.5	33.2	34.5	37.8	42.4	43.0
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 7-1-3. Body weights of male rats (g)

HA 300 mg/kg

Male No.	Days of administration							
	1	4	7	14	21	28	35	42
M03025	379.1	389.4	394.8					
M03026	377.6	384.1	383.8	394.2	406.2	429.0	440.9	460.7
M03027	416.6	432.6	446.7	473.2	476.8	497.6	515.4	508.9
M03028	409.2	426.7	431.2	444.8	462.6	485.0	499.3	501.8
M03029	412.5	431.0	445.3	480.6	508.4	539.0	569.5	587.2
M03030	403.0	415.7	423.3	453.2	472.0	501.4	527.1	530.7
M03031	422.6	447.3	473.2	494.8	517.3	549.3	571.9	597.8
M03032	388.2	403.6	413.5	442.9	477.4	499.8	524.4	535.2
M03033	373.4	379.7	392.6	408.5	424.5	451.4	469.2	470.2
M03034	399.7	406.1	413.2	439.6	455.3	473.5	490.0	495.7
M03035	419.8	435.8	450.2	480.8	501.1	528.8	543.0	558.7
M03036	407.5	429.5	448.6	470.5	494.5	517.1	541.8	553.9
Number of males	12	12	12	11	11	11	11	11
Mean	400.8	415.1	426.4	453.0	472.4	497.4	517.5	527.3
S.D.	17.2	22.3	27.5	31.3	34.3	36.5	40.4	44.7
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 7-1-4. Body weights of male rats (g)

HA 1000 mg/kg

Male No.	Days of administration							
	1	4	7	14	21	28	35	42
M04037	406.0	427.4	443.6	461.2	481.3	504.0	533.9	532.3
M04038	425.9	448.5	463.5	502.5	543.8	579.2	603.7	621.7
M04039	410.5	428.0	443.8	474.0	487.9	516.7	542.8	561.9
M04040	401.1	421.0	426.9	447.4	455.1	482.4	496.4	510.9
M04041	378.0	391.0	401.8	422.0	442.4	469.2	473.4	492.8
M04042	417.1	429.3	446.2	476.2	507.8	538.1	568.7	594.9
M04043	369.4	377.2	390.7	411.2	422.0	437.7	448.1	455.7
M04044	402.0	414.7	431.4	472.3	498.5	530.1	551.3	558.1
M04045	410.0	421.1	432.1	455.4	481.8	504.3	521.7	523.8
M04046	429.5	447.4	462.8	503.6	527.0	555.6	586.4	612.7
M04047	404.0	409.9	423.4	445.5	469.7	483.5	513.1	525.4
M04048	370.6	384.5	397.2	415.8	438.5	459.5	484.0	494.9
Number of males	12	12	12	12	12	12	12	12
Mean	402.0	416.7	430.3	457.3	479.7	505.0	527.0	540.4
S.D.	19.9	22.8	24.0	30.7	36.5	41.3	46.8	50.9
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 7-2-1. Body weights of male rats at the recovery period (g)

Control (vehicle: corn oil)

Male No.	Days of recovery		
	1	7	14
M01008	528.6	545.9	561.0
M01009	501.7	520.2	540.3
M01010	526.9	542.0	549.2
M01011	531.9	554.3	570.2
M01012	514.3	522.3	531.6
Number of males	5	5	5
Mean	520.7	536.9	550.5
S.D.	12.5	15.0	15.5

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 7-2-2. Body weights of male rats at the recovery period (g)

HA 1000 mg/kg

Male No.	Days of recovery		
	1	7	14
M04044	560.4	580.2	591.4
M04045	525.9	558.2	571.8
M04046	615.3	631.3	628.0
M04047	525.1	547.2	568.9
M04048	491.3	500.6	506.1
Number of males	5	5	5
Mean	543.6	563.5	573.2
S.D.	46.9	47.8	44.3
Significance	NS	NS	NS
Statistical method	AW	AW	TT

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AW: Analysis by Aspin-Welch t-test.
TT: Analysis by Student's t-test.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 8-1-1. Body weights of female rats (g)

Control (vehicle: corn oil)

Female No.	Days of administration								
	1	4	7	14	21	28	35	42	49
F01001	236.6	247.7	250.4	254.3					
F01002	240.6	241.8	237.2	245.5					
F01003	242.2	259.8	261.1	277.1	306.7	340.0	324.8	336.3	344.1
F01004	258.6	261.0	256.2	267.2					
F01005	253.3	258.8	258.9	268.4					
F01006	230.3	234.1	235.5	241.6					
F01007	231.6	230.8	241.1	244.0	251.6				
F01008	238.3	238.2	248.7	257.6					
F01009	257.5	256.2	259.8	270.2					
F01010	230.9	231.7	240.4	247.9					
F01011	251.2	270.2	274.7	284.1					
F01012	236.6	248.0	251.0	258.5					
Number of females	12	12	12	12					
Mean	242.3	248.2	251.3	259.7					
S.D.	10.3	13.1	11.6	13.8					

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 8-1-2. Body weights of female rats (g)

HA 100 mg/kg

Female No.	Days of administration					
	1	4	7	14	21	28
F02013	242.3	248.3	248.8	255.5		
F02014	247.4	253.0	255.5	267.3		
F02015	221.8	219.3	215.9	229.9		
F02016	224.5	243.7	248.1	257.3		
F02017	233.4	250.6	252.9	262.4		
F02018	245.0	244.0	246.7	252.4	270.7	
F02019	230.6	232.3	242.2	251.0		
F02020	243.3	246.2	248.1	258.7		
F02021	216.4	220.0	215.2	227.5		
F02022	234.5	232.3	240.8	251.9		
F02023	235.5	255.6	259.3	273.3		
F02024	238.9	250.3	259.5	270.8	319.1	346.0
Number of females	12	12	12	12		
Mean	234.5	241.3	244.4	254.8		
S.D.	9.7	12.4	14.7	14.2		
Significance	NS	NS	NS	NS	---	---
Statistical method	AN	AN	AN	AN	NA	NA

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 8-1-3. Body weights of female rats (g)

HA 300 mg/kg

Female No.	Days of administration			
	1	4	7	14
F03025	237.2	252.2	250.0	257.8
F03026	222.8	221.4	229.1	238.3
F03027	245.7	252.3	250.0	262.3
F03028	234.9	229.9	243.1	236.6
F03029	245.3	255.8	253.8	264.6
F03030	244.4	246.5	256.1	274.6
F03031	240.4	240.6	252.0	257.0
F03032	231.2	233.1	242.0	245.6
F03033	232.2	234.6	241.8	246.7
F03034	232.2	234.7	231.9	239.2
F03035	251.4	257.7	260.8	268.3
F03036	221.5	222.9	231.1	239.8
Number of females	12	12	12	12
Mean	236.6	240.1	245.1	252.6
S.D.	9.3	12.6	10.4	13.2
Significance	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 8-1-4. Body weights of female rats (g)

HA 1000 mg/kg

Female No.	Days of administration								
	1	4	7	14	21	28	35	42	49
F04037	263.9	269.4	279.5	294.5					
F04038	221.0	221.3	225.3	233.0					
F04039	237.5	244.1	247.6	251.4					
F04040	227.2	238.0	232.9	231.8					
F04041	226.1	248.1	261.6	265.4	255.0	285.0	285.4	287.5	288.7
F04042	248.7	255.7	257.5	274.3					
F04043	239.6	250.2	256.7	259.9					
F04044	244.6	244.5	256.2	267.0					
F04045	226.1	227.8	235.6	243.7					
F04046	243.9	250.6	248.3	249.8					
F04047	230.8	235.8	242.4	245.7					
F04048	252.2	250.7	248.3	255.0					
Number of females	12	12	12	12					
Mean	238.5	244.7	249.3	256.0					
S.D.	12.8	12.8	14.5	17.8					
Significance	NS	NS	NS	NS	---	---	---	---	---
Statistical method	AN	AN	AN	AN	NA	NA	NA	NA	NA

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 8-2-1. Body weights of female rats, satellite group (g)

Control (vehicle: corn oil)

Female No.	Days of administration							
	1	4	7	14	21	28	35	42
F05049	246.0	251.1	257.5	272.0	284.0	285.3	298.6	305.6
F05050	258.6	266.1	261.7	277.2	282.5	286.6	280.7	289.6
F05051	266.5	265.4	265.6	286.7	301.7	305.3	302.7	307.2
F05052	233.6	247.7	252.9	261.3	270.7	281.4	286.4	287.9
F05053	228.1	240.2	243.3	252.0	256.4	263.4	270.8	277.4
F05054	235.6	244.4	254.3	264.2	267.3	273.0	285.8	285.5
F05055	243.4	254.5	262.5	277.0	283.8	293.4	304.5	309.1
F05056	234.3	239.0	255.8	273.6	282.4	281.3	294.5	300.5
F05057	237.4	243.0	240.6	257.4	268.6	274.3	281.0	294.1
F05058	220.4	221.1	227.6	231.2	236.5	241.1	244.2	246.5
Number of females	10	10	10	10	10	10	10	10
Mean	240.4	247.3	252.2	265.3	273.4	278.5	284.9	290.3
S.D.	13.8	13.3	11.7	15.9	18.0	17.5	17.9	18.6

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 8-2-2. Body weights of female rats, satellite group (g)

HA 1000 mg/kg

Female No.	Days of administration							
	1	4	7	14	21	28	35	42
F06059	251.7	270.3	282.9	296.3	290.3	308.5	319.7	326.0
F06060	250.0	244.6	259.0	273.9	281.7	284.2	295.7	303.1
F06061	249.2	255.9	270.1	287.4	298.5	303.4	322.3	330.3
F06062	232.8	233.1	245.4	244.1	260.4	256.8	274.4	277.3
F06063	253.4	259.5	259.0	276.6	287.1	300.7	318.5	331.1
F06064	216.5	236.2	244.2	244.9	247.8	260.4	268.4	276.3
F06065	224.1	237.0	241.2	249.0	258.8	275.9	282.0	299.5
F06066	251.3	266.0	269.6	282.6	274.9	287.5	297.9	295.1
F06067	245.8	249.5	247.1	262.3	272.8	283.7	287.8	298.2
F06068	228.3	242.2	247.2	255.4	256.2	265.5	274.3	271.7
Number of females	10	10	10	10	10	10	10	10
Mean	240.3	249.4	256.6	267.3	272.9	282.7	294.1	300.9
S.D.	13.6	13.0	13.9	18.7	16.7	18.1	20.2	22.3
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	TT	TT	TT	TT	TT	TT	TT	TT

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
TT: Analysis by Student's t-test.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 8-3-1. Body weights of female rats at the recovery period (g)

Control (vehicle: corn oil)

Female No.	Days of recovery		
	1	7	14
F05054	287.8	290.5	293.7
F05055	312.0	311.5	334.0
F05056	301.7	305.0	302.1
F05057	292.4	306.5	307.7
F05058	246.5	252.2	251.5
Number of females	5	5	5
Mean	288.1	293.1	297.8
S.D.	25.0	24.2	29.9

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 8-3-2. Body weights of female rats at the recovery period (g)

HA 1000 mg/kg

Female No.	Days of recovery		
	1	7	14
F06064	276.5	280.3	286.2
F06065	292.7	300.2	314.4
F06066	301.7	297.4	307.4
F06067	294.2	308.6	311.8
F06068	277.1	284.7	289.0
Number of females	5	5	5
Mean	288.4	294.2	301.8
S.D.	11.2	11.6	13.2
Significance	NS	NS	NS
Statistical method	TT	TT	TT

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
TT: Analysis by Student's t-test.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 9-1. Body weights of dams during pregnancy (g)

Control (vehicle: corn oil)

Dam No.	Days of pregnancy			
	0	7	14	20
F01001	269.0	296.6	325.7	403.2
F01002	261.1	295.5	329.9	408.0
F01004	287.4	337.2	378.2	472.2
F01005	281.6	328.5	362.9	444.6
F01006	267.1	292.8	331.9	414.5
F01007	259.5	296.1	327.8	395.0
F01008	274.1	305.7	340.3	422.4
F01009	277.7	318.8	359.6	439.9
F01010	246.1	282.5	315.7	397.3
F01011	289.5	319.0	360.8	445.7
F01012	273.1	297.1	332.9	411.1
Number of dams	11	11	11	11
Mean	271.5	306.3	342.3	423.1
S.D.	12.8	17.1	19.8	24.4

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 9-2. Body weights of dams during pregnancy (g)

HA 100 mg/kg

Dam No.		Days of pregnancy				
		0	7	14	20	26
F02013	>	258.2 >	297.0 >	297.7 >	289.1 >	299.7 >
F02014		280.9	316.1	354.5	441.3	
F02015		241.4	283.7	325.4	405.4	
F02016		264.4	302.5	345.4	446.2	
F02017		271.0	306.1	335.5	388.3	
F02018		268.4	321.0	367.5	451.4	
F02019		245.8	284.2	311.5	404.4	
F02020		273.2	310.4	348.4	439.7	
F02021		243.4	273.8	307.9	378.5	
F02022		245.0	296.6	335.7	414.0	
F02023		275.8	305.1	340.6	421.1	
F02024	>	351.7 >	363.1 >	378.2 >	359.0 >	366.7 >
Number of dams		10	10	10	10	
Mean		260.9	300.0	337.2	419.0	
S.D.		15.3	15.2	18.5	25.2	
Significance		NS	NS	NS	NS	---
Statistical method		AN	AN	AN	AN	NA

>: Excluded from analysis (not pregnant)

Significantly different from the control group (*: P<0.05, **: P<0.01).

NS: Not significantly different from the control group.

AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 9-3. Body weights of dams during pregnancy (g)

HA 300 mg/kg

Dam No.	Days of pregnancy			
	0	7	14	20
F03025	273.7	308.3	357.3	446.1
F03026	242.9	288.8	321.3	392.7
F03027	274.7	288.6	320.1	394.6
F03028	256.5	293.4	328.7	404.6
F03029	283.8	325.4	369.4	469.3
F03030	275.1	303.6	331.4	425.1
F03031	272.3	304.6	337.8	418.5
F03032	256.7	299.7	336.2	377.5
F03033	264.9	286.8	320.3	372.1
F03034	254.0	280.2	297.2	371.4
F03035	280.5	339.0	375.7	464.9
F03036	243.4	284.5	321.1	411.4
Number of dams	12	12	12	12
Mean	264.9	300.2	334.7	412.4
S.D.	13.9	17.5	22.7	33.9
Significance	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 9-4. Body weights of dams during pregnancy (g)

HA 1000 mg/kg

Dam No.	Days of pregnancy			
	0	7	14	20
F04037	294.1	334.7	366.2	434.4
F04038	239.4	274.6	308.7	384.3
F04039	265.1	300.3	327.8	394.1
F04040	251.3	302.6	342.5	417.6
F04042	270.9	317.7	363.5	450.8
F04043	273.1	308.3	345.8	419.6
F04044	263.6	312.5	352.4	438.9
F04045	246.7	287.5	314.0	401.7
F04046	263.5	304.1	328.6	392.6
F04047	252.1	276.2	306.6	346.9
F04048	272.4	301.0	332.4	410.8
Number of dams	11	11	11	11
Mean	262.9	301.8	335.3	408.3
S.D.	15.2	17.6	20.7	29.1
Significance	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 10-1. Body weights of dams during lactation (g)

Control (vehicle: corn oil)

Dam No.	Days of lactation	
	0	4
F01001	302.1	322.0
F01002	304.5	330.7
F01004	343.9	360.3
F01005	328.1	334.5
F01006	326.9	351.9
F01007	342.2	327.5
F01008	344.9	325.4
F01009	317.9	340.3
F01010	319.9	306.2
F01011	364.9	365.3
F01012	303.5	322.2
Number of dams	11	11
Mean	327.2	335.1
S.D.	20.2	17.9

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 10-2. Body weights of dams during lactation (g)

HA 100 mg/kg

Dam No.	Days of lactation	
	0	4
F02014	325.9	351.5
F02015	301.0	314.0
F02016	311.7	353.5
F02017	357.5	335.7
F02018	335.2	355.9
F02019	286.3	310.7
F02020	360.5	339.8
F02021	304.7	311.0
F02022	309.6	345.1
F02023	341.3	339.0
Number of dams	10	10
Mean	323.4	335.6
S.D.	24.9	17.6
Significance	NS	NS
Statistical method	AN	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 10-3. Body weights of dams during lactation (g)

HA 300 mg/kg

Dam No.	Days of lactation	
	0	4
F03025	335.3	340.6
F03026	326.6	314.2
F03027	315.8	325.8
F03028	293.3	320.2
F03029	350.1	358.1
F03030	322.3	335.1
F03031	316.3	349.6
F03033	328.4	312.9
F03034	266.5	294.0
F03035	367.8	388.4
F03036	296.3	330.8
Number of dams	11	11
Mean	319.9	333.6
S.D.	27.8	25.6
Significance	NS	NS
Statistical method	AN	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 10-4. Body weights of dams during lactation (g)

HA 1000 mg/kg

Dam No.	Days of lactation	
	0	4
F04037	362.0	358.4
F04038	313.8	322.1
F04039	318.5	312.1
F04040	338.9	352.8
F04042	376.1	350.4
F04043	343.4	364.7
F04044	326.8	364.4
F04045	318.3	309.5
F04046	327.4	334.5
F04047	317.4	306.1
F04048	329.0	332.8
Number of dams	11	11
Mean	333.8	337.1
S.D.	19.9	22.3
Significance	NS	NS
Statistical method	AN	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 11-1-1. Food consumption of male rats (g/day)

Control (vehicle: corn oil)

Male No.	Days of administration					
	1	7	14	29	35	41
M01001	26.5	25.0	25.3	25.5	21.9	25.0
M01002	25.0	21.7	23.7	21.6	16.1	20.2
M01003	25.4	26.5	24.5	24.6	21.8	24.8
M01004	24.4	23.8	22.4	23.8	19.2	23.9
M01005	25.8	21.2	24.4	27.1	24.4	23.3
M01006	25.8	22.9	20.9	20.5	19.1	20.9
M01007	34.9	32.2	30.0	30.1	33.5	34.4
M01008	25.8	26.3	24.8	25.5	26.7	25.8
M01009	25.6	27.5	23.0	25.3	22.6	25.2
M01010	27.0	28.0	26.9	26.5	27.8	27.0
M01011	19.6	26.2	20.2	25.3	22.4	24.3
M01012	33.2	27.1	22.7	19.3	17.9	24.9
Number of males	12	12	12	12	12	12
Mean	26.6	25.7	24.1	24.6	22.8	25.0
S.D.	4.0	3.0	2.6	3.0	4.8	3.5

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 11-1-2. Food consumption of male rats (g/day)

HA 100 mg/kg

Male No.	Days of administration					
	1	7	14	29	35	41
M02013	29.2	28.0	25.9	25.9	21.0	27.1
M02014	32.1	30.8	23.3	28.2	25.5	29.1
M02015	25.1	22.3	21.7	23.8	22.5	21.2
M02016	25.7	29.3	23.3	29.0	25.0	25.2
M02017	24.3	27.5	27.0	24.5	22.5	23.9
M02018	24.8	24.6	24.6	24.9	24.7	25.5
M02019	28.0	25.9	23.3	20.8	18.8	24.3
M02020	31.0	32.6	26.6	27.2	25.0	34.3
M02021	27.9	24.1	24.6	24.8	23.0	24.4
M02022	24.2	25.2	20.1	22.1	23.9	22.0
M02023	25.1	24.9	25.1	22.2	23.1	22.5
M02024	31.6	28.1	21.8	29.5	22.1	27.0
Number of males	12	12	12	12	12	12
Mean	27.4	26.9	23.9	25.2	23.1	25.5
S.D.	3.0	3.0	2.1	2.8	1.9	3.6
Significance	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	KW	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).
KW: Analysis by Kruskal-Wallis' test (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 11-1-3. Food consumption of male rats (g/day)

HA 300 mg/kg

Male No.	Days of administration					
	1	7	14	29	35	41
M03025	22.4	23.9				
M03026	26.1	21.0	19.8	20.8	19.1	20.4
M03027	29.3	26.0	23.8	27.9	21.8	21.8
M03028	25.0	24.6	23.2	23.4	21.7	21.6
M03029	27.8	28.3	33.0	28.1	29.9	29.4
M03030	27.9	26.1	24.0	25.7	24.5	24.0
M03031	32.5	30.6	28.5	30.1	27.9	30.5
M03032	29.9	26.5	27.6	24.1	22.8	26.4
M03033	23.2	18.1	17.3	19.4	16.0	19.8
M03034	25.7	26.8	24.9	23.8	24.3	23.1
M03035	29.5	30.6	28.0	26.3	26.9	26.5
M03036	31.2	28.1	26.2	25.1	23.3	24.4
Number of males	12	12	11	11	11	11
Mean	27.5	25.9	25.1	25.0	23.5	24.4
S.D.	3.1	3.6	4.3	3.2	3.9	3.5
Significance	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	KW	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).
KW: Analysis by Kruskal-Wallis' test (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 11-1-4. Food consumption of male rats (g/day)

HA 1000 mg/kg

Male No.	Days of administration					
	1	7	14	29	35	41
M04037	35.4	26.8	22.9	21.6	22.9	22.2
M04038	26.8	25.6	28.9	28.1	26.9	28.0
M04039	26.1	27.2	24.7	27.5	27.3	28.9
M04040	26.1	22.5	21.4	23.5	21.3	20.2
M04041	25.2	25.9	22.6	23.2	20.7	27.0
M04042	25.9	26.5	25.2	24.6	21.6	30.5
M04043	23.9	22.0	22.8	22.5	21.9	19.9
M04044	28.6	30.1	28.2	27.8	22.6	24.5
M04045	27.2	28.6	24.5	25.6	21.7	23.8
M04046	33.1	32.4	28.5	33.8	30.6	32.6
M04047	22.0	21.9	23.7	22.6	22.0	19.7
M04048	23.3	23.8	22.6	25.5	23.0	23.4
Number of males	12	12	12	12	12	12
Mean	27.0	26.1	24.7	25.5	23.5	25.1
S.D.	3.9	3.3	2.6	3.4	3.0	4.3
Significance	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	KW	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).
KW: Analysis by Kruskal-Wallis' test (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 11-2-1. Food consumption of male rats at the recovery period (g/day)

Control (vehicle: corn oil)

Male No.	Days of recovery	
	6	12
M01008	31.7	31.1
M01009	32.4	30.8
M01010	32.3	33.0
M01011	34.1	33.6
M01012	25.7	26.0
Number of males	5	5
Mean	31.2	30.9
S.D.	3.2	3.0

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 11-2-2. Food consumption of male rats at the recovery period (g/day)

HA 1000 mg/kg

Male No.	Days of recovery	
	6	12
M04044	30.7	31.8
M04045	38.5	36.3
M04046	37.2	35.9
M04047	30.5	34.2
M04048	26.4	29.5
Number of males	5	5
Mean	32.7	33.5
S.D.	5.1	2.9
Significance	NS	NS
Statistical method	TT	TT

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
TT: Analysis by Student's t-test.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 12-1-1. Food consumption of female rats (g/day)

Control (vehicle: corn oil)

Female No.	Days of administration						
	1	7	14	29	35	41	48
F01001	12.6	17.8	17.0				
F01002	20.7	17.4	11.3				
F01003	19.8	18.6	19.3	21.5	16.6	22.9	21.7
F01004	18.8	16.8	10.4				
F01005	11.9	21.1	21.4				
F01006	12.3	15.8	16.3				
F01007	15.8	14.0	18.6				
F01008	17.6	13.8	21.4				
F01009	17.4	14.1	19.3				
F01010	20.4	11.2	18.5				
F01011	19.8	16.7	21.3				
F01012	15.1	19.5	18.1				
Number of females	12	12	12				
Mean	16.9	16.4	17.7				
S.D.	3.3	2.8	3.6				

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 12-1-2. Food consumption of female rats (g/day)

HA 100 mg/kg

Female No.	Days of administration		
	1	7	14
F02013	16.7	16.6	14.9
F02014	20.5	18.1	13.6
F02015	14.9	14.8	7.9
F02016	17.6	19.7	19.6
F02017	17.3	18.5	13.6
F02018	14.6	13.8	20.6
F02019	20.6	15.9	17.2
F02020	18.3	15.5	12.1
F02021	14.6	15.9	13.3
F02022	20.8	12.4	17.2
F02023	22.6	21.0	20.4
F02024	19.8	19.1	13.0
Number of females	12	12	12
Mean	18.2	16.8	15.3
S.D.	2.7	2.6	3.8
Significance	NS	NS	NS
Statistical method	AN	AN	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 12-1-3. Food consumption of female rats (g/day)

HA 300 mg/kg

Female No.	Days of administration		
	1	7	14
F03025	20.5	19.1	15.3
F03026	18.7	10.6	16.0
F03027	17.7	18.4	11.3
F03028	18.4	14.2	16.1
F03029	12.2	19.3	17.8
F03030	19.9	13.1	16.7
F03031	21.4	16.5	18.9
F03032	18.0	13.9	17.4
F03033	20.5	20.0	19.4
F03034	13.5	19.6	19.1
F03035	15.1	21.6	16.9
F03036	19.6	12.7	17.3
Number of females	12	12	12
Mean	18.0	16.6	16.9
S.D.	2.9	3.6	2.2
Significance	NS	NS	NS
Statistical method	AN	AN	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 12-1-4. Food consumption of female rats (g/day)

HA 1000 mg/kg

Female No.	Days of administration						
	1	7	14	29	35	41	48
F04037	22.1	14.1	19.0				
F04038	17.0	13.5	17.6				
F04039	14.1	21.7	18.8				
F04040	13.8	18.3	15.7				
F04041	19.3	22.4	10.8	17.6	19.0	17.2	5.9
F04042	16.4	15.9	16.5				
F04043	14.7	18.4	19.1				
F04044	21.5	13.2	19.5				
F04045	21.4	9.5	18.8				
F04046	12.9	16.7	12.6				
F04047	20.9	19.5	16.8				
F04048	11.0	20.3	19.4				
Number of females	12	12	12				
Mean	17.1	17.0	17.1				
S.D.	3.9	3.9	2.8				
Significance	NS	NS	NS	---	---	---	---
Statistical method	AN	AN	AN	NA	NA	NA	NA

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 12-2-1. Food consumption of female rats, satellite group (g/day)

Control (vehicle: corn oil)

Female No.	Days of administration						
	1	7	14	21	29	35	41
F05049	21.0	13.5	18.5	22.1	19.0	13.0	16.6
F05050	21.4	20.7	15.3	18.0	15.5	14.1	12.8
F05051	19.5	23.2	15.5	19.2	16.9	13.7	18.0
F05052	16.9	19.9	20.9	18.4	16.5	17.5	13.9
F05053	19.3	17.1	17.3	16.2	17.0	17.4	16.4
F05054	21.5	16.5	17.9	19.5	19.4	12.7	18.4
F05055	20.9	19.1	19.1	18.3	17.1	16.9	17.4
F05056	19.1	14.8	17.2	19.1	20.8	9.4	17.7
F05057	22.5	19.4	16.6	18.0	21.2	19.0	21.4
F05058	17.0	14.5	15.8	16.9	15.7	10.0	8.1
Number of females	10	10	10	10	10	10	10
Mean	19.9	17.9	17.4	18.6	17.9	14.4	16.1
S.D.	1.9	3.1	1.8	1.6	2.0	3.3	3.7

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 12-2-2. Food consumption of female rats, satellite group (g/day)

HA 1000 mg/kg

Female No.	Days of administration						
	1	7	14	21	29	35	41
F06059	26.4	23.9	21.8	20.6	17.6	19.9	21.0
F06060	19.0	12.5	15.6	17.6	18.5	12.1	16.0
F06061	20.0	16.5	19.3	19.9	20.2	16.4	19.4
F06062	20.0	16.8	17.7	18.1	18.1	16.4	15.8
F06063	17.6	17.4	16.2	21.9	22.7	15.9	21.4
F06064	18.3	17.5	20.5	16.9	18.9	15.2	17.1
F06065	16.7	17.8	13.8	18.5	18.6	19.5	22.7
F06066	21.2	20.7	20.7	19.0	17.7	18.4	17.6
F06067	19.1	18.1	13.6	18.7	18.8	17.9	17.7
F06068	18.9	16.7	19.6	16.5	15.8	17.0	15.8
Number of females	10	10	10	10	10	10	10
Mean	19.7	17.8	17.9	18.8	18.7	16.9	18.5
S.D.	2.7	2.9	2.9	1.7	1.8	2.3	2.5
Significance	NS	NS	NS	NS	NS	NS	NS
Statistical method	TT	TT	TT	TT	TT	TT	TT

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
TT: Analysis by Student's t-test.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 12-3-1. Food consumption of female rats at the recovery period (g/day)

Control (vehicle: corn oil)

Female No.	Days of recovery	
	6	12
F05054	19.4	23.7
F05055	18.8	21.2
F05056	18.1	22.5
F05057	24.4	19.1
F05058	20.2	20.6
Number of females	5	5
Mean	20.2	21.4
S.D.	2.5	1.8

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 12-3-2. Food consumption of female rats at the recovery period (g/day)

HA 1000 mg/kg

Female No.	Days of recovery	
	6	12
F06064	17.0	22.3
F06065	19.0	20.7
F06066	16.4	23.3
F06067	23.3	16.9
F06068	19.4	20.9
Number of females	5	5
Mean	19.0	20.8
S.D.	2.7	2.4
Significance	NS	NS
Statistical method	TT	TT

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
TT: Analysis by Student's t-test.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 13-1. Food consumption in dams during pregnancy (g/day)

Control (vehicle: corn oil)

Dam No.	Days of pregnancy			
	0	7	14	20
F01001	16.3	22.2	20.9	24.0
F01002	18.5	22.6	22.6	22.0
F01004	17.5	28.1	27.1	19.3
F01005	16.6	29.3	25.4	18.1
F01006	15.6	21.6	25.5	21.3
F01007	16.9	21.3	26.3	19.4
F01008	15.3	25.9	25.9	25.7
F01009	21.0	28.2	25.0	20.7
F01010	20.2	24.4	19.3	21.1
F01011	19.4	26.8	22.1	21.0
F01012	19.3	14.1	24.8	20.4
Number of dams	11	11	11	11
Mean	17.9	24.0	24.1	21.2
S.D.	1.9	4.4	2.5	2.1

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 13-2. Food consumption in dams during pregnancy (g/day)

HA 100 mg/kg

Dam No.		Days of pregnancy			
		0	7	14	20
F02013	>	16.4 >	21.2 >	10.2 >	14.4 >
F02014		19.6	21.0	23.5	22.5
F02015		18.4	23.4	20.4	26.5
F02016		19.6	21.7	23.3	18.3
F02017		18.4	22.0	26.6	22.3
F02018		19.4	28.0	24.7	27.1
F02019		16.3	21.5	21.2	21.1
F02020		18.0	22.1	24.7	23.8
F02021		18.9	22.2	18.0	18.3
F02022		22.2	26.8	23.7	25.6
F02023		17.5	26.6	21.8	21.1
F02024	>	24.5 >	24.2 >	20.6 >	15.2 >
Number of dams		10	10	10	10
Mean		18.8	23.5	22.8	22.7
S.D.		1.6	2.6	2.5	3.1
Significance		NS	NS	NS	NS
Statistical method		KW	AN	AN	AN

>: Excluded from analysis (not pregnant)
Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
KW: Analysis by Kruskal-Wallis' test (one-way layout).
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 13-3. Food consumption in dams during pregnancy (g/day)

HA 300 mg/kg

Dam No.	Days of pregnancy			
	0	7	14	20
F03025	17.7	25.6	22.0	23.3
F03026	20.1	25.5	19.1	23.9
F03027	14.9	18.0	17.4	25.5
F03028	17.8	22.2	24.5	14.0
F03029	20.6	25.6	27.4	28.3
F03030	18.7	20.4	20.0	21.1
F03031	17.1	20.3	19.5	22.9
F03032	20.6	24.4	25.3	21.7
F03033	14.4	23.0	23.7	16.9
F03034	17.7	19.5	22.3	16.1
F03035	19.4	28.6	28.1	25.9
F03036	19.8	23.7	19.8	23.8
Number of dams	12	12	12	12
Mean	18.2	23.1	22.4	22.0
S.D.	2.1	3.1	3.4	4.3
Significance	NS	NS	NS	NS
Statistical method	KW	AN	AN	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
KW: Analysis by Kruskal-Wallis' test (one-way layout).
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 13-4. Food consumption in dams during pregnancy (g/day)

HA 1000 mg/kg

Dam No.	Days of pregnancy			
	0	7	14	20
F04037	19.0	23.5	19.3	19.7
F04038	15.3	22.4	21.7	22.1
F04039	12.1	22.7	28.3	19.5
F04040	20.6	28.3	29.2	26.6
F04042	17.0	23.9	24.5	25.1
F04043	14.6	19.6	19.2	17.3
F04044	16.9	23.6	22.3	28.2
F04045	21.6	23.9	18.9	24.5
F04046	17.1	20.3	22.6	20.6
F04047	9.5	20.7	23.1	18.4
F04048	22.8	26.1	28.4	19.3
Number of dams	11	11	11	11
Mean	17.0	23.2	23.4	21.9
S.D.	4.0	2.5	3.8	3.6
Significance	NS	NS	NS	NS
Statistical method	KW	AN	AN	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
KW: Analysis by Kruskal-Wallis' test (one-way layout).
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 14-1. Food consumption in dams during lactation (g/day)

Control (vehicle: corn oil)

Dam No.	Days of lactation
	3
F01001	40.0
F01002	41.6
F01004	46.9
F01005	33.7
F01006	43.5
F01007	32.4
F01008	28.8
F01009	43.3
F01010	34.5
F01011	41.5
F01012	44.0
Number of dams	11
Mean	39.1
S.D.	5.8

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 14-2. Food consumption in dams during lactation (g/day)

HA 100 mg/kg

Dam No.	Days of lactation
	3
F02014	43.3
F02015	37.6
F02016	44.5
F02017	24.4
F02018	43.6
F02019	42.6
F02020	34.5
F02021	36.4
F02022	50.0
F02023	38.8
Number of dams	10
Mean	39.6
S.D.	7.0
Significance	NS
Statistical method	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 14-3. Food consumption in dams during lactation (g/day)

HA 300 mg/kg

Dam No.	Days of lactation
	3
F03025	48.3
F03026	38.1
F03027	28.1
F03028	39.7
F03029	35.9
F03030	38.2
F03031	38.5
F03033	25.5
F03034	39.6
F03035	48.8
F03036	55.0
Number of dams	11
Mean	39.6
S.D.	8.6
Significance	NS
Statistical method	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 14-4. Food consumption in dams during lactation (g/day)

HA 1000 mg/kg

Dam No.	Days of lactation
	3
F04037	37.0
F04038	37.6
F04039	28.4
F04040	43.6
F04042	25.5
F04043	42.1
F04044	55.7
F04045	34.4
F04046	40.7
F04047	25.9
F04048	36.1
Number of dams	11
Mean	37.0
S.D.	8.8
Significance	NS
Statistical method	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 15-1. Functional findings of male rats at the end of the dosing period

Control (vehicle: corn oil)

Male No.	Righting reflex	Visual placing	Pupillary reflex	Startle reaction	Preyer's reaction	Withdrawal reflex	Eyelid reflex
M01001	2	2	2	2	+	+	+
M01002	2	2	2	2	+	+	+
M01003	2	2	2	2	+	+	+
M01004	2	2	2	2	+	+	+
M01005	2	2	2	2	+	+	+
Total	2: 5	2: 5	2: 5	2: 5	+: 5	+: 5	+: 5

2 or +, normal

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 15-2. Functional findings of male rats at the end of the dosing period

HA 100 mg/kg

Male No.	Righting reflex	Visual placing	Pupillary reflex	Startle reaction	Preyer's reaction	Withdrawal reflex	Eyelid reflex
M02013	2	2	2	2	+	+	+
M02014	2	2	2	2	+	+	+
M02015	2	2	2	2	+	+	+
M02016	2	2	2	2	+	+	+
M02017	2	2	2	2	+	+	+
Total	2: 5	2: 5	2: 5	2: 5	+: 5	+: 5	+: 5

2 or +, normal

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 15-3. Functional findings of male rats at the end of the dosing period

HA 300 mg/kg

Male No.	Righting reflex	Visual placing	Pupillary reflex	Startle reaction	Preyer's reaction	Withdrawal reflex	Eyelid reflex
M03026	2	2	2	2	+	+	+
M03027	2	2	2	2	+	+	+
M03028	2	2	2	2	+	+	+
M03029	2	2	2	2	+	+	+
M03030	2	2	2	2	+	+	+
Total	2: 5	2: 5	2: 5	2: 5	+: 5	+: 5	+: 5

2 or +, normal

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 15-4. Functional findings of male rats at the end of the dosing period

HA 1000 mg/kg

Male No.	Righting reflex	Visual placing	Pupillary reflex	Startle reaction	Preyer's reaction	Withdrawal reflex	Eyelid reflex
M04037	2	2	2	2	+	+	+
M04038	2	2	2	2	+	+	+
M04039	2	2	2	2	+	+	+
M04040	2	2	2	2	+	+	+
M04041	2	2	2	2	+	+	+
Total	2: 5	2: 5	2: 5	2: 5	+: 5	+: 5	+: 5

2 or +, normal

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 16-1-1. Functional findings of female rats at the end of the dosing period

Control (vehicle: corn oil)
Female, dam

Female No.	Righting reflex	Visual placing	Pupillary reflex	Startle reaction	Preyer's reaction	Withdrawal reflex	Eyelid reflex
F01001	2	2	2	2	+	+	+
F01005	2	2	2	2	+	+	+
F01008	2	2	2	2	+	+	+
F01010	2	2	2	2	+	+	+
F01011	2	2	2	2	+	+	+
Total	2: 5	2: 5	2: 5	2: 5	+: 5	+: 5	+: 5

2 or +, normal

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 16-1-2. Functional findings of female rats at the end of the dosing period

HA 100 mg/kg

Female, dam

Female No.	Righting reflex	Visual placing	Pupillary reflex	Startle reaction	Preyer's reaction	Withdrawal reflex	Eyelid reflex
F02016	2	2	2	2	+	+	+
F02019	2	2	2	2	+	+	+
F02021	2	2	2	2	+	+	+
F02022	2	2	2	2	+	+	+
F02023	2	2	2	2	+	+	+
Total	2: 5	2: 5	2: 5	2: 5	+: 5	+: 5	+: 5

2 or +, normal

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 16-1-3. Functional findings of female rats at the end of the dosing period

HA 300 mg/kg

Female, dam

Female No.	Righting reflex	Visual placing	Pupillary reflex	Startle reaction	Preyer's reaction	Withdrawal reflex	Eyelid reflex
F03026	2	2	2	2	+	+	+
F03028	2	2	2	2	+	+	+
F03029	2	2	2	2	+	+	+
F03030	2	2	2	2	+	+	+
F03036	2	2	2	2	+	+	+
Total	2: 5	2: 5	2: 5	2: 5	+: 5	+: 5	+: 5

2 or +, normal

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 16-1-4. Functional findings of female rats at the end of the dosing period

HA 1000 mg/kg

Female, dam

Female No.	Righting reflex	Visual placing	Pupillary reflex	Startle reaction	Preyer's reaction	Withdrawal reflex	Eyelid reflex
F04037	2	2	2	2	+	+	+
F04038	2	2	2	2	+	+	+
F04042	2	2	2	2	+	+	+
F04044	2	2	2	2	+	+	+
F04045	2	2	2	2	+	+	+
Total	2: 5	2: 5	2: 5	2: 5	+: 5	+: 5	+: 5

2 or +, normal

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 16-2-1. Functional findings of female rats at the end of the dosing period, satellite group

Control (vehicle: corn oil)
Female, satellite groups

Female No.	Righting reflex	Visual placing	Pupillary reflex	Startle reaction	Preyer's reaction	Withdrawal reflex	Eyelid reflex
F05049	2	2	2	2	+	+	+
F05050	2	2	2	2	+	+	+
F05051	2	2	2	2	+	+	+
F05052	2	2	2	2	+	+	+
F05053	2	2	2	2	+	+	+
Total	2: 5	2: 5	2: 5	2: 5	+: 5	+: 5	+: 5

2 or +, normal

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 16-2-2. Functional findings of female rats at the end of the dosing period, satellite group

HA 1000 mg/kg

Female, satellite groups

Female No.	Righting reflex	Visual placing	Pupillary reflex	Startle reaction	Preyer's reaction	Withdrawal reflex	Eyelid reflex
F06059	2	2	2	2	+	+	+
F06060	2	2	2	2	+	+	+
F06061	2	2	2	2	+	+	+
F06062	2	2	2	2	+	+	+
F06063	2	2	2	2	+	+	+
Total	2: 5	2: 5	2: 5	2: 5	+: 5	+: 5	+: 5

2 or +, normal

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 17-1. Assessment of grip strength of male rats

Control (vehicle: corn oil)

Male No.	Administration period	
	Forelimb	Hindlimb
	(kg)	(kg)
M01001	0.728	0.498
M01002	0.922	0.461
M01003	0.881	0.452
M01004	0.938	0.578
M01005	1.141	0.416
Number of males	5	5
Mean	0.922	0.481
S.D.	0.148	0.062

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 17-2. Assessment of grip strength of male rats

HA 100 mg/kg

Male No.	Administration period	
	Forelimb	Hindlimb
	(kg)	(kg)
M02013	0.652	0.413
M02014	0.759	0.341
M02015	0.973	0.476
M02016	1.005	0.471
M02017	0.870	0.397
Number of males	5	5
Mean	0.852	0.420
S.D.	0.147	0.056

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 17-3. Assessment of grip strength of male rats

HA 300 mg/kg

Male No.	Administration period	
	Forelimb	Hindlimb
	(kg)	(kg)
M03026	0.538	0.440
M03027	1.205	0.321
M03028	0.859	0.482
M03029	1.120	0.545
M03030	1.044	0.474
Number of males	5	5
Mean	0.953	0.452
S.D.	0.265	0.083

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 17-4. Assessment of grip strength of male rats

HA 1000 mg/kg

Male No.	Administration period	
	Forelimb	Hindlimb
	(kg)	(kg)
M04037	0.725	0.480
M04038	0.859	0.372
M04039	1.284	0.446
M04040	1.100	0.476
M04041	0.812	0.752
Number of males	5	5
Mean	0.956	0.505
S.D.	0.230	0.145

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 18-1. Assessment of grip strength of female rats

Control (vehicle: corn oil)

Female No.	Administration period	
	Forelimb	Hindlimb
	(kg)	(kg)
F01001	0.662	0.454
F01005	0.861	0.527
F01008	0.913	0.266
F01010	0.944	0.427
F01011	0.668	0.560
Number of females	5	5
Mean	0.810	0.447
S.D.	0.135	0.114

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 18-2. Assessment of grip strength of female rats

HA 100 mg/kg

Female No.	Administration period	
	Forelimb	Hindlimb
	(kg)	(kg)
F02016	0.718	0.384
F02019	0.891	0.528
F02021	0.867	0.336
F02022	0.796	0.423
F02023	0.843	0.636
Number of females	5	5
Mean	0.823	0.461
S.D.	0.068	0.121

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 18-3. Assessment of grip strength of female rats

HA 300 mg/kg

Female No.	Administration period	
	Forelimb (kg)	Hindlimb (kg)
F03026	0.704	0.472
F03028	0.869	0.534
F03029	0.996	0.416
F03030	0.913	0.534
F03036	0.980	0.511
Number of females	5	5
Mean	0.892	0.493
S.D.	0.117	0.050

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 18-4. Assessment of grip strength of female rats

HA 1000 mg/kg

Female No.	Administration period	
	Forelimb (kg)	Hindlimb (kg)
F04037	0.780	0.427
F04038	0.876	0.603
F04042	0.962	0.554
F04044	1.021	0.492
F04045	0.853	0.433
Number of females	5	5
Mean	0.898	0.502
S.D.	0.094	0.076

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 19-1. Assessment of grip strength of female rats, satellite group

Control (vehicle: corn oil)

Female No.	Administration period	
	Forelimb	Hindlimb
	(kg)	(kg)
F05049	0.527	0.396
F05050	0.896	0.434
F05051	0.933	0.398
F05052	0.517	0.428
F05053	0.530	0.409
Number of females	5	5
Mean	0.681	0.413
S.D.	0.214	0.017

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 19-2. Assessment of grip strength of female rats, satellite group

HA 1000 mg/kg

Female No.	Administration period	
	Forelimb	Hindlimb
	(kg)	(kg)
F06059	0.963	0.555
F06060	0.823	0.420
F06061	0.925	0.560
F06062	0.869	0.421
F06063	0.875	0.367
Number of females	5	5
Mean	0.891	0.465
S.D.	0.054	0.088

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 20-1. Motor activity of male rats

Control (vehicle: corn oil)

Male No.	Administration period									
	Ambulation (counts)					Rearing (counts)				
	5min	10min	15min	20min	Total	5min	10min	15min	20min	Total
M01001	1820	1913	1564	1120	6417	29	19	16	3	67
M01002	1125	1118	747	969	3959	25	28	10	16	79
M01003	1167	929	630	691	3417	27	16	9	11	63
M01004	1238	1167	1109	720	4234	29	24	22	3	78
M01005	1195	940	781	974	3890	24	14	16	21	75
Number of males	5	5	5	5	5	5	5	5	5	5
Mean	1309	1213	966	895	4383	27	20	15	11	72
S.D.	289	405	379	183	1174	2	6	5	8	7

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 20-2. Motor activity of male rats

HA 100 mg/kg

Male No.	Administration period									
	Ambulation (counts)					Rearing (counts)				
	5min	10min	15min	20min	Total	5min	10min	15min	20min	Total
M02013	1315	1195	1139	926	4575	23	21	22	3	69
M02014	1272	1116	682	528	3598	31	21	4	7	63
M02015	1071	895	734	431	3131	21	12	12	5	50
M02016	1450	924	717	617	3708	29	11	4	5	49
M02017	1180	1099	966	963	4208	27	27	14	25	93
Number of males	5	5	5	5	5	5	5	5	5	5
Mean	1258	1046	848	693	3844	26	18	11	9	65
S.D.	143	130	198	239	560	4	7	8	9	18

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 20-3. Motor activity of male rats

HA 300 mg/kg

Male No.	Administration period									
	Ambulation (counts)					Rearing (counts)				
	5min	10min	15min	20min	Total	5min	10min	15min	20min	Total
M03026	1154	827	977	521	3479	25	11	11	3	50
M03027	1108	969	968	620	3665	32	28	22	6	88
M03028	1359	1216	1153	1042	4770	44	37	22	13	116
M03029	1186	1207	1157	1005	4555	20	24	14	14	72
M03030	1277	918	1013	861	4069	33	8	18	11	70
Number of males	5	5	5	5	5	5	5	5	5	5
Mean	1217	1027	1054	810	4108	31	22	17	9	79
S.D.	101	176	94	231	555	9	12	5	5	25

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 20-4. Motor activity of male rats

HA 1000 mg/kg

Male No.	Administration period									
	Ambulation (counts)					Rearing (counts)				
	5min	10min	15min	20min	Total	5min	10min	15min	20min	Total
M04037	1177	1275	831	657	3940	34	36	9	16	95
M04038	868	730	761	467	2826	36	25	22	8	91
M04039	1336	1041	1204	961	4542	29	22	25	8	84
M04040	1073	679	440	105	2297	26	4	6	0	36
M04041	1129	961	639	505	3234	26	16	8	10	60
Number of males	5	5	5	5	5	5	5	5	5	5
Mean	1117	937	775	539	3368	30	21	14	8	73
S.D.	170	242	282	311	889	5	12	9	6	25

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 21-1. Motor activity of female rats

Control (vehicle: corn oil)

Female No.	Administration period									
	Ambulation (counts)					Rearing (counts)				
	5min	10min	15min	20min	Total	5min	10min	15min	20min	Total
F01001	1203	645	746	583	3177	36	4	11	3	54
F01005	1597	1230	1459	1170	5456	22	7	1	11	41
F01008	1334	1149	978	888	4349	43	26	8	13	90
F01010	1295	779	765	779	3618	38	14	1	16	69
F01011	1115	836	1055	378	3384	30	16	37	1	84
Number of females	5	5	5	5	5	5	5	5	5	5
Mean	1309	928	1001	760	3997	34	13	12	9	68
S.D.	182	250	289	301	928	8	9	15	6	20

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 21-2. Motor activity of female rats

HA 100 mg/kg

Female No.	Administration period									
	Ambulation (counts)					Rearing (counts)				
	5min	10min	15min	20min	Total	5min	10min	15min	20min	Total
F02016	1080	926	645	762	3413	32	17	11	13	73
F02019	1022	923	849	616	3410	27	21	7	6	61
F02021	1185	1010	1121	1000	4316	22	20	9	11	62
F02022	1240	1141	888	852	4121	41	36	24	18	119
F02023	1085	876	893	605	3459	35	27	18	4	84
Number of females	5	5	5	5	5	5	5	5	5	5
Mean	1122	975	879	767	3744	31	24	14	10	80
S.D.	88	105	169	166	439	7	8	7	6	24

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 21-3. Motor activity of female rats

HA 300 mg/kg

Female No.	Administration period									
	Ambulation (counts)					Rearing (counts)				
	5min	10min	15min	20min	Total	5min	10min	15min	20min	Total
F03026	780	617	462	386	2245	31	17	1	3	52
F03028	1101	678	264	110	2153	19	5	0	0	24
F03029	1231	992	367	298	2888	37	23	0	0	60
F03030	1239	768	812	662	3481	25	9	15	3	52
F03036	1012	830	916	628	3386	20	10	12	7	49
Number of females	5	5	5	5	5	5	5	5	5	5
Mean	1073	777	564	417	2831	26	13	6	3	47
S.D.	189	145	285	231	620	8	7	7	3	14

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 21-4. Motor activity of female rats

HA 1000 mg/kg

Female No.	Administration period									
	Ambulation (counts)					Rearing (counts)				
	5min	10min	15min	20min	Total	5min	10min	15min	20min	Total
F04037	1401	1165	823	736	4125	30	22	5	2	59
F04038	1051	854	447	509	2861	28	22	6	6	62
F04042	1245	1068	580	623	3516	29	13	3	15	60
F04044	1034	981	998	891	3904	28	14	22	8	72
F04045	1092	520	453	487	2552	40	9	5	2	56
Number of females	5	5	5	5	5	5	5	5	5	5
Mean	1165	918	660	649	3392	31	16	8	7	62
S.D.	156	250	243	168	671	5	6	8	5	6

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 22-1. Motor activity of female rats, satellite group

Control (vehicle: corn oil)

Female No.	Administration period									
	Ambulation (counts)					Rearing (counts)				
	5min	10min	15min	20min	Total	5min	10min	15min	20min	Total
F05049	900	742	761	665	3068	49	36	24	18	127
F05050	1279	1067	1025	840	4211	32	24	30	17	103
F05051	1126	1212	999	1060	4397	30	35	22	38	125
F05052	1747	1594	1476	1358	6175	31	22	14	7	74
F05053	1268	1275	1168	1003	4714	42	53	55	33	183
Number of females	5	5	5	5	5	5	5	5	5	5
Mean	1264	1178	1086	985	4513	37	34	29	23	122
S.D.	310	311	263	259	1118	8	12	16	13	40

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 22-2. Motor activity of female rats, satellite group

HA 1000 mg/kg

Female No.	Administration period									
	Ambulation (counts)					Rearing (counts)				
	5min	10min	15min	20min	Total	5min	10min	15min	20min	Total
F06059	1249	1238	1380	916	4783	22	22	47	15	106
F06060	1335	1383	1400	1310	5428	35	34	71	61	201
F06061	1212	1058	1117	1009	4396	38	25	29	25	117
F06062	1288	1039	1193	1039	4559	46	30	30	41	147
F06063	1308	1307	1172	1401	5188	40	42	21	18	121
Number of females	5	5	5	5	5	5	5	5	5	5
Mean	1278	1205	1252	1135	4871	36	31	40	32	138
S.D.	49	152	129	209	431	9	8	20	19	38

Significantly different from the control group (*: P<0.05, **: P<0.01).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 23-1-1. Urinalysis in male rats

Control (vehicle: corn oil)

Male No.	Quality									Urinary sediments				
	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen	Color	Turbidity	Red blood cells	White blood cells	Casts	Crystals	Epithelial cells
M01001	6.5	2+	-	+	-	-	+	yellow	-	-	-	-	±	-
M01002	≧9.0	2+	-	+	-	-	+	yellow	-	-	-	-	±	-
M01003	8.0	2+	-	+	-	-	+	light yellow	-	-	-	-	±	-
M01004	7.0	+	-	+	-	-	+	light yellow	-	-	-	-	±	-
M01005	7.0	+	-	±	-	-	±	light yellow	-	-	-	-	±	-

Protein, -: negative; ±: 10≦and<30 mg/dL; +: 30≦and<100 mg/dL; 2+: 100≦and<300 mg/dL; 3+: 300≦and<600 mg/dL; 4+: 600 mg/dL≦
Glucose, -: negative; ±: 30≦and<70 mg/dL; +: 70≦and<150 mg/dL; 2+: 150≦and<300 mg/dL; 3+: 300≦and<1,000 mg/dL; 4+: 1,000 mg/dL≦
Ketone, -: negative; ±(5≦and<10 mg/dL; +: 10≦and<40 mg/dL; 2+: 40≦and<80 mg/dL; 3+: 80≦and<150 mg/dL; 4+: 150 mg/dL≦
Bilirubin, -: negative; +: 0.5≦and<2.0 mg/dL; 2+: 2.0≦and<6.0 mg/dL; 3+: 6.0≦and<10.0 mg/dL; 4+: 10.0 mg/dL≦
Occult blood, -: negative; ±: 0.03≦and<0.06 mg/dL; +: 0.06≦and<0.20 mg/dL; 2+: 0.20≦and<1.00 mg/dL; 3+: 1.00 mg/dL≦
Urobilinogen, ±: normal; +: 2.0≦and<4.0 mg/dL; 2+: 4.0≦and<8.0 mg/dL; 3+: 8.0≦and<12.0 mg/dL; 4+: 12.0 mg/dL≦
Turbidity, -: negative; ±: trace; +: slight; 2+: moderate; 3+: marked
Red Blood cells, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≧300/3 visual field
White Blood cells, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field, 2+: 100-299/3 visual field; 3+: ≧300/3 visual field
Casts, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≧300/3 visual field
Cristals, -: not observed; ±: a few; +: abundant
Epithelial cells, -: not observed; ±: a few; +: abundant

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 23-1-2. Urinalysis in male rats

HA 100 mg/kg

Male No.	Quality									Urinary sediments				
	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen	Color	Turbidity	Red blood cells	White blood cells	Casts	Crystals	Epithelial cells
M02013	6.5	2+	-	+	-	-	2+	yellow	-	-	-	-	±	-
M02014	8.0	+	-	+	-	-	±	light yellow	-	-	-	-	±	-
M02015	7.0	2+	-	+	-	-	+	light yellow	-	-	-	-	±	-
M02016	7.5	2+	-	+	-	-	+	light yellow	-	-	-	-	±	-
M02017	7.0	2+	-	+	-	-	2+	yellow	-	-	-	-	±	-

Protein, -: negative; ±: 10≦and<30 mg/dL; +: 30≦and<100 mg/dL; 2+: 100≦and<300 mg/dL; 3+: 300≦and<600 mg/dL; 4+: 600 mg/dL≦
Glucose, -: negative; ±: 30≦and<70 mg/dL; +: 70≦and<150 mg/dL; 2+: 150≦and<300 mg/dL; 3+: 300≦and<1,000 mg/dL; 4+: 1,000 mg/dL≦
Ketone, -: negative; ±(5≦and<10 mg/dL; +: 10≦and<40 mg/dL; 2+: 40≦and<80 mg/dL; 3+: 80≦and<150 mg/dL; 4+: 150 mg/dL≦
Bilirubin, -: negative; +: 0.5≦and<2.0 mg/dL; 2+: 2.0≦and<6.0 mg/dL; 3+: 6.0≦and<10.0 mg/dL; 4+: 10.0 mg/dL≦
Occult blood, -: negative; ±: 0.03≦and<0.06 mg/dL; +: 0.06≦and<0.20 mg/dL; 2+: 0.20≦and<1.00 mg/dL; 3+: 1.00 mg/dL≦
Urobilinogen, ±: normal; +: 2.0≦and<4.0 mg/dL; 2+: 4.0≦and<8.0 mg/dL; 3+: 8.0≦and<12.0 mg/dL; 4+: 12.0 mg/dL≦
Turbidity, -: negative; ±: trace; +: slight; 2+: moderate; 3+: marked
Red Blood cells, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≧300/3 visual field
White Blood cells, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field, 2+: 100-299/3 visual field; 3+: ≧300/3 visual field
Casts, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≧300/3 visual field
Cristals, -: not observed; ±: a few; +: abundant
Epithelial cells, -: not observed; ±: a few; +: abundant

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 23-1-3. Urinalysis in male rats

HA 300 mg/kg

Male No.	Quality									Urinary sediments				
	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen	Color	Turbidity	Red blood cells	White blood cells	Casts	Crystals	Epithelial cells
M03026	8.5	+	-	+	-	-	±	light yellow	-	-	-	-	±	-
M03027	8.0	+	-	+	-	-	±	light yellow	-	-	-	-	±	-
M03028	8.0	2+	-	+	-	-	+	light yellow	-	-	-	-	±	-
M03029	7.5	±	-	-	-	-	±	light yellow	-	-	-	-	-	-
M03030	6.5	+	-	+	-	-	±	light yellow	-	-	-	-	±	-

Protein, -: negative; ±: 10≦and<30 mg/dL; +: 30≦and<100 mg/dL; 2+: 100≦and<300 mg/dL; 3+: 300≦and<600 mg/dL; 4+: 600 mg/dL≦
Glucose, -: negative; ±: 30≦and<70 mg/dL; +: 70≦and<150 mg/dL; 2+: 150≦and<300 mg/dL; 3+: 300≦and<1,000 mg/dL; 4+: 1,000 mg/dL≦
Ketone, -: negative; ±(5≦and<10 mg/dL; +: 10≦and<40 mg/dL; 2+: 40≦and<80 mg/dL; 3+: 80≦and<150 mg/dL; 4+: 150 mg/dL≦
Bilirubin, -: negative; +: 0.5≦and<2.0 mg/dL; 2+: 2.0≦and<6.0 mg/dL; 3+: 6.0≦and<10.0 mg/dL; 4+: 10.0 mg/dL≦
Occult blood, -: negative; ±: 0.03≦and<0.06 mg/dL; +: 0.06≦and<0.20 mg/dL; 2+: 0.20≦and<1.00 mg/dL; 3+: 1.00 mg/dL≦
Urobilinogen, ±: normal; +: 2.0≦and<4.0 mg/dL; 2+: 4.0≦and<8.0 mg/dL; 3+: 8.0≦and<12.0 mg/dL; 4+: 12.0 mg/dL≦
Turbidity, -: negative; ±: trace; +: slight; 2+: moderate; 3+: marked
Red Blood cells, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≧300/3 visual field
White Blood cells, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field, 2+: 100-299/3 visual field; 3+: ≧300/3 visual field
Casts, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≧300/3 visual field
Cristals, -: not observed; ±: a few; +: abundant
Epithelial cells, -: not observed; ±: a few; +: abundant

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 23-1-4. Urinalysis in male rats

HA 1000 mg/kg

Male No.	Quality									Urinary sediments				
	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen	Color	Turbidity	Red blood cells	White blood cells	Casts	Crystals	Epithelial cells
M04037	8.0	+	-	+	-	-	±	light yellow	-	-	-	-	±	-
M04038	6.5	2+	-	+	-	-	+	yellow	-	-	-	-	±	-
M04039	7.5	±	-	-	-	-	±	light yellow	-	-	-	-	±	-
M04040	7.0	±	-	±	-	-	±	light yellow	-	-	-	-	-	-
M04041	7.0	2+	-	+	-	-	±	light yellow	-	-	-	-	±	-

Protein, -: negative; ±: 10≦and<30 mg/dL; +: 30≦and<100 mg/dL; 2+: 100≦and<300 mg/dL; 3+: 300≦and<600 mg/dL; 4+: 600 mg/dL≦
Glucose, -: negative; ±: 30≦and<70 mg/dL; +: 70≦and<150 mg/dL; 2+: 150≦and<300 mg/dL; 3+: 300≦and<1,000 mg/dL; 4+: 1,000 mg/dL≦
Ketone, -: negative; ±(5≦and<10 mg/dL; +: 10≦and<40 mg/dL; 2+: 40≦and<80 mg/dL; 3+: 80≦and<150 mg/dL; 4+: 150 mg/dL≦
Bilirubin, -: negative; +: 0.5≦and<2.0 mg/dL; 2+: 2.0≦and<6.0 mg/dL; 3+: 6.0≦and<10.0 mg/dL; 4+: 10.0 mg/dL≦
Occult blood, -: negative; ±: 0.03≦and<0.06 mg/dL; +: 0.06≦and<0.20 mg/dL; 2+: 0.20≦and<1.00 mg/dL; 3+: 1.00 mg/dL≦
Urobilinogen, ±: normal; +: 2.0≦and<4.0 mg/dL; 2+: 4.0≦and<8.0 mg/dL; 3+: 8.0≦and<12.0 mg/dL; 4+: 12.0 mg/dL≦
Turbidity, -: negative; ±: trace; +: slight; 2+: moderate; 3+: marked
Red Blood cells, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≧300/3 visual field
White Blood cells, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field, 2+: 100-299/3 visual field; 3+: ≧300/3 visual field
Casts, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≧300/3 visual field
Cristals, -: not observed; ±: a few; +: abundant
Epithelial cells, -: not observed; ±: a few; +: abundant

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 23-2-1. Urinalysis in male rats

Control (vehicle: corn oil)

Male No.	Urine volume	S.G.	Electrolyte, density			Electrolyte, gross volume		
			Na	K	Cl	Na	K	Cl
	mL/24hr		mEq/L	mEq/L	mEq/L	mEq/24hr	mEq/24hr	mEq/24hr
M01001	11.4	1.061	100.2	277.33	139.5	1.14	3.16	1.59
M01002	10.9	1.071	169.4	338.74 #	205.3	1.85	3.69	2.24
M01003	11.2	1.076	140.5	356.38 #	210.1	1.57	3.99	2.35
M01004	12.0	1.061	113.4	249.66	151.4	1.36	3.00	1.82
M01005	32.8	1.028	59.7	120.92	75.2	1.96	3.97	2.47
Number of males	5	5	5	5	5	5	5	5
Mean	15.7	1.059	116.6	268.61	156.3	1.58	3.56	2.09
S.D.	9.6	0.019	41.5	93.37	55.2	0.34	0.46	0.37

S.G.: Specific gravity

#: The specimen was diluted to two folds with distilled water.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 23-2-2. Urinalysis in male rats

HA 100 mg/kg

Male No.	Urine volume	S.G.	Electrolyte, density			Electrolyte, gross volume		
			Na	K	Cl	Na	K	Cl
	mL/24hr		mEq/L	mEq/L	mEq/L	mEq/24hr	mEq/24hr	mEq/24hr
M02013	10.9	1.079	158.0	380.32 #	219.8	1.72	4.15	2.40
M02014	24.3	1.039	79.5	177.30	95.9	1.93	4.31	2.33
M02015	13.9	1.065	128.8	298.79	184.2	1.79	4.15	2.56
M02016	14.6	1.062	105.1	275.25	151.9	1.53	4.02	2.22
M02017	12.0	1.067	129.5	322.48 #	178.6	1.55	3.87	2.14
Number of males	5	5	5	5	5	5	5	5
Mean	15.1	1.062	120.2	290.83	166.1	1.70	4.10	2.33
S.D.	5.3	0.015	29.5	74.51	46.1	0.17	0.16	0.16
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN

S.G.: Specific gravity

#: The specimen was diluted to two folds with distilled water.

Significantly different from the control group (*: P<0.05, **: P<0.01).

NS: Not significantly different from the control group.

AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 23-2-3. Urinalysis in male rats

HA 300 mg/kg

Male No.	Urine volume	S.G.	Electrolyte, density			Electrolyte, gross volume		
			Na	K	Cl	Na	K	Cl
	mL/24hr		mEq/L	mEq/L	mEq/L	mEq/24hr	mEq/24hr	mEq/24hr
M03026	11.1	1.075	160.9	361.52 #	228.8	1.79	4.01	2.54
M03027	14.8	1.061	139.3	267.20	181.5	2.06	3.95	2.69
M03028	9.6	1.077	129.8	337.58 #	166.4	1.25	3.24	1.60
M03029	53.5	1.017	38.8	73.21	41.4	2.08	3.92	2.21
M03030	9.8	1.070	89.9	279.65	128.9	0.88	2.74	1.26
Number of males	5	5	5	5	5	5	5	5
Mean	19.8	1.060	111.7	263.83	149.4	1.61	3.57	2.06
S.D.	19.0	0.025	48.2	113.56	70.2	0.53	0.56	0.61
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN

S.G.: Specific gravity

#: The specimen was diluted to two folds with distilled water.

Significantly different from the control group (*: P<0.05, **: P<0.01).

NS: Not significantly different from the control group.

AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 23-2-4. Urinalysis in male rats

HA 1000 mg/kg

Male No.	Urine volume	S.G.	Electrolyte, density			Electrolyte, gross volume		
			Na	K	Cl	Na	K	Cl
	mL/24hr		mEq/L	mEq/L	mEq/L	mEq/24hr	mEq/24hr	mEq/24hr
M04037	15.0	1.060	109.7	247.45	159.8	1.65	3.71	2.40
M04038	11.9	1.078	168.2	386.44 #	225.7	2.00	4.60	2.69
M04039	44.5	1.022	49.1	97.25	60.6	2.18	4.33	2.70
M04040	15.0	1.056	102.5	261.77	163.7	1.54	3.93	2.46
M04041	11.3	1.069	138.1	318.62 #	185.5	1.56	3.60	2.10
Number of males	5	5	5	5	5	5	5	5
Mean	19.5	1.057	113.5	262.31	159.1	1.79	4.03	2.47
S.D.	14.1	0.021	44.4	107.29	60.9	0.29	0.42	0.25
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN

S.G.: Specific gravity

#: The specimen was diluted to two folds with distilled water.

Significantly different from the control group (*: P<0.05, **: P<0.01).

NS: Not significantly different from the control group.

AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 23-3-1. Urinalysis in male rats of the recovery period

Control (vehicle: corn oil)

Male No.	Quality									Urinary sediments				
	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen	Color	Turbidity	Red blood cells	White blood cells	Casts	Crystals	Epithelial cells
M01008	8.0	+	-	-	-	-	±	light yellow	-	-	-	-	±	-
M01009	8.5	±	-	-	-	-	±	light yellow	-	-	-	-	±	-
M01010	8.0	+	-	-	-	-	±	light yellow	+	-	-	-	±	-
M01011	8.5	+	-	±	-	-	±	light yellow	-	-	-	-	±	-
M01012	7.5	±	-	-	-	-	±	light yellow	-	-	-	-	-	-

Protein, -: negative; ±: 10≦and<30 mg/dL; +: 30≦and<100 mg/dL; 2+: 100≦and<300 mg/dL; 3+: 300≦and<600 mg/dL; 4+: 600 mg/dL≦
Glucose, -: negative; ±: 30≦and<70 mg/dL; +: 70≦and<150 mg/dL; 2+: 150≦and<300 mg/dL; 3+: 300≦and<1,000 mg/dL; 4+: 1,000 mg/dL≦
Ketone, -: negative; ±(5≦and<10 mg/dL; +: 10≦and<40 mg/dL; 2+: 40≦and<80 mg/dL; 3+: 80≦and<150 mg/dL; 4+: 150 mg/dL≦
Bilirubin, -: negative; +: 0.5≦and<2.0 mg/dL; 2+: 2.0≦and<6.0 mg/dL; 3+: 6.0≦and<10.0 mg/dL; 4+: 10.0 mg/dL≦
Occult blood, -: negative; ±: 0.03≦and<0.06 mg/dL; +: 0.06≦and<0.20 mg/dL; 2+: 0.20≦and<1.00 mg/dL; 3+: 1.00 mg/dL≦
Urobilinogen, ±: normal; +: 2.0≦and<4.0 mg/dL; 2+: 4.0≦and<8.0 mg/dL; 3+: 8.0≦and<12.0 mg/dL; 4+: 12.0 mg/dL≦
Turbidity, -: negative; ±: trace; +: slight; 2+: moderate; 3+: marked
Red Blood cells, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≧300/3 visual field
White Blood cells, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field, 2+: 100-299/3 visual field; 3+: ≧300/3 visual field
Casts, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≧300/3 visual field
Cristals, -: not observed; ±: a few; +: abundant
Epithelial cells, -: not observed; ±: a few; +: abundant

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 23-3-2. Urinalysis in male rats of the recovery period

HA 1000 mg/kg

Male No.	Quality									Urinary sediments				
	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen	Color	Turbidity	Red blood cells	White blood cells	Casts	Crystals	Epithelial cells
M04044	8.0	+	-	±	-	-	±	light yellow	-	-	-	-	±	-
M04045	8.0	+	-	-	-	-	±	light yellow	-	-	-	-	±	-
M04046	7.5	+	-	+	-	-	±	light yellow	-	-	-	-	±	-
M04047	7.0	+	-	±	-	-	±	light yellow	-	-	-	-	±	-
M04048	7.0	+	-	±	-	-	+	light yellow	-	-	-	-	±	-

Protein, -: negative; ±: 10≦and<30 mg/dL; +: 30≦and<100 mg/dL; 2+: 100≦and<300 mg/dL; 3+: 300≦and<600 mg/dL; 4+: 600 mg/dL≦
Glucose, -: negative; ±: 30≦and<70 mg/dL; +: 70≦and<150 mg/dL; 2+: 150≦and<300 mg/dL; 3+: 300≦and<1,000 mg/dL; 4+: 1,000 mg/dL≦
Ketone, -: negative; ±(5≦and<10 mg/dL; +: 10≦and<40 mg/dL; 2+: 40≦and<80 mg/dL; 3+: 80≦and<150 mg/dL; 4+: 150 mg/dL≦
Bilirubin, -: negative; +: 0.5≦and<2.0 mg/dL; 2+: 2.0≦and<6.0 mg/dL; 3+: 6.0≦and<10.0 mg/dL; 4+: 10.0 mg/dL≦
Occult blood, -: negative; ±: 0.03≦and<0.06 mg/dL; +: 0.06≦and<0.20 mg/dL; 2+: 0.20≦and<1.00 mg/dL; 3+: 1.00 mg/dL≦
Urobilinogen, ±: normal; +: 2.0≦and<4.0 mg/dL; 2+: 4.0≦and<8.0 mg/dL; 3+: 8.0≦and<12.0 mg/dL; 4+: 12.0 mg/dL≦
Turbidity, -: negative; ±: trace; +: slight; 2+: moderate; 3+: marked
Red Blood cells, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≧300/3 visual field
White Blood cells, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field, 2+: 100-299/3 visual field; 3+: ≧300/3 visual field
Casts, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≧300/3 visual field
Cristals, -: not observed; ±: a few; +: abundant
Epithelial cells, -: not observed; ±: a few; +: abundant

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 23-4-1. Urinalysis in male rats of the recovery period

Control (vehicle: corn oil)

Male No.	Urine volume	S.G.	Electrolyte, density			Electrolyte, gross volume		
			Na	K	Cl	Na	K	Cl
	mL/24hr		mEq/L	mEq/L	mEq/L	mEq/24hr	mEq/24hr	mEq/24hr
M01008	28.4	1.043	99.5	183.82	130.5	2.83	5.22	3.71
M01009	16.1	1.067	124.5	297.36	186.9	2.00	4.79	3.01
M01010	26.5	1.043	95.1	198.96	125.3	2.52	5.27	3.32
M01011	33.0	1.041	97.4	195.69	132.7	3.21	6.46	4.38
M01012	32.6	1.032	70.6	156.20	106.9	2.30	5.09	3.48
Number of males	5	5	5	5	5	5	5	5
Mean	27.3	1.045	97.4	206.41	136.5	2.57	5.37	3.58
S.D.	6.9	0.013	19.1	53.56	30.0	0.47	0.64	0.51

S.G.: Specific gravity

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 23-4-2. Urinalysis in male rats of the recovery period

HA 1000 mg/kg

Male No.	Urine volume	S.G.	Electrolyte, density			Electrolyte, gross volume		
			Na	K	Cl	Na	K	Cl
	mL/24hr		mEq/L	mEq/L	mEq/L	mEq/24hr	mEq/24hr	mEq/24hr
M04044	22.6	1.044	93.1	195.18	120.8	2.10	4.41	2.73
M04045	25.2	1.045	103.8	205.71	126.0	2.62	5.18	3.18
M04046	14.8	1.079	135.4	358.68 #	191.3	2.00	5.31	2.83
M04047	17.4	1.058	126.0	272.54	170.7	2.19	4.74	2.97
M04048	13.8	1.077	159.0	378.42 #	234.9	2.19	5.22	3.24
Number of males	5	5	5	5	5	5	5	5
Mean	18.8	1.061	123.5	282.11	168.7	2.22	4.97	2.99
S.D.	5.0	0.017	26.1	84.59	47.5	0.24	0.38	0.22
Significance	NS	NS	NS	NS	NS	NS	NS	*
Statistical method	TT	TT	TT	TT	TT	TT	TT	TT

S.G.: Specific gravity

#: The specimen was diluted to two folds with distilled water.

Significantly different from the control group (*: P<0.05, **: P<0.01).

NS: Not significantly different from the control group.

TT: Analysis by Student's t-test.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 24-1-1. Urinalysis in female rats, satellite group

Control (vehicle: corn oil)

Female No.	Quality									Urinary sediments				
	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen	Color	Turbidity	Red blood cells	White blood cells	Casts	Crystals	Epithelial cells
F05049	6.5	+	-	±	-	-	+	light yellow	-	-	-	-	-	-
F05050	7.0	+	-	±	-	-	+	light yellow	-	-	-	-	±	-
F05051	6.5	+	-	±	-	-	±	light yellow	-	-	-	-	-	-
F05052	6.5	±	-	±	-	-	±	light yellow	-	-	-	-	-	-
F05053	6.5	2+	-	+	+	-	+	yellow	-	-	-	-	±	-

Protein, -: negative; ±: 10≦and<30 mg/dL; +: 30≦and<100 mg/dL; 2+: 100≦and<300 mg/dL; 3+: 300≦and<600 mg/dL; 4+: 600 mg/dL≦
Glucose, -: negative; ±: 30≦and<70 mg/dL; +: 70≦and<150 mg/dL; 2+: 150≦and<300 mg/dL; 3+: 300≦and<1,000 mg/dL; 4+: 1,000 mg/dL≦
Ketone, -: negative; ±(5≦and<10 mg/dL; +: 10≦and<40 mg/dL; 2+: 40≦and<80 mg/dL; 3+: 80≦and<150 mg/dL; 4+: 150 mg/dL≦
Bilirubin, -: negative; +: 0.5≦and<2.0 mg/dL; 2+: 2.0≦and<6.0 mg/dL; 3+: 6.0≦and<10.0 mg/dL; 4+: 10.0 mg/dL≦
Occult blood, -: negative; ±: 0.03≦and<0.06 mg/dL; +: 0.06≦and<0.20 mg/dL; 2+: 0.20≦and<1.00 mg/dL; 3+: 1.00 mg/dL≦
Urobilinogen, ±: normal; +: 2.0≦and<4.0 mg/dL; 2+: 4.0≦and<8.0 mg/dL; 3+: 8.0≦and<12.0 mg/dL; 4+: 12.0 mg/dL≦
Turbidity, -: negative; ±: trace; +: slight; 2+: moderate; 3+: marked
Red Blood cells, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≧300/3 visual field
White Blood cells, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field, 2+: 100-299/3 visual field; 3+: ≧300/3 visual field
Casts, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≧300/3 visual field
Cristals, -: not observed; ±: a few; +: abundant
Epithelial cells, -: not observed; ±: a few; +: abundant

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 24-1-2. Urinalysis in female rats, satellite group

HA 1000 mg/kg

Female No.	Quality									Urinary sediments				
	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen	Color	Turbidity	Red blood cells	White blood cells	Casts	Crystals	Epithelial cells
F06059	7.0	2+	-	+	-	-	+	yellow	-	-	-	-	±	-
F06060	6.5	±	-	±	-	-	±	light yellow	-	-	-	-	-	-
F06061	7.0	-	-	-	-	-	±	light yellow	-	-	-	-	-	-
F06062	6.5	2+	-	+	+	-	+	yellow	-	-	-	-	±	-
F06063	6.5	-	-	-	-	-	±	light yellow	-	-	-	-	-	-

Protein, -: negative; ±: 10≦and<30 mg/dL; +: 30≦and<100 mg/dL; 2+: 100≦and<300 mg/dL; 3+: 300≦and<600 mg/dL; 4+: 600 mg/dL≦
Glucose, -: negative; ±: 30≦and<70 mg/dL; +: 70≦and<150 mg/dL; 2+: 150≦and<300 mg/dL; 3+: 300≦and<1,000 mg/dL; 4+: 1,000 mg/dL≦
Ketone, -: negative; ±(5≦and<10 mg/dL; +: 10≦and<40 mg/dL; 2+: 40≦and<80 mg/dL; 3+: 80≦and<150 mg/dL; 4+: 150 mg/dL≦
Bilirubin, -: negative; +: 0.5≦and<2.0 mg/dL; 2+: 2.0≦and<6.0 mg/dL; 3+: 6.0≦and<10.0 mg/dL; 4+: 10.0 mg/dL≦
Occult blood, -: negative; ±: 0.03≦and<0.06 mg/dL; +: 0.06≦and<0.20 mg/dL; 2+: 0.20≦and<1.00 mg/dL; 3+: 1.00 mg/dL≦
Urobilinogen, ±: normal; +: 2.0≦and<4.0 mg/dL; 2+: 4.0≦and<8.0 mg/dL; 3+: 8.0≦and<12.0 mg/dL; 4+: 12.0 mg/dL≦
Turbidity, -: negative; ±: trace; +: slight; 2+: moderate; 3+: marked
Red Blood cells, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≧300/3 visual field
White Blood cells, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field, 2+: 100-299/3 visual field; 3+: ≧300/3 visual field
Casts, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≧300/3 visual field
Cristals, -: not observed; ±: a few; +: abundant
Epithelial cells, -: not observed; ±: a few; +: abundant

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 24-2-1. Urinalysis in female rats, satellite group

Control (vehicle: corn oil)

Female No.	Urine volume	S.G.	Electrolyte, density			Electrolyte, gross volume		
			Na	K	Cl	Na	K	Cl
	mL/24hr		mEq/L	mEq/L	mEq/L	mEq/24hr	mEq/24hr	mEq/24hr
F05049	20.4	1.037	84.3	189.43	119.8	1.72	3.86	2.44
F05050	11.4	1.047	112.1	231.97	157.0	1.28	2.64	1.79
F05051	9.1	1.043	30.0	138.32	47.3	0.27	1.26	0.43
F05052	12.4	1.052	109.6	249.11	160.3	1.36	3.09	1.99
F05053	4.3	1.094	187.0	459.14 #	276.4	0.80	1.97	1.19
Number of females	5	5	5	5	5	5	5	5
Mean	11.5	1.055	104.6	253.59	152.2	1.09	2.56	1.57
S.D.	5.9	0.023	56.7	122.62	83.0	0.56	1.00	0.78

S.G.: Specific gravity

#: The specimen was diluted to two folds with distilled water.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 24-2-2. Urinalysis in female rats, satellite group

HA 1000 mg/kg

Female No.	Urine volume	S.G.	Electrolyte, density			Electrolyte, gross volume		
			Na	K	Cl	Na	K	Cl
	mL/24hr		mEq/L	mEq/L	mEq/L	mEq/24hr	mEq/24hr	mEq/24hr
F06059	8.2	1.063	97.8	253.37	153.4	0.80	2.08	1.26
F06060	12.8	1.057	124.5	269.43	184.4	1.59	3.45	2.36
F06061	19.8	1.037	72.7	165.57	102.7	1.44	3.28	2.03
F06062	5.4	1.096	147.8	418.28 #	262.5	0.80	2.26	1.42
F06063	23.7	1.032	66.3	156.43	92.4	1.57	3.71	2.19
Number of females	5	5	5	5	5	5	5	5
Mean	14.0	1.057	101.8	252.62	159.1	1.24	2.96	1.85
S.D.	7.7	0.025	34.5	105.54	68.9	0.41	0.74	0.49
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	TT	TT	TT	TT	TT	TT	TT	TT

S.G.: Specific gravity

#: The specimen was diluted to two folds with distilled water.

Significantly different from the control group (*: P<0.05, **: P<0.01).

NS: Not significantly different from the control group.

TT: Analysis by Student's t-test.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 24-3-1. Urinalysis in female rats of the recovery period

Control (vehicle: corn oil)

Female No.	Quality									Urinary sediments				
	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen	Color	Turbidity	Red blood cells	White blood cells	Casts	Crystals	Epithelial cells
F05054	6.5	±	-	-	-	-	±	light yellow	-	-	-	-	±	-
F05055	7.0	-	-	-	-	-	±	light yellow	-	-	-	-	-	-
F05056	7.0	-	-	-	-	-	±	light yellow	-	-	-	-	-	-
F05057	6.5	-	-	-	-	-	±	light yellow	-	-	-	-	-	-
F05058	7.0	±	-	-	-	-	±	light yellow	-	-	-	-	±	-

Protein, -: negative; ±: 10≦and<30 mg/dL; +: 30≦and<100 mg/dL; 2+: 100≦and<300 mg/dL; 3+: 300≦and<600 mg/dL; 4+: 600 mg/dL≦
Glucose, -: negative; ±: 30≦and<70 mg/dL; +: 70≦and<150 mg/dL; 2+: 150≦and<300 mg/dL; 3+: 300≦and<1,000 mg/dL; 4+: 1,000 mg/dL≦
Ketone, -: negative; ±(5≦and<10 mg/dL; +: 10≦and<40 mg/dL; 2+: 40≦and<80 mg/dL; 3+: 80≦and<150 mg/dL; 4+: 150 mg/dL≦
Bilirubin, -: negative; +: 0.5≦and<2.0 mg/dL; 2+: 2.0≦and<6.0 mg/dL; 3+: 6.0≦and<10.0 mg/dL; 4+: 10.0 mg/dL≦
Occult blood, -: negative; ±: 0.03≦and<0.06 mg/dL; +: 0.06≦and<0.20 mg/dL; 2+: 0.20≦and<1.00 mg/dL; 3+: 1.00 mg/dL≦
Urobilinogen, ±: normal; +: 2.0≦and<4.0 mg/dL; 2+: 4.0≦and<8.0 mg/dL; 3+: 8.0≦and<12.0 mg/dL; 4+: 12.0 mg/dL≦
Turbidity, -: negative; ±: trace; +: slight; 2+: moderate; 3+: marked
Red Blood cells, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≧300/3 visual field
White Blood cells, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field, 2+: 100-299/3 visual field; 3+: ≧300/3 visual field
Casts, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≧300/3 visual field
Cristals, -: not observed; ±: a few; +: abundant
Epithelial cells, -: not observed; ±: a few; +: abundant

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 24-3-2. Urinalysis in female rats of the recovery period

HA 1000 mg/kg

Female No.	Quality									Urinary sediments				
	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen	Color	Turbidity	Red blood cells	White blood cells	Casts	Crystals	Epithelial cells
F06064	6.5	+	-	-	-	-	±	light yellow	-	-	-	-	±	-
F06065	7.0	±	-	-	-	-	±	light yellow	-	-	-	-	±	-
F06066	7.5	-	-	-	-	-	±	light yellow	-	-	-	-	-	-
F06067	7.0	-	-	-	-	-	±	light yellow	-	-	-	-	±	-
F06068	7.0	+	-	-	-	-	±	light yellow	-	-	-	-	±	-

Protein, -: negative; ±: 10≦and<30 mg/dL; +: 30≦and<100 mg/dL; 2+: 100≦and<300 mg/dL; 3+: 300≦and<600 mg/dL; 4+: 600 mg/dL≦
Glucose, -: negative; ±: 30≦and<70 mg/dL; +: 70≦and<150 mg/dL; 2+: 150≦and<300 mg/dL; 3+: 300≦and<1,000 mg/dL; 4+: 1,000 mg/dL≦
Ketone, -: negative; ±(5≦and<10 mg/dL; +: 10≦and<40 mg/dL; 2+: 40≦and<80 mg/dL; 3+: 80≦and<150 mg/dL; 4+: 150 mg/dL≦
Bilirubin, -: negative; +: 0.5≦and<2.0 mg/dL; 2+: 2.0≦and<6.0 mg/dL; 3+: 6.0≦and<10.0 mg/dL; 4+: 10.0 mg/dL≦
Occult blood, -: negative; ±: 0.03≦and<0.06 mg/dL; +: 0.06≦and<0.20 mg/dL; 2+: 0.20≦and<1.00 mg/dL; 3+: 1.00 mg/dL≦
Urobilinogen, ±: normal; +: 2.0≦and<4.0 mg/dL; 2+: 4.0≦and<8.0 mg/dL; 3+: 8.0≦and<12.0 mg/dL; 4+: 12.0 mg/dL≦
Turbidity, -: negative; ±: trace; +: slight; 2+: moderate; 3+: marked
Red Blood cells, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≧300/3 visual field
White Blood cells, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field, 2+: 100-299/3 visual field; 3+: ≧300/3 visual field
Casts, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≧300/3 visual field
Cristals, -: not observed; ±: a few; +: abundant
Epithelial cells, -: not observed; ±: a few; +: abundant

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 24-4-1. Urinalysis in female rats of the recovery period

Control (vehicle: corn oil)

Female No.	Urine volume	S.G.	Electrolyte, density			Electrolyte, gross volume		
			Na	K	Cl	Na	K	Cl
	mL/24hr		mEq/L	mEq/L	mEq/L	mEq/24hr	mEq/24hr	mEq/24hr
F05054	16.3	1.047	113.3	183.33	113.6	1.85	2.99	1.85
F05055	28.5	1.031	67.7	136.99	83.8	1.93	3.90	2.39
F05056	11.8	1.054	123.4	225.56	141.5	1.46	2.66	1.67
F05057	21.7	1.035	91.0	160.28	113.5	1.97	3.48	2.46
F05058	7.7	1.053	95.0	201.55	119.6	0.73	1.55	0.92
Number of females	5	5	5	5	5	5	5	5
Mean	17.2	1.044	98.1	181.54	114.4	1.59	2.92	1.86
S.D.	8.2	0.010	21.5	34.56	20.6	0.52	0.90	0.62

S.G.: Specific gravity

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 24-4-2. Urinalysis in female rats of the recovery period

HA 1000 mg/kg

Female No.	Urine volume	S.G.	Electrolyte, density			Electrolyte, gross volume		
			Na	K	Cl	Na	K	Cl
	mL/24hr		mEq/L	mEq/L	mEq/L	mEq/24hr	mEq/24hr	mEq/24hr
F06064	14.2	1.046	112.3	197.91	141.3	1.59	2.81	2.01
F06065	13.0	1.063	150.1	286.99	205.1	1.95	3.73	2.67
F06066	23.7	1.042	100.4	194.24	128.6	2.38	4.60	3.05
F06067	17.1	1.044	104.6	203.15	135.2	1.79	3.47	2.31
F06068	14.3	1.061	169.8	288.62	206.8	2.43	4.13	2.96
Number of females	5	5	5	5	5	5	5	5
Mean	16.5	1.051	127.4	234.18	163.4	2.03	3.75	2.60
S.D.	4.3	0.010	30.8	49.06	39.1	0.37	0.68	0.44
Significance	NS	NS	NS	NS	*	NS	NS	NS
Statistical method	TT	TT	TT	TT	TT	TT	TT	TT

S.G.: Specific gravity

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
TT: Analysis by Student's t-test.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 25-1-1. Hematological findings of male rats at the end of the dosing period

Control (vehicle: corn oil)

Male No.	RBC	HGB	Hematocrit	MCV	MCH	MCHC	Platelet	PT	APTT	WBC	Neutrophil	Eosinophil	Basophil	Monocyte	Lymphocyte	Reticulocyte
	10000/μL	g/dL	%	fL	pg	g/dL	10000/μL	sec.	sec.	100/μL	%	%	%	%	%	%
M01001	749	13.6	40.4	53.9	18.2	33.7	92.9	16.3	19.5	82.5	13.4	1.2	0.1	4.8	80.5	3.05
M01002	874	15.0	44.0	50.3	17.2	34.1	107.1	15.3	20.5	69.6	12.4	2.3	0.0	4.0	81.3	2.69
M01003	738	13.8	40.4	54.7	18.7	34.2	86.7	13.9	16.8	59.7	20.1	2.3	0.0	6.4	71.2	3.56
M01004	812	15.0	44.7	55.0	18.5	33.6	81.2	17.4	17.9	89.8	25.3	2.9	0.0	4.9	66.9	3.27
M01005	817	16.2	46.4	56.8	19.8	34.9	75.6	19.9	20.0	40.9	21.1	3.2	0.0	4.6	71.1	3.28
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	798	14.7	43.2	54.1	18.5	34.1	88.7	16.6	18.9	68.5	18.5	2.4	0.0	4.9	74.2	3.17
S.D.	56	1.1	2.7	2.4	0.9	0.5	12.1	2.3	1.5	19.3	5.4	0.8	0.0	0.9	6.4	0.32

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 25-1-2. Hematological findings of male rats at the end of the dosing period

HA 100 mg/kg

Male No.	RBC 10000/μL	HGB g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelet 10000/μL	PT sec.	APTT sec.	WBC 100/μL	Neutrophil %	Eosinophil %	Basophil %	Monocyte %	Lymphocyte %	Reticulocyte %
M02013	837	14.7	42.2	50.4	17.6	34.8	96.6	15.7	20.3	84.2	13.8	1.0	0.0	3.8	81.4	2.40
M02014	816	14.8	44.5	54.5	18.1	33.3	98.9	23.7	28.0	83.0	27.0	1.7	0.0	4.3	67.0	3.11
M02015	777	14.6	42.3	54.4	18.8	34.5	95.8	19.3	20.9	70.3	16.0	1.6	0.0	4.3	78.1	2.86
M02016	748	13.1	39.4	52.7	17.5	33.2	91.1	14.9	17.0	59.6	19.4	2.0	0.0	4.4	74.2	3.27
M02017	759	14.6	43.9	57.8	19.2	33.3	84.1	27.6	31.3	153.5	42.5	0.9	0.1	1.3	55.2	3.86
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	787	14.4	42.5	54.0	18.2	33.8	93.3	20.2	23.5	90.1	23.7	1.4	0.0	3.6	71.2	3.10
S.D.	38	0.7	2.0	2.7	0.7	0.8	5.9	5.4	5.9	36.8	11.6	0.5	0.0	1.3	10.4	0.54
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN	KW	AN	AN	DU	AN	AN	AN	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).
KW: Analysis by Kruskal-Wallis' test (one-way layout).
DU: Analysis by Dunnett's test.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 25-1-3. Hematological findings of male rats at the end of the dosing period

HA 300 mg/kg

Male No.	RBC 10000/μL	HGB g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelet 10000/μL	PT sec.	APTT sec.	WBC 100/μL	Neutrophil %	Eosinophil %	Basophil %	Monocyte %	Lymphocyte %	Reticulocyte %
M03026	805	14.4	42.3	52.5	17.9	34.0	92.8	19.4	22.4	89.3	15.5	1.0	0.0	3.4	80.1	3.54
M03027	804	14.2	40.7	50.6	17.7	34.9	95.7	16.9	19.4	61.6	18.5	2.3	0.0	5.7	73.5	2.71
M03028	805	15.0	44.7	55.5	18.6	33.6	90.0	22.0	22.7	66.7	23.0	1.6	0.0	4.6	70.8	2.78
M03029	839	14.7	42.9	51.1	17.5	34.3	110.3	15.7	19.0	97.8	23.2	2.9	0.0	6.2	67.7	4.08
M03030	817	15.0	43.3	53.0	18.4	34.6	104.7	16.5	21.1	77.2	19.7	1.7	0.0	4.0	74.6	2.84
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	814	14.7	42.8	52.5	18.0	34.3	98.7	18.1	20.9	78.5	20.0	1.9	0.0	4.8	73.3	3.19
S.D.	15	0.4	1.5	1.9	0.5	0.5	8.5	2.6	1.7	15.1	3.2	0.7	0.0	1.2	4.6	0.60
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN	KW	AN	AN	DU	AN	AN	AN	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).
KW: Analysis by Kruskal-Wallis' test (one-way layout).
DU: Analysis by Dunnett's test.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 25-1-4. Hematological findings of male rats at the end of the dosing period

HA 1000 mg/kg

Male No.	RBC 10000/μL	HGB g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelet 10000/μL	PT sec.	APTT sec.	WBC 100/μL	Neutrophil %	Eosinophil %	Basophil %	Monocyte %	Lymphocyte %	Reticulocyte %
M04037	777	14.2	42.8	55.1	18.3	33.2	98.6	16.9	21.5	85.4	17.7	1.1	0.1	4.2	76.9	3.17
M04038	751	13.7	41.9	55.8	18.2	32.7	84.0	18.5	19.8	105.6	17.7	1.1	0.1	4.0	77.1	3.52
M04039	785	14.1	41.9	53.4	18.0	33.7	90.8	14.4	17.0	77.0	19.6	1.8	0.0	5.5	73.1	3.02
M04040	783	14.2	40.9	52.2	18.1	34.7	101.1	14.9	19.1	79.2	26.5	1.0	0.0	3.7	68.8	1.86
M04041	849	14.8	42.9	50.5	17.4	34.5	104.6	21.5	23.1	105.8	16.7	1.3	0.0	5.9	76.1	2.90
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	789	14.2	42.1	53.4	18.0	33.8	95.8	17.2	20.1	90.6	19.6	1.3	0.0	4.7	74.4	2.89
S.D.	36	0.4	0.8	2.2	0.4	0.8	8.3	2.9	2.3	14.1	4.0	0.3	0.1	1.0	3.5	0.62
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	*	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN	KW	AN	AN	DU	AN	AN	AN	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).
KW: Analysis by Kruskal-Wallis' test (one-way layout).
DU: Analysis by Dunnett's test.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 25-2-1. Hematological findings of male rats at the end of the recovery period

Control (vehicle: corn oil)

Male No.	RBC	HGB	Hematocrit	MCV	MCH	MCHC	Platelet	PT	APTT	WBC	Neutrophil	Eosinophil	Basophil	Monocyte	Lymphocyte	Reticulocyte
	10000/μL	g/dL	%	fL	pg	g/dL	10000/μL	sec.	sec.	100/μL	%	%	%	%	%	%
M01008	805	14.4	43.0	53.4	17.9	33.5	100.3	18.1	22.1	121.5	9.9	1.2	0.0	4.4	84.5	3.53
M01009	732	12.6	37.5	51.2	17.2	33.6	103.3	13.8	16.5	105.0	6.9	0.8	0.0	2.2	90.1	3.50
M01010	782	13.9	41.0	52.4	17.8	33.9	110.5	13.7	16.8	85.3	10.7	1.3	0.0	2.8	85.2	3.40
M01011	769	13.9	41.4	53.8	18.1	33.6	72.6	16.6	17.4	67.0	21.2	1.8	0.0	4.2	72.8	3.24
M01012	761	12.8	38.2	50.2	16.8	33.5	102.0	13.6	12.2	61.5	24.9	1.8	0.0	2.6	70.7	4.18
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	770	13.5	40.2	52.2	17.6	33.6	97.7	15.2	17.0	88.1	14.7	1.4	0.0	3.2	80.7	3.57
S.D.	27	0.8	2.3	1.5	0.5	0.2	14.6	2.1	3.5	25.3	7.8	0.4	0.0	1.0	8.4	0.36

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 25-2-2. Hematological findings of male rats at the end of the recovery period

HA 1000 mg/kg

Male No.	RBC 10000/μL	HGB g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelet 10000/μL	PT sec.	APTT sec.	WBC 100/μL	Neutrophil %	Eosinophil %	Basophil %	Monocyte %	Lymphocyte %	Reticulocyte %
M04044	791	13.7	40.3	50.9	17.3	34.0	92.2	15.5	18.4	92.6	15.9	1.1	0.1	4.5	78.4	3.39
M04045	780	13.3	39.9	51.2	17.1	33.3	122.7	13.7	15.4	105.1	11.2	0.9	0.1	3.9	83.9	4.34
M04046	783	14.3	42.3	54.0	18.3	33.8	91.7	13.8	17.5	97.5	13.6	1.1	0.0	3.6	81.7	3.11
M04047	750	13.9	40.8	54.4	18.5	34.1	100.8	16.5	16.9	57.0	21.9	1.8	0.0	4.2	72.1	3.18
M04048	738	13.5	40.4	54.7	18.3	33.4	99.4	14.4	15.1	47.1	19.2	3.8	0.0	5.9	71.1	3.32
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	768	13.7	40.7	53.0	17.9	33.7	101.4	14.8	16.7	79.9	16.4	1.7	0.0	4.4	77.4	3.47
S.D.	23	0.4	0.9	1.8	0.6	0.4	12.6	1.2	1.4	26.0	4.3	1.2	0.1	0.9	5.7	0.50
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
TT: Analysis by Student's t-test.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 26-1-1. Hematological findings of female rats at the end of the dosing period

Control (vehicle: corn oil)

Female No.	RBC	HGB	Hematocrit	MCV	MCH	MCHC	Platelet	PT	APTT	WBC	Neutrophil	Eosinophil	Basophil	Monocyte	Lymphocyte	Reticulocyte
	10000/μL	g/dL	%	fL	pg	g/dL	10000/μL	sec.	sec.	100/μL	%	%	%	%	%	%
F01001	611	12.7	39.5	64.6	20.8	32.2	108.0	13.5	13.8	77.8	29.9	0.5	0.0	4.6	65.0	8.79
F01005	621	11.7	35.1	56.5	18.8	33.3	107.6	13.1	14.9	87.0	28.5	0.7	0.0	1.6	69.2	7.49
F01008	643	12.8	37.8	58.8	19.9	33.9	96.5	14.0	14.6	80.8	22.6	1.5	0.0	4.2	71.7	8.42
F01010	584	11.7	36.1	61.8	20.0	32.4	98.6	12.7	14.4	115.0	33.6	0.9	0.0	3.2	62.3	9.63
F01011	628	12.5	38.4	61.1	19.9	32.6	122.0	14.1	15.1	101.9	20.5	0.5	0.0	2.6	76.4	7.80
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	617	12.3	37.4	60.6	19.9	32.9	106.5	13.5	14.6	92.5	27.0	0.8	0.0	3.2	68.9	8.43
S.D.	22	0.5	1.8	3.1	0.7	0.7	10.1	0.6	0.5	15.6	5.4	0.4	0.0	1.2	5.5	0.84

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 26-1-2. Hematological findings of female rats at the end of the dosing period

HA 100 mg/kg

Female No.	RBC 10000/μL	HGB g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelet 10000/μL	PT sec.	APTT sec.	WBC 100/μL	Neutrophil %	Eosinophil %	Basophil %	Monocyte %	Lymphocyte %	Reticulocyte %
F02016	624	11.8	35.5	56.9	18.9	33.2	102.1	13.9	15.6	87.4	32.6	1.0	0.0	3.9	62.5	8.95
F02019	711	13.3	41.1	57.8	18.7	32.4	93.8	15.2	14.6	154.3	37.9	0.5	0.1	3.6	57.9	8.49
F02021	620	12.1	37.4	60.3	19.5	32.4	101.5	12.9	13.9	70.1	26.3	1.7	0.0	2.4	69.6	6.99
F02022	627	12.2	36.9	58.9	19.5	33.1	88.1	12.9	14.1	102.0	44.8	0.4	0.0	3.6	51.2	5.87
F02023	579	11.6	36.1	62.3	20.0	32.1	107.1	13.2	16.4	89.0	35.6	0.7	0.0	3.1	60.6	9.42
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	632	12.2	37.4	59.2	19.3	32.6	98.5	13.6	14.9	100.6	35.4	0.9	0.0	3.3	60.4	7.94
S.D.	48	0.7	2.2	2.1	0.5	0.5	7.5	1.0	1.1	32.1	6.8	0.5	0.0	0.6	6.7	1.47
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 26-1-3. Hematological findings of female rats at the end of the dosing period

HA 300 mg/kg

Female No.	RBC 10000/μL	HGB g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelet 10000/μL	PT sec.	APTT sec.	WBC 100/μL	Neutrophil %	Eosinophil %	Basophil %	Monocyte %	Lymphocyte %	Reticulocyte %
F03026	641	12.3	37.3	58.2	19.2	33.0	92.0	13.5	16.2	86.1	52.4	1.5	0.0	5.6	40.5	6.86
F03028	599	12.6	39.3	65.6	21.0	32.1	100.8	13.4	14.8	69.0	31.3	0.9	0.0	4.5	63.3	8.99
F03029	628	11.6	35.0	55.7	18.5	33.1	97.7	13.0	15.5	51.1	21.1	1.2	0.0	4.9	72.8	6.52
F03030	642	12.9	39.0	60.7	20.1	33.1	109.2	14.2	15.7	101.2	25.4	0.7	0.0	4.1	69.8	6.97
F03036	587	11.7	36.7	62.5	19.9	31.9	90.4	12.6	18.9	80.9	52.2	0.4	0.0	5.4	42.0	9.47
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	619	12.2	37.5	60.5	19.7	32.6	98.0	13.3	16.2	77.7	36.5	0.9	0.0	4.9	57.7	7.76
S.D.	25	0.6	1.8	3.8	0.9	0.6	7.5	0.6	1.6	18.8	14.9	0.4	0.0	0.6	15.4	1.36
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 26-1-4. Hematological findings of female rats at the end of the dosing period

HA 1000 mg/kg

Female No.	RBC 10000/μL	HGB g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelet 10000/μL	PT sec.	APTT sec.	WBC 100/μL	Neutrophil %	Eosinophil %	Basophil %	Monocyte %	Lymphocyte %	Reticulocyte %
F04037	614	11.8	36.1	58.8	19.2	32.7	123.6	12.5	15.3	116.4	42.6	0.4	0.0	4.2	52.8	9.27
F04038	693	13.4	39.6	57.1	19.3	33.8	126.2	13.3	15.0	103.0	33.4	0.8	0.0	3.3	62.5	7.11
F04042	656	12.8	39.2	59.8	19.5	32.7	124.6	12.7	11.9	81.3	34.5	0.4	0.0	4.6	60.5	5.58
F04044	642	12.5	37.8	58.9	19.5	33.1	72.2	13.4	15.4	83.2	48.2	1.0	0.0	6.9	43.9	6.79
F04045	679	12.9	39.4	58.0	19.0	32.7	109.0	13.6	18.2	132.2	27.6	0.5	0.0	3.0	68.9	7.59
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	657	12.7	38.4	58.5	19.3	33.0	111.1	13.1	15.2	103.2	37.3	0.6	0.0	4.4	57.7	7.27
S.D.	31	0.6	1.5	1.0	0.2	0.5	22.8	0.5	2.2	21.8	8.1	0.3	0.0	1.5	9.6	1.34
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 26-2-1. Hematological findings of female rats at the end of the dosing period, satellite group

Control (vehicle: corn oil)

Female No.	RBC	HGB	Hematocrit	MCV	MCH	MCHC	Platelet	PT	APTT	WBC	Neutrophil	Eosinophil	Basophil	Monocyte	Lymphocyte	Reticulocyte
	10000/μL	g/dL	%	fL	pg	g/dL	10000/μL	sec.	sec.	100/μL	%	%	%	%	%	%
F05049	698	13.4	39.1	56.0	19.2	34.3	95.6	12.8	12.8	82.4	8.8	1.1	0.1	2.3	87.7	3.41
F05050	687	13.1	39.3	57.2	19.1	33.3	90.7	12.0	13.0	59.0	8.3	1.9	0.0	2.2	87.6	3.85
F05051	674	12.5	38.0	56.4	18.5	32.9	91.8	13.3	17.9	52.6	12.0	1.7	0.0	3.6	82.7	3.78
F05052	714	13.8	40.1	56.2	19.3	34.4	94.3	12.0	15.9	43.2	14.1	2.3	0.0	3.0	80.6	2.75
F05053	697	13.3	39.2	56.2	19.1	33.9	94.2	11.9	14.9	61.2	21.2	1.6	0.0	4.2	73.0	3.35
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	694	13.2	39.1	56.4	19.0	33.8	93.3	12.4	14.9	59.7	12.9	1.7	0.0	3.1	82.3	3.43
S.D.	15	0.5	0.8	0.5	0.3	0.6	2.0	0.6	2.1	14.5	5.2	0.4	0.0	0.9	6.1	0.44

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 26-2-2. Hematological findings of female rats at the end of the dosing period, satellite group

HA 1000 mg/kg

Female No.	RBC	HGB	Hematocrit	MCV	MCH	MCHC	Platelet	PT	APTT	WBC	Neutrophil	Eosinophil	Basophil	Monocyte	Lymphocyte	Reticulocyte
	10000/μL	g/dL	%	fL	pg	g/dL	10000/μL	sec.	sec.	100/μL	%	%	%	%	%	%
F06059	684	13.3	39.5	57.7	19.4	33.7	67.8	13.4	14.6	76.9	13.4	1.8	0.1	4.6	80.1	3.41
F06060	710	12.8	39.6	55.8	18.0	32.3	74.9	13.5	15.4	37.0	11.3	1.4	0.0	3.8	83.5	3.80
F06061	673	12.6	37.3	55.4	18.7	33.8	86.8	11.9	11.4	72.0	16.7	1.0	0.0	1.9	80.4	3.96
F06062	628	12.4	37.3	59.4	19.7	33.2	92.5	13.1	20.4	32.5	11.1	2.2	0.0	1.8	84.9	3.14
F06063	645	12.3	36.4	56.4	19.1	33.8	101.3	12.7	13.8	41.6	23.5	2.9	0.0	2.4	71.2	3.97
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	668	12.7	38.0	56.9	19.0	33.4	84.7	12.9	15.1	52.0	15.2	1.9	0.0	2.9	80.0	3.66
S.D.	32	0.4	1.4	1.6	0.7	0.6	13.4	0.6	3.3	20.8	5.2	0.7	0.0	1.2	5.3	0.37
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	TT	TT	TT	AW	TT	TT	AW	TT	TT	TT	TT	TT	TT	TT	TT	TT

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
TT: Analysis by Student's t-test.
AW: Analysis by Aspin-Welch t-test.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 26-3-1. Hematological findings of female rats at the end of the recovery period

Control (vehicle: corn oil)

Female No.	RBC	HGB	Hematocrit	MCV	MCH	MCHC	Platelet	PT	APTT	WBC	Neutrophil	Eosinophil	Basophil	Monocyte	Lymphocyte	Reticulocyte
	10000/μL	g/dL	%	fL	pg	g/dL	10000/μL	sec.	sec.	100/μL	%	%	%	%	%	%
F05054	797	14.4	42.3	53.1	18.1	34.0	86.8	13.0	14.6	48.7	11.8	2.1	0.0	2.7	83.4	2.93
F05055	702	13.5	40.0	57.0	19.2	33.8	90.8	12.8	15.1	46.8	17.5	3.2	0.0	3.0	76.3	5.04
F05056	720	13.3	38.5	53.5	18.5	34.5	100.2	13.1	15.9	28.8	19.8	2.8	0.0	2.4	75.0	2.59
F05057	756	13.6	39.3	52.0	18.0	34.6	107.2	13.3	14.4	46.5	17.7	2.8	0.0	3.4	76.1	2.52
F05058	759	13.5	39.6	52.2	17.8	34.1	96.1	12.5	14.6	34.4	17.4	3.2	0.0	2.9	76.5	2.71
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	747	13.7	39.9	53.6	18.3	34.2	96.2	12.9	14.9	41.0	16.8	2.8	0.0	2.9	77.5	3.16
S.D.	37	0.4	1.4	2.0	0.6	0.3	8.0	0.3	0.6	8.9	3.0	0.4	0.0	0.4	3.4	1.06

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 26-3-2. Hematological findings of female rats at the end of the recovery period

HA 1000 mg/kg

Female No.	RBC 10000/μL	HGB g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelet 10000/μL	PT sec.	APTT sec.	WBC 100/μL	Neutrophil %	Eosinophil %	Basophil %	Monocyte %	Lymphocyte %	Reticulocyte %
F06064	727	13.4	39.7	54.6	18.4	33.8	92.2	13.3	15.1	28.1	18.5	1.8	0.0	2.8	76.9	3.06
F06065	693	12.8	37.9	54.7	18.5	33.8	100.1	12.9	15.2	42.8	22.4	1.9	0.0	2.6	73.1	2.76
F06066	716	13.3	40.4	56.4	18.6	32.9	94.1	13.0	17.1	27.9	21.8	2.2	0.0	3.2	72.8	4.42
F06067	742	13.3	39.4	53.1	17.9	33.8	102.3	12.9	14.0	41.3	18.1	2.7	0.0	3.4	75.8	2.39
F06068	736	13.9	40.3	54.8	18.9	34.5	88.1	12.6	16.7	31.5	15.8	1.9	0.0	2.9	79.4	3.87
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	723	13.3	39.5	54.7	18.5	33.8	95.4	12.9	15.6	34.3	19.3	2.1	0.0	3.0	75.6	3.30
S.D.	19	0.4	1.0	1.2	0.4	0.6	5.8	0.3	1.3	7.2	2.7	0.4	0.0	0.3	2.8	0.83
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	*	NS	NS	NS	NS
Statistical method	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
TT: Analysis by Student's t-test.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 27-1-1. Biochemical findings of male rats at the end of the dosing period

Control (vehicle: corn oil)

Male No.	Total protein g/dL	Albumin g/dL	A/G	Glucose mg/dL	Total cholesterol mg/dL	Triglyceride mg/dL	Phospholipid mg/dL	AST U/L	ALT U/L	γ-GTP U/L	LDH U/L	Bile acid μmol/L	BUN mg/dL	Creatinine mg/dL	Total bilirubin mg/dL	ALP U/L
M01001	4.8	3.2	2.00	136	39	26	67	61	26	0	66	7.4	10.8	0.24	0.10	473
M01002	4.7	3.3	2.36	151	51	49	91	52	29	0	77	8.9	12.8	0.22	0.07	611
M01003	4.6	3.3	2.54	111	39	40	73	51	25	0	76	13.6	12.7	0.27	0.08	723
M01004	4.5	3.1	2.21	105	41	51	76	50	20	0	64	10.3	9.8	0.22	0.08	489
M01005	4.7	3.2	2.13	120	44	41	83	45	21	0	102	7.1	14.7	0.17	0.08	784
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	4.7	3.2	2.25	125	43	41	78	52	24	0	77	9.5	12.2	0.22	0.08	616
S.D.	0.1	0.1	0.21	19	5	10	9	6	4	0	15	2.6	1.9	0.04	0.01	138

Control (vehicle: corn oil)

Male No.	Inorganic phosphorus mg/dL	Ca mg/dL	Na mEq/L	K mEq/L	Cl mEq/L
M01001	5.5	8.4	144.9	3.85	110.6
M01002	5.7	8.3	146.0	3.54	113.4
M01003	5.2	8.2	145.7	4.00	113.1 §
M01004	5.1	8.2	147.1	3.69	112.8
M01005	5.5	8.0	148.4	3.73	114.1
Number of males	5	5	5	5	5
Mean	5.4	8.2	146.4	3.76	112.8
S.D.	0.2	0.1	1.4	0.17	1.3

§: The re-measurement was carried out because the difference between two measured values exceeded the permissible limit. The re-measured values were employed as the data.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 27-1-2. Biochemical findings of male rats at the end of the dosing period

HA 100 mg/kg

Male No.	Total protein g/dL	Albumin g/dL	A/G	Glucose mg/dL	Total cholesterol mg/dL	Triglyceride mg/dL	Phospholipid mg/dL	AST U/L	ALT U/L	γ-GTP U/L	LDH U/L	Bile acid μmol/L	BUN mg/dL	Creatinine mg/dL	Total bilirubin mg/dL	ALP U/L
M02013	4.7	3.2	2.13	132	43	52	86	49	23	0	74	12.2	15.2	0.25	0.10	571
M02014	4.9	3.4	2.27	125	52	71	90	46	23	0	72	3.2	7.9	0.21	0.08	281
M02015	4.4	3.0	2.14	122	41	22	74	48	22	0	178	9.3	12.3	0.23	0.07	535
M02016	4.6	2.9	1.71	117	34	19	58	51	26	0	115	6.0	13.4	0.26	0.06	586
M02017	5.5	3.3	1.50	135	55	39	101	41	25	0	314	5.2	18.4	0.34	0.06	481
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	4.8	3.2	1.95	126	45	41	82	47	24	0	151	7.2	13.4	0.26	0.07	491
S.D.	0.4	0.2	0.33	7	9	22	16	4	2	0	101	3.6	3.9	0.05	0.02	124
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN	KW	AN	KW	KW	AN	AN	AN	AN

HA 100 mg/kg

Male No.	Inorganic phosphorus mg/dL	Ca mg/dL	Na mEq/L	K mEq/L	Cl mEq/L
M02013	5.7	8.3	146.2	3.73	112.1
M02014	5.5	8.6	147.0	3.82	112.1
M02015	5.2	8.2	145.8	4.12	113.0
M02016	5.0	8.2	147.2	3.58	113.8
M02017	5.8	8.8	143.9	4.15	112.0 §
Number of males	5	5	5	5	5
Mean	5.4	8.4	146.0	3.88	112.6
S.D.	0.3	0.3	1.3	0.25	0.8
Significance	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).
KW: Analysis by Kruskal-Wallis' test (one-way layout).
§: The re-measurement was carried out because the difference between two measured values exceeded the permissible limit. The re-measured values were employed as the data.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 27-1-3. Biochemical findings of male rats at the end of the dosing period

HA 300 mg/kg

Male No.	Total protein g/dL	Albumin g/dL	A/G	Glucose mg/dL	Total cholesterol mg/dL	Triglyceride mg/dL	Phospholipid mg/dL	AST U/L	ALT U/L	γ-GTP U/L	LDH U/L	Bile acid μmol/L	BUN mg/dL	Creatinine mg/dL	Total bilirubin mg/dL	ALP U/L
M03026	4.2	2.8	2.00	129	36	26	66	53	26	0	124	27.7	13.2	0.25	0.09	512
M03027	4.7	3.0	1.76	150	46	49	82	53	27	0	153	16.3	12.6	0.27	0.08	505
M03028	4.5	3.0	2.00	133	53	33	87	54	26	0	242	11.7	12.9	0.23	0.08	592
M03029	5.1	3.5	2.19	146	60	62	99	57	26	0	296	6.7	11.6	0.31	0.09	541
M03030	4.7	3.2	2.13	131	42	19	72	46	25	0	98	3.8	13.7	0.27	0.06	522
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	4.6	3.1	2.02	138	47	38	81	53	26	0	183	13.2	12.8	0.27	0.08	534
S.D.	0.3	0.3	0.17	10	9	18	13	4	1	0	83	9.4	0.8	0.03	0.01	35
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN	KW	AN	KW	KW	AN	AN	AN	AN

HA 300 mg/kg

Male No.	Inorganic phosphorus mg/dL	Ca mg/dL	Na mEq/L	K mEq/L	Cl mEq/L
M03026	6.6	7.8	145.9	3.77	112.8
M03027	5.6	8.2	146.5	3.55	112.4
M03028	5.1	8.1	146.4	3.93	114.6
M03029	5.6	8.8	146.2	3.80	110.8
M03030	4.8	8.1	144.4	3.71	111.0
Number of males	5	5	5	5	5
Mean	5.5	8.2	145.9	3.75	112.3
S.D.	0.7	0.4	0.9	0.14	1.5
Significance	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).
KW: Analysis by Kruskal-Wallis' test (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 27-1-4. Biochemical findings of male rats at the end of the dosing period

HA 1000 mg/kg

Male No.	Total protein g/dL	Albumin g/dL	A/G	Glucose mg/dL	Total cholesterol mg/dL	Triglyceride mg/dL	Phospholipid mg/dL	AST U/L	ALT U/L	γ-GTP U/L	LDH U/L	Bile acid μmol/L	BUN mg/dL	Creatinine mg/dL	Total bilirubin mg/dL	ALP U/L
M04037	4.4	3.0	2.14	117	39	27	64	45	21	0	151	7.5	11.2	0.31	0.06	405
M04038	5.5	3.5	1.75	119	56	52	102	59	26	0	313	25.4	11.3	0.27	0.07	475
M04039	4.8	3.2	2.00	108	52	49	81	51	22	0	89	8.5	11.3	0.23	0.07	523
M04040	4.7	3.1	1.94	122	65	38	96	47	22	0	68	6.7	15.7	0.26	0.07	585
M04041	4.7	3.2	2.13	118	41	39	77	58	24	0	162	25.8	11	0.26	0.09	665
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	4.8	3.2	1.99	117	51	41	84	52	23	0	157	14.8	12.1	0.27	0.07	531
S.D.	0.4	0.2	0.16	5	11	10	15	6	2	0	96	9.9	2	0.03	0.01	100
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN	KW	AN	KW	KW	AN	AN	AN	AN

HA 1000 mg/kg

Male No.	Inorganic phosphorus mg/dL	Ca mg/dL	Na mEq/L	K mEq/L	Cl mEq/L
M04037	5.1	7.9	148.2	3.53 §	114.4
M04038	5.3	8.8	145.9	4.10	111.2
M04039	5.5	8.4	145.2	3.76	111.9
M04040	5.7	8.2	146.4	3.58	112.9
M04041	5.5	8.3	145.6	3.76	112.5
Number of males	5	5	5	5	5
Mean	5.4	8.3	146.3	3.75	112.6
S.D.	0.2	0.3	1.2	0.22	1.2
Significance	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).
KW: Analysis by Kruskal-Wallis' test (one-way layout).
§: The re-measurement was carried out because the difference between two measured values exceeded the permissible limit. The re-measured values were employed as the data.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 27-2-1. Biochemical findings of male rats at the end of the recovery period

Control (vehicle: corn oil)

Male No.	Total protein g/dL	Albumin g/dL	A/G	Glucose mg/dL	Total cholesterol mg/dL	Triglyceride mg/dL	Phospholipid mg/dL	AST U/L	ALT U/L	γ-GTP U/L	LDH U/L	Bile acid μmol/L	BUN mg/dL	Creatinine mg/dL	Total bilirubin mg/dL	ALP U/L
M01008	5.6	3.7	1.95	130	46	100	82	46	24	0	50	9.8	14.1	0.33	0.06	304
M01009	5.2	3.3	1.74	158	43	44	72	55	23	0	97	17.5	14.3	0.26	0.07	409
M01010	5.7	3.6	1.71	134	70	30	96	57	22	0	170	6.6	16.1	0.36	0.06	420
M01011	5.0	3.3	1.94	129	44	20	66	66	30	0	73	32.5	17.8	0.33	0.07	416
M01012	5.3	3.5	1.94	156	48	39	76	62	27	0	122	8.9	14.2	0.29	0.05	399
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	5.4	3.5	1.86	141	50	47	78	57	25	0	102	15.1	15.3	0.31	0.06	390
S.D.	0.3	0.2	0.12	14	11	31	11	8	3	0	46	10.6	1.6	0.04	0.01	49

Control (vehicle: corn oil)

Male No.	Inorganic phosphorus mg/dL	Ca mg/dL	Na mEq/L	K mEq/L	Cl mEq/L
M01008	6.6	9.4	142.4	3.94	108.4
M01009	6.7	9.2	144.6	3.45	112.9
M01010	5.4	9.1	144.5	3.85	113.1
M01011	6.1	8.6	143.1	3.59	110.1
M01012	4.8	8.8	145.4	3.56	111.6
Number of males	5	5	5	5	5
Mean	5.9	9.0	144.0	3.68	111.2
S.D.	0.8	0.3	1.2	0.21	2.0

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 27-2-2. Biochemical findings of male rats at the end of the recovery period

HA 1000 mg/kg

Male No.	Total protein g/dL	Albumin g/dL	A/G	Glucose mg/dL	Total cholesterol mg/dL	Triglyceride mg/dL	Phospholipid mg/dL	AST U/L	ALT U/L	γ-GTP U/L	LDH U/L	Bile acid μmol/L	BUN mg/dL	Creatinine mg/dL	Total bilirubin mg/dL	ALP U/L
M04044	5.9	3.7	1.68	142	59	26	83	54	22	0	72	15.0	12.7	0.33	0.07	455
M04045	5.7	3.5	1.59	160	64	40	90	76	35	0	161	9.6	14.1	0.30	0.06	383
M04046	5.2	3.3	1.74	140	69	37	98	55	57	0	102	7.6	15.1	0.38	0.06	362
M04047	5.5	3.6	1.89	129	53	37	81	59	24	0	70	14.5	12.5	0.30	0.05	513
M04048	5.3	3.4	1.79	128	43	17	67	66	29	0	135	8.1	15.9	0.30	0.06	501
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	5.5	3.5	1.74	140	58	31	84	62	33	0	108	11.0	14.1	0.32	0.06	443
S.D.	0.3	0.2	0.11	13	10	10	12	9	14	0	40	3.5	1.5	0.03	0.01	68
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	TT	TT	TT	TT	TT	AW	TT	TT	AW	TT	TT	TT	TT	TT	TT	TT

HA 1000 mg/kg

Male No.	Inorganic phosphorus mg/dL	Ca mg/dL	Na mEq/L	K mEq/L	Cl mEq/L
M04044	5.9	9.3	142.2	3.92	110.0
M04045	6.7	9.3	144.2	3.64	109.7
M04046	5.7	8.8	144.0	3.48	110.5
M04047	5.7	9.1	145.3	3.70	113.3
M04048	5.1	8.7	146.0	3.27	112.4 §
Number of males	5	5	5	5	5
Mean	5.8	9.0	144.3	3.60	111.2
S.D.	0.6	0.3	1.4	0.24	1.6
Significance	NS	NS	NS	NS	NS
Statistical method	TT	TT	TT	TT	TT

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
TT: Analysis by Student's t-test.
AW: Analysis by Aspin-Welch t-test.
§: The re-measurement was carried out because the difference between two measured values exceeded the permissible limit. The re-measured values were employed as the data.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 28-1-1. Biochemical findings of female rats at the end of the dosing period

Control (vehicle: corn oil)

Female No.	Total protein g/dL	Albumin g/dL	A/G	Glucose mg/dL	Total cholesterol mg/dL	Triglyceride mg/dL	Phospholipid mg/dL	AST U/L	ALT U/L	γ-GTP U/L	LDH U/L	Bile acid μmol/L	BUN mg/dL	Creatinine mg/dL	Total bilirubin mg/dL	ALP U/L
F01001	5.7	3.9	2.17	128	42	45	88	57	38	0	77	10.2	11.8	0.31	0.05	164
F01005	5.6	3.7	1.95	129	56	23	100	67	34	0	63	57.0	13.4	0.31	0.06	218
F01008	5.3	3.7	2.31	117	38	16	73	63	30	0	39	4.9	11.2	0.31	0.05	272
F01010	5.3	3.6	2.12	118	51	13	90	74	37	0	87	10.5	10.0	0.34	0.06	231
F01011	5.3	3.7	2.31	118	45	33	92	66	37	0	111	25.5	11.5	0.34	0.07	363
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	5.4	3.7	2.17	122	46	26	89	65	35	0	75	21.6	11.6	0.32	0.06	250
S.D.	0.2	0.1	0.15	6	7	13	10	6	3	0	27	21.2	1.2	0.02	0.01	74

Control (vehicle: corn oil)

Female No.	Inorganic phosphorus mg/dL	Ca mg/dL	Na mEq/L	K mEq/L	Cl mEq/L
F01001	5.5	9.2	144.2	3.57	113.1
F01005	8.0	9.3	144.2	3.70	110.3
F01008	5.0	9.0	141.9	4.00	113.3
F01010	5.9	8.8	142.7	3.66	114.0
F01011	5.8	8.8	141.5	3.46	109.4
Number of females	5	5	5	5	5
Mean	6.0	9.0	142.9	3.68	112.0
S.D.	1.2	0.2	1.3	0.20	2.0

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 28-1-2. Biochemical findings of female rats at the end of the dosing period

HA 100 mg/kg

Female No.	Total protein g/dL	Albumin g/dL	A/G	Glucose mg/dL	Total cholesterol mg/dL	Triglyceride mg/dL	Phospholipid mg/dL	AST U/L	ALT U/L	γ-GTP U/L	LDH U/L	Bile acid μmol/L	BUN mg/dL	Creatinine mg/dL	Total bilirubin mg/dL	ALP U/L
F02016	5.2	3.6	2.25	129	41	50	84	60	38	1	32	8.9	12.1	0.29	0.07	212
F02019	5.2	3.5	2.06	116	41	23	84	123	54	0	149	15.4	14.6	0.36	0.07	349
F02021	5.8	3.9	2.05	127	54	23	106	179	49	0	127	9.5	13.8	0.37	0.06	194
F02022	5.5	3.7	2.06	134	58	24	103	74	42	0	172	10.1	14.8	0.44	0.05	237
F02023	5.9	3.9	1.95	112	44	33	88	80	37	0	105	10.9	11.9	0.31	0.07	236
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	5.5	3.7	2.07	124	48	31	93	103	44	0	117	11.0	13.4	0.35	0.06	246
S.D.	0.3	0.2	0.11	9	8	12	11	48	7	0	54	2.6	1.4	0.06	0.01	61
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	KW	AN	AN	AN	KW	AN	AN	AN	KW

HA 100 mg/kg

Female No.	Inorganic phosphorus mg/dL	Ca mg/dL	Na mEq/L	K mEq/L	Cl mEq/L
F02016	5.2	8.7	143.6	3.42	112.7
F02019	6.0	8.8	141.8	3.42	110.5
F02021	5.6	9.5	144.1	3.30	111.5
F02022	6.4	9.1	144.0	4.05	111.1
F02023	5.1	9.4	142.7	3.90	111.2
Number of females	5	5	5	5	5
Mean	5.7	9.1	143.2	3.62	111.4
S.D.	0.5	0.4	1.0	0.33	0.8
Significance	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	DU

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).
KW: Analysis by Kruskal-Wallis' test (one-way layout).
DU: Analysis by Dunnett's test.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 28-1-3. Biochemical findings of female rats at the end of the dosing period

HA 300 mg/kg

Female No.	Total protein g/dL	Albumin g/dL	A/G	Glucose mg/dL	Total cholesterol mg/dL	Triglyceride mg/dL	Phospholipid mg/dL	AST U/L	ALT U/L	γ-GTP U/L	LDH U/L	Bile acid μmol/L	BUN mg/dL	Creatinine mg/dL	Total bilirubin mg/dL	ALP U/L
F03026	5.6	3.7	1.95	115	35	15	78	112	53	0	262	4.3	10.1	0.37	0.04	250
F03028	5.5	3.7	2.06	113	44	21	78	63	37	0	123	12.7	10.7	0.31	0.05	271
F03029	5.7	3.8	2.00	110	52	37	100	66	38	0	170	9.7	13.7	0.32	0.03	324
F03030	5.5	3.9	2.44	113	41	18	84	84	36	0	95	12.9	13.2	0.31	0.08	197
F03036	5.8	4.0	2.22	131	43	25	94	135	54	0	229	13.9	14.0	0.37	0.05	272
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	5.6	3.8	2.13	116	43	23	87	92	44	0	176	10.7	12.3	0.34	0.05	263
S.D.	0.1	0.1	0.20	8	6	9	10	31	9	0	70	3.9	1.8	0.03	0.02	46
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	KW	AN	AN	AN	KW	AN	AN	AN	KW

HA 300 mg/kg

Female No.	Inorganic phosphorus mg/dL	Ca mg/dL	Na mEq/L	K mEq/L	Cl mEq/L
F03026	5.9	9.2	145.2	3.49	112.6
F03028	5.7	9.1	142.9	3.41	110.0
F03029	5.9	9.0	142.3	3.67	109.3
F03030	5.9	9.3	143.4	3.77	109.5
F03036	6.8	9.3	144.0	3.20	111.1 §
Number of females	5	5	5	5	5
Mean	6.0	9.2	143.6	3.51	110.5
S.D.	0.4	0.1	1.1	0.22	1.4
Significance	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	DU

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).
KW: Analysis by Kruskal-Wallis' test (one-way layout).
DU: Analysis by Dunnett's test.
§: The re-measurement was carried out because the difference between two measured values exceeded the permissible limit. The re-measured values were employed as the data.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 28-1-4. Biochemical findings of female rats at the end of the dosing period

HA 1000 mg/kg

Female No.	Total protein g/dL	Albumin g/dL	A/G	Glucose mg/dL	Total cholesterol mg/dL	Triglyceride mg/dL	Phospholipid mg/dL	AST U/L	ALT U/L	γ-GTP U/L	LDH U/L	Bile acid μmol/L	BUN mg/dL	Creatinine mg/dL	Total bilirubin mg/dL	ALP U/L
F04037	5.7	4.0	2.35	118	51	38	104	64	31	0	91	7.7	10.7	0.37	0.07	191
F04038	5.6	3.8	2.11	145	54	36	110	73	39	0	80	11.4	12.9	0.34	0.07	601
F04042	5.5	3.9	2.44	106	56	17	97	64	33	0	92	11.2	10.7	0.40	0.08	195
F04044	5.9	4.0	2.11	117	52	39	107	92	44	0	189	8.3	16.2	0.45	0.06	246
F04045	5.8	4.0	2.22	121	50	14	88	122	43	0	149	7.0	13.4	0.31	0.07	152
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	5.7	3.9	2.25	121	53	29	101	83	38	0	120	9.1	12.8	0.37	0.07	277
S.D.	0.2	0.1	0.15	14	2	12	9	25	6	0	47	2.0	2.3	0.05	0.01	184
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	KW	AN	AN	AN	KW	AN	AN	AN	KW

HA 1000 mg/kg

Female No.	Inorganic phosphorus mg/dL	Ca mg/dL	Na mEq/L	K mEq/L	Cl mEq/L
F04037	6.4	9.7	143.9	3.91	111.2
F04038	6.0	8.7	141.6	3.11	107.1
F04042	6.7	9.7	142.6	3.87	108.2
F04044	6.9	9.4	142.5	3.49 §	108.4
F04045	6.1	9.4	142.6	3.39 §	108.1
Number of females	5	5	5	5	5
Mean	6.4	9.4	142.6	3.55	108.6
S.D.	0.4	0.4	0.8	0.34	1.5
Significance	NS	NS	NS	NS	**
Statistical method	AN	AN	AN	AN	DU

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).
KW: Analysis by Kruskal-Wallis' test (one-way layout).
DU: Analysis by Dunnett's test.
§: The re-measurement was carried out because the difference between two measured values exceeded the permissible limit. The re-measured values were employed as the data.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 28-2-1. Biochemical findings of female rats at the end of the dosing period, satellite group

Control (vehicle: corn oil)

Female No.	Total protein g/dL	Albumin g/dL	A/G	Glucose mg/dL	Total cholesterol mg/dL	Triglyceride mg/dL	Phospholipid mg/dL	AST U/L	ALT U/L	γ-GTP U/L	LDH U/L	Bile acid μmol/L	BUN mg/dL	Creatinine mg/dL	Total bilirubin mg/dL	ALP U/L
F05049	4.9	3.4	2.27	113	52	27	107	49	19	0	64	9.3	16.1	0.42	0.11	257
F05050	5.2	3.7	2.47	117	58	15	110	79	31	1	67	17.0	12.3	0.40	0.09	350
F05051	4.8	3.5	2.69	109	60	29	124	43	15	1	93	15.4	10.8	0.35	0.09	190
F05052	4.6	3.2	2.29	89	43	13	85	40	15	1	29	8.6	14.0	0.43	0.05	196
F05053	4.8	3.5	2.69	90	55	8	101	58	24	1	38	8.8	14.6	0.39	0.09	343
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	4.9	3.5	2.48	104	54	18	105	54	21	1	58	11.8	13.6	0.40	0.09	267
S.D.	0.2	0.2	0.21	13	7	9	14	16	7	0	25	4.0	2.1	0.03	0.02	77

Control (vehicle: corn oil)

Female No.	Inorganic phosphorus mg/dL	Ca mg/dL	Na mEq/L	K mEq/L	Cl mEq/L
F05049	4.4	8.1	144.3	3.60	112.6
F05050	4.3	8.2	144.7	3.57	113.3
F05051	3.9	7.4	146.6	3.20	114.6
F05052	3.4	7.5	145.6	3.66	114.7
F05053	3.8	7.9	145.5	3.55	113.9
Number of females	5	5	5	5	5
Mean	4.0	7.8	145.3	3.52	113.8
S.D.	0.4	0.4	0.9	0.18	0.9

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 28-2-2. Biochemical findings of female rats at the end of the dosing period, satellite group

HA 1000 mg/kg

Female No.	Total protein g/dL	Albumin g/dL	A/G	Glucose mg/dL	Total cholesterol mg/dL	Triglyceride mg/dL	Phospholipid mg/dL	AST U/L	ALT U/L	γ-GTP U/L	LDH U/L	Bile acid μmol/L	BUN mg/dL	Creatinine mg/dL	Total bilirubin mg/dL	ALP U/L
F06059	4.5	3.0	2.00	92	46	11	89	56	20	0	77	8.8	16.7	0.37	0.10	248
F06060	4.7	3.3	2.36	112	69	20	123	54	19	0	67	9.8	16.4	0.43	0.10	348
F06061	5.1	3.6	2.40	108	63	16	115	53	24	0	90	7.0	17.7	0.46	0.10	245
F06062	4.9	3.3	2.06	87	38	5	74	55	22	0	35	10.4	13.2	0.38	0.07	199
F06063	5.0	3.5	2.33	109	48	7	89	68	22	0	99	23.3	18.2	0.47	0.10	372
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	4.8	3.3	2.23	102	53	12	98	57	21	0	74	11.9	16.4	0.42	0.09	282
S.D.	0.2	0.2	0.19	11	13	6	20	6	2	0	25	6.5	2.0	0.05	0.01	74
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	**	NS	NS	NS	NS	NS	NS
Statistical method	TT	TT	TT	TT	TT	TT	TT	TT	AW	TT	TT	TT	TT	TT	TT	TT

HA 1000 mg/kg

Female No.	Inorganic phosphorus mg/dL	Ca mg/dL	Na mEq/L	K mEq/L	Cl mEq/L
F06059	4.4	7.9	145.7	3.56	115.3
F06060	4.2	7.9	145.6	3.66	112.5
F06061	4.0	8.0	145.1	3.63	113.0
F06062	4.6	8.1	145.3	3.92	112.3
F06063	4.2	7.9	146.3	3.50	113.9 §
Number of females	5	5	5	5	5
Mean	4.3	8.0	145.6	3.65	113.4
S.D.	0.2	0.1	0.5	0.16	1.2
Significance	NS	NS	NS	NS	NS
Statistical method	TT	AW	TT	TT	TT

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
TT: Analysis by Student's t-test.
AW: Analysis by Aspin-Welch t-test.
§: The re-measurement was carried out because the difference between two measured values exceeded the permissible limit. The re-measured values were employed as the data.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 28-3-1. Biochemical findings of female rats at the end of the recovery period

Control (vehicle: corn oil)

Female No.	Total protein g/dL	Albumin g/dL	A/G	Glucose mg/dL	Total cholesterol mg/dL	Triglyceride mg/dL	Phospholipid mg/dL	AST U/L	ALT U/L	γ-GTP U/L	LDH U/L	Bile acid μmol/L	BUN mg/dL	Creatinine mg/dL	Total bilirubin mg/dL	ALP U/L
F05054	5.1	3.4	2.00	101	61	14	107	52	19	0	49	7.3	18.2	0.40	0.07	200
F05055	5.9	3.9	1.95	132	92	52	156	96	40	0	89	17.3	17.5	0.45	0.08	191
F05056	5.9	4.4	2.93	131	80	20	138	73	25	0	119	9.0	21.9	0.54	0.08	213
F05057	5.7	4.0	2.35	104	58	18	105	58	22	0	43	14.0	18.4	0.40	0.10	148
F05058	6.0	4.0	2.00	105	81	9	127	61	25	0	105	10.2	24.3	0.52	0.08	255
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	5.7	3.9	2.25	115	74	23	127	68	26	0	81	11.6	20.1	0.46	0.08	201
S.D.	0.4	0.4	0.41	16	14	17	21	17	8	0	34	4.0	2.9	0.07	0.01	39

Control (vehicle: corn oil)

Female No.	Inorganic phosphorus mg/dL	Ca mg/dL	Na mEq/L	K mEq/L	Cl mEq/L
F05054	3.5	8.0	145.4	3.23	113.2
F05055	3.7	9.1	143.6	3.30	113.1
F05056	4.5	9.2	143.7	3.56	111.5
F05057	4.6	8.8	144.6	3.42	111.5
F05058	4.9	9.0	143.5	3.69	112.5
Number of females	5	5	5	5	5
Mean	4.2	8.8	144.2	3.44	112.4
S.D.	0.6	0.5	0.8	0.19	0.8

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 28-3-2. Biochemical findings of female rats at the end of the recovery period

HA 1000 mg/kg

Female No.	Total protein g/dL	Albumin g/dL	A/G	Glucose mg/dL	Total cholesterol mg/dL	Triglyceride mg/dL	Phospholipid mg/dL	AST U/L	ALT U/L	γ-GTP U/L	LDH U/L	Bile acid μmol/L	BUN mg/dL	Creatinine mg/dL	Total bilirubin mg/dL	ALP U/L
F06064	5.5	3.8	2.24	131	76	17	130	56	20	0	63	8.9	17.3	0.49	0.07	240
F06065	6.5	4.7	2.61	137	62	46	131	56	26	0	156	8.7	17.8	0.38	0.07	156
F06066	5.9	4.0	2.11	135	64	16	118	64	25	0	40	10.2	20.2	0.52	0.07	231
F06067	5.6	3.9	2.29	106	50	20	90	61	24	0	58	8.1	20.3	0.45	0.08	211
F06068	5.9	3.9	1.95	140	54	15	107	68	38	0	107	9.1	22.5	0.48	0.06	195
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	5.9	4.1	2.24	130	61	23	115	61	27	0	85	9.0	19.6	0.46	0.07	207
S.D.	0.4	0.4	0.25	14	10	13	17	5	7	0	47	0.8	2.1	0.05	0.01	33
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	TT	TT	TT	TT	TT	TT	TT	AW	TT	TT	TT	AW	TT	TT	TT	TT

HA 1000 mg/kg

Female No.	Inorganic phosphorus mg/dL	Ca mg/dL	Na mEq/L	K mEq/L	Cl mEq/L
F06064	3.5	8.6	144.5	3.10	113.9
F06065	3.3	9.7	144.0	3.45	112.2
F06066	3.2	8.8	143.7	3.34	113.4
F06067	4.1	8.8	143.9	3.13	111.8 §
F06068	3.8	8.9	143.8	3.11	113.8
Number of females	5	5	5	5	5
Mean	3.6	9.0	144.0	3.23	113.0
S.D.	0.4	0.4	0.3	0.16	1.0
Significance	NS	NS	NS	NS	NS
Statistical method	TT	TT	TT	TT	TT

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
TT: Analysis by Student's t-test.
AW: Analysis by Aspin-Welch t-test.
§: The re-measurement was carried out because the difference between two measured values exceeded the permissible limit. The re-measured values were employed as the data.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 29-1-1. Organ weights of male rats at the end of the dosing period

Control (vehicle: corn oil)

Male No.	Body weight (g)	Brain (mg)	Brain (mg/g)	Thymus (mg)	Thymus (mg/g)	Heart (mg)	Heart (mg/g)	Liver (mg)	Liver (mg/g)	Kidney (R) (mg)	Kidney (R) (mg/g)	Kidney (L) (mg)	Kidney (L) (mg/g)	Kidneys (mg)	Kidneys (mg/g)	Spleen (mg)	Spleen (mg/g)
M01001	504.1	2143.4	4.252	303.2	0.601	1543.9	3.063	13535.9	26.852	1796.7	3.564	1812.8	3.596	3609.5	7.160	990.6	1.965
M01002	449.1	2030.9	4.522	363.3	0.809	1430.4	3.185	12638.4	28.142	1475.4	3.285	1455.5	3.241	2930.9	6.526	709.1	1.579
M01003	533.7	2020.2	3.785	186.7	0.350	1537.5	2.881	13544.9	25.379	1641.0	3.075	1663.0	3.116	3304.0	6.191	807.4	1.513
M01004	505.7	2126.1	4.204	252.5	0.499	1580.0	3.124	12986.9	25.681	1715.3	3.392	1712.5	3.386	3427.8	6.778	912.3	1.804
M01005	449.4	2039.8	4.539	235.8	0.525	1331.6	2.963	12420.7	27.638	1510.5	3.361	1464.7	3.259	2975.2	6.620	715.7	1.593
M01006	462.7	2048.1	4.426	205.5	0.444	1374.7	2.971	11212.4	24.233	1475.9	3.190	1453.1	3.140	2929.0	6.330	721.0	1.558
M01007	568.6	2107.6	3.707	339.5	0.597	1450.8	2.552	17238.9	30.318	1772.7	3.118	1835.9	3.229	3608.6	6.346	782.5	1.376
Number of males	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7
Mean	496.2	2073.7	4.205	269.5	0.546	1464.1	2.963	13368.3	26.892	1626.8	3.284	1628.2	3.281	3255.0	6.564	805.5	1.627
S.D.	45.3	50.4	0.339	67.3	0.145	93.1	0.209	1882.6	2.028	139.9	0.171	169.7	0.164	308.9	0.328	108.5	0.196

Control (vehicle: corn oil)

Male No.	Testis (R) (mg)	Testis (R) (mg/g)	Testis (L) (mg)	Testis (L) (mg/g)	Testes (mg)	Testes (mg/g)	Epididymis (R) (mg)	Epididymis (R) (mg/g)	Epididymis (L) (mg)	Epididymis (L) (mg/g)	Epididymides (mg)	Epididymides (mg/g)
M01001	1581.3	3.137	1619.2	3.212	3200.5	6.349	538.7	1.069	521.2	1.034	1059.9	2.103
M01002	1786.7	3.978	1745.1	3.886	3531.8	7.864	584.1	1.301	587.6	1.308	1171.7	2.609
M01003	1565.1	2.933	1527.8	2.863	3092.9	5.795	584.8	1.096	576.9	1.081	1161.7	2.177
M01004	1746.3	3.453	1717.4	3.396	3463.7	6.849	681.8	1.348	686.0	1.357	1367.8	2.705
M01005	1895.2	4.217	1916.2	4.264	3811.4	8.481	693.9	1.544	675.9	1.504	1369.8	3.048
M01006	1740.9	3.762	1722.2	3.722	3463.1	7.485	668.3	1.444	619.7	1.339	1288.0	2.784
M01007	1626.6	2.861	1683.5	2.961	3310.1	5.821	625.5	1.100	640.2	1.126	1265.7	2.226
Number of males	7	7	7	7	7	7	7	7	7	7	7	7
Mean	1706.0	3.477	1704.5	3.472	3410.5	6.949	625.3	1.272	615.4	1.250	1240.7	2.522
S.D.	120.3	0.528	119.6	0.511	236.7	1.036	58.6	0.188	58.3	0.172	115.0	0.358

Control (vehicle: corn oil)

Male No.	Prostate, ventral (mg)	Prostate, ventral (mg/g)	Seminal vesicles (mg)	Seminal vesicles (mg/g)	Thyroid gland (mg)	Thyroid gland (mg/g)	Adrenal gland (R) (mg)	Adrenal gland (R) (mg/g)	Adrenal gland (L) (mg)	Adrenal gland (L) (mg/g)	Adrenal glands (mg)	Adrenal glands (mg/g)
M01001	663.7	1.317	1328.7	2.636	23.2	0.046	32.1	0.064	31.1	0.062	63.2	0.125
M01002	462.0	1.029	1015.7	2.262	21.4	0.048	21.6	0.048	21.6	0.048	43.2	0.096
M01003	637.0	1.194	1656.4	3.104	18.9	0.035	20.5	0.038	21.8	0.041	42.3	0.079
M01004	592.3	1.171	1577.8	3.120	26.7	0.053	28.5	0.056	25.9	0.051	54.4	0.108
M01005	621.2	1.382	1971.5	4.387	32.5	0.072	26.4	0.059	32.9	0.073	59.3	0.132
M01006	741.9	1.603	1930.6	4.172	25.8	0.056	24.5	0.053	26.6	0.057	51.1	0.110
M01007	618.6	1.088	1899.1	3.340	24.8	0.044	22.6	0.040	21.6	0.038	44.2	0.078
Number of males	7	7	7	7	7	7	7	7	7	7	7	7
Mean	619.5	1.255	1625.7	3.289	24.8	0.051	25.2	0.051	25.9	0.053	51.1	0.104
S.D.	84.5	0.196	353.8	0.767	4.3	0.012	4.1	0.010	4.7	0.012	8.3	0.021

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 29-1-2. Organ weights of male rats at the end of the dosing period

HA 100 mg/kg

Male No.	Body	Brain		Thymus		Heart		Liver		Kidney (R)		Kidney (L)		Kidneys		Spleen	
	weight (g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
M02013	523.1	2230.6	4.264	291.7	0.558	1567.9	2.997	13778.0	26.339	1569.5	3.000	1597.3	3.054	3166.8	6.054	760.4	1.454
M02014	549.9	2033.6	3.698	248.9	0.453	1393.9	2.535	15478.9	28.149	1796.4	3.267	1812.3	3.296	3608.7	6.562	736.4	1.339
M02015	460.5	1948.5	4.231	267.8	0.582	1571.5	3.413	11916.3	25.877	1461.9	3.175	1489.9	3.235	2951.8	6.410	688.4	1.495
M02016	499.6	1944.5	3.892	240.0	0.480	1524.9	3.052	13412.2	26.846	1650.5	3.304	1670.2	3.343	3320.7	6.647	1069.5	2.141
M02017	458.4	2017.2	4.401	299.3	0.653	1244.2	2.714	15472.1	33.752	1493.5	3.258	1396.3	3.046	2889.8	6.304	915.3	1.997
M02018	495.2	2001.0	4.041	207.8	0.420	1439.6	2.907	14404.8	29.089	1690.7	3.414	1660.3	3.353	3351.0	6.767	549.0	1.109
M02019	491.2	2041.2	4.156	291.7	0.594	1369.1	2.787	13229.6	26.933	1707.9	3.477	1649.6	3.358	3357.5	6.835	720.4	1.467
M02020	583.2	2066.7	3.544	354.6	0.608	1702.0	2.918	16916.8	29.007	1869.0	3.205	1886.3	3.234	3755.3	6.439	1024.5	1.757
M02021	474.9	1843.9	3.883	282.0	0.594	1200.0	2.527	11829.4	24.909	1547.5	3.259	1530.4	3.223	3077.9	6.481	686.9	1.446
M02022	439.7	2035.6	4.630	217.9	0.496	1252.8	2.849	10671.2	24.269	1428.5	3.249	1459.4	3.319	2887.9	6.568	587.6	1.336
M02023	468.6	2123.8	4.532	318.2	0.679	1433.1	3.058	12928.2	27.589	1919.1	4.095	1843.4	3.934	3762.5	8.029	744.5	1.589
M02024	468.7	2042.1	4.357	328.6	0.701	1371.2	2.926	12437.6	26.536	1569.1	3.348	1628.7	3.475	3197.8	6.823	573.5	1.224
Number of males	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
Mean	492.8	2027.4	4.136	279.0	0.568	1422.5	2.890	13539.6	27.441	1642.0	3.338	1635.3	3.323	3277.3	6.660	754.7	1.530
S.D.	41.5	95.4	0.333	44.5	0.090	150.4	0.242	1788.7	2.470	159.1	0.267	154.1	0.229	309.5	0.486	168.3	0.303
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN

HA 100 mg/kg

Male No.	Testis (R)		Testis (L)		Testes		Epididymis (R)		Epididymis (L)		Epididymides	
	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
M02013	1899.1	3.630	1933.1	3.695	3832.2	7.326	673.7	1.288	649.2	1.241	1322.9	2.529
M02014	1955.2	3.556	1945.7	3.538	3900.9	7.094	731.8	1.331	727.0	1.322	1458.8	2.653
M02015	1552.6	3.372	1578.1	3.427	3130.7	6.798	551.2	1.197	539.8	1.172	1091.0	2.369
M02016	1591.8	3.186	1618.0	3.239	3209.8	6.425	609.1	1.219	622.7	1.246	1231.8	2.466
M02017	1484.1	3.238	1534.8	3.348	3018.9	6.586	568.0	1.239	562.3	1.227	1130.3	2.466
M02018	1639.0	3.310	1671.4	3.375	3310.4	6.685	600.3	1.212	583.1	1.178	1183.4	2.390
M02019	1613.3	3.284	1593.7	3.245	3207.0	6.529	680.0	1.384	694.5	1.414	1374.5	2.798
M02020	1718.6	2.947	1579.1	2.708	3297.7	5.654	544.6	0.934	566.0	0.971	1110.6	1.904
M02021	1705.6	3.591	1672.2	3.521	3377.8	7.113	605.6	1.275	591.9	1.246	1197.5	2.522
M02022	1835.6	4.175	1791.8	4.075	3627.4	8.250	698.6	1.589	640.8	1.457	1339.4	3.046
M02023	2000.0	4.268	1978.6	4.222	3978.6	8.490	628.9	1.342	614.6	1.312	1243.5	2.654
M02024	1558.1	3.324	1518.0	3.239	3076.1	6.563	594.8	1.269	622.6	1.328	1217.4	2.597
Number of males	12	12	12	12	12	12	12	12	12	12	12	12
Mean	1712.8	3.490	1701.2	3.469	3414.0	6.959	623.9	1.273	617.9	1.260	1241.8	2.533
S.D.	171.4	0.390	167.9	0.399	335.3	0.784	59.9	0.150	54.9	0.126	112.5	0.273
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 29-1-2 (continued). Organ weights of male rats at the end of the dosing period

HA 100 mg/kg

Male No.	Prostate, ventral		Seminal vesicles		Thyroid gland		Adrenal gland (R)		Adrenal gland (L)		Adrenal glands	
	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
M02013	470.3	0.899	1591.8	3.043	21.0	0.040	28.6	0.055	35.2	0.067	63.8	0.122
M02014	489.4	0.890	2205.2	4.010	26.5	0.048	24.9	0.045	26.2	0.048	51.1	0.093
M02015	930.2	2.020	1815.9	3.943	22.8	0.050	20.9	0.045	22.5	0.049	43.4	0.094
M02016	808.1	1.617	1760.5	3.524	21.7	0.043	28.1	0.056	29.6	0.059	57.7	0.115
M02017	548.3	1.196	1643.0	3.584	20.7	0.045	24.4	0.053	26.9	0.059	51.3	0.112
M02018	935.6	1.889	1440.5	2.909	19.7	0.040	24.6	0.050	26.3	0.053	50.9	0.103
M02019	819.6	1.669	1725.9	3.514	31.6	0.064	22.6	0.046	22.0	0.045	44.6	0.091
M02020	495.5	0.850	1536.7	2.635	34.2	0.059	30.5	0.052	31.0	0.053	61.5	0.105
M02021	670.1	1.411	1910.6	4.023	15.5	0.033	27.4	0.058	26.6	0.056	54.0	0.114
M02022	621.8	1.414	1664.3	3.785	21.4	0.049	28.5	0.065	32.6	0.074	61.1	0.139
M02023	658.9	1.406	2068.9	4.415	28.0	0.060	24.1	0.051	27.0	0.058	51.1	0.109
M02024	728.4	1.554	1388.6	2.963	21.2	0.045	31.5	0.067	38.2	0.082	69.7	0.149
Number of males	12	12	12	12	12	12	12	12	12	12	12	12
Mean	681.4	1.401	1729.3	3.529	23.7	0.048	26.3	0.054	28.7	0.059	55.0	0.112
S.D.	165.6	0.384	243.1	0.543	5.4	0.009	3.2	0.007	4.9	0.011	7.9	0.018
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 29-1-3. Organ weights of male rats at the end of the dosing period

HA 300 mg/kg

Male No.	Body weight (g)	Brain (mg)	Brain (mg/g)	Thymus (mg)	Thymus (mg/g)	Heart (mg)	Heart (mg/g)	Liver (mg)	Liver (mg/g)	Kidney (R) (mg)	Kidney (R) (mg/g)	Kidney (L) (mg)	Kidney (L) (mg/g)	Kidneys (mg)	Kidneys (mg/g)	Spleen (mg)	Spleen (mg/g)
M03026	437.9	1966.6	4.491	226.9	0.518	1338.4	3.056	10712.8	24.464	1559.6	3.562	1482.3	3.385	3041.9	6.947	736.4	1.682
M03027	484.2	2129.9	4.399	262.9	0.543	1499.7	3.097	12901.4	26.645	1671.9	3.453	1705.7	3.523	3377.6	6.976	571.7	1.181
M03028	482.6	2047.7	4.243	225.5	0.467	1406.0	2.913	12220.4	25.322	1628.6	3.375	1695.2	3.513	3323.8	6.887	698.2	1.447
M03029	555.5	2126.7	3.828	410.2	0.738	1517.1	2.731	15038.6	27.072	1654.9	2.979	1703.8	3.067	3358.7	6.046	741.0	1.334
M03030	511.0	1961.0	3.838	267.0	0.523	1573.6	3.079	14962.1	29.280	1648.5	3.226	1637.8	3.205	3286.3	6.431	705.3	1.380
M03031	572.7	2042.7	3.567	359.9	0.628	1589.6	2.776	15994.6	27.928	1745.6	3.048	1684.7	2.942	3430.3	5.990	923.9	1.613
M03032	509.9	2222.1	4.358	194.2	0.381	1532.7	3.006	15377.3	30.157	1770.3	3.472	1791.0	3.512	3561.3	6.984	713.7	1.400
M03033	447.4	1949.4	4.357	258.9	0.579	1492.4	3.336	10692.9	23.900	1538.1	3.438	1545.4	3.454	3083.5	6.892	662.8	1.481
M03034	470.4	2039.0	4.335	132.4	0.281	1550.8	3.297	13265.7	28.201	1982.9	4.215	1888.7	4.015	3871.6	8.230	745.7	1.585
M03035	537.2	2096.3	3.902	197.3	0.367	1711.4	3.186	17804.4	33.143	2000.4	3.724	2016.8	3.754	4017.2	7.478	870.9	1.621
M03036	529.8	1983.5	3.744	344.7	0.651	1699.0	3.207	14171.6	26.749	1697.9	3.205	1674.5	3.161	3372.4	6.365	921.8	1.740
Number of males	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
Mean	503.5	2051.4	4.097	261.8	0.516	1537.3	3.062	13922.0	27.533	1718.1	3.427	1711.4	3.412	3429.5	6.839	753.8	1.497
S.D.	43.3	85.8	0.323	81.6	0.135	110.2	0.196	2212.9	2.667	151.7	0.342	148.0	0.310	295.1	0.643	109.5	0.168
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN

HA 300 mg/kg

Male No.	Testis (R) (mg)	Testis (R) (mg/g)	Testis (L) (mg)	Testis (L) (mg/g)	Testes (mg)	Testes (mg/g)	Epididymis (R) (mg)	Epididymis (R) (mg/g)	Epididymis (L) (mg)	Epididymis (L) (mg/g)	Epididymides (mg)	Epididymides (mg/g)
M03026	1460.6	3.335	1487.5	3.397	2948.1	6.732	509.5	1.164	551.2	1.259	1060.7	2.422
M03027	1744.7	3.603	1741.2	3.596	3485.9	7.199	658.9	1.361	644.2	1.330	1303.1	2.691
M03028	1709.3	3.542	1698.8	3.520	3408.1	7.062	596.4	1.236	583.0	1.208	1179.4	2.444
M03029	1614.2	2.906	1610.4	2.899	3224.6	5.805	596.9	1.075	612.9	1.103	1209.8	2.178
M03030	1666.6	3.261	1644.6	3.218	3311.2	6.480	666.0	1.303	620.0	1.213	1286.0	2.517
M03031	1781.1	3.110	1807.3	3.156	3588.4	6.266	715.8	1.250	686.7	1.199	1402.5	2.449
M03032	1856.2	3.640	1761.5	3.455	3617.7	7.095	579.5	1.136	510.5	1.001	1090.0	2.138
M03033	1960.4	4.382	1883.2	4.209	3843.6	8.591	631.6	1.412	615.8	1.376	1247.4	2.788
M03034	1833.1	3.897	1890.6	4.019	3723.7	7.916	652.1	1.386	645.8	1.373	1297.9	2.759
M03035	1931.3	3.595	1931.5	3.595	3862.8	7.191	677.7	1.262	675.6	1.258	1353.3	2.519
M03036	1600.1	3.020	1634.1	3.084	3234.2	6.105	659.5	1.245	647.5	1.222	1307.0	2.467
Number of males	11	11	11	11	11	11	11	11	11	11	11	11
Mean	1741.6	3.481	1735.5	3.468	3477.1	6.949	631.3	1.257	617.6	1.231	1248.8	2.488
S.D.	151.3	0.423	136.8	0.390	284.8	0.809	56.9	0.105	52.6	0.111	105.6	0.208
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 29-1-3 (continued). Organ weights of male rats at the end of the dosing period

HA 300 mg/kg

Male No.	Prostate, ventral		Seminal vesicles		Thyroid gland		Adrenal gland (R)		Adrenal gland (L)		Adrenal glands	
	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
M03026	633.5	1.447	1781.2	4.068	26.5	0.061	21.8	0.050	23.5	0.054	45.3	0.103
M03027	439.6	0.908	1555.3	3.212	29.3	0.061	34.6	0.071	35.7	0.074	70.3	0.145
M03028	543.9	1.127	1722.1	3.568	21.0	0.044	29.9	0.062	28.9	0.060	58.8	0.122
M03029	820.0	1.476	1818.7	3.274	20.5	0.037	21.9	0.039	26.4	0.048	48.3	0.087
M03030	575.9	1.127	2102.4	4.114	29.1	0.057	22.2	0.043	25.3	0.050	47.5	0.093
M03031	857.4	1.497	1944.1	3.395	32.3	0.056	23.5	0.041	26.1	0.046	49.6	0.087
M03032	455.8	0.894	1948.2	3.821	20.7	0.041	33.2	0.065	33.9	0.066	67.1	0.132
M03033	643.9	1.439	1966.5	4.395	28.0	0.063	21.9	0.049	23.4	0.052	45.3	0.101
M03034	981.1	2.086	1998.6	4.249	22.2	0.047	34.4	0.073	31.6	0.067	66.0	0.140
M03035	859.6	1.600	1732.7	3.225	20.6	0.038	33.5	0.062	38.0	0.071	71.5	0.133
M03036	591.7	1.117	1527.9	2.884	27.3	0.052	32.9	0.062	33.7	0.064	66.6	0.126
Number of males	11	11	11	11	11	11	11	11	11	11	11	11
Mean	672.9	1.338	1827.1	3.655	25.2	0.051	28.2	0.056	29.7	0.059	57.8	0.115
S.D.	179.5	0.348	184.0	0.501	4.3	0.010	5.8	0.012	5.1	0.010	10.7	0.022
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 29-1-4. Organ weights of male rats at the end of the dosing period

HA 1000 mg/kg

Male No.	Body	Brain		Thymus		Heart		Liver		Kidney (R)		Kidney (L)		Kidneys		Spleen	
	weight (g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
M04037	512.0	2073.1	4.049	384.5	0.751	1490.7	2.912	13463.2	26.295	1516.7	2.962	1555.6	3.038	3072.3	6.001	788.3	1.540
M04038	587.1	2264.6	3.857	447.0	0.761	1739.4	2.963	17618.0	30.009	1994.3	3.397	1897.4	3.232	3891.7	6.629	1043.2	1.777
M04039	532.9	2065.8	3.877	416.3	0.781	1621.5	3.043	14393.7	27.010	1778.0	3.336	1793.0	3.365	3571.0	6.701	802.1	1.505
M04040	484.8	1996.1	4.117	219.7	0.453	1272.4	2.625	13530.8	27.910	1364.0	2.814	1430.4	2.950	2794.4	5.764	732.3	1.511
M04041	463.2	2096.6	4.526	286.6	0.619	1425.0	3.076	11611.9	25.069	1496.4	3.231	1490.3	3.217	2986.7	6.448	681.7	1.472
M04042	560.6	2057.6	3.670	358.3	0.639	1717.5	3.064	15116.9	26.966	1698.6	3.030	1730.9	3.088	3429.5	6.118	806.4	1.438
M04043	437.4	2017.7	4.613	286.5	0.655	1120.0	2.561	10993.3	25.133	1619.4	3.702	1534.8	3.509	3154.2	7.211	729.2	1.667
Number of males	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7
Mean	511.1	2081.6	4.101	342.7	0.666	1483.8	2.892	13818.3	26.913	1638.2	3.210	1633.2	3.200	3271.4	6.410	797.6	1.559
S.D.	53.4	87.6	0.351	81.4	0.114	230.7	0.213	2217.8	1.710	208.3	0.301	174.2	0.194	378.9	0.491	117.5	0.120
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN

HA 1000 mg/kg

Male No.	Testis (R)		Testis (L)		Testes		Epididymis (R)		Epididymis (L)		Epididymides	
	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
M04037	1740.8	3.400	1759.3	3.436	3500.1	6.836	639.9	1.250	612.9	1.197	1252.8	2.447
M04038	1817.9	3.096	1879.8	3.202	3697.7	6.298	656.8	1.119	657.4	1.120	1314.2	2.238
M04039	1533.2	2.877	1552.0	2.912	3085.2	5.789	704.4	1.322	682.4	1.281	1386.8	2.602
M04040	1723.6	3.555	1702.1	3.511	3425.7	7.066	612.2	1.263	596.8	1.231	1209.0	2.494
M04041	1787.9	3.860	1726.6	3.728	3514.5	7.587	622.7	1.344	612.5	1.322	1235.2	2.667
M04042	1636.8	2.920	1631.1	2.910	3267.9	5.829	540.5	0.964	605.1	1.079	1145.6	2.044
M04043	1672.5	3.824	1663.9	3.804	3336.4	7.628	583.6	1.334	595.1	1.361	1178.7	2.695
Number of males	7	7	7	7	7	7	7	7	7	7	7	7
Mean	1701.8	3.362	1702.1	3.358	3403.9	6.719	622.9	1.228	623.2	1.227	1246.0	2.455
S.D.	97.0	0.409	103.7	0.363	197.0	0.769	52.5	0.140	33.4	0.103	82.3	0.239
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 29-1-4 (continued). Organ weights of male rats at the end of the dosing period

HA 1000 mg/kg

Male No.	Prostate, ventral		Seminal vesicles		Thyroid gland		Adrenal gland (R)		Adrenal gland (L)		Adrenal glands	
	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
M04037	741.1	1.447	1603.8	3.132	17.5	0.034	29.7	0.058	32.2	0.063	61.9	0.121
M04038	531.5	0.905	2042.8	3.479	33.4	0.057	32.5	0.055	31.9	0.054	64.4	0.110
M04039	677.3	1.271	1848.6	3.469	30.1	0.056	27.5	0.052	28.2	0.053	55.7	0.105
M04040	747.5	1.542	1827.3	3.769	23.3	0.048	22.9	0.047	27.5	0.057	50.4	0.104
M04041	770.6	1.664	1626.8	3.512	29.2	0.063	29.9	0.065	31.5	0.068	61.4	0.133
M04042	516.2	0.921	1953.2	3.484	28.7	0.051	28.7	0.051	29.7	0.053	58.4	0.104
M04043	715.6	1.636	1807.1	4.131	27.2	0.062	27.1	0.062	28.7	0.066	55.8	0.128
Number of males	7	7	7	7	7	7	7	7	7	7	7	7
Mean	671.4	1.341	1815.7	3.568	27.1	0.053	28.3	0.056	30.0	0.059	58.3	0.115
S.D.	105.0	0.320	159.4	0.310	5.2	0.010	3.0	0.006	1.9	0.006	4.7	0.012
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 29-2-1. Organ weights of male rats at the end of the recovery period

Control (vehicle: corn oil)

Male No.	Body weight (g)	Brain (mg)	Brain (mg/g)	Thymus (mg)	Thymus (mg/g)	Heart (mg)	Heart (mg/g)	Liver (mg)	Liver (mg/g)	Kidney (R) (mg)	Kidney (R) (mg/g)	Kidney (L) (mg)	Kidney (L) (mg/g)	Kidneys (mg)	Kidneys (mg/g)	Spleen (mg)	Spleen (mg/g)
M01008	526.9	1951.2	3.703	314.4	0.597	1457.8	2.767	15075.3	28.611	1685.7	3.199	1664.3	3.159	3350.0	6.358	727.1	1.380
M01009	514.2	2168.9	4.218	237.0	0.461	1546.5	3.008	14044.0	27.312	1648.5	3.206	1647.8	3.205	3296.3	6.411	883.1	1.717
M01010	517.8	2120.4	4.095	218.2	0.421	1556.3	3.006	12725.2	24.576	1533.0	2.961	1522.8	2.941	3055.8	5.902	828.1	1.599
M01011	533.7	2152.9	4.034	311.4	0.583	1433.2	2.685	12765.8	23.919	1826.1	3.422	1739.6	3.260	3565.7	6.681	759.9	1.424
M01012	511.6	2061.9	4.030	222.5	0.435	1506.7	2.945	13542.2	26.470	1613.2	3.153	1644.2	3.214	3257.4	6.367	721.3	1.410
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	520.8	2091.1	4.016	260.7	0.499	1500.1	2.882	13630.5	26.178	1661.3	3.188	1643.7	3.156	3305.0	6.344	783.9	1.506
S.D.	9.2	88.3	0.191	48.2	0.084	53.9	0.148	979.0	1.934	108.0	0.164	77.9	0.125	183.3	0.280	69.8	0.146

Control (vehicle: corn oil)

Male No.	Testis (R) (mg)	Testis (R) (mg/g)	Testis (L) (mg)	Testis (L) (mg/g)	Testes (mg)	Testes (mg/g)	Epididymis (R) (mg)	Epididymis (R) (mg/g)	Epididymis (L) (mg)	Epididymis (L) (mg/g)	Epididymides (mg)	Epididymides (mg/g)
M01008	1509.6	2.865	1443.0	2.739	2952.6	5.604	631.2	1.198	596.6	1.132	1227.8	2.330
M01009	1930.7	3.755	1869.5	3.636	3800.2	7.391	711.0	1.383	669.1	1.301	1380.1	2.684
M01010	1886.2	3.643	1881.2	3.633	3767.4	7.276	640.8	1.238	631.3	1.219	1272.1	2.457
M01011	1632.2	3.058	1610.8	3.018	3243.0	6.076	712.1	1.334	673.5	1.262	1385.6	2.596
M01012	1597.3	3.122	1641.8	3.209	3239.1	6.331	727.4	1.422	691.7	1.352	1419.1	2.774
Number of males	5	5	5	5	5	5	5	5	5	5	5	5
Mean	1711.2	3.289	1689.3	3.247	3400.5	6.536	684.5	1.315	652.4	1.253	1336.9	2.568
S.D.	186.2	0.388	186.0	0.391	369.4	0.775	44.9	0.095	38.2	0.084	82.3	0.177

Control (vehicle: corn oil)

Male No.	Prostate, ventral (mg)	Prostate, ventral (mg/g)	Seminal vesicles (mg)	Seminal vesicles (mg/g)	Thyroid gland (mg)	Thyroid gland (mg/g)	Adrenal gland (R) (mg)	Adrenal gland (R) (mg/g)	Adrenal gland (L) (mg)	Adrenal gland (L) (mg/g)	Adrenal glands (mg)	Adrenal glands (mg/g)
M01008	676.7	1.284	1695.5	3.218	30.0	0.057	23.9	0.045	24.2	0.046	48.1	0.091
M01009	690.4	1.343	1590.1	3.092	28.3	0.055	32.6	0.063	32.7	0.064	65.3	0.127
M01010	583.2	1.126	1885.0	3.640	33.2	0.064	23.1	0.045	23.5	0.045	46.6	0.090
M01011	548.2	1.027	1737.5	3.256	30.6	0.057	26.4	0.049	29.5	0.055	55.9	0.105
M01012	484.2	0.946	1468.1	2.870	18.0	0.035	24.6	0.048	26.7	0.052	51.3	0.100
Number of males	5	5	5	5	5	5	5	5	5	5	5	5
Mean	596.5	1.145	1675.2	3.215	28.0	0.054	26.1	0.050	27.3	0.052	53.4	0.103
S.D.	87.1	0.168	156.9	0.281	5.9	0.011	3.8	0.007	3.8	0.008	7.5	0.015

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 29-2-2. Organ weights of male rats at the end of the recovery period

HA 1000 mg/kg

Male No.	Body weight (g)	Brain (mg)	Brain (mg/g)	Thymus (mg)	Thymus (mg/g)	Heart (mg)	Heart (mg/g)	Liver (mg)	Liver (mg/g)	Kidney (R) (mg)	Kidney (R) (mg/g)	Kidney (L) (mg)	Kidney (L) (mg/g)	Kidneys (mg)	Kidneys (mg/g)	Spleen (mg)	Spleen (mg/g)
M04044	555.3	2053.1	3.697	293.3	0.528	1658.5	2.987	15382.6	27.701	1751.0	3.153	1773.0	3.193	3524.0	6.346	691.7	1.246
M04045	547.6	2112.6	3.858	190.6	0.348	1619.7	2.958	15194.3	27.747	1822.1	3.327	1880.7	3.434	3702.8	6.762	818.4	1.495
M04046	601.7	2007.6	3.337	309.3	0.514	1633.7	2.715	16847.5	28.000	1958.1	3.254	1955.7	3.250	3913.8	6.505	848.7	1.411
M04047	541.1	2189.0	4.045	228.7	0.423	1437.0	2.656	11756.4	21.727	1689.7	3.123	1613.2	2.981	3302.9	6.104	770.8	1.425
M04048	484.5	2130.7	4.398	214.9	0.444	1494.3	3.084	12170.6	25.120	1697.9	3.504	1625.4	3.355	3323.3	6.859	700.4	1.446
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	546.0	2098.6	3.867	247.4	0.451	1568.6	2.880	14270.3	26.059	1783.8	3.272	1769.6	3.243	3553.4	6.515	766.0	1.405
S.D.	41.8	70.3	0.395	51.4	0.073	97.2	0.185	2205.8	2.691	110.9	0.153	151.9	0.173	259.2	0.307	69.7	0.094
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AW	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT

HA 1000 mg/kg

Male No.	Testis (R) (mg)	Testis (R) (mg/g)	Testis (L) (mg)	Testis (L) (mg/g)	Testes (mg)	Testes (mg/g)	Epididymis (R) (mg)	Epididymis (R) (mg/g)	Epididymis (L) (mg)	Epididymis (L) (mg/g)	Epididymides (mg)	Epididymides (mg/g)
M04044	1896.7	3.416	2007.9	3.616	3904.6	7.032	716.0	1.289	712.4	1.283	1428.4	2.572
M04045	1810.1	3.306	1859.4	3.396	3669.5	6.701	692.8	1.265	692.2	1.264	1385.0	2.529
M04046	1833.8	3.048	1840.0	3.058	3673.8	6.106	794.3	1.320	724.9	1.205	1519.2	2.525
M04047	1945.6	3.596	1954.4	3.612	3900.0	7.208	755.4	1.396	692.4	1.280	1447.8	2.676
M04048	1758.7	3.630	1714.2	3.538	3472.9	7.168	710.1	1.466	678.7	1.401	1388.8	2.866
Number of males	5	5	5	5	5	5	5	5	5	5	5	5
Mean	1849.0	3.399	1875.2	3.444	3724.2	6.843	733.7	1.347	700.1	1.287	1433.8	2.634
S.D.	73.3	0.237	113.2	0.233	181.8	0.458	40.9	0.083	18.3	0.071	54.6	0.143
Significance	NS	NS	NS	NS	NS	NS	NS	NS	*	NS	NS	NS
Statistical method	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT

HA 1000 mg/kg

Male No.	Prostate, ventral (mg)	Prostate, ventral (mg/g)	Seminal vesicles (mg)	Seminal vesicles (mg/g)	Thyroid gland (mg)	Thyroid gland (mg/g)	Adrenal gland (R) (mg)	Adrenal gland (R) (mg/g)	Adrenal gland (L) (mg)	Adrenal gland (L) (mg/g)	Adrenal glands (mg)	Adrenal glands (mg/g)
M04044	458.5	0.826	1968.9	3.546	31.9	0.057	32.4	0.058	33.7	0.061	66.1	0.119
M04045	607.1	1.109	1813.1	3.311	19.8	0.036	34.4	0.063	30.1	0.055	64.5	0.118
M04046	618.5	1.028	1745.9	2.902	28.7	0.048	27.2	0.045	26.8	0.045	54.0	0.090
M04047	553.1	1.022	2074.4	3.834	30.7	0.057	29.2	0.054	31.2	0.058	60.4	0.112
M04048	664.0	1.370	1951.0	4.027	21.6	0.045	24.6	0.051	28.6	0.059	53.2	0.110
Number of males	5	5	5	5	5	5	5	5	5	5	5	5
Mean	580.2	1.071	1910.7	3.524	26.5	0.049	29.6	0.054	30.1	0.056	59.6	0.110
S.D.	78.7	0.197	130.9	0.442	5.5	0.009	3.9	0.007	2.6	0.006	5.9	0.012
Significance	NS	NS	*	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AW: Analysis by Aspin-Welch t-test.
TT: Analysis by Student's t-test.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 30-1-1. Organ weights of female rats at the end of the dosing period

Control (vehicle: corn oil)

Female No.	Body weight (g)	Brain (mg)	Brain (mg/g)	Thymus (mg)	Thymus (mg/g)	Heart (mg)	Heart (mg/g)	Liver (mg)	Liver (mg/g)	Kidney (R) (mg)	Kidney (R) (mg/g)	Kidney (L) (mg)	Kidney (L) (mg/g)	Kidneys (mg)	Kidneys (mg/g)	Spleen (mg)	Spleen (mg/g)
F01001	290.5	1920.4	6.611	267.0	0.919	950.1	3.271	9416.9	32.416	956.8	3.294	947.6	3.262	1904.4	6.556	604.3	2.080
F01002	290.2	1839.7	6.339	268.4	0.925	873.4	3.010	9779.3	33.698	954.4	3.289	925.3	3.188	1879.7	6.477	641.2	2.210
F01003	344.6 a	2012.6 a	5.840 a	224.5 a	0.651 a	998.1 a	2.896 a	11888.2 a	34.499 a	1019.8 a	2.959 a	979.5 a	2.842 a	1999.3 a	5.802 a	541.1 a	1.570 a
F01004	329.5	1871.8	5.681	193.6	0.588	1028.9	3.123	11314.5	34.338	1147.0	3.481	1141.8	3.465	2288.8	6.946	594.3	1.804
F01005	306.4	1942.2	6.339	194.0	0.633	988.8	3.227	10172.2	33.199	982.9	3.208	929.7	3.034	1912.6	6.242	673.1	2.197
F01006	313.9	1938.8	6.176	282.5	0.900	1034.7	3.296	9966.2	31.750	1045.9	3.332	1056.3	3.365	2102.2	6.697	662.8	2.112
F01007	294.3	1785.6	6.067	264.4	0.898	998.0	3.391	9802.8	33.309	982.1	3.337	979.6	3.329	1961.7	6.666	562.3	1.911
F01008	294.6	1907.5	6.475	267.0	0.906	946.8	3.214	9129.6	30.990	940.3	3.192	942.9	3.201	1883.2	6.392	598.3	2.031
F01009	309.3	1968.0	6.363	242.9	0.785	1163.7	3.762	11022.1	35.636	1137.4	3.677	1095.0	3.540	2232.4	7.218	871.0	2.816
F01010	278.2	1805.2	6.489	164.5	0.591	1015.7	3.651	8567.4	30.796	949.5	3.413	935.4	3.362	1884.9	6.775	709.0	2.549
F01011	341.1	1769.0	5.186	311.2	0.912	1058.1	3.102	9770.1	28.643	1031.5	3.024	1012.8	2.969	2044.3	5.993	617.0	1.809
F01012	289.4	1907.8	6.592	167.5	0.579	956.2	3.304	9854.8	34.053	1020.0	3.525	987.6	3.413	2007.6	6.937	723.3	2.499
Number of females	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
Mean	303.4	1877.8	6.211	238.5	0.785	1001.3	3.305	9890.5	32.621	1013.4	3.343	995.8	3.284	2009.3	6.627	659.7	2.183
S.D.	18.9	68.3	0.431	49.9	0.154	74.7	0.226	773.5	1.967	72.6	0.178	73.2	0.175	144.4	0.348	86.1	0.321

Control (vehicle: corn oil)

Female No.	Ovary (R) (mg)	Ovary (R) (mg/g)	Ovary (L) (mg)	Ovary (L) (mg/g)	Ovaries (mg)	Ovaries (mg/g)	Uterus (mg)	Uterus (mg/g)	Thyroid gland (mg)	Thyroid gland (mg/g)	Adrenal gland (R) (mg)	Adrenal gland (R) (mg/g)	Adrenal gland (L) (mg)	Adrenal gland (L) (mg/g)	Adrenal glands (mg)	Adrenal glands (mg/g)
F01001	43.3	0.149	54.2	0.187	97.5	0.336	592.8	2.041	22.5	0.077	32.4	0.112	30.4	0.105	62.8	0.216
F01002	50.8	0.175	58.4	0.201	109.2	0.376	550.0	1.895	15.7	0.054	37.2	0.128	41.3	0.142	78.5	0.271
F01003	55.0 a	0.160 a	51.3 a	0.149 a	106.3 a	0.308 a	556.3 a	1.614 a	23.2 a	0.067 a	28.1 a	0.082 a	32.4 a	0.094 a	60.5 a	0.176 a
F01004	51.8	0.157	47.0	0.143	98.8	0.300	624.8	1.896	16.5	0.050	34.4	0.104	37.4	0.114	71.8	0.218
F01005	58.5	0.191	57.7	0.188	116.2	0.379	727.6	2.375	24.2	0.079	33.3	0.109	31.2	0.102	64.5	0.211
F01006	46.9	0.149	51.1	0.163	98.0	0.312	562.1	1.791	13.4	0.043	34.4	0.110	36.9	0.118	71.3	0.227
F01007	56.3	0.191	50.2	0.171	106.5	0.362	653.4	2.220	23.1	0.078	30.7	0.104	31.1	0.106	61.8	0.210
F01008	54.6	0.185	57.6	0.196	112.2	0.381	725.9	2.464	17.3	0.059	31.2	0.106	32.3	0.110	63.5	0.216
F01009	66.0	0.213	65.3	0.211	131.3	0.425	735.2	2.377	22.4	0.072	36.4	0.118	41.1	0.133	77.5	0.251
F01010	67.2	0.242	44.0	0.158	111.2	0.400	697.7	2.508	23.0	0.083	36.1	0.130	41.0	0.147	77.1	0.277
F01011	62.0	0.182	37.6	0.110	99.6	0.292	689.9	2.023	19.7	0.058	36.1	0.106	44.4	0.130	80.5	0.236
F01012	51.9	0.179	50.0	0.173	101.9	0.352	531.1	1.835	19.7	0.068	37.0	0.128	38.3	0.132	75.3	0.260
Number of females	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
Mean	55.4	0.183	52.1	0.173	107.5	0.356	644.6	2.130	19.8	0.066	34.5	0.114	36.9	0.122	71.3	0.236
S.D.	7.6	0.028	7.7	0.029	10.2	0.042	76.4	0.267	3.6	0.013	2.3	0.010	4.9	0.016	7.0	0.025

a, Excluded from data analysis (not copulated).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 30-1-2. Organ weights of female rats at the end of the dosing period

HA 100 mg/kg

Female No.	Body weight (g)	Brain (mg)	Brain (mg/g)	Thymus (mg)	Thymus (mg/g)	Heart (mg)	Heart (mg/g)	Liver (mg)	Liver (mg/g)	Kidney (R) (mg)	Kidney (R) (mg/g)	Kidney (L) (mg)	Kidney (L) (mg/g)	Kidneys (mg)	Kidneys (mg/g)	Spleen (mg)	Spleen (mg/g)
F02013	299.7 b	1922.8 b	6.416 b	264.8 b	0.884 b	939.9 b	3.136 b	9918.7 b	33.095 b	982.0 b	3.277 b	973.8 b	3.249 b	1955.8 b	6.526 b	595.9 b	1.988 b
F02014	313.8	1956.1	6.234	176.4	0.562	1098.5	3.501	9870.2	31.454	1096.3	3.494	1145.5	3.650	2241.8	7.144	787.4	2.509
F02015	281.9	1999.5	7.093	304.4	1.080	1077.1	3.821	9767.5	34.649	963.8	3.419	985.9	3.497	1949.7	6.916	669.0	2.373
F02016	320.2	1916.9	5.987	229.9	0.718	934.2	2.918	10973.2	34.270	1005.2	3.139	955.1	2.983	1960.3	6.122	824.1	2.574
F02017	314.0	1897.2	6.042	246.3	0.784	960.1	3.058	9914.2	31.574	992.4	3.161	942.9	3.003	1935.3	6.163	910.0	2.898
F02018	310.9	2032.0	6.536	227.6	0.732	1210.0	3.892	11453.6	36.840	1030.0	3.313	1061.9	3.416	2091.9	6.729	722.3	2.323
F02019	272.5	1882.2	6.907	189.6	0.696	905.4	3.323	8985.8	32.975	850.0	3.119	852.4	3.128	1702.4	6.247	747.8	2.744
F02020	310.7	1874.4	6.033	143.4	0.462	1076.0	3.463	10595.2	34.101	1126.9	3.627	1043.6	3.359	2170.5	6.986	667.4	2.148
F02021	269.8	1845.7	6.841	195.0	0.723	1021.6	3.787	9552.9	35.407	899.5	3.334	857.7	3.179	1757.2	6.513	535.0	1.983
F02022	301.8	1930.9	6.398	176.4	0.584	996.7	3.303	10952.1	36.289	1136.4	3.765	1125.6	3.730	2262.0	7.495	659.0	2.184
F02023	301.2	1892.7	6.284	172.7	0.573	1010.2	3.354	9645.3	32.023	1009.0	3.350	957.4	3.179	1966.4	6.529	698.9	2.320
F02024	366.7 b	1982.3 b	5.406 b	262.1 b	0.715 b	982.6 b	2.680 b	11845.6 b	32.303 b	1202.6 b	3.280 b	1121.9 b	3.059 b	2324.5 b	6.339 b	582.8 b	1.589 b
Number of females	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
Mean	299.7	1922.8	6.436	206.2	0.691	1029.0	3.442	10171.0	33.958	1011.0	3.372	992.8	3.312	2003.8	6.684	722.1	2.406
S.D.	18.3	58.2	0.396	46.6	0.169	89.8	0.322	779.0	1.918	93.0	0.212	100.8	0.260	189.0	0.453	103.3	0.280
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN

HA 100 mg/kg

Female No.	Ovary (R) (mg)	Ovary (R) (mg/g)	Ovary (L) (mg)	Ovary (L) (mg/g)	Ovaries (mg)	Ovaries (mg/g)	Uterus (mg)	Uterus (mg/g)	Thyroid gland (mg)	Thyroid gland (mg/g)	Adrenal gland (R) (mg)	Adrenal gland (R) (mg/g)	Adrenal gland (L) (mg)	Adrenal gland (L) (mg/g)	Adrenal glands (mg)	Adrenal glands (mg/g)
F02013	43.7 b	0.146 b	43.9 b	0.146 b	87.6 b	0.292 b	989.7 b	3.302 b	22.1 b	0.074 b	34.3 b	0.114 b	35.0 b	0.117 b	69.3 b	0.231 b
F02014	53.1	0.169	56.4	0.180	109.5	0.349	677.0	2.157	19.0	0.061	43.7	0.139	47.3	0.151	91.0	0.290
F02015	62.3	0.221	46.7	0.166	109.0	0.387	788.4	2.797	17.5	0.062	31.6	0.112	33.9	0.120	65.5	0.232
F02016	59.2	0.185	61.8	0.193	121.0	0.378	677.4	2.116	16.8	0.052	43.9	0.137	45.1	0.141	89.0	0.278
F02017	53.5	0.170	48.4	0.154	101.9	0.325	523.7	1.668	16.9	0.054	25.3	0.081	29.8	0.095	55.1	0.175
F02018	69.2	0.223	66.9	0.215	136.1	0.438	737.9	2.373	18.9	0.061	42.8	0.138	46.0	0.148	88.8	0.286
F02019	55.5	0.204	40.7	0.149	96.2	0.353	498.1	1.828	17.1	0.063	40.0	0.147	41.2	0.151	81.2	0.298
F02020	59.2	0.191	53.3	0.172	112.5	0.362	803.6	2.586	25.9	0.083	33.8	0.109	32.5	0.105	66.3	0.213
F02021	62.5	0.232	37.8	0.140	100.3	0.372	654.6	2.426	22.7	0.084	38.6	0.143	39.4	0.146	78.0	0.289
F02022	61.4	0.203	46.1	0.153	107.5	0.356	520.9	1.726	25.9	0.086	42.0	0.139	49.2	0.163	91.2	0.302
F02023	52.9	0.176	62.5	0.208	115.4	0.383	597.9	1.985	17.2	0.057	30.6	0.102	34.1	0.113	64.7	0.215
F02024	50.5 b	0.138 b	53.1 b	0.145 b	103.6 b	0.283 b	334.4 b	0.912 b	14.0 b	0.038 b	28.8 b	0.079 b	29.8 b	0.081 b	58.6 b	0.160 b
Number of females	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
Mean	58.9	0.197	52.1	0.173	110.9	0.370	648.0	2.166	19.8	0.066	37.2	0.125	39.9	0.133	77.1	0.258
S.D.	5.2	0.023	9.7	0.026	11.5	0.030	110.7	0.377	3.7	0.013	6.5	0.022	6.9	0.023	13.2	0.045
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	AN	AN	DU	DU	AN	AN	AN	AN	KW	AN	AN	AN	AN	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).
DU: Analysis by Dunnett's test.
KW: Analysis by Kruskal-Wallis' test (one-way layout).
b, Excluded from data analysis (not pregnant).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 30-1-3. Organ weights of female rats at the end of the dosing period

HA 300 mg/kg

Female No.	Body weight (g)	Brain (mg)	Brain (mg/g)	Thymus (mg)	Thymus (mg/g)	Heart (mg)	Heart (mg/g)	Liver (mg)	Liver (mg/g)	Kidney (R) (mg)	Kidney (R) (mg/g)	Kidney (L) (mg)	Kidney (L) (mg/g)	Kidneys (mg)	Kidneys (mg/g)	Spleen (mg)	Spleen (mg/g)
F03025	311.4	1694.5	5.442	156.3	0.502	1032.3	3.315	10974.8	35.243	1010.2	3.244	1048.4	3.367	2058.6	6.611	697.2	2.239
F03026	284.0	1879.7	6.619	128.8	0.454	930.3	3.276	9279.4	32.674	904.8	3.186	891.3	3.138	1796.1	6.324	559.5	1.970
F03027	299.7	1914.4	6.388	146.8	0.490	955.2	3.187	9411.0	31.401	1159.7	3.870	1092.1	3.644	2251.8	7.514	614.8	2.051
F03028	282.0	1901.2	6.742	245.8	0.872	962.9	3.415	10034.0	35.582	957.2	3.394	998.8	3.542	1956.0	6.936	751.4	2.665
F03029	335.2	1978.7	5.903	187.7	0.560	1026.2	3.061	10723.9	31.993	1031.2	3.076	1015.0	3.028	2046.2	6.104	694.8	2.073
F03030	287.9	1873.0	6.506	329.9	1.146	926.6	3.218	9614.3	33.395	960.2	3.335	985.4	3.423	1945.6	6.758	596.6	2.072
F03031	306.5	1958.1	6.389	390.8	1.275	955.4	3.117	10065.8	32.841	1082.0	3.530	1058.7	3.454	2140.7	6.984	564.0	1.840
F03032	380.8 c	1999.4 c	5.251 c	367.3 c	0.965 c	1138.0 c	2.988 c	12213.6 c	32.074 c	1125.1 c	2.955 c	1149.9 c	3.020 c	2275.0 c	5.974 c	713.6 c	1.874 c
F03033	287.8	1838.0	6.386	323.9	1.125	840.2	2.919	9905.4	34.418	908.0	3.155	869.9	3.023	1777.9	6.178	693.6	2.410
F03034	266.5	1756.6	6.591	146.2	0.549	972.4	3.649	8506.6	31.920	880.5	3.304	888.6	3.334	1769.1	6.638	657.3	2.466
F03035	344.6	1942.9	5.638	326.4	0.947	1085.9	3.151	10581.1	30.705	1215.5	3.527	1248.2	3.622	2463.7	7.149	772.9	2.243
F03036	290.0	1865.6	6.433	130.7	0.451	992.9	3.424	10263.9	35.393	965.9	3.331	904.8	3.120	1870.7	6.451	788.4	2.719
Number of females	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
Mean	299.6	1873.0	6.276	228.5	0.761	970.9	3.248	9941.8	33.233	1006.8	3.359	1000.1	3.336	2006.9	6.695	671.9	2.250
S.D.	23.4	85.2	0.423	97.7	0.317	64.6	0.200	714.4	1.707	107.5	0.221	112.5	0.228	216.6	0.430	80.7	0.285
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN

HA 300 mg/kg

Female No.	Ovary (R) (mg)	Ovary (R) (mg/g)	Ovary (L) (mg)	Ovary (L) (mg/g)	Ovaries (mg)	Ovaries (mg/g)	Uterus (mg)	Uterus (mg/g)	Thyroid gland (mg)	Thyroid gland (mg/g)	Adrenal gland (R) (mg)	Adrenal gland (R) (mg/g)	Adrenal gland (L) (mg)	Adrenal gland (L) (mg/g)	Adrenal glands (mg)	Adrenal glands (mg/g)
F03025	54.6	0.175	60.6	0.195	115.2	0.370	805.4	2.586	14.4	0.046	33.9	0.109	38.6	0.124	72.5	0.233
F03026	55.3	0.195	59.7	0.210	115.0	0.405	533.1	1.877	18.9	0.067	41.5	0.146	45.7	0.161	87.2	0.307
F03027	54.5	0.182	45.5	0.152	100.0	0.334	691.1	2.306	17.0	0.057	28.4	0.095	30.7	0.102	59.1	0.197
F03028	54.4	0.193	52.9	0.188	107.3	0.380	577.2	2.047	20.2	0.072	33.3	0.118	34.0	0.121	67.3	0.239
F03029	61.2	0.183	56.1	0.167	117.3	0.350	637.2	1.901	14.9	0.044	32.7	0.098	34.0	0.101	66.7	0.199
F03030	53.7	0.187	62.8	0.218	116.5	0.405	700.8	2.434	24.0	0.083	38.4	0.133	42.6	0.148	81.0	0.281
F03031	50.7	0.165	46.2	0.151	96.9	0.316	535.7	1.748	24.0	0.078	32.2	0.105	31.8	0.104	64.0	0.209
F03032	47.7 c	0.125 c	54.1 c	0.142 c	101.8 c	0.267 c	1610.0 c	4.228 c	21.9 c	0.058 c	30.0 c	0.079 c	33.2 c	0.087 c	63.2 c	0.166 c
F03033	63.7	0.221	46.0	0.160	109.7	0.381	640.2	2.224	31.1	0.108	26.0	0.090	27.6	0.096	53.6	0.186
F03034	54.2	0.203	57.3	0.215	111.5	0.418	699.7	2.626	17.8	0.067	26.8	0.101	29.2	0.110	56.0	0.210
F03035	69.1	0.201	58.8	0.171	127.9	0.371	759.7	2.205	22.1	0.064	38.9	0.113	42.0	0.122	80.9	0.235
F03036	69.8	0.241	57.8	0.199	127.6	0.440	451.1	1.556	19.5	0.067	47.0	0.162	48.8	0.168	95.8	0.330
Number of females	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
Mean	58.3	0.195	54.9	0.184	113.2	0.379	639.2	2.137	20.4	0.068	34.5	0.115	36.8	0.123	71.3	0.239
S.D.	6.6	0.021	6.3	0.025	9.7	0.037	106.5	0.345	4.8	0.018	6.5	0.023	7.1	0.025	13.5	0.048
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	AN	AN	DU	DU	AN	AN	AN	AN	KW	AN	AN	AN	AN	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).
DU: Analysis by Dunnett's test.
KW: Analysis by Kruskal-Wallis' test (one-way layout).
c, Excluded from data analysis (not delivery).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 30-1-4. Organ weights of female rats at the end of the dosing period

HA 1000 mg/kg

Female No.	Body weight (g)	Brain (mg)	Brain (mg/g)	Thymus (mg)	Thymus (mg/g)	Heart (mg)	Heart (mg/g)	Liver (mg)	Liver (mg/g)	Kidney (R) (mg)	Kidney (R) (mg/g)	Kidney (L) (mg)	Kidney (L) (mg/g)	Kidneys (mg)	Kidneys (mg/g)	Spleen (mg)	Spleen (mg/g)
F04037	328.9	1940.0	5.898	286.5	0.871	948.3	2.883	9918.2	30.156	925.9	2.815	920.2	2.798	1846.1	5.613	701.6	2.133
F04038	287.7	1796.0	6.243	172.8	0.601	902.2	3.136	8976.9	31.202	968.3	3.366	912.5	3.172	1880.8	6.537	548.7	1.907
F04039	271.6	1996.3	7.350	159.4	0.587	1031.3	3.797	9460.4	34.832	946.9	3.486	895.0	3.295	1841.9	6.782	606.5	2.233
F04040	321.3	1884.5	5.865	228.5	0.711	1083.8	3.373	10631.2	33.088	968.6	3.015	965.5	3.005	1934.1	6.020	681.1	2.120
F04041	289.0 a	1898.8 a	6.570 a	188.1 a	0.651 a	944.9 a	3.270 a	10873.4 a	37.624 a	1305.9 a	4.519 a	1172.2 a	4.056 a	2478.1 a	8.575 a	864.6 a	2.992 a
F04042	316.9	1811.3	5.716	316.5	0.999	1016.3	3.207	9316.4	29.399	915.6	2.889	890.7	2.811	1806.3	5.700	535.2	1.689
F04043	320.2	1946.7	6.080	264.0	0.824	1033.6	3.228	9339.0	29.166	1097.8	3.428	1009.1	3.151	2106.9	6.580	709.8	2.217
F04044	317.4	1885.5	5.940	159.6	0.503	1091.8	3.440	10596.3	33.385	1000.6	3.152	1007.0	3.173	2007.6	6.325	596.1	1.878
F04045	273.7	1898.7	6.937	273.3	0.999	965.3	3.527	10261.6	37.492	951.9	3.478	963.1	3.519	1915.0	6.997	626.3	2.288
F04046	305.7	1889.5	6.181	200.1	0.655	938.0	3.068	9789.6	32.024	982.7	3.215	949.1	3.105	1931.8	6.319	709.3	2.320
F04047	279.5	1881.8	6.733	332.3	1.189	887.8	3.176	8185.7	29.287	993.4	3.554	1067.6	3.820	2061.0	7.374	525.8	1.881
F04048	300.6	1769.1	5.885	205.8	0.685	910.0	3.027	9235.5	30.724	931.4	3.098	887.2	2.951	1818.6	6.050	651.6	2.168
Number of females	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
Mean	302.1	1881.8	6.257	236.3	0.784	982.6	3.260	9610.1	31.887	971.2	3.227	951.5	3.164	1922.7	6.391	626.5	2.076
S.D.	20.8	67.9	0.523	62.0	0.212	72.4	0.258	729.3	2.626	50.2	0.255	58.1	0.301	99.5	0.538	69.9	0.205
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN

HA 1000 mg/kg

Female No.	Ovary (R) (mg)	Ovary (R) (mg/g)	Ovary (L) (mg)	Ovary (L) (mg/g)	Ovaries (mg)	Ovaries (mg/g)	Uterus (mg)	Uterus (mg/g)	Thyroid gland (mg)	Thyroid gland (mg/g)	Adrenal gland (R) (mg)	Adrenal gland (R) (mg/g)	Adrenal gland (L) (mg)	Adrenal gland (L) (mg/g)	Adrenal glands (mg)	Adrenal glands (mg/g)
F04037	48.8	0.148	50.8	0.154	99.6	0.303	569.8	1.732	18.9	0.057	38.1	0.116	39.2	0.119	77.3	0.235
F04038	38.3	0.133	53.2	0.185	91.5	0.318	536.1	1.863	11.0	0.038	28.3	0.098	32.3	0.112	60.6	0.211
F04039	45.4	0.167	52.7	0.194	98.1	0.361	609.8	2.245	18.5	0.068	40.1	0.148	43.1	0.159	83.2	0.306
F04040	40.5	0.126	53.8	0.167	94.3	0.293	580.8	1.808	22.1	0.069	33.3	0.104	34.4	0.107	67.7	0.211
F04041	53.0 a	0.183 a	49.3 a	0.171 a	102.3 a	0.354 a	817.0 a	2.827 a	18.9 a	0.065 a	40.0 a	0.138 a	39.9 a	0.138 a	79.9 a	0.276 a
F04042	40.6	0.128	65.5	0.207	106.1	0.335	573.5	1.810	21.8	0.069	42.7	0.135	45.3	0.143	88.0	0.278
F04043	47.9	0.150	44.5	0.139	92.4	0.289	712.1	2.224	21.1	0.066	29.9	0.093	34.3	0.107	64.2	0.200
F04044	52.0	0.164	54.8	0.173	106.8	0.336	405.4	1.277	20.7	0.065	45.4	0.143	51.3	0.162	96.7	0.305
F04045	48.1	0.176	42.2	0.154	90.3	0.330	636.1	2.324	15.6	0.057	45.5	0.166	47.6	0.174	93.1	0.340
F04046	49.6	0.162	53.3	0.174	102.9	0.337	577.5	1.889	19.6	0.064	31.4	0.103	29.8	0.097	61.2	0.200
F04047	43.2	0.155	55.7	0.199	98.9	0.354	611.7	2.189	13.0	0.047	29.7	0.106	31.2	0.112	60.9	0.218
F04048	52.1	0.173	47.9	0.159	100.0	0.333	513.3	1.708	20.2	0.067	34.6	0.115	39.4	0.131	74.0	0.246
Number of females	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
Mean	46.0	0.153	52.2	0.173	98.3	0.326	575.1	1.915	18.4	0.061	36.3	0.121	38.9	0.129	75.2	0.250
S.D.	4.8	0.018	6.2	0.021	5.7	0.023	77.0	0.309	3.7	0.010	6.4	0.024	7.2	0.026	13.4	0.049
Significance	**	**	NS	NS	*	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	AN	AN	DU	DU	AN	AN	AN	AN	KW	AN	AN	AN	AN	AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).
DU: Analysis by Dunnett's test.
KW: Analysis by Kruskal-Wallis' test (one-way layout).
a, Excluded from data analysis (not copulated).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 30-2-1. Organ weights of female rats at the end of the dosing period, satellite group

Control (vehicle: corn oil)

Female No.	Body weight (g)	Brain (mg)	Brain (mg/g)	Thymus (mg)	Thymus (mg/g)	Heart (mg)	Heart (mg/g)	Liver (mg)	Liver (mg/g)	Kidney (R) (mg)	Kidney (R) (mg/g)	Kidney (L) (mg)	Kidney (L) (mg/g)	Kidneys (mg)	Kidneys (mg/g)	Spleen (mg)	Spleen (mg/g)
F05049	289.0	1884.1	6.519	395.5	1.369	882.4	3.053	7412.5	25.649	788.3	2.728	824.7	2.854	1613.0	5.581	515.8	1.785
F05050	275.1	1848.4	6.719	337.6	1.227	967.9	3.518	6689.8	24.318	843.8	3.067	835.1	3.036	1678.9	6.103	469.9	1.708
F05051	294.9	1979.3	6.712	245.3	0.832	990.4	3.358	8306.3	28.166	1029.9	3.492	1118.7	3.793	2148.6	7.286	412.7	1.399
F05052	268.4	1896.1	7.064	272.5	1.015	888.1	3.309	6342.9	23.632	813.7	3.032	873.0	3.253	1686.7	6.284	511.5	1.906
F05053	261.4	1762.5	6.743	236.2	0.904	845.5	3.235	6526.7	24.968	944.1	3.612	896.0	3.428	1840.1	7.039	480.8	1.839
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	277.8	1874.1	6.751	297.4	1.069	914.9	3.295	7055.6	25.347	884.0	3.186	909.5	3.273	1793.5	6.459	478.1	1.727
S.D.	14.0	78.7	0.196	67.7	0.224	61.4	0.170	808.3	1.745	100.8	0.362	120.4	0.363	215.3	0.698	41.5	0.197

Control (vehicle: corn oil)

Female No.	Ovary (R) (mg)	Ovary (R) (mg/g)	Ovary (L) (mg)	Ovary (L) (mg/g)	Ovaries (mg)	Ovaries (mg/g)	Uterus (mg)	Uterus (mg/g)	Thyroid gland (mg)	Thyroid gland (mg/g)	Adrenal gland (R) (mg)	Adrenal gland (R) (mg/g)	Adrenal gland (L) (mg)	Adrenal gland (L) (mg/g)	Adrenal glands (mg)	Adrenal glands (mg/g)
F05049	43.0	0.149	42.4	0.147	85.4	0.296	774.2	2.679	20.1	0.070	33.0	0.114	34.3	0.119	67.3	0.233
F05050	40.5	0.147	33.4	0.121	73.9	0.269	678.7	2.467	18.0	0.065	26.4	0.096	27.7	0.101	54.1	0.197
F05051	46.3	0.157	39.7	0.135	86.0	0.292	562.6	1.908	27.8	0.094	29.5	0.100	30.8	0.104	60.3	0.204
F05052	34.2	0.127	41.7	0.155	75.9	0.283	465.4	1.734	19.8	0.074	31.4	0.117	32.9	0.123	64.3	0.240
F05053	31.5	0.121	41.9	0.160	73.4	0.281	512.1	1.959	19.1	0.073	25.9	0.099	30.9	0.118	56.8	0.217
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	39.1	0.140	39.8	0.144	78.9	0.284	598.6	2.149	21.0	0.075	29.2	0.105	31.3	0.113	60.6	0.218
S.D.	6.1	0.015	3.7	0.016	6.3	0.011	126.3	0.403	3.9	0.011	3.1	0.010	2.5	0.010	5.4	0.018

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 30-2-2. Organ weights of female rats at the end of the dosing period, satellite group

HA 1000 mg/kg

Female No.	Body weight (g)	Brain (mg)	Brain (mg/g)	Thymus (mg)	Thymus (mg/g)	Heart (mg)	Heart (mg/g)	Liver (mg)	Liver (mg/g)	Kidney (R) (mg)	Kidney (R) (mg/g)	Kidney (L) (mg)	Kidney (L) (mg/g)	Kidneys (mg)	Kidneys (mg/g)	Spleen (mg)	Spleen (mg/g)
F06059	307.0	1852.1	6.033	258.5	0.842	1076.5	3.507	7243.7	23.595	888.7	2.895	908.2	2.958	1796.9	5.853	648.4	2.112
F06060	283.9	1915.3	6.746	387.6	1.365	889.9	3.135	7867.9	27.714	958.2	3.375	973.0	3.427	1931.2	6.802	493.1	1.737
F06061	310.6	1829.3	5.890	453.1	1.459	855.0	2.753	7810.6	25.147	907.1	2.920	881.2	2.837	1788.3	5.758	627.2	2.019
F06062	262.3	1948.7	7.429	180.1	0.687	820.6	3.128	7470.9	28.482	1143.3	4.359	1123.2	4.282	2266.5	8.641	603.0	2.299
F06063	305.6	1897.4	6.209	345.5	1.131	1094.8	3.582	7968.1	26.074	904.8	2.961	909.8	2.977	1814.6	5.938	651.4	2.132
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	293.9	1888.6	6.461	325.0	1.097	947.4	3.221	7672.2	26.202	960.4	3.302	959.1	3.296	1919.5	6.598	604.6	2.060
S.D.	20.5	48.1	0.631	107.4	0.331	128.8	0.334	303.8	1.963	105.5	0.623	97.7	0.595	202.4	1.216	65.3	0.207
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	**	*
Statistical method	TT	TT	AW	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT

HA 1000 mg/kg

Female No.	Ovary (R) (mg)	Ovary (R) (mg/g)	Ovary (L) (mg)	Ovary (L) (mg/g)	Ovaries (mg)	Ovaries (mg/g)	Uterus (mg)	Uterus (mg/g)	Thyroid gland (mg)	Thyroid gland (mg/g)	Adrenal gland (R) (mg)	Adrenal gland (R) (mg/g)	Adrenal gland (L) (mg)	Adrenal gland (L) (mg/g)	Adrenal glands (mg)	Adrenal glands (mg/g)
F06059	47.7	0.155	53.2	0.173	100.9	0.329	484.3	1.578	20.5	0.067	36.8	0.120	36.2	0.118	73.0	0.238
F06060	38.1	0.134	33.2	0.117	71.3	0.251	1119.0	3.942	13.2	0.046	28.1	0.099	27.2	0.096	55.3	0.195
F06061	44.5	0.143	45.3	0.146	89.8	0.289	804.3	2.590	14.6	0.047	28.4	0.091	28.1	0.090	56.5	0.182
F06062	52.5	0.200	51.3	0.196	103.8	0.396	448.6	1.710	19.9	0.076	34.5	0.132	37.5	0.143	72.0	0.274
F06063	62.8	0.205	54.2	0.177	117.0	0.383	797.1	2.608	16.2	0.053	35.6	0.116	39.4	0.129	75.0	0.245
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	49.1	0.167	47.4	0.162	96.6	0.330	730.7	2.486	16.9	0.058	32.7	0.112	33.7	0.115	66.4	0.227
S.D.	9.3	0.033	8.7	0.031	17.1	0.061	274.3	0.945	3.2	0.013	4.1	0.017	5.6	0.022	9.6	0.038
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	TT	TT	TT	TT	TT	AW	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
TT: Analysis by Student's t-test.
AW: Analysis by Aspin-Welch t-test.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 30-3-1. Organ weights of female rats at the end of the recovery period

Control (vehicle: corn oil)

Female No.	Body	Brain		Thymus		Heart		Liver		Kidney (R)		Kidney (L)		Kidneys		Spleen	
	weight (g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
F05054	276.0	1943.7	7.042	305.8	1.108	873.3	3.164	6903.1	25.011	890.0	3.225	906.5	3.284	1796.5	6.509	678.0	2.457
F05055	302.3	1835.1	6.070	330.0	1.092	896.5	2.966	8070.1	26.696	848.0	2.805	787.2	2.604	1635.2	5.409	622.1	2.058
F05056	289.0	1952.1	6.755	357.7	1.238	967.6	3.348	7229.0	25.014	931.8	3.224	920.3	3.184	1852.1	6.409	573.2	1.983
F05057	290.0	1934.0	6.669	264.0	0.910	970.2	3.346	7033.6	24.254	851.3	2.936	850.6	2.933	1701.9	5.869	566.9	1.955
F05058	237.3	1869.5	7.878	245.0	1.032	792.9	3.341	5362.1	22.596	788.9	3.324	778.3	3.280	1567.2	6.604	455.9	1.921
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	278.9	1906.9	6.883	300.5	1.076	900.1	3.233	6919.6	24.714	862.0	3.103	848.6	3.057	1710.6	6.160	579.2	2.075
S.D.	25.1	51.7	0.659	46.3	0.119	73.6	0.169	982.1	1.484	53.2	0.221	65.6	0.291	115.9	0.507	82.1	0.220

Control (vehicle: corn oil)

Female No.	Ovary (R)		Ovary (L)		Ovaries		Uterus		Thyroid gland		Adrenal gland (R)		Adrenal gland (L)		Adrenal glands	
	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
F05054	42.2	0.153	42.9	0.155	85.1	0.308	483.7	1.753	16.1	0.058	31.9	0.116	33.4	0.121	65.3	0.237
F05055	44.7	0.148	45.4	0.150	90.1	0.298	607.9	2.011	20.5	0.068	33.8	0.112	32.0	0.106	65.8	0.218
F05056	50.1	0.173	44.7	0.155	94.8	0.328	576.8	1.996	25.0	0.087	27.8	0.096	36.4	0.126	64.2	0.222
F05057	34.6	0.119	43.2	0.149	77.8	0.268	451.3	1.556	18.5	0.064	32.3	0.111	38.0	0.131	70.3	0.242
F05058	34.0	0.143	34.0	0.143	68.0	0.287	478.6	2.017	25.5	0.107	26.5	0.112	26.6	0.112	53.1	0.224
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	41.1	0.147	42.0	0.150	83.2	0.298	519.7	1.867	21.1	0.077	30.5	0.109	33.3	0.119	63.7	0.229
S.D.	6.9	0.019	4.6	0.005	10.6	0.022	68.4	0.206	4.1	0.020	3.1	0.008	4.4	0.010	6.4	0.010

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 30-3-2. Organ weights of female rats at the end of the recovery period

HA 1000 mg/kg

Female No.	Body	Brain		Thymus		Heart		Liver		Kidney (R)		Kidney (L)		Kidneys		Spleen	
	weight (g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
F06064	270.1	1849.7	6.848	268.5	0.994	802.2	2.970	6695.9	24.790	851.7	3.153	844.0	3.125	1695.7	6.278	384.2	1.422
F06065	294.5	1898.7	6.447	228.6	0.776	883.3	2.999	7632.0	25.915	902.9	3.066	929.9	3.158	1832.8	6.223	559.6	1.900
F06066	287.6	2024.1	7.038	316.8	1.102	955.8	3.323	7503.8	26.091	941.2	3.273	936.5	3.256	1877.7	6.529	461.1	1.603
F06067	287.6	1863.6	6.480	261.2	0.908	860.3	2.991	7110.5	24.724	747.9	2.600	746.6	2.596	1494.5	5.196	500.1	1.739
F06068	269.4	1825.5	6.776	291.6	1.082	790.7	2.935	6903.3	25.625	904.5	3.357	896.8	3.329	1801.3	6.686	500.6	1.858
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	281.8	1892.3	6.718	273.3	0.972	858.5	3.044	7169.1	25.429	869.6	3.090	870.8	3.093	1740.4	6.182	481.1	1.704
S.D.	11.4	78.3	0.251	33.1	0.134	66.8	0.158	395.1	0.636	75.1	0.296	78.5	0.289	152.9	0.583	64.6	0.196
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	*
Statistical method	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT

HA 1000 mg/kg

Female No.	Ovary (R)		Ovary (L)		Ovaries		Uterus		Thyroid gland		Adrenal gland (R)		Adrenal gland (L)		Adrenal glands	
	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
F06064	41.2	0.153	42.5	0.157	83.7	0.310	538.7	1.994	20.0	0.074	36.6	0.136	37.8	0.140	74.4	0.275
F06065	59.7	0.203	46.3	0.157	106.0	0.360	489.9	1.663	18.8	0.064	31.0	0.105	30.0	0.102	61.0	0.207
F06066	46.1	0.160	57.4	0.200	103.5	0.360	462.3	1.607	19.0	0.066	39.1	0.136	42.2	0.147	81.3	0.283
F06067	56.7	0.197	48.1	0.167	104.8	0.364	427.0	1.485	22.5	0.078	37.7	0.131	40.3	0.140	78.0	0.271
F06068	35.9	0.133	36.5	0.135	72.4	0.269	538.8	2.000	18.0	0.067	32.2	0.120	33.0	0.122	65.2	0.242
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	47.9	0.169	46.2	0.163	94.1	0.333	491.3	1.750	19.7	0.070	35.3	0.126	36.7	0.130	72.0	0.256
S.D.	10.1	0.030	7.7	0.024	15.2	0.042	48.7	0.235	1.7	0.006	3.5	0.013	5.1	0.018	8.6	0.031
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	*	NS	NS	NS	NS
Statistical method	TT	TT	TT	AW	TT	TT	TT	TT	TT	AW	TT	TT	TT	TT	TT	TT

Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
TT: Analysis by Student's t-test.
AW: Analysis by Aspin-Welch t-test.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 31-1. Macroscopic findings of male rats at the end of the dosing period

Animal No.	Organs	Findings	Notes
M01001	All organs/	Within normal limits	
M01002	All organs/	Within normal limits	
M01003	All organs/	Within normal limits	
M01004	All organs/	Within normal limits	
M01005	All organs/	Within normal limits	
M01006	All organs/	Within normal limits	
M01007	All organs/	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 31-1 (continued). Macroscopic findings of male rats at the end of the dosing period

Animal No.	Organs	Findings	Notes
M02013	All organs/	Within normal limits	
M02014	All organs/	Within normal limits	
M02015	All organs/	Within normal limits	
M02016	All organs/	Within normal limits	
M02017	All organs/	Within normal limits	
M02018	Liver/	Diaphragmatic nodule	
M02019	All organs/	Within normal limits	
M02020	All organs/	Within normal limits	
M02021	All organs/	Within normal limits	
M02022	All organs/	Within normal limits	
M02023	Skin/	Crust	Dorsal neck
M02024	All organs/	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 31-1 (continued). Macroscopic findings of male rats at the end of the dosing period

Animal No.	Fate	Organs	Findings	Notes
M03025	D	Kidney/	Enlargement	
		Liver/	Enlargement	
		Lung/	Dark colored area	Scattered
			Discoloration, dark reddish	
		Thymus/	Dark reddish spot	Scattered
M03026		All organs/	Within normal limits	
M03027		All organs/	Within normal limits	
M03028		All organs/	Within normal limits	
M03029		All organs/	Within normal limits	
M03030		All organs/	Within normal limits	
M03031		All organs/	Within normal limits	
M03032		All organs/	Within normal limits	
M03033		All organs/	Within normal limits	
M03034		Thymus/	Small	
M03035		All organs/	Within normal limits	
M03036		Epididymis/	Nodule	Yellowish, Bilateral, Caudal

D: Died during dosing period

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 31-1 (continued). Macroscopic findings of male rats at the end of the dosing period

Animal No.	Organs	Findings	Notes
M04037	All organs/	Within normal limits	
M04038	All organs/	Within normal limits	
M04039	All organs/	Within normal limits	
M04040	All organs/	Within normal limits	
M04041	Skin/	Crust	Forelimb, Bilateral
M04042	All organs/	Within normal limits	
M04043	All organs/	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 31-2. Macroscopic findings of male rats at the end of the recovery period

Animal No.	Organs	Findings	Notes
M01008	All organs/	Within normal limits	
M01009	All organs/	Within normal limits	
M01010	All organs/	Within normal limits	
M01011	All organs/	Within normal limits	
M01012	Epididymis/	Nodule	Yellowish white, Caudal, Right

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 31-2 (continued). Macroscopic findings of male rats at the end of the recovery period

Animal No.	Organs	Findings	Notes
M04044	All organs/	Within normal limits	
M04045	Skin/	Alopecia	Dorsal neck
M04046	All organs/	Within normal limits	
M04047	All organs/	Within normal limits	
M04048	All organs/	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 32-1. Macroscopic findings of female rats at the end of the dosing period

Animal No.	Fate	Organs	Findings	Notes
F01001		All organs/	Within normal limits	
F01002		All organs/	Within normal limits	
F01003	NC	All organs/	Within normal limits	
F01004		All organs/	Within normal limits	
F01005		All organs/	Within normal limits	
F01006		All organs/	Within normal limits	
F01007		All organs/	Within normal limits	
F01008		All organs/	Within normal limits	
F01009		Stomach/	Dark reddish spot	Mucosa, Glandular stomach
F01010		All organs/	Within normal limits	
F01011		All organs/	Within normal limits	
F01012		All organs/	Within normal limits	

NC: Not copulated

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 32-1 (continued). Macroscopic findings of female rats at the end of the dosing period

Animal No.	Fate	Organs	Findings	Notes
F02013	NP	All organs/	Within normal limits	
F02014		All organs/	Within normal limits	
F02015		All organs/	Within normal limits	
F02016		Stomach/	Attachment, black content, mucosa	Glandular stomach
F02017		All organs/	Within normal limits	
F02018		All organs/	Within normal limits	
F02019		All organs/	Within normal limits	
F02020		All organs/	Within normal limits	
F02021		All organs/	Within normal limits	
F02022		All organs/	Within normal limits	
F02023		All organs/	Within normal limits	
F02024	NP	All organs/	Within normal limits	

NP: Not pregnant

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 32-1 (continued). Macroscopic findings of female rats at the end of the dosing period

Animal No.	Fate	Organs	Findings	Notes
F03025		All organs/	Within normal limits	
F03026		Stomach/	Dark colored spot	Mucosa, Glandular stomach
			Recessed area	Mucosa, Glandular stomach
F03027		All organs/	Within normal limits	
F03028		All organs/	Within normal limits	
F03029		Liver/	Whitish spot	Lateral left lobe
		Spleen/	Accessory spleen	
		Stomach/	Reddish spot	Mucosa, Glandular stomach
F03030		All organs/	Within normal limits	
F03031		All organs/	Within normal limits	
F03032	ND	Lung/	Dark colored area	Right caudal lobe
		Uterus/	Discoloration, dark colored	
			Remnant, fetal	
			Retention, watery content	Reddish, Yellowish
F03033		All organs/	Within normal limits	
F03034		All organs/	Within normal limits	
F03035		All organs/	Within normal limits	
F03036		All organs/	Within normal limits	

ND: Not delivery

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 32-1 (continued). Macroscopic findings of female rats at the end of the dosing period

Animal No.	Fate	Organs	Findings	Notes
F04037		All organs/	Within normal limits	
F04038		All organs/	Within normal limits	
F04039		All organs/	Within normal limits	
F04040		All organs/	Within normal limits	
F04041	NC	Kidney/ Urinary bladder/	Elevated area Thickening	Whitish, Right Wall
F04042		All organs/	Within normal limits	
F04043		All organs/	Within normal limits	
F04044		All organs/	Within normal limits	
F04045		All organs/	Within normal limits	
F04046		All organs/	Within normal limits	
F04047		All organs/	Within normal limits	
F04048		All organs/	Within normal limits	

NC: Not copulated

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 32-2. Macroscopic findings of female rats at the end of the dosing period, satellite group

Animal No.	Organs	Findings	Notes
F05049	All organs/	Within normal limits	
F05050	All organs/	Within normal limits	
F05051	All organs/	Within normal limits	
F05052	All organs/	Within normal limits	
F05053	All organs/	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 32-2 (continued). Macroscopic findings of female rats at the end of the dosing period, satellite group

Animal No.	Organs	Findings	Notes
F06059	All organs/	Within normal limits	
F06060	All organs/	Within normal limits	
F06061	All organs/	Within normal limits	
F06062	All organs/	Within normal limits	
F06063	All organs/	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 32-3. Macroscopic findings of female rats at the end of the recovery period

Animal No.	Organs	Findings	Notes
F05054	All organs/	Within normal limits	
F05055	All organs/	Within normal limits	
F05056	All organs/	Within normal limits	
F05057	All organs/	Within normal limits	
F05058	All organs/	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 32-3 (continued). Macroscopic findings of female rats at the end of the recovery period

Animal No.	Organs	Findings	Notes
F06064	All organs/	Within normal limits	
F06065	All organs/	Within normal limits	
F06066	All organs/	Within normal limits	
F06067	All organs/	Within normal limits	
F06068	All organs/	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 33-1. Histopathological findings of male rats at the end of the dosing period [H.E. staining]

Animal No.	Organs	Findings	Notes
M01001	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Degeneration/fibrosis, myocardial ±	Focal
	Trachea /	Within normal limits	
	Lung /	Accumulation, foam cell ±	Alveolus, Focal
		Metaplasia, osseous P	Focal
		Microgranuloma ±	
	Bronchus /	Within normal limits	
	Liver /	Within normal limits	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown ±	
		Hematopoiesis, extramedullary ±	
	Kidney /	Basophilic tubule, cortex +	
		Cellular infiltration, lymphocyte +	Interstitial
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Testis /	Degeneration, seminiferous tubule ±	Unilateral
	Epididymis /	Within normal limits	
	Prostate /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 33-1 (continued). Histopathological findings of male rats at the end of the dosing period [H.E. staining]

Animal No.	Organs	Findings	Notes
M01001	Seminal vesicle /	Within normal limits	
	Coagulating gland /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	
M01002	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Metaplasia, osseous P	Focal
	Bronchus /	Within normal limits	
	Liver /	Fatty change, hepatocyte ±	Periportal
		Microgranuloma ±	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown +	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 33-1 (continued). Histopathological findings of male rats at the end of the dosing period [H.E. staining]

Animal No.	Organs	Findings	Notes
M01002	Spleen /	Hematopoiesis, extramedullary ±	
	Kidney /	Basophilic tubule, cortex ±	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Testis /	Within normal limits	
	Epididymis /	Within normal limits	
	Prostate /	Within normal limits	
	Seminal vesicle /	Within normal limits	
	Coagulating gland /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	
M01003	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Fatty change, hepatocyte ±	Periportal
		Microgranuloma ±	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 33-1 (continued). Histopathological findings of male rats at the end of the dosing period [H.E. staining]

Animal No.	Organs	Findings	Notes
M01003	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown ±	
		Hematopoiesis, extramedullary ±	
	Kidney /	Cellular infiltration, lymphocyte ±	Renal pelvis, Interstitial
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Testis /	Within normal limits	
	Epididymis /	Within normal limits	
	Prostate /	Within normal limits	
	Seminal vesicle /	Within normal limits	
	Coagulating gland /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	
M01004	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 33-1 (continued). Histopathological findings of male rats at the end of the dosing period [H.E. staining]

Animal No.	Organs	Findings	Notes
M01004	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Microgranuloma ±	
	Pancreas /	Within normal limits	
	Stomach /	Cellular infiltration, lymphocyte ±	Limiting ridge, Submucosa, Perivascular, Focal
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown ±	
		Hematopoiesis, extramedullary +	
	Kidney /	Mineralization ±	Cortex
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Testis /	Within normal limits	
	Epididymis /	Within normal limits	
	Prostate /	Within normal limits	
	Seminal vesicle /	Within normal limits	
	Coagulating gland /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	
M01005	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 33-1 (continued). Histopathological findings of male rats at the end of the dosing period [H.E. staining]

Animal No.	Organs	Findings	Notes
M01005	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Hematopoiesis, extramedullary ±	
		Microgranuloma ±	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown ±	
		Hematopoiesis, extramedullary ±	
	Kidney /	Basophilic tubule, cortex ±	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Testis /	Within normal limits	
	Epididymis /	Within normal limits	
	Prostate /	Cellular infiltration, lymphocyte ±	Interstitial
	Seminal vesicle /	Within normal limits	
	Coagulating gland /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 33-1 (continued). Histopathological findings of male rats at the end of the dosing period [H.E. staining]

Animal No.	Organs	Findings	Notes
M01005	Marrow, femur /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 33-1 (continued). Histopathological findings of male rats at the end of the dosing period [H.E. staining]

Animal No.	Organs	Findings	Notes
M02018	Liver /	Nodule, hepatodiaphragmatic P	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 33-1 (continued). Histopathological findings of male rats at the end of the dosing period [H.E. staining]

Animal No.	Fate	Organs	Findings	Notes
M03025	D	Brain /	Within normal limits	
		Spinal cord /	Within normal limits	
		Pituitary gland /	Congestion P	Postmortem change
		Submandibular gland /	Within normal limits	
		Sublingual gland /	Within normal limits	
		Lymph node, submandibular /	Within normal limits	
		Thyroid gland /	Within normal limits	
		Parathyroid gland /	Within normal limits	
		Thymus /	Congestion P	Postmortem change
		Heart /	Within normal limits	
		Trachea /	Within normal limits	
		Lung /	Congestion P	Postmortem change
		Bronchus /	Within normal limits	
		Liver /	Congestion P	Postmortem change
		Pancreas /	Within normal limits	
		Stomach /	Within normal limits	
		Duodenum /	Autolysis	
		Jejunum /	Autolysis	
		Ileum /	Autolysis	
		Cecum /	Within normal limits	
		Colon /	Within normal limits	
		Rectum /	Within normal limits	
		Lymph node, mesenteric /	Within normal limits	
		Spleen /	Deposit, pigment, brown ±	
			Hematopoiesis, extramedullary +	
		Kidney /	Autolysis	
		Urinary bladder /	Within normal limits	
		Adrenal gland /	Within normal limits	
		Testis /	Degeneration, seminiferous tubule 3+	Bilateral
		Epididymis /	Cell debris +	Lumen, bilateral
		Prostate /	Within normal limits	
		Seminal vesicle /	Within normal limits	
		Coagulating gland /	Within normal limits	
		Eyeball /	Within normal limits	

D: Died during dosing period

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 33-1 (continued). Histopathological findings of male rats at the end of the dosing period [H.E. staining]

Animal No.	Fate	Organs	Findings	Notes
M03025	D	Harderian gland /	Within normal limits	
		Sciatic nerve /	Within normal limits	
		Skeletal muscle /	Within normal limits	
		Femur /	Within normal limits	
		Marrow, femur /	Within normal limits	
M03034		Thymus /	Within normal limits	
M03036		Epididymis /	Granuloma, spermatic P	Caudal, unilateral

D: Died during dosing period

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 33-1 (continued). Histopathological findings of male rats at the end of the dosing period [H.E. staining]

M04037	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Degeneration/fibrosis, myocardial ±	Focal
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Microgranuloma ±	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown ±	
		Hematopoiesis, extramedullary ±	
	Kidney /	Basophilic tubule, cortex ±	
		Cellular infiltration, lymphocyte ±	Interstitial
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Testis /	Within normal limits	
	Epididymis /	Within normal limits	
	Prostate /	Cellular infiltration, lymphocyte ±	Interstitial
	Seminal vesicle /	Within normal limits	
	Coagulating gland /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 33-1 (continued). Histopathological findings of male rats at the end of the dosing period [H.E. staining]

Animal No.	Organs	Findings	Notes
M04037	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	
M04038	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Microgranuloma ±	
	Bronchus /	Within normal limits	
	Liver /	Fibrosis, focal ±	With macrophage containing brown pigment, Subcapsule
		Hematopoiesis, extramedullary ±	
		Microgranuloma ±	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown ±	
		Hematopoiesis, extramedullary +	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 33-1 (continued). Histopathological findings of male rats at the end of the dosing period [H.E. staining]

Animal No.	Organs	Findings	Notes
M04038	Kidney /	Basophilic tubule, cortex ±	
		Cellular infiltration, lymphocyte ±	Interstitial
		Eosinophilic body ±	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Testis /	Within normal limits	
	Epididymis /	Within normal limits	
	Prostate /	Within normal limits	
	Seminal vesicle /	Within normal limits	
	Coagulating gland /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	
M04039	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Ultimobranchial body P	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Microgranuloma ±	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 33-1 (continued). Histopathological findings of male rats at the end of the dosing period [H.E. staining]

Animal No.	Organs	Findings	Notes
M04039	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown +	
		Hematopoiesis, extramedullary ±	
	Kidney /	Basophilic tubule, cortex ±	
		Mineralization ±	Cortex
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Testis /	Within normal limits	
	Epididymis /	Within normal limits	
	Prostate /	Cellular infiltration, lymphocyte ±	Interstitial
	Seminal vesicle /	Within normal limits	
	Coagulating gland /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	
M04040	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 33-1 (continued). Histopathological findings of male rats at the end of the dosing period [H.E. staining]

Animal No.	Organs	Findings	Notes
M04040	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Microgranuloma ±	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown ±	
		Hematopoiesis, extramedullary ±	
	Kidney /	Dilatation, lumen ±	Medulla
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Testis /	Within normal limits	
	Epididymis /	Within normal limits	
	Prostate /	Within normal limits	
	Seminal vesicle /	Within normal limits	
	Coagulating gland /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	
M04041	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 33-1 (continued). Histopathological findings of male rats at the end of the dosing period [H.E. staining]

Animal No.	Organs	Findings	Notes
M04041	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Ultimobranchial body P	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Degeneration/fibrosis, myocardial ±	Focal
	Trachea /	Within normal limits	
	Lung /	Accumulation, foam cell ±	Alveolus, Focal
	Bronchus /	Within normal limits	
	Liver /	Within normal limits	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown ±	
		Hematopoiesis, extramedullary +	
	Kidney /	Basophilic tubule, cortex ±	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Testis /	Within normal limits	
	Epididymis /	Within normal limits	
	Prostate /	Within normal limits	
	Seminal vesicle /	Within normal limits	
	Coagulating gland /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 33-1 (continued). Histopathological findings of male rats at the end of the dosing period [H.E. staining]

Animal No.	Organs	Findings	Notes
M04041	Marrow, femur /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 33-2. Histopathological findings of male rats at the end of the recovery period [H.E. staining]

Animal No.	Organs	Findings	Notes
M01012	Epididymis /	Granuloma, spermatic P	Caudal, unilateral

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 34-1. Histopathological findings of female rats at the end of the dosing period [H.E. staining]

Animal No.	Organs	Findings	Notes
F01001	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Ultimobranchial body P	
	Parathyroid gland /	Within normal limits	
	Thymus /	Hyperplasia, epithelial tubule/cord ±	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Accumulation, foam cell ±	Alveolus, focal
	Bronchus /	Within normal limits	
	Liver /	Cellular infiltration, mononuclear cell ±	Periportal
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown +	
		Hematopoiesis, extramedullary 2+	
	Kidney /	Basophilic tubule, cortex ±	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 34-1 (continued). Histopathological findings of female rats at the end of the dosing period [H.E. staining]

Animal No.	Organs	Findings	Notes
F01001	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	
F01005	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Hyperplasia, epithelial tubule/cord ±	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Fatty change, hepatocyte ±	Periportal
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown ±	
		Hematopoiesis, extramedullary +	
	Kidney /	Mineralization ±	Medulla
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 34-1 (continued). Histopathological findings of female rats at the end of the dosing period [H.E. staining]

Animal No.	Organs	Findings	Notes
F01005	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	
F01008	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Ultimobranchial body P	
	Parathyroid gland /	Within normal limits	
	Thymus /	Hyperplasia, epithelial tubule/cord ±	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Cellular infiltration, mononuclear cell +	Periarterial
	Bronchus /	Within normal limits	
	Liver /	Within normal limits	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown +	
		Hematopoiesis, extramedullary +	
	Kidney /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 34-1 (continued). Histopathological findings of female rats at the end of the dosing period [H.E. staining]

Animal No.	Organs	Findings	Notes
F01008	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	
F01009	Stomach /	Erosion ±	Glandular stomach, focal
F01010	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Degeneration/fibrosis, myocardial ±	Focal
	Trachea /	Within normal limits	
	Lung /	Accumulation, foam cell ±	Alveolus, focal
	Bronchus /	Within normal limits	
	Liver /	Fatty change, hepatocyte ±	Periportal
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 34-1 (continued). Histopathological findings of female rats at the end of the dosing period [H.E. staining]

Animal No.	Organs	Findings	Notes
F01010	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown +	
		Hematopoiesis, extramedullary 2+	
	Kidney /	Within normal limits	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	
F01011	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Ultimobranchial body P	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Within normal limits	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 34-1 (continued). Histopathological findings of female rats at the end of the dosing period [H.E. staining]

Animal No.	Organs	Findings	Notes
F01011	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown +	
		Hematopoiesis, extramedullary 2+	
	Kidney /	Within normal limits	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 34-1 (continued). Histopathological findings of female rats at the end of the dosing period [H.E. staining]

Animal No.	Organs	Findings	Notes
F02016	Stomach /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 34-1 (continued). Histopathological findings of female rats at the end of the dosing period [H.E. staining]

Animal No.	Fate	Organs	Findings	Notes
F03026		Stomach /	Erosion ±	Glandular stomach, focal
F03029		Liver /	Microgranuloma ± Necrosis, focal +	
		Spleen /	Deposit, pigment, brown ± Hematopoiesis, extramedullary +	
		Stomach /	Erosion +	Glandular stomach, focal
F03032	ND	Lung /	Accumulation, foam cell ±	Alveolus, focal

ND: Not delivery

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 34-1 (continued). Histopathological findings of female rats at the end of the dosing period [H.E. staining]

Animal No.	Organs	Findings	Notes
F04037	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Hyperplasia, epithelial tubule/cord ±	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Cellular infiltration, mononuclear cell ±	Periportal
		Microgranuloma ±	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown ±	
		Hematopoiesis, extramedullary 2+	
	Kidney /	Mineralization ±	Cortex
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 34-1 (continued). Histopathological findings of female rats at the end of the dosing period [H.E. staining]

Animal No.	Organs	Findings	Notes
F04037	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	
F04038	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Ultimobranchial body P	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Within normal limits	
	Pancreas /	Cellular infiltration, lymphocyte ±	Intersitial, focal
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown ±	
		Hematopoiesis, extramedullary +	
	Kidney /	Within normal limits	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 34-1 (continued). Histopathological findings of female rats at the end of the dosing period [H.E. staining]

Animal No.	Fate	Organs	Findings	Notes
F04038		Uterus /	Within normal limits	
		Vagina /	Within normal limits	
		Eyeball /	Within normal limits	
		Harderian gland /	Within normal limits	
		Sciatic nerve /	Within normal limits	
		Skeletal muscle /	Within normal limits	
		Femur /	Within normal limits	
		Marrow, femur /	Within normal limits	
F04041	NC	Kidney /	Basophilic tubule, cortex 3+	Unilateral
			Cellular infiltration, inflammatory 3+	Interstitial, lumen, unilateral
			Hyperplasia, transitional cell 2+	Unilateral, papillary, renal pelvis
		Urinary bladder /	Cellular infiltration, neutrophil +	Epithelial layer, submucosa
			Hyperplasia, transitional cell 2+	Diffuse
F04042		Brain /	Within normal limits	
		Spinal cord /	Within normal limits	
		Pituitary gland /	Within normal limits	
		Submandibular gland /	Within normal limits	
		Sublingual gland /	Within normal limits	
		Lymph node, submandibular /	Within normal limits	
		Thyroid gland /	Within normal limits	
		Parathyroid gland /	Within normal limits	
		Thymus /	Within normal limits	
		Heart /	Degeneration/fibrosis, myocardial ±	Focal
		Trachea /	Within normal limits	
		Lung /	Within normal limits	
		Bronchus /	Within normal limits	
		Liver /	Fatty change, hepatocyte ±	Periportal
		Pancreas /	Within normal limits	
		Stomach /	Within normal limits	
		Duodenum /	Within normal limits	
		Jejunum /	Within normal limits	
		Ileum /	Within normal limits	

NC: Not copulated

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 34-1 (continued). Histopathological findings of female rats at the end of the dosing period [H.E. staining]

Animal No.	Organs	Findings	Notes
F04042	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown ±	
		Hematopoiesis, extramedullary ±	
	Kidney /	Within normal limits	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	
F04044	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Ultimobranchial body P	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Within normal limits	
	Pancreas /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 34-1 (continued). Histopathological findings of female rats at the end of the dosing period [H.E. staining]

Animal No.	Organs	Findings	Notes
F04044	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown +	
		Hematopoiesis, extramedullary +	
	Kidney /	Within normal limits	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	
F04045	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Hyperplasia, epithelial tubule/cord ±	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 34-1 (continued). Histopathological findings of female rats at the end of the dosing period [H.E. staining]

Animal No.	Organs	Findings	Notes
F04045	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Microgranuloma ±	
	Pancreas /	Within normal limits	
	Stomach /	Dilatation, fundic gland ±	Glandular stomach, focal
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown +	
		Hematopoiesis, extramedullary 2+	
	Kidney /	Cellular infiltration, lymphocyte ±	Interstitial
		Mineralization ±	Medulla
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 34-2. Histopathological findings of female rats at the end of the dosing period, satellite group [H.E. staining]

Animal No.	Organs	Findings	Notes
F05049	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Hyperplasia, epithelial tubule/cord ±	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Accumulation, foam cell ±	Alveolus, focal
	Bronchus /	Within normal limits	
	Liver /	Microgranuloma ±	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown +	
		Hematopoiesis, extramedullary +	
	Kidney /	Basophilic tubule, cortex ±	
		Mineralization ±	Cortico-medullary junction
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 34-2 (continued). Histopathological findings of female rats at the end of the dosing period, satellite group [H.E. staining]

Animal No.	Organs	Findings	Notes
F05049	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	
F05050	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Within normal limits	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown +	
		Hematopoiesis, extramedullary ±	
	Kidney /	Within normal limits	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 34-2 (continued). Histopathological findings of female rats at the end of the dosing period, satellite group [H.E. staining]

Animal No.	Organs	Findings	Notes
F05050	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Cellular infiltration, lymphocyte ±	Interstitial
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	
F05051	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Ultimobranchial body P	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Microgranuloma ±	
	Pancreas /	Atrophy, acinar cell ±	Focal
		Cellular infiltration, lymphocyte ±	Interstitial
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown +	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 34-2 (continued). Histopathological findings of female rats at the end of the dosing period, satellite group [H.E. staining]

Animal No.	Organs	Findings	Notes
F05051	Spleen /	Hematopoiesis, extramedullary ±	
	Kidney /	Cast, hyalin P	Cortex
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	
F05052	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Cellular infiltration, lymphocyte ±	Interstitial
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Within normal limits	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 34-2 (continued). Histopathological findings of female rats at the end of the dosing period, satellite group [H.E. staining]

Animal No.	Organs	Findings	Notes
F05052	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown ±	
		Hematopoiesis, extramedullary ±	
	Kidney /	Basophilic tubule, cortex ±	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	
F05053	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Hyperplasia, epithelial tubule/cord ±	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Hematopoiesis, extramedullary ±	
		Microgranuloma ±	
	Pancreas /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 34-2 (continued). Histopathological findings of female rats at the end of the dosing period, satellite group [H.E. staining]

Animal No.	Organs	Findings	Notes
F05053	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown +	
		Hematopoiesis, extramedullary ±	
	Kidney /	Basophilic tubule, cortex ±	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 34-2 (continued). Histopathological findings of female rats at the end of the dosing period, satellite group [H.E. staining]

Animal No.	Organs	Findings	Notes
F06059	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Hyperplasia, epithelial tubule/cord ±	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Microgranuloma ±	
	Pancreas /	Atrophy, acinar cell ±	Focal
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown +	
		Hematopoiesis, extramedullary +	
	Kidney /	Within normal limits	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 34-2 (continued). Histopathological findings of female rats at the end of the dosing period, satellite group [H.E. staining]

Animal No.	Organs	Findings	Notes
F06059	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	
F06060	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Hyperplasia, epithelial tubule/cord ±	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Within normal limits	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown +	
		Hematopoiesis, extramedullary ±	
	Kidney /	Basophilic tubule, cortex ±	
		Mineralization ±	Cortico-medullary junction
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 34-2 (continued). Histopathological findings of female rats at the end of the dosing period, satellite group [H.E. staining]

Animal No.	Organs	Findings	Notes
F06060	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	
F06061	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Microgranuloma ±	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown +	
		Hematopoiesis, extramedullary +	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 34-2 (continued). Histopathological findings of female rats at the end of the dosing period, satellite group [H.E. staining]

Animal No.	Organs	Findings	Notes
F06061	Kidney /	Basophilic tubule, cortex ±	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	
F06062	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Hyperplasia, epithelial tubule/cord ±	
	Heart /	Degeneration/fibrosis, myocardial ±	Focal
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Within normal limits	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 34-2 (continued). Histopathological findings of female rats at the end of the dosing period, satellite group [H.E. staining]

Animal No.	Organs	Findings	Notes
F06062	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown +	
		Hematopoiesis, extramedullary +	
	Kidney /	Within normal limits	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Cellular infiltration, lymphocyte ±	Interstitial
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	
F06063	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Cellular infiltration, lymphocyte ±	Interstitial
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Within normal limits	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 34-2 (continued). Histopathological findings of female rats at the end of the dosing period, satellite group [H.E. staining]

Animal No.	Organs	Findings	Notes
F06063	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown ±	
		Hematopoiesis, extramedullary +	
	Kidney /	Within normal limits	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 35-1. Results of observations about estrous cycle

Control (vehicle: corn oil)

Animal No.	Pre-mating period						Mating period	
	Pre-treatment period			Treatment period				Times of vaginal estrus observed
	Stage	Type	Mean length (days)	Stage	Type	Mean length (days)	Stage	
F01001	D D E D D D E D D D E D D P	4-day	4.0	E D D P E D D P E D D P E D	4-day	4.0	D P PL	1
F01002	D E D D P E E D D D E E D D	5-day	5.0	P E D D P E D D P E D D D E	4-day	4.0	D D P PL	1
F01003	D D P E D D D P E D D D P E	5-day	5.0	D D P E E D D P E E D D P E	4/5-day	4.5	D D D D D D D D D D D D D D	
F01004	D D D E D D D E D D D E D D	4-day	4.0	D E D D D E D D P E D D D E	4-day	4.0	D D D PL	1
F01005	D P E D D D E D D D E D D D	4-day	4.0	E D D D E D D D E D D D E D	4-day	4.0	D P PL	1
F01006	D E D D D E D D D P E D D D	4/5-day	4.5	E D D P E D D P E D D D E D	4-day	4.0	D P PL	1
F01007	E E D D P E E D D D P E D D	5-day	5.0	D P E D D D E E D D D P E D	5-day	5.0	D D E D D P PL	2
F01008	E D D D P E D D P E E D D D	5-day	5.0	P E D D D P E D D P P E D D	5-day	5.0	D P PL	1
F01009	E D D D P E D D D P E D D D	5-day	5.0	P E D D D P E D D D P E D D	5-day	5.0	D PL	1
F01010	E D D D E D D P E D D P E D	4-day	4.0	D D E D D P E D D D E D D D	4-day	4.0	PL	1
F01011	D E D D P E D D D E D D D E	4-day	4.0	D D P E D D P E D D P E D D	4-day	4.0	D PL	1
F01012	D D E D D D E D D P E D D P	4-day	4.0	E D D D E D D D E D D P E D	4-day	4.0	D P PL	1
Mean			4.5			4.3		1.1
S.D.			0.5			0.5		0.3
(N)			(12)			(12)		(11)

D, diestrus; P, proestrus; E, estrus; PL, vaginal plug; SP, sperm positive

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 35-2. Results of observations about estrous cycle

HA 100 mg/kg

Animal No.	Pre-mating period						Mating period	
	Pre-treatment period			Treatment period				Times of vaginal estrus observed
	Stage	Type	Mean length (days)	Stage	Type	Mean length (days)	Stage	
F02013	D D E D D D E D D D E D D D	4-day	4.0	E D D D E D D D E E D D D E	4/5-day	4.3	PL	1
F02014	D D D E D D D E D D D E D D	4-day	4.0	D E D D D E D D D E D D D E	4-day	4.0	D D D PL	1
F02015	D D P E D D P E D D P E D D	4-day	4.0	P E D D P E D D P E D D P E	4-day	4.0	D D P PL	1
F02016	D D D P E D D D D E D D D E	4/5-day	4.5	D D D E D D P E D D D E D D	4-day	4.0	P PL	1
F02017	D E D D P E D D D E D D P E	4-day	4.0	D D P E D D P E D D D D P E	irregular	5.0	D D D PL	1
F02018	P E D D D E D D D P E D D D	4/5-day	4.5	E E D D D P E D D D P E D D	5-day	5.0	P E E D D D E PL	2
F02019	E D D P E D D P E D D D E D	4-day	4.0	D D E D D P E D D P E D D D	4-day	4.0	E PL	1
F02020	D D D E D D P E D D D E D D	4-day	4.0	P E D D D E D D P E D D D E	4-day	4.0	D D P PL	1
F02021	D D D E D D P E D D D E D D	4-day	4.0	P E D D D E D D D E D D D E	4-day	4.0	D D D PL	1
F02022	E D D D E D D D E D D D E D	4-day	4.0	D D E D D D E D D D E D D D	4-day	4.0	PL	1
F02023	P E D D P E D D P E D D P E	4-day	4.0	D D P E D D P E D D P E D D	4-day	4.0	D PL	1
F02024	D P E D D D D E D D D D E D	5-day	5.0	D P E E D D D P E D D D P E	5-day	5.0	D D D D P D D D D D D D D PL	1
Mean			4.2			4.3		1.1
S.D.			0.3			0.4		0.3
(N)			(12)			(12)		(12)

Significantly different from the control group (*: $p<0.05$, **: $p<0.01$).
D, diestrus; P, proestrus; E, estrus; PL, vaginal plug; SP, sperm positive

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 35-3. Results of observations about estrous cycle

HA 300 mg/kg

Animal No.	Pre-mating period						Mating period	
	Pre-treatment period			Treatment period				Times of vaginal estrus observed
	Stage	Type	Mean length (days)	Stage	Type	Mean length (days)	Stage	
F03025	D D D E D D D P E D D D E E	5-day	5.0	D D D E E D D D P E D D D E E D	5-day	5.0	D P PL	1
F03026	E D D P E D D D E D D P E D	4-day	4.0	D D E D D P E D D D E D D P	4-day	4.0	PL	1
F03027	D E D D D P E D D D E D D D	4/5-day	4.5	P E D D D E D D D E D D D E	4-day	4.0	D D D PL	1
F03028	P E D D D D E D D D D E D D	5-day	5.0	D D E D D D P E D D D P E D	5-day	5.0	D D SP	1
F03029	E D D D D E D D D E E D D D	5-day	5.0	E D D D E D D D E D D D P D	4-day	4.0	D D PL	1
F03030	E D D P E D D P E D D P E D	4-day	4.0	D P E D D P E D D P E D D P	4-day	4.0	PL	1
F03031	D E D D D P E D D D P E D D	5-day	5.0	D P E D D D P E D D D P E D	5-day	5.0	D D E PL	1
F03032	E D D P E D D P E D D P E D	4-day	4.0	D P E D D P E D D P E D D P	4-day	4.0	PL	1
F03033	D D E D D D P E D D D E E D	5-day	5.0	D D P E D D D E E D D D E D	4/5-day	4.5	D D PL	1
F03034	D D E D D P E D D D E D D D	4-day	4.0	E D D P E D D D E D D P E D	4-day	4.0	D D PL	1
F03035	D D E D D D E D D D E D D D	4-day	4.0	E D D D E D D D E D D D E D	4-day	4.0	D D PL	1
F03036	E D D D E D D D E D D P E D	4-day	4.0	D D E D D D E D D D E D D D	4-day	4.0	PL	1
Mean			4.5			4.3		1.0
S.D.			0.5			0.5		0.0
(N)			(12)			(12)		(12)

Significantly different from the control group (*: $p<0.05$, **: $p<0.01$).
D, diestrus; P, proestrus; E, estrus; PL, vaginal plug; SP, sperm positive

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 35-4. Results of observations about estrous cycle

HA 1000 mg/kg

Animal No.	Pre-mating period						Mating period	
	Pre-treatment period			Treatment period				Times of vaginal estrus observed
	Stage	Type	Mean length (days)	Stage	Type	Mean length (days)	Stage	
F04037	D D D D E D D P E D D P E D	4-day	4.0	D P E D D D E D D P E D D P	4-day	4.0	PL	1
F04038	E D D D D E D D D E E D D P	5-day	5.0	E E D D D D E D D P E E D D	5-day	5.0	D PL	1
F04039	D P E D D P E D D D E D D P	4-day	4.0	E D D P E D D P E D D P E D	4-day	4.0	D D PL	1
F04040	D P E D D P E D D P E D D P	4-day	4.0	E D D P E D D P E D D D E D	4-day	4.0	D P PL	1
F04041	D E D D D E D D D E D D D E	4-day	4.0	D D D D D D D D D D D D D P	irregular		D D D E D D D D D D D D D D	
F04042	E D D D E E D D D E E D D D	5-day	5.0	P E D D P E D D D E D D D E	4-day	4.0	PL	1
F04043	D D E D D D E D D P E D D P	4-day	4.0	E D D P E D D P E D D P E D	4-day	4.0	D D PL	1
F04044	E D D D E D D D E D D D E D	4-day	4.0	D D E D D P E D D P E D D P	4-day	4.0	PL	1
F04045	E D D D E D D P E D D P E D	4-day	4.0	D P E D D P E D D P E D D P	4-day	4.0	PL	1
F04046	D D E D D D E D D D E D D D	4-day	4.0	E D D D E D D D E D D D E E	4/5-day	4.3	D D D PL	1
F04047	P E D D D D E D D D P E D D	5-day	5.0	D P E D D D P E D D D P E D	5-day	5.0	D P E PL	1
F04048	D P E D D P E D D P E D D P	4-day	4.0	E D D D E D D P E D D P E D	4-day	4.0	D D PL	1
Mean			4.3			4.2		1.0
S.D.			0.5			0.4		0.0
(N)			(12)			(11)		(11)

Significantly different from the control group (*: $p<0.05$, **: $p<0.01$).
D, diestrus; P, proestrus; E, estrus; PL, vaginal plug; SP, sperm positive

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 36-1. Results of observations about reproductive performance

Control (vehicle: corn oil)

Male No.	Female No.	Copulation	Conception	Pairing days until copulation
M01001	F01001	+	+	3
M01002	F01002	+	+	4
M01003	F01003	-		
M01004	F01004	+	+	4
M01005	F01005	+	+	3
M01006	F01006	+	+	3
M01007	F01007	+	+	7
M01008	F01008	+	+	3
M01009	F01009	+	+	2
M01010	F01010	+	+	1
M01011	F01011	+	+	2
M01012	F01012	+	+	3
Total		+: 11, -: 1	+: 11, -: 0	
Mean				3.2
S.D.				1.5
(N)				(11)

+, confirmed

-, not confirmed

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 36-2. Results of observations about reproductive performance

HA 100 mg/kg

Male No.	Female No.	Copulation	Conception	Pairing days until copulation
M02013	F02013	+	-	1
M02014	F02014	+	+	4
M02015	F02015	+	+	4
M02016	F02016	+	+	2
M02017	F02017	+	+	4
M02018	F02018	+	+	8
M02019	F02019	+	+	2
M02020	F02020	+	+	4
M02021	F02021	+	+	4
M02022	F02022	+	+	1
M02023	F02023	+	+	2
M02024	F02024	+	-	14
Total		+: 12, -: 0	+: 10, -: 2	
Mean				4.2
S.D.				3.6
(N)				(12)

Significantly different from the control group (*: $p<0.05$, **: $p<0.01$).

+, confirmed

-, not confirmed

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 36-3. Results of observations about reproductive performance

HA 300 mg/kg

Male No.	Female No.	Copulation	Conception	Pairing days until copulation
M03026	F03025	+	+	3
M03026	F03026	+	+	1
M03027	F03027	+	+	4
M03028	F03028	+	+	3
M03029	F03029	+	+	3
M03030	F03030	+	+	1
M03031	F03031	+	+	4
M03032	F03032	+	+	1
M03033	F03033	+	+	3
M03034	F03034	+	+	3
M03035	F03035	+	+	3
M03036	F03036	+	+	1
Total		+: 12, -: 0	+: 12, -: 0	
Mean				2.5
S.D.				1.2
(N)				(12)

Significantly different from the control group (*: $p<0.05$, **: $p<0.01$).

+, confirmed

-, not confirmed

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 36-4. Results of observations about reproductive performance

HA 1000 mg/kg

Male No.	Female No.	Copulation	Conception	Pairing days until copulation
M04037	F04037	+	+	1
M04038	F04038	+	+	2
M04039	F04039	+	+	3
M04040	F04040	+	+	3
M04041	F04041	-		
M04042	F04042	+	+	1
M04043	F04043	+	+	3
M04044	F04044	+	+	1
M04045	F04045	+	+	1
M04046	F04046	+	+	4
M04047	F04047	+	+	4
M04048	F04048	+	+	3
Total		+: 11, -: 1	+: 11, -: 0	
Mean				2.4
S.D.				1.2
(N)				(11)

Significantly different from the control group (*: $p<0.05$, **: $p<0.01$).

+, confirmed

-, not confirmed

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 37-1. Observation of offspring (F_1)

Control (vehicle: corn oil)

Dam No.	Gestation length	Number of corpora lutea	Number of implan-tation scars	Implan-tation index	Delivery index (dams)	Number of offspring at birth						Delivery index (offspring)	Birth index	Live birth index	Number of live offspring				External abnormalities [b]	
						Number of offspring	Live			Sex ratio	Dead offspring				4 days		Sex ratio	Viability index		
	(days)			(%)	(%)		Male	Female	Total			(%)	(%)	(%)	Male	Female		(%)	(Number)	(%)
F01001	22	15	14	93.3	+	13	6	7	13	0.46	0	92.9	92.9	100.0	6	7	0.46	100.0	0	0.0
F01002	22	14	14	100.0	+	14	10	4	14	0.71	0	100.0	100.0	100.0	10	4	0.71	100.0	0	0.0
F01003	Not copulated																			
F01004	22	19	19	100.0	+	19	10	9	19	0.53	0	100.0	100.0	100.0	10	9	0.53	100.0	0	0.0
F01005	22	21	19	90.5	+	19	7	11	18	0.39	1	100.0	94.7	94.7	6	11	0.35	94.4	0	0.0
F01006	22	15	14	93.3	+	13	5	8	13	0.38	0	92.9	92.9	100.0	5	8	0.38	100.0	0	0.0
F01007	22	9	9	100.0	+	8	6	2	8	0.75	0	88.9	88.9	100.0	6	2	0.75	100.0	0	0.0
F01008	21	16	15	93.8	+	14	9	5	14	0.64	0	93.3	93.3	100.0	9	5	0.64	100.0	0	0.0
F01009	23	16	16	100.0	+	15	8	7	15	0.53	0	93.8	93.8	100.0	8	7	0.53	100.0	0	0.0
F01010	21	14	14	100.0	+	14	6	8	14	0.43	0	100.0	100.0	100.0	6	8	0.43	100.0	0	0.0
F01011	22	14	14	100.0	+	14	7	7	14	0.50	0	100.0	100.0	100.0	7	7	0.50	100.0	0	0.0
F01012	22	16	16	100.0	+	16	10	6	16	0.63	0	100.0	100.0	100.0	10	6	0.63	100.0	0	0.0
Number of dams	11	11	11	11	11 [a]	11			11	11	11	11	11	11			11	11	11	11
Total		169	164			159	84	74	158		1				83	74			0	
Mean	21.9	15.4	14.9	97.4		14.5	7.6	6.7	14.4	0.54	0.1	96.5	96.0	99.5	7.5	6.7	0.54	99.5		0.0
S.D.	0.5	3.0	2.7	3.8		3.0	1.9	2.5	2.9	0.13	0.3	4.2	4.0	1.6	1.9	2.5	0.13	1.7		0.0
%					100.0															

+: Dams with live offspring, -: dams without live offspring.

a): Number of dams with live offspring.

b): Number of external abnormalities in live offspring at birth.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 37-2. Observation of offspring (F_1)

HA 100 mg/kg

Dam No.	Gestation length (days)	Number of corpora lutea	Number of implan-tation scars	Implan-tation index (%)	Delivery index (dams) (%)	Number of offspring at birth: Number of offspring	Live: Male	Live: Female	Live: Total	Sex ratio	Dead offspring	Delivery index (offspring) (%)	Birth index (%)	Live birth index (%)	Number of live offspring: 4 days: Male	4 days: Female	Sex ratio	Viability index (%)	External abnormalities b) (Number)	(%)
F02013	Not pregnant																			
F02014	22	17	17	100.0	+	14	8	6	14	0.57	0	82.4	82.4	100.0	8	6	0.57	100.0	0	0.0
F02015	22	16	16	100.0	+	15	8	7	15	0.53	0	93.8	93.8	100.0	8	7	0.53	100.0	0	0.0
F02016	22	19	18	94.7	+	18	8	10	18	0.44	0	100.0	100.0	100.0	8	10	0.44	100.0	0	0.0
F02017	22	12	6	50.0	+	6	0	6	6	0.00	0	100.0	100.0	100.0	0	6	0.00	100.0	0	0.0
F02018	22	17	17	100.0	+	16	6	10	16	0.38	0	94.1	94.1	100.0	6	10	0.38	100.0	0	0.0
F02019	22	16	16	100.0	+	15	9	6	15	0.60	0	93.8	93.8	100.0	9	6	0.60	100.0	0	0.0
F02020	22	18	16	88.9	+	15	7	8	15	0.47	0	93.8	93.8	100.0	7	8	0.47	100.0	0	0.0
F02021	21	16	16	100.0	+	13	8	5	13	0.62	0	81.3	81.3	100.0	8	5	0.62	100.0	0	0.0
F02022	22	15	15	100.0	+	14	7	7	14	0.50	0	93.3	93.3	100.0	7	7	0.50	100.0	0	0.0
F02023	21	17	17	100.0	+	15	5	10	15	0.33	0	88.2	88.2	100.0	5	10	0.33	100.0	0	0.0
F02024	Not pregnant																			
Number of dams	10	10	10	10	10 a)	10			10	10	10	10	10	10			10	10	10	10
Total		163	154			141	66	75	141		0				66	75			0	
Mean	21.8	16.3	15.4	93.4		14.1	6.6	7.5	14.1	0.44	0.0	92.1	92.1	100.0	6.6	7.5	0.44	100.0		0.0
S.D.	0.4	1.9	3.4	15.7		3.1	2.6	1.9	3.1	0.18	0.0	6.4	6.4	0.0	2.6	1.9	0.18	0.0		0.0
%					100.0															
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS		NS
Statistical method	AN	AN	AN	KW	AN	AN	AN	AN	AN	AN	AN	DU	DU	KW	AN	AN	AN	AN		AN

Significantly different from the control group (*: P<0.05, **: P<0.01).

+: Dams with live offspring, -: dams without live offspring.

a): Number of dams with live offspring.

b): Number of external abnormalities in live offspring at birth.

NS: Not significantly different from the control group.

AN: Analysis by variance (one-way layout).

DU: Analysis by Dunnett's test.

KW: Analysis by Kruskal-Wallis' test (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 37-3. Observation of offspring (F_1)

HA 300 mg/kg

Dam No.	Gestation length (days)	Number of corpora lutea	Number of implantation scars	Implantation index (%)	Delivery index (dams) (%)	Number of offspring at birth: Number of offspring	Live: Male	Live: Female	Live: Total	Sex ratio	Dead offspring	Delivery index (offspring) (%)	Birth index (%)	Live birth index (%)	Number of live offspring 4 days: Male	4 days: Female	Sex ratio	Viability index (%)	External abnormalities b) (Number)	(%)
F03025	22	17	17	100.0	+	17	11	6	17	0.65	0	100.0	100.0	100.0	11	6	0.65	100.0	0	0.0
F03026	22	15	15	100.0	+	13	6	7	13	0.46	0	86.7	86.7	100.0	6	7	0.46	100.0	0	0.0
F03027	22	12	12	100.0	+	11	7	4	11	0.64	0	91.7	91.7	100.0	7	4	0.64	100.0	0	0.0
F03028	22	15	15	100.0	+	15	5	10	15	0.33	0	100.0	100.0	100.0	5	10	0.33	100.0	0	0.0
F03029	22	19	19	100.0	+	18	11	7	18	0.61	0	94.7	94.7	100.0	11	7	0.61	100.0	0	0.0
F03030	21	16	16	100.0	+	15	8	7	15	0.53	0	93.8	93.8	100.0	8	7	0.53	100.0	0	0.0
F03031	22	14	14	100.0	+	14	8	6	14	0.57	0	100.0	100.0	100.0	8	6	0.57	100.0	0	0.0
F03032	-	14	2	14.3	-	Not delivery														
F03033	22	13	7	53.8	+	7	3	3	6	0.50	1	100.0	85.7	85.7	3	3	0.50	100.0	0	0.0
F03034	22	14	14	100.0	+	12	5	7	12	0.42	0	85.7	85.7	100.0	5	7	0.42	100.0	0	0.0
F03035	22	16	16	100.0	+	16	10	6	16	0.63	0	100.0	100.0	100.0	10	6	0.63	100.0	0	0.0
F03036	22	17	17	100.0	+	16	9	7	16	0.56	0	94.1	94.1	100.0	9	7	0.56	100.0	0	0.0
Number of dams	11	12	12	12	11 a)	11			11	11	11	11	11	11			11	11	11	11
Total		182	164			154	83	70	153		1				83	70			0	
Mean	21.9	15.2	13.7	89.0		14.0	7.5	6.4	13.9	0.54	0.1	95.2	93.9	98.7	7.5	6.4	0.54	100.0		0.0
S.D.	0.3	1.9	4.8	27.0		3.1	2.6	1.8	3.4	0.10	0.3	5.4	5.8	4.3	2.6	1.8	0.10	0.0		0.0
%					91.7															
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS		NS
Statistical method	AN	AN	AN	KW	AN	AN	AN	AN	AN	AN	AN	DU	DU	KW	AN	AN	AN	AN		AN

Significantly different from the control group (*: P<0.05, **: P<0.01).

+: Dams with live offspring, -: dams without live offspring.

a): Number of dams with live offspring.

b): Number of external abnormalities in live offspring at birth.

NS: Not significantly different from the control group.

AN: Analysis by variance (one-way layout).

DU: Analysis by Dunnett's test.

KW: Analysis by Kruskal-Wallis' test (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 37-4. Observation of offspring (F_1)

HA 1000 mg/kg

Dam No.	Gestation length (days)	Number of corpora lutea	Number of implan-tation scars	Implan-tation index (%)	Delivery index (dams) (%)	Number of offspring at birth: Number of offspring	Live: Male	Live: Female	Live: Total	Sex ratio	Dead offspring	Delivery index (offspring) (%)	Birth index (%)	Live birth index (%)	Number of live offspring 4 days: Male	4 days: Female	Sex ratio	Viability index (%)	External abnormalities b) (Number)	(%)
F04037	22	14	14	100.0	+	12	5	7	12	0.42	0	85.7	85.7	100.0	5	7	0.42	100.0	0	0.0
F04038	22	17	14	82.4	+	12	9	3	12	0.75	0	85.7	85.7	100.0	9	3	0.75	100.0	0	0.0
F04039	21	16	15	93.8	+	14	7	7	14	0.50	0	93.3	93.3	100.0	7	7	0.50	100.0	0	0.0
F04040	22	15	15	100.0	+	12	6	6	12	0.50	0	80.0	80.0	100.0	6	6	0.50	100.0	0	0.0
F04041	Not copulated																			
F04042	21	16	16	100.0	+	14	11	3	14	0.79	0	87.5	87.5	100.0	11	3	0.79	100.0	0	0.0
F04043	22	15	15	100.0	+	14	9	5	14	0.64	0	93.3	93.3	100.0	9	5	0.64	100.0	0	0.0
F04044	22	14	14	100.0	+	14	8	6	14	0.57	0	100.0	100.0	100.0	8	6	0.57	100.0	0	0.0
F04045	21	16	16	100.0	+	15	8	7	15	0.53	0	93.8	93.8	100.0	8	7	0.53	100.0	0	0.0
F04046	22	14	14	100.0	+	11	5	6	11	0.45	0	78.6	78.6	100.0	5	6	0.45	100.0	0	0.0
F04047	22	10	8	80.0	+	6	3	3	6	0.50	0	75.0	75.0	100.0	3	3	0.50	100.0	0	0.0
F04048	21	15	14	93.3	+	14	7	6	13	0.54	1	100.0	92.9	92.9	7	6	0.54	100.0	0	0.0
Number of dams	11	11	11	11	11 a)	11			11	11	11	11	11	11			11	11	11	11
Total		162	155			138	78	59	137		1				78	59			0	
Mean	21.6	14.7	14.1	95.4		12.5	7.1	5.4	12.5	0.56	0.1	88.4	87.8	99.4	7.1	5.4	0.56	100.0		0.0
S.D.	0.5	1.8	2.2	7.5		2.5	2.3	1.6	2.5	0.12	0.3	8.4	7.7	2.1	2.3	1.6	0.12	0.0		0.0
%					100.0															
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	*	**	NS	NS	NS	NS	NS		NS
Statistical method	AN	AN	AN	KW	AN	AN	AN	AN	AN	AN	AN	DU	DU	KW	AN	AN	AN	AN		AN

Significantly different from the control group (*: P<0.05, **: P<0.01).
+: Dams with live offspring, -: dams without live offspring.
a): Number of dams with live offspring.
b): Number of external abnormalities in live offspring at birth.
Significantly different from control (vehicle: corn oil) (**: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).
DU: Analysis by Dunnett's test.
KW: Analysis by Kruskal-Wallis' test (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 38-1. Body weights of offspring (F_1) before weaning

Control (vehicle: corn oil)

Dam No.	Days after birth							
	Male body weight				Female body weight			
	0		4		0		4	
F01001	6.8	(6)	12.0	(6)	6.4	(7)	11.4	(7)
F01002	6.5	(10)	11.0	(10)	6.2	(4)	10.3	(4)
F01003	Not copulated							
F01004	6.0	(10)	9.3	(10)	5.8	(9)	9.1	(9)
F01005	5.8	(7)	8.7	(6)	5.7	(11)	8.3	(11)
F01006	7.0	(5)	11.6	(5)	6.7	(8)	11.2	(8)
F01007	7.6	(6)	13.4	(6)	7.0	(2)	12.6	(2)
F01008	6.2	(9)	9.7	(9)	5.9	(5)	9.6	(5)
F01009	7.6	(8)	11.0	(8)	7.1	(7)	11.0	(7)
F01010	6.0	(6)	8.9	(6)	5.9	(8)	8.9	(8)
F01011	6.8	(7)	11.5	(7)	6.4	(7)	10.7	(7)
F01012	6.1	(10)	9.6	(10)	5.9	(6)	9.8	(6)
Number of dams	11		11		11		11	
Mean	6.6		10.6		6.3		10.3	
S.D.	0.6		1.5		0.5		1.3	

Each value shows mean per dam (g).

Figures in parentheses indicate number of offspring.

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 38-2. Body weights of offspring (F_1) before weaning

HA 100 mg/kg

Dam No.	Days after birth							
	Male body weight				Female body weight			
	0		4		0		4	
F02013	Not pregnant							
F02014	6.9	(8)	11.5	(8)	6.5	(6)	10.6	(6)
F02015	6.6	(8)	10.4	(8)	6.2	(7)	10.1	(7)
F02016	6.3	(8)	10.4	(8)	5.9	(10)	9.4	(10)
F02017					6.8	(6)	13.3	(6)
F02018	6.5	(6)	10.6	(6)	6.2	(10)	10.0	(10)
F02019	6.5	(9)	10.5	(9)	6.4	(6)	10.6	(6)
F02020	6.5	(7)	10.8	(7)	6.3	(8)	10.3	(8)
F02021	6.0	(8)	9.7	(8)	5.8	(5)	9.3	(5)
F02022	6.9	(7)	11.4	(7)	6.7	(7)	11.5	(7)
F02023	5.8	(5)	9.6	(5)	5.7	(10)	9.5	(10)
F02024	Not pregnant							
Number of dams	9		9		10		10	
Mean	6.4		10.5		6.3		10.5	
S.D.	0.4		0.6		0.4		1.2	
Significance	NS		NS		NS		NS	
Statistical method	AN		AN		AN		AN	

Each value shows mean per dam (g).
Figures in parentheses indicate number of offspring.
Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 38-3. Body weights of offspring (F_1) before weaning

HA 300 mg/kg

Dam No.	Days after birth							
	Male body weight				Female body weight			
	0		4		0		4	
F03025	6.5	(11)	9.7	(11)	6.1	(6)	9.3	(6)
F03026	6.8	(6)	11.3	(6)	6.4	(7)	10.7	(7)
F03027	7.1	(7)	12.2	(7)	6.9	(4)	11.8	(4)
F03028	7.0	(5)	11.9	(5)	6.5	(10)	11.0	(10)
F03029	6.1	(11)	9.5	(11)	5.8	(7)	8.8	(7)
F03030	6.3	(8)	9.4	(8)	6.1	(7)	9.3	(7)
F03031	6.7	(8)	10.8	(8)	6.2	(6)	10.2	(6)
F03032	Not delivery							
F03033	7.5	(3)	14.1	(3)	7.2	(3)	13.0	(3)
F03034	7.6	(5)	12.5	(5)	7.2	(7)	12.2	(7)
F03035	6.4	(10)	10.2	(10)	6.1	(6)	9.8	(6)
F03036	6.5	(9)	10.5	(9)	6.1	(7)	9.8	(7)
Number of dams	11		11		11		11	
Mean	6.8		11.1		6.4		10.5	
S.D.	0.5		1.5		0.5		1.3	
Significance	NS		NS		NS		NS	
Statistical method	AN		AN		AN		AN	

Each value shows mean per dam (g).
Figures in parentheses indicate number of offspring.
Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 38-4. Body weights of offspring (F_1) before weaning

HA 1000 mg/kg

Dam No.	Days after birth							
	Male body weight				Female body weight			
	0		4		0		4	
F04037	7.0	(5)	11.9	(5)	7.0	(7)	11.8	(7)
F04038	6.7	(9)	11.5	(9)	6.2	(3)	10.6	(3)
F04039	6.1	(7)	9.5	(7)	5.7	(7)	8.6	(7)
F04040	7.4	(6)	12.7	(6)	7.1	(6)	12.5	(6)
F04041	Not copulated							
F04042	6.0	(11)	9.9	(11)	6.1	(3)	10.1	(3)
F04043	6.5	(9)	11.0	(9)	6.3	(5)	10.7	(5)
F04044	6.6	(8)	11.6	(8)	6.8	(6)	11.7	(6)
F04045	6.2	(8)	9.6	(8)	5.5	(7)	8.6	(7)
F04046	7.0	(5)	12.4	(5)	6.6	(6)	11.9	(6)
F04047	7.3	(3)	13.7	(3)	7.1	(3)	14.0	(3)
F04048	5.7	(7)	9.4	(7)	5.4	(6)	9.2	(6)
Number of dams	11		11		11		11	
Mean	6.6		11.2		6.3		10.9	
S.D.	0.6		1.5		0.6		1.7	
Significance	NS		NS		NS		NS	
Statistical method	AN		AN		AN		AN	

Each value shows mean per dam (g).
Figures in parentheses indicate number of offspring.
Significantly different from the control group (*: P<0.05, **: P<0.01).
NS: Not significantly different from the control group.
AN: Analysis by variance (one-way layout).

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 39-1. General conditions in offspring (F_1) before weaning

Control (vehicle: corn oil)

Dam No.	Number of offspring and general conditions	Days after birth				
		0	1	2	3	4
F01001	Number of offspring	13	13	13	13	13
	General appearance, No abnormality	13	13	13	13	13
F01002	Number of offspring	14	14	14	14	14
	General appearance, No abnormality	14	14	14	14	14
F01003	Not copulated					
F01004	Number of offspring	19	19	19	19	19
	General appearance, No abnormality	19	19	19	19	19
F01005	Number of offspring	18	18	17	17	17
	General appearance, No abnormality	18	17	17	17	17
	General appearance, Death	0	1	0	0	0
F01006	Number of offspring	13	13	13	13	13
	General appearance, No abnormality	13	13	13	13	13
F01007	Number of offspring	8	8	8	8	8
	General appearance, No abnormality	8	8	8	8	8
F01008	Number of offspring	14	14	14	14	14
	General appearance, No abnormality	14	14	14	14	14
F01009	Number of offspring	15	15	15	15	15
	General appearance, No abnormality	15	15	15	15	15
F01010	Number of offspring	14	14	14	14	14
	General appearance, No abnormality	14	14	14	14	14
F01011	Number of offspring	14	14	14	14	14
	General appearance, No abnormality	14	14	14	14	14
F01012	Number of offspring	16	16	16	16	16
	General appearance, No abnormality	16	16	16	16	16
	Number of offspring	158	158	157	157	157
	General appearance, No abnormality	158	157	157	157	157
	General appearance, Death		1			

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 39-2. General conditions in offspring (F_1) before weaning

HA 100 mg/kg

Dam No.	Number of offspring and general conditions	Days after birth				
		0	1	2	3	4
F02013	Not pregnant					
F02014	Number of offspring	14	14	14	14	14
	General appearance, No abnormality	14	14	14	14	14
F02015	Number of offspring	15	15	15	15	15
	General appearance, No abnormality	15	15	15	15	15
F02016	Number of offspring	18	18	18	18	18
	General appearance, No abnormality	18	18	18	18	18
F02017	Number of offspring	6	6	6	6	6
	General appearance, No abnormality	6	6	6	6	6
F02018	Number of offspring	16	16	16	16	16
	General appearance, No abnormality	16	16	16	16	16
F02019	Number of offspring	15	15	15	15	15
	General appearance, No abnormality	15	15	15	15	15
F02020	Number of offspring	15	15	15	15	15
	General appearance, No abnormality	15	15	15	15	15
F02021	Number of offspring	13	13	13	13	13
	General appearance, No abnormality	13	13	13	13	13
F02022	Number of offspring	14	14	14	14	14
	General appearance, No abnormality	14	14	14	14	14
F02023	Number of offspring	15	15	15	15	15
	General appearance, No abnormality	15	15	15	15	15
F02024	Not pregnant					
	Number of offspring	141	141	141	141	141
	General appearance, No abnormality	141	141	141	141	141

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 39-3. General conditions in offspring (F_1) before weaning

HA 300 mg/kg

Dam No.	Number of offspring and general conditions	Days after birth				
		0	1	2	3	4
F03025	Number of offspring	17	17	17	17	17
	General appearance, No abnormality	17	17	17	17	17
F03026	Number of offspring	13	13	13	13	13
	General appearance, No abnormality	13	13	13	13	13
F03027	Number of offspring	11	11	11	11	11
	General appearance, No abnormality	11	11	11	11	11
F03028	Number of offspring	15	15	15	15	15
	General appearance, No abnormality	15	15	15	15	15
F03029	Number of offspring	18	18	18	18	18
	General appearance, No abnormality	18	18	18	18	18
F03030	Number of offspring	15	15	15	15	15
	General appearance, No abnormality	15	15	15	15	15
F03031	Number of offspring	14	14	14	14	14
	General appearance, No abnormality	14	14	14	14	14
F03032	Not delivery					
F03033	Number of offspring	6	6	6	6	6
	General appearance, No abnormality	6	6	6	6	6
F03034	Number of offspring	12	12	12	12	12
	General appearance, No abnormality	12	12	12	12	12
F03035	Number of offspring	16	16	16	16	16
	General appearance, No abnormality	16	16	16	16	16
F03036	Number of offspring	16	16	16	16	16
	General appearance, No abnormality	16	16	16	16	16
	Number of offspring	153	153	153	153	153
	General appearance, No abnormality	153	153	153	153	153

Combined repeat dose and reproductive/developmental toxicity screening test of Hexyl acetate by oral administration in rats

Appendix 39-4. General conditions in offspring (F_1) before weaning

HA 1000 mg/kg

Dam No.	Number of offspring and general conditions	Days after birth				
		0	1	2	3	4
F04037	Number of offspring	12	12	12	12	12
	General appearance, No abnormality	12	12	12	12	12
F04038	Number of offspring	12	12	12	12	12
	General appearance, No abnormality	12	12	12	12	12
F04039	Number of offspring	14	14	14	14	14
	General appearance, No abnormality	14	14	14	14	14
F04040	Number of offspring	12	12	12	12	12
	General appearance, No abnormality	12	12	12	12	12
F04041	Not copulated					
F04042	Number of offspring	14	14	14	14	14
	General appearance, No abnormality	14	14	14	14	14
F04043	Number of offspring	14	14	14	14	14
	General appearance, No abnormality	14	14	14	14	14
F04044	Number of offspring	14	14	14	14	14
	General appearance, No abnormality	14	14	14	14	14
F04045	Number of offspring	15	15	15	15	15
	General appearance, No abnormality	15	15	15	15	15
F04046	Number of offspring	11	11	11	11	11
	General appearance, No abnormality	11	11	11	11	11
F04047	Number of offspring	6	6	6	6	6
	General appearance, No abnormality	6	6	6	6	6
F04048	Number of offspring	13	13	13	13	13
	General appearance, No abnormality	13	13	13	13	13
	Number of offspring	137	137	137	137	137
	General appearance, No abnormality	137	137	137	137	137

信頼性保証書

表題　　酢酸ヘキシルのラットを用いる反復投与毒性・生殖発生毒性併合試験

試験番号　　R-15-003

この試験に関する信頼性保証部門による査察および監査状況等は下記のとおりであった。

査察・監査項目	査察・監査年月日	運営管理者および試験責任者への報告年月日
試験計画書	2015年 9月 7日	2015年 9月 7日
試験計画書変更書 R-15-003-No.1	2015年10月13日	2015年10月13日
動物の受入れおよび検疫	2015年 9月14日	2015年 9月15日
性周期観察	2015年 9月16日	2015年 9月16日
原体の安定性(実験開始前)	2015年 9月16日	2015年 9月16日
媒体中の安定性(安定性試験開始日)	2015年 9月17日	2015年 9月17日
群分け、検体調製および含量試験	2015年 9月28日	2015年 9月28日
体重測定、給餌量測定、投与および一般状態の観察	2015年 9月29日	2015年 9月29日
詳細な症状観察	2015年10月 6日	2015年10月 6日
交尾確認	2015年10月14日	2015年10月14日
尿検査	2015年11月4、5日	2015年11月 5日
分娩状態および出生児の観察	2015年11月 5日	2015年11月 5日
機能検査	2015年11月 6日	2015年11月 6日
出生児剖検、採血、雄雌動物剖検、血液学的検査、血液生化学的検査、器官重量測定および固定	2015年11月10日	2015年11月10日
病理組織学検査(標本作製:包埋)	2015年11月25日	2015年11月25日
報告書草案および生データ	2016年 1月27～29日、2016年 2月 1日	2016年 2月 1日
最終報告書	2016年 3月 1日	2016年 3月 1日

試験は、「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)を遵守して実施され、また、この報告書は試験に使用された方法および手順を正確に記載し、記載された結果は試験の生データを正確に反映していることを保証する。

2016年3月1日

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