R-1100

原本

最　終　報　告　書

酢酸ヘキセニルのラットを用いた
経口投与による反復投与毒性･生殖発生毒性併合試験

試験番号：R-1100

試験期間：2012 年 9 月 3 日-2013 年 3 月 28 日

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

試験委託者
厚生労働省　医薬食品局　審査管理課　化学物質安全対策室
〒100-8916　東京都千代田区霞が関 1-2-2

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

1. GLP 陳述書

試験番号　：　R-1100

試験表題　：　酢酸ヘキセニルのラットを用いた経口投与による
反復投与毒性・生殖発生毒性併合試験

本試験は以下に示す基準を遵守して実施したものであります。

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

[redacted]　2013 年 3 月 28 日 [redacted]

試験責任者
株式会社ボゾリサーチセンター　御殿場研究所

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3. 試験実施概要

3.1 試験番号

R-1100

3.2 試験表題

酢酸ヘキセニルのラットを用いた経口投与による反復投与毒性･生殖発生毒性併合試験

（Combined repeated dose toxicity study with the reproduction / developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats）

3.3 試験目的

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

3.4 試験委託者

厚生労働省　医薬食品局　審査管理課　化学物質安全対策室

〒100-8916　東京都千代田区霞が関 1-2-2

3.5 試験受託者

株式会社ボゾリサーチセンター

〒151-0065　東京都渋谷区大山町 36-7

3.6 試験実施施設

株式会社ボゾリサーチセンター　御殿場研究所

〒412-0039　静岡県御殿場市かまど 1284

3.7 被験物質

製造者	:	Atomax Chemicals Co., Ltd
名称	:	酢酸ヘキセニル
別名	:	Leaf acetate
CAS 番号	:	3681-71-8
官報公示整理番号	:	2-760、2-2533
入手日	:	2012 年 7 月 20 日

3.8 試験日程

試験開始日	:	2012 年　9 月　3 日
被験物質出庫日	:	2012 年　9 月 19 日

動物入荷日　　：　2012 年　9 月　5 日
実験開始日（投与開始日）
　　：　2012 年　9 月 25 日
交配開始日　　：　2012 年 10 月　9 日
分娩開始日　　：　2012 年 10 月 31 日
母動物剖検開始日　：　2012 年 11 月　5 日
投与終了剖検日　：　2012 年 11 月　6 日　（雄及び非交配群）
回復開始日　　：　2012 年 11 月　6 日
回復終了剖検日　：　2012 年 11 月 20 日
動物試験終了日　：　2012 年 11 月 20 日
実験終了日（病理組織学検査終了日）
　　：　2012 年 12 月 28 日
試験終了日　　：　2013 年　3 月 28 日

3.9　試験責任者

株式会社ボゾリサーチセンター　御殿場研究所　研究部
[redacted]

3.10　試験担当者

試験主担当者　　：
被験物質保存責任者：
臨床検査責任者　：
化学分析責任者　：
病理検査責任者　：
統計解析責任者　：
[redacted]

3.11　試験成績の信頼性に影響を及ぼしたと思われる環境要因

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

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

動物番号 1009、2008、1104、1116、1119 の上皮小体が標本上欠落していた。しかし、検索動物では 1 例（動物番号 1116）のみであり、その他は検索対象外の動物であることから、病理組織学的評価は可能と判断されたため、試験成績へ及ぼす影響はなかった。

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

3.13　資料保存

株式会社ボゾリサーチセンターの保存方法に従い、試験計画書原本、記録文書、生データ、報告書類（最終報告書は原本）及び標本（被験物質保存サンプルを含む）は株式会社ボゾリサーチセンター御殿場研究所の資料保存施設に最終報告書提出後5年間保存する。期間終了後の保存については、厚生労働省医薬食品局審査管理課化学物質安全対策室と株式会社ボゾリサーチセンター間で協議し、その処置を決定する。ただし、長期保存に耐えられない生体試料（尿、血漿、血清）及び膣垢標本については、試験終了までに廃棄した。また、死産児、死亡児及び生後4日生存児については、出生率及び生後4日生存率に被験物質投与の影響が認められなかったため試験終了までに廃棄した。

3.14　試験責任者の記名・なつ印

[redacted]　2013 年 3 月 28 日 [redacted]

4. 要約

酢酸ヘキセニルの 0（対照群：コーン油）、100、300 及び 1000 mg/kg を Sprague-Dawley 系 SPF ラット（交配群として雌雄各 12 匹/群、雌には非交配群として対照群及び 1000 mg/kg 投与群に各 10 匹を追加）の雄には交配前 14 日間に加え交配期間を通して剖検前日まで（42 日間）、雌には交配前 14 日間に加え交配期間及び妊娠期間を通して授乳 4 日まで(41~48 日間)、非交配群雌には 42 日間強制経口投与し、反復投与毒性及び生殖発生毒性を検討した。更に、0 及び 1000 mg/kg 投与群の一部の動物（交配群雄 5 匹と非交配群雌 5 匹）については雄及び非交配群雌ともに 42 日間投与した後 14 日間の回復期間を設け、毒性変化の可逆性を検討した。

4.1 反復投与毒性

いずれの投与群においても死亡動物はみられず、1000 mg/kg 投与群で精嚢及び前立腺の重量に高値が認められた以外には、いずれの検査にも被験物質投与の影響は認められなかった。

4.2 生殖発生毒性

親動物及び児動物のいずれの検査においても、被験物質投与による影響は認められなかった。

これらの結果から、本試験条件下において、本被験物質の反復投与毒性に対する無影響量は雄で 300 mg/kg、雌で 1000 mg/kg、無毒性量は雌雄ともに 1000 mg/kg と判断した。また、雌雄親動物と児動物における生殖発生毒性に対する無影響量及び無毒性量はいずれも 1000 mg/kg と判断した。

5. 緒言

厚生労働省医薬食品局審査管理課化学物質安全対策室の委託により、酢酸ヘキセニルのラットを用いた経口投与による反復投与毒性･生殖発生毒性併合試験を実施したので、その成績を報告する。

なお、本試験は以下の基準を遵守し、ガイドライン等に準拠して、株式会社ボゾリサーチセンターで実施した。また、本試験は試験実施施設の動物実験委員会の承認を受けて実施した。

5.1 GLP

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

5.2 毒性試験ガイドライン

- 「新規化学物質等に係る試験の方法について」
  （平成 23 年 3 月 31 日：薬食発 0331 第 7 号、平成 23･03･29 製局第 5 号、環保企発第 110331009 号）

5.3 動物の福祉

- 「動物の愛護及び管理に関する法律」
  （昭和 48 年 10 月 1 日法律第 105 号、最終改正：平成 23 年 8 月 30 日法律第 105 号）
- 「実験動物の飼養及び保管並びに苦痛の軽減に関する基準」
  （平成 18 年 4 月 28 日環境省告示第 88 号）
- 「動物実験の適正な実施に向けたガイドライン」
  （日本学術会議 平成 18 年 6 月 1 日）

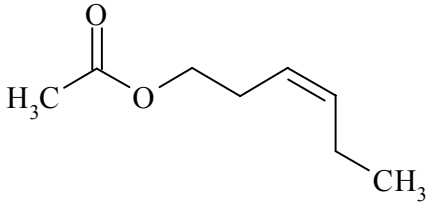
6. 試験材料及び方法

6.1 被験物質及び媒体

6.1.1 被験物質

酢酸ヘキセニルは[redacted]から以下の情報とともに購入した。また、試験開始前に赤外吸収スペクトルの測定により特性が確認されている（試験番号：A-2511、添付資料 1）。

製造者	:	Atomax Chemicals Co., Ltd
名称	:	酢酸ヘキセニル
別名	:	Leaf acetate
英語名称	:	(Z)-hex-3-enyl acetate
CAS 番号	:	3681-71-8
官報公示整理番号	:	2-760、2-2533
構造式又は示性式	:	



分子式	:	$C_8H_{14}O_2$
分子量	:	142.20
常温における性状	:	無色透明液体
沸点	:	66°C(12 mmHg)*
引火点	:	57°C(closed cup)*
ロット番号	:	120707K2-2
純度	:	99.16%
不純物	:	不明
比重	:	0.899(25/25°C)
屈折率	:	1.428(20°C)
保存条件	:	密栓、冷暗所
保存方法	:	気密容器に入れ冷蔵庫内（許容値：1~10°C、実測値：2~8°C）に保存した。
保存場所	:	御殿場研究所被験物質保存室、第 2 研究棟 4 階被験物質調製室及び生化学部標準物質保存場所
安定性	:	投与期間終了後に株式会社ボゾリサーチセンター御殿場研究所において、残余被験物質の赤外吸収スペクトルを確認した結果、実験実施前に確認した参照スペク

トルとほぼ同様であり安定性に問題はなかった（添付資料 2）。

取扱い上の注意　：　作業場の換気を十分に行い、マスク、保護眼鏡、保護手袋等の適切な保護具を着用し、直接の接触を防ぐ。取り扱い後は、手、顔等を良く洗い、うがいをする。

残量の処理　：　被験物質 5 g を保存試料として御殿場研究所の資料保存施設に保存した。動物試験及び分析終了後の残量は全て焼却処分した。

*　：独立行政法人製品評価技術基盤機構化学物質総合情報システム(CHRIP)に基づく

6.1.2　媒体

名称　：　コーン油
規格　：　生化学用
製造者　：　和光純薬工業株式会社
ロット番号　：　WEN1861
有効期限　：　2017 年 8 月 29 日、2017 年 9 月 30 日
保存方法　：　室温
保存場所　：　御殿場研究所第 2 研究棟 4 階被験物質調製室

なお、媒体については、本試験に先立って実施した被験液中濃度測定法バリデーション及び安定性試験（試験番号：A-2511）[1]において、コーン油中での被験物質の安定性に良好な結果が得られていることから、コーン油を選択した。

6.2　投与液の調製及び保存方法

6.2.1　対照群投与液の採取

被験液調製当日の被験物質を取り扱う前に、対照群投与液として、必要量の媒体を褐色ガラス瓶に貼付したラベルを確認しながら分注した。

6.2.2　被験液の調製

濃度ごとに必要量の被験物質をガラスシリンジで採り、ビーカーに正確に秤取した。秤取した被験物質をメスシリンダーに移すとともに、ビーカーを少量の媒体で数回洗い、その液もメスシリンダーに加えた。手で振り攪拌して混合し、完全に溶解したことを目視により確認した。更に媒体をメスシリンダーに加え規定量にメスアップし、20、60 及び 200 mg/mL 液（低、中及び高用量群投与液）を調製した。調製は 7 日に 1 回以上の頻度で最大 7 日分を一括して行った。残液はポリ瓶に回収又はペーパータオル等に吸着させて焼却処分した。

6.2.3　投与液の保存

褐色ガラス瓶に入れて冷所（冷蔵庫内、許容値：1~10°C、実測値：3.6~8°C）に保

存し、安定性の確認された範囲内で投与に使用した。

6.2.4　　被験液の安定性

本被験物質の 1.01 及び 200 mg/mL 濃度の被験液（媒体：コーン油）は、褐色ガラス瓶に入れ冷所（冷蔵庫内、許容値：1~10°C）で 9 日間、その後室温で 24 時間安定であることが株式会社ボゾリサーチセンターで確認されている（試験番号：A-2511、添付資料 3）[1]。

6.2.5　　被験液の濃度確認

初回投与及び投与 6 週の投与に使用する各濃度の被験液(各 10 mL 採取)について、株式会社ボゾリサーチセンター御殿場研究所で GC により濃度確認を実施した。なお、初回投与に使用する被験液については、投与開始前に確認を行った。その結果、各濃度液における表示値に対する被験物質の割合は 96.8~110.0%であり、いずれも許容範囲内（濃度：表示値に対する割合；100.0±10.0%）であった（添付資料 4、5）ことから、被験液の調製に問題はなかったと考えられた。なお、GC を用いた被験液中濃度測定法バリデーションは株式会社ボゾリサーチセンター御殿場研究所（試験番号：A-2511）[1]で実施された。分析法の概略を以下に示した。

[標準物質]

被験物質から一部分配したものを用いた。

名称	:	酢酸ヘキセニル
ロット番号	:	120707K2-2
保存条件	:	密栓、冷暗所
保存方法	:	気密容器に入れ冷蔵庫内（実測値：3~8°C）に保存した。
保存場所	:	御殿場研究所　被験物質保存室、第 2 研究棟 4 階被験物質調製室及び生化学部標準物質保存場所

[測定実測試料の調製]

各測定試料を任意の場所から n=1 で採取し、以下の表に従い、アセトンで溶解・希釈した測定実測試料を用時調製した。

濃度 (mg/mL)	溶解		希釈		希釈率
	採取量 (mL)	定容量 (mL)	溶解溶液 採取量 (mL)	定容量 (mL)	
20	1	20	2.5	50	400
60	1	30	2.5	100	1200
200	1	100	2.5	100	4000

溶媒：アセトン

[GC システム]

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

[GC 測定条件]

カラム : DB-5（0.53 mm I.D.×25 m、膜厚 5 μm、Agilent Technologies Inc.）
キャリアガス : He
流量モード : コンスタントフローモード
流量 : 5.0 mL/min
注入口 : スプリット注入口
スプリット比 : 5:1
注入口温度 : 250°C
検出器 : Flame ionization detector（FID）
検出器温度 : 250°C
H_2 流量 : 45 mL/min
Air 流量 : 450 mL/min
メイクアップガス（N_2）流量 : 40 mL/min
オーブン温度 : 120°C（Hold 0 分）→200°C（10°C/min、Hold 0 分）
注入量 : 1 μL

6.3 試験動物種及び系統の選択理由

毒性試験法ガイドラインによりげっ歯類を用いた試験が必要とされていることからラットを選択した。また、この試験に使用された系統のラットは一般毒性試験、生殖発生毒性試験に広く用いられ、かつ、その特性がよく知られており、背景資料が豊富であることから選択した。

6.4 試験動物

Sprague-Dawley 系 SPF ラット〔Crl:CD(SD)、日本チャールス・リバー株式会社、筑波飼育センター〕の雄 62 匹及び雌 83 匹をそれぞれ 8 週齢で入手[注)]し、入荷日を馴化 1 日と起算して、3 日間の検疫期間を含む 20 日間の馴化飼育を行った。その間、一般状態の観察（1 回/日）、体重測定（馴化 1、3、6、13 及び 20 日の 5 回）、詳細な一般状態の観察（群分け 3 日前の馴化 17 日に 1 回）を実施した。更に、雄について馴化終了日に陰嚢内の精巣の触診及び陰茎亀頭の観察を実施し、雌については膣垢を検疫期間終了後群分け日まで採取して性周期（検疫期間終了後 14 日間）を調べた。そ

の結果、性周期の異常が 1 例（耳標番号：715）にみられ、赤色尿が雌 1 例（耳標番号：755）、外傷（頸部）が雌 1 例（耳標番号：767）にみられた。それらの異常例を除き、検疫・馴化期間中の一般状態、詳細な一般状態、体重推移、精巣の触診結果及び性周期に異常がなく、性成熟に達した陰茎亀頭であり、健康と思われる雄 62 匹中 48 匹及び雌 80 匹中 68 匹を選択し、10 週齢で投与に使用した。投与開始時（10 週齢）の体重の変動範囲は雄で 372~446 g（平均体重：403 g）、雌は 207~263 g（平均体重：229 g）であり、雌雄それぞれ平均体重の±20%以内であった。

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

注）：試験計画書に従い、動物発注数は雄 60 匹及び雌 80 匹であったが、実際には雄 62 匹及び雌 83 匹が納入された。

6.5　飼育条件

動物は、温度 23±3°C（実測値：21~23°C）、相対湿度 50±20%（実測値：49~55%）、換気回数 10~15 回/h、照明 12 時間/日（07:00~19:00）の動物飼育室（飼育室番号：905 号室）でブラケット式金属製網ケージ（W254×D350×H170 mm：リードエンジニアリング株式会社）に交配中を除いて個別に収容した。なお、妊娠 17 日から授乳 4 日までは、床敷（ホワイトフレーク：日本チャールス・リバー株式会社、ロット番号：2012-2）を入れたプラスチック製エコンケージ（W340×D400×H185 mm：日本クレア株式会社）に 1 腹単位で収容した。

飼料は NMF 固形（放射線滅菌、オリエンタル酵母工業株式会社、ロット番号：120413、120815、120919）をステンレス製給餌器により自由に摂取させた。

飲料水は御殿場市営水道水を自動給水装置（ブラケット式金属製網ケージでの飼育時）又は給水瓶（プラスチック製エコンケージでの飼育時）により自由に摂取させた。

飼料及び床敷中の混入物質の分析に関しては、使用したロットについて Eurofins Scientific Analytics で実施した分析結果を入手した。また、飲料水については、水道法に準拠した施設全体の水質の分析を定期的（年 4 回）に芝浦セムテック株式会社に依頼して得られたデータを入手した。これらのデータにより飼料、床敷及び飲料水中の混入物質が試験成績に影響を与える可能性のないことを確認し、分析報告書の写しを保存した。

6.6　動物の識別

動物は番号（雄：629~690、雌：691~773）が刻印された耳標を入荷時に装着し、個体識別を行った。群分け後は、1000 の位は群（対照群、低、中及び高用量の順）、100 の位は性別（0 番を雄、1 番を雌）、10 と 1 の位は個体番号を示す 4 桁の動物番号を設定した。各飼育ケージに投与量（群）ごとに色分けしたケージラベルを付け、試験番号、投与経路、投与量、性別、動物番号、耳標番号、剖検予定日（雄及び非交配群の雌）、交尾成立日（交配群の雌雄）及び分娩日（交配群の雌）を明記した。

6.7　投与経路、投与期間及び投与回数並びに回復期間とそれらの選択理由

投与経路は毒性試験法ガイドラインに準じ、経口投与を選択した。投与期間は、投与日数として、交配群雌雄ともに交配前 14 日、更に、雄については交配開始後 28 日（計 42 日）、雌については交配期間及び妊娠期間を通して授乳 4 日まで（計 41~48 日）とした。非交配群の雌については 42 日とした。また、不妊であった動物（動物番号 2104）については 40 日とした。回復動物については、42 日の投与期間が終了した後、被験物質投与に起因した変化の可逆性、持続性並びに遅発性毒性等について観察するため、14 日間の回復期間を設けた。投与回数は反復投与試験で一般的に行われている 1 日 1 回とした。

6.8　投与方法

投与方法は、げっ歯類の経口投与に際して一般的な強制経口投与とした。投与容量は 5 mL/kg 体重とし、胃ゾンデを用いて投与液を 08:46~12:23 の間に投与した。ただし、投与時に分娩中であった動物は分娩終了を待って、14:11~16:07 の間に投与した。対照群には媒体のみを同様に投与した。個体ごとの投与液量（表示単位 : 0.1 mL）は、直近の体重を基準に算出した。

6.9　投与量及び群構成

投与量は 100、300 及び 1000 mg/kg の 3 用量とし、試験群はこれらの用量群に媒体を投与する対照群を加え 4 群構成とした。1 群当たりの動物数は交配を行う交配群として各群で雌雄各 12 匹、交配しない非交配群として対照群及び高用量群で雌各 10 匹とした。なお、対照群及び高用量群における雄の群内番号 8 番以降、非交配群雌の群内番号 18 番以降の各 5 匹は、最終投与終了日以降、回復動物とした。群構成を表 1-1. 及び 1-2.に示した。

表 1-1.群構成表（雄）

試験群	投与量 (mg/kg)	被験液濃度 (mg/mL)	投与容量 (mL/kg)	交配群	
				動物数	動物番号
対照群	0	0	5	12	1001~1012 注 1
低用量群	100	20	5	12	2001~2012
中用量群	300	60	5	12	3001~3012
高用量群	1000	200	5	12	4001~4012 注 1

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

表 1-2.群構成表（雌）

試験群	投与量 (mg/kg)	被験液濃度 (mg/mL)	投与容量 (mL/kg)	交配群		非交配群	
				動物数	動物番号	動物数	動物番号
対照群	0	0	5	12	1101~1112	10	1113~1122 注 2
低用量群	100	20	5	12	2101~2112	－	－
中用量群	300	60	5	12	3101~3112	－	－
高用量群	1000	200	5	12	4101~4112	10	4113~4122 注 2

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

6.10　投与量の設定根拠

本試験の投与量は、先に実施した「酢酸ヘキセニルのラットを用いた 14 日間反復経口投与毒性試験（投与量設定試験）、株式会社ボゾリサーチセンター、試験番号:N-R031、投与量：250、500 及び 1000 mg/kg/day」[2]の結果（添付資料 6）を参考に設定した。投与量設定試験では、高用量の 1000 mg/kg 投与群においても死亡はみられず、一般状態、体重、摂餌量、血液化学検査、器官重量及び剖検所見に被験物質投与の影響はみられなかった。しかし、1000 mg/kg 投与群の雌で網赤血球率の高値及び白血球数の低値が認められ、500 mg/kg 投与群の雌で白血球数の低値が認められた。したがって、本試験では毒性試験法ガイドラインに示されている限度試験の最高投与量である 1000 mg/kg を高用量とし、以下公比約 3 で除して 300 及び 100 mg/kg をそれぞれ中及び低用量に設定した。

6.11　観察及び検査の方法

試験日の起算は、投与開始日を投与 1 日、投与 1 日から 7 日を投与 1 週、回復開始日（投与 42 日の翌日）を回復 1 日、回復 1 日から 7 日を回復 1 週、交尾成立日を妊娠 0 日、分娩終了日（出産日）を授乳 0 日、出生日を生後 0 日とし、以下に示す項目について、それぞれ記載の時期に観察及び検査を実施した。

6.11.1　　一般状態の観察

全個体について、検疫・馴化期間中は毎日 1 回、投与期間中は毎日 3 回（投与前、投与直後及び投与 1~3 時間後）、回復期間中は毎日 2 回（午前・午後）、それぞれ生死、身体の外観、姿勢、行動及び排泄物（尿、糞）などの一般状態における異常の有無を観察した。なお、投与 2 週以降の動物のハンドリングを伴った定期的な観察は、

詳細な一般状態の観察と兼ねて行った。

6.11.2　詳細な一般状態の観察、機能検査、握力及び自発運動量の測定

詳細な一般状態の観察は全個体について行った。投与開始前（馴化期間中）に 1 回、また、雄及び非交配群は投与期間中及び回復期間中毎週 1 回、交配群雌は交配前投与期間中毎週 1 回、交配期間中、妊娠期間中及び授乳期間中は指定された日（交尾動物は妊娠 1、7、14 及び 20 日、未交尾動物は交配開始後 6 日、分娩動物は授乳 4 日）にそれぞれ行った。

機能検査、握力測定及び自発運動量測定は、各群の 5 匹（雄の群内番号 8~12 番、交配群雌の各群の分娩順で動物番号が若い順[注]、非交配群の群内番号 18~22 番）について行った。投与期間中は交配群の雌で授乳 4 日（投与 41~43 日）に、その他は投与期間終了週（投与 6 週、投与 39 日）に、回復期間中は対照群及び高用量群の雌雄で回復期間終了週（回復 2 週、雌雄ともに回復 11 日）に行った。

上記の観察、検査及び測定は、動物をランダムに配置し、観察者に対して投与量などの情報を制限（ブラインド化）した状態で行った。ただし、自発運動量測定に関しては、ブラインド化を行わなかった。なお、詳細な一般状態の観察及び機能検査の観察・検査結果について、実数データ以外はスコア化した評点法を用いて記録した。

注：交配群雌の検査対象動物を以下に示した。

試験群	動物番号
対照群	1101、1102、1103、1105、1108
低用量群	2101、2105、2106、2108、2112
中用量群	3101、3102、3104、3106、3108
高用量群	4101、4102、4103、4106、4109

1)　詳細な一般状態の観察

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

2)　機能検査

聴覚反応、接近反応、接触反応、痛覚反応、瞳孔反射、空中正向反射、着地開脚幅について検査した。

3)　握力測定

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

4)　自発運動量の測定

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

6.11.3　　体重測定

全個体について、馴化 1、3、6、13 及び 20 日に体重を測定した。交配群の雄及び非交配群の雌は投与 1、8、15、22、29、36、42 日及び剖検日に、回復動物は更に回復 1、8、14 日及び剖検日に、交配群の雌は投与 1、8、15 日、妊娠 0、7、14 及び 20 日、授乳 0 及び 4 日並びに剖検日に体重を測定した。なお、午後の分娩観察時に分娩の終了が確認された個体の授乳 0 日の体重測定（13:46~16:57 の間）を除き、体重測定は測定日の 08:03~11:09 の間（投与期間中は投与前）に行った。剖検日には、前日から約 16 時間絶食させた後､相対器官重量算出に備えて体重を 07:30~09:06 の間に測定した。また、妊娠 25 日未分娩動物及び授乳期間中に全哺育児が死亡した母動物については、搬出前に体重を測定した。

6.11.4　　摂餌量測定

全個体について、交配群の雄及び非交配群の雌は投与 2、8、15、30、36 及び 42 日に、回復動物は更に回復 1、8 及び 14 日に、交配群の雌は投与 2、8 及び 15 日、妊娠 1、7、14 及び 20 日並びに授乳 2 及び 4 日に残餌量を測定し、前日の給餌量との差から 1 匹当たりの 1 日摂餌量を算出した。給餌量及び残餌量の測定は測定日の 08:18~11:09 の間（投与期間中は投与前）に行った。

6.11.5　　腟垢検査

馴化期間中は雌全個体について検疫期間終了後から群分け日まで毎日（午前）腟垢を採取し、性周期異常の有無について調べた。

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

非交配群については、剖検 6 日前から剖検日まで毎日（午前）腟垢を採取し、鏡検した。鏡検結果については、剖検時における性周期ステージの判別のための参考データとした。

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

6.11.6　交配方法

交配前投与期間終了後、交配群の同じ投与群の雌雄を 1:1 で終夜同居させ、翌朝、腟栓形成あるいは腟垢中に精子を確認したものを交尾成立とみなした。交配開始日を 0 日と起算して交尾までに要した日数を求めた。同一雌雄による同居期間は最長 7 日間であった。

6.11.7　分娩及び哺育観察

1)　母動物の観察

交尾の確認された雌動物は妊娠 21 日から妊娠 25 日の午前まで 1 日 2 回（午前・午後、妊娠 25 日は午前に 1 回）分娩の有無並びにその終了を確認するとともに分娩状態の異常の有無（胎盤及び羊膜の処理の有無など）を観察した。交尾成立から分娩終了までを妊娠期間とし、妊娠期間を 0.5 日単位で求めた。ただし、1 日単位で集計した。なお、分娩終了の確認は 17:00 までとした。

分娩が終了した母動物は授乳 4 日まで出生児を哺育させ、児集め、営巣及び授乳を指標として哺育状態を観察し、授乳 5 日に病理学検査に供した。なお、妊娠 25 日の午前までに分娩が終了しなかった 100 mg/kg 投与群の 1 例（動物番号 2104）は、イソフルラン麻酔下で採血後、腹大動脈切断により放血致死させ、病理学検査に供した。妊娠の有無を確認した結果、着床が認められなかったため不妊とみなした。また、授乳期間中に全哺育児が死亡した母動物は、その時点で同様に検査を行った。

2)　出生児の観察

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

生後 4 日まで毎日 1 回、死亡児の有無を確認した。死亡児は肉眼による異常の有無を観察した後、ブアン液で固定して保存した。

生後 4 日に全生存児の性別を判定し、個体別に体重を測定後、肉眼による異常の有無を観察した後、イソフルラン深麻酔下でブアン液に浸漬し、固定して保存した。

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

6.11.8　尿検査（摂水量測定を含む）

投与期間終了週（投与 6 週、投与 36~37 日）及び回復期間終了週（回復 2 週、回復 8~9 日）に検査を実施した。投与期間中は検査当日の投与後に各群の 5 匹（雄の群内番号 8~12 番、非交配群の群内番号 18~22 番）について、回復期間中は回復動物の全個体について、それぞれ採尿器をセットしたケージに収容し、絶食・自由摂水下で 4 時間尿を、次いで自由摂食・自由摂水下でその後の 20 時間尿を採取した。検査項目を表 2.に示した。採取した最初の 4 時間尿について pH 以下沈渣までの検査と尿量を、その後に得られた 20 時間尿について浸透圧、電解質（ナトリウム、カリウム、塩素）及び尿量の測定を行った。尿量は 4 時間の尿量と 20 時間の尿量を合計して 1 日量を算出した。電解質は 20 時間尿について濃度を測定し、測定濃度と 24 時間の尿量から 1 日当たりの排泄量を算出した。摂水量は、採尿器をセットしたケージに収容した状態で前日からの 1 日の摂取量を、給水瓶を用いて測定した。

表 2.尿検査の項目、測定法及び使用機器など

検査項目	測定方法
pH	ﾏﾙﾃｨｽﾃｨｯｸｽ試験紙［ｼｰﾒﾝｽﾍﾙｽｹｱ・ﾀﾞｲｱｸﾞﾉｽﾃｨｸｽ株式会社］[a)]
たん白質	ﾏﾙﾃｨｽﾃｨｯｸｽ試験紙［ｼｰﾒﾝｽﾍﾙｽｹｱ・ﾀﾞｲｱｸﾞﾉｽﾃｨｸｽ株式会社］[a)]
ケトン体	ﾏﾙﾃｨｽﾃｨｯｸｽ試験紙［ｼｰﾒﾝｽﾍﾙｽｹｱ・ﾀﾞｲｱｸﾞﾉｽﾃｨｸｽ株式会社］[a)]
グルコース	ﾏﾙﾃｨｽﾃｨｯｸｽ試験紙［ｼｰﾒﾝｽﾍﾙｽｹｱ・ﾀﾞｲｱｸﾞﾉｽﾃｨｸｽ株式会社］[a)]
潜血	ﾏﾙﾃｨｽﾃｨｯｸｽ試験紙［ｼｰﾒﾝｽﾍﾙｽｹｱ・ﾀﾞｲｱｸﾞﾉｽﾃｨｸｽ株式会社］[a)]
ビリルビン	ﾏﾙﾃｨｽﾃｨｯｸｽ試験紙［ｼｰﾒﾝｽﾍﾙｽｹｱ・ﾀﾞｲｱｸﾞﾉｽﾃｨｸｽ株式会社］[a)]
ウロビリノーゲン	ﾏﾙﾃｨｽﾃｨｯｸｽ試験紙［ｼｰﾒﾝｽﾍﾙｽｹｱ・ﾀﾞｲｱｸﾞﾉｽﾃｨｸｽ株式会社］[a)]
色調	肉眼観察
沈渣	鏡検法
尿量（4 時間量）	目盛付スピッツ管を用いた容量測定（単位：mL）
浸透圧	氷点降下法[b)]（単位：mOsm/kg）
ナトリウム	イオン選択電極法[c)]（単位：mmol/24h）
カリウム	イオン選択電極法[c)]（単位：mmol/24h）
塩素	イオン選択電極法[c)]（単位：mmol/24h）
尿量（20 時間量）	メスシリンダーを用いた容量測定（単位：mL）
摂水量（24 時間量）	重量測定

使用測定機器
a)：尿自動分析装置　クリニテック 500（Siemens Healthcare Diagnostics Inc., Illinois, USA）
b)：自動浸透圧測定装置 オートアンドスタット OM-6030（アークレイ株式会社）
c)：臨床化学自動分析装置　TBA-120FR 形（東芝メディカルシステムズ株式会社）

6.11.9　血液学検査

全例について剖検前日（最終投与日あるいは回復 14 日）から一夜（16~19 時間）絶食させた。各群雌雄各 5 匹（動物番号が若い順、ただし、交配群雌は分娩順の 5 匹[注]）について、イソフルラン麻酔下に開腹し、腹大動脈から EDTA-2K 加採血瓶（SB-41：シスメックス株式会社）に血液を採取した。得られた血液について、次の表 3.-1)に記載した項目及び方法により検査した。なお、採血した全例について、May-Grünwald-Giemsa 染色法による血液塗抹標本を作製した。また、3.8%クエン酸ナトリウム溶液加試験管（血液 9 容に対し 1 容の割合）に採取した血液を遠心分離（3,000 rpm、1,600×g、10 分間）し、得られた血漿について表 3.-2)に記載の項目及び方法により検査した。妊娠 25 日未分娩動物及び授乳期間中に全哺育児が死亡した母動物についても採血し同様に検査した。

注：交配群雌の検査対象動物を以下に示した。

試験群	動物番号
対照群	1101、1102、1103、1105、1108
低用量群	2101、2105、2106、2108、2112
中用量群	3101、3102、3104、3106、3108
高用量群	4101、4102、4103、4106、4109

表 3.血液学検査の項目、測定法及び使用機器など

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

6.11.10　血液化学検査

血液学検査用試料と同時に採取した血液を凝固促進剤入り試験管（ベノジェクト II-オートセップ：テルモ株式会社）に採り、遠心分離（3,000 rpm、1,670×g、10 分間）し、得られた血清について表 4.-1)に記載の項目及び方法により検査した。また、ヘパリン加試験管（血液 1 mL 当たり約 20 単位のヘパリン）に採取した血液を遠心分離（3,000 rpm、1,600×g、10 分間）して得られた血漿について表 4.-2)に記載の項目及び方法により検査した。妊娠 25 日未分娩動物及び授乳期間中に全哺育児が死亡した母動物についても同様に検査した。血清の一部（妊娠 25 日未分娩動物及び授乳期間中に全哺育児が死亡した母動物を除く）は血中ホルモン測定に備え、約 0.5 mL×3 本をサンプルチューブに分注し、−80°C の冷凍庫（許容範囲：−70°C 以下）に保存した。

表 4.血液化学検査の項目、測定法及び使用機器など

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

6.11.11　血中ホルモン測定

他の観察及び検査結果から下垂体-甲状腺系への影響が認められなかったため 6.11.10 で得られた血清について血中ホルモン（T_3、T_4 及び TSH）測定は実施しなかった。

6.11.12　病理学検査

1)　剖検及び器官重量測定

最終投与翌日及び回復期間終了日に全ての生存動物について、採血した動物は採血後に、その他の動物はイソフルラン麻酔下で、腹大動脈切断により放血致死させ、それぞれ体外表並びに頭部、胸部及び腹部の器官・組織の肉眼検査を行った。妊娠 25 日未分娩動物及び授乳期間中に全哺育児が死亡した母動物については、採血して放血致死させた後に剖検を行った。なお、母動物については剖検時に黄体数及び着床痕数を数えた。次いで、全例について、以下に示す器官の重量を測定した。それら器官重量（絶対重量）と剖検時の体重から体重 100 g 当たりの相対重量を算出した。なお、*印をつけた両側性の器官については左右別々に測定し、その合計値で評価した。また、妊娠 25 日未分娩動物及び授乳期間中に全哺育児が死亡した母動物についても同様に器官重量を測定したが、剖検日の体重も含め統計解析の対象から除外した。

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

2)　病理組織学検査

全ての個体について、以下に示す全検査対象器官/組織をリン酸緩衝 10 vol%ホルマリン液で固定し、保存した。固定時に肺にはリン酸緩衝 10 vol%ホルマリン液を注入した。ただし、眼球、視神経はリン酸緩衝液で調製した 3 vol%グルタルアルデヒド・2.5 vol%ホルマリン液で固定後、精巣及び精巣上体はブアン液で固定した後、リン酸緩衝 10 vol%ホルマリン液に置換し保存した。次いで、パラフィン包埋した後、切片とし（下線を施した器官・組織は固定・保存のみとした）、ヘマトキシリン・エオジン（H・E）染色標本を作製した。鏡検は、まず投与終了時剖検群における対照群及び高用量群の採血を行った動物、妊娠 25 日未分娩動物及びその交配相手雄並びに授乳期間中に全哺育児が死亡した母動物の全検査対象器官/組織について行った。両側性の器官については両側を摘出し、坐骨神経、眼球、甲状腺、上皮小体、副腎、顎下腺、腎臓、大腿骨（骨髄を含む）及び大腿部骨格筋は片側、精巣、卵巣、精巣上体及び精嚢（凝固腺含む）は両側並びに子宮は両角部を鏡検した。なお、舌下腺及び視神経は H･E 染色標本作製までとし、病理組織学検査は実施しなかった。その結果、高用量群の雌雄ともに被験物質投与によると考えられる変化はみられなかったため、その他の中及び低用量群並びに回復動物〔肉眼的異常部位（動物番号 4012 の肺、動物番号 1118 の腎臓）を除く〕については、鏡検しなかった。

大脳、小脳（橋を含む）、坐骨神経、脊髄（胸部）、眼球、視神経、ハーダー腺、下垂体、甲状腺、上皮小体、副腎、胸腺、脾臓、顎下リンパ節、腸間膜リンパ節、心臓、胸大動脈、気管、肺（気管支を含む）、舌、喉頭、食道、胃、十二指腸、空腸、回腸（パイエル板を含む）、盲腸、結腸、直腸、顎下腺、舌下腺、肝臓、

膵臓、腎臓、膀胱、精巣、卵巣、精巣上体、子宮、腟、前立腺、精嚢（凝固腺を含む）、皮膚（鼠径部）、乳腺（鼠径部）、胸骨（骨髄を含む）、大腿骨（骨髄を含む）、大腿部骨格筋、個体識別部（耳標を装着した耳介）

6.12　統計解析

6.12.1　　パラメータの算出

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

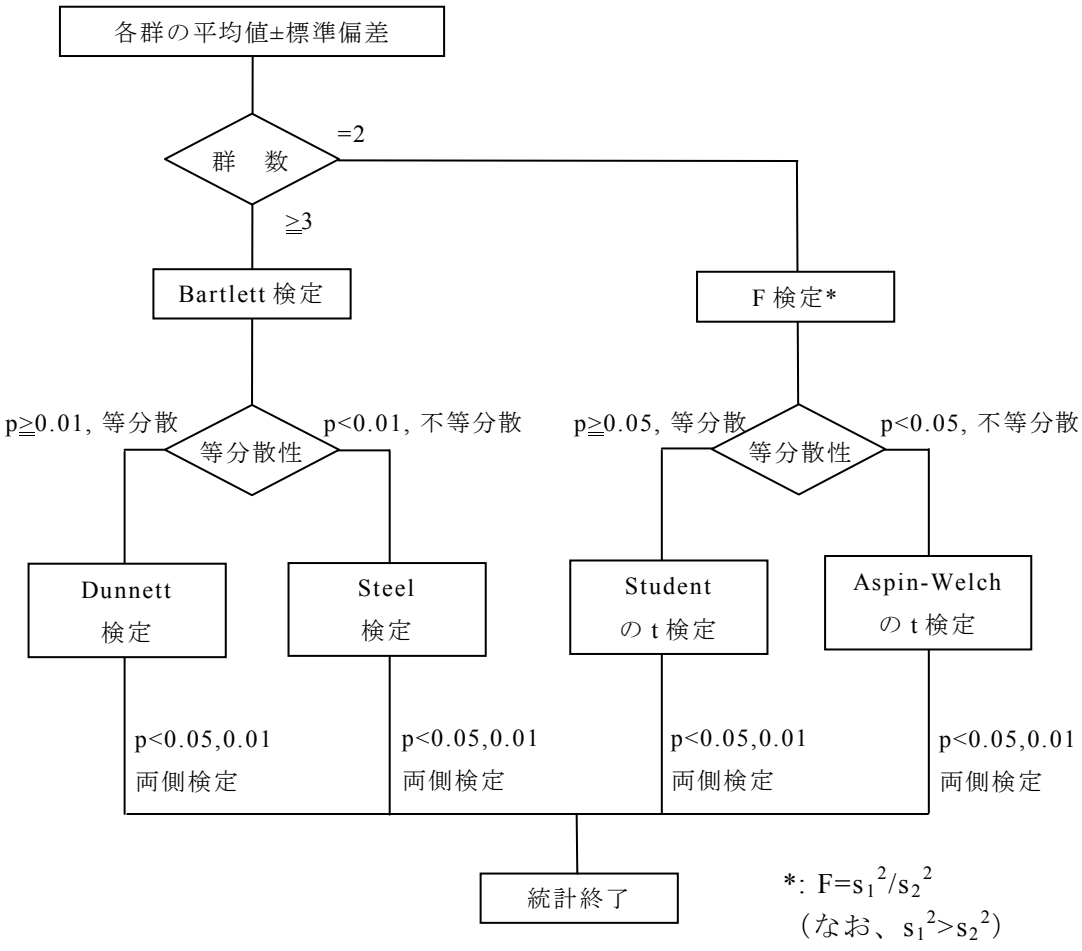
性周期異常率(%) =（性周期異常を示した個体数/観察雌個体数）×100
交尾率(%) =（交尾動物数/同居動物数）×100
授精率(%) =（雌を妊娠させた雄の数/交尾した雄の数）×100
受胎率(%) =（妊娠した雌の数/交尾した雌の数）×100
出産率(%) =（出生児出産雌数/妊娠雌数）×100
妊娠期間(日) = 妊娠 0 日から分娩した日までの日数
着床率(%) =（着床痕数/黄体数）×100
分娩率(%) =（出産児数/着床痕数）×100
死産児率(%) =（死産児数/出産児数）×100
外表異常率(%) =（外表異常児数/出産児数）×100
出生率(%) =（出生児数/出産児数）×100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

6.12.2　　検定

対照群と各用量群との差について以下の手法により統計学的有意性の検定を行った。

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

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



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

性周期異常率、交尾率、授精率、受胎率及び出産率並びに聴覚反応、接近反応、接触反応、痛覚反応、瞳孔反射及び空中正向反射の各反応・反射率は、各群の性周期異常を示した個体数、交尾動物数、雌を妊娠させた雄動物数、妊娠雌動物数、出生児出産雌動物数、正常反射のみられた動物数より算出し、期待度数が 5 以下のセルがみられたため Fisher の直接確率計算法により検定（有意水準 0.05 及び 0.01、両側）を行った[6]。

7. 試験結果

7.1 一般状態（Table 1-1~1-7、Appendix 1-1~1-22）

いずれの投与群においても死亡動物はみられず、いずれの動物にも投与期間及び回復期間を通じて哺育状態を含め異常はみられなかった。なお、100 mg/kg 投与群の 1 例で授乳 1 日に全哺育児が死亡したが、用量との関連性はみられなかった。

7.2 詳細な一般状態の観察、機能検査、握力測定及び自発運動量の測定（Fig. 1~5、Table 2-1~2-84、Appendix 2-1~2-258）

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

いずれの動物にも異常はみられなかった。

7.2.2 手に持っての観察（Table 2-24~2-46、Appendix 2-73~2-144）

いずれの動物にも被験物質投与に関連すると考えられる異常はみられなかった。

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

いずれの動物にも被験物質投与に関連すると考えられる異常はみられなかった。

なお、100 mg/kg 投与群の雄で投与 1 及び 6 週の立ち上がり回数に対照群と比べ有意な高値が認められたが、用量に関連しない変化であった。非交配群雌の投与 2 週の立ち上がり回数に対照群と比べ有意な低値が認められたが、以降の観察時点及び交配群雌の同時点に異常はないことから偶発性と判断した。非交配群雌の回復 1 及び 2 週の立ち上がり回数に対照群と比べ有意な低値が認められたが、僅かな低値でありその他の詳細な一般状態に異常はみられないことから、毒性学的意義はないと判断した。排糞の個数には対照群と各被験物質投与群との間に有意差は認められなかった。

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

1) 投与期間終了週検査

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

2) 回復期間終了週検査

いずれの動物にも聴覚反応、接近反応、接触反応、痛覚反応、瞳孔反射及び空中正向反射に異常はみられず、着地開脚幅には対照群と 1000 mg/kg 投与群との間に有意差は認められなかった。

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

1)　投与期間終了週測定

対照群と各被験物質投与群との間に有意差は認められなかった。

2)　回復期間終了週測定

1000 mg/kg 投与群の雌で対照群と比べ後肢の握力に有意な高値が認められたが、後肢のみの変化であり、投与期間終了週測定に異常はみられていないことから、毒性学的意義はないと判断した。

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

1)　投与期間終了週測定

対照群と各被験物質投与群との間に有意差は認められなかった。

2)　回復期間終了週測定

対照群と 1000 mg/kg 投与群との間に有意差は認められなかった。

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

1)　投与期間

雄の各被験物質投与群ともに投与期間を通じて対照群と同様な体重推移を示し、有意差は認められなかった。

交配群雌及び非交配群雌では交配前、妊娠及び授乳の各期間中、各被験物質投与群ともに対照群と同様な体重推移を示し、有意差は認められなかった。

2)　回復期間

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。

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

1)　投与期間

雄の各被験物質投与群ともに投与期間を通じて対照群と同様な摂餌量を示し、有意差は認められなかった。

交配群雌及び非交配群雌では交配前、妊娠及び授乳の各期間中、各被験物質投与群ともに対照群と同様な摂餌量を示し、有意差は認められなかった。

2)　回復期間

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。

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

1)　投与期間終了週検査

定性項目については、いずれの動物にも異常はみられなかった。

定量項目については、いずれの検査項目においても被験物質投与群と対照群との間に有意差は認められなかった。

2) 回復期間終了週検査

定性項目については、いずれの動物にも異常はみられなかった。

定量項目については、いずれの検査項目においても 1000 mg/kg 投与群と対照群との間に有意差は認められなかった。

7.6 血液学検査（Table 6-1~6-10、Appendix 6-1~6-28）

1) 投与期間終了時検査

雄では 100 及び 300 mg/kg 投与群で対照群と比べフィブリノーゲン量の有意な低値、300 mg/kg 投与群で白血球数及び好中球数の有意な低値が認められたが、用量に依存性のない変化であった。

交配群雌では 1000 mg/kg 投与群で平均赤血球血色素濃度に対照群と比べ有意な高値が認められたが、軽微な変化であり他の赤血球系パラメータに変動はないことから偶発性と判断した。その他に 300 mg/kg 投与群で好酸球数に有意な高値が認められたが、用量に依存性のない変化であった。

非交配群雌の 1000 mg/kg 投与群で、対照群と比べ血小板数に有意な高値が認められたが、軽微な変化であり他の血液凝固系パラメータに変動はないことから生理的変動範囲内と判断した。

2) 回復期間終了時検査

1000 mg/kg 投与群の雌雄ではいずれの検査項目においても対照群との間に有意差は認められなかった。

7.7 血液化学検査（Table 7-1~7-10、Appendix 7-1~7-28）

1) 投与期間終了時検査

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

交配群雌では 100 mg/kg 投与群で対照群と比べナトリウムの有意な低値が認められたが、用量に依存性のない変化であった。

非交配群雌の 1000 mg/kg 投与群で尿素窒素に対照群と比べ有意な低値が認められたが、軽微な変化であり生理的変動範囲内と判断した。

2) 回復期間終了時検査

1000 mg/kg 投与群の雄ではいずれの検査項目においても対照群との間に有意差は認められなかった。

1000 mg/kg 投与群の雌で LDH に対照群と比べ有意な高値が認められたが、軽微な変化であり投与期間終了時検査には異常がなく、弊社背景データ（Mean±S.D.：47±14、n=69、2009/04-2013/03）の範囲内であることから生理的変動範囲内と判断した。

7.8　器官重量（Table 8-1~8-10、Appendix 8-1~8-48）

1)　投与期間終了時検査

雄では 1000 mg/kg 投与群で精嚢及び前立腺の絶対及び相対重量に対照群と比べ有意な高値が認められた。なお、100 mg/kg 投与群で精巣の絶対重量に対照群と比べ有意な高値が認められたが、用量に依存性のない変化であった。

交配群雌では 300 mg/kg 投与群で卵巣の絶対重量に対照群と比べ有意な低値が認められたが、用量に依存性のない変化であった。

非交配群雌ではいずれの器官重量にも各被験物質投与群と対照群との間に有意差は認められなかった。

2)　回復期間終了時検査

1000 mg/kg 投与群の雄ではいずれの器官重量にも対照群との間に有意差は認められなかった。

1000 mg/kg 投与群の雌で腎臓の絶対重量に対照群と比べ有意な低値が認められたが、絶対重量のみの軽微な変化であり投与終了時検査には異常はないことから偶発性と判断した。

7.9　剖検所見（Table 9-1~9-6、Appendix 9-1~9-116）

1)　投与期間終了時検査

いずれの動物にも被験物質投与に起因すると考えられる変化はみられなかった。

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

妊娠 25 日未分娩（不妊）であった 100 mg/kg 投与群の 1 例（動物番号 2104）及び授乳期間中に全哺育児が死亡した 100 mg/kg 投与群の 1 例（動物番号 2107）では肉眼的異常はみられなかった。

2)　回復期間終了時検査

1000 mg/kg 投与群の雄 1/5 例で肺に暗赤色巣が、対照群の雌 1/5 例で腎臓に嚢胞がみられたが、その発現状況から偶発性変化と考えられた。

7.10　病理組織学検査（Table 10-1~10-16、Appendix 9-1~9-116）

1)　投与期間終了時検査

いずれの器官/組織にも被験物質投与に起因する考えられる変化はみられなかった。

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

妊娠 25 日未分娩（不妊）であった 100 mg/kg 投与群の 1 例では脾臓の髄外造血が、その交配相手雄（動物番号 2004）では腎臓の再生尿細管、肝臓の微小肉芽腫、下垂体の嚢胞、前立腺の細胞浸潤及び脾臓の髄外造血がそれぞれ軽微にみられたのみで不妊を示唆する変化はみられなかった。授乳期間中に全哺育児が死亡した 100 mg/kg 投与群の 1 例では腎臓に軽微な腎乳頭の鉱質沈着、脾臓に軽度な髄外造血がみられたのみ

で全哺育児死亡と関連すると考えられる変化はみられなかった。
不妊あるいは全哺育児死亡は低用量群の各 1 例のみであり、偶発性にも発現しうることから、被験物質投与による影響は否定した。
2) 回復期間終了時検査
肉眼的に肺に暗赤色巣のみられた 1000 mg/kg 投与群の雄 1 例で肺に軽微な細胞浸潤が、腎臓に嚢胞のみられた対照群の雌 1 例で腎臓に軽度な嚢胞がみられたが、偶発性変化と考えられた。

7.11 性周期（Table 11、Appendix 10-1~10-4）

性周期異常の動物はみられず、性周期異常率、発情期像発現回数及び平均性周期日数には対照群と各被験物質投与群との間に有意差は認められなかった。

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

交配 7 日までに全例の交尾が成立し、交尾までに要した日数、交尾率、授精率及び受胎率には対照群と各被験物質投与群との間に有意差は認められなかった。

7.13 分娩成績（Table 13、Appendix 12-1~12-4）並びに分娩及び哺育状態（Table 1-3 及び 1-4、Appendix 1-9~1-16）

出産率、妊娠期間、黄体数、着床痕数、着床率、分娩率、死産児率、出生児数及び外表異常率には対照群と各被験物質投与群との間に有意差は認められなかった。
妊娠動物の分娩状態では妊娠 21 から 23 日に全例が分娩し、胎盤及び羊膜の処理は正常に行われ、哺育状態ではいずれの母動物にも児集め、営巣及び授乳行動に異常はみられなかった。

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

出生率及び生後 4 日生存率には対照群と各被験物質投与群との間に有意差は認められなかった。

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

出産児並びに出生児の生後 0 及び 4 日の性比には対照群と各被験物質投与群との間に有意差は認められなかった。

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

生後 0 及び 4 日の雌雄体重並びに生後 0~4 日の間の体重増加量には対照群と各被験物質投与群との間に有意差は認められなかった。

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

いずれの死亡児にも肉眼的異常はみられなかった。

7.18　出生児の生後 4 日肉眼観察所見（Table 18、Appendix 17-1~17-4）

いずれの出生児にも肉眼的異常はみられなかった。

8. 考察

酢酸ヘキセニルの 0（対照群：コーン油）、100、300 及び 1000 mg/kg を、Sprague-Dawley 系 SPF ラットの雄には交配前 14 日間に加え交配期間を通して剖検前日まで（42 日間）、雌には交配前 14 日間に加え交配期間及び妊娠期間を通して授乳 4 日まで（41~48 日間）、非交配群雌には 42 日間強制経口投与し、反復投与毒性及び生殖発生毒性を検討した。更に、0 及び 1000 mg/kg 群の一部の動物については雌雄ともに 42 日間投与した後、14 日間の回復期間を設け、毒性変化の可逆性を検討した。

8.1 反復投与毒性

いずれの投与群においても死亡動物はみられず、一般状態、詳細な一般状態、機能検査、握力、自発運動量、体重、摂餌量、尿検査（摂水量を含む）、血液学検査、血液化学検査、剖検及び病理組織学検査には被験物質投与の影響は認められなかった。

器官重量では、1000 mg/kg 投与群で精嚢及び前立腺の重量に高値が認められた。精嚢及び前立腺の病理組織に重量増加を示唆する変化はみられず、試験施設の背景データ[Mean±S.D., n=77, 2009/04-2013/03]（精嚢：絶対；1.82±0.22/相対；0.36±0.05、前立腺：絶対；1.34±0.19/相対；0.26±0.04）の範囲内であり、雄の交尾能及び授精能に被験物質投与の影響は認められないことから、重量変化の毒性学的意義は低いと判断した。

8.2 生殖発生毒性

いずれの投与群においても性周期、交尾までに要した日数、交尾率、授精率及び受胎率には被験物質投与の影響は認められなかった。更に、出産率、妊娠期間、黄体数、着床痕数、着床率、分娩率、死産児率、死産児の外表観察、出生児数、外表異常率及び出生率に被験物質投与の影響は認められず、授乳期間中の哺育状態にも異常が認められないことから、1000 mg/kg 投与群においても雌雄動物の交尾能、授精能及び受胎能、母動物の妊娠維持、分娩及び哺育行動などの生殖機能への影響はないと判断した。

出生児では、生後 0 日の外表観察、生後 0 及び 4 日の雌雄体重並びに性比、死亡児の肉眼観察所見、生後 4 日の生存率及び肉眼観察所見に被験物質投与による影響は認められないことから、1000 mg/kg 投与群においても児の子宮内発生、発育及び分化並びに生存性などへの影響はないと判断した。

これらの結果から、本試験条件下で酢酸ヘキセニルを反復経口投与することにより、1000 mg/kg で精嚢及び前立腺に重量変化が認められた以外に被験物質に起因すると考えられる変化はみられなかった。したがって、本被験物質の反復投与毒性に対する無影響量は雄で 300 mg/kg、雌で 1000 mg/kg、無毒性量は雌雄ともに 1000 mg/kg と判断した。また、雌雄親動物と児動物における生殖発生毒性に対する無影響量及び無毒性量はいずれも 1000 mg/kg と判断した。

9. 文献

[1] [redacted]: 酢酸ヘキセニルの GC を用いた被験液中濃度測定法バリデーション及び安定性試験（媒体：コーン油）並びに IR を用いた特性及び安定性試験（株式会社ボゾリサーチセンター　御殿場研究所、試験番号：A-2511、2012 年）

[2] [redacted]: 酢酸ヘキセニルのラットを用いた 14 日間反復経口投与毒性試験（投与量設定試験）（株式会社ボゾリサーチセンター、試験番号：N-R031、2012 年）

[3] Snedecor GW, Cochran WG. Statistical methods. 8th ed. Ames: Iowa State University Press; 1989.

[4] Dunnett, CW. New tables for multiple comparisons with a control. Biometrics 1964; 20: 482-91.

[5] Steel RGD. A multiple comparison rank sum test: Treatments versus control. Biometrics 1959; 15: 560-72.

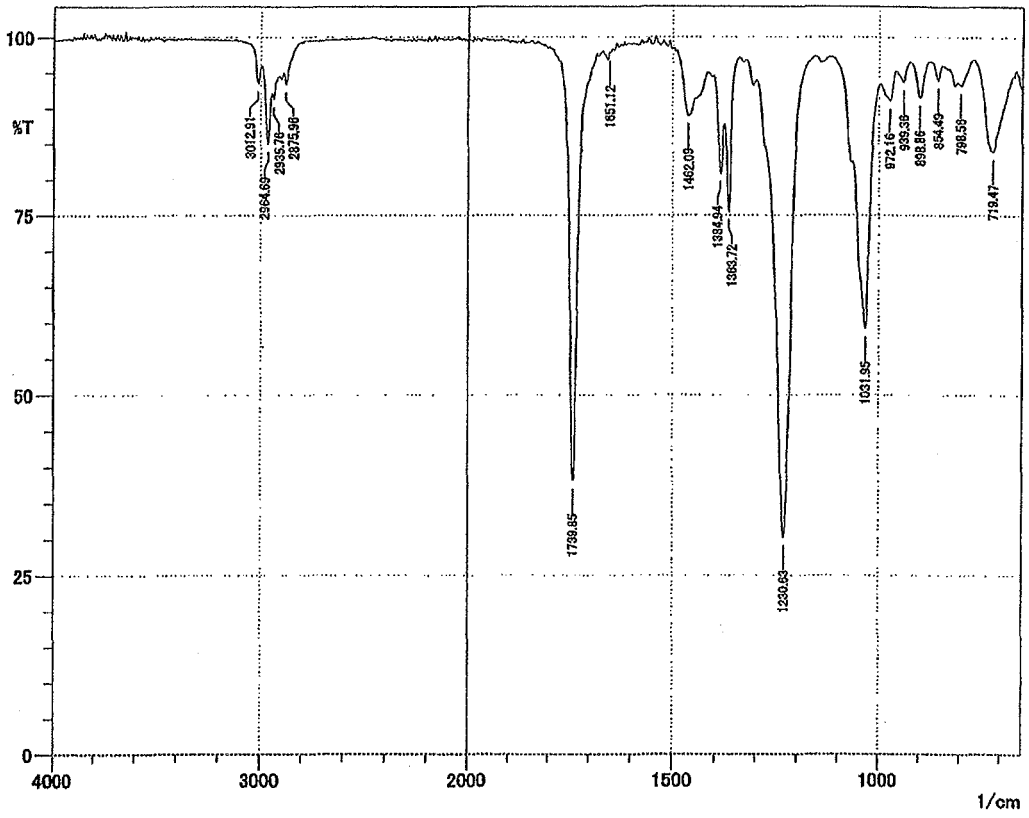
[6] 佐久間昭（1981）：薬効評価－計画と分析–II, pp.23-27, 387-389, 東京大学出版会, 東京.

R-1100
添付資料 1

試験番号：A-2511

試験成績書
[酢酸ヘキセニルの特性]

ステージ	:	被験物質の使用前
測定日	:	2012 年 8 月 3 日
被験物質	:	酢酸ヘキセニル（ロット番号 120707K2-2）
試験項目	:	赤外吸収スペクトルの確認（ATR 法）
結果	:	特性のスペクトルを以下に示す。



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

[redacted]　2012年 8月 9日

試験責任者
株式会社ボゾリサーチセンター　御殿場研究所

R-1100
添付資料 2 (1/2)

試験番号：R-1100（1/2）

試験成績書
［酢酸ヘキセニルの安定性］

ステージ	:	投与期間終了後
測定日	:	2012 年 11 月 26 日
被験物質	:	酢酸ヘキセニル（ロット番号：120707K2-2）
試験項目	:	赤外吸収スペクトルの確認（ATR 法）
評価基準	:	安定性のスペクトルを特性のスペクトル（A-2511）と比較するとき、同様な赤外吸収スペクトルである。
結果	:	安定性のスペクトルを特性のスペクトルと比較したとき、同様な赤外吸収スペクトルが得られた。 なお、赤外吸収スペクトルは次のページに示す。
基準	:	「新規化学物質等に係る試験を実施する試験施設に関する基準」（平成 23 年 3 月 31 日：薬食発 0331 第 8 号、平成 23･03･29 製局第 6 号、環保企発第 110331010 号）
判定	:	適

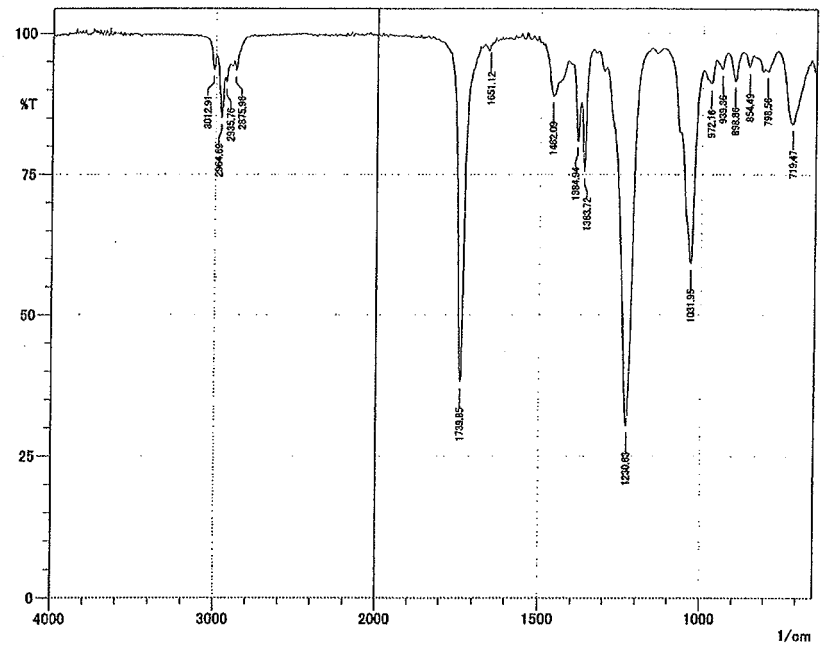
[redacted]　2012 年 12 月 12 日

化学分析責任者
株式会社ボゾリサーチセンター　御殿場研究所

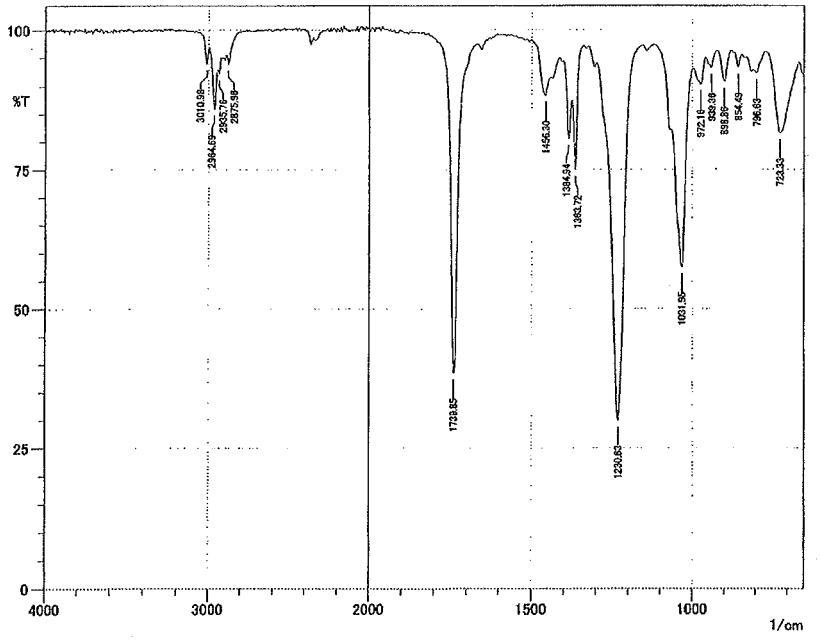
試験番号：R-1100（2/2）

結果　　：　赤外吸収スペクトル

（特性のスペクトル：A-2511）



（安定性のスペクトル）



R-1100
添付資料 3

試験番号：A-2511（訂正版）

試験成績書
（被験液中酢酸ヘキセニルの安定性）

被験物質	：	酢酸ヘキセニル（ロット番号：120707K2-2）
形態（媒体）	：	溶液（コーン油）
保存条件	：	褐色ガラスビンにて、冷所（冷蔵庫内、許容値：1~10°C）及び室温保存
保存期間	：	冷所 9 日間 + 室温 24 時間保存
評価基準		
安定性	：	残存率が 100.0 ±10.0%以内。

結果：

調製濃度 (mg/mL)		測定濃度（mg/mL）	
		調製直後	冷所 9 日間+ 室温 24 時間保存後
1.01		1.06	0.987
		1.05	0.990
		1.02	0.958
	平均値	1.04	0.978
	残存率（%）	–	94.0
200		218	200
		212	197
		215	197
	平均値	215	198
	残存率（%）	–	92.1

判定　：　適

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

[redacted]　2012 年 9 月 7 日

試験責任者
株式会社ボゾリサーチセンター　御殿場研究所

R-1100
添付資料 4

試験番号：R-1100

試験成績書
（被験液中酢酸ヘキセニルの濃度）

ステージ　：　初回投与
分析日　：　2012 年 9 月 20 日

測定試料
　被験物質　：　酢酸ヘキセニル（ロット番号；120707K2-2）
　形態（媒体）　：　溶液（コーン油）
　調製日　：　2012 年 9 月 20 日

評価基準
　濃度　：　表示値に対する割合；100.0 ± 10.0%

結果：

表示値 (mg/mL)	測定濃度 (mg/mL)	表示値に対する割合 (%)
20	20.5	102.5
60	61.1	101.8
200	220	110.0

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

判定　：　適

[redacted]　2013 年 1 月 8 日

化学分析責任者
株式会社ボゾリサーチセンター　御殿場研究所

R-1100
添付資料 5

試験番号：R-1100

試験成績書
（被験液中酢酸ヘキセニルの濃度）

ステージ　：　投与 6 週
分析日　：　2012 年 10 月 26 日

測定試料
　被験物質　：　酢酸ヘキセニル（ロット番号；120707K2-2）
　形態（媒体）　：　溶液（コーン油）
　調製日　：　2012 年 10 月 25 日

評価基準
　濃度　：　表示値に対する割合；100.0 ± 10.0%

結果：

表示値 (mg/mL)	測定濃度 (mg/mL)	表示値に対する割合 (%)
20	20.1	100.5
60	58.1	96.8
200	205	102.5

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

判定　：　適

[redacted]　2013 年 1 月 8 日

化学分析責任者
株式会社ボゾリサーチセンター　御殿場研究所

R-1100
添付資料 6

酢酸ヘキセニルのラットを用いた
14 日間反復経口投与毒性試験（投与量設定試験）における所見

試験番号：N-R031

被験物質		媒体 a)	酢酸ヘキセニル		
投与量(mg/kg)		0	250	500	1000
投与容量 (mL/kg)		5	5	5	5
使用動物数 (♂/♀)		5/5	5/5	5/5	5/5
死亡動物数 (♂/♀)		0/0	0/0	0/0	0/0
死亡発現時期		–	–	–	–
一般状態	生存	–	–	–	–
	死亡				
体重			–	–	–
摂餌量			–	–	–
血液学検査			–	白血球数：↓（♀）	白血球数：↓（♀） 網赤血球率:↑↑(♀)
血液化学検査			–	–	–
器官重量	絶対		–	–	–
	相対		–	–	–
剖検	生存	–	–	–	–
	死亡				

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

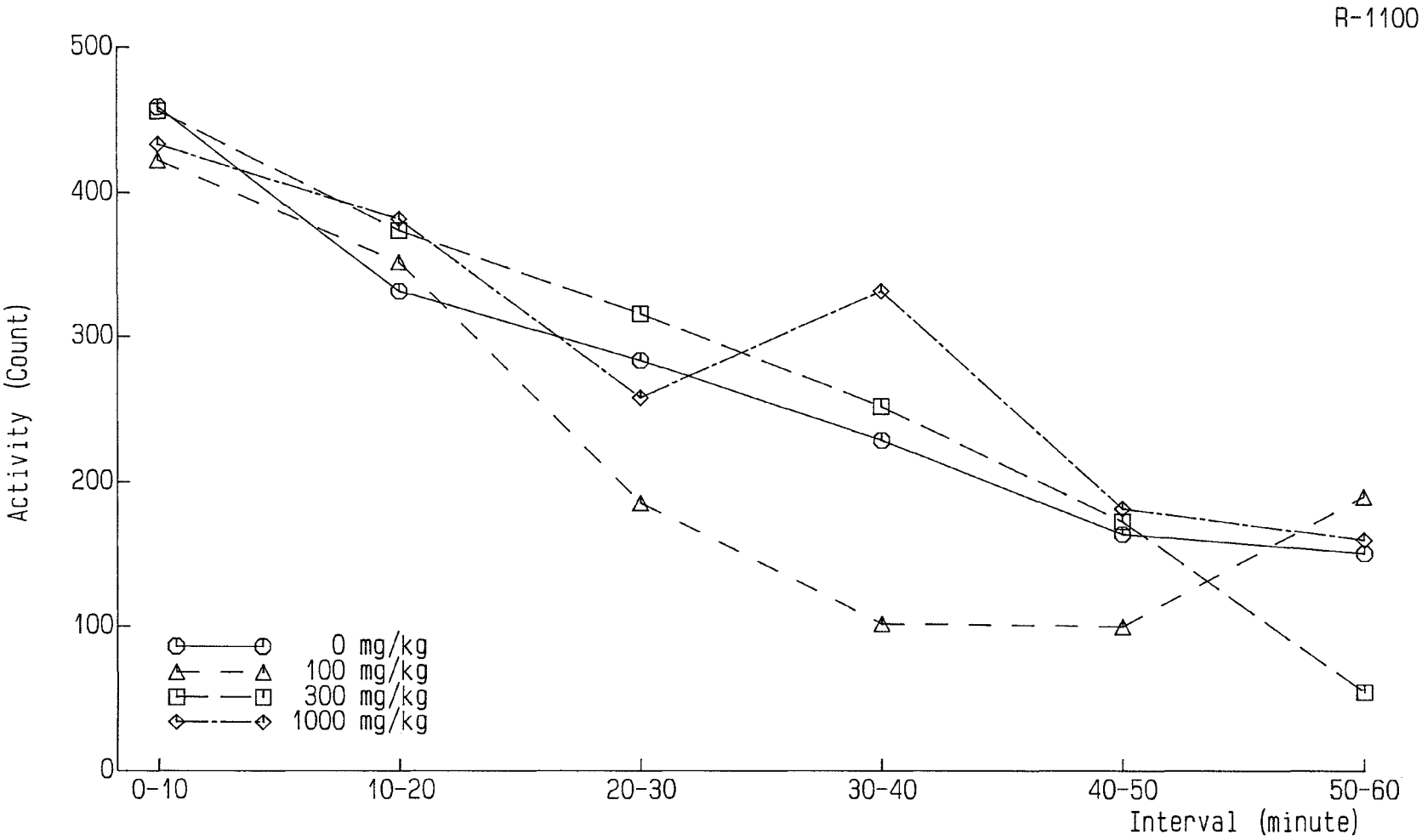


Fig.1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Motor activity of male rats (Week 6 of administration)

R-1100

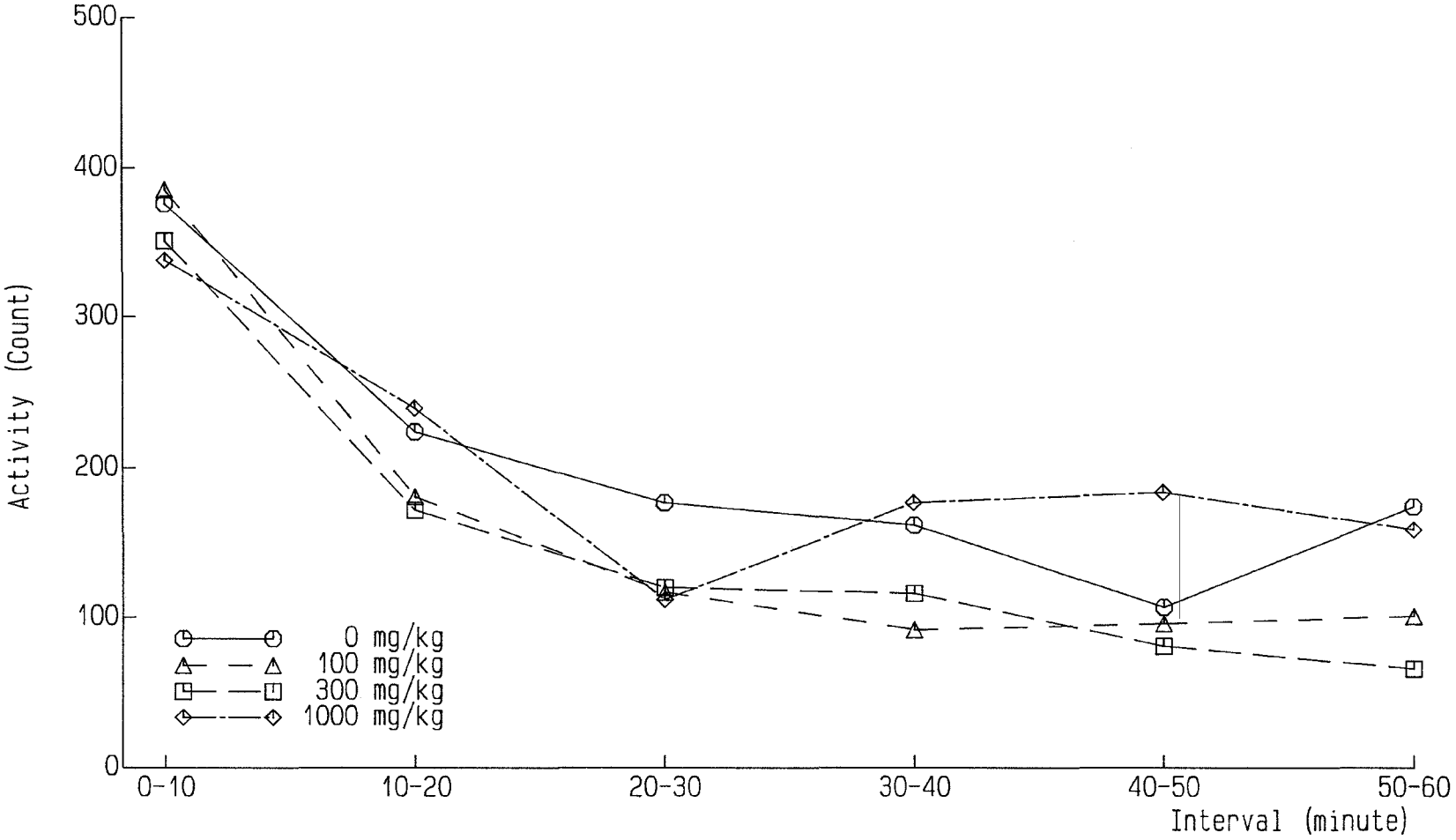


Fig.2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

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

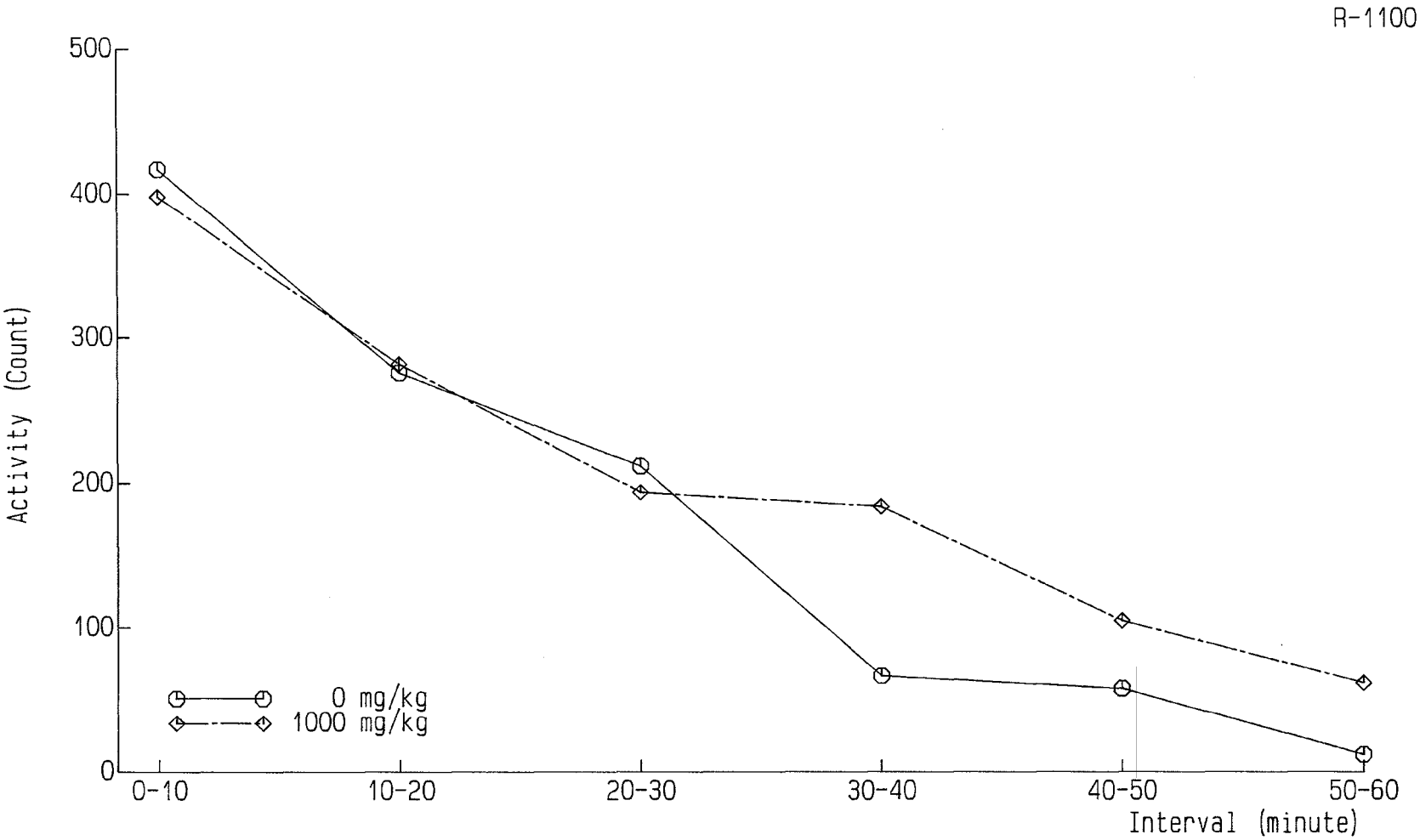


Fig.3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

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

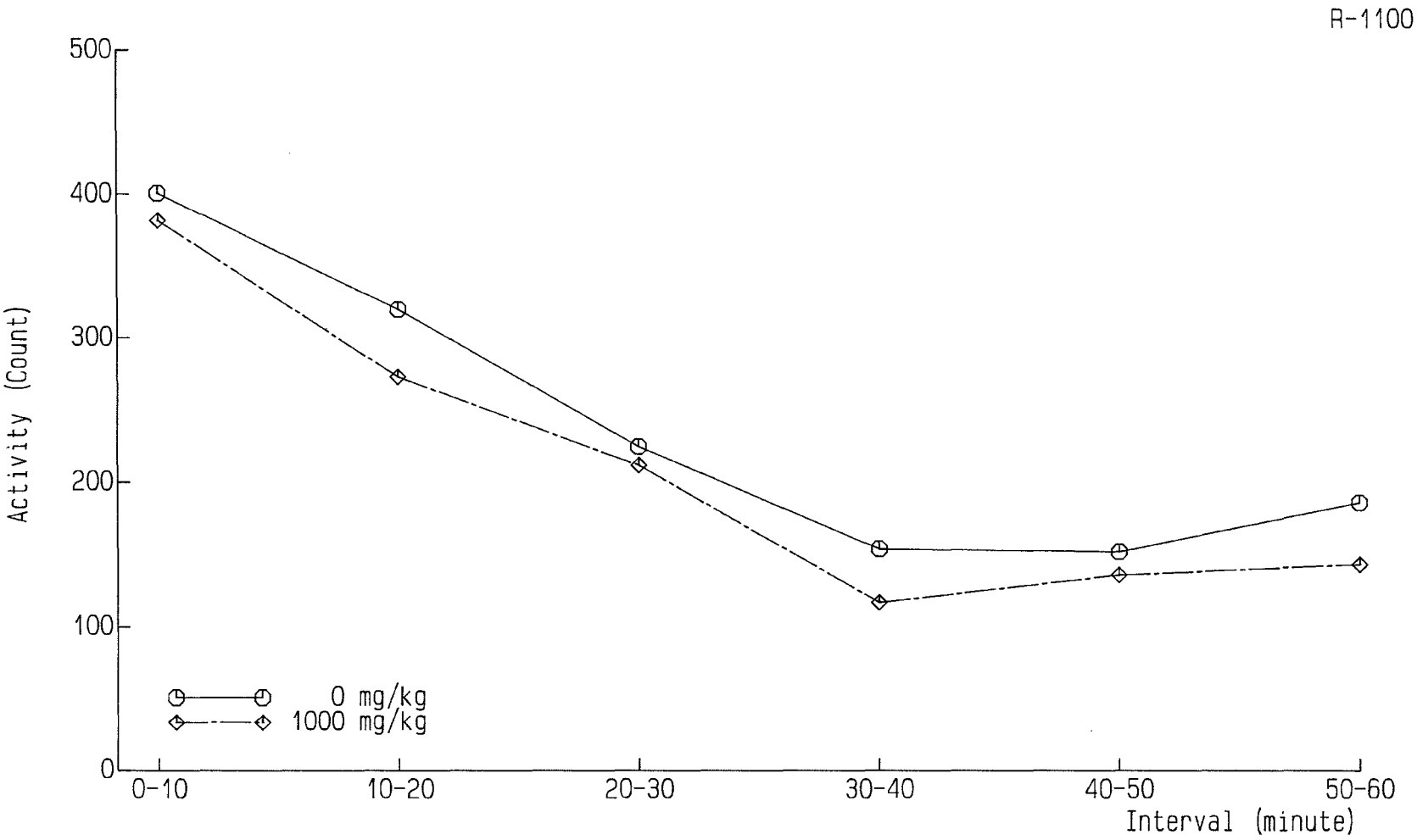


Fig.4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Motor activity of male rats (Week 2 of recovery)

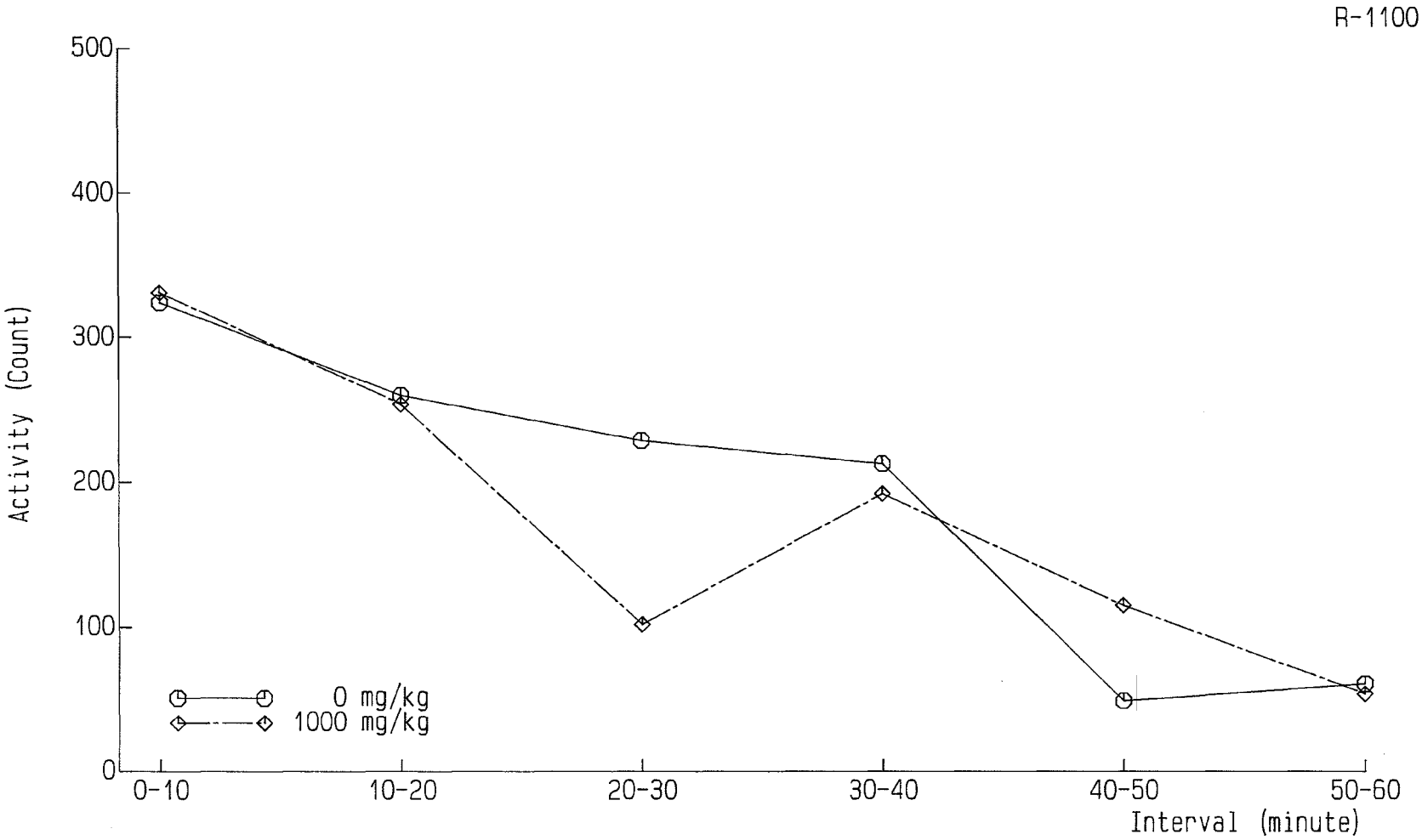


Fig.5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Motor activity of female rats (Week 2 of recovery)

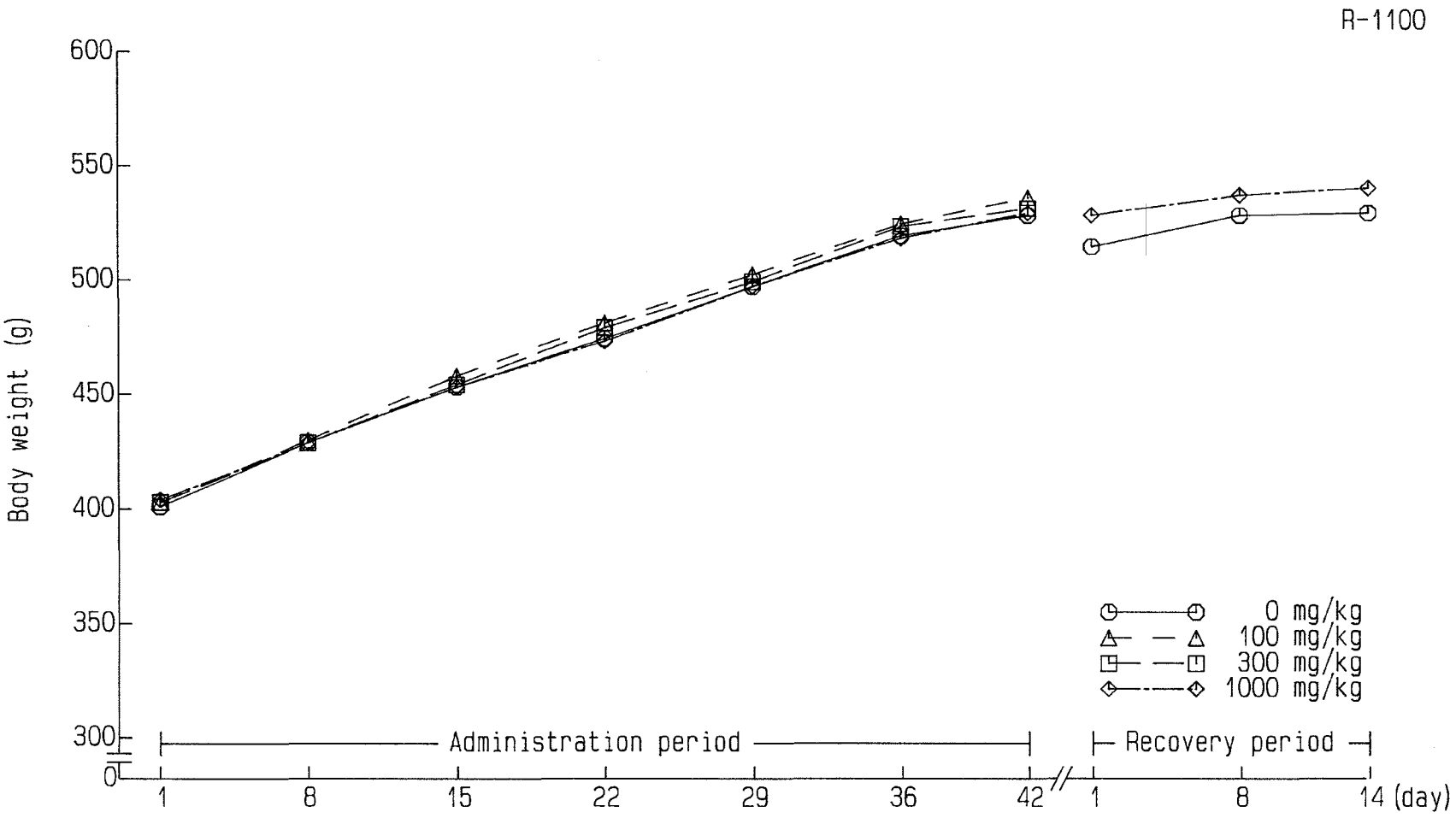


Fig.6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Body weight of male rats

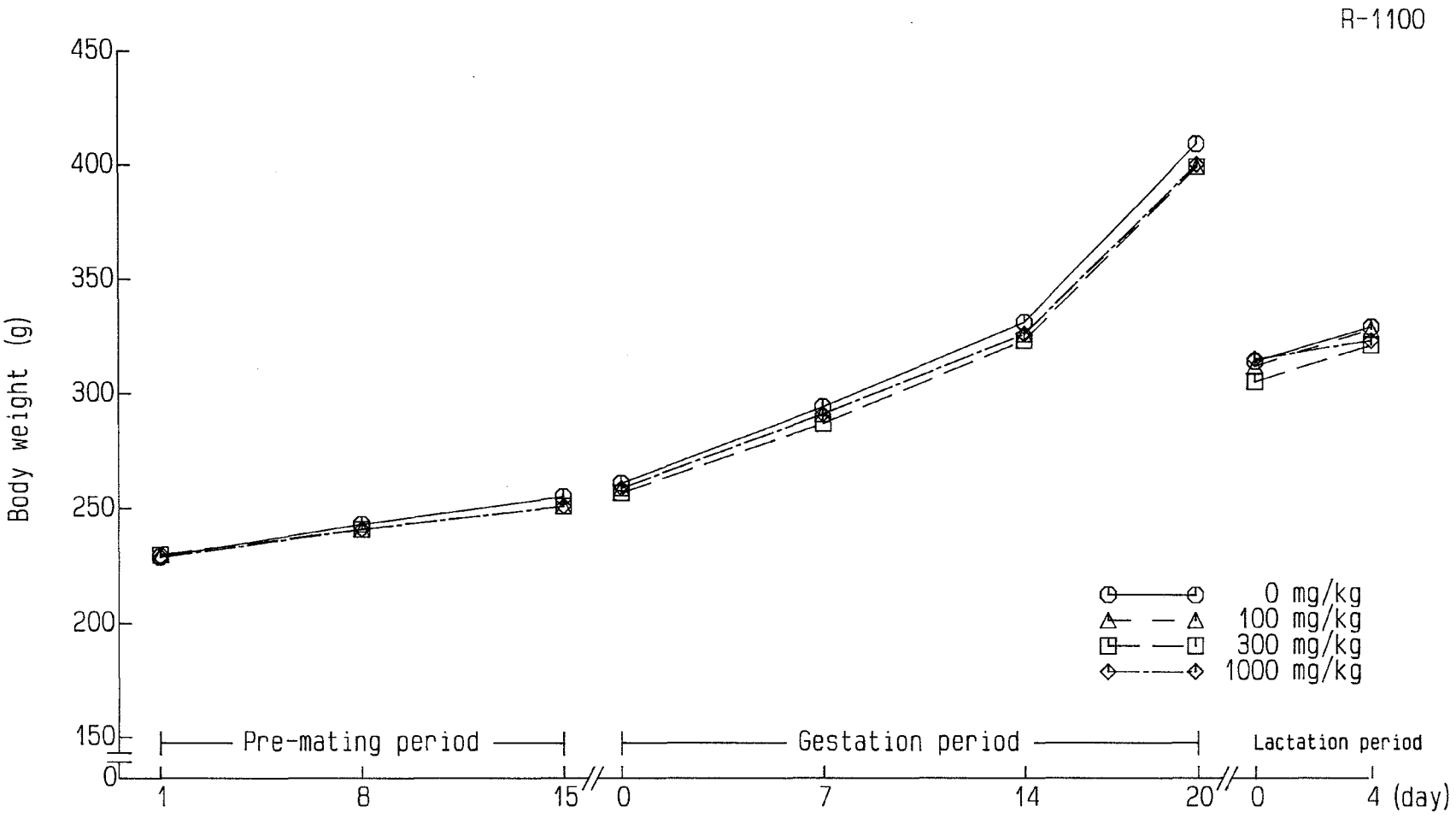


Fig.7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Body weight of female rats (Main group)

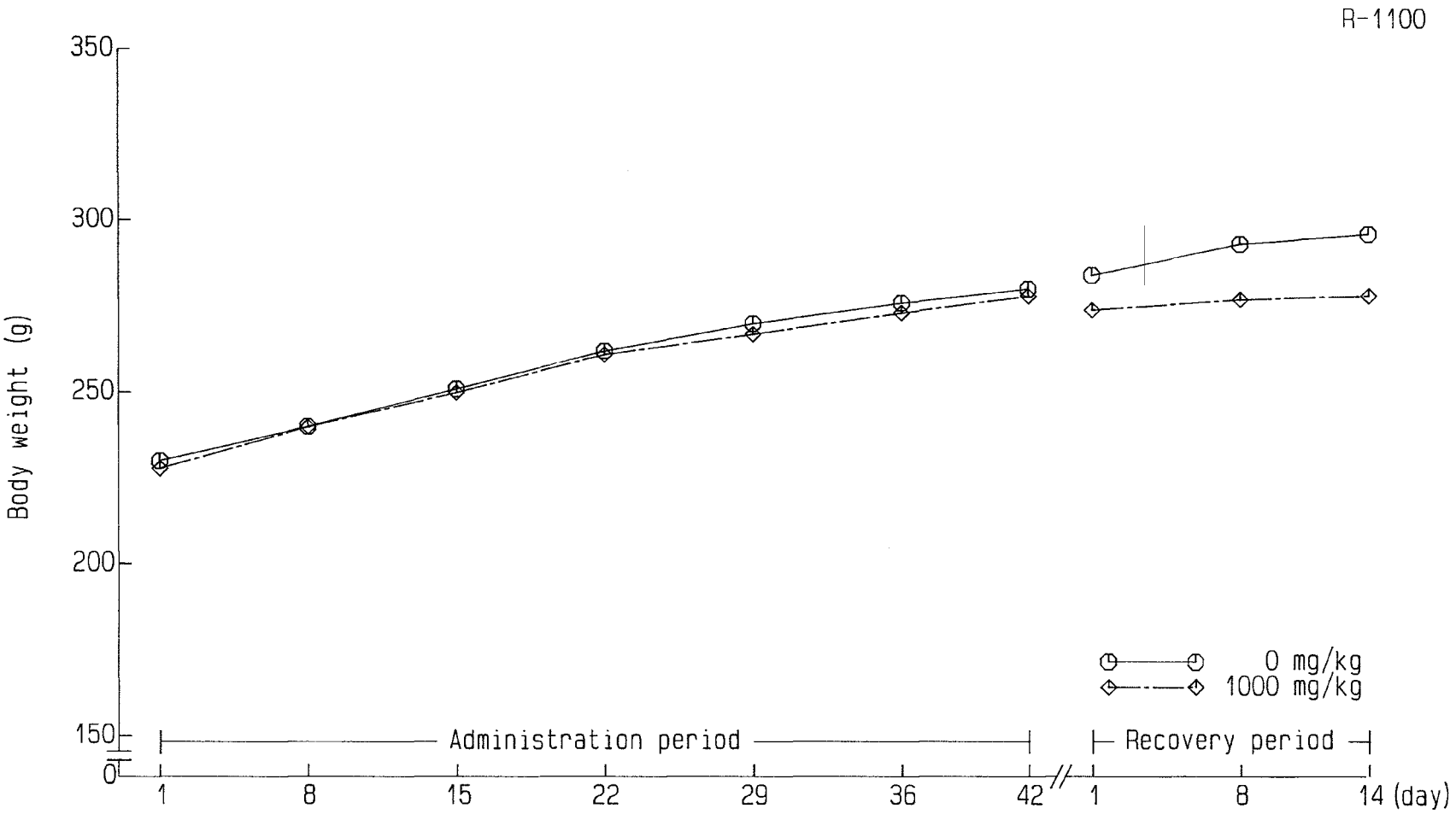


Fig.8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Body weight of female rats (Satellite group)

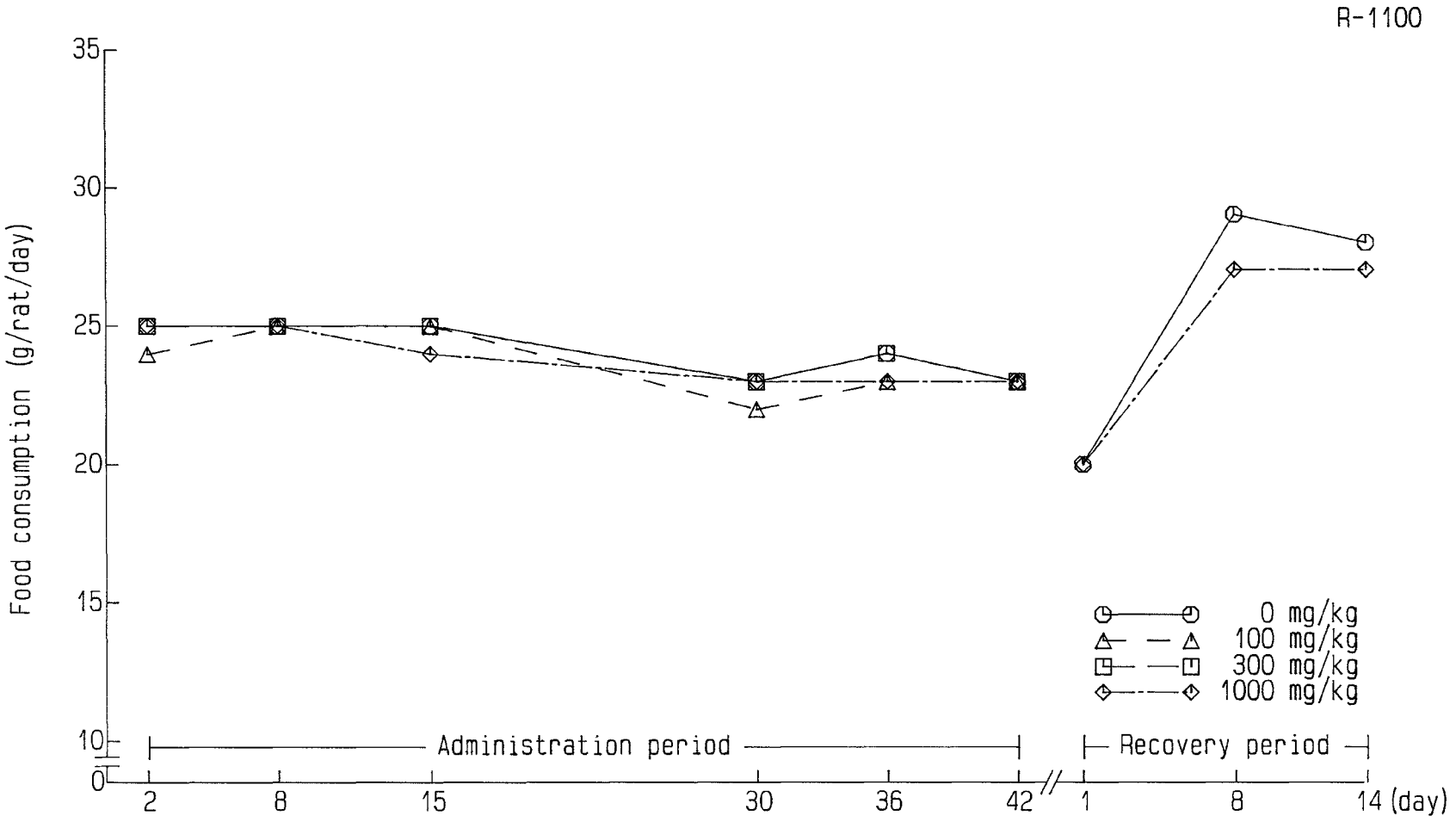


Fig.9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Food consumption of male rats

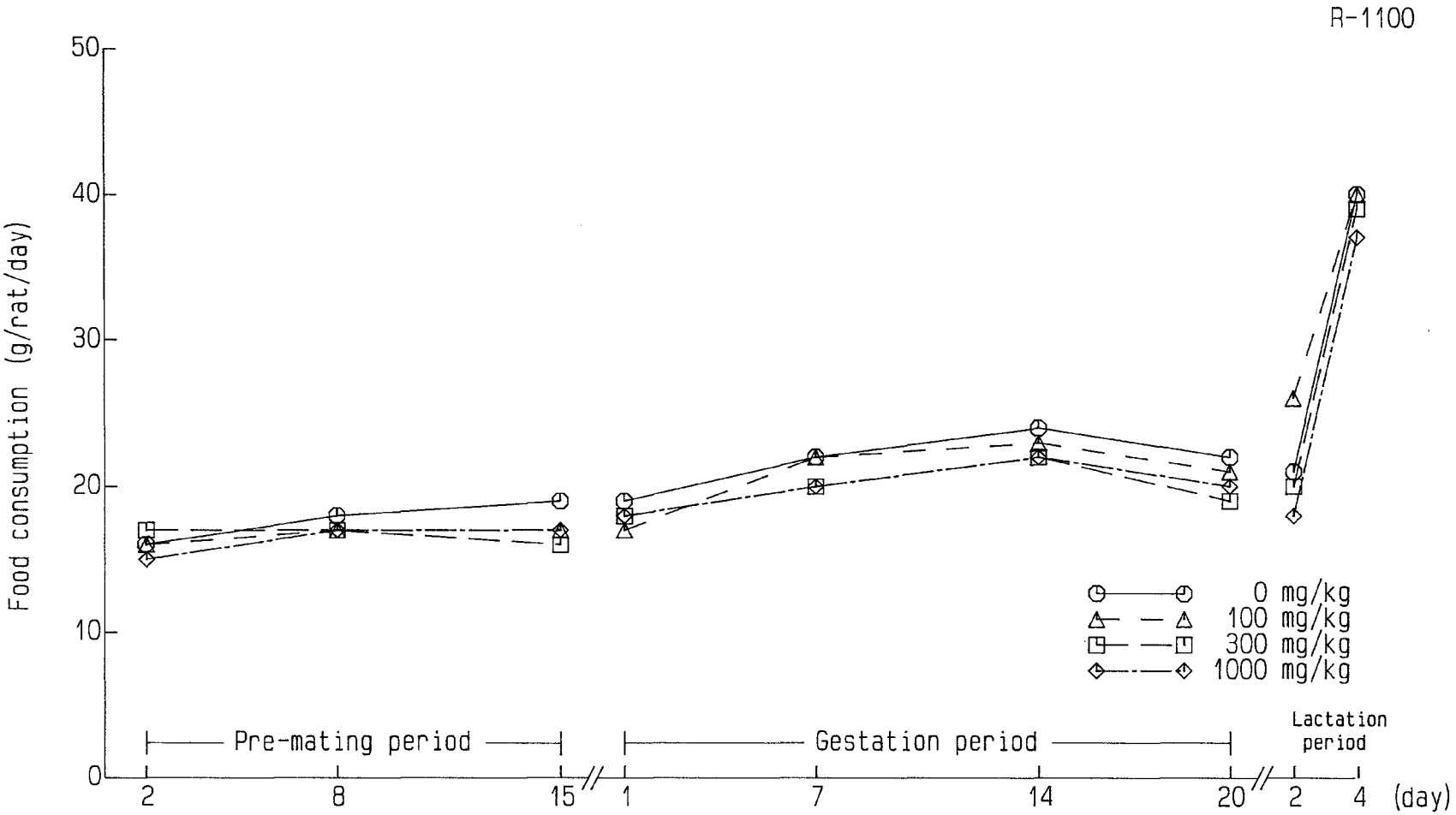


Fig.10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Food consumption of female rats (Main group)

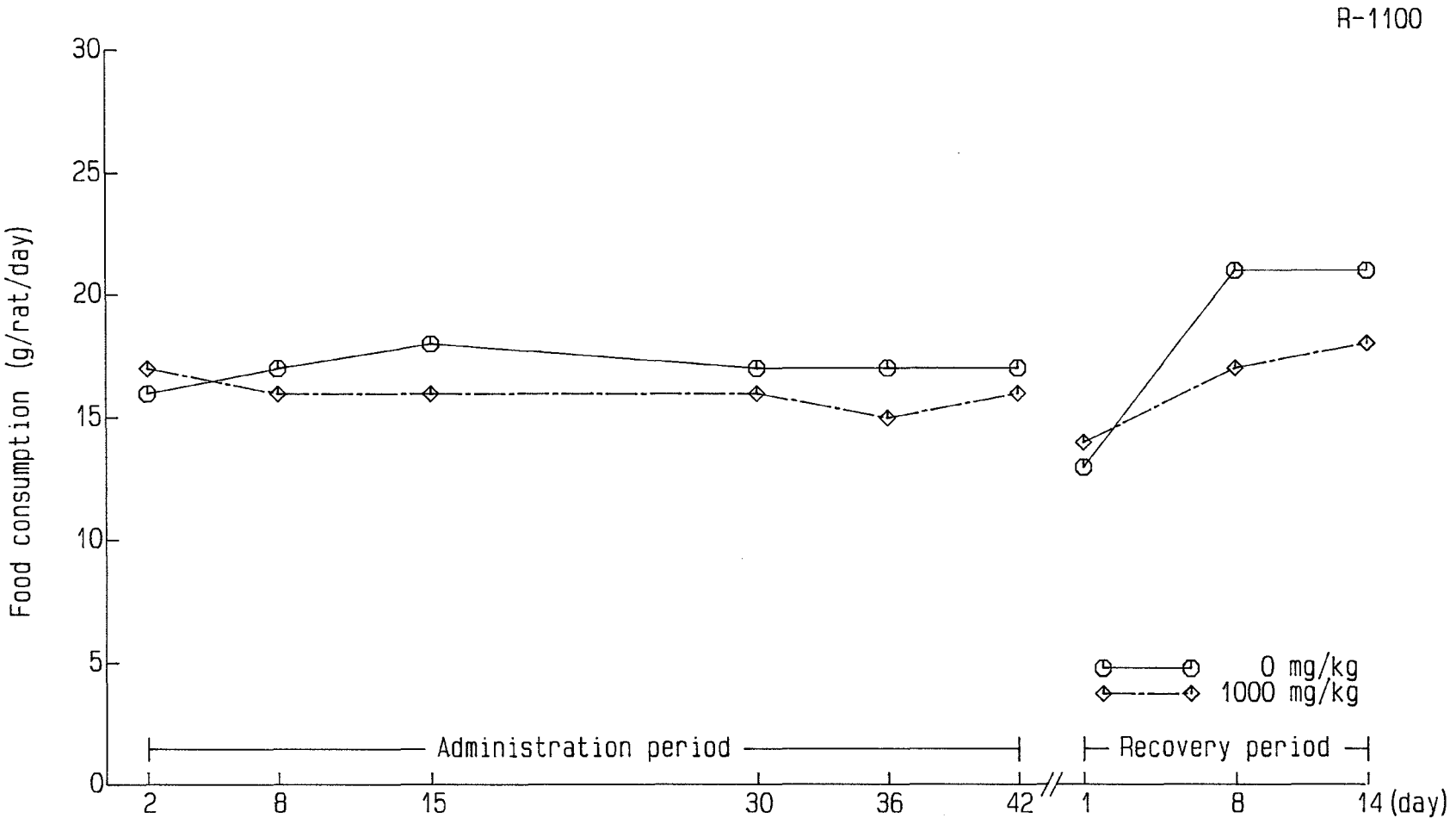


Fig.11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Food consumption of female rats (Satellite group)

Table 1-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Clinical signs in male rats (Administration period)

Dose mg/kg	Signs	Day of administration 1-7	8-14	15-21	22-28	29-35	36-42	43a)
0	No. of animals	12	12	12	12	12	12	7
	No. of animals with abnormal findings	0	0	0	0	0	0	0
100	No. of animals	12	12	12	12	12	12	12
	No. of animals with abnormal findings	0	0	0	0	0	0	0
300	No. of animals	12	12	12	12	12	12	12
	No. of animals with abnormal findings	0	0	0	0	0	0	0
1000	No. of animals	12	12	12	12	12	12	7
	No. of animals with abnormal findings	0	0	0	0	0	0	0

a): Day of necropsy

Table 1-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Clinical signs in female rats during the pre-mating period (Main group)

Dose mg/kg	Signs	Day of administration														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
0	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
100	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
300	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1000	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Table 1-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Clinical signs in dams during the gestation period (Main group)

Dose mg/kg	Signs	Administration																							
		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23a)
0	No. of dams	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	0	
	No. of dams with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
100	No. of dams	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	1	0
	No. of dams with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
300	No. of dams	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	3	0
	No. of dams with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
1000	No. of dams	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	4	0
	No. of dams with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	

a): Gestation day

Table 1-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Clinical signs in dams during the lactation period (Main group)

Dose mg/kg	Signs	Administration 0	1	2	3	4a)	5b)
0	No. of dams	12	12	12	12	12	12
	No. of dams with abnormal findings	0	0	0	0	0	0
100	No. of dams	11	11	10c)	10	10	10
	No. of dams with abnormal findings	0	0	0	0	0	0
300	No. of dams	12	12	12	12	12	12
	No. of dams with abnormal findings	0	0	0	0	0	0
1000	No. of dams	12	12	12	12	12	12
	No. of dams with abnormal findings	0	0	0	0	0	0

a): Lactation day
b): Day of necropsy
c): One dam was necropsied on lactation day 1 because all pups died.

Table 1-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Clinical signs in female rats (Satellite group, Administration period)

Dose mg/kg	Signs	Day of administration 1-7	8-14	15-21	22-28	29-35	36-42	43a)
0	No. of animals	10	10	10	10	10	10	5
	No. of animals with abnormal findings	0	0	0	0	0	0	0
1000	No. of animals	10	10	10	10	10	10	5
	No. of animals with abnormal findings	0	0	0	0	0	0	0

a): Day of necropsy

Table 1-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Clinical signs in male rats (Recovery period)

Dose mg/kg	Signs	Day of recovery														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)
0	No. of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1000	No. of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

a): Day of necropsy

Table 1-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Clinical signs in female rats (Recovery period)

Dose mg/kg	Signs	Day of recovery														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)
0	No. of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1000	No. of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

a): Day of necropsy

Table 2-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in male rats: home cage observation (Week 1 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in male rats: home cage observation (Week 2 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in male rats: home cage observation (Week 3 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in male rats: home cage observation (Week 4 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in male rats: home cage observation (Week 5 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in male rats: home cage observation (Week 6 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: home cage observation (Main group, Week 1 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: home cage observation (Main group, Week 2 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: home cage observation (Main group, Gestation day 1)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	11	12	12
Posture					
Normal		12	11	12	12
Convulsion					
None		12	11	12	12
Abnormal behavior					
None		12	11	12	12

Table 2-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: home cage observation (Main group, Gestation day 7)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	11	12	12
Posture					
Normal		12	11	12	12
Convulsion					
None		12	11	12	12
Abnormal behavior					
None		12	11	12	12

Table 2-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: home cage observation (Main group, Gestation day 14)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	11	12	12
Posture					
Normal		12	11	12	12
Convulsion					
None		12	11	12	12
Abnormal behavior					
None		12	11	12	12

Table 2-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: home cage observation (Main group, Gestation day 20)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	11	12	12
Posture					
Normal		12	11	12	12
Convulsion					
None		12	11	12	12
Abnormal behavior					
None		12	11	12	12

Table 2-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: home cage observation (Main group, Lactation day 4)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	10	12	12
Posture					
Normal		12	10	12	12
Convulsion					
None		12	10	12	12
Abnormal behavior					
None		12	10	12	12

Table 2-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: home cage observation (Satellite group, Week 1 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	10	10
Posture			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10

Table 2-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: home cage observation (Satellite group, Week 2 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	10	10
Posture			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10

Table 2-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: home cage observation (Satellite group, Week 3 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	10	10
Posture			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10

Table 2-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: home cage observation (Satellite group, Week 4 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	10	10
Posture			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10

Table 2-18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: home cage observation (Satellite group, Week 5 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	10	10
Posture			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10

Table 2-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: home cage observation (Satellite group, Week 6 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	10	10
Posture			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10

Table 2-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in male rats: home cage observation (Week 1 of recovery)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Posture			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5

Table 2-21 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in male rats: home cage observation (Week 2 of recovery)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Posture			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5

Table 2-22 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: home cage observation (Week 1 of recovery)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Posture			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5

Table 2-23 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: home cage observation (Week 2 of recovery)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Posture			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5

Table 2-24 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in male rats: in-the-hand observation (Week 1 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	12	12
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	11	12	12
Soft		0	1	0	0
Reactivity to handling					
Easy		12	12	12	12

Table 2-25 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in male rats: in-the-hand observation (Week 2 of administration)

Parameter \ Dose (mg/kg)	0	100	300	1000
No. of animals	12	12	12	12
Ease of removal from cage				
Easy	12	12	12	12
Fur condition				
Normal	12	12	12	12
Skin				
Normal	12	12	12	12
Secretions-Eye, Nose				
Absent	12	12	12	12
Exophthalmos				
Absent	12	12	12	12
Palpebral closure				
Normal	12	12	12	12
Mucosal membranes				
Normal	12	12	12	12
Lacrimation				
Normal	12	12	12	12
Piloerection				
Absent	12	12	12	12
Pupil size				
Normal	12	12	12	12
Salivation				
None	12	12	12	12
Abnormal respiration				
Absent	12	12	12	12
Vocalization				
None	12	12	11	10
Soft	0	0	1	2
Reactivity to handling				
Easy	12	12	11	11
Slightly awkward	0	0	1	1

Table 2-26 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in male rats: in-the-hand observation (Week 3 of administration)

Parameter \ Dose (mg/kg)	0	100	300	1000
No. of animals	12	12	12	12
Ease of removal from cage				
Easy	12	12	12	12
Fur condition				
Normal	12	12	12	12
Skin				
Normal	12	12	12	12
Secretions-Eye, Nose				
Absent	12	12	12	12
Exophthalmos				
Absent	12	12	12	12
Palpebral closure				
Normal	12	12	12	12
Mucosal membranes				
Normal	12	12	12	12
Lacrimation				
Normal	12	12	12	12
Piloerection				
Absent	12	12	12	12
Pupil size				
Normal	12	12	12	12
Salivation				
None	12	12	12	12
Abnormal respiration				
Absent	12	12	12	12
Vocalization				
None	12	12	11	11
Soft	0	0	1	1
Reactivity to handling				
Easy	12	12	12	12

Table 2-27 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in male rats: in-the-hand observation (Week 4 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	12	12
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	12	11	11
Soft		0	0	1	1
Reactivity to handling					
Easy		12	12	11	12
Slightly awkward		0	0	1	0

Table 2-28 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in male rats: in-the-hand observation (Week 5 of administration)

Parameter \ Dose (mg/kg)	0	100	300	1000
No. of animals	12	12	12	12
Ease of removal from cage				
Easy	11	12	12	12
Some resistance/avoidance	1	0	0	0
Fur condition				
Normal	12	12	12	12
Skin				
Normal	12	12	12	12
Secretions-Eye, Nose				
Absent	12	12	12	12
Exophthalmos				
Absent	12	12	12	12
Palpebral closure				
Normal	12	12	12	12
Mucosal membranes				
Normal	12	12	12	12
Lacrimation				
Normal	12	12	12	12
Piloerection				
Absent	12	12	12	12
Pupil size				
Normal	12	12	12	12
Salivation				
None	12	12	12	12
Abnormal respiration				
Absent	12	12	12	12
Vocalization				
None	12	12	12	10
Soft	0	0	0	2
Reactivity to handling				
Easy	12	12	12	12

Table 2-29 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in male rats: in-the-hand observation (Week 6 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	12	12
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	12	12	11
Soft		0	0	0	1
Reactivity to handling					
Easy		12	12	12	12

Table 2-30 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: in-the-hand observation (Main group, Week 1 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	12	12
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	12	12	12
Reactivity to handling					
Easy		12	12	12	12

Table 2-31 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: in-the-hand observation (Main group, Week 2 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	12	12
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	12	12	12
Reactivity to handling					
Easy		12	12	12	12

Table 2-32 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: in-the-hand observation (Main group, Gestation day 1)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	11	12	12
Ease of removal from cage					
Easy		12	11	12	12
Fur condition					
Normal		12	11	12	12
Skin					
Normal		12	11	12	12
Secretions-Eye, Nose					
Absent		12	11	12	12
Exophthalmos					
Absent		12	11	12	12
Palpebral closure					
Normal		12	11	12	12
Mucosal membranes					
Normal		12	11	12	12
Lacrimation					
Normal		12	11	12	12
Piloerection					
Absent		12	11	12	12
Pupil size					
Normal		12	11	12	12
Salivation					
None		12	11	12	12
Abnormal respiration					
Absent		12	11	12	12
Vocalization					
None		12	11	12	12
Reactivity to handling					
Easy		12	11	12	12

Table 2-33 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: in-the-hand observation (Main group, Gestation day 7)

Parameter \ Dose (mg/kg)	0	100	300	1000
No. of animals	12	11	12	12
Ease of removal from cage				
Easy	12	11	12	11
Some resistance/avoidance	0	0	0	1
Fur condition				
Normal	12	11	12	12
Skin				
Normal	12	11	12	12
Secretions-Eye, Nose				
Absent	12	11	12	12
Exophthalmos				
Absent	12	11	12	12
Palpebral closure				
Normal	12	11	12	12
Mucosal membranes				
Normal	12	11	12	12
Lacrimation				
Normal	12	11	12	12
Piloerection				
Absent	12	11	12	12
Pupil size				
Normal	12	11	12	12
Salivation				
None	12	11	12	12
Abnormal respiration				
Absent	12	11	12	12
Vocalization				
None	12	11	12	12
Reactivity to handling				
Easy	12	11	12	11
Slightly awkward	0	0	0	1

Table 2-34 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: in-the-hand observation (Main group, Gestation day 14)

Parameter \ Dose (mg/kg)	0	100	300	1000
No. of animals	12	11	12	12
Ease of removal from cage				
Easy	12	11	12	12
Fur condition				
Normal	12	11	12	12
Skin				
Normal	12	11	12	12
Secretions-Eye, Nose				
Absent	12	11	12	12
Exophthalmos				
Absent	12	11	12	12
Palpebral closure				
Normal	12	11	12	12
Mucosal membranes				
Normal	12	11	12	12
Lacrimation				
Normal	12	11	12	12
Piloerection				
Absent	12	11	12	12
Pupil size				
Normal	12	11	12	12
Salivation				
None	12	11	12	12
Abnormal respiration				
Absent	12	11	12	12
Vocalization				
None	12	11	12	12
Reactivity to handling				
Easy	12	11	12	12

Table 2-35 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: in-the-hand observation (Main group, Gestation day 20)

Parameter \ Dose (mg/kg)	0	100	300	1000
No. of animals	12	11	12	12
Ease of removal from cage				
Easy	12	11	12	12
Fur condition				
Normal	12	11	12	12
Skin				
Normal	12	11	12	12
Secretions-Eye, Nose				
Absent	12	11	12	12
Exophthalmos				
Absent	12	11	12	12
Palpebral closure				
Normal	12	11	12	12
Mucosal membranes				
Normal	12	11	12	12
Lacrimation				
Normal	12	11	12	12
Piloerection				
Absent	12	11	12	12
Pupil size				
Normal	12	11	12	12
Salivation				
None	12	11	12	12
Abnormal respiration				
Absent	12	11	12	12
Vocalization				
None	12	11	12	12
Reactivity to handling				
Easy	12	11	12	12

Table 2-36 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: in-the-hand observation (Main group, Lactation day 4)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	10	12	12
Ease of removal from cage					
Easy		12	10	12	12
Fur condition					
Normal		12	10	12	12
Skin					
Normal		12	10	12	12
Secretions-Eye, Nose					
Absent		12	10	12	12
Exophthalmos					
Absent		12	10	12	12
Palpebral closure					
Normal		12	10	12	12
Mucosal membranes					
Normal		12	10	12	12
Lacrimation					
Normal		12	10	12	12
Piloerection					
Absent		12	10	12	12
Pupil size					
Normal		12	10	12	12
Salivation					
None		12	10	12	12
Abnormal respiration					
Absent		12	10	12	12
Vocalization					
None		12	10	12	12
Reactivity to handling					
Easy		12	10	12	12

Table 2-37 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: in-the-hand observation (Satellite group, Week 1 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	10	10
Ease of removal from cage			
Easy		10	10
Fur condition			
Normal		10	10
Skin			
Normal		10	10
Secretions-Eye, Nose			
Absent		10	10
Exophthalmos			
Absent		10	10
Palpebral closure			
Normal		10	10
Mucosal membranes			
Normal		10	10
Lacrimation			
Normal		10	10
Piloerection			
Absent		10	10
Pupil size			
Normal		10	10
Salivation			
None		10	10
Abnormal respiration			
Absent		10	10
Vocalization			
None		10	10
Reactivity to handling			
Easy		10	10

Table 2-38 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: in-the-hand observation (Satellite group, Week 2 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	10	10
Ease of removal from cage			
Easy		10	10
Fur condition			
Normal		10	10
Skin			
Normal		10	10
Secretions-Eye, Nose			
Absent		10	10
Exophthalmos			
Absent		10	10
Palpebral closure			
Normal		10	10
Mucosal membranes			
Normal		10	10
Lacrimation			
Normal		10	10
Piloerection			
Absent		10	10
Pupil size			
Normal		10	10
Salivation			
None		10	10
Abnormal respiration			
Absent		10	10
Vocalization			
None		10	10
Reactivity to handling			
Easy		10	10

Table 2-39 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: in-the-hand observation (Satellite group, Week 3 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	10	10
Ease of removal from cage			
Easy		10	10
Fur condition			
Normal		10	10
Skin			
Normal		10	10
Secretions-Eye, Nose			
Absent		10	10
Exophthalmos			
Absent		10	10
Palpebral closure			
Normal		10	10
Mucosal membranes			
Normal		10	10
Lacrimation			
Normal		10	10
Piloerection			
Absent		10	10
Pupil size			
Normal		10	10
Salivation			
None		10	10
Abnormal respiration			
Absent		10	10
Vocalization			
None		10	10
Reactivity to handling			
Easy		10	10

Table 2-40 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: in-the-hand observation (Satellite group, Week 4 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	10	10
Ease of removal from cage			
Easy		10	10
Fur condition			
Normal		10	10
Skin			
Normal		10	10
Secretions-Eye, Nose			
Absent		10	10
Exophthalmos			
Absent		10	10
Palpebral closure			
Normal		10	10
Mucosal membranes			
Normal		10	10
Lacrimation			
Normal		10	10
Piloerection			
Absent		10	10
Pupil size			
Normal		10	10
Salivation			
None		10	10
Abnormal respiration			
Absent		10	10
Vocalization			
None		10	10
Reactivity to handling			
Easy		10	10

Table 2-41 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: in-the-hand observation (Satellite group, Week 5 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	10	10
Ease of removal from cage			
Easy		10	10
Fur condition			
Normal		10	10
Skin			
Normal		10	10
Secretions-Eye, Nose			
Absent		10	10
Exophthalmos			
Absent		10	10
Palpebral closure			
Normal		10	10
Mucosal membranes			
Normal		10	10
Lacrimation			
Normal		10	10
Piloerection			
Absent		10	10
Pupil size			
Normal		10	10
Salivation			
None		10	10
Abnormal respiration			
Absent		10	10
Vocalization			
None		10	10
Reactivity to handling			
Easy		10	10

Table 2-42 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: in-the-hand observation (Satellite group, Week 6 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	10	10
Ease of removal from cage			
Easy		10	10
Fur condition			
Normal		10	10
Skin			
Normal		10	10
Secretions-Eye, Nose			
Absent		10	10
Exophthalmos			
Absent		10	10
Palpebral closure			
Normal		10	10
Mucosal membranes			
Normal		10	10
Lacrimation			
Normal		10	10
Piloerection			
Absent		10	10
Pupil size			
Normal		10	10
Salivation			
None		10	10
Abnormal respiration			
Absent		10	10
Vocalization			
None		10	10
Reactivity to handling			
Easy		10	10

Table 2-43 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in male rats: in-the-hand observation (Week 1 of recovery)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Ease of removal from cage			
Easy		5	5
Fur condition			
Normal		5	5
Skin			
Normal		5	5
Secretions-Eye, Nose			
Absent		5	5
Exophthalmos			
Absent		5	5
Palpebral closure			
Normal		5	5
Mucosal membranes			
Normal		5	5
Lacrimation			
Normal		5	5
Piloerection			
Absent		5	5
Pupil size			
Normal		5	5
Salivation			
None		5	5
Abnormal respiration			
Absent		5	5
Vocalization			
None		5	5
Reactivity to handling			
Easy		5	5

Table 2-44 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in male rats: in-the-hand observation (Week 2 of recovery)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Ease of removal from cage			
Easy		5	5
Fur condition			
Normal		5	5
Skin			
Normal		5	5
Secretions-Eye, Nose			
Absent		5	5
Exophthalmos			
Absent		5	5
Palpebral closure			
Normal		5	5
Mucosal membranes			
Normal		5	5
Lacrimation			
Normal		5	5
Piloerection			
Absent		5	5
Pupil size			
Normal		5	5
Salivation			
None		5	5
Abnormal respiration			
Absent		5	5
Vocalization			
None		5	5
Reactivity to handling			
Easy		5	5

Table 2-45 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: in-the-hand observation (Week 1 of recovery)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Ease of removal from cage			
Easy		5	5
Fur condition			
Normal		5	5
Skin			
Normal		5	5
Secretions-Eye, Nose			
Absent		5	5
Exophthalmos			
Absent		5	5
Palpebral closure			
Normal		5	5
Mucosal membranes			
Normal		5	5
Lacrimation			
Normal		5	5
Piloerection			
Absent		5	5
Pupil size			
Normal		5	5
Salivation			
None		5	5
Abnormal respiration			
Absent		5	5
Vocalization			
None		5	5
Reactivity to handling			
Easy		5	5

Table 2-46 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: in-the-hand observation (Week 2 of recovery)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Ease of removal from cage			
Easy		5	5
Fur condition			
Normal		5	5
Skin			
Normal		5	5
Secretions-Eye, Nose			
Absent		5	5
Exophthalmos			
Absent		5	5
Palpebral closure			
Normal		5	5
Mucosal membranes			
Normal		5	5
Lacrimation			
Normal		5	5
Piloerection			
Absent		5	5
Pupil size			
Normal		5	5
Salivation			
None		5	5
Abnormal respiration			
Absent		5	5
Vocalization			
None		5	5
Reactivity to handling			
Easy		5	5

Table 2-47 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in male rats: open field observation (Week 1 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		3± 1	5± 2*D	5± 2	5± 2
Defecation count (Mean±S.D.)		1± 1	0± 0	0± 0	0± 0
Urination					
None		11	12	10	11
Small amount		1	0	2	1

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

Table 2-48 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in male rats: open field observation (Week 2 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		4± 1	4± 1	4± 2	4± 2
Defecation count (Mean±S.D.)		0± 1	0± 1	0± 0	0± 1
Urination					
None		10	12	12	11
Small amount		2	0	0	1

No significant difference in any treated groups from control group.

Table 2-49 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in male rats: open field observation (Week 3 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		5± 2	6± 1	5± 3	5± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 1
Urination					
None		11	12	11	9
Small amount		1	0	1	3

No significant difference in any treated groups from control group.

Table 2-50 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in male rats: open field observation (Week 4 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
No/minimal location		0	0	0	1
Normal		12	12	12	11
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		4± 1	6± 2	5± 2	4± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		10	12	11	8
Small amount		2	0	1	4

No significant difference in any treated groups from control group.

Table 2-51 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in male rats: open field observation (Week 5 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		5± 2	6± 2	5± 1	5± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		10	11	7	11
Small amount		2	1	5	1

No significant difference in any treated groups from control group.

Table 2-52 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in male rats: open field observation (Week 6 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
No/minimal location		0	0	0	1
Normal		12	12	12	11
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		3± 1	5± 2*D	4± 1	4± 2
Defecation count (Mean±S.D.)		0± 0	0± 1	0± 0	0± 0
Urination					
None		8	12	9	9
Small amount		4	0	3	3

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

Table 2-53 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Main group, Week 1 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		8± 3	6± 2	6± 3	7± 3
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	12	12	12

No significant difference in any treated groups from control group.

Table 2-54 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Main group, Week 2 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		8± 2	8± 2	7± 3	8± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	12	12	12

No significant difference in any treated groups from control group.

Table 2-55 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Main group, Gestation day 1)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	11	12	12
Arousal					
Normal		12	11	12	12
Convulsion					
None		12	11	12	12
Abnormal behavior					
None		12	11	12	12
Stereotypy					
None		12	11	12	12
Gait					
No/minimal location		0	0	0	1
Normal		12	11	12	11
Posture					
Normal		12	11	12	12
Grooming					
None		12	11	12	12
Rearing (Mean±S.D.)		6± 2	6± 2	7± 4	6± 3
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	11	12	12

No significant difference in any treated groups from control group.

Table 2-56 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Main group, Gestation day 7)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	11	12	12
Arousal					
Normal		12	11	12	12
Convulsion					
None		12	11	12	12
Abnormal behavior					
None		12	11	12	12
Stereotypy					
None		12	11	12	12
Gait					
Normal		12	11	12	12
Posture					
Normal		12	11	12	12
Grooming					
None		12	11	12	12
Rearing (Mean±S.D.)		5± 2	5± 2	5± 2	5± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	11	12	12

No significant difference in any treated groups from control group.

Table 2-57 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Main group, Gestation day 14)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	11	12	12
Arousal					
Normal		12	11	12	12
Convulsion					
None		12	11	12	12
Abnormal behavior					
None		12	11	12	12
Stereotypy					
None		12	11	12	12
Gait					
Normal		12	11	12	12
Posture					
Normal		12	11	12	12
Grooming					
None		12	11	12	12
Rearing (Mean±S.D.)		6± 3	5± 2	5± 2	6± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	11	11	11
Small amount		0	0	1	1

No significant difference in any treated groups from control group.

Table 2-58 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Main group, Gestation day 20)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	11	12	12
Arousal					
Normal		12	11	12	12
Convulsion					
None		12	11	12	12
Abnormal behavior					
None		12	11	12	12
Stereotypy					
None		12	11	12	12
Gait					
Normal		12	11	12	12
Posture					
Normal		12	11	12	12
Grooming					
None		12	11	12	12
Rearing (Mean±S.D.)		6± 1	5± 2	5± 2	6± 3
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	11	12	10
Small amount		0	0	0	2

No significant difference in any treated groups from control group.

Table 2-59 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Main group, Lactation day 4)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	10	12	12
Arousal					
Normal		12	10	12	12
Convulsion					
None		12	10	12	12
Abnormal behavior					
None		12	10	12	12
Stereotypy					
None		12	10	12	12
Gait					
Normal		12	10	12	12
Posture					
Normal		12	10	12	12
Grooming					
None		12	10	12	12
Rearing (Mean±S.D.)		7± 1	8± 4	8± 3	8± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	10	12	12

No significant difference in any treated groups from control group.

Table 2-60 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Satellite group, Week 1 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	10	10
Arousal			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10
Stereotypy			
None		10	10
Gait			
Normal		10	10
Posture			
Normal		10	10
Grooming			
None		10	10
Rearing (Mean±S.D.)		8± 2	7± 1
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		9	10
Small amount		1	0

No significant difference between treated group and control group.

Table 2-61 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Satellite group, Week 2 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	10	10
Arousal			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10
Stereotypy			
None		10	10
Gait			
Normal		10	10
Posture			
Normal		10	10
Grooming			
None		10	10
Rearing (Mean±S.D.)		9± 1	7± 2*T
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	10

*: p<0.05 (Significant difference from control group)
T: Student's t-test

Table 2-62 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Satellite group, Week 3 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	10	10
Arousal			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10
Stereotypy			
None		10	10
Gait			
Normal		10	10
Posture			
Normal		10	10
Grooming			
None		10	10
Rearing (Mean±S.D.)		10± 2	9± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	10

No significant difference between treated group and control group.

Table 2-63 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Satellite group, Week 4 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	10	10
Arousal			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10
Stereotypy			
None		10	10
Gait			
Normal		10	10
Posture			
Normal		10	10
Grooming			
None		10	10
Rearing (Mean±S.D.)		9± 2	9± 3
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	10

No significant difference between treated group and control group.

Table 2-64 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Satellite group, Week 5 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	10	10
Arousal			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10
Stereotypy			
None		10	10
Gait			
Normal		10	10
Posture			
Normal		10	10
Grooming			
None		10	10
Rearing (Mean±S.D.)		10± 3	9± 3
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	10

No significant difference between treated group and control group.

Table 2-65 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Satellite group, Week 6 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	10	10
Arousal			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10
Stereotypy			
None		10	10
Gait			
Normal		10	10
Posture			
Normal		10	10
Grooming			
None		10	10
Rearing (Mean±S.D.)		8± 2	7± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	10

No significant difference between treated group and control group.

Table 2-66 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in male rats: open field observation (Week 1 of recovery)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Arousal			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5
Stereotypy			
None		5	5
Gait			
Normal		5	5
Posture			
Normal		5	5
Grooming			
None		5	5
Rearing (Mean±S.D.)		6± 2	5± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		4	3
Small amount		1	2

No significant difference between treated group and control group.

Table 2-67 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in male rats: open field observation (Week 2 of recovery)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Arousal			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5
Stereotypy			
None		5	5
Gait			
Normal		5	5
Posture			
Normal		5	5
Grooming			
None		5	5
Rearing (Mean±S.D.)		6± 1	5± 1
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		5	3
Small amount		0	2

No significant difference between treated group and control group.

Table 2-68 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Week 1 of recovery)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Arousal			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5
Stereotypy			
None		5	5
Gait			
Normal		5	5
Posture			
Normal		5	5
Grooming			
None		5	5
Rearing (Mean±S.D.)		10± 2	7± 2*T
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		5	5

*: p<0.05 (Significant difference from control group)
T: Student's t-test

Table 2-69 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Week 2 of recovery)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Arousal			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5
Stereotypy			
None		5	5
Gait			
Normal		5	5
Posture			
Normal		5	5
Grooming			
None		5	5
Rearing (Mean±S.D.)		9± 1	7± 1**T
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		5	5

**: p<0.01 (Significant difference from control group)
T: Student's t-test

Table 2-70 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Manipulative test of male rats (Week 6 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	5	5	5	5
Auditory response					
Normal		5	5	5	5
Approach response					
Normal		5	5	5	5
Touch response					
Normal		5	5	5	5
Tail pinch response					
Normal		5	5	5	5
Pupillary reflex					
Pass, both		5	5	5	5
Aerial righting reflex					
(Total score: Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Landing foot splay (mm: Mean±S.D.)		90±20	90±14	96±10	77±17

No significant difference in any treated groups from control group.

Table 2-71 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Manipulative test of female rats (Main group, Lactation day 4)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	5	5	5	5
Auditory response					
Normal		5	5	5	5
Approach response					
Normal		5	5	5	5
Touch response					
Normal		5	5	5	5
Tail pinch response					
Normal		5	5	5	5
Pupillary reflex					
Pass, both		5	5	5	5
Aerial righting reflex					
(Total score: Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Landing foot splay (mm: Mean±S.D.)		43±17	53±16	46± 9	42±15

No significant difference in any treated groups from control group.

Table 2-72 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Manipulative test of female rats (Satellite group, Week 6 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Auditory response			
Normal		5	5
Approach response			
Normal		5	5
Touch response			
Normal		5	5
Tail pinch response			
Normal		5	5
Pupillary reflex			
Pass, both		5	5
Aerial righting reflex			
(Total score: Mean±S.D.)		0± 0	0± 0
Landing foot splay (mm: Mean±S.D.)		62±21	74±17

No significant difference between treated group and control group.

Table 2-73 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Manipulative test of male rats (Week 2 of recovery)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Auditory response			
Normal		5	5
Approach response			
Normal		5	5
Touch response			
Normal		5	5
Tail pinch response			
Normal		5	5
Pupillary reflex			
Pass, both		5	5
Aerial righting reflex			
(Total score: Mean±S.D.)		0± 0	0± 0
Landing foot splay (mm: Mean±S.D.)		101±13	85±12

No significant difference between treated group and control group.

Table 2-74 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Manipulative test of female rats (Week 2 of recovery)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Auditory response			
Normal		5	5
Approach response			
Normal		5	5
Touch response			
Normal		5	5
Tail pinch response			
Normal		5	5
Pupillary reflex			
Pass, both		5	5
Aerial righting reflex			
(Total score: Mean±S.D.)		0± 0	0± 0
Landing foot splay (mm: Mean±S.D.)		60±32	82±13

No significant difference between treated group and control group.

Table 2-75 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Grip strength of male rats (Week 6 of administration)

Dose mg/kg		Fore limb g	Hind limb g
0	No.	5	5
	Mean	1547	1136
	S.D.	216	178
100	No.	5	5
	Mean	1367	1037
	S.D.	318	249
300	No.	5	5
	Mean	1602	1108
	S.D.	298	94
1000	No.	5	5
	Mean	1454	1022
	S.D.	253	124

No.: No. of animals
No significant difference in any treated groups from control group.

Table 2-76 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Grip strength of female rats (Main group, Lactation day 4)

Dose mg/kg		Fore limb g	Hind limb g
0	No.	5	5
	Mean	1139	791
	S.D.	239	181
100	No.	5	5
	Mean	1203	906
	S.D.	212	128
300	No.	5	5
	Mean	1192	710
	S.D.	130	48
1000	No.	5	5
	Mean	1229	762
	S.D.	219	183

No.: No. of animals
No significant difference in any treated groups from control group.

Table 2-77 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Grip strength of female rats (Satellite group, Week 6 of administration)

Dose mg/kg		Fore limb g	Hind limb g
0	No.	5	5
	Mean	1010	602
	S.D.	129	156
1000	No.	5	5
	Mean	1110	828
	S.D.	215	183

No.: No. of animals
No significant difference between treated group and control group.

Table 2-78 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Grip strength of male rats (Week 2 of recovery)

Dose mg/kg		Fore limb g	Hind limb g
0	No.	5	5
	Mean	1732	1052
	S.D.	90	224
1000	No.	5	5
	Mean	1478	980
	S.D.	325	137

No.: No. of animals
No significant difference between treated group and control group.

Table 2-79 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Grip strength of female rats (Week 2 of recovery)

Dose mg/kg		Fore limb g	Hind limb g
0	No.	5	5
	Mean	1094	668
	S.D.	163	107
1000	No.	5	5
	Mean	1027	869*
	S.D.	131	159T

No.: No. of animals
*: p<0.05 (Significant difference from control group)
T: Student's t-test

Table 2-80 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Motor activity of male rats (Week 6 of administration)

Dose mg/kg		Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
0	No.	5	5	5	5	5	5	5
	Mean	459	332	284	229	164	151	1620
	S.D.	52	82	79	157	143	84	452
100	No.	5	5	5	5	5	5	5
	Mean	422	352	186	102	100	190	1351
	S.D.	37	58	136	85	59	159	264
300	No.	5	5	5	5	5	5	5
	Mean	456	374	316	252	173	55	1626
	S.D.	23	60	99	134	103	53	372
1000	No.	5	5	5	5	5	5	5
	Mean	433	382	258	332	182	160	1747
	S.D.	25	70	158	83	152	87	491

Unit: Count
No.: No. of animals
No significant difference in any treated groups from control group.

Table 2-81 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Motor activity of female rats (Main group, Lactation day 4)

Dose mg/kg		Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
0	No.	5	5	5	5	5	5	5
	Mean	376	224	177	162	107	174	1220
	S.D.	88	112	86	111	144	117	584
100	No.	5	5	5	5	5	5	5
	Mean	385	181	117	92	96	101	973
	S.D.	49	98	120	88	104	139	523
300	No.	5	5	5	5	5	5	5
	Mean	351	172	120	116	81	66	906
	S.D.	69	103	24	61	64	47	274
1000	No.	5	5	5	5	5	5	5
	Mean	338	240	112	177	184	159	1212
	S.D.	57	74	80	143	118	128	533

Unit: Count
No.: No. of animals
No significant difference in any treated groups from control group.

Table 2-82 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Motor activity of female rats (Satellite group, Week 6 of administration)

Dose mg/kg		Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
0	No.	5	5	5	5	5	5	5
	Mean	417	276	212	67	58	12	1042
	S.D.	41	80	120	69	116	10	112
1000	No.	5	5	5	5	5	5	5
	Mean	398	282	194	184	105	62	1224
	S.D.	35	74	110	124	128	71	423

Unit: Count
No.: No. of animals
No significant difference between treated group and control group.

Table 2-83 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Motor activity of male rats (Week 2 of recovery)

Dose mg/kg		Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
0	No.	5	5	5	5	5	5	5
	Mean	401	320	225	154	152	186	1438
	S.D.	64	87	85	147	118	107	385
1000	No.	5	5	5	5	5	5	5
	Mean	382	273	212	117	136	143	1263
	S.D.	40	87	109	100	65	122	392

Unit: Count
No.: No. of animals
No significant difference between treated group and control group.

Table 2-84 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Motor activity of female rats (Week 2 of recovery)

Dose mg/kg		Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
0	No.	5	5	5	5	5	5	5
	Mean	324	260	229	213	49	61	1137
	S.D.	68	51	64	65	85	82	248
1000	No.	5	5	5	5	5	5	5
	Mean	331	254	102	192	115	54	1048
	S.D.	95	123	121	62	128	85	314

Unit: Count
No.: No. of animals
No significant difference between treated group and control group.

Table 3-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Body weight of male rats (Administration period)

Dose mg/kg		Day of administration 1	8	15	22	29	36	42	Gain 1-42
0	No.	12	12	12	12	12	12	12	12
	Mean	401	429	453	474	497	519	528	128
	S.D.	17	20	23	23	25	25	26	19
100	No.	12	12	12	12	12	12	12	12
	Mean	403	430	458	481	502	524	536	133
	S.D.	20	22	26	24	30	32	33	23
300	No.	12	12	12	12	12	12	12	12
	Mean	403	429	454	479	499	523	531	128
	S.D.	18	20	23	28	29	30	31	15
1000	No.	12	12	12	12	12	12	12	12
	Mean	404	429	453	473	497	518	529	125
	S.D.	17	20	24	26	28	32	32	22

Unit: g
No.: No. of animals
No significant difference in any treated groups from control group.

Table 3-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Body weight of female rats during the pre-mating period (Main group)

Dose mg/kg		Day of administration 1	8	15	Gain 1-15
0	No.	12	12	12	12
	Mean	229	243	255	26
	S.D.	11	11	12	8
100	No.	12	12	12	12
	Mean	230	241	251	21
	S.D.	13	17	19	10
300	No.	12	12	12	12
	Mean	230	241	251	21
	S.D.	15	15	17	9
1000	No.	12	12	12	12
	Mean	229	241	251	22
	S.D.	12	12	12	7

Unit: g
No.: No. of animals
No significant difference in any treated groups from control group.

Table 3-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Body weight of dams during the gestation period (Main group)

Dose mg/kg		Administration 0	7	14	20a)	Gain 0-20
0	No.	12	12	12	12	12
	Mean	261	294	331	409	148
	S.D.	12	15	18	20	14
100	No.	11	11	11	11	11
	Mean	259	291	326	399	140
	S.D.	17	17	21	20	16
300	No.	12	12	12	12	12
	Mean	257	287	323	399	142
	S.D.	20	21	20	24	14
1000	No.	12	12	12	12	12
	Mean	259	291	326	400	141
	S.D.	14	14	17	26	22

Unit: g
No.: No. of dams
a): Gestation day
No significant difference in any treated groups from control group.

Table 3-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Body weight of dams during the lactation period (Main group)

Dose mg/kg		Administration 0	Administration 4a)	Gain 0-4
0	No.	12	12	12
	Mean	314	329	15
	S.D.	20	18	19
100	No.	11	10b)	10
	Mean	312	328	20
	S.D.	23	17	10
300	No.	12	12	12
	Mean	305	321	17
	S.D.	20	22	15
1000	No.	12	12	12
	Mean	315	323	9
	S.D.	21	14	15

Unit: g
No.: No. of dams
a): Lactation day
b): One dam was necropsied on lactation day 1 because all pups died.
No significant difference in any treated groups from control group.

Table 3-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Body weight of female rats (Satellite group, Administration period)

Dose mg/kg		Day of administration 1	8	15	22	29	36	42	Gain 1-42
0	No.	10	10	10	10	10	10	10	10
	Mean	230	240	251	262	270	276	280	50
	S.D.	11	15	16	21	28	22	19	13
1000	No.	10	10	10	10	10	10	10	10
	Mean	228	240	250	261	267	273	278	50
	S.D.	8	11	14	14	13	14	14	11

Unit: g
No.: No. of animals
No significant difference between treated group and control group.

Table 3-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Body weight of male rats (Recovery period)

Dose mg/kg		Day of recovery 1	8	14	Gain 1-14
0	No.	5	5	5	5
	Mean	514	528	529	15
	S.D.	20	19	13	13
1000	No.	5	5	5	5
	Mean	528	537	540	12
	S.D.	48	46	49	2

Unit: g
No.: No. of animals
No significant difference between treated group and control group.

Table 3-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Body weight of female rats (Recovery period)

Dose mg/kg		Day of recovery 1	8	14	Gain 1-14
0	No.	5	5	5	5
	Mean	284	293	296	12
	S.D.	24	26	28	7
1000	No.	5	5	5	5
	Mean	274	277	278	4
	S.D.	11	8	10	5

Unit: g
No.: No. of animals
No significant difference between treated group and control group.

Table 4-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Food consumption of male rats (Administration period)

Dose mg/kg		Day of administration 2	8	15	30	36	42
	No.	12	12	12	12	12	12
0	Mean	25	25	25	23	24	23
	S.D.	2	2	2	2	2	3
	No.	12	12	12	12	12	12
100	Mean	24	25	25	22	23	23
	S.D.	2	2	3	2	2	2
	No.	12	12	12	12	12	12
300	Mean	25	25	25	23	24	23
	S.D.	2	2	2	2	2	1
	No.	12	12	12	12	12	12
1000	Mean	25	25	24	23	23	23
	S.D.	3	1	2	2	2	2

Unit: g/rat/day
No.: No. of animals
No significant difference in any treated groups from control group.

Table 4-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Food consumption of female rats during the pre-mating period (Main group)

Dose mg/kg		Day of administration 2	8	15
	No.	12	12	12
0	Mean	16	18	19
	S.D.	4	3	2
	No.	12	12	12
100	Mean	16	17	17
	S.D.	2	3	3
	No.	12	12	12
300	Mean	17	17	16
	S.D.	2	2	3
	No.	12	12	12
1000	Mean	15	17	17
	S.D.	2	4	2

Unit: g/rat/day
No.: No. of animals
No significant difference in any treated groups from control group.

Table 4-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Food consumption of dams during the gestation period (Main group)

Dose mg/kg		Administration 1	7	14	20a)
0	No.	12	12	12	12
	Mean	19	22	24	22
	S.D.	2	3	2	4
100	No.	11	11	11	11
	Mean	17	22	23	21
	S.D.	3	2	3	2
300	No.	12	12	12	12
	Mean	18	20	22	19
	S.D.	3	2	2	3
1000	No.	12	12	12	12
	Mean	18	20	22	20
	S.D.	2	3	2	3

Unit: g/rat/day
No.: No. of dams
a): Gestation day
No significant difference in any treated groups from control group.

Table 4-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Food consumption of dams during the lactation period (Main group)

Dose mg/kg		Administration 2	Administration 4a)
0	No.	12	12
	Mean	21	40
	S.D.	8	8
100	No.	10b)	10
	Mean	26	40
	S.D.	5	6
300	No.	12	12
	Mean	20	39
	S.D.	5	6
1000	No.	12	12
	Mean	18	37
	S.D.	5	7

Unit: g/rat/day
No.: No. of dams
a): Lactation day
b): One dam was necropsied on lactation day 1 because all pups died.
No significant difference in any treated groups from control group.

Table 4-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Food consumption of female rats (Satellite group, Administration period)

Dose mg/kg		Day of administration 2	8	15	30	36	42
0	No.	10	10	10	10	10	10
	Mean	16	17	18	17	17	17
	S.D.	3	3	3	2	3	1
1000	No.	10	10	10	10	10	10
	Mean	17	16	16	16	15	16
	S.D.	2	3	3	2	3	3

Unit: g/rat/day
No.: No. of animals
No significant difference between treated group and control group.

Table 4-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Food consumption of male rats (Recovery period)

Dose mg/kg		Day of recovery 1	8	14
0	No.	5	5	5
	Mean	20	29	28
	S.D.	3	4	3
1000	No.	5	5	5
	Mean	20	27	27
	S.D.	2	2	2

Unit: g/rat/day
No.: No. of animals
No significant difference between treated group and control group.

Table 4-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Food consumption of female rats (Recovery period)

Dose mg/kg		Day of recovery 1	8	14
	No.	5	5	5
0	Mean	13	21	21
	S.D.	2	3	3
	No.	5	5	5
1000	Mean	14	17	18
	S.D.	2	2	3

Unit: g/rat/day
No.: No. of animals
No significant difference between treated group and control group.

Table 5-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Urinalysis of male rats (Week 6 of administration)

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

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL

Table 5-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Urinalysis of male rats (Week 6 of administration)

Dose mg/kg	No.	Occult blood 4)					Bilirubin 5)				Urobilinogen 6)				Color 7)		
		-	+-	+	++	+++	-	+	++	+++	+-	+	++	+++	LY	Y	DY
0	5	2	2	0	0	1	4	1	0	0	4	1	0	0	0	5	0
100	5	2	3	0	0	0	5	0	0	0	5	0	0	0	0	5	0
300	5	3	2	0	0	0	3	2	0	0	4	1	0	0	0	5	0
1000	5	4	1	0	0	0	4	1	0	0	3	1	1	0	0	5	0

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

Table 5-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Urinalysis of male rats (Week 6 of administration)

Dose mg/kg	No.	URINE SEDIMENT																																	
		RBC					WBC					SEC					SREC					Cast			CRYSTALLIZATION PS					CRYSTALLIZATION CO				
		-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	-	+-	+	++	+++	-	+-	+	++	+++
0	5	4	1	0	0	0	5	0	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0	0	1	4	0	0	0	5	0	0	0	0
100	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0	0	2	2	1	0	0	5	0	0	0	0
300	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0	0	2	3	0	0	0	5	0	0	0	0
1000	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0	0	0	5	0	0	0	5	0	0	0	0

SEC : Squamous Epithelial Cell
SREC : Small Round Epithelial Cell
PS : Phosphate Salts
CO : Calcium Oxalate

\- : Negative
+- : Slight
\+ : Mild
++ : Moderate
+++ : Severe

Table 5-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Water intake and urinalysis of male rats (Week 6 of administration)

Dose mg/kg	No.		Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
0	5	Mean	38	12.3	1903	1.11	3.39	1.50
		S.D.	8	3.8	646	0.34	0.62	0.42
100	5	Mean	39	15.3	1807	1.25	4.33	1.78
		S.D.	7	5.6	444	0.22	0.90	0.38
300	5	Mean	33	8.8	2055	0.97	3.02	1.33
		S.D.	8	1.2	376	0.11	0.27	0.18
1000	5	Mean	32	10.4	1921	1.00	3.12	1.38
		S.D.	3	3.6	283	0.29	0.85	0.43

No significant difference in any treated groups from control group.

Table 5-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Urinalysis of female rats (Satellite group, Week 6 of administration)

Dose mg/kg	No.	pH									Protein 1)						Ketone body 2)						Glucose 3)					
		5.0	5.5	6.0	6.5	7.0	7.5	8.0	8.5	>=9.0	-	+-	+	++	+++		-	+-	+	++	+++		-	+	++	+++	++++	
0	5	0	0	0	1	2	1	0	0	1	3	1	1	0	0		2	3	0	0	0		5	0	0	0	0	
1000	5	0	0	2	0	1	2	0	0	0	1	0	4	0	0		1	3	1	0	0		5	0	0	0	0	

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL

Table 5-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Urinalysis of female rats (Satellite group, Week 6 of administration)

Dose mg/kg	No.	Occult blood 4) -	+-	+	++	+++	Bilirubin 5) -	+	++	+++	Urobilinogen 6) +-	+	++	+++	Color 7) LY	Y	DY
0	5	5	0	0	0	0	5	0	0	0	4	0	1	0	0	5	0
1000	5	5	0	0	0	0	4	1	0	0	3	2	0	0	0	5	0

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

Table 5-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Urinalysis of female rats (Satellite group, Week 6 of administration)

Dose mg/kg	No.	URINE SEDIMENT																																					
		RBC					WBC					SEC					SREC					Cast			CRYSTALLIZATION PS					CRYSTALLIZATION CO									
		-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	-	+-	+	++	+++	-	+-	+	++	+++					
0	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0	0	2	3	0	0	0	5	0	0	0	0					
1000	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0	0	1	4	0	0	0	5	0	0	0	0					

SEC : Squamous Epithelial Cell
SREC : Small Round Epithelial Cell
PS : Phosphate Salts
CO : Calcium Oxalate

\- : Negative
+- : Slight
\+ : Mild
++ : Moderate
+++ : Severe

Table 5-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Water intake and urinalysis of female rats (Satellite group, Week 6 of administration)

Dose mg/kg	No.		Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
0	5	Mean	26	5.9	2197	0.69	1.94	0.82
		S.D.	2	2.3	322	0.25	0.83	0.40
1000	5	Mean	24	7.9	2001	0.81	2.21	1.02
		S.D.	7	5.2	433	0.24	0.87	0.34

No significant difference between treated group and control group.

Table 5-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Urinalysis of male rats (Week 2 of recovery)

Dose	No.	pH								Protein 1)					Ketone body 2)					Glucose 3)				
mg/kg		5.0	5.5	6.0	6.5	7.0	7.5	8.0	8.5	>=9.0	-	+-	+	++	+++	-	+-	+	++	+++	-	+	++	+++	++++
0	5	0	0	0	0	0	2	2	1	0	1	1	2	1	0	1	1	2	1	0	5	0	0	0	0
1000	5	0	0	0	0	0	0	2	2	1	0	4	1	0	0	0	1	4	0	0	5	0	0	0	0

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL

Table 5-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Urinalysis of male rats (Week 2 of recovery)

Dose mg/kg	No.	Occult blood 4) -	+-	+	++	+++	Bilirubin 5) -	+	++	+++	Urobilinogen 6) +-	+	++	+++	Color 7) LY	Y	DY
0	5	2	3	0	0	0	5	0	0	0	5	0	0	0	0	5	0
1000	5	2	3	0	0	0	5	0	0	0	5	0	0	0	0	5	0

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

Table 5-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Urinalysis of male rats (Week 2 of recovery)

URINE SEDIMENT

Dose mg/kg	No.	RBC -	RBC +-	RBC +	RBC ++	RBC +++	WBC -	WBC +-	WBC +	WBC ++	WBC +++	SEC -	SEC +-	SEC +	SEC ++	SEC +++	SREC -	SREC +-	SREC +	SREC ++	SREC +++	Cast -	Cast +-	Cast +	CRYSTALLIZATION PS -	PS +-	PS +	PS ++	PS +++	CRYSTALLIZATION CO -	CO +-	CO +	CO ++	CO +++
0	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0	0	0	2	3	0	0	5	0	0	0	0
1000	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0	0	0	3	2	0	0	5	0	0	0	0

SEC : Squamous Epithelial Cell
SREC : Small Round Epithelial Cell
PS : Phosphate Salts
CO : Calcium Oxalate

\- : Negative
+- : Slight
\+ : Mild
++ : Moderate
+++ : Severe

Table 5-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Water intake and urinalysis of male rats (Week 2 of recovery)

Dose mg/kg	No.		Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
0	5	Mean	41	19.9	1817	1.78	5.58	2.31
		S.D.	9	5.4	368	0.22	0.94	0.29
1000	5	Mean	37	15.2	2037	1.45	5.12	2.06
		S.D.	8	3.8	210	0.36	1.13	0.43

No significant difference between treated group and control group.

Table 5-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Urinalysis of female rats (Week 2 of recovery)

Dose mg/kg	No.	pH									Protein 1)					Ketone body 2)					Glucose 3)				
		5.0	5.5	6.0	6.5	7.0	7.5	8.0	8.5	>=9.0	-	+-	+	++	+++	-	+-	+	++	+++	-	+	++	+++	++++
0	5	0	0	0	1	3	0	0	1	0	3	1	1	0	0	3	2	0	0	0	5	0	0	0	0
1000	5	0	0	1	1	1	0	1	1	0	4	1	0	0	0	3	2	0	0	0	5	0	0	0	0

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL

Table 5-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Urinalysis of female rats (Week 2 of recovery)

Dose mg/kg	No.	Occult blood 4)					Bilirubin 5)				Urobilinogen 6)				Color 7)		
		-	+-	+	++	+++	-	+	++	+++	+-	+	++	+++	LY	Y	DY
0	5	4	0	1	0	0	5	0	0	0	5	0	0	0	0	5	0
1000	5	5	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0

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

Table 5-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Urinalysis of female rats (Week 2 of recovery)

Dose mg/kg	No.	URINE SEDIMENT																																	
		RBC					WBC					SEC					SREC					Cast			CRYSTALLIZATION PS					CRYSTALLIZATION CO				
		-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	-	+-	+	++	+++	-	+-	+	++	+++
0	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0	0	1	2	2	0	0	5	0	0	0	0
1000	5	5	0	0	0	0	4	1	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0	0	1	4	0	0	0	5	0	0	0	0

SEC : Squamous Epithelial Cell
SREC : Small Round Epithelial Cell
PS : Phosphate Salts
CO : Calcium Oxalate

\- : Negative
+- : Slight
\+ : Mild
++ : Moderate
+++ : Severe

Table 5-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Water intake and urinalysis of female rats (Week 2 of recovery)

Dose mg/kg	No.		Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
0	5	Mean	27	8.9	2220	1.04	2.91	1.14
		S.D.	6	2.0	112	0.16	0.51	0.25
1000	5	Mean	27	7.6	2220	0.81	2.59	1.00
		S.D.	8	2.8	259	0.25	0.94	0.35

No significant difference between treated group and control group.

Table 6-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Hematology of male rats (End of administration)

Dose mg/kg	No.		RBC 10E4/μL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/μL	PT s	APTT s	FIB mg/dL
0	5	Mean	867	15.7	44.3	51.2	18.1	35.4	2.1	93.8	14.0	18.3	283
		S.D.	56	0.7	2.1	2.1	0.7	0.3	0.3	11.0	1.2	1.9	18
100	5	Mean	896	15.8	44.5	49.6	17.6	35.5	1.9	91.9	14.6	20.2	240*
		S.D.	37	0.5	1.5	1.1	0.4	0.4	0.2	7.7	2.6	4.0	30D
300	5	Mean	880	15.7	44.3	50.4	17.9	35.5	1.7	92.3	16.3	21.3	243*
		S.D.	57	0.4	1.2	2.6	1.1	0.5	0.4	10.8	3.8	3.8	18D
1000	5	Mean	839	15.2	43.3	51.7	18.2	35.2	2.3	103.9	16.0	21.8	264
		S.D.	29	0.4	1.2	1.9	0.5	0.5	0.5	19.5	2.6	2.7	25

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

Table 6-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Hematology of male rats (End of administration)

Dose mg/kg	No.		WBC	Differential leukocyte ratio (%)						Differential leukocyte counts (10E2/μL)					
			10E2/μL	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	5	Mean	79.4	70.9	25.4	1.3	0.2	1.7	0.5	56.5	20.0	1.0	0.2	1.4	0.4
		S.D.	15.9	8.9	8.5	0.2	0.1	0.5	0.2	14.7	7.1	0.3	0.1	0.4	0.1
100	5	Mean	66.2	66.5	29.2	1.5	0.2	2.0	0.6	44.0	19.4	1.0	0.1	1.3	0.4
		S.D.	13.0	6.9	7.0	0.4	0.0	0.5	0.3	10.1	5.6	0.3	0.0	0.4	0.2
300	5	Mean	55.7*	76.1	20.0	1.4	0.2	1.7	0.6	42.8	10.8*	0.8	0.1	0.9	0.3
		S.D.	11.7D	6.3	5.9	0.4	0.1	0.5	0.2	11.0	3.1D	0.2	0.0	0.1	0.1
1000	5	Mean	71.6	73.2	22.2	1.3	0.2	2.3	0.8	52.2	16.0	0.9	0.1	1.7	0.6
		S.D.	11.1	3.2	2.1	0.4	0.1	0.8	0.4	7.7	3.3	0.3	0.1	0.7	0.4

LUC: Large unstained cells
*: $p<0.05$ (Significant difference from control group)
D: Dunnett's test

Table 6-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Hematology of female rats (Lactation day 5)

Dose mg/kg	No.		RBC 10E4/μL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/μL	PT s	APTT s	FIB mg/dL
0	5	Mean	685	12.9	37.1	54.3	18.8	34.7	7.1	139.4	11.0	14.3	321
		S.D.	36	0.8	1.7	2.6	1.0	0.5	1.9	25.9	0.8	1.2	32
100	5	Mean	703	13.7	39.2	55.8	19.5	34.9	6.5	134.9	12.0	15.6	306
		S.D.	41	0.4	0.9	2.9	0.8	0.5	1.2	12.1	0.8	1.7	82
300	5	Mean	720	13.4	38.5	53.5	18.7	34.9	5.5	140.8	11.2	14.7	269
		S.D.	42	0.6	1.6	1.6	0.5	0.3	1.4	18.9	0.6	1.0	73
1000	5	Mean	714	13.7	38.8	54.4	19.3	35.4*	6.0	131.9	11.6	15.4	267
		S.D.	27	0.1	0.6	2.1	0.7	0.3D	1.1	18.2	0.8	1.7	36

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

Table 6-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Hematology of female rats (Lactation day 5)

Dose mg/kg	No.		WBC	Differential leukocyte ratio (%)						Differential leukocyte counts (10E2/μL)					
			10E2/μL	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	5	Mean	107.7	47.7	49.3	0.7	0.2	1.7	0.4	51.3	53.2	0.8	0.2	1.9	0.5
		S.D.	21.9	6.6	6.3	0.2	0.1	0.7	0.1	11.6	14.2	0.2	0.1	0.9	0.1
100	5	Mean	111.1	50.3	45.8	0.6	0.1	2.7	0.4	56.3	50.6	0.7	0.2	2.9	0.4
		S.D.	27.3	7.6	6.7	0.3	0.1	1.0	0.1	17.5	13.9	0.2	0.1	1.4	0.2
300	5	Mean	136.4	54.4	41.5	0.9	0.2	2.5	0.6	73.1	57.8	1.2*	0.3	3.3	0.8
		S.D.	17.9	11.6	11.9	0.3	0.1	0.5	0.3	13.2	24.3	0.4D	0.1	0.4	0.4
1000	5	Mean	97.3	52.7	43.4	0.9	0.1	2.4	0.4	50.4	43.2	0.8	0.1	2.4	0.4
		S.D.	26.0	10.2	10.1	0.4	0.0	0.4	0.2	14.5	15.3	0.2	0.1	0.9	0.2

LUC: Large unstained cells
*: $p<0.05$ (Significant difference from control group)
D: Dunnett's test

Table 6-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Hematology of female rats (Satellite group, End of administration)

Dose mg/kg	No.		RBC 10E4/μL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/μL	PT s	APTT s	FIB mg/dL
0	5	Mean	812	14.9	41.8	51.4	18.4	35.8	1.5	100.7	11.8	12.8	186
		S.D.	29	0.5	1.3	1.1	0.5	0.3	0.3	7.9	0.3	0.8	16
1000	5	Mean	819	15.0	42.1	51.4	18.3	35.6	1.6	111.2*	11.7	14.7	178
		S.D.	34	0.7	2.3	0.9	0.3	0.4	0.3	6.1T	0.7	1.9	21

*: $p<0.05$ (Significant difference from control group)
T: Student's t-test

Table 6-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Hematology of female rats (Satellite group, End of administration)

Dose mg/kg	No.		WBC	Differential leukocyte ratio (%)						Differential leukocyte counts (10E2/μL)					
			10E2/μL	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	5	Mean	43.7	77.3	18.9	1.7	0.1	1.3	0.6	33.7	8.4	0.7	0.0	0.6	0.2
		S.D.	5.6	10.1	10.3	0.4	0.0	0.3	0.3	5.4	5.2	0.1	0.1	0.1	0.1
1000	5	Mean	48.1	77.2	18.9	1.6	0.2	1.7	0.5	37.4	8.7	0.8	0.1	0.8	0.3
		S.D.	10.8	7.2	7.1	0.5	0.1	0.6	0.2	10.9	3.3	0.3	0.1	0.2	0.2

LUC: Large unstained cells
No significant difference between treated group and control group.

Table 6-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Hematology of male rats (End of recovery)

Dose mg/kg	No.		RBC 10E4/μL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/μL	PT s	APTT s	FIB mg/dL
0	5	Mean	927	15.6	44.8	48.5	16.9	34.8	2.0	102.5	19.1	22.4	281
		S.D.	85	0.9	2.4	2.2	0.8	0.5	0.8	7.5	2.9	2.0	26
1000	5	Mean	914	15.9	45.9	50.3	17.4	34.7	1.8	99.8	16.3	21.2	262
		S.D.	32	0.4	1.5	1.5	0.4	0.4	0.1	11.7	2.5	3.8	31

No significant difference between treated group and control group.

Table 6-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Hematology of male rats (End of recovery)

Dose mg/kg	No.		WBC	Differential leukocyte ratio (%)						Differential leukocyte counts (10E2/μL)					
			10E2/μL	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	5	Mean	68.6	72.7	22.9	1.4	0.2	2.1	0.6	50.0	15.6	0.9	0.1	1.5	0.5
		S.D.	13.6	7.5	6.8	0.5	0.1	0.7	0.2	12.5	5.8	0.2	0.1	0.7	0.2
1000	5	Mean	59.5	73.2	21.8	1.6	0.3	2.4	0.7	43.6	13.0	0.9	0.2	1.4	0.4
		S.D.	11.4	7.9	8.1	0.5	0.1	0.6	0.5	9.5	6.4	0.4	0.1	0.4	0.3

LUC: Large unstained cells
No significant difference between treated group and control group.

Table 6-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Hematology of female rats (End of recovery)

Dose mg/kg	No.		RBC 10E4/μL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/μL	PT s	APTT s	FIB mg/dL
0	5	Mean	844	15.5	43.2	51.2	18.3	35.9	1.9	106.5	12.2	15.3	174
		S.D.	27	0.4	1.2	0.5	0.3	0.4	0.7	9.7	0.7	1.1	18
1000	5	Mean	865	15.9	44.7	51.7	18.4	35.6	1.5	107.0	12.4	16.9	172
		S.D.	30	0.4	1.4	1.6	0.4	0.4	0.4	5.1	0.4	1.2	23

No significant difference between treated group and control group.

Table 6-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Hematology of female rats (End of recovery)

Dose mg/kg	No.		WBC	Differential leukocyte ratio (%)						Differential leukocyte counts (10E2/μL)					
			10E2/μL	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	5	Mean	42.8	78.1	17.3	1.5	0.2	2.0	0.9	33.3	7.5	0.6	0.1	0.9	0.4
		S.D.	11.8	3.8	3.2	0.6	0.1	0.8	0.5	8.5	2.9	0.2	0.0	0.4	0.4
1000	5	Mean	43.0	77.2	18.1	1.7	0.2	1.7	1.1	32.9	8.1	0.7	0.1	0.7	0.5
		S.D.	16.1	4.1	3.4	0.6	0.1	0.6	0.6	11.4	4.1	0.3	0.0	0.3	0.4

LUC: Large unstained cells
No significant difference between treated group and control group.

Table 7-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Blood chemistry of male rats (End of administration)

Dose mg/kg	No.		AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
0	5	Mean	87	39	73	1	393	18.3	57	48	96	0.1	134
		S.D.	52	28	55	0	71	20.0	9	18	11	0.0	18
100	5	Mean	62	25	50	1	428	12.3	49	30	83	0.1	137
		S.D.	7	2	15	0	115	9.5	10	17	11	0.0	26
300	5	Mean	61	29	48	1	423	9.1	53	27	88	0.1	145
		S.D.	6	2	8	1	113	4.8	7	7	8	0.1	10
1000	5	Mean	60	27	43	1	378	14.0	55	34	91	0.1	149
		S.D.	5	2	11	0	58	4.2	11	15	11	0.1	22

No significant difference in any treated groups from control group.

Table 7-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Blood chemistry of male rats (End of administration)

Dose mg/kg	No.		BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
0	5	Mean	14	0.23	143	4.5	106	10.1	6.1	5.9	3.2	1.22
		S.D.	2	0.00	1	0.2	2	0.4	0.8	0.3	0.1	0.08
100	5	Mean	12	0.25	143	4.4	106	9.9	6.1	5.7	3.2	1.29
		S.D.	2	0.01	1	0.2	1	0.3	0.6	0.3	0.2	0.10
300	5	Mean	14	0.25	143	4.5	106	9.7	6.1	5.7	3.2	1.24
		S.D.	2	0.02	1	0.2	2	0.2	0.7	0.3	0.1	0.10
1000	5	Mean	13	0.25	143	4.7	106	9.7	6.3	5.6	3.1	1.24
		S.D.	2	0.02	1	0.2	1	0.3	0.5	0.2	0.1	0.06

No significant difference in any treated groups from control group.

Table 7-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Blood chemistry of female rats (Lactation day 5)

Dose mg/kg	No.		AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
0	5	Mean	83	58	40	1	238	15.8	59	44	112	0.1	125
		S.D.	12	10	8	0	22	7.7	10	22	10	0.0	10
100	5	Mean	73	48	32	1	255	16.6	62	50	129	0.1	133
		S.D.	14	9	6	0	66	12.6	14	11	14	0.0	9
300	5	Mean	89	49	52	1	199	10.5	52	40	110	0.1	121
		S.D.	18	4	10	1	46	4.3	11	25	26	0.0	4
1000	5	Mean	86	44	48	1	213	9.9	50	43	105	0.1	122
		S.D.	16	13	12	0	16	4.0	17	28	32	0.1	7

No significant difference in any treated groups from control group.

Table 7-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Blood chemistry of female rats (Lactation day 5)

Dose mg/kg	No.		BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
0	5	Mean	14	0.26	141	3.7	104	10.2	7.0	5.8	3.4	1.45
		S.D.	1	0.05	1	0.3	2	0.3	0.9	0.2	0.1	0.11
100	5	Mean	15	0.28	139*	3.9	104	10.2	6.8	6.1	3.5	1.36
		S.D.	2	0.05	1D	0.4	2	0.2	0.8	0.1	0.1	0.14
300	5	Mean	14	0.25	139	4.0	103	10.2	7.6	6.0	3.5	1.35
		S.D.	2	0.02	1	0.1	1	0.5	0.2	0.2	0.2	0.14
1000	5	Mean	14	0.28	139	3.9	104	10.2	6.5	5.9	3.4	1.34
		S.D.	1	0.02	1	0.5	1	0.2	0.7	0.3	0.2	0.11

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

Table 7-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Blood chemistry of female rats (Satellite group, End of administration)

Dose mg/kg	No.		AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
0	5	Mean	60	24	50	1	262	12.4	51	9	102	0.1	125
		S.D.	8	4	16	0	77	3.4	7	2	14	0.0	11
1000	5	Mean	57	23	45	1	209	13.3	56	14	114	0.1	126
		S.D.	6	4	6	1	36	8.0	7	5	13	0.0	8

No significant difference between treated group and control group.

Table 7-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Blood chemistry of female rats (Satellite group, End of administration)

Dose mg/kg	No.		BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
0	5	Mean	19	0.32	141	4.4	107	10.1	4.9	6.1	3.6	1.44
		S.D.	1	0.05	1	0.1	2	0.2	0.3	0.1	0.1	0.07
1000	5	Mean	16*	0.31	141	4.5	107	10.1	4.5	6.2	3.7	1.47
		S.D.	2T	0.02	1	0.2	1	0.2	0.8	0.3	0.2	0.13

*: p<0.05 (Significant difference from control group)
T: Student's t-test

Table 7-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Blood chemistry of male rats (End of recovery)

Dose mg/kg	No.		AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
0	5	Mean	61	29	43	1	264	9.1	47	42	83	0.1	143
		S.D.	3	3	7	1	45	4.1	12	16	16	0.0	13
1000	5	Mean	90	54	62	1	351	9.7	53	32	88	0.1	152
		S.D.	62	57	37	0	89	4.9	13	15	16	0.0	8

No significant difference between treated group and control group.

Table 7-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Blood chemistry of male rats (End of recovery)

Dose mg/kg	No.		BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
0	5	Mean	15	0.20	142	4.4	106	9.5	5.5	5.7	3.1	1.18
		S.D.	2	0.02	0	0.2	1	0.3	0.4	0.2	0.1	0.07
1000	5	Mean	15	0.21	142	4.5	106	9.5	5.4	5.8	3.1	1.20
		S.D.	2	0.04	1	0.1	1	0.3	0.4	0.2	0.1	0.10

No significant difference between treated group and control group.

Table 7-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Blood chemistry of female rats (End of recovery)

Dose mg/kg	No.		AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
0	5	Mean	62	28	36	1	163	14.6	65	12	125	0.1	128
		S.D.	6	8	6	0	47	7.5	28	6	51	0.0	22
1000	5	Mean	71	39	48*	1	127	8.6	62	11	119	0.1	115
		S.D.	11	14	8T	0	23	2.6	10	3	18	0.0	11

*: p<0.05 (Significant difference from control group)
T: Student's t-test

Table 7-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Blood chemistry of female rats (End of recovery)

Dose mg/kg	No.		BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
0	5	Mean	19	0.26	141	4.2	107	10.0	5.9	6.4	3.8	1.44
		S.D.	2	0.02	1	0.3	1	0.4	0.6	0.5	0.4	0.14
1000	5	Mean	17	0.27	142	4.5	108	10.1	5.7	6.6	3.9	1.47
		S.D.	1	0.01	1	0.2	1	0.2	0.8	0.2	0.2	0.12

No significant difference between treated group and control group.

Table 8-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Organ weight of male rats (End of administration)

	Dose mg/kg		Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)	Liver g(g/100g BW)
Absolute	0	No.	7	7	7	7	7	7	7
		Mean	513	2.14	12.8	22.2	283	1.39	14.57
		S.D.	26	0.11	1.5	3.5	64	0.09	0.86
	100	No.	12	12	12	12	12	12	12
		Mean	514	2.15	13.8	21.1	243	1.42	14.04
		S.D.	33	0.03	1.2	4.5	57	0.08	1.37
	300	No.	12	12	12	12	12	12	12
		Mean	508	2.16	13.2	21.7	247	1.46	13.67
		S.D.	30	0.09	1.3	3.1	37	0.15	1.37
	1000	No.	7	7	7	7	7	7	7
		Mean	504	2.14	13.9	21.9	291	1.48	13.55
		S.D.	20	0.05	1.4	2.0	80	0.07	0.86
Relative	0	No.		7	7	7	7	7	7
		Mean		0.42	2.5	4.3	55	0.27	2.84
		S.D.		0.02	0.3	0.8	11	0.02	0.05
	100	No.		12	12	12	12	12	12
		Mean		0.42	2.7	4.1	47	0.28	2.73
		S.D.		0.03	0.3	1.0	9	0.02	0.13
	300	No.		12	12	12	12	12	12
		Mean		0.43	2.6	4.3	49	0.29	2.69
		S.D.		0.02	0.2	0.7	7	0.03	0.15
	1000	No.		7	7	7	7	7	7
		Mean		0.42	2.8	4.3	58	0.29	2.69
		S.D.		0.01	0.2	0.5	14	0.01	0.19

No significant difference in any treated groups from control group.

Table 8-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Organ weight of male rats (End of administration)

	Dose mg/kg		Spleen g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Testis (R+L) g(g/100g BW)	Epididymis (R+L) mg(mg/100g BW)	Seminal vesicle g(g/100g BW)	Prostate g(g/100g BW)
Absolute	0	No.	7	7	7	7	7	7	7
		Mean	0.72	3.21	61	3.22	1294	1.70	1.16
		S.D.	0.09	0.23	8	0.14	67	0.16	0.14
	100	No.	12	12	12	12	12	12	12
		Mean	0.73	3.29	66	3.41*	1350	1.89	1.28
		S.D.	0.10	0.30	7	0.61ST	199	0.25	0.22
	300	No.	12	12	12	12	12	12	12
		Mean	0.70	3.24	65	3.31	1258	1.84	1.24
		S.D.	0.12	0.23	8	0.25	71	0.24	0.16
	1000	No.	7	7	7	7	7	7	7
		Mean	0.76	3.84	59	3.31	1311	2.03*	1.42*
		S.D.	0.10	1.76	6	0.30	56	0.25D	0.22D
Relative	0	No.	7	7	7	7	7	7	7
		Mean	0.14	0.63	12	0.63	253	0.33	0.23
		S.D.	0.01	0.05	2	0.04	16	0.04	0.02
	100	No.	12	12	12	12	12	12	12
		Mean	0.14	0.64	13	0.67	265	0.37	0.25
		S.D.	0.02	0.05	1	0.14	47	0.05	0.05
	300	No.	12	12	12	12	12	12	12
		Mean	0.14	0.64	13	0.65	248	0.36	0.24
		S.D.	0.02	0.03	1	0.06	19	0.05	0.04
	1000	No.	7	7	7	7	7	7	7
		Mean	0.15	0.76	12	0.66	260	0.40*	0.28*
		S.D.	0.02	0.33	1	0.05	9	0.06D	0.04D

*: p<0.05 (Significant difference from control group)
D: Dunnett's test
ST: Steel's test

Table 8-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Organ weight of female rats (Main group, End of administration)

	Dose mg/kg		Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)	Liver g(g/100g BW)
Absolute	0	No.	12	12	12	12	12	12	12
		Mean	304	1.99	16.9	17.2	176	0.99	10.46
		S.D.	12	0.10	2.5	2.5	69	0.06	0.75
	100	No.	10	10	10	10	10	10	10
		Mean	301	1.96	15.7	16.4	209	1.00	10.55
		S.D.	16	0.07	2.2	2.4	62	0.11	0.91
	300	No.	12	12	12	12	12	12	12
		Mean	297	1.97	16.0	16.9	161	0.92	10.10
		S.D.	20	0.06	2.5	2.0	52	0.09	1.03
	1000	No.	12	12	12	12	12	12	12
		Mean	298	2.00	16.1	16.6	187	0.98	10.01
		S.D.	18	0.09	3.3	2.6	71	0.08	0.87
Relative	0	No.		12	12	12	12	12	12
		Mean		0.65	5.5	5.7	58	0.33	3.44
		S.D.		0.03	0.8	0.9	24	0.02	0.22
	100	No.		10	10	10	10	10	10
		Mean		0.65	5.3	5.5	69	0.33	3.50
		S.D.		0.03	0.6	0.9	20	0.03	0.20
	300	No.		12	12	12	12	12	12
		Mean		0.66	5.4	5.7	54	0.31	3.39
		S.D.		0.05	0.8	0.8	16	0.02	0.14
	1000	No.		12	12	12	12	12	12
		Mean		0.67	5.4	5.6	62	0.33	3.36
		S.D.		0.04	0.9	0.9	22	0.03	0.24

No significant difference in any treated groups from control group.

Table 8-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Organ weight of female rats (Main group, End of administration)

	Dose mg/kg		Spleen g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	0	No.	12	12	12	12	12
		Mean	0.57	2.11	88	109.3	614
		S.D.	0.07	0.14	8	12.9	65
	100	No.	10	10	10	10	10
		Mean	0.63	2.15	90	101.3	648
		S.D.	0.05	0.18	13	7.9	102
	300	No.	12	12	12	12	12
		Mean	0.59	2.05	84	98.6*	674
		S.D.	0.07	0.12	11	9.3D	77
	1000	No.	12	12	12	12	12
		Mean	0.61	2.10	85	100.8	669
		S.D.	0.09	0.14	10	7.4	66
Relative	0	No.	12	12	12	12	12
		Mean	0.19	0.70	29	35.9	201
		S.D.	0.02	0.06	2	4.0	15
	100	No.	10	10	10	10	10
		Mean	0.21	0.71	30	33.7	215
		S.D.	0.01	0.04	4	2.7	32
	300	No.	12	12	12	12	12
		Mean	0.20	0.69	28	33.3	227
		S.D.	0.02	0.04	3	3.8	29
	1000	No.	12	12	12	12	12
		Mean	0.20	0.71	29	33.9	226
		S.D.	0.02	0.05	4	2.9	30

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

Table 8-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Organ weight of female rats (Satellite group, End of administration)

	Dose mg/kg		Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)	Liver g(g/100g BW)
Absolute	0	No.	5	5	5	5	5	5	5
		Mean	262	1.93	14.8	16.3	250	0.84	6.67
		S.D.	14	0.04	1.6	2.2	62	0.03	0.40
	1000	No.	5	5	5	5	5	5	5
		Mean	266	1.98	15.4	18.0	255	0.85	6.86
		S.D.	17	0.07	0.8	3.6	70	0.03	0.40
Relative	0	No.		5	5	5	5	5	5
		Mean		0.74	5.7	6.2	95	0.32	2.55
		S.D.		0.03	0.7	0.9	19	0.03	0.16
	1000	No.		5	5	5	5	5	5
		Mean		0.74	5.8	6.8	96	0.32	2.58
		S.D.		0.03	0.5	1.7	30	0.02	0.05

No significant difference between treated group and control group.

Table 8-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Organ weight of female rats (Satellite group, End of administration)

	Dose mg/kg		Spleen g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	0	No.	5	5	5	5	5
		Mean	0.46	1.85	72	77.4	545
		S.D.	0.05	0.15	8	11.6	62
	1000	No.	5	5	5	5	5
		Mean	0.46	1.91	65	83.7	562
		S.D.	0.06	0.13	8	9.8	68
Relative	0	No.	5	5	5	5	5
		Mean	0.18	0.71	27	29.5	208
		S.D.	0.02	0.06	2	3.8	25
	1000	No.	5	5	5	5	5
		Mean	0.17	0.72	24	31.5	211
		S.D.	0.02	0.05	3	3.6	15

No significant difference between treated group and control group.

Table 8-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Organ weight of male rats (End of recovery)

	Dose mg/kg		Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)	Liver g(g/100g BW)
Absolute	0	No.	5	5	5	5	5	5	5
		Mean	498	2.15	12.8	21.8	231	1.46	13.00
		S.D.	14	0.07	1.3	4.6	51	0.16	1.13
	1000	No.	5	5	5	5	5	5	5
		Mean	512	2.13	13.8	20.1	245	1.45	12.74
		S.D.	50	0.06	1.3	4.8	85	0.13	1.34
Relative	0	No.		5	5	5	5	5	5
		Mean		0.43	2.6	4.4	46	0.29	2.61
		S.D.		0.02	0.3	0.9	10	0.03	0.18
	1000	No.		5	5	5	5	5	5
		Mean		0.42	2.7	3.9	48	0.29	2.49
		S.D.		0.04	0.2	0.8	15	0.04	0.09

No significant difference between treated group and control group.

Table 8-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Organ weight of male rats (End of recovery)

	Dose mg/kg		Spleen g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Testis (R+L) g(g/100g BW)	Epididymis (R+L) mg(mg/100g BW)	Seminal vesicle g(g/100g BW)	Prostate g(g/100g BW)
Absolute	0	No.	5	5	5	5	5	5	5
		Mean	0.73	3.35	62	3.54	1406	1.76	1.28
		S.D.	0.08	0.29	3	0.25	112	0.27	0.12
	1000	No.	5	5	5	5	5	5	5
		Mean	0.63	3.28	62	3.63	1387	1.56	1.26
		S.D.	0.13	0.32	9	0.28	88	0.27	0.11
Relative	0	No.	5	5	5	5	5	5	5
		Mean	0.14	0.67	12	0.71	282	0.35	0.25
		S.D.	0.02	0.05	1	0.05	23	0.05	0.02
	1000	No.	5	5	5	5	5	5	5
		Mean	0.12	0.64	12	0.71	274	0.31	0.25
		S.D.	0.02	0.06	1	0.08	41	0.07	0.03

No significant difference between treated group and control group.

Table 8-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Organ weight of female rats (End of recovery)

	Dose mg/kg		Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)	Liver g(g/100g BW)
Absolute	0	No.	5	5	5	5	5	5	5
		Mean	278	2.01	15.6	17.0	261	0.88	7.07
		S.D.	20	0.08	2.7	2.2	23	0.08	0.75
	1000	No.	5	5	5	5	5	5	5
		Mean	262	1.96	15.4	19.5	253	0.84	6.29
		S.D.	8	0.07	1.7	3.2	93	0.05	0.29
Relative	0	No.		5	5	5	5	5	5
		Mean		0.72	5.6	6.2	94	0.32	2.54
		S.D.		0.04	1.0	1.0	7	0.03	0.21
	1000	No.		5	5	5	5	5	5
		Mean		0.75	5.9	7.4	96	0.32	2.40
		S.D.		0.04	0.7	1.2	33	0.02	0.17

No significant difference between treated group and control group.

Table 8-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Organ weight of female rats (End of recovery)

	Dose mg/kg		Spleen g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	0	No.	5	5	5	5	5
		Mean	0.51	2.00	71	85.4	615
		S.D.	0.07	0.11	10	19.5	47
	1000	No.	5	5	5	5	5
		Mean	0.44	1.83*	68	72.5	526
		S.D.	0.10	0.05T	5	6.6	81
Relative	0	No.	5	5	5	5	5
		Mean	0.18	0.72	25	30.6	222
		S.D.	0.02	0.03	3	5.6	17
	1000	No.	5	5	5	5	5
		Mean	0.17	0.70	26	27.7	201
		S.D.	0.03	0.04	2	2.6	30

*: $p<0.05$ (Significant difference from control group)
T: Student's t-test

Table 9-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Gross pathological findings (End of administration period (D42))

Organs	Sex:	M	M	M	M
	Dose(mg/kg):	0	100	300	1000
Findings	Number:	7	12	12	7
Epididymis					
Nodule		0	1	0	0
Kidney					
Nodule		0	0	0	1
Lung(bronchus)					
Focus,dark red		0	1	0	0
Stomach					
Focus,raised,forestomach		0	1	0	0
Testis					
Small		0	1	0	0

M : Male

Table 9-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Gross pathological findings (End of administration period (D42))

Organs	Sex:	F	F
	Dose(mg/kg):	0	1000
Findings	Number:	5	5
All tissues			
Not remarkable		5	5

F : Female

R-1100

Table 9-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Gross pathological findings (End of administration period (L4))

Organs	Sex:	F	F	F	F
	Dose(mg/kg):	0	100	300	1000
Findings	Number:	12	10	12	12
Stomach					
Focus,dark red,glandular stomach		1	0	1	1

F : Female

R-1100

Table 9-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Gross pathological findings (End of recovery period)

Organs	Sex:	M	M	F	F
	Dose(mg/kg):	0	1000	0	1000
Findings	Number:	5	5	5	5
Kidney					
Cyst		0	0	1	0
Lung(bronchus)					
Focus,dark red		0	1	0	0

M : Male, F : Female

Table 9-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Gross pathological findings (Undelivered)

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

F : Female

Table 9-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Gross pathological findings (All littermates died)

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

F : Female

Table 10-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Histopathological findings (End of administration period (D42))

Organs	Sex:	M	M	M	M
	Dose(mg/kg):	0	100	300	1000
Findings	Number:	7	12	12	7
Adrenal					
Number examined		5	1	0	5
Not remarkable		5	1	0	5
Bone+Bone marrow,femoral					
Number examined		5	1	0	5
Not remarkable		5	1	0	5
Cerebellum(Pons)					
Number examined		5	1	0	5
Not remarkable		5	1	0	5
Cerebrum					
Number examined		5	1	0	5
Not remarkable		5	1	0	5
Epididymis					
Number examined		5	1	0	5
Not remarkable		5	1	0	5
Eye					
Number examined		5	1	0	5
Not remarkable		5	1	0	5
Heart					
Number examined		5	1	0	5
Not remarkable		4	1	0	3
Cell infiltration		1	0	0	2
minimal		1	0	0	2
Intestine,duodenum					
Number examined		5	1	0	5
Not remarkable		5	1	0	5
Intestine,jejunum					
Number examined		5	1	0	5
Not remarkable		5	1	0	5
Intestine,ileum(Peyer's patch)					
Number examined		5	1	0	5
Not remarkable		5	1	0	5
Intestine,cecum					
Number examined		5	1	0	5
Not remarkable		5	1	0	5
Intestine,colon					
Number examined		5	1	0	5
Not remarkable		5	1	0	5
Intestine,rectum					
Number examined		5	1	0	5
Not remarkable		5	1	0	5

M : Male

Table 10-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Histopathological findings (End of administration period (D42))

Organs	Sex:	M	M	M	M
	Dose(mg/kg):	0	100	300	1000
Findings	Number:	7	12	12	7
Kidney					
Number examined		5	1	0	5
Not remarkable		2	0	0	1
Regeneration,tubular		3	1	0	4
minimal		3	1	0	4
Mineralization,papillary		1	0	0	0
minimal		1	0	0	0
NEPHROBLASTOMA		0	0	0	1
present		0	0	0	1
Liver					
Number examined		5	1	0	5
Not remarkable		1	0	0	1
Vacuolation,hepatocyte,periportal		2	0	0	0
minimal		2	0	0	0
Microgranuloma		4	1	0	4
minimal		4	1	0	4
Lung(bronchus)					
Number examined		5	1	0	5
Not remarkable		3	1	0	4
Aggregation,macrophage		2	0	0	1
minimal		2	0	0	1
Lymph node,mesenteric					
Number examined		5	1	0	5
Not remarkable		5	1	0	5
Lymph node,submandibular					
Number examined		5	1	0	5
Not remarkable		5	1	0	5
Pancreas					
Number examined		5	1	0	5
Not remarkable		5	1	0	5
Parathyroid					
Number examined		5	1	0	5
Not remarkable		5	1	0	5
Pituitary					
Number examined		5	1	0	5
Not remarkable		5	0	0	5
Cyst		0	1	0	0
minimal		0	1	0	0
Prostate					
Number examined		5	1	0	5
Not remarkable		3	0	0	2
Cell infiltration		2	1	0	3
minimal		1	1	0	3
mild		1	0	0	0
Salivary gland,submandibular					
Number examined		5	1	0	5
Not remarkable		5	1	0	5

M : Male

Table 10-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Histopathological findings (End of administration period (D42))

Organs	Sex:	M	M	M	M
	Dose(mg/kg):	0	100	300	1000
Findings	Number:	7	12	12	7
Sciatic nerve					
Number examined		5	1	0	5
Not remarkable		5	1	0	5
Seminal vesicle(coagulation gland)					
Number examined		5	1	0	5
Not remarkable		5	1	0	5
Skeletal muscle,femoral					
Number examined		5	1	0	5
Not remarkable		4	1	0	5
Degeneration,muscular		1	0	0	0
minimal		1	0	0	0
Spinal cord,thoracic					
Number examined		5	1	0	5
Not remarkable		5	1	0	5
Spleen					
Number examined		5	1	0	5
Not remarkable		1	0	0	1
Hematopoiesis,extramedullary		4	1	0	4
minimal		4	1	0	4
Stomach					
Number examined		5	1	0	5
Not remarkable		5	1	0	5
Testis					
Number examined		5	1	0	5
Not remarkable		5	1	0	4
Atrophy,seminiferous tubular		0	0	0	1
minimal		0	0	0	1
Thymus					
Number examined		5	1	0	5
Not remarkable		5	1	0	5
Thyroid					
Number examined		5	1	0	5
Not remarkable		5	1	0	5
Trachea					
Number examined		5	1	0	5
Not remarkable		5	1	0	5
Urinary bladder					
Number examined		5	1	0	5
Not remarkable		5	1	0	5

M : Male

Table 10-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Histopathological findings (End of administration period (D42))

Organs / Findings	Sex: / Dose(mg/kg): / Number:	F 0 5	F 1000 5
Adrenal			
Number examined		5	5
Not remarkable		5	5
Bone+Bone marrow,femoral			
Number examined		5	5
Not remarkable		5	5
Cerebellum(Pons)			
Number examined		5	5
Not remarkable		5	5
Cerebrum			
Number examined		5	5
Not remarkable		5	5
Eye			
Number examined		5	5
Not remarkable		5	5
Heart			
Number examined		5	5
Not remarkable		5	5
Intestine,duodenum			
Number examined		5	5
Not remarkable		5	5
Intestine,jejunum			
Number examined		5	5
Not remarkable		5	5
Intestine,ileum(Peyer's patch)			
Number examined		5	5
Not remarkable		5	5
Intestine,cecum			
Number examined		5	5
Not remarkable		5	5
Intestine,colon			
Number examined		5	5
Not remarkable		5	5
Intestine,rectum			
Number examined		5	5
Not remarkable		5	5
Kidney			
Number examined		5	5
Not remarkable		4	4
Regeneration,tubular		1	1
minimal		1	1

F : Female

Table 10-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Histopathological findings (End of administration period (D42))

Organs / Findings	Sex: / Dose(mg/kg): / Number:	F 0 5	F 1000 5
Liver			
Number examined		5	5
Not remarkable		2	0
Microgranuloma		3	5
minimal		3	5
Lung(bronchus)			
Number examined		5	5
Not remarkable		5	4
Aggregation,macrophage		0	1
minimal		0	1
Lymph node,mesenteric			
Number examined		5	5
Not remarkable		5	5
Lymph node,submandibular			
Number examined		5	5
Not remarkable		5	5
Ovary			
Number examined		5	5
Not remarkable		5	5
Pancreas			
Number examined		5	5
Not remarkable		5	5
Parathyroid			
Number examined		4	5
Not remarkable		4	5
No sample		1	0
Pituitary			
Number examined		5	5
Not remarkable		3	5
Cyst		2	0
minimal		2	0
Salivary gland,submandibular			
Number examined		5	5
Not remarkable		5	5
Sciatic nerve			
Number examined		5	5
Not remarkable		5	5
Skeletal muscle,femoral			
Number examined		5	5
Not remarkable		5	5
Spinal cord,thoracic			
Number examined		5	5
Not remarkable		5	5

F : Female

Table 10-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Histopathological findings (End of administration period (D42))

Organs	Sex:	F	F
	Dose(mg/kg):	0	1000
Findings	Number:	5	5
Spleen			
Number examined		5	5
Not remarkable		2	3
Hematopoiesis,extramedullary		3	2
minimal		3	2
Stomach			
Number examined		5	5
Not remarkable		5	5
Thymus			
Number examined		5	5
Not remarkable		5	5
Thyroid			
Number examined		5	5
Not remarkable		5	5
Trachea			
Number examined		5	5
Not remarkable		5	5
Urinary bladder			
Number examined		5	5
Not remarkable		5	5
Uterus			
Number examined		5	5
Not remarkable		5	5
Vagina			
Number examined		5	5
Not remarkable		5	5

F : Female

Table 10-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Histopathological findings (End of administration period (L4))

Organs / Findings	Sex: / Dose(mg/kg): / Number:	F 0 12	F 100 10	F 300 12	F 1000 12
Adrenal					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Bone+Bone marrow,femoral					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Cerebellum(Pons)					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Cerebrum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Eye					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Heart					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,duodenum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,jejunum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,ileum(Peyer's patch)					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,cecum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,colon					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,rectum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Kidney					
Number examined		5	0	0	5
Not remarkable		3	0	0	3
Regeneration,tubular		1	0	0	2
minimal		1	0	0	2
Mineralization,papillary		1	0	0	0
minimal		1	0	0	0

F : Female

Table 10-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Histopathological findings (End of administration period (L4))

Organs	Sex:	F	F	F	F
	Dose(mg/kg):	0	100	300	1000
Findings	Number:	12	10	12	12
Liver					
Number examined		5	0	0	5
Not remarkable		5	0	0	4
Microgranuloma		0	0	0	1
minimal		0	0	0	1
Lung(bronchus)					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Lymph node,mesenteric					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Lymph node,submandibular					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Ovary					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Pancreas					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Parathyroid					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Pituitary					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Salivary gland,submandibular					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Sciatic nerve					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Skeletal muscle,femoral					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Spinal cord,thoracic					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Spleen					
Number examined		5	0	0	5
Hematopoiesis,extramedullary		5	0	0	5
minimal		1	0	0	1
mild		4	0	0	4

F : Female

Table 10-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Histopathological findings (End of administration period (L4))

Organs / Findings	Sex: / Dose(mg/kg): / Number:	F 0 12	F 100 10	F 300 12	F 1000 12
Stomach					
Number examined		5	0	0	5
Not remarkable		4	0	0	5
Erosion,glandular stomach		1	0	0	0
mild		1	0	0	0
Thymus					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Thyroid					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Trachea					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Urinary bladder					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Uterus					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Vagina					
Number examined		5	0	0	5
Not remarkable		5	0	0	5

F : Female

Table 10-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Histopathological findings (End of recovery period)

Organs	Sex:	M	M	F	F
	Dose(mg/kg):	0	1000	0	1000
Findings	Number:	5	5	5	5
Kidney					
Number examined		0	0	1	0
Cyst		0	0	1	0
mild		0	0	1	0
Lung(bronchus)					
Number examined		0	1	0	0
Cell infiltration		0	1	0	0
minimal		0	1	0	0

M : Male, F : Female

Table 10-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Histopathological findings (Undelivered)

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

F : Female

Table 10-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Histopathological findings (Undelivered)

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

F : Female

Table 10-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Histopathological findings (Undelivered)

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

F : Female

Table 10-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Histopathological findings (All littermates died)

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

F : Female

Table 10-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Histopathological findings (All littermates died)

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

F : Female

Table 10-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Histopathological findings (All littermates died)

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

F : Female

Table 11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Estrous cycle in female rats during the pre-mating period (Main group)

Dose mg/kg	No. of animals	Count of estrus						Mean duration of cycles	Index of animals with abnormal estrous cycle (%)a)
		0	1	2	3	4	Mean±S.D.	Mean±S.D.	
0	12	0	0	0	4	8	3.7±0.5	4.1±0.3	0/12(0.0)
100	12	0	0	0	5	7	3.6±0.5	4.2±0.4	0/12(0.0)
300	12	0	0	0	4	8	3.7±0.5	4.0±0.0	0/12(0.0)
1000	12	0	0	0	5	7	3.6±0.5	4.0±0.1	0/12(0.0)

a): (No. of animals with abnormal estrous cycle / No. of animals examined)×100
No significant difference in any treated groups from control group.

Table 12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Mating and fertility of animals

	Male				Female			
Dose mg/kg	No. of males	Days until copulation Mean±S.D.	Copulation index (%) a)	Insemination index (%) b)	No. of females	Days until copulation Mean±S.D.	Copulation index (%) a)	Fertility index (%) c)
0	12	2.7±1.6	12/12(100.0)	12/12(100.0)	12	2.7±1.6	12/12(100.0)	12/12(100.0)
100	12	2.4±1.1	12/12(100.0)	11/12(91.7)	12	2.4±1.1	12/12(100.0)	11/12(91.7)
300	12	2.3±1.2	12/12(100.0)	12/12(100.0)	12	2.3±1.2	12/12(100.0)	12/12(100.0)
1000	12	2.3±1.2	12/12(100.0)	12/12(100.0)	12	2.3±1.2	12/12(100.0)	12/12(100.0)

a): (No. of copulated animals / No. of mated animals)×100
b): (No. of males which impregnated females / No. of copulated males)×100
c): (No. of pregnant females / No. of copulated females)×100
No significant difference in any treated groups from control group.

Table 13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Delivery data on dams

Dose mg/kg		No. of pregnant females	No. of females with liveborns	Gestation index % a)	Gestation length in days	No. of corpora lutea	No. of implan-tation sites	Implan-tation index % b)	Delivery index % c)	No. of still-borns (%)d)	No. of live-borns	External e) abnor-malities(%)f)
	Total	12	12	100.0		194	178			1	168	0
0	Mean				21.9	16.2	14.8	92.5	95.0	(0.6)	14.0	(0.0)
	S.D.				0.3	1.9	1.0	8.9	5.7	(1.9)	1.1	(0.0)
	Total	11	11	100.0		172	150			2	139	0
100	Mean				22.0	15.6	13.6	85.8	94.7	(1.3)	12.6	(0.0)
	S.D.				0.4	2.5	4.1	23.3	7.3	(2.9)	3.7	(0.0)
	Total	12	12	100.0		181	170			5	160	0
300	Mean				21.9	15.1	14.2	94.2	97.0	(3.5)	13.3	(0.0)
	S.D.				0.5	1.3	1.1	6.4	5.8	(12.0)	2.4	(0.0)
	Total	12	12	100.0		184	167			2	155	0
1000	Mean				21.8	15.3	13.9	89.4	92.9	(1.1)	12.9	(0.0)
	S.D.				0.5	2.8	3.3	13.8	7.4	(3.8)	3.3	(0.0)

a): (No. of females which delivered liveborns / No. of pregnant females)×100
b): (No. of implantation sites / No. of corpora lutea)×100
c): (No. of delivered pups / No. of implantation sites)×100
d): (No. of stillborns / No. of delivered pups)×100
e): No. of delivered pups with external abnormalities
f): (No. of delivered pups with external abnormalities / No. of delivered pups)×100
No significant difference in any treated groups from control group.

Table 14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Viability index of pups

Dose mg/kg		No. of dams	No. of live-borns	No. of delivered pups	Live birth index % a)	No. of dams	No. of live pups		Viability index on postnatal day 4 % b)
							Day 0	Day 4	
	Total	12	168	169		12	168	167	
0	Mean		14.0	14.1	99.4		14.0	13.9	99.4
	S.D.		1.1	1.2	1.9		1.1	1.2	2.0
	Total	11	139	141		11	139	136	
100	Mean		12.6	12.8	98.7		12.6	12.4	90.2
	S.D.		3.7	3.8	2.9		3.7	4.3	30.0
	Total	12	160	165		12	160	159	
300	Mean		13.3	13.8	96.5		13.3	13.3	99.4
	S.D.		2.4	1.4	12.0		2.4	2.4	2.0
	Total	12	155	157		12	155	152	
1000	Mean		12.9	13.1	98.9		12.9	12.7	96.0
	S.D.		3.3	3.4	3.8		3.3	3.6	9.7

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

Table 15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Sex ratio of pups

Dose mg/kg	No. of dams		Liveborns: No. of males	Liveborns: No. of females	Stillborns: No. of males	Stillborns: No. of females	Sex ratio of delivered pups a)	Sex ratio of liveborns b)	Postnatal day 4: No. of dams	Postnatal day 4: No. of males	Postnatal day 4: No. of females	Sex ratio of live pups on day 4 c)
		Total	78	90	0	1				78	89	
0	12	Mean	6.5	7.5	0.0	0.1	0.46	0.46	12	6.5	7.4	0.47
		S.D.	2.5	2.3	0.0	0.3	0.16	0.16		2.5	2.4	0.16
		Total	62	77	0	2				60	76	
100	11	Mean	5.6	7.0	0.0	0.2	0.48	0.49	10d)	6.0	7.6	0.45
		S.D.	2.0	3.0	0.0	0.4	0.21	0.21		1.7	2.2	0.14
		Total	77	83	2	3				76	83	
300	12	Mean	6.4	6.9	0.2	0.3	0.47	0.47	12	6.3	6.9	0.47
		S.D.	2.2	1.6	0.6	0.9	0.11	0.11		2.1	1.6	0.11
		Total	79	76	2	0				79	73	
1000	12	Mean	6.6	6.3	0.2	0.0	0.53	0.52	12	6.6	6.1	0.56
		S.D.	2.6	2.6	0.6	0.0	0.16	0.15		2.6	2.8	0.21

a): No. of delivered males / No. of delivered pups
b): No. of liveborn males / No. of liveborns
c): No. of live males on day 4 / No. of live pups on day 4
d): All pups from one dam died on postnatal day 1.
No significant difference in any treated groups from control group.

Table 16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Body weight of pups

Dose mg/kg		Male			Female		
		0	4a)	Gain	0	4a)	Gain
0	No.	12	12	12	12	12	12
	Mean	6.7	10.3	3.6	6.2	9.6	3.4
	S.D.	0.4	1.0	0.8	0.4	1.0	0.8
100	No.	11	10b)	10	10c)	10	10
	Mean	6.7	10.5	3.9	6.2	9.9	3.7
	S.D.	0.3	0.7	0.5	0.2	0.6	0.5
300	No.	12	12	12	12	12	12
	Mean	6.7	10.4	3.7	6.3	9.8	3.5
	S.D.	0.5	1.4	1.2	0.5	1.4	1.1
1000	No.	12	12	12	12	11d)	11
	Mean	6.7	9.9	3.2	6.1	9.4	3.1
	S.D.	0.4	0.9	0.5	0.7	0.9	0.6

Unit: g
No.: No. of dams
a): Postnatal day
b): All male pups from one dam died.
c): Female pups were not born in one dam.
d): All female pups from one dam died.
No significant difference in any treated groups from control group.

Table 17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Externally for gross abnormalities in dead pups

Dose (mg/kg)	0	100	300	1000
Male				
No. of pups examined	0	1	1	0
No. of pups with abnormal findings	0	0	0	0
Female				
No. of pups examined	1	0	0	2
No. of pups with abnormal findings	0	0	0	0

Table 18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Externally for gross abnormalities in pups on postnatal day 4

Dose (mg/kg)	0	100	300	1000
Male				
No. of pups examined	78	60	76	79
No. of pups with abnormal findings	0	0	0	0
Female				
No. of pups examined	89	76	83	73
No. of pups with abnormal findings	0	0	0	0

Appendix 1-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual clinical signs in male rats (Administration period)
Dose (mg/kg): 0

Animal number	Day of administration 1-7	8-14	15-21	22-28	29-35	36-42	43a)
1001	-	-	-	-	-	-	-
1002	-	-	-	-	-	-	-
1003	-	-	-	-	-	-	-
1004	-	-	-	-	-	-	-
1005	-	-	-	-	-	-	-
1006	-	-	-	-	-	-	-
1007	-	-	-	-	-	-	-
1008	-	-	-	-	-	-	
1009	-	-	-	-	-	-	
1010	-	-	-	-	-	-	
1011	-	-	-	-	-	-	
1012	-	-	-	-	-	-	

a): Day of necropsy
-: No abnormal findings

Appendix 1-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual clinical signs in male rats (Administration period)
Dose (mg/kg): 100

Animal number	Day of administration 1-7	8-14	15-21	22-28	29-35	36-42	43a)
2001	-	-	-	-	-	-	-
2002	-	-	-	-	-	-	-
2003	-	-	-	-	-	-	-
2004	-	-	-	-	-	-	-
2005	-	-	-	-	-	-	-
2006	-	-	-	-	-	-	-
2007	-	-	-	-	-	-	-
2008	-	-	-	-	-	-	-
2009	-	-	-	-	-	-	-
2010	-	-	-	-	-	-	-
2011	-	-	-	-	-	-	-
2012	-	-	-	-	-	-	-

a): Day of necropsy
-: No abnormal findings

Appendix 1-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual clinical signs in male rats (Administration period)
Dose (mg/kg): 300

Animal number	Day of administration 1-7	8-14	15-21	22-28	29-35	36-42	43a)
3001	-	-	-	-	-	-	-
3002	-	-	-	-	-	-	-
3003	-	-	-	-	-	-	-
3004	-	-	-	-	-	-	-
3005	-	-	-	-	-	-	-
3006	-	-	-	-	-	-	-
3007	-	-	-	-	-	-	-
3008	-	-	-	-	-	-	-
3009	-	-	-	-	-	-	-
3010	-	-	-	-	-	-	-
3011	-	-	-	-	-	-	-
3012	-	-	-	-	-	-	-

a): Day of necropsy
-: No abnormal findings

Appendix 1-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual clinical signs in male rats (Administration period)
Dose (mg/kg): 1000

Animal number	Day of administration 1-7	8-14	15-21	22-28	29-35	36-42	43a)
4001	-	-	-	-	-	-	-
4002	-	-	-	-	-	-	-
4003	-	-	-	-	-	-	-
4004	-	-	-	-	-	-	-
4005	-	-	-	-	-	-	-
4006	-	-	-	-	-	-	-
4007	-	-	-	-	-	-	-
4008	-	-	-	-	-	-	
4009	-	-	-	-	-	-	
4010	-	-	-	-	-	-	
4011	-	-	-	-	-	-	
4012	-	-	-	-	-	-	

a): Day of necropsy
-: No abnormal findings

Appendix 1-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

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

Dose (mg/kg): 0

Animal number	Day of administration														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1111	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1112	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-: No abnormal findings

Appendix 1-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual clinical signs in female rats during the pre-mating period (Main group)
Dose (mg/kg): 100

Animal number	Day of administration														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
2101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2111	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2112	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-: No abnormal findings

Appendix 1-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual clinical signs in female rats during the pre-mating period (Main group)
Dose (mg/kg): 300

Animal number	Day of administration														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
3101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3111	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3112	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-: No abnormal findings

Appendix 1-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual clinical signs in female rats during the pre-mating period (Main group)
Dose (mg/kg): 1000

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

-: No abnormal findings

Appendix 1-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual clinical signs in dams during the gestation period (Main group)
Dose (mg/kg): 0

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

a): Gestation day
-: No abnormal findings
d: Delivery
/d: Found delivery after the observation of general conditions.

Appendix 1-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual clinical signs in dams during the gestation period (Main group)
Dose (mg/kg): 100

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

a): Gestation day
-: No abnormal findings
d: Delivery
/d: Found delivery after the observation of general conditions.

Appendix 1-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual clinical signs in dams during the gestation period (Main group)
Dose (mg/kg): 300

Dam number	Administration																							
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23a)
3101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
3102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
3103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
3104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
3105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
3106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d		
3107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d	
3108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
3109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
3110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d		
3111	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d	
3112	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	

a): Gestation day
-: No abnormal findings
d: Delivery
/d: Found delivery after the observation of general conditions.

Appendix 1-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual clinical signs in dams during the gestation period (Main group)
Dose (mg/kg): 1000

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

a): Gestation day
-: No abnormal findings
d: Delivery
/d: Found delivery after the observation of general conditions.

Appendix 1-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual clinical signs in dams during the lactation period (Main group)
Dose (mg/kg): 0

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

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

Appendix 1-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual clinical signs in dams during the lactation period (Main group)
Dose (mg/kg): 100

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

a): Lactation day
b): Day of necropsy
c): Necropsied on lactation day 1 because all pups died
-: No abnormal findings

Appendix 1-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual clinical signs in dams during the lactation period (Main group)
Dose (mg/kg): 300

Dam number	Administration					
	0	1	2	3	4a)	5b)
3101	-	-	-	-	-	-
3102	-	-	-	-	-	-
3103	-	-	-	-	-	-
3104	-	-	-	-	-	-
3105	-	-	-	-	-	-
3106	-	-	-	-	-	-
3107	-	-	-	-	-	-
3108	-	-	-	-	-	-
3109	-	-	-	-	-	-
3110	-	-	-	-	-	-
3111	-	-	-	-	-	-
3112	-	-	-	-	-	-

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

Appendix 1-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual clinical signs in dams during the lactation period (Main group)
Dose (mg/kg): 1000

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

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

Appendix 1-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual clinical signs in female rats (Satellite group, Administration period)
Dose (mg/kg): 0

Animal number	Day of administration 1-7	8-14	15-21	22-28	29-35	36-42	43a)
1113	-	-	-	-	-	-	-
1114	-	-	-	-	-	-	-
1115	-	-	-	-	-	-	-
1116	-	-	-	-	-	-	-
1117	-	-	-	-	-	-	-
1118	-	-	-	-	-	-	
1119	-	-	-	-	-	-	
1120	-	-	-	-	-	-	
1121	-	-	-	-	-	-	
1122	-	-	-	-	-	-	

a): Day of necropsy
-: No abnormal findings

Appendix 1-18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual clinical signs in female rats (Satellite group, Administration period)
Dose (mg/kg): 1000

Animal number	Day of administration 1-7	8-14	15-21	22-28	29-35	36-42	43a)
4113	-	-	-	-	-	-	-
4114	-	-	-	-	-	-	-
4115	-	-	-	-	-	-	-
4116	-	-	-	-	-	-	-
4117	-	-	-	-	-	-	-
4118	-	-	-	-	-	-	
4119	-	-	-	-	-	-	
4120	-	-	-	-	-	-	
4121	-	-	-	-	-	-	
4122	-	-	-	-	-	-	

a): Day of necropsy
-: No abnormal findings

Appendix 1-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual clinical signs in male rats (Recovery period)
Dose (mg/kg): 0

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

a): Day of necropsy
-: No abnormal findings

Appendix 1-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual clinical signs in male rats (Recovery period)
Dose (mg/kg): 1000

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

a): Day of necropsy
-: No abnormal findings

Appendix 1-21 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual clinical signs in female rats (Recovery period)
Dose (mg/kg): 0

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

a): Day of necropsy
-: No abnormal findings

Appendix 1-22 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual clinical signs in female rats (Recovery period)
Dose (mg/kg): 1000

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

a): Day of necropsy
-: No abnormal findings

Appendix 2-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 1 of administration)
Dose (mg/kg): 0

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

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 1 of administration)
Dose (mg/kg): 100

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

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 1 of administration)
Dose (mg/kg): 300

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

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 1 of administration)
Dose (mg/kg): 1000

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

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 2 of administration)
Dose (mg/kg): 0

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

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 2 of administration)
Dose (mg/kg): 100

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

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 2 of administration)
Dose (mg/kg): 300

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

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 2 of administration)
Dose (mg/kg): 1000

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

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 3 of administration)
Dose (mg/kg): 0

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

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 3 of administration)
Dose (mg/kg): 100

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

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 3 of administration)
Dose (mg/kg): 300

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

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 3 of administration)
Dose (mg/kg): 1000

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

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 4 of administration)
Dose (mg/kg): 0

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

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 4 of administration)
Dose (mg/kg): 100

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

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 4 of administration)
Dose (mg/kg): 300

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

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 4 of administration)
Dose (mg/kg): 1000

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

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 5 of administration)
Dose (mg/kg): 0

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

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 5 of administration)
Dose (mg/kg): 100

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

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 5 of administration)
Dose (mg/kg): 300

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

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 5 of administration)
Dose (mg/kg): 1000

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

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-21 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 6 of administration)
Dose (mg/kg): 0

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

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-22 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 6 of administration)
Dose (mg/kg): 100

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

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-23 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 6 of administration)
Dose (mg/kg): 300

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

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-24 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 6 of administration)
Dose (mg/kg): 1000

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

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-25 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 1 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-26 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 1 of administration)
Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-27 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 1 of administration)
Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-28 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 1 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-29 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 2 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-30 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 2 of administration)
Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-31 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 2 of administration)
Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-32 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 2 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-33 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 1)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-34 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 1)
Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4 NP	5	6	7	8	9	10	11	12
Posture a)	N	N	N		N	N	N	N	N	N	N	N
Convulsion b)	0	0	0		0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0		0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
NP: Non-pregnant

Appendix 2-35 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 1)
Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-36 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 1)
Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-37 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 7)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-38 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 7)
Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4 NP	5	6	7	8	9	10	11	12
Posture a)	N	N	N		N	N	N	N	N	N	N	N
Convulsion b)	0	0	0		0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0		0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
NP: Non-pregnant

Appendix 2-39 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 7)
Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-40 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 7)
Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-41 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 14)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-42 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 14)
Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4 NP	5	6	7	8	9	10	11	12
Posture a)	N	N	N		N	N	N	N	N	N	N	N
Convulsion b)	0	0	0		0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0		0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
NP: Non-pregnant

Appendix 2-43 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 14)
Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-44 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 14)
Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-45 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 20)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-46 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 20)
Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4 NP	5	6	7	8	9	10	11	12
Posture a)	N	N	N		N	N	N	N	N	N	N	N
Convulsion b)	0	0	0		0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0		0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
NP: Non-pregnant

Appendix 2-47 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 20)
Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-48 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 20)
Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-49 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Lactation day 4)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-50 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Lactation day 4)
Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
				NP			d)					
Posture a)	N	N	N		N	N		N	N	N	N	N
Convulsion b)	0	0	0		0	0		0	0	0	0	0
Abnormal behavior c)	0	0	0		0	0		0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) Necropsied on lactation day 1 because all pups died
NP: Non-pregnant

Appendix 2-51 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Lactation day 4)
Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-52 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Lactation day 4)
Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-53 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 1 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-54 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 1 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-55 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 2 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-56 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 2 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-57 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 3 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-58 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 3 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-59 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 4 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-60 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 4 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-61 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 5 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-62 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 5 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-63 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 6 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-64 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 6 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-65 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 1 of recovery)
Dose (mg/kg): 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-66 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 1 of recovery)
Dose (mg/kg): 1000

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-67 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 2 of recovery)
Dose (mg/kg): 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-68 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 2 of recovery)
Dose (mg/kg): 1000

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-69 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Week 1 of recovery)
Dose (mg/kg): 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-70 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Week 1 of recovery)
Dose (mg/kg): 1000

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-71 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Week 2 of recovery)
Dose (mg/kg): 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-72 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Week 2 of recovery)
Dose (mg/kg): 1000

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-73 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 1 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-74 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 1 of administration)
Dose (mg/kg): 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	1	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-75 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 1 of administration)
Dose (mg/kg): 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-76 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 1 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-77 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 2 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-78 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 2 of administration)
Dose (mg/kg): 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-79 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 2 of administration)
Dose (mg/kg): 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	1	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	1	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-80 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 2 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	1	0	0	0	1	0	0	0
Reactivity to handling n)	0	0	0	0	1	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-81 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 3 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-82 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 3 of administration)
Dose (mg/kg): 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-83 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 3 of administration)
Dose (mg/kg): 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	1	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-84 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 3 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	1	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-85 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 4 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-86 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 4 of administration)
Dose (mg/kg): 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-87 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 4 of administration)
Dose (mg/kg): 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	1	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	1	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-88 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 4 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	1	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-89 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 5 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	1	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-90 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 5 of administration)
Dose (mg/kg): 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-91 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 5 of administration)
Dose (mg/kg): 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-92 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 5 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	1	0	0	0	1	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-93 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 6 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-94 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 6 of administration)
Dose (mg/kg): 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-95 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 6 of administration)
Dose (mg/kg): 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-96 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 6 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	1	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-97 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 1 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-98 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 1 of administration)
Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-99 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 1 of administration)
Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-100 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 1 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-101 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 2 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-102 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 2 of administration)
Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-103 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 2 of administration)
Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-104 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 2 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-105 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 1)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-106 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 1)
Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4 NP	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0		0	0	0	0	0	0	0	0
Fur condition b)	0	0	0		0	0	0	0	0	0	0	0
Skin c)	0	0	0		0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0		0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0		0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0		0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0		0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0		0	0	0	0	0	0	0	0
Piloerection i)	0	0	0		0	0	0	0	0	0	0	0
Pupil size j)	0	0	0		0	0	0	0	0	0	0	0
Salivation k)	0	0	0		0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0		0	0	0	0	0	0	0	0
Vocalization m)	0	0	0		0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0		0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult
NP: Non-pregnant

Appendix 2-107 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 1)
Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-108 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 1)
Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-109 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 7)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-110 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 7)
Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4 NP	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0		0	0	0	0	0	0	0	0
Fur condition b)	0	0	0		0	0	0	0	0	0	0	0
Skin c)	0	0	0		0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0		0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0		0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0		0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0		0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0		0	0	0	0	0	0	0	0
Piloerection i)	0	0	0		0	0	0	0	0	0	0	0
Pupil size j)	0	0	0		0	0	0	0	0	0	0	0
Salivation k)	0	0	0		0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0		0	0	0	0	0	0	0	0
Vocalization m)	0	0	0		0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0		0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult
NP: Non-pregnant

Appendix 2-111 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 7)
Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-112 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 7)
Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	1	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	1	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-113 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 14)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-114 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 14)
Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4 NP	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0		0	0	0	0	0	0	0	0
Fur condition b)	0	0	0		0	0	0	0	0	0	0	0
Skin c)	0	0	0		0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0		0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0		0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0		0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0		0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0		0	0	0	0	0	0	0	0
Piloerection i)	0	0	0		0	0	0	0	0	0	0	0
Pupil size j)	0	0	0		0	0	0	0	0	0	0	0
Salivation k)	0	0	0		0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0		0	0	0	0	0	0	0	0
Vocalization m)	0	0	0		0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0		0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult
NP: Non-pregnant

Appendix 2-115 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 14)
Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-116 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 14)
Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-117 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 20)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-118 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 20)
Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4 NP	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0		0	0	0	0	0	0	0	0
Fur condition b)	0	0	0		0	0	0	0	0	0	0	0
Skin c)	0	0	0		0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0		0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0		0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0		0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0		0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0		0	0	0	0	0	0	0	0
Piloerection i)	0	0	0		0	0	0	0	0	0	0	0
Pupil size j)	0	0	0		0	0	0	0	0	0	0	0
Salivation k)	0	0	0		0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0		0	0	0	0	0	0	0	0
Vocalization m)	0	0	0		0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0		0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult
NP: Non-pregnant

Appendix 2-119 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 20)
Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-120 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 20)
Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-121 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Lactation day 4)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-122 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Lactation day 4)
Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4 NP	5	6	7 o)	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0		0	0	0	0	0	
Fur condition b)	0	0	0	0	0		0	0	0	0	0	
Skin c)	0	0	0	0	0		0	0	0	0	0	
Secretions-Eye, Nose d)	0	0	0	0	0		0	0	0	0	0	
Exophthalmos e)	0	0	0	0	0		0	0	0	0	0	
Palpebral closure f)	0	0	0	0	0		0	0	0	0	0	
Mucosal membranes g)	0	0	0	0	0		0	0	0	0	0	
Lacrimation h)	0	0	0	0	0		0	0	0	0	0	
Piloerection i)	0	0	0	0	0		0	0	0	0	0	
Pupil size j)	0	0	0	0	0		0	0	0	0	0	
Salivation k)	0	0	0	0	0		0	0	0	0	0	
Abnormal respiration l)	0	0	0	0	0		0	0	0	0	0	
Vocalization m)	0	0	0	0	0		0	0	0	0	0	
Reactivity to handling n)	0	0	0	0	0		0	0	0	0	0	

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult
o) Necropsied on lactation day 1 because all pups died
NP: Non-pregnant

Appendix 2-123 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Lactation day 4)
Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-124 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Lactation day 4)
Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-125 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 1 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-126 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 1 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-127 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 2 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-128 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 2 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-129 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 3 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-130 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 3 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-131 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 4 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-132 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 4 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-133 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 5 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-134 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 5 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-135 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 6 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-136 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 6 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-137 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 1 of recovery)
Dose (mg/kg): 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-138 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 1 of recovery)
Dose (mg/kg): 1000

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-139 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 2 of recovery)
Dose (mg/kg): 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-140 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 2 of recovery)
Dose (mg/kg): 1000

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-141 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Week 1 of recovery)
Dose (mg/kg): 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-142 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Week 1 of recovery)
Dose (mg/kg): 1000

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-143 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Week 2 of recovery)
Dose (mg/kg): 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-144 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Week 2 of recovery)
Dose (mg/kg): 1000

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-145 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 1 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	3	5	4	2	5	4	2	2	3	4	3	4
Defecation count	1	0	0	0	0	3	2	0	0	0	0	0
Urination h)	1	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-146 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 1 of administration)
Dose (mg/kg): 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	1	6	6	4	6	5	7	6	7	3	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-147 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 1 of administration)
Dose (mg/kg): 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	5	5	3	0	7	5	4	6	3	5	7
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	1	0	0	0	0	0	0	0	1	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-148 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 1 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	8	7	6	3	7	6	3	7	5	3	1	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	1	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-149 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 2 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	1	6	5	4	6	4	5	4	5	5	3	4
Defecation count	3	0	0	0	0	0	0	0	0	0	0	0
Urination h)	1	0	0	0	0	0	0	0	0	1	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-150 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 2 of administration)
Dose (mg/kg): 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	3	1	6	4	4	5	4	6	4	3	3	4
Defecation count	0	0	0	0	0	0	0	0	0	0	0	3
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-151 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 2 of administration)
Dose (mg/kg): 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	2	3	5	2	7	4	4	2	5	6	6
Defecation count	0	0	0	0	0	0	0	0	1	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-152 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 2 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	7	5	2	3	4	3	5	3	5	5	2
Defecation count	0	0	0	0	0	0	3	0	0	0	0	0
Urination h)	0	0	0	0	0	0	1	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-153 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 3 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	6	5	5	6	6	2	3	4	9	2	5
Defecation count	1	0	0	0	0	0	0	0	0	0	0	0
Urination h)	1	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-154 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 3 of administration)
Dose (mg/kg): 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	5	3	6	8	6	6	7	6	5	4	4
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-155 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 3 of administration)
Dose (mg/kg): 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	10	1	4	5	3	5	6	6	1	5	8	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	1	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-156 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 3 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	8	4	2	9	2	4	4	4	6	7	3
Defecation count	0	0	0	0	0	0	3	0	0	0	0	0
Urination h)	1	0	0	0	0	0	1	1	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-157 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 4 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	5	6	4	4	2	5	2	7	4	5	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	1	0	0	0	0	0	1

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-158 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 4 of administration)
Dose (mg/kg): 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	10	3	4	4	7	7	3	5	6	6	6	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-159 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 4 of administration)
Dose (mg/kg): 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	2	2	7	6	3	7	5	3	4	8	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	1	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-160 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 4 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	U	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	5	5	1	6	1	2	4	2	6	3	4
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	1	1	0	0	0	0	0	1	1	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-161 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 5 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	4	3	4	4	4	4	2	8	6	6	7
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	1	0	0	0	1	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-162 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 5 of administration)
Dose (mg/kg): 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	8	4	4	4	7	8	6	6	5	5	6	4
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	1	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-163 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 5 of administration)
Dose (mg/kg): 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	5	5	3	4	4	4	6	7	5	5	6
Defecation count	0	0	0	0	0	0	0	0	1	0	0	0
Urination h)	0	0	1	0	0	0	0	1	1	1	0	1

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-164 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 5 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	7	8	2	6	3	2	3	6	6	6	4
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	1	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-165 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 6 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	2	4	4	4	4	3	1	4	3	1	4
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	1	0	1	1	0	0	0	0	1	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-166 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 6 of administration)
Dose (mg/kg): 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	4	1	5	7	5	6	6	5	3	7	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	2
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-167 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 6 of administration)
Dose (mg/kg): 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	3	3	3	2	3	5	5	3	2	4	6
Defecation count	0	0	0	0	0	0	0	0	1	0	0	0
Urination h)	0	0	1	0	0	0	0	0	0	1	0	1

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-168 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 6 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	U	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	6	7	0	4	2	3	5	3	6	2	4
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	1	0	0	0	0	1	0	1	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-169 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Week 1 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	10	11	5	8	9	7	3	9	8	3	7	10
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-170 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Week 1 of administration)
Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	7	6	4	3	8	4	7	9	7	8	8
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-171 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Week 1 of administration)
Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	2	6	10	8	3	5	6	5	8	7	3	9
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-172 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Week 1 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	13	6	7	7	8	5	9	7	7	8	2
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-173 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Week 2 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	10	8	6	7	12	8	4	8	9	7	6	11
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-174 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Week 2 of administration)
Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	7	5	7	7	8	6	10	12	10	10	10
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-175 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Week 2 of administration)
Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	7	11	8	2	10	6	6	7	3	6	10
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-176 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Week 2 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	8	12	10	7	10	9	9	7	4	8	6	4
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-177 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 1)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	8	6	4	4	8	6	6	5	7	8	8
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-178 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 1)
Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4 NP	5	6	7	8	9	10	11	12
Arousal a)	0	0	0		0	0	0	0	0	0	0	0
Convulsion b)	0	0	0		0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0		0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0		0	0	0	0	0	0	0	0
Gait e)	0	0	0		0	0	0	0	0	0	0	0
Posture f)	N	N	N		N	N	N	N	N	N	N	N
Grooming g)	0	0	0		0	0	0	0	0	0	0	0
Rearing	5	5	3		6	8	5	7	8	4	6	7
Defecation count	0	0	0		0	0	0	0	0	0	0	0
Urination h)	0	0	0		0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
NP: Non-pregnant

Appendix 2-179 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 1)
Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	6	7	7	4	12	8	0	10	4	4	12
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-180 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 1)
Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	U
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	10	5	8	8	5	9	7	5	5	6	0
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-181 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 7)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	3	5	2	6	7	5	5	6	7	1	4	7
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-182 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 7)
Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4 NP	5	6	7	8	9	10	11	12
Arousal a)	0	0	0		0	0	0	0	0	0	0	0
Convulsion b)	0	0	0		0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0		0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0		0	0	0	0	0	0	0	0
Gait e)	0	0	0		0	0	0	0	0	0	0	0
Posture f)	N	N	N		N	N	N	N	N	N	N	N
Grooming g)	0	0	0		0	0	0	0	0	0	0	0
Rearing	5	3	3		3	4	5	9	6	6	6	1
Defecation count	0	0	0		0	0	0	0	0	0	0	0
Urination h)	0	0	0		0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
NP: Non-pregnant

Appendix 2-183 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 7)
Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	7	7	7	4	7	2	3	6	4	1	7
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-184 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 7)
Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	8	4	8	6	5	6	1	3	7	6	3
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-185 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 14)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	10	3	10	6	4	1	6	5	5	7	10
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-186 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 14)
Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4 NP	5	6	7	8	9	10	11	12
Arousal a)	0	0	0		0	0	0	0	0	0	0	0
Convulsion b)	0	0	0		0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0		0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0		0	0	0	0	0	0	0	0
Gait e)	0	0	0		0	0	0	0	0	0	0	0
Posture f)	N	N	N		N	N	N	N	N	N	N	N
Grooming g)	0	0	0		0	0	0	0	0	0	0	0
Rearing	5	5	4		3	6	4	7	4	4	7	1
Defecation count	0	0	0		0	0	0	0	0	0	0	0
Urination h)	0	0	0		0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
NP: Non-pregnant

Appendix 2-187 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 14)
Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	6	8	6	4	7	1	3	7	4	5	4
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	1	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-188 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 14)
Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	8	3	8	9	5	8	4	5	5	5	2
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	1	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-189 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 20)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	7	6	5	5	4	6	5	6	5	5	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-190 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 20)
Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4 NP	5	6	7	8	9	10	11	12
Arousal a)	0	0	0		0	0	0	0	0	0	0	0
Convulsion b)	0	0	0		0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0		0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0		0	0	0	0	0	0	0	0
Gait e)	0	0	0		0	0	0	0	0	0	0	0
Posture f)	N	N	N		N	N	N	N	N	N	N	N
Grooming g)	0	0	0		0	0	0	0	0	0	0	0
Rearing	6	5	4		3	3	5	5	7	5	7	2
Defecation count	0	0	0		0	0	0	0	0	0	0	1
Urination h)	0	0	0		0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
NP: Non-pregnant

Appendix 2-191 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 20)
Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	6	7	6	4	6	3	2	6	5	4	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-192 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 20)
Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	8	15	6	6	7	6	6	2	4	6	2
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	1	0	0	1

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-193 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Lactation day 4)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	6	6	9	7	7	6	5	9	5	5	7
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-194 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Lactation day 4)
Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
				NP			i)					
Arousal a)	0	0	0		0	0		0	0	0	0	0
Convulsion b)	0	0	0		0	0		0	0	0	0	0
Abnormal behavior c)	0	0	0		0	0		0	0	0	0	0
Stereotypy d)	0	0	0		0	0		0	0	0	0	0
Gait e)	0	0	0		0	0		0	0	0	0	0
Posture f)	N	N	N		N	N		N	N	N	N	N
Grooming g)	0	0	0		0	0		0	0	0	0	0
Rearing	8	13	6		4	7		6	12	9	12	2
Defecation count	0	0	0		0	0		0	0	0	0	0
Urination h)	0	0	0		0	0		0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
i) Necropsied on lactation day 1 because all pups died
NP: Non-pregnant

Appendix 2-195 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Lactation day 4)
Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	15	8	9	8	5	4	7	5	9	6	7	9
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-196 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Lactation day 4)
Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	9	11	5	9	9	8	7	5	6	8	10	7
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-197 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 1 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	9	10	6	5	9	6	6	11	8	9
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	1	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-198 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 1 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	9	6	6	7	9	7	6	6	5	9
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-199 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 2 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	10	10	6	10	10	7	9	9	9	7
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-200 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 2 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	7	7	9	6	12	5	5	6	6	5
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-201 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 3 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	13	9	8	9	13	8	11	9	11	12
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-202 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 3 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	10	10	8	7	13	6	7	8	8	10
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-203 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 4 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	11	9	9	9	12	6	8	6	11	10
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-204 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 4 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	12	9	13	7	13	7	5	8	7	10
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-205 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 5 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	12	10	11	9	11	6	9	7	16	9
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-206 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 5 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	12	11	9	5	10	11	4	9	6	9
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-207 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 6 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	12	5	7	9	10	8	6	7	8	7
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-208 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 6 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	8	8	4	6	12	7	6	6	6	7
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-209 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 1 of recovery)
Dose (mg/kg): 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	4	8	6	5	5
Defecation count	0	0	0	0	0
Urination h)	0	0	0	1	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-210 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 1 of recovery)
Dose (mg/kg): 1000

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	5	3	7	4	4
Defecation count	0	0	0	0	0
Urination h)	1	0	1	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-211 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 2 of recovery)
Dose (mg/kg): 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	4	7	7	5	6
Defecation count	0	0	0	0	0
Urination h)	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-212 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 2 of recovery)
Dose (mg/kg): 1000

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	6	5	7	4	4
Defecation count	0	0	0	0	0
Urination h)	1	0	0	0	1

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-213 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Week 1 of recovery)
Dose (mg/kg): 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	10	9	9	12	8
Defecation count	0	0	0	0	0
Urination h)	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-214 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Week 1 of recovery)
Dose (mg/kg): 1000

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	9	4	5	6	9
Defecation count	0	0	0	0	0
Urination h)	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-215 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Week 2 of recovery)
Dose (mg/kg): 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	9	9	8	10	8
Defecation count	0	0	0	0	0
Urination h)	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-216 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Week 2 of recovery)
Dose (mg/kg): 1000

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	8	7	7	6	6
Defecation count	0	0	0	0	0
Urination h)	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-217 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual manipulative test of male rats (Week 6 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	113	105	78	90	63

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-218 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual manipulative test of male rats (Week 6 of administration)
Dose (mg/kg): 100

Parameter	Animal number (2008-2012)				
	8	9	10	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	71	109	90	87	94

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-219 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual manipulative test of male rats (Week 6 of administration)
Dose (mg/kg): 300

Parameter	Animal number (3008-3012)				
	8	9	10	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	99	94	107	81	101

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-220 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual manipulative test of male rats (Week 6 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	91	97	61	79	59

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-221 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual manipulative test of female rats (Main group, Lactation day 4)
Dose (mg/kg): 0

Parameter	Animal number (1101-1108)				
	1	2	3	5	8
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	47	36	71	34	28

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-222 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual manipulative test of female rats (Main group, Lactation day 4)
Dose (mg/kg): 100

Parameter	Animal number (2101-2112)				
	1	5	6	8	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	34	71	69	48	44

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-223 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual manipulative test of female rats (Main group, Lactation day 4)
Dose (mg/kg): 300

Parameter	Animal number (3101-3108)				
	1	2	4	6	8
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	62	45	37	43	45

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-224 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual manipulative test of female rats (Main group, Lactation day 4)
Dose (mg/kg): 1000

Parameter	Animal number (4101-4109)				
	1	2	3	6	9
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	41	25	55	29	59

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-225 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual manipulative test of female rats (Satellite group, Week 6 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	84	37	82	54	51

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-226 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual manipulative test of female rats (Satellite group, Week 6 of administration)
Dose (mg/kg): 1000

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	55	63	83	98	71

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-227 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual manipulative test of male rats (Week 2 of recovery)
Dose (mg/kg): 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	110	117	85	100	92

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-228 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual manipulative test of male rats (Week 2 of recovery)
Dose (mg/kg): 1000

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	96	93	89	78	67

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-229 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual manipulative test of female rats (Week 2 of recovery)
Dose (mg/kg): 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	73	91	84	28	22

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-230 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual manipulative test of female rats (Week 2 of recovery)
Dose (mg/kg): 1000

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	80	84	64	101	80

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-231 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual grip strength of male rats (Week 6 of administration)
Dose (mg/kg): 0

Animal number	Fore limb g	Hind limb g
1008	1524	1202
1009	1764	1257
1010	1231	825
1011	1482	1240
1012	1733	1157
Mean	1547	1136
S.D.	216	178

Appendix 2-232 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual grip strength of male rats (Week 6 of administration)
Dose (mg/kg): 100

Animal number	Fore limb g	Hind limb g
2008	930	772
2009	1348	1229
2010	1492	1263
2011	1268	763
2012	1799	1159
Mean	1367	1037
S.D.	318	249

Appendix 2-233 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual grip strength of male rats (Week 6 of administration)
Dose (mg/kg): 300

Animal number	Fore limb g	Hind limb g
3008	1625	1183
3009	1403	1207
3010	2036	994
3011	1257	1026
3012	1687	1128
Mean	1602	1108
S.D.	298	94

Appendix 2-234 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual grip strength of male rats (Week 6 of administration)
Dose (mg/kg): 1000

Animal number	Fore limb g	Hind limb g
4008	1620	1133
4009	1744	1169
4010	1082	974
4011	1382	879
4012	1444	954
Mean	1454	1022
S.D.	253	124

Appendix 2-235 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual grip strength of female rats (Main group, Lactation day 4)
Dose (mg/kg): 0

Animal number	Fore limb g	Hind limb g
1101	1076	769
1102	899	605
1103	1378	1072
1105	1404	672
1108	938	839
Mean	1139	791
S.D.	239	181

Appendix 2-236 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual grip strength of female rats (Main group, Lactation day 4)
Dose (mg/kg): 100

Animal number	Fore limb g	Hind limb g
2101	958	703
2105	1440	1033
2106	1046	995
2108	1398	894
2112	1174	905
Mean	1203	906
S.D.	212	128

Appendix 2-237 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual grip strength of female rats (Main group, Lactation day 4)
Dose (mg/kg): 300

Animal number	Fore limb g	Hind limb g
3101	1247	638
3102	1284	744
3104	1123	703
3106	1307	704
3108	997	763
Mean	1192	710
S.D.	130	48

Appendix 2-238 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual grip strength of female rats (Main group, Lactation day 4)
Dose (mg/kg): 1000

Animal number	Fore limb g	Hind limb g
4101	1516	748
4102	1059	503
4103	1112	690
4106	1047	953
4109	1413	918
Mean	1229	762
S.D.	219	183

Appendix 2-239 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual grip strength of female rats (Satellite group, Week 6 of administration)
Dose (mg/kg): 0

Animal number	Fore limb g	Hind limb g
1118	868	459
1119	1155	825
1120	1072	572
1121	1075	689
1122	878	463
Mean	1010	602
S.D.	129	156

Appendix 2-240 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual grip strength of female rats (Satellite group, Week 6 of administration)
Dose (mg/kg): 1000

Animal number	Fore limb g	Hind limb g
4118	1184	885
4119	1324	1097
4120	762	846
4121	1214	660
4122	1064	654
Mean	1110	828
S.D.	215	183

Appendix 2-241 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual grip strength of male rats (Week 2 of recovery)
Dose (mg/kg): 0

Animal number	Fore limb g	Hind limb g
1008	1661	1024
1009	1787	1251
1010	1610	882
1011	1794	796
1012	1807	1307
Mean	1732	1052
S.D.	90	224

Appendix 2-242 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual grip strength of male rats (Week 2 of recovery)
Dose (mg/kg): 1000

Animal number	Fore limb g	Hind limb g
4008	1652	924
4009	1956	1064
4010	1345	1174
4011	1290	834
4012	1145	905
Mean	1478	980
S.D.	325	137

Appendix 2-243 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual grip strength of female rats (Week 2 of recovery)
Dose (mg/kg): 0

Animal number	Fore limb g	Hind limb g
1118	1234	772
1119	1217	783
1120	899	565
1121	936	563
1122	1183	656
Mean	1094	668
S.D.	163	107

Appendix 2-244 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual grip strength of female rats (Week 2 of recovery)
Dose (mg/kg): 1000

Animal number	Fore limb g	Hind limb g
4118	1121	737
4119	1159	1129
4120	1077	894
4121	916	747
4122	861	839
Mean	1027	869
S.D.	131	159

Appendix 2-245 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual motor activity of male rats (Week 6 of administration)
Dose (mg/kg): 0

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
1008	384	341	284	176	259	239	1683
1009	528	465	359	388	320	247	2307
1010	472	293	359	213	213	97	1647
1011	467	247	175	367	25	87	1368
1012	442	316	245	2	2	86	1093
Mean	459	332	284	229	164	151	1620
S.D.	52	82	79	157	143	84	452

Unit: Count

Appendix 2-246 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual motor activity of male rats (Week 6 of administration)
Dose (mg/kg): 100

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
2008	430	270	77	33	106	9	925
2009	444	364	115	32	100	375	1430
2010	427	396	391	128	72	235	1649
2011	358	318	259	237	191	42	1405
2012	451	410	87	79	30	290	1347
Mean	422	352	186	102	100	190	1351
S.D.	37	58	136	85	59	159	264

Unit: Count

Appendix 2-247 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual motor activity of male rats (Week 6 of administration)
Dose (mg/kg): 300

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
3008	461	389	406	367	252	64	1939
3009	486	465	332	293	195	16	1787
3010	442	319	227	21	5	6	1020
3011	426	321	201	274	257	48	1527
3012	463	378	416	305	156	139	1857
Mean	456	374	316	252	173	55	1626
S.D.	23	60	99	134	103	53	372

Unit: Count

Appendix 2-248 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual motor activity of male rats (Week 6 of administration)
Dose (mg/kg): 1000

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
4008	428	382	328	367	331	50	1886
4009	394	331	67	273	27	148	1240
4010	463	418	381	401	217	286	2166
4011	444	300	111	216	19	126	1216
4012	436	477	405	401	318	192	2229
Mean	433	382	258	332	182	160	1747
S.D.	25	70	158	83	152	87	491

Unit: Count

Appendix 2-249 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual motor activity of female rats (Main group, Lactation day 4)
Dose (mg/kg): 0

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
1101	401	236	246	199	271	273	1626
1102	469	356	267	305	258	274	1929
1103	232	56	51	11	0	81	431
1105	410	282	145	100	3	222	1162
1108	369	191	174	196	3	18	951
Mean	376	224	177	162	107	174	1220
S.D.	88	112	86	111	144	117	584

Unit: Count

Appendix 2-250 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual motor activity of female rats (Main group, Lactation day 4)
Dose (mg/kg): 100

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
2101	446	350	235	181	237	347	1796
2105	340	108	44	14	33	59	598
2106	397	123	25	43	12	19	619
2108	332	172	261	194	178	60	1197
2112	412	151	20	27	21	22	653
Mean	385	181	117	92	96	101	973
S.D.	49	98	120	88	104	139	523

Unit: Count

Appendix 2-251 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual motor activity of female rats (Main group, Lactation day 4)
Dose (mg/kg): 300

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
3101	393	275	118	188	56	19	1049
3102	308	133	162	87	12	19	721
3104	251	23	106	32	39	66	517
3106	407	170	103	156	147	119	1102
3108	398	261	109	116	151	106	1141
Mean	351	172	120	116	81	66	906
S.D.	69	103	24	61	64	47	274

Unit: Count

Appendix 2-252 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual motor activity of female rats (Main group, Lactation day 4)
Dose (mg/kg): 1000

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
4101	372	217	90	70	236	204	1189
4102	373	296	126	262	198	263	1518
4103	242	221	46	172	26	24	731
4106	376	328	244	368	339	284	1939
4109	329	138	56	15	122	21	681
Mean	338	240	112	177	184	159	1212
S.D.	57	74	80	143	118	128	533

Unit: Count

Appendix 2-253 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual motor activity of female rats (Satellite group, Week 6 of administration)
Dose (mg/kg): 0

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
1118	462	349	233	5	5	3	1057
1119	416	156	2	69	265	26	934
1120	417	350	287	167	1	5	1227
1121	352	264	281	94	13	7	1011
1122	437	259	259	1	8	19	983
Mean	417	276	212	67	58	12	1042
S.D.	41	80	120	69	116	10	112

Unit: Count

Appendix 2-254 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual motor activity of female rats (Satellite group, Week 6 of administration)
Dose (mg/kg): 1000

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
4118	420	374	189	307	282	60	1632
4119	351	310	197	19	0	34	911
4120	423	247	20	154	23	5	872
4121	370	177	245	131	20	27	970
4122	424	303	317	308	201	184	1737
Mean	398	282	194	184	105	62	1224
S.D.	35	74	110	124	128	71	423

Unit: Count

Appendix 2-255 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual motor activity of male rats (Week 2 of recovery)
Dose (mg/kg): 0

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
1008	422	256	213	145	203	283	1522
1009	341	291	250	226	159	175	1442
1010	445	316	356	362	319	230	2028
1011	327	266	174	3	32	236	1038
1012	470	469	133	32	47	8	1159
Mean	401	320	225	154	152	186	1438
S.D.	64	87	85	147	118	107	385

Unit: Count

Appendix 2-256 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual motor activity of male rats (Week 2 of recovery)
Dose (mg/kg): 1000

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
4008	380	166	75	46	48	9	724
4009	405	310	331	214	125	320	1705
4010	436	383	291	38	152	155	1455
4011	349	205	124	51	230	49	1008
4012	339	302	240	238	124	181	1424
Mean	382	273	212	117	136	143	1263
S.D.	40	87	109	100	65	122	392

Unit: Count

Appendix 2-257 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual motor activity of female rats (Week 2 of recovery)
Dose (mg/kg): 0

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
1118	386	320	330	277	13	117	1443
1119	394	192	155	117	3	6	867
1120	281	289	207	177	200	178	1332
1121	326	272	225	253	30	3	1109
1122	235	228	230	239	0	1	933
Mean	324	260	229	213	49	61	1137
S.D.	68	51	64	65	85	82	248

Unit: Count

Appendix 2-258 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual motor activity of female rats (Week 2 of recovery)
Dose (mg/kg): 1000

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
4118	342	315	148	197	53	10	1065
4119	348	358	295	84	0	205	1290
4120	391	215	1	212	274	34	1127
4121	406	327	38	238	230	10	1249
4122	168	57	30	229	16	11	511
Mean	331	254	102	192	115	54	1048
S.D.	95	123	121	62	128	85	314

Unit: Count

Appendix 3-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual body weight of male rats (Administration period)
Dose (mg/kg): 0

Animal number	Day of administration 1	8	15	22	29	36	42	Gain 1-42
1001	407	441	461	485	512	535	548	141
1002	396	419	444	467	486	510	530	134
1003	418	460	496	510	540	565	586	168
1004	400	429	444	466	491	515	529	129
1005	382	406	428	452	478	498	516	134
1006	425	457	482	511	531	556	549	124
1007	372	399	428	445	472	492	506	134
1008	417	443	471	492	516	531	509	92
1009	388	415	436	459	480	503	511	123
1010	388	419	442	451	480	502	509	121
1011	418	450	469	491	514	534	550	132
1012	398	414	430	457	464	488	497	99
Mean	401	429	453	474	497	519	528	128
S.D.	17	20	23	23	25	25	26	19

Unit: g

Appendix 3-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual body weight of male rats (Administration period)
Dose (mg/kg): 100

Animal number	Day of administration 1	8	15	22	29	36	42	Gain 1-42
2001	418	434	458	474	491	513	526	108
2002	379	411	443	470	488	517	535	156
2003	418	439	458	483	506	525	542	124
2004	391	402	413	437	452	468	486	95
2005	446	477	516	523	560	582	607	161
2006	402	434	469	489	515	548	555	153
2007	408	451	482	513	546	573	582	174
2008	417	447	472	496	515	533	539	122
2009	375	402	433	458	474	494	508	133
2010	394	425	461	480	492	519	525	131
2011	387	410	435	461	476	497	513	126
2012	401	433	457	483	505	517	518	117
Mean	403	430	458	481	502	524	536	133
S.D.	20	22	26	24	30	32	33	23

Unit: g

Appendix 3-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual body weight of male rats (Administration period)
Dose (mg/kg): 300

Animal number	Day of administration 1	8	15	22	29	36	42	Gain 1-42
3001	402	427	452	477	491	517	530	128
3002	423	444	471	506	517	550	557	134
3003	383	410	442	442	457	479	485	102
3004	427	447	474	493	520	553	566	139
3005	378	402	423	448	470	493	485	107
3006	412	443	469	499	519	538	549	137
3007	429	456	489	521	542	569	564	135
3008	414	456	481	515	544	561	575	161
3009	387	410	432	449	470	496	513	126
3010	391	421	445	470	488	508	511	120
3011	402	430	453	475	492	514	527	125
3012	383	404	421	450	473	496	509	126
Mean	403	429	454	479	499	523	531	128
S.D.	18	20	23	28	29	30	31	15

Unit: g

Appendix 3-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual body weight of male rats (Administration period)
Dose (mg/kg): 1000

Animal number	Day of administration 1	8	15	22	29	36	42	Gain 1-42
4001	416	440	470	483	513	530	544	128
4002	393	420	449	478	506	534	553	160
4003	415	448	468	488	513	531	530	115
4004	396	421	441	468	479	502	523	127
4005	402	428	452	473	506	530	547	145
4006	404	421	443	452	480	502	513	109
4007	382	399	426	443	467	490	503	121
4008	392	424	458	469	487	506	509	117
4009	383	398	407	424	449	453	464	81
4010	442	471	502	531	558	586	598	156
4011	407	430	456	486	510	530	536	129
4012	419	445	469	480	501	523	532	113
Mean	404	429	453	473	497	518	529	125
S.D.	17	20	24	26	28	32	32	22

Unit: g

Appendix 3-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual body weight of female rats during the pre-mating period (Main group)
Dose (mg/kg): 0

Animal number	Day of administration 1	8	15	Gain 1-15
1101	229	249	260	31
1102	214	230	239	25
1103	238	262	278	40
1104	219	231	242	23
1105	248	257	273	25
1106	217	231	243	26
1107	221	247	257	36
1108	225	231	248	23
1109	240	246	252	12
1110	228	238	247	19
1111	228	246	262	34
1112	241	246	263	22
Mean	229	243	255	26
S.D.	11	11	12	8

Unit: g

Appendix 3-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual body weight of female rats during the pre-mating period (Main group)
Dose (mg/kg): 100

Animal number	Day of administration 1	8	15	Gain 1-15
2101	229	244	251	22
2102	238	261	262	24
2103	234	244	247	13
2104	261	272	294	33
2105	232	245	258	26
2106	215	227	236	21
2107	244	252	271	27
2108	229	223	235	6
2109	211	219	232	21
2110	219	225	235	16
2111	228	228	232	4
2112	223	251	261	38
Mean	230	241	251	21
S.D.	13	17	19	10

Unit: g

Appendix 3-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual body weight of female rats during the pre-mating period (Main group)
Dose (mg/kg): 300

Animal number	Day of administration 1	8	15	Gain 1-15
3101	239	243	252	13
3102	227	227	249	22
3103	232	236	235	3
3104	227	238	252	25
3105	223	235	245	22
3106	213	225	238	25
3107	217	229	237	20
3108	263	269	289	26
3109	229	245	244	15
3110	207	224	234	27
3111	247	262	261	14
3112	239	259	277	38
Mean	230	241	251	21
S.D.	15	15	17	9

Unit: g

Appendix 3-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual body weight of female rats during the pre-mating period (Main group)
Dose (mg/kg): 1000

Animal number	Day of administration 1	8	15	Gain 1-15
4101	226	235	254	28
4102	211	226	237	26
4103	242	248	248	6
4104	250	267	280	30
4105	224	236	244	20
4106	232	244	254	22
4107	210	229	240	30
4108	234	246	255	21
4109	230	239	256	26
4110	222	226	244	22
4111	236	250	260	24
4112	229	242	240	11
Mean	229	241	251	22
S.D.	12	12	12	7

Unit: g

Appendix 3-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual body weight of dams during the gestation period (Main group)
Dose (mg/kg): 0

Dam number	Administration 0	7	14	20a)	Gain 0-20
1101	265	289	324	405	140
1102	248	272	301	375	127
1103	287	322	363	443	156
1104	248	283	333	418	170
1105	269	308	335	404	135
1106	243	271	304	373	130
1107	263	297	336	427	164
1108	253	288	319	398	145
1109	260	308	349	425	165
1110	260	290	324	407	147
1111	265	292	336	412	147
1112	273	308	344	417	144
Mean	261	294	331	409	148
S.D.	12	15	18	20	14

Unit: g
a): Gestation day

Appendix 3-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual body weight of dams during the gestation period (Main group)
Dose (mg/kg): 100

Dam number	Administration 0	7	14	20a)	Gain 0-20
2101	252	288	330	402	150
2102	288	326	360	442	154
2103	255	284	321	396	141
2104	Non-pregnant				
2105	261	289	318	398	137
2106	241	277	316	394	153
2107	283	316	361	387	104
2108	242	275	306	398	156
2109	241	270	296	362	121
2110	253	297	337	407	154
2111	256	283	313	386	130
2112	275	296	333	419	144
Mean	259	291	326	399	140
S.D.	17	17	21	20	16

Unit: g
a): Gestation day

Appendix 3-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual body weight of dams during the gestation period (Main group)
Dose (mg/kg): 300

Dam number	Administration 0	7	14	20a)	Gain 0-20
3101	251	280	322	383	132
3102	245	276	319	404	159
3103	242	275	315	389	147
3104	250	278	308	386	136
3105	253	271	305	372	119
3106	238	272	311	391	153
3107	241	262	301	394	153
3108	295	326	358	441	146
3109	262	288	316	383	121
3110	242	281	313	385	143
3111	277	315	342	404	127
3112	289	318	363	451	162
Mean	257	287	323	399	142
S.D.	20	21	20	24	14

Unit: g
a): Gestation day

Appendix 3-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual body weight of dams during the gestation period (Main group)
Dose (mg/kg): 1000

Dam number	Administration 0	7	14	20a)	Gain 0-20
4101	257	292	330	400	143
4102	245	278	308	380	135
4103	251	290	305	343	92
4104	295	329	369	448	153
4105	250	279	316	406	156
4106	264	296	332	419	155
4107	243	279	315	393	150
4108	270	287	315	375	105
4109	263	290	333	407	144
4110	245	275	328	411	166
4111	256	295	329	400	144
4112	264	300	337	413	149
Mean	259	291	326	400	141
S.D.	14	14	17	26	22

Unit: g
a): Gestation day

Appendix 3-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual body weight of dams during the lactation period (Main group)
Dose (mg/kg): 0

Dam number	Administration 0	Administration 4a)	Gain 0-4
1101	300	340	40
1102	309	307	-2
1103	340	353	13
1104	316	350	34
1105	310	330	20
1106	302	292	-10
1107	358	345	-13
1108	284	320	36
1109	306	311	5
1110	333	334	1
1111	300	335	35
1112	312	333	21
Mean	314	329	15
S.D.	20	18	19

Unit: g
a): Lactation day

Appendix 3-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual body weight of dams during the lactation period (Main group)
Dose (mg/kg): 100

Dam number	Administration 0	Administration 4a)	Gain 0-4
2101	326	333	7
2102	351	359	8
2103	296	316	20
2104	Non-pregnant		
2105	305	339	34
2106	295	315	20
2107b)	354		
2108	296	325	29
2109	285	294	9
2110	318	335	17
2111	292	324	32
2112	310	335	25
Mean	312	328	20
S.D.	23	17	10

Unit: g
a): Lactation day
b): Necropsied on lactation day 1 because all pups died

Appendix 3-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual body weight of dams during the lactation period (Main group)
Dose (mg/kg): 300

Dam number	Administration 0	Administration 4a)	Gain 0-4
3101	298	322	24
3102	284	314	30
3103	289	301	12
3104	287	328	41
3105	279	306	27
3106	316	322	6
3107	290	296	6
3108	333	358	25
3109	301	318	17
3110	312	297	-15
3111	331	333	2
3112	334	362	28
Mean	305	321	17
S.D.	20	22	15

Unit: g
a): Lactation day

Appendix 3-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual body weight of dams during the lactation period (Main group)
Dose (mg/kg): 1000

Dam number	Administration 0	Administration 4a)	Gain 0-4
4101	301	336	35
4102	304	298	-6
4103	319	321	2
4104	365	350	-15
4105	316	319	3
4106	328	326	-2
4107	281	304	23
4108	301	319	18
4109	330	335	5
4110	314	321	7
4111	297	326	29
4112	318	321	3
Mean	315	323	9
S.D.	21	14	15

Unit: g
a): Lactation day

Appendix 3-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual body weight of female rats (Satellite group, Administration period)
Dose (mg/kg): 0

Animal number	Day of administration 1	8	15	22	29	36	42	Gain 1-42
1113	242	256	271	277	292	296	299	57
1114	230	230	242	246	255	267	267	37
1115	212	227	241	247	247	261	267	55
1116	231	232	248	261	267	264	279	48
1117	217	220	238	241	247	247	260	43
1118	240	253	252	270	278	283	288	48
1119	244	268	280	311	339	327	324	80
1120	227	233	226	243	250	263	264	37
1121	221	240	247	254	258	273	276	55
1122	237	245	260	265	269	281	276	39
Mean	230	240	251	262	270	276	280	50
S.D.	11	15	16	21	28	22	19	13

Unit: g

Appendix 3-18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual body weight of female rats (Satellite group, Administration period)
Dose (mg/kg): 1000

Animal number	Day of administration 1	8	15	22	29	36	42	Gain 1-42
4113	229	234	237	261	269	269	277	48
4114	240	258	262	271	269	279	280	40
4115	242	252	276	292	300	302	312	70
4116	218	231	239	243	260	262	272	54
4117	223	240	250	258	259	270	265	42
4118	225	237	251	259	265	281	287	62
4119	224	234	247	261	267	267	282	58
4120	224	227	238	248	250	249	261	37
4121	224	236	236	251	260	266	268	44
4122	230	255	264	269	275	281	274	44
Mean	228	240	250	261	267	273	278	50
S.D.	8	11	14	14	13	14	14	11

Unit: g

Appendix 3-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual body weight of male rats (Recovery period)
Dose (mg/kg): 0

Animal number	Day of recovery 1	8	14	Gain 1-14
1008	512	521	513	1
1009	509	522	531	22
1010	510	539	535	25
1011	547	553	547	0
1012	493	503	520	27
Mean	514	528	529	15
S.D.	20	19	13	13

Unit: g

Appendix 3-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual body weight of male rats (Recovery period)
Dose (mg/kg): 1000

Animal number	Day of recovery 1	8	14	Gain 1-14
4008	506	515	517	11
4009	467	483	480	13
4010	599	607	614	15
4011	534	538	544	10
4012	535	544	544	9
Mean	528	537	540	12
S.D.	48	46	49	2

Unit: g

Appendix 3-21 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual body weight of female rats (Recovery period)
Dose (mg/kg): 0

Animal number	Day of recovery 1	8	14	Gain 1-14
1118	279	292	294	15
1119	322	337	341	19
1120	257	272	267	10
1121	282	281	283	1
1122	280	283	293	13
Mean	284	293	296	12
S.D.	24	26	28	7

Unit: g

Appendix 3-22 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual body weight of female rats (Recovery period)
Dose (mg/kg): 1000

Animal number	Day of recovery 1	8	14	Gain 1-14
4118	287	289	292	5
4119	278	279	276	-2
4120	264	269	266	2
4121	262	270	273	11
4122	281	278	285	4
Mean	274	277	278	4
S.D.	11	8	10	5

Unit: g

Appendix 4-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual food consumption of male rats (Administration period)
Dose (mg/kg): 0

Animal number	Day of administration 2	8	15	30	36	42
1001	26	26	25	23	24	22
1002	28	24	20	19	22	22
1003	24	25	28	27	28	27
1004	27	24	25	25	24	26
1005	21	24	26	21	22	22
1006	24	26	25	22	23	18
1007	24	22	24	22	24	24
1008	22	25	25	20	23	17
1009	21	24	22	22	25	23
1010	26	26	24	25	27	25
1011	27	28	26	24	25	25
1012	25	25	26	24	24	25
Mean	25	25	25	23	24	23
S.D.	2	2	2	2	2	3

Unit: g/rat/day

Appendix 4-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual food consumption of male rats (Administration period)
Dose (mg/kg): 100

Animal number	Day of administration 2	8	15	30	36	42
2001	27	23	27	21	23	24
2002	22	23	25	22	24	25
2003	22	25	21	21	19	25
2004	26	21	22	21	21	20
2005	24	29	30	25	23	26
2006	24	27	26	24	25	24
2007	28	27	27	27	27	24
2008	28	28	27	21	22	22
2009	23	26	25	23	22	23
2010	24	24	27	21	22	24
2011	20	23	22	20	22	23
2012	24	26	23	22	21	21
Mean	24	25	25	22	23	23
S.D.	2	2	3	2	2	2

Unit: g/rat/day

Appendix 4-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual food consumption of male rats (Administration period)
Dose (mg/kg): 300

Animal number	Day of administration 2	8	15	30	36	42
3001	26	23	26	20	24	24
3002	27	24	26	25	26	23
3003	24	21	25	22	24	25
3004	27	24	25	24	26	26
3005	23	23	25	22	23	21
3006	28	28	25	24	25	22
3007	26	27	26	24	23	23
3008	27	29	24	24	26	24
3009	23	23	24	23	23	23
3010	24	25	27	21	26	22
3011	25	23	23	20	19	22
3012	25	27	21	23	23	23
Mean	25	25	25	23	24	23
S.D.	2	2	2	2	2	1

Unit: g/rat/day

Appendix 4-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual food consumption of male rats (Administration period)
Dose (mg/kg): 1000

Animal number	Day of administration 2	8	15	30	36	42
4001	24	27	25	27	21	21
4002	26	24	24	24	25	26
4003	23	25	23	23	22	20
4004	22	25	22	22	22	23
4005	26	24	23	23	22	23
4006	23	23	27	22	23	23
4007	23	26	24	24	25	22
4008	25	26	24	22	21	22
4009	21	22	21	21	20	20
4010	29	25	25	24	26	24
4011	24	24	21	19	22	24
4012	29	25	23	22	23	23
Mean	25	25	24	23	23	23
S.D.	3	1	2	2	2	2

Unit: g/rat/day

Appendix 4-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

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

Dose (mg/kg): 0

Animal number	Day of administration 2	8	15
1101	20	21	19
1102	14	19	19
1103	18	19	21
1104	12	22	22
1105	18	16	18
1106	17	15	19
1107	16	18	19
1108	15	12	16
1109	7	19	18
1110	18	19	16
1111	17	18	18
1112	20	19	22
Mean	16	18	19
S.D.	4	3	2

Unit: g/rat/day

Appendix 4-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual food consumption of female rats during the pre-mating period (Main group)
Dose (mg/kg): 100

Animal number	Day of administration 2	8	15
2101	15	17	15
2102	18	23	13
2103	13	18	15
2104	17	17	23
2105	11	16	16
2106	16	19	19
2107	17	14	21
2108	16	11	16
2109	14	16	17
2110	17	12	17
2111	17	19	11
2112	17	21	20
Mean	16	17	17
S.D.	2	3	3

Unit: g/rat/day

Appendix 4-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual food consumption of female rats during the pre-mating period (Main group)
Dose (mg/kg): 300

Animal number	Day of administration 2	8	15
3101	17	14	14
3102	18	15	18
3103	16	18	12
3104	20	15	21
3105	15	17	17
3106	16	16	18
3107	13	17	14
3108	21	15	20
3109	17	21	12
3110	14	19	19
3111	18	21	12
3112	17	19	20
Mean	17	17	16
S.D.	2	2	3

Unit: g/rat/day

Appendix 4-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual food consumption of female rats during the pre-mating period (Main group)
Dose (mg/kg): 1000

Animal number	Day of administration 2	8	15
4101	18	13	18
4102	10	20	18
4103	16	22	15
4104	13	21	21
4105	14	17	18
4106	17	15	16
4107	17	20	19
4108	15	18	16
4109	14	12	17
4110	13	12	18
4111	17	16	18
4112	18	20	11
Mean	15	17	17
S.D.	2	4	2

Unit: g/rat/day

Appendix 4-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual food consumption of dams during the gestation period (Main group)
Dose (mg/kg): 0

Dam number	Administration 1	7	14	20a)
1101	18	21	19	20
1102	18	20	25	29
1103	20	24	26	21
1104	21	20	26	25
1105	21	19	22	16
1106	16	21	21	19
1107	17	21	22	25
1108	20	22	24	21
1109	17	28	27	18
1110	15	24	25	26
1111	19	19	22	19
1112	23	21	23	22
Mean	19	22	24	22
S.D.	2	3	2	4

Unit: g/rat/day
a): Gestation day

Appendix 4-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual food consumption of dams during the gestation period (Main group)
Dose (mg/kg): 100

Dam number	Administration			
	1	7	14	20a)
2101	15	21	23	20
2102	20	25	24	21
2103	14	20	21	18
2104	Non-pregnant			
2105	12	19	20	22
2106	15	22	26	24
2107	18	22	30	21
2108	15	21	21	21
2109	18	19	21	17
2110	20	27	23	21
2111	21	23	24	21
2112	21	20	22	26
Mean	17	22	23	21
S.D.	3	2	3	2

Unit: g/rat/day
a): Gestation day

Appendix 4-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual food consumption of dams during the gestation period (Main group)
Dose (mg/kg): 300

Dam number	Administration 1	7	14	20a)
3101	16	19	25	17
3102	14	17	23	18
3103	17	23	24	16
3104	20	16	19	18
3105	18	19	19	23
3106	19	21	22	20
3107	10	17	19	24
3108	19	20	23	21
3109	19	20	22	14
3110	17	21	21	19
3111	21	24	23	16
3112	22	22	25	25
Mean	18	20	22	19
S.D.	3	2	2	3

Unit: g/rat/day
a): Gestation day

Appendix 4-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual food consumption of dams during the gestation period (Main group)
Dose (mg/kg): 1000

Dam number	Administration 1	7	14	20a)
4101	17	23	20	15
4102	18	19	25	21
4103	21	20	19	18
4104	21	24	25	20
4105	18	16	22	24
4106	17	22	20	21
4107	19	23	21	19
4108	16	16	19	15
4109	17	20	23	21
4110	15	20	21	21
4111	17	19	22	21
4112	15	21	25	21
Mean	18	20	22	20
S.D.	2	3	2	3

Unit: g/rat/day
a): Gestation day

Appendix 4-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual food consumption of dams during the lactation period (Main group)
Dose (mg/kg): 0

Dam number	Administration	
	2	4a)
1101	24	43
1102	20	31
1103	20	41
1104	28	49
1105	29	41
1106	7	27
1107	22	31
1108	27	42
1109	7	34
1110	26	46
1111	25	47
1112	15	50
Mean	21	40
S.D.	8	8

Unit: g/rat/day
a): Lactation day

Appendix 4-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual food consumption of dams during the lactation period (Main group)
Dose (mg/kg): 100

Dam number	Administration	
	2	4a)
2101	21	38
2102	31	32
2103	18	39
2104	Non-pregnant	
2105	24	45
2106	26	41
2107b)		
2108	27	44
2109	19	31
2110	32	37
2111	28	47
2112	32	50
Mean	26	40
S.D.	5	6

Unit: g/rat/day
a): Lactation day
b): Necropsied on lactation day 1 because all pups died

Appendix 4-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual food consumption of dams during the lactation period (Main group)
Dose (mg/kg): 300

Dam number	Administration	
	2	4a)
3101	27	36
3102	17	43
3103	20	37
3104	27	44
3105	23	28
3106	23	35
3107	10	37
3108	21	48
3109	26	37
3110	12	35
3111	18	41
3112	21	47
Mean	20	39
S.D.	5	6

Unit: g/rat/day
a): Lactation day

Appendix 4-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual food consumption of dams during the lactation period (Main group)
Dose (mg/kg): 1000

Dam number	Administration	
	2	4a)
4101	28	43
4102	15	34
4103	11	19
4104	20	35
4105	24	34
4106	15	34
4107	17	39
4108	14	40
4109	25	44
4110	20	43
4111	18	45
4112	14	31
Mean	18	37
S.D.	5	7

Unit: g/rat/day
a): Lactation day

Appendix 4-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual food consumption of female rats (Satellite group, Administration period)
Dose (mg/kg): 0

Animal number	Day of administration 2	8	15	30	36	42
1113	13	20	21	14	21	16
1114	17	15	21	16	19	16
1115	15	16	19	16	15	16
1116	19	15	20	19	12	19
1117	18	12	19	17	13	19
1118	15	19	13	21	17	17
1119	20	21	21	17	20	17
1120	10	17	11	17	16	16
1121	18	19	18	17	17	17
1122	15	14	19	15	18	17
Mean	16	17	18	17	17	17
S.D.	3	3	3	2	3	1

Unit: g/rat/day

Appendix 4-18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual food consumption of female rats (Satellite group, Administration period)
Dose (mg/kg): 1000

Animal number	Day of administration					
	2	8	15	30	36	42
4113	17	16	16	17	17	16
4114	16	20	16	14	13	13
4115	21	13	21	17	11	19
4116	11	17	17	13	16	16
4117	16	14	16	15	15	14
4118	17	17	19	17	17	17
4119	17	14	15	20	14	20
4120	17	12	14	16	11	16
4121	17	19	11	16	18	16
4122	18	18	18	12	18	11
Mean	17	16	16	16	15	16
S.D.	2	3	3	2	3	3

Unit: g/rat/day

Appendix 4-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual food consumption of male rats (Recovery period)
Dose (mg/kg): 0

Animal number	Day of recovery 1	8	14
1008	15	24	25
1009	19	25	25
1010	21	33	31
1011	24	31	30
1012	20	30	29
Mean	20	29	28
S.D.	3	4	3

Unit: g/rat/day

Appendix 4-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual food consumption of male rats (Recovery period)
Dose (mg/kg): 1000

Animal number	Day of recovery 1	8	14
4008	17	26	26
4009	19	27	26
4010	21	30	30
4011	20	25	29
4012	21	27	24
Mean	20	27	27
S.D.	2	2	2

Unit: g/rat/day

Appendix 4-21 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual food consumption of female rats (Recovery period)
Dose (mg/kg): 0

Animal number	Day of recovery 1	8	14
1118	14	20	19
1119	12	26	26
1120	10	21	19
1121	15	19	20
1122	16	18	21
Mean	13	21	21
S.D.	2	3	3

Unit: g/rat/day

Appendix 4-22 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual food consumption of female rats (Recovery period)
Dose (mg/kg): 1000

Animal number	Day of recovery 1	8	14
4118	17	19	21
4119	14	18	13
4120	15	18	16
4121	11	17	20
4122	14	14	20
Mean	14	17	18
S.D.	2	2	3

Unit: g/rat/day

Appendix 5-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual urinalysis of male rats (Week 6 of administration)
Dose (mg/kg): 0

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
1008	>=9.0	+	+	-	+-	-	+-	Y
1009	8.0	+	+	-	+-	-	+-	Y
1010	8.5	+	+	-	+++	-	+-	Y
1011	7.0	++	++	-	-	+	+	Y
1012	6.5	+	+	-	-	-	+-	Y

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL
4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 5-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual urinalysis of male rats (Week 6 of administration)
Dose (mg/kg): 0

Animal number	URINE SEDIMENT						
						CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
1008	-	-	+-	-	-	+-	-
1009	-	-	+-	-	-	+-	-
1010	+-	-	+-	-	-	+-	-
1011	-	-	+-	-	-	-	-
1012	-	-	+-	-	-	+-	-

SEC : Squamous Epithelial Cell
SREC : Small Round Epithelial Cell
PS : Phosphate Salts
CO : Calcium Oxalate

\- : Negative
+- : Slight
\+ : Mild
++ : Moderate
+++ : Severe

Appendix 5-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual water intake and urinalysis of male rats (Week 6 of administration)
Dose (mg/kg): 0

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
1008	39	14.4	1412	1.01	3.07	1.35
1009	35	15.5	1822	1.64	4.46	2.20
1010	51	14.6	1308	1.05	3.24	1.26
1011	30	6.4	2926	0.69	2.90	1.15
1012	35	10.5	2046	1.16	3.28	1.53
Mean	38	12.3	1903	1.11	3.39	1.50
S.D.	8	3.8	646	0.34	0.62	0.42

Appendix 5-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual urinalysis of male rats (Week 6 of administration)
Dose (mg/kg): 100

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
2008	8.0	++	+	-	+-	-	+-	Y
2009	>=9.0	+	+	-	-	-	+-	Y
2010	7.5	+-	+	-	+-	-	+-	Y
2011	8.0	-	-	-	-	-	+-	Y
2012	6.5	-	+	-	+-	-	+-	Y

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL
4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 5-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual urinalysis of male rats (Week 6 of administration)
Dose (mg/kg): 100

Animal number	URINE SEDIMENT						
						CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
2008	-	-	+-	-	-	+-	-
2009	-	-	+-	-	-	+-	-
2010	-	-	+-	-	-	+	-
2011	-	-	+-	-	-	-	-
2012	-	-	+-	-	-	-	-

SEC : Squamous Epithelial Cell
SREC : Small Round Epithelial Cell
PS : Phosphate Salts
CO : Calcium Oxalate

\- : Negative
+- : Slight
\+ : Mild
++ : Moderate
+++ : Severe

Appendix 5-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual water intake and urinalysis of male rats (Week 6 of administration)
Dose (mg/kg): 100

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
2008	31	7.5	2286	0.87	2.88	1.14
2009	34	14.5	2058	1.39	5.16	1.94
2010	39	15.9	1576	1.34	4.08	1.81
2011	48	23.4	1158	1.26	4.68	1.83
2012	41	15.1	1956	1.39	4.83	2.17
Mean	39	15.3	1807	1.25	4.33	1.78
S.D.	7	5.6	444	0.22	0.90	0.38

Appendix 5-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual urinalysis of male rats (Week 6 of administration)
Dose (mg/kg): 300

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
3008	7.0	+	+	-	+-	-	+-	Y
3009	>=9.0	+	+	-	-	-	+-	Y
3010	>=9.0	++	++	-	+-	+	+	Y
3011	>=9.0	+	+	-	-	-	+-	Y
3012	7.0	+	++	-	-	+	+-	Y

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL
4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 5-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual urinalysis of male rats (Week 6 of administration)
Dose (mg/kg): 300

Animal number	URINE SEDIMENT						
						CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
3008	-	-	+-	-	-	-	-
3009	-	-	+-	-	-	+-	-
3010	-	-	+-	-	-	+-	-
3011	-	-	+-	-	-	-	-
3012	-	-	+-	-	-	+-	-

SEC : Squamous Epithelial Cell
SREC : Small Round Epithelial Cell
PS : Phosphate Salts
CO : Calcium Oxalate

\- : Negative
+- : Slight
\+ : Mild
++ : Moderate
+++ : Severe

Appendix 5-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual water intake and urinalysis of male rats (Week 6 of administration)
Dose (mg/kg): 300

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
3008	41	9.1	2158	0.91	3.35	1.16
3009	24	6.9	2628	1.12	3.11	1.61
3010	31	8.7	1934	0.99	2.74	1.27
3011	27	9.2	1946	0.83	3.16	1.38
3012	40	10.3	1608	1.01	2.75	1.22
Mean	33	8.8	2055	0.97	3.02	1.33
S.D.	8	1.2	376	0.11	0.27	0.18

Appendix 5-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual urinalysis of male rats (Week 6 of administration)
Dose (mg/kg): 1000

Animal number	pH	1) Pro-tein	2) Ketone body	3) Glu-cose	4) Occult blood	5) Bili-rubin	6) Urobi-linogen	7) Color
4008	8.5	++	++	-	-	+	++	Y
4009	>=9.0	+	+	-	+-	-	+-	Y
4010	>=9.0	++	++	-	-	-	+	Y
4011	7.0	+	++	-	-	-	+-	Y
4012	>=9.0	+-	+	-	-	-	+-	Y

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL
4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 5-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual urinalysis of male rats (Week 6 of administration)
Dose (mg/kg): 1000

Animal number	URINE SEDIMENT						
						CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
4008	-	-	+-	-	-	+-	-
4009	-	-	+-	-	-	+-	-
4010	-	-	+-	-	-	+-	-
4011	-	-	+-	-	-	+-	-
4012	-	-	+-	-	-	+-	-

SEC : Squamous Epithelial Cell
SREC : Small Round Epithelial Cell
PS : Phosphate Salts
CO : Calcium Oxalate

\- : Negative
+- : Slight
\+ : Mild
++ : Moderate
+++ : Severe

Appendix 5-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual water intake and urinalysis of male rats (Week 6 of administration)
Dose (mg/kg): 1000

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
4008	28	5.6	2308	0.68	2.15	0.86
4009	31	10.4	1752	0.87	2.72	1.31
4010	36	13.9	1802	1.25	4.30	1.70
4011	33	13.9	1624	1.36	3.66	1.92
4012	33	8.4	2118	0.82	2.75	1.09
Mean	32	10.4	1921	1.00	3.12	1.38
S.D.	3	3.6	283	0.29	0.85	0.43

Appendix 5-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual urinalysis of female rats (Satellite group, Week 6 of administration)
Dose (mg/kg): 0

Animal number	pH	1) Pro-tein	2) Ketone body	3) Glu-cose	4) Occult blood	5) Bili-rubin	6) Urobi-linogen	7) Color
1118	7.5	-	+-	-	-	-	+-	Y
1119	7.0	-	-	-	-	-	+-	Y
1120	7.0	-	+-	-	-	-	+-	Y
1121	6.5	+	+-	-	-	-	++	Y
1122	>=9.0	+-	-	-	-	-	+-	Y

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL
4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 5-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual urinalysis of female rats (Satellite group, Week 6 of administration)
Dose (mg/kg): 0

Animal number	URINE SEDIMENT						
						CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
1118	-	-	+-	-	-	+-	-
1119	-	-	+-	-	-	-	-
1120	-	-	+-	-	-	-	-
1121	-	-	+-	-	-	+-	-
1122	-	-	+-	-	-	+-	-

SEC : Squamous Epithelial Cell
SREC : Small Round Epithelial Cell
PS : Phosphate Salts
CO : Calcium Oxalate

\- : Negative
+- : Slight
\+ : Mild
++ : Moderate
+++ : Severe

Appendix 5-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual water intake and urinalysis of female rats (Satellite group, Week 6 of administration)
Dose (mg/kg): 0

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
1118	29	6.8	1740	0.71	1.79	0.86
1119	28	9.5	2230	1.10	3.39	1.48
1120	25	4.2	2630	0.66	1.74	0.78
1121	23	4.4	2286	0.54	1.44	0.51
1122	26	4.4	2098	0.44	1.34	0.48
Mean	26	5.9	2197	0.69	1.94	0.82
S.D.	2	2.3	322	0.25	0.83	0.40

Appendix 5-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual urinalysis of female rats (Satellite group, Week 6 of administration)
Dose (mg/kg): 1000

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
4118	6.0	+	+-	-	-	-	+-	Y
4119	7.0	+	+-	-	-	+	+	Y
4120	6.0	+	-	-	-	-	+-	Y
4121	7.5	+	+	-	-	-	+	Y
4122	7.5	-	+-	-	-	-	+-	Y

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL
4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 5-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual urinalysis of female rats (Satellite group, Week 6 of administration)
Dose (mg/kg): 1000

Animal number	URINE SEDIMENT						
						CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
4118	-	-	+-	-	-	-	-
4119	-	-	+-	-	-	+-	-
4120	-	-	+-	-	-	+-	-
4121	-	-	+-	-	-	+-	-
4122	-	-	+-	-	-	+-	-

SEC : Squamous Epithelial Cell
SREC : Small Round Epithelial Cell
PS : Phosphate Salts
CO : Calcium Oxalate

\- : Negative
+- : Slight
\+ : Mild
++ : Moderate
+++ : Severe

Appendix 5-18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual water intake and urinalysis of female rats (Satellite group, Week 6 of administration)
Dose (mg/kg): 1000

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
4118	14	6.9	2016	0.83	1.97	0.83
4119	27	5.1	2338	0.58	1.86	0.86
4120	23	5.0	2436	0.83	1.90	1.01
4121	26	5.5	1868	0.63	1.57	0.78
4122	32	17.1	1346	1.20	3.73	1.61
Mean	24	7.9	2001	0.81	2.21	1.02
S.D.	7	5.2	433	0.24	0.87	0.34

Appendix 5-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual urinalysis of male rats (Week 2 of recovery)
Dose (mg/kg): 0

Animal number	pH	1) Pro-tein	2) Ketone body	3) Glu-cose	4) Occult blood	5) Bili-rubin	6) Urobi-linogen	7) Color
1008	7.5	++	++	-	-	-	+-	Y
1009	8.0	+-	-	-	+-	-	+-	Y
1010	8.0	-	+-	-	-	-	+-	Y
1011	8.5	+	+	-	+-	-	+-	Y
1012	7.5	+	+	-	+-	-	+-	Y

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL
4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 5-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual urinalysis of male rats (Week 2 of recovery)
Dose (mg/kg): 0

Animal number	URINE SEDIMENT						
						CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
1008	-	-	+-	-	-	+	-
1009	-	-	+-	-	-	+-	-
1010	-	-	+-	-	-	+	-
1011	-	-	+-	-	-	+-	-
1012	-	-	+-	-	-	+	-

SEC : Squamous Epithelial Cell
SREC : Small Round Epithelial Cell
PS : Phosphate Salts
CO : Calcium Oxalate

\- : Negative
+- : Slight
\+ : Mild
++ : Moderate
+++ : Severe

Appendix 5-21 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual water intake and urinalysis of male rats (Week 2 of recovery)
Dose (mg/kg): 0

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
1008	33	16.3	1750	1.70	4.21	1.96
1009	54	26.7	1580	1.71	6.81	2.40
1010	43	24.5	1470	2.11	5.90	2.70
1011	33	14.0	2416	1.85	5.58	2.41
1012	44	18.1	1868	1.52	5.38	2.10
Mean	41	19.9	1817	1.78	5.58	2.31
S.D.	9	5.4	368	0.22	0.94	0.29

Appendix 5-22 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual urinalysis of male rats (Week 2 of recovery)
Dose (mg/kg): 1000

Animal number	pH	1) Pro-tein	2) Ketone body	3) Glu-cose	4) Occult blood	5) Bili-rubin	6) Urobi-linogen	7) Color
4008	8.5	+	+	-	+-	-	+-	Y
4009	8.0	+-	+-	-	-	-	+-	Y
4010	8.5	+-	+	-	-	-	+-	Y
4011	8.0	+-	+	-	+-	-	+-	Y
4012	>=9.0	+-	+	-	+-	-	+-	Y

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL
4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 5-23 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual urinalysis of male rats (Week 2 of recovery)
Dose (mg/kg): 1000

	URINE SEDIMENT						
						CRYSTALLIZATION	
Animal number	RBC	WBC	SEC	SREC	Cast	PS	CO
4008	-	-	+-	-	-	+	-
4009	-	-	+-	-	-	+-	-
4010	-	-	+-	-	-	+-	-
4011	-	-	+-	-	-	+	-
4012	-	-	+-	-	-	+-	-

SEC : Squamous Epithelial Cell
SREC : Small Round Epithelial Cell
PS : Phosphate Salts
CO : Calcium Oxalate

\- : Negative
+- : Slight
\+ : Mild
++ : Moderate
+++ : Severe

Appendix 5-24 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual water intake and urinalysis of male rats (Week 2 of recovery)
Dose (mg/kg): 1000

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
4008	24	10.9	2310	1.16	4.11	1.70
4009	39	15.3	1894	1.07	4.85	1.87
4010	46	20.2	1806	1.98	6.11	2.50
4011	35	12.2	1980	1.49	4.05	1.68
4012	39	17.6	2196	1.55	6.49	2.53
Mean	37	15.2	2037	1.45	5.12	2.06
S.D.	8	3.8	210	0.36	1.13	0.43

Appendix 5-25 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual urinalysis of female rats (Week 2 of recovery)
Dose (mg/kg): 0

Animal number	pH	1) Pro-tein	2) Ketone body	3) Glu-cose	4) Occult blood	5) Bili-rubin	6) Urobi-linogen	7) Color
1118	7.0	-	-	-	-	-	+-	Y
1119	7.0	-	-	-	-	-	+-	Y
1120	6.5	-	-	-	-	-	+-	Y
1121	7.0	+-	+-	-	-	-	+-	Y
1122	8.5	+	+-	-	+	-	+-	Y

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL
4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 5-26 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual urinalysis of female rats (Week 2 of recovery)
Dose (mg/kg): 0

	URINE SEDIMENT						
						CRYSTALLIZATION	
Animal number	RBC	WBC	SEC	SREC	Cast	PS	CO
1118	-	-	+-	-	-	+-	-
1119	-	-	+-	-	-	+-	-
1120	-	-	+-	-	-	-	-
1121	-	-	+-	-	-	+	-
1122	-	-	+-	-	-	+	-

SEC : Squamous Epithelial Cell
SREC : Small Round Epithelial Cell
PS : Phosphate Salts
CO : Calcium Oxalate

\- : Negative
+- : Slight
\+ : Mild
++ : Moderate
+++ : Severe

Appendix 5-27 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual water intake and urinalysis of female rats (Week 2 of recovery)
Dose (mg/kg): 0

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
1118	23	6.5	2340	0.77	2.42	0.85
1119	30	11.8	2110	1.11	3.61	1.20
1120	18	7.7	2298	1.09	2.44	0.97
1121	31	9.2	2256	1.18	3.19	1.51
1122	31	9.4	2094	1.05	2.89	1.18
Mean	27	8.9	2220	1.04	2.91	1.14
S.D.	6	2.0	112	0.16	0.51	0.25

Appendix 5-28 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual urinalysis of female rats (Week 2 of recovery)
Dose (mg/kg): 1000

Animal number	pH	1) Pro-tein	2) Ketone body	3) Glu-cose	4) Occult blood	5) Bili-rubin	6) Urobi-linogen	7) Color
4118	7.0	-	-	-	-	-	+-	Y
4119	8.0	-	-	-	-	-	+-	Y
4120	8.5	+-	+-	-	-	-	+-	Y
4121	6.0	-	-	-	-	-	+-	Y
4122	6.5	-	+-	-	-	-	+-	Y

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL
4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 5-29 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual urinalysis of female rats (Week 2 of recovery)
Dose (mg/kg): 1000

	URINE SEDIMENT						
						CRYSTALLIZATION	
Animal number	RBC	WBC	SEC	SREC	Cast	PS	CO
4118	-	+-	+-	-	-	+-	-
4119	-	-	+-	-	-	+-	-
4120	-	-	+-	-	-	+-	-
4121	-	-	+-	-	-	-	-
4122	-	-	+-	-	-	+-	-

SEC : Squamous Epithelial Cell
SREC : Small Round Epithelial Cell
PS : Phosphate Salts
CO : Calcium Oxalate

\- : Negative
+- : Slight
\+ : Mild
++ : Moderate
+++ : Severe

Appendix 5-30 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual water intake and urinalysis of female rats (Week 2 of recovery)
Dose (mg/kg): 1000

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
4118	19	9.8	1824	0.82	2.74	1.12
4119	39	11.1	2340	1.24	4.11	1.53
4120	23	5.1	2272	0.64	1.79	0.75
4121	23	4.6	2518	0.64	1.86	0.62
4122	29	7.3	2144	0.69	2.43	0.98
Mean	27	7.6	2220	0.81	2.59	1.00
S.D.	8	2.8	259	0.25	0.94	0.35

Appendix 6-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual hematology of male rats (End of administration)
Dose (mg/kg): 0

Animal number	RBC 10E4/μL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/μL	PT s	APTT s	FIB mg/dL
1001	928	15.8	44.6	48.1	17.0	35.4	1.8	110.3	13.8	15.9	268
1002	815	14.9	41.5	50.9	18.3	35.9	2.3	90.6	13.6	17.2	270
1003	872	16.3	46.3	53.1	18.6	35.1	2.2	80.0	13.3	19.8	307
1004	805	15.1	42.9	53.3	18.7	35.2	2.4	92.1	16.0	20.6	297
1005	916	16.4	46.2	50.5	17.9	35.5	1.6	96.2	13.2	18.0	273
Mean	867	15.7	44.3	51.2	18.1	35.4	2.1	93.8	14.0	18.3	283
S.D.	56	0.7	2.1	2.1	0.7	0.3	0.3	11.0	1.2	1.9	18

Appendix 6-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual hematology of male rats (End of administration)
Dose (mg/kg): 0

Animal number	WBC	Differential leukocyte ratio (%)						Differential leukocyte counts (10E2/μL)					
	10E2/μL	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
1001	94.8	80.3	16.0	1.3	0.3	1.8	0.3	76.2	15.2	1.2	0.3	1.7	0.3
1002	62.7	74.9	21.7	1.0	0.3	1.8	0.4	47.0	13.6	0.6	0.2	1.2	0.2
1003	72.6	56.6	38.4	1.6	0.1	2.4	0.8	41.1	27.9	1.2	0.1	1.8	0.5
1004	97.9	68.9	28.2	1.1	0.2	1.2	0.4	67.5	27.6	1.1	0.2	1.2	0.4
1005	69.2	73.6	22.7	1.3	0.2	1.4	0.7	50.9	15.7	0.9	0.1	0.9	0.5
Mean	79.4	70.9	25.4	1.3	0.2	1.7	0.5	56.5	20.0	1.0	0.2	1.4	0.4
S.D.	15.9	8.9	8.5	0.2	0.1	0.5	0.2	14.7	7.1	0.3	0.1	0.4	0.1

LUC: Large unstained cells

Appendix 6-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual hematology of male rats (End of administration)
Dose (mg/kg): 100

Animal number	RBC 10E4/µL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/µL	PT s	APTT s	FIB mg/dL
2001	897	15.4	43.9	48.9	17.1	35.0	2.0	94.8	13.4	20.2	202
2002	844	15.4	43.4	51.4	18.3	35.6	1.8	92.9	13.8	16.2	227
2003	902	15.9	44.9	49.7	17.7	35.5	1.9	93.9	14.2	20.5	232
2004	947	16.6	46.8	49.4	17.5	35.5	2.0	78.9	19.0	26.6	276
2005	890	15.6	43.3	48.7	17.5	36.0	1.6	99.2	12.4	17.4	263
Mean	896	15.8	44.5	49.6	17.6	35.5	1.9	91.9	14.6	20.2	240
S.D.	37	0.5	1.5	1.1	0.4	0.4	0.2	7.7	2.6	4.0	30

Appendix 6-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual hematology of male rats (End of administration)
Dose (mg/kg): 100

Animal number	WBC	Differential leukocyte ratio (%)						Differential leukocyte counts (10E2/μL)					
	10E2/μL	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
2001	87.4	70.2	25.6	1.3	0.2	1.8	0.9	61.4	22.4	1.2	0.2	1.6	0.7
2002	64.8	67.7	26.9	2.2	0.2	2.2	0.9	43.9	17.4	1.4	0.1	1.4	0.6
2003	65.7	56.5	39.3	1.1	0.2	2.6	0.4	37.1	25.8	0.7	0.1	1.7	0.3
2004	60.6	63.3	33.1	1.5	0.2	1.4	0.5	38.4	20.1	0.9	0.1	0.8	0.3
2005	52.4	74.7	21.3	1.3	0.2	2.2	0.3	39.2	11.1	0.7	0.1	1.2	0.2
Mean	66.2	66.5	29.2	1.5	0.2	2.0	0.6	44.0	19.4	1.0	0.1	1.3	0.4
S.D.	13.0	6.9	7.0	0.4	0.0	0.5	0.3	10.1	5.6	0.3	0.0	0.4	0.2

LUC: Large unstained cells

Appendix 6-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual hematology of male rats (End of administration)
Dose (mg/kg): 300

Animal number	RBC 10E4/μL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/μL	PT s	APTT s	FIB mg/dL
3001	912	15.9	44.5	48.7	17.4	35.7	2.0	109.9	15.8	26.7	224
3002	797	15.2	42.7	53.6	19.1	35.7	1.9	92.1	14.6	21.7	243
3003	906	16.2	46.1	50.8	17.9	35.3	1.6	80.7	15.8	21.2	235
3004	848	15.9	44.0	51.9	18.7	36.1	2.0	89.5	12.5	16.1	273
3005	938	15.3	44.0	46.9	16.3	34.8	1.0	89.1	22.7	20.9	239
Mean	880	15.7	44.3	50.4	17.9	35.5	1.7	92.3	16.3	21.3	243
S.D.	57	0.4	1.2	2.6	1.1	0.5	0.4	10.8	3.8	3.8	18

Appendix 6-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual hematology of male rats (End of administration)
Dose (mg/kg): 300

Animal number	WBC	Differential leukocyte ratio (%)						Differential leukocyte counts (10E2/μL)					
	10E2/μL	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
3001	64.9	77.0	19.2	1.2	0.2	1.6	0.8	50.0	12.5	0.8	0.1	1.0	0.5
3002	59.7	83.8	13.1	1.2	0.1	1.2	0.5	50.1	7.8	0.7	0.1	0.7	0.3
3003	59.0	80.3	15.5	1.7	0.2	1.6	0.7	47.4	9.1	1.0	0.1	1.0	0.4
3004	59.7	71.2	25.9	1.1	0.1	1.5	0.3	42.5	15.5	0.6	0.1	0.9	0.2
3005	35.2	68.4	26.1	2.0	0.2	2.6	0.7	24.0	9.2	0.7	0.1	0.9	0.2
Mean	55.7	76.1	20.0	1.4	0.2	1.7	0.6	42.8	10.8	0.8	0.1	0.9	0.3
S.D.	11.7	6.3	5.9	0.4	0.1	0.5	0.2	11.0	3.1	0.2	0.0	0.1	0.1

LUC: Large unstained cells

Appendix 6-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual hematology of male rats (End of administration)
Dose (mg/kg): 1000

Animal number	RBC 10E4/µL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/µL	PT s	APTT s	FIB mg/dL
4001	851	14.9	42.2	49.6	17.5	35.4	2.4	136.1	15.1	20.5	263
4002	800	14.8	42.2	52.8	18.5	35.0	3.1	99.4	13.1	19.0	224
4003	819	15.3	44.6	54.4	18.7	34.4	1.9	94.5	19.9	25.5	278
4004	854	15.4	43.3	50.7	18.0	35.5	2.1	104.8	14.8	20.3	264
4005	872	15.7	44.4	50.9	18.1	35.5	1.9	84.7	16.9	23.7	291
Mean	839	15.2	43.3	51.7	18.2	35.2	2.3	103.9	16.0	21.8	264
S.D.	29	0.4	1.2	1.9	0.5	0.5	0.5	19.5	2.6	2.7	25

Appendix 6-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual hematology of male rats (End of administration)
Dose (mg/kg): 1000

Animal number	WBC	Differential leukocyte ratio (%)						Differential leukocyte counts (10E2/μL)					
	10E2/μL	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
4001	79.4	75.8	20.3	0.6	0.1	2.2	1.0	60.2	16.1	0.5	0.1	1.7	0.8
4002	75.5	71.3	23.2	1.1	0.3	2.9	1.3	53.8	17.5	0.8	0.2	2.2	1.0
4003	52.2	75.5	20.6	1.6	0.2	1.7	0.4	39.4	10.8	0.8	0.1	0.9	0.2
4004	72.7	74.8	21.7	1.6	0.1	1.5	0.3	54.4	15.7	1.1	0.1	1.1	0.2
4005	78.0	68.5	25.4	1.6	0.3	3.4	0.9	53.4	19.8	1.2	0.2	2.6	0.7
Mean	71.6	73.2	22.2	1.3	0.2	2.3	0.8	52.2	16.0	0.9	0.1	1.7	0.6
S.D.	11.1	3.2	2.1	0.4	0.1	0.8	0.4	7.7	3.3	0.3	0.1	0.7	0.4

LUC: Large unstained cells

Appendix 6-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual hematology of female rats (Lactation day 5)
Dose (mg/kg): 0

Animal number	RBC 10E4/µL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/µL	PT s	APTT s	FIB mg/dL
1101	674	13.7	39.0	57.9	20.2	35.0	7.6	107.5	11.5	15.8	292
1102	707	13.6	38.3	54.3	19.2	35.4	5.8	123.9	11.2	13.5	326
1103	629	12.0	34.9	55.5	19.0	34.2	10.3	166.1	12.0	15.3	350
1105	694	12.3	35.7	51.4	17.7	34.4	5.7	165.6	10.1	13.1	354
1108	720	13.0	37.6	52.2	18.0	34.5	6.2	133.9	10.4	13.7	285
Mean	685	12.9	37.1	54.3	18.8	34.7	7.1	139.4	11.0	14.3	321
S.D.	36	0.8	1.7	2.6	1.0	0.5	1.9	25.9	0.8	1.2	32

Appendix 6-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual hematology of female rats (Lactation day 5)
Dose (mg/kg): 0

Animal number	WBC	Differential leukocyte ratio (%)						Differential leukocyte counts (10E2/μL)					
	10E2/μL	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
1101	121.8	51.7	45.0	0.7	0.3	2.0	0.3	63.0	54.8	0.9	0.3	2.4	0.4
1102	75.9	43.2	54.1	1.0	0.1	1.3	0.4	32.8	41.0	0.8	0.1	1.0	0.3
1103	133.6	39.4	57.5	0.7	0.2	1.8	0.5	52.6	76.8	1.0	0.2	2.4	0.7
1105	105.1	55.9	42.3	0.4	0.1	0.7	0.5	58.7	44.5	0.5	0.1	0.8	0.5
1108	102.1	48.3	47.8	0.6	0.2	2.6	0.5	49.3	48.8	0.6	0.2	2.7	0.5
Mean	107.7	47.7	49.3	0.7	0.2	1.7	0.4	51.3	53.2	0.8	0.2	1.9	0.5
S.D.	21.9	6.6	6.3	0.2	0.1	0.7	0.1	11.6	14.2	0.2	0.1	0.9	0.1

LUC: Large unstained cells

Appendix 6-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual hematology of female rats (Lactation day 5)
Dose (mg/kg): 100

Animal number	RBC 10E4/µL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/µL	PT s	APTT s	FIB mg/dL
2101	689	13.6	39.8	57.7	19.8	34.3	7.6	135.6	11.5	12.8	243
2104NP	780Z	15.1Z	41.5Z	53.2Z	19.4Z	36.4Z	2.2Z	129.1Z	11.7Z	12.8Z	208Z
2105	696	13.8	39.3	56.4	19.8	35.2	7.3	119.0	12.5	16.2	429
2106	655	13.5	38.9	59.3	20.5	34.6	7.0	131.9	12.1	16.1	349
2107a)	688Z	13.5Z	38.7Z	56.2Z	19.6Z	34.8Z	4.8Z	109.0Z	11.7Z	15.8Z	240Z
2108	708	13.2	37.9	53.6	18.7	34.8	5.4	153.0	11.0	15.4	238
2112	768	14.3	40.1	52.2	18.6	35.6	5.0	135.1	13.0	17.4	269
Mean	703	13.7	39.2	55.8	19.5	34.9	6.5	134.9	12.0	15.6	306
S.D.	41	0.4	0.9	2.9	0.8	0.5	1.2	12.1	0.8	1.7	82

NP: Non-pregnant
a): Necropsied on lactation day 1 because all pups died
Z: Data was excluded from statistical analysis.

Appendix 6-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual hematology of female rats (Lactation day 5)
Dose (mg/kg): 100

Animal number	WBC	Differential leukocyte ratio (%)						Differential leukocyte counts (10E2/μL)					
	10E2/μL	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
2101	139.6	57.4	39.2	0.5	0.2	2.2	0.5	80.2	54.8	0.7	0.3	3.0	0.7
2104NP	84.0Z	85.9Z	9.8Z	1.3Z	0.4Z	2.2Z	0.4Z	72.2Z	8.3Z	1.1Z	0.3Z	1.8Z	0.4Z
2105	113.2	55.5	41.9	0.5	0.1	1.4	0.6	62.8	47.4	0.6	0.2	1.6	0.6
2106	92.4	54.6	41.9	0.6	0.1	2.5	0.4	50.5	38.7	0.5	0.1	2.3	0.3
2107a)	107.6Z	77.7Z	17.8Z	1.4Z	0.3Z	1.8Z	1.0Z	83.6Z	19.2Z	1.5Z	0.3Z	1.9Z	1.1Z
2108	75.7	42.8	52.4	1.1	0.1	3.4	0.2	32.4	39.7	0.9	0.1	2.6	0.1
2112	134.7	41.3	53.8	0.5	0.2	3.9	0.4	55.7	72.5	0.6	0.2	5.2	0.5
Mean	111.1	50.3	45.8	0.6	0.1	2.7	0.4	56.3	50.6	0.7	0.2	2.9	0.4
S.D.	27.3	7.6	6.7	0.3	0.1	1.0	0.1	17.5	13.9	0.2	0.1	1.4	0.2

LUC: Large unstained cells
NP: Non-pregnant
a): Necropsied on lactation day 1 because all pups died
Z: Data was excluded from statistical analysis.

Appendix 6-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual hematology of female rats (Lactation day 5)
Dose (mg/kg): 300

Animal number	RBC 10E4/µL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/µL	PT s	APTT s	FIB mg/dL
3101	702	13.4	38.0	54.2	19.1	35.3	4.6	140.7	10.4	13.7	230
3102	716	13.2	37.8	52.8	18.4	34.9	7.0	166.2	10.9	13.8	226
3104	775	13.9	39.6	51.1	17.9	35.0	3.7	117.1	12.0	16.0	232
3106	743	14.0	40.6	54.6	18.9	34.5	6.0	129.7	11.6	15.5	261
3108	663	12.6	36.5	54.9	19.1	34.7	6.4	150.4	11.0	14.5	398
Mean	720	13.4	38.5	53.5	18.7	34.9	5.5	140.8	11.2	14.7	269
S.D.	42	0.6	1.6	1.6	0.5	0.3	1.4	18.9	0.6	1.0	73

Appendix 6-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual hematology of female rats (Lactation day 5)
Dose (mg/kg): 300

Animal number	WBC	Differential leukocyte ratio (%)						Differential leukocyte counts (10E2/μL)					
	10E2/μL	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
3101	137.5	58.1	37.7	1.3	0.3	2.3	0.4	79.9	51.9	1.7	0.4	3.1	0.5
3102	139.3	66.0	30.7	0.5	0.1	2.1	0.6	91.9	42.8	0.7	0.2	2.9	0.8
3104	127.2	53.8	41.6	0.9	0.2	2.4	1.2	68.4	52.9	1.2	0.2	3.1	1.5
3106	114.7	59.1	35.9	0.9	0.2	3.4	0.5	67.8	41.2	1.1	0.3	3.8	0.6
3108	163.2	35.2	61.5	0.7	0.1	2.1	0.5	57.5	100.3	1.1	0.2	3.4	0.7
Mean	136.4	54.4	41.5	0.9	0.2	2.5	0.6	73.1	57.8	1.2	0.3	3.3	0.8
S.D.	17.9	11.6	11.9	0.3	0.1	0.5	0.3	13.2	24.3	0.4	0.1	0.4	0.4

LUC: Large unstained cells

Appendix 6-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual hematology of female rats (Lactation day 5)
Dose (mg/kg): 1000

Animal number	RBC 10E4/µL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/µL	PT s	APTT s	FIB mg/dL
4101	759	13.7	38.8	51.1	18.1	35.4	4.4	136.3	11.5	14.2	263
4102	712	13.7	39.1	54.9	19.3	35.2	6.4	113.3	12.3	17.0	239
4103	710	13.7	38.3	54.0	19.3	35.8	5.5	141.4	12.1	17.3	265
4106	689	13.6	38.2	55.5	19.7	35.5	7.3	155.0	11.7	15.2	327
4109	699	13.9	39.6	56.7	19.9	35.1	6.4	113.6	10.2	13.4	241
Mean	714	13.7	38.8	54.4	19.3	35.4	6.0	131.9	11.6	15.4	267
S.D.	27	0.1	0.6	2.1	0.7	0.3	1.1	18.2	0.8	1.7	36

Appendix 6-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual hematology of female rats (Lactation day 5)
Dose (mg/kg): 1000

Animal number	WBC	Differential leukocyte ratio (%)						Differential leukocyte counts (10E2/μL)					
	10E2/μL	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
4101	130.6	56.0	39.9	0.8	0.2	2.7	0.4	73.1	52.2	1.0	0.3	3.5	0.5
4102	100.8	52.1	44.9	0.7	0.1	2.0	0.2	52.5	45.2	0.7	0.1	2.0	0.2
4103	57.5	66.5	29.5	1.7	0.1	1.9	0.3	38.2	17.0	1.0	0.1	1.1	0.2
4106	97.7	38.3	57.4	0.8	0.1	2.9	0.5	37.4	56.1	0.8	0.1	2.9	0.5
4109	99.9	50.8	45.3	0.7	0.1	2.3	0.7	50.8	45.3	0.7	0.1	2.3	0.7
Mean	97.3	52.7	43.4	0.9	0.1	2.4	0.4	50.4	43.2	0.8	0.1	2.4	0.4
S.D.	26.0	10.2	10.1	0.4	0.0	0.4	0.2	14.5	15.3	0.2	0.1	0.9	0.2

LUC: Large unstained cells

Appendix 6-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual hematology of female rats (Satellite group, End of administration)
Dose (mg/kg): 0

Animal number	RBC 10E4/µL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/µL	PT s	APTT s	FIB mg/dL
1113	808	15.5	42.9	53.1	19.2	36.1	1.3	97.9	11.4	12.4	185
1114	803	14.6	40.7	50.7	18.2	36.0	1.4	112.4	11.6	12.8	164
1115	813	14.8	42.0	51.7	18.2	35.3	1.4	91.2	12.1	12.2	208
1116	858	15.4	43.1	50.2	17.9	35.7	1.5	98.4	11.9	14.1	189
1117	778	14.4	40.1	51.5	18.5	35.9	2.1	103.6	12.0	12.3	184
Mean	812	14.9	41.8	51.4	18.4	35.8	1.5	100.7	11.8	12.8	186
S.D.	29	0.5	1.3	1.1	0.5	0.3	0.3	7.9	0.3	0.8	16

Appendix 6-18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual hematology of female rats (Satellite group, End of administration)
Dose (mg/kg): 0

Animal number	WBC	Differential leukocyte ratio (%)						Differential leukocyte counts (10E2/μL)					
	10E2/μL	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
1113	40.5	85.5	10.4	2.2	0.1	1.1	0.7	34.6	4.2	0.9	0.0	0.5	0.3
1114	36.5	82.2	13.7	2.1	0.1	1.4	0.4	30.0	5.0	0.8	0.0	0.5	0.1
1115	50.2	85.3	11.4	1.6	0.2	0.9	0.6	42.8	5.7	0.8	0.1	0.5	0.3
1116	43.0	70.9	25.0	1.4	0.1	1.5	1.0	30.5	10.8	0.6	0.0	0.7	0.4
1117	48.4	62.8	34.2	1.2	0.1	1.4	0.3	30.4	16.5	0.6	0.1	0.7	0.1
Mean	43.7	77.3	18.9	1.7	0.1	1.3	0.6	33.7	8.4	0.7	0.0	0.6	0.2
S.D.	5.6	10.1	10.3	0.4	0.0	0.3	0.3	5.4	5.2	0.1	0.1	0.1	0.1

LUC: Large unstained cells

Appendix 6-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual hematology of female rats (Satellite group, End of administration)
Dose (mg/kg): 1000

Animal number	RBC 10E4/µL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/µL	PT s	APTT s	FIB mg/dL
4113	804	15.0	42.0	52.2	18.7	35.8	1.9	100.6	11.1	17.0	176
4114	787	14.1	39.4	50.1	17.9	35.6	1.8	115.3	12.2	14.4	170
4115	828	15.2	42.1	50.9	18.3	36.0	1.4	111.6	12.0	14.2	213
4116	802	14.7	41.5	51.8	18.4	35.5	1.7	114.8	10.7	12.0	174
4117	875	16.0	45.7	52.2	18.3	35.0	1.3	113.9	12.3	15.8	156
Mean	819	15.0	42.1	51.4	18.3	35.6	1.6	111.2	11.7	14.7	178
S.D.	34	0.7	2.3	0.9	0.3	0.4	0.3	6.1	0.7	1.9	21

Appendix 6-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual hematology of female rats (Satellite group, End of administration)
Dose (mg/kg): 1000

Animal number	WBC	Differential leukocyte ratio (%)						Differential leukocyte counts (10E2/μL)					
	10E2/μL	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
4113	52.3	68.3	27.8	1.4	0.1	1.8	0.5	35.7	14.5	0.8	0.1	1.0	0.3
4114	49.1	79.5	15.4	2.2	0.2	2.2	0.6	39.0	7.6	1.1	0.1	1.1	0.3
4115	45.7	78.5	17.6	2.1	0.1	1.5	0.3	35.9	8.0	1.0	0.1	0.7	0.1
4116	31.9	72.5	23.8	1.1	0.1	2.3	0.4	23.1	7.6	0.3	0.0	0.7	0.1
4117	61.4	87.2	9.7	1.3	0.3	0.8	0.8	53.5	6.0	0.8	0.2	0.5	0.5
Mean	48.1	77.2	18.9	1.6	0.2	1.7	0.5	37.4	8.7	0.8	0.1	0.8	0.3
S.D.	10.8	7.2	7.1	0.5	0.1	0.6	0.2	10.9	3.3	0.3	0.1	0.2	0.2

LUC: Large unstained cells

Appendix 6-21 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual hematology of male rats (End of recovery)
Dose (mg/kg): 0

Animal number	RBC 10E4/µL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/µL	PT s	APTT s	FIB mg/dL
1008	987	16.1	46.6	47.2	16.3	34.5	1.3	97.9	18.7	23.4	273
1009	880	15.5	43.6	49.6	17.6	35.5	2.1	100.7	24.0	19.9	295
1010	961	16.3	46.6	48.4	17.0	35.1	1.6	107.5	16.1	20.6	309
1011	802	14.1	41.2	51.4	17.6	34.2	3.4	112.5	18.5	24.1	241
1012	1005	15.9	46.0	45.8	15.8	34.6	1.8	93.7	18.3	24.0	289
Mean	927	15.6	44.8	48.5	16.9	34.8	2.0	102.5	19.1	22.4	281
S.D.	85	0.9	2.4	2.2	0.8	0.5	0.8	7.5	2.9	2.0	26

Appendix 6-22 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual hematology of male rats (End of recovery)
Dose (mg/kg): 0

Animal number	WBC	Differential leukocyte ratio (%)						Differential leukocyte counts (10E2/μL)					
	10E2/μL	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
1008	83.1	83.2	13.7	0.8	0.3	1.5	0.5	69.2	11.4	0.7	0.2	1.2	0.4
1009	79.8	62.4	32.4	1.4	0.1	2.8	0.9	49.8	25.8	1.1	0.1	2.3	0.8
1010	53.9	71.1	24.6	1.7	0.2	1.8	0.6	38.3	13.3	0.9	0.1	1.0	0.3
1011	55.1	71.9	23.9	2.0	0.1	1.7	0.5	39.6	13.1	1.1	0.1	0.9	0.3
1012	70.9	75.1	20.1	1.0	0.3	2.9	0.7	53.2	14.2	0.7	0.2	2.1	0.5
Mean	68.6	72.7	22.9	1.4	0.2	2.1	0.6	50.0	15.6	0.9	0.1	1.5	0.5
S.D.	13.6	7.5	6.8	0.5	0.1	0.7	0.2	12.5	5.8	0.2	0.1	0.7	0.2

LUC: Large unstained cells

Appendix 6-23 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual hematology of male rats (End of recovery)
Dose (mg/kg): 1000

Animal number	RBC 10E4/µL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/µL	PT s	APTT s	FIB mg/dL
4008	911	16.1	46.0	50.5	17.7	35.1	1.9	100.9	13.7	18.7	246
4009	933	16.0	46.9	50.3	17.2	34.2	1.7	81.2	20.3	27.6	226
4010	909	16.3	47.4	52.2	17.9	34.3	1.9	110.7	15.4	21.6	259
4011	866	15.3	43.5	50.2	17.6	35.1	1.9	97.7	15.6	19.7	267
4012	952	16.0	45.8	48.1	16.8	34.9	1.6	108.5	16.7	18.5	310
Mean	914	15.9	45.9	50.3	17.4	34.7	1.8	99.8	16.3	21.2	262
S.D.	32	0.4	1.5	1.5	0.4	0.4	0.1	11.7	2.5	3.8	31

Appendix 6-24 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual hematology of male rats (End of recovery)
Dose (mg/kg): 1000

Animal number	WBC	Differential leukocyte ratio (%)						Differential leukocyte counts (10E2/μL)					
	10E2/μL	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
4008	60.2	80.5	14.6	2.5	0.3	1.5	0.5	48.5	8.8	1.5	0.2	0.9	0.3
4009	45.5	70.6	24.9	1.4	0.3	2.5	0.3	32.1	11.3	0.6	0.2	1.1	0.1
4010	68.4	81.4	13.5	1.6	0.2	2.6	0.7	55.7	9.2	1.1	0.1	1.8	0.5
4011	72.7	62.4	33.3	1.1	0.3	2.4	0.5	45.4	24.2	0.8	0.2	1.8	0.4
4012	50.9	71.2	22.8	1.4	0.2	3.0	1.5	36.2	11.6	0.7	0.1	1.5	0.8
Mean	59.5	73.2	21.8	1.6	0.3	2.4	0.7	43.6	13.0	0.9	0.2	1.4	0.4
S.D.	11.4	7.9	8.1	0.5	0.1	0.6	0.5	9.5	6.4	0.4	0.1	0.4	0.3

LUC: Large unstained cells

Appendix 6-25 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual hematology of female rats (End of recovery)
Dose (mg/kg): 0

Animal number	RBC 10E4/µL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/µL	PT s	APTT s	FIB mg/dL
1118	869	15.6	43.9	50.5	17.9	35.5	1.1	112.2	13.3	14.0	161
1119	808	15.0	41.4	51.2	18.6	36.4	2.5	107.9	11.4	14.9	190
1120	872	16.0	44.6	51.1	18.4	36.0	1.3	101.9	12.2	17.1	173
1121	833	15.3	42.7	51.2	18.3	35.8	2.0	92.5	12.0	15.2	193
1122	837	15.5	43.5	52.0	18.5	35.6	2.8	117.8	12.0	15.3	152
Mean	844	15.5	43.2	51.2	18.3	35.9	1.9	106.5	12.2	15.3	174
S.D.	27	0.4	1.2	0.5	0.3	0.4	0.7	9.7	0.7	1.1	18

Appendix 6-26 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual hematology of female rats (End of recovery)
Dose (mg/kg): 0

Animal number	WBC	Differential leukocyte ratio (%)						Differential leukocyte counts (10E2/μL)					
	10E2/μL	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
1118	32.4	82.0	13.3	2.2	0.1	1.7	0.7	26.5	4.3	0.7	0.0	0.5	0.2
1119	39.7	80.5	16.6	0.7	0.1	1.2	0.8	32.0	6.6	0.3	0.1	0.5	0.3
1120	46.4	79.9	15.5	2.0	0.3	1.6	0.8	37.0	7.2	0.9	0.1	0.7	0.4
1121	61.5	74.6	20.0	1.1	0.2	2.4	1.7	45.9	12.3	0.7	0.1	1.5	1.1
1122	34.0	73.5	21.2	1.5	0.2	3.1	0.5	25.0	7.2	0.5	0.1	1.1	0.2
Mean	42.8	78.1	17.3	1.5	0.2	2.0	0.9	33.3	7.5	0.6	0.1	0.9	0.4
S.D.	11.8	3.8	3.2	0.6	0.1	0.8	0.5	8.5	2.9	0.2	0.0	0.4	0.4

LUC: Large unstained cells

Appendix 6-27 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual hematology of female rats (End of recovery)
Dose (mg/kg): 1000

Animal number	RBC 10E4/µL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/µL	PT s	APTT s	FIB mg/dL
4118	845	16.0	45.8	54.2	19.0	35.0	2.1	112.9	12.4	17.2	211
4119	830	15.2	42.4	51.1	18.4	35.9	1.1	101.7	12.3	16.2	160
4120	908	16.1	45.5	50.1	17.8	35.4	1.3	106.3	11.8	17.8	159
4121	865	16.1	45.2	52.3	18.6	35.6	1.3	102.6	12.3	15.3	155
4122	879	16.0	44.5	50.6	18.2	36.0	1.7	111.7	13.0	18.1	175
Mean	865	15.9	44.7	51.7	18.4	35.6	1.5	107.0	12.4	16.9	172
S.D.	30	0.4	1.4	1.6	0.4	0.4	0.4	5.1	0.4	1.2	23

Appendix 6-28 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual hematology of female rats (End of recovery)
Dose (mg/kg): 1000

Animal number	WBC	Differential leukocyte ratio (%)						Differential leukocyte counts (10E2/μL)					
	10E2/μL	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
4118	63.1	74.3	20.7	1.3	0.2	1.7	1.8	46.9	13.1	0.8	0.1	1.1	1.2
4119	28.8	84.4	12.3	0.9	0.2	1.9	0.4	24.3	3.5	0.3	0.0	0.5	0.1
4120	38.8	74.6	18.9	2.6	0.2	2.2	1.5	29.0	7.4	1.0	0.1	0.9	0.6
4121	27.8	76.5	18.1	1.8	0.4	2.1	1.2	21.3	5.0	0.5	0.1	0.6	0.3
4122	56.4	76.1	20.5	1.8	0.2	0.6	0.8	43.0	11.6	1.0	0.1	0.3	0.5
Mean	43.0	77.2	18.1	1.7	0.2	1.7	1.1	32.9	8.1	0.7	0.1	0.7	0.5
S.D.	16.1	4.1	3.4	0.6	0.1	0.6	0.6	11.4	4.1	0.3	0.0	0.3	0.4

LUC: Large unstained cells

Appendix 7-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual blood chemistry of male rats (End of administration)
Dose (mg/kg): 0

Animal number	AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
1001	62	25	57	1	514	5.2	57	58	94	0.1	140
1002	80	29	41	1	392	4.7	49	51	90	0.0	153
1003	62	28	41	1	375	16.3	68	70	111	0.1	146
1004	178	89	171	1	341	53.0	62	22	101	0.1	113
1005	52	24	54	1	341	12.2	47	40	82	0.1	116
Mean	87	39	73	1	393	18.3	57	48	96	0.1	134
S.D.	52	28	55	0	71	20.0	9	18	11	0.0	18

Appendix 7-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual blood chemistry of male rats (End of administration)
Dose (mg/kg): 0

Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
1001	12	0.23	142	4.3	104	9.8	5.7	5.8	3.1	1.15
1002	13	0.23	142	4.7	107	9.6	6.0	5.4	3.1	1.35
1003	13	0.23	143	4.2	108	10.3	5.2	6.2	3.3	1.14
1004	16	0.24	144	4.5	106	10.5	6.7	6.0	3.3	1.22
1005	15	0.23	144	4.7	105	10.2	7.1	6.0	3.3	1.22
Mean	14	0.23	143	4.5	106	10.1	6.1	5.9	3.2	1.22
S.D.	2	0.00	1	0.2	2	0.4	0.8	0.3	0.1	0.08

Appendix 7-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual blood chemistry of male rats (End of administration)
Dose (mg/kg): 100

Animal number	AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
2001	63	23	60	1	426	7.5	37	15	66	0.1	149
2002	53	23	29	1	480	6.0	51	19	81	0.0	175
2003	73	28	68	1	381	11.2	56	30	88	0.1	131
2004	60	26	48	1	580	8.0	42	59	84	0.1	112
2005	61	25	44	1	271	29.0	61	26	96	0.1	117
Mean	62	25	50	1	428	12.3	49	30	83	0.1	137
S.D.	7	2	15	0	115	9.5	10	17	11	0.0	26

Appendix 7-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual blood chemistry of male rats (End of administration)
Dose (mg/kg): 100

Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
2001	12	0.27	142	4.3	106	9.8	5.4	5.4	3.1	1.35
2002	16	0.25	142	4.6	106	9.5	5.8	5.5	2.9	1.12
2003	10	0.24	144	4.3	105	10.1	6.0	5.9	3.3	1.27
2004	11	0.24	144	4.5	106	10.1	6.7	6.0	3.4	1.31
2005	13	0.25	144	4.2	105	10.2	6.7	5.7	3.3	1.38
Mean	12	0.25	143	4.4	106	9.9	6.1	5.7	3.2	1.29
S.D.	2	0.01	1	0.2	1	0.3	0.6	0.3	0.2	0.10

Appendix 7-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual blood chemistry of male rats (End of administration)
Dose (mg/kg): 300

Animal number	AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
3001	56	28	60	0	294	5.5	53	32	94	0.1	154
3002	58	30	46	1	372	8.7	61	22	95	0.0	137
3003	65	29	38	2	437	3.7	49	22	82	0.0	144
3004	56	30	50	1	601	12.3	59	36	90	0.1	155
3005	69	26	47	1	413	15.5	43	21	77	0.1	133
Mean	61	29	48	1	423	9.1	53	27	88	0.1	145
S.D.	6	2	8	1	113	4.8	7	7	8	0.1	10

Appendix 7-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual blood chemistry of male rats (End of administration)
Dose (mg/kg): 300

Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
3001	11	0.23	142	4.7	103	9.4	5.5	5.9	3.2	1.19
3002	14	0.26	142	4.6	105	9.6	5.9	5.7	3.1	1.19
3003	13	0.27	143	4.3	107	9.7	5.4	5.7	3.1	1.19
3004	15	0.24	144	4.7	107	9.9	6.4	6.0	3.3	1.22
3005	15	0.24	144	4.4	107	10.0	7.2	5.3	3.1	1.41
Mean	14	0.25	143	4.5	106	9.7	6.1	5.7	3.2	1.24
S.D.	2	0.02	1	0.2	2	0.2	0.7	0.3	0.1	0.10

Appendix 7-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual blood chemistry of male rats (End of administration)
Dose (mg/kg): 1000

Animal number	AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
4001	66	27	59	1	398	16.2	48	55	86	0.1	151
4002	58	27	37	1	325	12.4	73	27	108	0.0	151
4003	54	27	34	1	430	19.1	49	14	82	0.1	180
4004	57	24	35	1	430	7.9	48	37	84	0.0	146
4005	64	29	51	1	307	14.6	57	37	94	0.1	119
Mean	60	27	43	1	378	14.0	55	34	91	0.1	149
S.D.	5	2	11	0	58	4.2	11	15	11	0.1	22

Appendix 7-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual blood chemistry of male rats (End of administration)
Dose (mg/kg): 1000

Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
4001	11	0.26	142	5.0	105	9.4	6.2	5.5	3.1	1.29
4002	14	0.29	141	4.6	105	9.4	5.7	5.6	3.0	1.15
4003	11	0.23	142	4.9	106	9.6	6.4	5.5	3.1	1.29
4004	12	0.25	144	4.7	107	9.8	6.2	5.6	3.1	1.24
4005	15	0.23	144	4.5	106	10.1	7.0	6.0	3.3	1.22
Mean	13	0.25	143	4.7	106	9.7	6.3	5.6	3.1	1.24
S.D.	2	0.02	1	0.2	1	0.3	0.5	0.2	0.1	0.06

Appendix 7-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual blood chemistry of female rats (Lactation day 5)
Dose (mg/kg): 0

Animal number	AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
1101	100	66	49	2	213	8.4	50	36	110	0.1	131
1102	73	45	32	1	216	21.9	47	28	98	0.1	134
1103	70	58	32	1	248	7.3	70	44	123	0.0	130
1105	88	53	44	1	255	24.2	64	30	111	0.1	116
1108	85	69	42	1	258	17.0	63	82	120	0.1	113
Mean	83	58	40	1	238	15.8	59	44	112	0.1	125
S.D.	12	10	8	0	22	7.7	10	22	10	0.0	10

Appendix 7-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual blood chemistry of female rats (Lactation day 5)
Dose (mg/kg): 0

Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
1101	12	0.32	140	3.3	103	9.7	5.7	5.6	3.4	1.55
1102	15	0.23	141	3.5	102	10.4	6.7	5.9	3.5	1.46
1103	15	0.28	142	4.1	107	10.2	6.9	6.1	3.4	1.26
1105	14	0.25	142	3.9	105	10.2	7.8	5.5	3.3	1.50
1108	14	0.20	139	3.6	102	10.4	7.8	5.9	3.5	1.46
Mean	14	0.26	141	3.7	104	10.2	7.0	5.8	3.4	1.45
S.D.	1	0.05	1	0.3	2	0.3	0.9	0.2	0.1	0.11

Appendix 7-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual blood chemistry of female rats (Lactation day 5)
Dose (mg/kg): 100

Animal number	AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
2101	85	53	38	1	322	16.0	55	51	119	0.1	135
2104NP	35Z	27Z	48Z	1Z	274Z	14.7Z	79Z	248Z	200Z	0.1Z	182Z
2105	90	61	22	2	302	12.1	87	43	151	0.1	142
2106	68	45	37	1	211	38.2	52	47	116	0.1	133
2107a)	54Z	19Z	42Z	1Z	294Z	6.2Z	86Z	42Z	144Z	0.0Z	162Z
2108	58	38	31	1	163	6.8	56	67	133	0.1	119
2112	66	44	34	1	276	9.7	61	40	126	0.1	138
Mean	73	48	32	1	255	16.6	62	50	129	0.1	133
S.D.	14	9	6	0	66	12.6	14	11	14	0.0	9

NP: Non-pregnant
a): Necropsied on lactation day 1 because all pups died
Z: Data was excluded from statistical analysis.

Appendix 7-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual blood chemistry of female rats (Lactation day 5)
Dose (mg/kg): 100

Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
2101	17	0.33	139	3.3	105	10.0	6.7	6.1	3.5	1.35
2104NP	20Z	0.27Z	138Z	4.6Z	103Z	11.3Z	6.0Z	7.1Z	4.3Z	1.54Z
2105	16	0.28	140	4.3	106	10.3	6.7	6.2	3.5	1.30
2106	16	0.33	139	3.9	105	10.1	6.3	6.0	3.4	1.31
2107a)	28Z	0.29Z	140Z	4.4Z	102Z	11.0Z	6.8Z	6.4Z	3.7Z	1.37Z
2108	14	0.20	137	4.0	101	10.5	8.2	6.0	3.7	1.61
2112	12	0.26	139	4.0	103	10.0	6.3	6.3	3.5	1.25
Mean	15	0.28	139	3.9	104	10.2	6.8	6.1	3.5	1.36
S.D.	2	0.05	1	0.4	2	0.2	0.8	0.1	0.1	0.14

NP: Non-pregnant
a): Necropsied on lactation day 1 because all pups died
Z: Data was excluded from statistical analysis.

Appendix 7-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual blood chemistry of female rats (Lactation day 5)
Dose (mg/kg): 300

Animal number	AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
3101	65	47	44	2	252	5.2	38	21	77	0.0	126
3102	92	54	66	0	205	11.6	55	34	113	0.1	114
3104	110	44	59	1	143	9.2	42	27	97	0.1	121
3106	101	48	44	0	161	17.1	57	33	116	0.1	122
3108	76	51	45	2	232	9.6	66	83	148	0.1	121
Mean	89	49	52	1	199	10.5	52	40	110	0.1	121
S.D.	18	4	10	1	46	4.3	11	25	26	0.0	4

Appendix 7-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual blood chemistry of female rats (Lactation day 5)
Dose (mg/kg): 300

Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
3101	13	0.26	141	4.0	104	9.3	7.6	6.1	3.3	1.18
3102	12	0.27	139	3.8	103	10.4	7.8	5.8	3.4	1.42
3104	16	0.24	140	4.2	104	10.1	7.8	6.1	3.7	1.54
3106	15	0.27	139	3.9	102	10.4	7.4	5.9	3.3	1.27
3108	12	0.22	138	4.0	102	10.6	7.3	6.3	3.6	1.33
Mean	14	0.25	139	4.0	103	10.2	7.6	6.0	3.5	1.35
S.D.	2	0.02	1	0.1	1	0.5	0.2	0.2	0.2	0.14

Appendix 7-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual blood chemistry of female rats (Lactation day 5)
Dose (mg/kg): 1000

Animal number	AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
4101	87	58	45	1	226	12.4	38	50	88	0.1	115
4102	81	46	44	1	219	7.8	46	17	91	0.0	129
4103	66	23	42	1	226	4.7	41	11	83	0.1	129
4106	111	51	69	1	188	14.9	80	63	160	0.0	120
4109	83	43	39	1	205	9.7	46	75	101	0.1	117
Mean	86	44	48	1	213	9.9	50	43	105	0.1	122
S.D.	16	13	12	0	16	4.0	17	28	32	0.1	7

Appendix 7-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual blood chemistry of female rats (Lactation day 5)
Dose (mg/kg): 1000

Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
4101	16	0.25	137	3.9	105	10.2	6.8	5.8	3.4	1.42
4102	15	0.28	140	4.1	106	9.8	6.8	5.8	3.2	1.23
4103	13	0.31	139	4.7	105	10.3	6.2	6.0	3.3	1.22
4106	13	0.28	140	3.5	103	10.1	5.6	6.3	3.7	1.42
4109	14	0.26	140	3.4	103	10.4	7.3	5.6	3.3	1.43
Mean	14	0.28	139	3.9	104	10.2	6.5	5.9	3.4	1.34
S.D.	1	0.02	1	0.5	1	0.2	0.7	0.3	0.2	0.11

Appendix 7-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual blood chemistry of female rats (Satellite group, End of administration)
Dose (mg/kg): 0

Animal number	AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
1113	64	23	56	1	301	11.1	46	7	87	0.1	133
1114	65	29	51	1	198	9.7	60	6	110	0.1	107
1115	64	26	73	1	225	11.7	45	8	91	0.1	120
1116	59	25	41	1	379	11.0	47	11	102	0.1	128
1117	46	17	31	1	208	18.3	58	11	120	0.1	135
Mean	60	24	50	1	262	12.4	51	9	102	0.1	125
S.D.	8	4	16	0	77	3.4	7	2	14	0.0	11

Appendix 7-18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual blood chemistry of female rats (Satellite group, End of administration)
Dose (mg/kg): 0

Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
1113	19	0.39	139	4.4	104	9.8	5.3	6.0	3.5	1.40
1114	18	0.28	141	4.3	106	10.2	4.8	6.3	3.6	1.33
1115	18	0.33	142	4.4	108	10.0	5.1	6.2	3.7	1.48
1116	21	0.27	141	4.5	109	10.2	4.9	6.2	3.7	1.48
1117	20	0.32	142	4.4	108	10.1	4.6	6.0	3.6	1.50
Mean	19	0.32	141	4.4	107	10.1	4.9	6.1	3.6	1.44
S.D.	1	0.05	1	0.1	2	0.2	0.3	0.1	0.1	0.07

Appendix 7-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual blood chemistry of female rats (Satellite group, End of administration)
Dose (mg/kg): 1000

Animal number	AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
4113	61	22	54	2	212	9.3	61	20	130	0.1	131
4114	47	19	46	1	175	7.0	53	16	111	0.1	135
4115	57	22	41	1	264	18.9	51	17	101	0.1	125
4116	64	29	46	1	215	24.5	66	10	125	0.1	126
4117	58	23	39	2	177	6.9	48	8	101	0.0	113
Mean	57	23	45	1	209	13.3	56	14	114	0.1	126
S.D.	6	4	6	1	36	8.0	7	5	13	0.0	8

Appendix 7-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual blood chemistry of female rats (Satellite group, End of administration)
Dose (mg/kg): 1000

Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
4113	12	0.31	141	4.3	107	9.9	3.3	6.6	3.8	1.36
4114	16	0.30	139	4.5	105	10.0	4.3	6.0	3.7	1.61
4115	17	0.33	142	4.6	107	9.8	4.7	6.0	3.4	1.31
4116	17	0.30	140	4.4	107	10.2	5.0	6.2	3.8	1.58
4117	17	0.29	142	4.8	109	10.4	5.4	6.0	3.6	1.50
Mean	16	0.31	141	4.5	107	10.1	4.5	6.2	3.7	1.47
S.D.	2	0.02	1	0.2	1	0.2	0.8	0.3	0.2	0.13

Appendix 7-21 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual blood chemistry of male rats (End of recovery)
Dose (mg/kg): 0

Animal number	AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
1008	59	27	48	0	227	6.5	35	27	69	0.1	147
1009	58	27	46	0	316	8.6	45	64	87	0.1	159
1010	63	28	44	1	233	11.8	61	54	103	0.1	131
1011	60	33	31	1	232	4.3	57	36	90	0.1	150
1012	66	28	46	1	311	14.5	36	30	65	0.0	130
Mean	61	29	43	1	264	9.1	47	42	83	0.1	143
S.D.	3	3	7	1	45	4.1	12	16	16	0.0	13

Appendix 7-22 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual blood chemistry of male rats (End of recovery)
Dose (mg/kg): 0

Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
1008	16	0.21	141	4.4	106	8.9	5.4	5.5	3.1	1.29
1009	13	0.19	142	4.5	106	9.5	4.9	5.8	3.1	1.15
1010	17	0.24	142	4.5	104	9.6	6.1	5.9	3.2	1.19
1011	15	0.20	142	4.5	106	9.8	5.5	5.6	3.0	1.15
1012	13	0.18	142	4.1	107	9.6	5.5	5.9	3.1	1.11
Mean	15	0.20	142	4.4	106	9.5	5.5	5.7	3.1	1.18
S.D.	2	0.02	0	0.2	1	0.3	0.4	0.2	0.1	0.07

Appendix 7-23 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual blood chemistry of male rats (End of recovery)
Dose (mg/kg): 1000

Animal number	AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
4008	54	27	50	1	438	7.2	62	23	96	0.1	159
4009	199	156	127	0	438	7.9	33	22	61	0.1	154
4010	58	23	51	1	251	5.9	62	47	100	0.1	159
4011	74	31	42	1	270	18.2	60	19	94	0.1	147
4012	64	34	40	1	360	9.1	48	51	88	0.1	142
Mean	90	54	62	1	351	9.7	53	32	88	0.1	152
S.D.	62	57	37	0	89	4.9	13	15	16	0.0	8

Appendix 7-24 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual blood chemistry of male rats (End of recovery)
Dose (mg/kg): 1000

Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
4008	16	0.17	141	4.4	106	9.5	5.6	6.0	3.2	1.14
4009	15	0.23	143	4.5	106	9.1	4.7	5.7	3.2	1.28
4010	14	0.25	142	4.4	105	9.8	5.7	5.8	3.1	1.15
4011	18	0.25	142	4.5	105	9.4	5.5	5.7	3.0	1.11
4012	13	0.17	143	4.6	107	9.7	5.5	5.6	3.2	1.33
Mean	15	0.21	142	4.5	106	9.5	5.4	5.8	3.1	1.20
S.D.	2	0.04	1	0.1	1	0.3	0.4	0.2	0.1	0.10

Appendix 7-25 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual blood chemistry of female rats (End of recovery)
Dose (mg/kg): 0

Animal number	AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
1118	70	38	45	1	132	11.0	52	10	103	0.1	118
1119	62	18	32	1	240	13.4	38	4	78	0.1	159
1120	67	34	40	1	171	10.6	51	13	97	0.1	103
1121	58	24	32	1	151	10.1	72	13	138	0.1	139
1122	54	24	32	1	122	27.7	110	20	208	0.1	121
Mean	62	28	36	1	163	14.6	65	12	125	0.1	128
S.D.	6	8	6	0	47	7.5	28	6	51	0.0	22

Appendix 7-26 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual blood chemistry of female rats (End of recovery)
Dose (mg/kg): 0

Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
1118	17	0.25	142	4.4	108	9.9	5.8	6.0	3.7	1.61
1119	19	0.28	142	3.8	105	9.6	5.8	6.1	3.5	1.35
1120	22	0.29	141	4.6	107	9.9	6.9	6.1	3.4	1.26
1121	17	0.23	141	3.9	108	9.9	5.5	6.4	3.8	1.46
1122	21	0.25	141	4.2	107	10.7	5.3	7.3	4.4	1.52
Mean	19	0.26	141	4.2	107	10.0	5.9	6.4	3.8	1.44
S.D.	2	0.02	1	0.3	1	0.4	0.6	0.5	0.4	0.14

Appendix 7-27 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual blood chemistry of female rats (End of recovery)
Dose (mg/kg): 1000

Animal number	AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
4118	82	48	43	2	131	5.4	74	15	136	0.1	118
4119	59	22	42	1	103	9.3	59	9	115	0.1	104
4120	84	58	44	1	109	10.7	70	13	135	0.1	132
4121	68	38	62	1	162	6.2	58	8	117	0.1	114
4122	63	29	51	1	132	11.2	48	8	91	0.1	109
Mean	71	39	48	1	127	8.6	62	11	119	0.1	115
S.D.	11	14	8	0	23	2.6	10	3	18	0.0	11

Appendix 7-28 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual blood chemistry of female rats (End of recovery)
Dose (mg/kg): 1000

Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
4118	16	0.27	141	4.4	106	10.3	6.4	6.6	3.7	1.28
4119	18	0.27	142	4.1	109	10.0	4.4	6.5	3.9	1.50
4120	19	0.26	141	4.7	108	10.3	5.7	6.8	4.2	1.62
4121	18	0.26	143	4.6	108	10.1	6.1	6.7	4.0	1.48
4122	16	0.27	142	4.6	108	10.0	6.1	6.2	3.7	1.48
Mean	17	0.27	142	4.5	108	10.1	5.7	6.6	3.9	1.47
S.D.	1	0.01	1	0.2	1	0.2	0.8	0.2	0.2	0.12

Appendix 8-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 0

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)
Absolute	1001	521	2.05	11.8	11.7	12.6	24.3	307
	1002	504	2.11	10.4	10.8	11.2	22.0	327
	1003	557	2.37	13.5	12.4	10.0	22.4	373
	1004	501	2.12	12.5	9.2	6.0	15.2	308
	1005	494	2.04	13.2	14.3	11.7	26.0	209
	1006	532	2.21	15.1	11.7	9.4	21.1	253
	1007	480	2.10	12.8	13.2	10.9	24.1	201
	Mean	513	2.14	12.8	11.9	10.3	22.2	283
	S.D.	26	0.11	1.5	1.6	2.2	3.5	64
Relative	1001		0.39	2.3	2.2	2.4	4.7	59
	1002		0.42	2.1	2.1	2.2	4.4	65
	1003		0.43	2.4	2.2	1.8	4.0	67
	1004		0.42	2.5	1.8	1.2	3.0	61
	1005		0.41	2.7	2.9	2.4	5.3	42
	1006		0.42	2.8	2.2	1.8	4.0	48
	1007		0.44	2.7	2.8	2.3	5.0	42
	Mean		0.42	2.5	2.3	2.0	4.3	55
	S.D.		0.02	0.3	0.4	0.4	0.8	11

Appendix 8-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 0

	Animal number	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	1001	1.26	15.28	0.66	1.38	1.43	2.81
	1002	1.27	13.91	0.80	1.56	1.54	3.10
	1003	1.47	15.86	0.78	1.64	1.68	3.32
	1004	1.51	14.19	0.82	1.58	1.66	3.24
	1005	1.39	14.23	0.58	1.56	1.59	3.15
	1006	1.41	15.10	0.76	1.77	1.75	3.52
	1007	1.42	13.44	0.67	1.67	1.69	3.36
	Mean	1.39	14.57	0.72	1.59	1.62	3.21
	S.D.	0.09	0.86	0.09	0.12	0.11	0.23
Relative	1001	0.24	2.93	0.13	0.26	0.27	0.54
	1002	0.25	2.76	0.16	0.31	0.31	0.62
	1003	0.26	2.85	0.14	0.29	0.30	0.60
	1004	0.30	2.83	0.16	0.32	0.33	0.65
	1005	0.28	2.88	0.12	0.32	0.32	0.64
	1006	0.27	2.84	0.14	0.33	0.33	0.66
	1007	0.30	2.80	0.14	0.35	0.35	0.70
	Mean	0.27	2.84	0.14	0.31	0.32	0.63
	S.D.	0.02	0.05	0.01	0.03	0.03	0.05

Appendix 8-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 0

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)
Absolute	1001	26	31	57	1.52	1.55	3.07
	1002	27	29	56	1.51	1.52	3.03
	1003	33	33	66	1.59	1.62	3.21
	1004	23	24	47	1.58	1.65	3.23
	1005	29	35	64	1.61	1.66	3.27
	1006	33	34	67	1.70	1.69	3.39
	1007	34	38	72	1.67	1.69	3.36
	Mean	29	32	61	1.60	1.63	3.22
	S.D.	4	5	8	0.07	0.07	0.14
Relative	1001	5	6	11	0.29	0.30	0.59
	1002	5	6	11	0.30	0.30	0.60
	1003	6	6	12	0.29	0.29	0.58
	1004	5	5	9	0.32	0.33	0.64
	1005	6	7	13	0.33	0.34	0.66
	1006	6	6	13	0.32	0.32	0.64
	1007	7	8	15	0.35	0.35	0.70
	Mean	6	6	12	0.31	0.32	0.63
	S.D.	1	1	2	0.02	0.02	0.04

Appendix 8-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 0

	Animal number	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)	Seminal vesicle g(g/100g BW)	Prostate g(g/100g BW)
Absolute	1001	677	664	1341	1.78	1.07
	1002	616	612	1228	1.47	1.10
	1003	707	682	1389	1.79	1.37
	1004	663	645	1308	1.75	1.01
	1005	643	652	1295	1.92	1.34
	1006	588	600	1188	1.53	1.19
	1007	658	652	1310	1.66	1.06
	Mean	650	644	1294	1.70	1.16
	S.D.	39	29	67	0.16	0.14
Relative	1001	130	127	257	0.34	0.21
	1002	122	121	244	0.29	0.22
	1003	127	122	249	0.32	0.25
	1004	132	129	261	0.35	0.20
	1005	130	132	262	0.39	0.27
	1006	111	113	223	0.29	0.22
	1007	137	136	273	0.35	0.22
	Mean	127	126	253	0.33	0.23
	S.D.	8	8	16	0.04	0.02

Appendix 8-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 100

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)
Absolute	2001	503	2.14	14.2	9.9	8.0	17.9	223
	2002	516	2.20	12.4	12.3	12.9	25.2	258
	2003	515	2.16	13.0	11.5	10.2	21.7	276
	2004	461	2.17	13.1	10.7	14.1	24.8	223
	2005	579	2.22	15.5	8.7	8.7	17.4	280
	2006	532	2.13	12.7	9.6	9.9	19.5	163
	2007	563	2.12	14.2	11.5	11.6	23.1	383
	2008	521	2.15	11.9	9.9	7.9	17.8	234
	2009	486	2.12	15.0	5.9	10.9	16.8	200
	2010	506	2.17	15.3	11.8	11.4	23.2	243
	2011	489	2.10	13.9	14.7	15.9	30.6	258
	2012	493	2.16	14.9	8.9	6.0	14.9	180
	Mean	514	2.15	13.8	10.5	10.6	21.1	243
	S.D.	33	0.03	1.2	2.2	2.8	4.5	57
Relative	2001		0.43	2.8	2.0	1.6	3.6	44
	2002		0.43	2.4	2.4	2.5	4.9	50
	2003		0.42	2.5	2.2	2.0	4.2	54
	2004		0.47	2.8	2.3	3.1	5.4	48
	2005		0.38	2.7	1.5	1.5	3.0	48
	2006		0.40	2.4	1.8	1.9	3.7	31
	2007		0.38	2.5	2.0	2.1	4.1	68
	2008		0.41	2.3	1.9	1.5	3.4	45
	2009		0.44	3.1	1.2	2.2	3.5	41
	2010		0.43	3.0	2.3	2.3	4.6	48
	2011		0.43	2.8	3.0	3.3	6.3	53
	2012		0.44	3.0	1.8	1.2	3.0	37
	Mean		0.42	2.7	2.0	2.1	4.1	47
	S.D.		0.03	0.3	0.5	0.6	1.0	9

Appendix 8-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 100

	Animal number	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	2001	1.53	13.28	0.89	1.45	1.46	2.91
	2002	1.33	14.09	0.58	1.44	1.58	3.02
	2003	1.42	13.09	0.76	1.55	1.57	3.12
	2004	1.32	11.86	0.80	1.63	1.49	3.12
	2005	1.42	16.18	0.81	1.72	1.86	3.58
	2006	1.43	14.92	0.73	1.79	1.76	3.55
	2007	1.56	16.74	0.86	1.85	1.86	3.71
	2008	1.33	13.86	0.64	1.75	1.85	3.60
	2009	1.37	13.43	0.70	1.38	1.47	2.85
	2010	1.43	13.76	0.63	1.55	1.62	3.17
	2011	1.46	14.29	0.65	1.56	1.75	3.31
	2012	1.46	12.93	0.71	1.74	1.82	3.56
	Mean	1.42	14.04	0.73	1.62	1.67	3.29
	S.D.	0.08	1.37	0.10	0.15	0.16	0.30
Relative	2001	0.30	2.64	0.18	0.29	0.29	0.58
	2002	0.26	2.73	0.11	0.28	0.31	0.59
	2003	0.28	2.54	0.15	0.30	0.30	0.61
	2004	0.29	2.57	0.17	0.35	0.32	0.68
	2005	0.25	2.79	0.14	0.30	0.32	0.62
	2006	0.27	2.80	0.14	0.34	0.33	0.67
	2007	0.28	2.97	0.15	0.33	0.33	0.66
	2008	0.26	2.66	0.12	0.34	0.36	0.69
	2009	0.28	2.76	0.14	0.28	0.30	0.59
	2010	0.28	2.72	0.12	0.31	0.32	0.63
	2011	0.30	2.92	0.13	0.32	0.36	0.68
	2012	0.30	2.62	0.14	0.35	0.37	0.72
	Mean	0.28	2.73	0.14	0.32	0.33	0.64
	S.D.	0.02	0.13	0.02	0.03	0.03	0.05

Appendix 8-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 100

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)
Absolute	2001	27	28	55	1.70	1.72	3.42
	2002	27	32	59	1.76	1.69	3.45
	2003	32	30	62	1.85	1.75	3.60
	2004	34	32	66	1.98	2.02	4.00
	2005	38	36	74	1.88	1.79	3.67
	2006	36	35	71	1.96	1.88	3.84
	2007	31	36	67	0.74	0.86	1.60
	2008	33	33	66	1.65	1.62	3.27
	2009	37	37	74	1.74	1.76	3.50
	2010	33	32	65	1.68	1.67	3.35
	2011	27	29	56	1.75	1.73	3.48
	2012	36	37	73	1.85	1.94	3.79
	Mean	33	33	66	1.71	1.70	3.41
	S.D.	4	3	7	0.32	0.29	0.61
Relative	2001	5	6	11	0.34	0.34	0.68
	2002	5	6	11	0.34	0.33	0.67
	2003	6	6	12	0.36	0.34	0.70
	2004	7	7	14	0.43	0.44	0.87
	2005	7	6	13	0.32	0.31	0.63
	2006	7	7	13	0.37	0.35	0.72
	2007	6	6	12	0.13	0.15	0.28
	2008	6	6	13	0.32	0.31	0.63
	2009	8	8	15	0.36	0.36	0.72
	2010	7	6	13	0.33	0.33	0.66
	2011	6	6	11	0.36	0.35	0.71
	2012	7	8	15	0.38	0.39	0.77
	Mean	6	7	13	0.34	0.33	0.67
	S.D.	1	1	1	0.07	0.07	0.14

Appendix 8-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 100

	Animal number	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)	Seminal vesicle g(g/100g BW)	Prostate g(g/100g BW)
Absolute	2001	690	664	1354	1.68	1.39
	2002	694	674	1368	1.69	1.14
	2003	767	678	1445	1.73	0.87
	2004	738	723	1461	1.80	1.28
	2005	716	642	1358	1.80	1.19
	2006	759	704	1463	2.49	1.48
	2007	365	393	758	1.74	1.17
	2008	691	661	1352	2.06	1.14
	2009	774	742	1516	1.82	1.17
	2010	598	665	1263	1.67	1.31
	2011	740	696	1436	2.04	1.62
	2012	711	716	1427	2.13	1.65
	Mean	687	663	1350	1.89	1.28
	S.D.	112	90	199	0.25	0.22
Relative	2001	137	132	269	0.33	0.28
	2002	134	131	265	0.33	0.22
	2003	149	132	281	0.34	0.17
	2004	160	157	317	0.39	0.28
	2005	124	111	235	0.31	0.21
	2006	143	132	275	0.47	0.28
	2007	65	70	135	0.31	0.21
	2008	133	127	260	0.40	0.22
	2009	159	153	312	0.37	0.24
	2010	118	131	250	0.33	0.26
	2011	151	142	294	0.42	0.33
	2012	144	145	289	0.43	0.33
	Mean	135	130	265	0.37	0.25
	S.D.	25	23	47	0.05	0.05

Appendix 8-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 300

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)
Absolute	3001	509	2.25	15.0	9.7	9.9	19.6	217
	3002	536	2.21	15.2	10.6	11.4	22.0	214
	3003	462	2.12	12.4	12.1	8.3	20.4	248
	3004	539	2.21	13.8	11.4	9.7	21.1	257
	3005	470	2.02	12.6	7.3	8.6	15.9	207
	3006	525	2.14	13.2	8.6	8.2	16.8	320
	3007	543	2.25	12.9	12.2	10.1	22.3	242
	3008	547	2.29	14.1	11.7	11.8	23.5	301
	3009	496	2.00	10.8	11.9	14.7	26.6	200
	3010	493	2.17	11.4	12.4	12.5	24.9	272
	3011	502	2.21	13.5	11.9	10.6	22.5	250
	3012	479	2.06	12.9	12.3	11.9	24.2	241
	Mean	508	2.16	13.2	11.0	10.6	21.7	247
	S.D.	30	0.09	1.3	1.6	1.9	3.1	37
Relative	3001		0.44	2.9	1.9	1.9	3.9	43
	3002		0.41	2.8	2.0	2.1	4.1	40
	3003		0.46	2.7	2.6	1.8	4.4	54
	3004		0.41	2.6	2.1	1.8	3.9	48
	3005		0.43	2.7	1.6	1.8	3.4	44
	3006		0.41	2.5	1.6	1.6	3.2	61
	3007		0.41	2.4	2.2	1.9	4.1	45
	3008		0.42	2.6	2.1	2.2	4.3	55
	3009		0.40	2.2	2.4	3.0	5.4	40
	3010		0.44	2.3	2.5	2.5	5.1	55
	3011		0.44	2.7	2.4	2.1	4.5	50
	3012		0.43	2.7	2.6	2.5	5.1	50
	Mean		0.43	2.6	2.2	2.1	4.3	49
	S.D.		0.02	0.2	0.3	0.4	0.7	7

Appendix 8-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 300

	Animal number	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	3001	1.48	13.85	0.60	1.67	1.72	3.39
	3002	1.44	13.51	0.62	1.59	1.67	3.26
	3003	1.34	11.91	0.76	1.45	1.49	2.94
	3004	1.41	14.34	0.61	1.71	1.68	3.39
	3005	1.48	11.55	0.53	1.54	1.54	3.08
	3006	1.37	14.06	0.89	1.84	1.80	3.64
	3007	1.67	15.37	0.90	1.84	1.76	3.60
	3008	1.79	16.62	0.71	1.57	1.57	3.14
	3009	1.26	13.09	0.67	1.57	1.58	3.15
	3010	1.48	13.15	0.75	1.62	1.64	3.26
	3011	1.35	13.40	0.58	1.49	1.49	2.98
	3012	1.50	13.22	0.78	1.50	1.55	3.05
	Mean	1.46	13.67	0.70	1.62	1.62	3.24
	S.D.	0.15	1.37	0.12	0.13	0.10	0.23
Relative	3001	0.29	2.72	0.12	0.33	0.34	0.67
	3002	0.27	2.52	0.12	0.30	0.31	0.61
	3003	0.29	2.58	0.16	0.31	0.32	0.64
	3004	0.26	2.66	0.11	0.32	0.31	0.63
	3005	0.31	2.46	0.11	0.33	0.33	0.66
	3006	0.26	2.68	0.17	0.35	0.34	0.69
	3007	0.31	2.83	0.17	0.34	0.32	0.66
	3008	0.33	3.04	0.13	0.29	0.29	0.57
	3009	0.25	2.64	0.14	0.32	0.32	0.64
	3010	0.30	2.67	0.15	0.33	0.33	0.66
	3011	0.27	2.67	0.12	0.30	0.30	0.59
	3012	0.31	2.76	0.16	0.31	0.32	0.64
	Mean	0.29	2.69	0.14	0.32	0.32	0.64
	S.D.	0.03	0.15	0.02	0.02	0.02	0.03

Appendix 8-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 300

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)
Absolute	3001	39	37	76	1.76	1.80	3.56
	3002	32	37	69	1.50	1.54	3.04
	3003	23	26	49	1.53	1.56	3.09
	3004	30	34	64	1.77	1.80	3.57
	3005	29	32	61	1.77	1.82	3.59
	3006	29	34	63	1.59	1.58	3.17
	3007	36	40	76	1.89	1.81	3.70
	3008	35	40	75	1.43	1.48	2.91
	3009	29	26	55	1.68	1.67	3.35
	3010	31	37	68	1.61	1.67	3.28
	3011	30	30	60	1.61	1.67	3.28
	3012	33	35	68	1.55	1.61	3.16
	Mean	31	34	65	1.64	1.67	3.31
	S.D.	4	5	8	0.14	0.12	0.25
Relative	3001	8	7	15	0.35	0.35	0.70
	3002	6	7	13	0.28	0.29	0.57
	3003	5	6	11	0.33	0.34	0.67
	3004	6	6	12	0.33	0.33	0.66
	3005	6	7	13	0.38	0.39	0.76
	3006	6	6	12	0.30	0.30	0.60
	3007	7	7	14	0.35	0.33	0.68
	3008	6	7	14	0.26	0.27	0.53
	3009	6	5	11	0.34	0.34	0.68
	3010	6	8	14	0.33	0.34	0.67
	3011	6	6	12	0.32	0.33	0.65
	3012	7	7	14	0.32	0.34	0.66
	Mean	6	7	13	0.32	0.33	0.65
	S.D.	1	1	1	0.03	0.03	0.06

Appendix 8-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 300

	Animal number	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)	Seminal vesicle g(g/100g BW)	Prostate g(g/100g BW)
Absolute	3001	623	664	1287	1.99	1.18
	3002	595	623	1218	1.82	1.23
	3003	583	590	1173	1.69	1.12
	3004	681	661	1342	2.38	1.09
	3005	653	666	1319	1.80	1.51
	3006	599	581	1180	1.91	1.39
	3007	714	651	1365	1.53	1.20
	3008	586	583	1169	1.86	0.92
	3009	678	664	1342	1.70	1.34
	3010	620	590	1210	1.83	1.20
	3011	605	654	1259	1.52	1.25
	3012	605	624	1229	2.09	1.41
	Mean	629	629	1258	1.84	1.24
	S.D.	43	35	71	0.24	0.16
Relative	3001	122	130	253	0.39	0.23
	3002	111	116	227	0.34	0.23
	3003	126	128	254	0.37	0.24
	3004	126	123	249	0.44	0.20
	3005	139	142	281	0.38	0.32
	3006	114	111	225	0.36	0.26
	3007	131	120	251	0.28	0.22
	3008	107	107	214	0.34	0.17
	3009	137	134	271	0.34	0.27
	3010	126	120	245	0.37	0.24
	3011	121	130	251	0.30	0.25
	3012	126	130	257	0.44	0.29
	Mean	124	124	248	0.36	0.24
	S.D.	10	10	19	0.05	0.04

Appendix 8-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 1000

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)
Absolute	4001	514	2.09	17.0	13.1	11.2	24.3	337
	4002	525	2.22	13.6	10.6	9.8	20.4	413
	4003	517	2.18	13.8	11.1	9.3	20.4	230
	4004	491	2.12	12.9	11.0	10.2	21.2	224
	4005	521	2.14	13.9	11.3	12.3	23.6	368
	4006	487	2.16	13.8	8.1	11.1	19.2	218
	4007	472	2.09	12.6	12.1	11.8	23.9	248
	Mean	504	2.14	13.9	11.0	10.8	21.9	291
	S.D.	20	0.05	1.4	1.5	1.1	2.0	80
Relative	4001		0.41	3.3	2.5	2.2	4.7	66
	4002		0.42	2.6	2.0	1.9	3.9	79
	4003		0.42	2.7	2.1	1.8	3.9	44
	4004		0.43	2.6	2.2	2.1	4.3	46
	4005		0.41	2.7	2.2	2.4	4.5	71
	4006		0.44	2.8	1.7	2.3	3.9	45
	4007		0.44	2.7	2.6	2.5	5.1	53
	Mean		0.42	2.8	2.2	2.2	4.3	58
	S.D.		0.01	0.2	0.3	0.3	0.5	14

Appendix 8-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 1000

	Animal number	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	4001	1.57	14.41	0.85	1.52	1.51	3.03
	4002	1.54	14.33	0.89	6.07	1.73	7.80
	4003	1.46	12.62	0.60	1.74	1.71	3.45
	4004	1.51	12.63	0.82	1.47	1.51	2.98
	4005	1.47	13.93	0.71	1.53	1.61	3.14
	4006	1.41	12.69	0.74	1.46	1.49	2.95
	4007	1.38	14.26	0.71	1.77	1.79	3.56
	Mean	1.48	13.55	0.76	2.22	1.62	3.84
	S.D.	0.07	0.86	0.10	1.70	0.12	1.76
Relative	4001	0.31	2.80	0.17	0.30	0.29	0.59
	4002	0.29	2.73	0.17	1.16	0.33	1.49
	4003	0.28	2.44	0.12	0.34	0.33	0.67
	4004	0.31	2.57	0.17	0.30	0.31	0.61
	4005	0.28	2.67	0.14	0.29	0.31	0.60
	4006	0.29	2.61	0.15	0.30	0.31	0.61
	4007	0.29	3.02	0.15	0.38	0.38	0.75
	Mean	0.29	2.69	0.15	0.44	0.32	0.76
	S.D.	0.01	0.19	0.02	0.32	0.03	0.33

Appendix 8-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 1000

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)
Absolute	4001	32	30	62	1.72	1.67	3.39
	4002	26	27	53	1.76	1.72	3.48
	4003	33	37	70	1.72	1.68	3.40
	4004	28	28	56	1.61	1.62	3.23
	4005	28	30	58	1.76	1.70	3.46
	4006	29	32	61	1.74	1.81	3.55
	4007	23	33	56	1.28	1.40	2.68
	Mean	28	31	59	1.66	1.66	3.31
	S.D.	3	3	6	0.17	0.13	0.30
Relative	4001	6	6	12	0.33	0.32	0.66
	4002	5	5	10	0.34	0.33	0.66
	4003	6	7	14	0.33	0.32	0.66
	4004	6	6	11	0.33	0.33	0.66
	4005	5	6	11	0.34	0.33	0.66
	4006	6	7	13	0.36	0.37	0.73
	4007	5	7	12	0.27	0.30	0.57
	Mean	6	6	12	0.33	0.33	0.66
	S.D.	1	1	1	0.03	0.02	0.05

Appendix 8-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 1000

	Animal number	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)	Seminal vesicle g(g/100g BW)	Prostate g(g/100g BW)
Absolute	4001	661	666	1327	1.92	1.42
	4002	646	646	1292	1.73	1.31
	4003	698	667	1365	2.31	1.76
	4004	641	660	1301	2.36	1.29
	4005	692	668	1360	1.77	1.67
	4006	692	641	1333	2.09	1.15
	4007	599	602	1201	2.01	1.35
	Mean	661	650	1311	2.03	1.42
	S.D.	36	24	56	0.25	0.22
Relative	4001	129	130	258	0.37	0.28
	4002	123	123	246	0.33	0.25
	4003	135	129	264	0.45	0.34
	4004	131	134	265	0.48	0.26
	4005	133	128	261	0.34	0.32
	4006	142	132	274	0.43	0.24
	4007	127	128	254	0.43	0.29
	Mean	131	129	260	0.40	0.28
	S.D.	6	3	9	0.06	0.04

Appendix 8-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 0

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)
Absolute	1101	306	1.86	14.4	10.0	8.8	18.8	191
	1102	286	1.93	14.3	10.1	8.6	18.7	332
	1103	324	2.18	19.2	12.0	7.9	19.9	167
	1104	313	2.09	19.5	10.2	8.5	18.7	247
	1105	309	1.93	14.7	8.6	6.5	15.1	251
	1106	285	1.94	15.0	8.0	9.0	17.0	135
	1107	312	2.06	15.1	7.1	8.1	15.2	104
	1108	290	1.93	16.2	10.0	7.2	17.2	140
	1109	301	1.89	19.0	11.9	7.7	19.6	94
	1110	314	1.92	16.0	5.7	5.6	11.3	158
	1111	306	2.07	17.1	8.9	7.1	16.0	136
	1112	307	2.06	22.2	10.7	8.3	19.0	161
	Mean	304	1.99	16.9	9.4	7.8	17.2	176
	S.D.	12	0.10	2.5	1.9	1.0	2.5	69
Relative	1101		0.61	4.7	3.3	2.9	6.1	62
	1102		0.67	5.0	3.5	3.0	6.5	116
	1103		0.67	5.9	3.7	2.4	6.1	52
	1104		0.67	6.2	3.3	2.7	6.0	79
	1105		0.62	4.8	2.8	2.1	4.9	81
	1106		0.68	5.3	2.8	3.2	6.0	47
	1107		0.66	4.8	2.3	2.6	4.9	33
	1108		0.67	5.6	3.4	2.5	5.9	48
	1109		0.63	6.3	4.0	2.6	6.5	31
	1110		0.61	5.1	1.8	1.8	3.6	50
	1111		0.68	5.6	2.9	2.3	5.2	44
	1112		0.67	7.2	3.5	2.7	6.2	52
	Mean		0.65	5.5	3.1	2.6	5.7	58
	S.D.		0.03	0.8	0.6	0.4	0.9	24

Appendix 8-18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 0

	Animal number	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	1101	0.94	10.92	0.66	0.95	0.97	1.92
	1102	1.06	10.13	0.52	1.11	1.14	2.25
	1103	1.03	11.39	0.60	0.98	1.05	2.03
	1104	1.04	9.29	0.66	0.96	0.99	1.95
	1105	1.06	9.67	0.48	1.11	1.01	2.12
	1106	0.88	9.26	0.62	0.97	0.97	1.94
	1107	1.03	11.33	0.59	1.05	1.10	2.15
	1108	0.97	10.45	0.61	1.18	1.17	2.35
	1109	0.99	10.54	0.49	1.02	0.96	1.98
	1110	0.88	10.64	0.52	1.11	1.07	2.18
	1111	0.98	10.58	0.46	1.13	1.12	2.25
	1112	1.05	11.31	0.61	1.09	1.11	2.20
	Mean	0.99	10.46	0.57	1.06	1.06	2.11
	S.D.	0.06	0.75	0.07	0.08	0.07	0.14
Relative	1101	0.31	3.57	0.22	0.31	0.32	0.63
	1102	0.37	3.54	0.18	0.39	0.40	0.79
	1103	0.32	3.52	0.19	0.30	0.32	0.63
	1104	0.33	2.97	0.21	0.31	0.32	0.62
	1105	0.34	3.13	0.16	0.36	0.33	0.69
	1106	0.31	3.25	0.22	0.34	0.34	0.68
	1107	0.33	3.63	0.19	0.34	0.35	0.69
	1108	0.33	3.60	0.21	0.41	0.40	0.81
	1109	0.33	3.50	0.16	0.34	0.32	0.66
	1110	0.28	3.39	0.17	0.35	0.34	0.69
	1111	0.32	3.46	0.15	0.37	0.37	0.74
	1112	0.34	3.68	0.20	0.36	0.36	0.72
	Mean	0.33	3.44	0.19	0.35	0.35	0.70
	S.D.	0.02	0.22	0.02	0.03	0.03	0.06

Appendix 8-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 0

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	1101	40	42	82	49.4	66.4	115.8	619
	1102	36	39	75	44.6	50.8	95.4	487
	1103	44	47	91	54.8	45.1	99.9	727
	1104	44	48	92	57.1	60.7	117.8	624
	1105	37	40	77	52.9	48.9	101.8	589
	1106	41	47	88	46.2	58.0	104.2	560
	1107	41	47	88	50.8	56.6	107.4	682
	1108	40	49	89	52.4	50.5	102.9	556
	1109	39	49	88	54.7	39.8	94.5	579
	1110	44	59	103	47.9	69.4	117.3	620
	1111	41	41	82	64.7	49.1	113.8	652
	1112	46	51	97	68.9	72.0	140.9	667
	Mean	41	47	88	53.7	55.6	109.3	614
	S.D.	3	6	8	7.2	10.0	12.9	65
Relative	1101	13	14	27	16.1	21.7	37.8	202
	1102	13	14	26	15.6	17.8	33.4	170
	1103	14	15	28	16.9	13.9	30.8	224
	1104	14	15	29	18.2	19.4	37.6	199
	1105	12	13	25	17.1	15.8	32.9	191
	1106	14	16	31	16.2	20.4	36.6	196
	1107	13	15	28	16.3	18.1	34.4	219
	1108	14	17	31	18.1	17.4	35.5	192
	1109	13	16	29	18.2	13.2	31.4	192
	1110	14	19	33	15.3	22.1	37.4	197
	1111	13	13	27	21.1	16.0	37.2	213
	1112	15	17	32	22.4	23.5	45.9	217
	Mean	14	15	29	17.6	18.3	35.9	201
	S.D.	1	2	2	2.2	3.3	4.0	15

Appendix 8-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 100

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)
Absolute	2101	301	2.04	11.6	7.5	6.0	13.5	214
	2102	333	2.02	18.5	9.5	5.3	14.8	215
	2103	297	1.99	15.3	6.7	7.3	14.0	129
	2104a)	359Z	1.74Z	12.3Z	8.5Z	7.8Z	16.3Z	344Z
	2105	312	1.90	15.9	10.5	9.5	20.0	247
	2106	287	1.87	13.6	7.9	8.0	15.9	275
	2107b)	352Z	1.93Z	15.8Z	12.5Z	8.3Z	20.8Z	497Z
	2108	294	1.86	16.7	9.2	8.4	17.6	208
	2109	277	1.93	14.3	10.3	9.0	19.3	94
	2110	309	2.06	16.9	7.4	6.4	13.8	298
	2111	290	1.95	16.1	9.7	6.7	16.4	235
	2112	309	2.02	18.5	10.4	8.5	18.9	177
	Mean	301	1.96	15.7	8.9	7.5	16.4	209
	S.D.	16	0.07	2.2	1.4	1.4	2.4	62
Relative	2101		0.68	3.9	2.5	2.0	4.5	71
	2102		0.61	5.6	2.9	1.6	4.4	65
	2103		0.67	5.2	2.3	2.5	4.7	43
	2104a)		0.48Z	3.4Z	2.4Z	2.2Z	4.5Z	96Z
	2105		0.61	5.1	3.4	3.0	6.4	79
	2106		0.65	4.7	2.8	2.8	5.5	96
	2107b)		0.55Z	4.5Z	3.6Z	2.4Z	5.9Z	141Z
	2108		0.63	5.7	3.1	2.9	6.0	71
	2109		0.70	5.2	3.7	3.2	7.0	34
	2110		0.67	5.5	2.4	2.1	4.5	96
	2111		0.67	5.6	3.3	2.3	5.7	81
	2112		0.65	6.0	3.4	2.8	6.1	57
	Mean		0.65	5.3	3.0	2.5	5.5	69
	S.D.		0.03	0.6	0.5	0.5	0.9	20

a): Non-pregnant
b): Necropsied on lactation day 1 because all pups died
Z: Data was excluded from statistical analysis.

Appendix 8-21 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 100

	Animal number	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	2101	1.05	10.48	0.67	1.11	1.12	2.23
	2102	0.96	11.17	0.71	1.28	1.22	2.50
	2103	0.94	10.20	0.61	1.09	1.02	2.11
	2104a)	1.01Z	14.60Z	0.42Z	1.02Z	1.00Z	2.02Z
	2105	1.21	10.89	0.64	1.03	1.07	2.10
	2106	0.99	9.87	0.62	0.92	0.93	1.85
	2107b)	1.15Z	11.99Z	0.55Z	1.05Z	1.12Z	2.17Z
	2108	0.87	10.65	0.54	1.15	1.15	2.30
	2109	0.90	8.89	0.55	1.03	0.96	1.99
	2110	1.16	11.16	0.62	1.11	1.03	2.14
	2111	0.98	9.91	0.68	1.08	0.99	2.07
	2112	0.96	12.24	0.66	1.11	1.13	2.24
	Mean	1.00	10.55	0.63	1.09	1.06	2.15
	S.D.	0.11	0.91	0.05	0.09	0.09	0.18
Relative	2101	0.35	3.48	0.22	0.37	0.37	0.74
	2102	0.29	3.35	0.21	0.38	0.37	0.75
	2103	0.32	3.43	0.21	0.37	0.34	0.71
	2104a)	0.28Z	4.07Z	0.12Z	0.28Z	0.28Z	0.56Z
	2105	0.39	3.49	0.21	0.33	0.34	0.67
	2106	0.34	3.44	0.22	0.32	0.32	0.64
	2107b)	0.33Z	3.41Z	0.16Z	0.30Z	0.32Z	0.62Z
	2108	0.30	3.62	0.18	0.39	0.39	0.78
	2109	0.32	3.21	0.20	0.37	0.35	0.72
	2110	0.38	3.61	0.20	0.36	0.33	0.69
	2111	0.34	3.42	0.23	0.37	0.34	0.71
	2112	0.31	3.96	0.21	0.36	0.37	0.72
	Mean	0.33	3.50	0.21	0.36	0.35	0.71
	S.D.	0.03	0.20	0.01	0.02	0.02	0.04

a): Non-pregnant
b): Necropsied on lactation day 1 because all pups died
Z: Data was excluded from statistical analysis.

Appendix 8-22 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 100

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	2101	46	48	94	44.3	51.1	95.4	808
	2102	46	51	97	50.8	50.3	101.1	693
	2103	35	35	70	52.1	43.6	95.7	555
	2104a)	37Z	39Z	76Z	63.8Z	61.4Z	125.2Z	566Z
	2105	39	39	78	45.4	59.7	105.1	535
	2106	36	44	80	40.2	51.7	91.9	587
	2107b)	39Z	46Z	85Z	53.8Z	52.0Z	105.8Z	951Z
	2108	52	58	110	52.6	63.8	116.4	562
	2109	37	41	78	51.5	46.7	98.2	614
	2110	44	55	99	51.9	56.7	108.6	827
	2111	43	43	86	37.7	55.7	93.4	658
	2112	52	53	105	53.3	54.0	107.3	641
	Mean	43	47	90	48.0	53.3	101.3	648
	S.D.	6	7	13	5.7	6.0	7.9	102
Relative	2101	15	16	31	14.7	17.0	31.7	268
	2102	14	15	29	15.3	15.1	30.4	208
	2103	12	12	24	17.5	14.7	32.2	187
	2104a)	10Z	11Z	21Z	17.8Z	17.1Z	34.9Z	158Z
	2105	13	13	25	14.6	19.1	33.7	171
	2106	13	15	28	14.0	18.0	32.0	205
	2107b)	11Z	13Z	24Z	15.3Z	14.8Z	30.1Z	270Z
	2108	18	20	37	17.9	21.7	39.6	191
	2109	13	15	28	18.6	16.9	35.5	222
	2110	14	18	32	16.8	18.3	35.1	268
	2111	15	15	30	13.0	19.2	32.2	227
	2112	17	17	34	17.2	17.5	34.7	207
	Mean	14	16	30	16.0	17.8	33.7	215
	S.D.	2	2	4	1.9	2.0	2.7	32

a): Non-pregnant
b): Necropsied on lactation day 1 because all pups died
Z: Data was excluded from statistical analysis.

Appendix 8-23 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 300

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)
Absolute	3101	298	1.92	15.4	8.8	8.9	17.7	212
	3102	284	2.02	18.9	8.4	8.2	16.6	114
	3103	286	2.00	12.3	7.7	8.3	16.0	95
	3104	287	1.91	17.7	9.9	8.4	18.3	158
	3105	282	1.95	17.9	7.7	11.5	19.2	86
	3106	290	2.02	17.2	10.2	9.6	19.8	232
	3107	274	2.09	12.7	9.4	5.3	14.7	115
	3108	333	2.04	19.0	9.5	8.1	17.6	150
	3109	296	1.93	16.9	10.6	8.3	18.9	176
	3110	288	1.87	11.6	7.0	7.7	14.7	155
	3111	315	1.96	16.1	7.6	6.7	14.3	221
	3112	336	1.93	16.7	8.2	6.6	14.8	221
	Mean	297	1.97	16.0	8.8	8.1	16.9	161
	S.D.	20	0.06	2.5	1.2	1.6	2.0	52
Relative	3101		0.64	5.2	3.0	3.0	5.9	71
	3102		0.71	6.7	3.0	2.9	5.8	40
	3103		0.70	4.3	2.7	2.9	5.6	33
	3104		0.67	6.2	3.4	2.9	6.4	55
	3105		0.69	6.3	2.7	4.1	6.8	30
	3106		0.70	5.9	3.5	3.3	6.8	80
	3107		0.76	4.6	3.4	1.9	5.4	42
	3108		0.61	5.7	2.9	2.4	5.3	45
	3109		0.65	5.7	3.6	2.8	6.4	59
	3110		0.65	4.0	2.4	2.7	5.1	54
	3111		0.62	5.1	2.4	2.1	4.5	70
	3112		0.57	5.0	2.4	2.0	4.4	66
	Mean		0.66	5.4	3.0	2.8	5.7	54
	S.D.		0.05	0.8	0.4	0.6	0.8	16

Appendix 8-24 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 300

	Animal number	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	3101	0.85	9.91	0.53	0.94	0.95	1.89
	3102	0.88	9.86	0.62	1.05	0.99	2.04
	3103	0.87	9.88	0.53	1.04	1.01	2.05
	3104	0.80	9.13	0.52	1.02	1.07	2.09
	3105	0.98	9.17	0.66	1.01	0.94	1.95
	3106	0.92	9.77	0.56	0.96	1.03	1.99
	3107	0.87	9.20	0.59	0.94	0.93	1.87
	3108	0.99	12.14	0.67	1.12	1.11	2.23
	3109	0.97	9.67	0.53	0.98	0.95	1.93
	3110	0.81	9.72	0.51	1.14	1.10	2.24
	3111	1.05	10.70	0.64	1.07	1.07	2.14
	3112	1.06	12.09	0.72	1.12	1.01	2.13
	Mean	0.92	10.10	0.59	1.03	1.01	2.05
	S.D.	0.09	1.03	0.07	0.07	0.06	0.12
Relative	3101	0.29	3.33	0.18	0.32	0.32	0.63
	3102	0.31	3.47	0.22	0.37	0.35	0.72
	3103	0.30	3.45	0.19	0.36	0.35	0.72
	3104	0.28	3.18	0.18	0.36	0.37	0.73
	3105	0.35	3.25	0.23	0.36	0.33	0.69
	3106	0.32	3.37	0.19	0.33	0.36	0.69
	3107	0.32	3.36	0.22	0.34	0.34	0.68
	3108	0.30	3.65	0.20	0.34	0.33	0.67
	3109	0.33	3.27	0.18	0.33	0.32	0.65
	3110	0.28	3.38	0.18	0.40	0.38	0.78
	3111	0.33	3.40	0.20	0.34	0.34	0.68
	3112	0.32	3.60	0.21	0.33	0.30	0.63
	Mean	0.31	3.39	0.20	0.35	0.34	0.69
	S.D.	0.02	0.14	0.02	0.02	0.02	0.04

Appendix 8-25 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 300

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	3101	41	47	88	37.4	53.2	90.6	609
	3102	42	47	89	49.7	57.6	107.3	580
	3103	41	36	77	53.0	43.0	96.0	657
	3104	40	43	83	65.9	50.0	115.9	580
	3105	43	43	86	45.1	62.1	107.2	597
	3106	37	40	77	44.0	45.1	89.1	686
	3107	31	38	69	57.2	39.0	96.2	790
	3108	51	54	105	56.5	41.9	98.4	669
	3109	35	37	72	49.8	42.9	92.7	819
	3110	43	46	89	47.3	39.5	86.8	697
	3111	35	38	73	48.3	44.5	92.8	706
	3112	46	50	96	70.0	39.9	109.9	699
	Mean	40	43	84	52.0	46.6	98.6	674
	S.D.	5	6	11	9.2	7.5	9.3	77
Relative	3101	14	16	30	12.6	17.9	30.4	204
	3102	15	17	31	17.5	20.3	37.8	204
	3103	14	13	27	18.5	15.0	33.6	230
	3104	14	15	29	23.0	17.4	40.4	202
	3105	15	15	30	16.0	22.0	38.0	212
	3106	13	14	27	15.2	15.6	30.7	237
	3107	11	14	25	20.9	14.2	35.1	288
	3108	15	16	32	17.0	12.6	29.5	201
	3109	12	13	24	16.8	14.5	31.3	277
	3110	15	16	31	16.4	13.7	30.1	242
	3111	11	12	23	15.3	14.1	29.5	224
	3112	14	15	29	20.8	11.9	32.7	208
	Mean	14	15	28	17.5	15.8	33.3	227
	S.D.	2	1	3	2.9	3.1	3.8	29

Appendix 8-26 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 1000

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)
Absolute	4101	303	1.98	13.7	10.0	8.5	18.5	128
	4102	273	2.02	13.8	8.4	7.3	15.7	169
	4103	298	2.10	15.2	8.7	8.4	17.1	326
	4104	330	2.12	23.2	9.4	9.5	18.9	233
	4105	297	1.93	14.6	8.3	8.6	16.9	132
	4106	306	2.09	13.5	7.2	6.5	13.7	233
	4107	259	1.97	13.9	9.3	8.4	17.7	130
	4108	288	1.95	16.1	6.1	7.3	13.4	131
	4109	314	2.10	13.8	7.7	6.8	14.5	285
	4110	309	1.97	21.5	12.2	9.7	21.9	220
	4111	298	1.91	15.5	7.7	9.2	16.9	148
	4112	300	1.86	18.4	7.3	6.2	13.5	104
	Mean	298	2.00	16.1	8.5	8.0	16.6	187
	S.D.	18	0.09	3.3	1.6	1.2	2.6	71
Relative	4101		0.65	4.5	3.3	2.8	6.1	42
	4102		0.74	5.1	3.1	2.7	5.8	62
	4103		0.70	5.1	2.9	2.8	5.7	109
	4104		0.64	7.0	2.8	2.9	5.7	71
	4105		0.65	4.9	2.8	2.9	5.7	44
	4106		0.68	4.4	2.4	2.1	4.5	76
	4107		0.76	5.4	3.6	3.2	6.8	50
	4108		0.68	5.6	2.1	2.5	4.7	45
	4109		0.67	4.4	2.5	2.2	4.6	91
	4110		0.64	7.0	3.9	3.1	7.1	71
	4111		0.64	5.2	2.6	3.1	5.7	50
	4112		0.62	6.1	2.4	2.1	4.5	35
	Mean		0.67	5.4	2.9	2.7	5.6	62
	S.D.		0.04	0.9	0.5	0.4	0.9	22

Appendix 8-27 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 1000

	Animal number	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	4101	0.94	9.62	0.58	0.95	1.10	2.05
	4102	0.95	8.42	0.51	0.98	0.98	1.96
	4103	0.98	9.32	0.51	1.00	0.90	1.90
	4104	1.06	11.16	0.83	1.24	1.20	2.44
	4105	1.02	10.02	0.69	1.09	1.08	2.17
	4106	1.16	10.03	0.60	1.01	0.99	2.00
	4107	0.95	9.70	0.57	1.04	1.02	2.06
	4108	0.87	9.68	0.64	1.07	1.02	2.09
	4109	0.94	10.44	0.63	1.05	1.06	2.11
	4110	1.03	11.40	0.60	1.05	1.01	2.06
	4111	0.91	11.00	0.54	1.03	1.04	2.07
	4112	0.95	9.29	0.62	1.11	1.14	2.25
	Mean	0.98	10.01	0.61	1.05	1.05	2.10
	S.D.	0.08	0.87	0.09	0.07	0.08	0.14
Relative	4101	0.31	3.17	0.19	0.31	0.36	0.68
	4102	0.35	3.08	0.19	0.36	0.36	0.72
	4103	0.33	3.13	0.17	0.34	0.30	0.64
	4104	0.32	3.38	0.25	0.38	0.36	0.74
	4105	0.34	3.37	0.23	0.37	0.36	0.73
	4106	0.38	3.28	0.20	0.33	0.32	0.65
	4107	0.37	3.75	0.22	0.40	0.39	0.80
	4108	0.30	3.36	0.22	0.37	0.35	0.73
	4109	0.30	3.32	0.20	0.33	0.34	0.67
	4110	0.33	3.69	0.19	0.34	0.33	0.67
	4111	0.31	3.69	0.18	0.35	0.35	0.69
	4112	0.32	3.10	0.21	0.37	0.38	0.75
	Mean	0.33	3.36	0.20	0.35	0.35	0.71
	S.D.	0.03	0.24	0.02	0.03	0.02	0.05

Appendix 8-28 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 1000

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	4101	35	40	75	56.3	48.2	104.5	617
	4102	47	49	96	56.8	51.7	108.5	764
	4103	34	38	72	35.8	58.0	93.8	549
	4104	42	46	88	55.6	45.6	101.2	619
	4105	43	47	90	45.9	46.4	92.3	656
	4106	38	43	81	55.5	43.6	99.1	744
	4107	42	46	88	49.8	46.7	96.5	652
	4108	40	45	85	40.7	46.6	87.3	686
	4109	49	58	107	54.7	54.3	109.0	594
	4110	39	42	81	59.8	52.3	112.1	732
	4111	39	48	87	46.1	55.5	101.6	730
	4112	36	38	74	54.5	49.3	103.8	682
	Mean	40	45	85	51.0	49.9	100.8	669
	S.D.	5	6	10	7.4	4.5	7.4	66
Relative	4101	12	13	25	18.6	15.9	34.5	204
	4102	17	18	35	20.8	18.9	39.7	280
	4103	11	13	24	12.0	19.5	31.5	184
	4104	13	14	27	16.8	13.8	30.7	188
	4105	14	16	30	15.5	15.6	31.1	221
	4106	12	14	26	18.1	14.2	32.4	243
	4107	16	18	34	19.2	18.0	37.3	252
	4108	14	16	30	14.1	16.2	30.3	238
	4109	16	18	34	17.4	17.3	34.7	189
	4110	13	14	26	19.4	16.9	36.3	237
	4111	13	16	29	15.5	18.6	34.1	245
	4112	12	13	25	18.2	16.4	34.6	227
	Mean	14	15	29	17.1	16.8	33.9	226
	S.D.	2	2	4	2.5	1.8	2.9	30

Appendix 8-29 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of female rats (Satellite group, End of administration)
Dose (mg/kg): 0

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)
Absolute	1113	286	1.95	14.4	8.4	9.1	17.5	349
	1114	257	1.95	17.1	7.6	9.0	16.6	196
	1115	254	1.87	14.3	6.4	6.1	12.5	197
	1116	263	1.98	15.4	8.0	8.6	16.6	256
	1117	251	1.92	12.9	9.8	8.5	18.3	254
	Mean	262	1.93	14.8	8.0	8.3	16.3	250
	S.D.	14	0.04	1.6	1.2	1.2	2.2	62
Relative	1113		0.68	5.0	2.9	3.2	6.1	122
	1114		0.76	6.7	3.0	3.5	6.5	76
	1115		0.74	5.6	2.5	2.4	4.9	78
	1116		0.75	5.9	3.0	3.3	6.3	97
	1117		0.76	5.1	3.9	3.4	7.3	101
	Mean		0.74	5.7	3.1	3.2	6.2	95
	S.D.		0.03	0.7	0.5	0.4	0.9	19

Appendix 8-30 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of female rats (Satellite group, End of administration)
Dose (mg/kg): 0

	Animal number	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	1113	0.81	6.85	0.40	0.91	0.97	1.88
	1114	0.84	7.16	0.45	1.02	0.99	2.01
	1115	0.89	6.13	0.46	0.84	0.81	1.65
	1116	0.85	6.77	0.54	0.99	0.97	1.96
	1117	0.81	6.43	0.45	0.89	0.88	1.77
	Mean	0.84	6.67	0.46	0.93	0.92	1.85
	S.D.	0.03	0.40	0.05	0.07	0.08	0.15
Relative	1113	0.28	2.40	0.14	0.32	0.34	0.66
	1114	0.33	2.79	0.18	0.40	0.39	0.78
	1115	0.35	2.41	0.18	0.33	0.32	0.65
	1116	0.32	2.57	0.21	0.38	0.37	0.75
	1117	0.32	2.56	0.18	0.35	0.35	0.71
	Mean	0.32	2.55	0.18	0.36	0.35	0.71
	S.D.	0.03	0.16	0.02	0.03	0.03	0.06

Appendix 8-31 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of female rats (Satellite group, End of administration)
Dose (mg/kg): 0

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	1113	36	42	78	40.2	45.0	85.2	570
	1114	36	39	75	34.7	41.4	76.1	457
	1115	32	36	68	35.4	26.3	61.7	505
	1116	36	41	77	47.4	44.3	91.7	584
	1117	28	32	60	39.9	32.5	72.4	607
	Mean	34	38	72	39.5	37.9	77.4	545
	S.D.	4	4	8	5.1	8.2	11.6	62
Relative	1113	13	15	27	14.1	15.7	29.8	199
	1114	14	15	29	13.5	16.1	29.6	178
	1115	13	14	27	13.9	10.4	24.3	199
	1116	14	16	29	18.0	16.8	34.9	222
	1117	11	13	24	15.9	12.9	28.8	242
	Mean	13	15	27	15.1	14.4	29.5	208
	S.D.	1	1	2	1.9	2.7	3.8	25

Appendix 8-32 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of female rats (Satellite group, End of administration)
Dose (mg/kg): 1000

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)
Absolute	4113	258	2.00	15.1	9.4	13.5	22.9	210
	4114	272	2.01	15.9	7.5	9.4	16.9	224
	4115	293	2.06	15.2	5.9	8.0	13.9	244
	4116	255	1.94	14.4	7.7	8.1	15.8	220
	4117	253	1.87	16.4	9.7	10.6	20.3	378
	Mean	266	1.98	15.4	8.0	9.9	18.0	255
	S.D.	17	0.07	0.8	1.5	2.3	3.6	70
Relative	4113		0.78	5.9	3.6	5.2	8.9	81
	4114		0.74	5.8	2.8	3.5	6.2	82
	4115		0.70	5.2	2.0	2.7	4.7	83
	4116		0.76	5.6	3.0	3.2	6.2	86
	4117		0.74	6.5	3.8	4.2	8.0	149
	Mean		0.74	5.8	3.0	3.8	6.8	96
	S.D.		0.03	0.5	0.7	1.0	1.7	30

Appendix 8-33 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of female rats (Satellite group, End of administration)
Dose (mg/kg): 1000

	Animal number	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	4113	0.89	6.70	0.44	0.89	0.87	1.76
	4114	0.84	6.84	0.40	1.07	1.04	2.11
	4115	0.88	7.53	0.54	0.93	0.99	1.92
	4116	0.83	6.72	0.41	0.93	1.00	1.93
	4117	0.81	6.49	0.52	0.91	0.91	1.82
	Mean	0.85	6.86	0.46	0.95	0.96	1.91
	S.D.	0.03	0.40	0.06	0.07	0.07	0.13
Relative	4113	0.34	2.60	0.17	0.34	0.34	0.68
	4114	0.31	2.51	0.15	0.39	0.38	0.78
	4115	0.30	2.57	0.18	0.32	0.34	0.66
	4116	0.33	2.64	0.16	0.36	0.39	0.76
	4117	0.32	2.57	0.21	0.36	0.36	0.72
	Mean	0.32	2.58	0.17	0.35	0.36	0.72
	S.D.	0.02	0.05	0.02	0.03	0.02	0.05

Appendix 8-34 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of female rats (Satellite group, End of administration)
Dose (mg/kg): 1000

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	4113	32	37	69	49.6	48.1	97.7	570
	4114	26	32	58	38.6	43.7	82.3	576
	4115	37	40	77	48.3	40.6	88.9	660
	4116	26	31	57	38.7	36.5	75.2	532
	4117	31	33	64	36.7	37.7	74.4	473
	Mean	30	35	65	42.4	41.3	83.7	562
	S.D.	5	4	8	6.1	4.7	9.8	68
Relative	4113	12	14	27	19.2	18.6	37.9	221
	4114	10	12	21	14.2	16.1	30.3	212
	4115	13	14	26	16.5	13.9	30.3	225
	4116	10	12	22	15.2	14.3	29.5	209
	4117	12	13	25	14.5	14.9	29.4	187
	Mean	11	13	24	15.9	15.6	31.5	211
	S.D.	1	1	3	2.0	1.9	3.6	15

Appendix 8-35 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of male rats (End of recovery)
Dose (mg/kg): 0

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)
Absolute	1008	482	2.16	13.9	6.9	9.1	16.0	242
	1009	499	2.07	11.0	10.9	12.3	23.2	201
	1010	502	2.11	14.0	12.7	14.0	26.7	316
	1011	518	2.26	12.8	11.1	6.8	17.9	203
	1012	489	2.15	12.1	11.9	13.2	25.1	193
	Mean	498	2.15	12.8	10.7	11.1	21.8	231
	S.D.	14	0.07	1.3	2.2	3.0	4.6	51
Relative	1008		0.45	2.9	1.4	1.9	3.3	50
	1009		0.41	2.2	2.2	2.5	4.6	40
	1010		0.42	2.8	2.5	2.8	5.3	63
	1011		0.44	2.5	2.1	1.3	3.5	39
	1012		0.44	2.5	2.4	2.7	5.1	39
	Mean		0.43	2.6	2.1	2.2	4.4	46
	S.D.		0.02	0.3	0.4	0.6	0.9	10

Appendix 8-36 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of male rats (End of recovery)
Dose (mg/kg): 0

	Animal number	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	1008	1.45	11.04	0.69	1.54	1.60	3.14
	1009	1.44	13.71	0.72	1.62	1.66	3.28
	1010	1.21	13.58	0.62	1.46	1.62	3.08
	1011	1.58	13.63	0.82	1.83	1.96	3.79
	1012	1.63	13.05	0.78	1.66	1.79	3.45
	Mean	1.46	13.00	0.73	1.62	1.73	3.35
	S.D.	0.16	1.13	0.08	0.14	0.15	0.29
Relative	1008	0.30	2.29	0.14	0.32	0.33	0.65
	1009	0.29	2.75	0.14	0.32	0.33	0.66
	1010	0.24	2.71	0.12	0.29	0.32	0.61
	1011	0.31	2.63	0.16	0.35	0.38	0.73
	1012	0.33	2.67	0.16	0.34	0.37	0.71
	Mean	0.29	2.61	0.14	0.32	0.35	0.67
	S.D.	0.03	0.18	0.02	0.02	0.03	0.05

Appendix 8-37 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of male rats (End of recovery)
Dose (mg/kg): 0

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)
Absolute	1008	30	32	62	1.89	1.95	3.84
	1009	29	32	61	1.75	1.73	3.48
	1010	31	35	66	1.67	1.73	3.40
	1011	31	32	63	1.93	1.83	3.76
	1012	29	29	58	1.62	1.61	3.23
	Mean	30	32	62	1.77	1.77	3.54
	S.D.	1	2	3	0.13	0.13	0.25
Relative	1008	6	7	13	0.39	0.40	0.80
	1009	6	6	12	0.35	0.35	0.70
	1010	6	7	13	0.33	0.34	0.68
	1011	6	6	12	0.37	0.35	0.73
	1012	6	6	12	0.33	0.33	0.66
	Mean	6	6	12	0.35	0.35	0.71
	S.D.	0	1	1	0.03	0.03	0.05

Appendix 8-38 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of male rats (End of recovery)
Dose (mg/kg): 0

	Animal number	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)	Seminal vesicle g(g/100g BW)	Prostate g(g/100g BW)
Absolute	1008	749	779	1528	1.88	1.32
	1009	704	690	1394	1.36	1.32
	1010	637	679	1316	1.77	1.25
	1011	767	746	1513	2.09	1.42
	1012	649	632	1281	1.72	1.09
	Mean	701	705	1406	1.76	1.28
	S.D.	58	58	112	0.27	0.12
Relative	1008	155	162	317	0.39	0.27
	1009	141	138	279	0.27	0.26
	1010	127	135	262	0.35	0.25
	1011	148	144	292	0.40	0.27
	1012	133	129	262	0.35	0.22
	Mean	141	142	282	0.35	0.25
	S.D.	11	13	23	0.05	0.02

Appendix 8-39 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of male rats (End of recovery)
Dose (mg/kg): 1000

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)
Absolute	4008	486	2.02	12.6	11.9	12.1	24.0	190
	4009	454	2.14	12.3	6.1	8.6	14.7	194
	4010	589	2.16	14.5	15.5	9.2	24.7	294
	4011	515	2.17	15.1	11.7	10.0	21.7	174
	4012	517	2.14	14.7	7.1	8.2	15.3	372
	Mean	512	2.13	13.8	10.5	9.6	20.1	245
	S.D.	50	0.06	1.3	3.9	1.5	4.8	85
Relative	4008		0.42	2.6	2.4	2.5	4.9	39
	4009		0.47	2.7	1.3	1.9	3.2	43
	4010		0.37	2.5	2.6	1.6	4.2	50
	4011		0.42	2.9	2.3	1.9	4.2	34
	4012		0.41	2.8	1.4	1.6	3.0	72
	Mean		0.42	2.7	2.0	1.9	3.9	48
	S.D.		0.04	0.2	0.6	0.4	0.8	15

Appendix 8-40 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of male rats (End of recovery)
Dose (mg/kg): 1000

	Animal number	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	4008	1.56	12.78	0.51	1.73	1.87	3.60
	4009	1.54	11.06	0.64	1.38	1.39	2.77
	4010	1.53	14.78	0.81	1.68	1.78	3.46
	4011	1.34	12.25	0.68	1.58	1.61	3.19
	4012	1.28	12.82	0.51	1.64	1.74	3.38
	Mean	1.45	12.74	0.63	1.60	1.68	3.28
	S.D.	0.13	1.34	0.13	0.14	0.19	0.32
Relative	4008	0.32	2.63	0.10	0.36	0.38	0.74
	4009	0.34	2.44	0.14	0.30	0.31	0.61
	4010	0.26	2.51	0.14	0.29	0.30	0.59
	4011	0.26	2.38	0.13	0.31	0.31	0.62
	4012	0.25	2.48	0.10	0.32	0.34	0.65
	Mean	0.29	2.49	0.12	0.32	0.33	0.64
	S.D.	0.04	0.09	0.02	0.03	0.03	0.06

Appendix 8-41 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of male rats (End of recovery)
Dose (mg/kg): 1000

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)
Absolute	4008	28	28	56	1.77	1.79	3.56
	4009	25	27	52	1.86	1.80	3.66
	4010	34	40	74	1.93	1.91	3.84
	4011	32	37	69	1.96	1.95	3.91
	4012	27	31	58	1.59	1.60	3.19
	Mean	29	33	62	1.82	1.81	3.63
	S.D.	4	6	9	0.15	0.14	0.28
Relative	4008	6	6	12	0.36	0.37	0.73
	4009	6	6	11	0.41	0.40	0.81
	4010	6	7	13	0.33	0.32	0.65
	4011	6	7	13	0.38	0.38	0.76
	4012	5	6	11	0.31	0.31	0.62
	Mean	6	6	12	0.36	0.36	0.71
	S.D.	0	1	1	0.04	0.04	0.08

Appendix 8-42 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of male rats (End of recovery)
Dose (mg/kg): 1000

	Animal number	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)	Seminal vesicle g(g/100g BW)	Prostate g(g/100g BW)
Absolute	4008	686	695	1381	1.24	1.27
	4009	785	752	1537	1.84	1.30
	4010	690	680	1370	1.38	1.41
	4011	689	643	1332	1.84	1.13
	4012	656	658	1314	1.50	1.18
	Mean	701	686	1387	1.56	1.26
	S.D.	49	42	88	0.27	0.11
Relative	4008	141	143	284	0.26	0.26
	4009	173	166	339	0.41	0.29
	4010	117	115	233	0.23	0.24
	4011	134	125	259	0.36	0.22
	4012	127	127	254	0.29	0.23
	Mean	138	135	274	0.31	0.25
	S.D.	21	20	41	0.07	0.03

Appendix 8-43 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of female rats (End of recovery)
Dose (mg/kg): 0

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)
Absolute	1118	280	1.93	15.0	7.4	8.4	15.8	269
	1119	311	2.13	14.7	8.3	8.5	16.8	284
	1120	258	1.98	12.9	8.6	7.9	16.5	260
	1121	267	1.98	15.1	10.8	10.0	20.8	222
	1122	275	2.03	20.2	7.8	7.5	15.3	268
	Mean	278	2.01	15.6	8.6	8.5	17.0	261
	S.D.	20	0.08	2.7	1.3	1.0	2.2	23
Relative	1118		0.69	5.4	2.6	3.0	5.6	96
	1119		0.68	4.7	2.7	2.7	5.4	91
	1120		0.77	5.0	3.3	3.1	6.4	101
	1121		0.74	5.7	4.0	3.7	7.8	83
	1122		0.74	7.3	2.8	2.7	5.6	97
	Mean		0.72	5.6	3.1	3.0	6.2	94
	S.D.		0.04	1.0	0.6	0.4	1.0	7

Appendix 8-44 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of female rats (End of recovery)
Dose (mg/kg): 0

	Animal number	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	1118	0.80	6.38	0.54	0.96	0.99	1.95
	1119	0.94	7.98	0.58	1.05	1.06	2.11
	1120	0.79	6.23	0.41	0.94	0.93	1.87
	1121	0.93	7.49	0.57	1.00	0.95	1.95
	1122	0.93	7.29	0.46	1.08	1.05	2.13
	Mean	0.88	7.07	0.51	1.01	1.00	2.00
	S.D.	0.08	0.75	0.07	0.06	0.06	0.11
Relative	1118	0.29	2.28	0.19	0.34	0.35	0.70
	1119	0.30	2.57	0.19	0.34	0.34	0.68
	1120	0.31	2.41	0.16	0.36	0.36	0.72
	1121	0.35	2.81	0.21	0.37	0.36	0.73
	1122	0.34	2.65	0.17	0.39	0.38	0.77
	Mean	0.32	2.54	0.18	0.36	0.36	0.72
	S.D.	0.03	0.21	0.02	0.02	0.01	0.03

Appendix 8-45 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of female rats (End of recovery)
Dose (mg/kg): 0

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	1118	39	40	79	45.1	35.6	80.7	615
	1119	38	43	81	63.1	51.6	114.7	630
	1120	30	34	64	48.4	34.0	82.4	535
	1121	34	38	72	43.5	45.2	88.7	648
	1122	27	30	57	30.0	30.4	60.4	646
	Mean	34	37	71	46.0	39.4	85.4	615
	S.D.	5	5	10	11.8	8.8	19.5	47
Relative	1118	14	14	28	16.1	12.7	28.8	220
	1119	12	14	26	20.3	16.6	36.9	203
	1120	12	13	25	18.8	13.2	31.9	207
	1121	13	14	27	16.3	16.9	33.2	243
	1122	10	11	21	10.9	11.1	22.0	235
	Mean	12	13	25	16.5	14.1	30.6	222
	S.D.	1	1	3	3.6	2.5	5.6	17

Appendix 8-46 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of female rats (End of recovery)
Dose (mg/kg): 1000

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)
Absolute	4118	269	1.88	16.1	11.0	9.9	20.9	258
	4119	264	2.03	15.6	12.7	10.8	23.5	186
	4120	251	1.96	13.3	10.7	9.4	20.1	186
	4121	256	2.03	17.6	7.1	7.8	14.9	224
	4122	270	1.91	14.2	8.7	9.2	17.9	410
	Mean	262	1.96	15.4	10.0	9.4	19.5	253
	S.D.	8	0.07	1.7	2.2	1.1	3.2	93
Relative	4118		0.70	6.0	4.1	3.7	7.8	96
	4119		0.77	5.9	4.8	4.1	8.9	70
	4120		0.78	5.3	4.3	3.7	8.0	74
	4121		0.79	6.9	2.8	3.0	5.8	88
	4122		0.71	5.3	3.2	3.4	6.6	152
	Mean		0.75	5.9	3.8	3.6	7.4	96
	S.D.		0.04	0.7	0.8	0.4	1.2	33

Appendix 8-47 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of female rats (End of recovery)
Dose (mg/kg): 1000

	Animal number	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	4118	0.91	6.47	0.55	0.89	0.91	1.80
	4119	0.81	5.97	0.39	0.88	0.91	1.79
	4120	0.79	6.44	0.36	0.92	0.90	1.82
	4121	0.88	6.57	0.35	0.93	0.99	1.92
	4122	0.80	5.98	0.53	0.89	0.94	1.83
	Mean	0.84	6.29	0.44	0.90	0.93	1.83
	S.D.	0.05	0.29	0.10	0.02	0.04	0.05
Relative	4118	0.34	2.41	0.20	0.33	0.34	0.67
	4119	0.31	2.26	0.15	0.33	0.34	0.68
	4120	0.31	2.57	0.14	0.37	0.36	0.73
	4121	0.34	2.57	0.14	0.36	0.39	0.75
	4122	0.30	2.21	0.20	0.33	0.35	0.68
	Mean	0.32	2.40	0.17	0.34	0.36	0.70
	S.D.	0.02	0.17	0.03	0.02	0.02	0.04

Appendix 8-48 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual organ weight of female rats (End of recovery)
Dose (mg/kg): 1000

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	4118	40	37	77	39.4	36.7	76.1	639
	4119	30	35	65	30.8	30.7	61.5	418
	4120	32	34	66	35.9	35.7	71.6	499
	4121	32	35	67	45.4	32.0	77.4	556
	4122	32	34	66	35.1	41.0	76.1	517
	Mean	33	35	68	37.3	35.2	72.5	526
	S.D.	4	1	5	5.5	4.1	6.6	81
Relative	4118	15	14	29	14.6	13.6	28.3	238
	4119	11	13	25	11.7	11.6	23.3	158
	4120	13	14	26	14.3	14.2	28.5	199
	4121	13	14	26	17.7	12.5	30.2	217
	4122	12	13	24	13.0	15.2	28.2	191
	Mean	13	14	26	14.3	13.4	27.7	201
	S.D.	1	1	2	2.2	1.4	2.6	30

Appendix 9-1(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1001 Male 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Parathyroid, Pancreas, Pituitary
Prostate, Salivary gland,submandibular, Sciatic nerve, Stomach
Skeletal muscle,femoral, Seminal vesicle(coagulation gland), Spinal cord,thoracic, Testis
Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-2(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1002 Male 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Heart	Cell infiltration: minimal, focal, mononuclear
Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal
Prostate	Cell infiltration: minimal, inflammatory acinar
Spleen	Hematopoiesis,extramedullary: minimal
Skeletal muscle,femoral	Degeneration,muscular: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Epididymis, Eye
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Sciatic nerve, Stomach, Seminal vesicle(coagulation gland)
Spinal cord,thoracic, Testis, Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-3(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1003 Male 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal Mineralization,papillary: minimal
Lung(bronchus)	Aggregation,macrophage: minimal
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Liver, Parathyroid, Pancreas, Pituitary, Prostate
Salivary gland,submandibular, Sciatic nerve, Stomach, Skeletal muscle,femoral
Seminal vesicle(coagulation gland), Spinal cord,thoracic, Testis, Thymus, Trachea, Thyroid
Urinary bladder

Appendix 9-4(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1004 Male 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Vacuolation,hepatocyte,periportal: minimal Microgranuloma: minimal
Prostate	Cell infiltration: mild, lymphocytic interstitial
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Parathyroid
Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve, Stomach
Skeletal muscle,femoral, Seminal vesicle(coagulation gland), Spinal cord,thoracic, Testis
Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-5(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1005 Male 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Vacuolation,hepatocyte,periportal: minimal Microgranuloma: minimal
Lung(bronchus)	Aggregation,macrophage: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Parathyroid, Pancreas
Pituitary, Prostate, Salivary gland,submandibular, Sciatic nerve, Spleen
Stomach, Skeletal muscle,femoral, Seminal vesicle(coagulation gland), Spinal cord,thoracic
Testis, Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-6(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1006 Male 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-7(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1007 Male 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-8(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1008 Male 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-9(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1009 Male 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-10(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1010 Male 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-11(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1011 Male 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-12(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1012 Male 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-13(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2001 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

Stomach	Focus,raised,forestomach: 1 present 2x2x1mm
Other tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-14(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2002 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-15(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2003 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

Epididymis	Nodule: 1 present, right cauda
Other tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-16(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2004 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal
Pituitary	Cyst: minimal pars diatalis
Prostate	Cell infiltration: minimal, interstitial lymphocytic
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Parathyroid, Pancreas
Salivary gland,submandibular, Sciatic nerve, Stomach, Skeletal muscle,femoral
Seminal vesicle(coagulation gland), Spinal cord,thoracic, Testis, Thymus, Trachea, Thyroid
Urinary bladder

Appendix 9-17(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2005 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-18(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2006 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

Lung(bronchus)	Focus,dark red: 1 present 2x2mm
Other tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-19(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2007 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

Testis	Small: mild, bilateral
Other tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-20(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2008 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-21(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2009 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-22(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2010 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-23(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2011 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-24(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2012 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-25(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3001 Male 300 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-26(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3002 Male 300 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-27(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3003 Male 300 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-28(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3004 Male 300 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-29(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3005 Male 300 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-30(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3006 Male 300 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-31(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3007 Male 300 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-32(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3008 Male 300 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-33(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3009 Male 300 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-34(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3010 Male 300 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-35(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3011 Male 300 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-36(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3012 Male 300 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-37(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4001 Male 1000 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Prostate	Cell infiltration: minimal, lymphocytic interstitial
Spleen	Hematopoiesis,extramedullary: minimal
Testis	Atrophy,seminiferous tubular: minimal, unilateral

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Parathyroid
Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve, Stomach
Skeletal muscle,femoral, Seminal vesicle(coagulation gland), Spinal cord,thoracic, Thymus
Trachea, Thyroid, Urinary bladder

Appendix 9-38(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4002 Male 1000 mg/kg Day 43 End of administration period (D42)

Gross pathology:

Kidney	Nodule: 1 present, right 30x20x20mm
Other tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal NEPHROBLASTOMA: 1 present
Liver	Microgranuloma: minimal
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Parathyroid, Pancreas, Pituitary
Prostate, Salivary gland,submandibular, Sciatic nerve, Stomach
Skeletal muscle,femoral, Seminal vesicle(coagulation gland), Spinal cord,thoracic, Testis
Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-39(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4003 Male 1000 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal with urinary cast
Lung(bronchus)	Aggregation,macrophage: minimal
Prostate	Cell infiltration: minimal, lymphocytic interstitial inflammatory, acinar

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Liver, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Sciatic nerve, Spleen, Stomach
Skeletal muscle,femoral, Seminal vesicle(coagulation gland), Spinal cord,thoracic, Testis
Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-40(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4004 Male 1000 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Heart	Cell infiltration: minimal, focal, mononuclear
Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Epididymis, Eye
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Parathyroid, Pancreas, Pituitary
Prostate, Salivary gland,submandibular, Sciatic nerve, Stomach
Skeletal muscle,femoral, Seminal vesicle(coagulation gland), Spinal cord,thoracic, Testis
Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-41(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4005 Male 1000 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Heart	Cell infiltration: minimal, focal, mononuclear
Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal
Prostate	Cell infiltration: minimal, lymphocytic interstitial inflammatory, acinar
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Epididymis, Eye
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Sciatic nerve, Stomach, Skeletal muscle,femoral
Seminal vesicle(coagulation gland), Spinal cord,thoracic, Testis, Thymus, Trachea, Thyroid
Urinary bladder

Appendix 9-42(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4006 Male 1000 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-43(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4007 Male 1000 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-44(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4008 Male 1000 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-45(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4009 Male 1000 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-46(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4010 Male 1000 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-47(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4011 Male 1000 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-48(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4012 Male 1000 mg/kg Day 57 End of recovery period

Gross pathology:

Lung(bronchus)	Focus,dark red: 1 present 2x3mm
Other tissues	Not remarkable

Histopathology:

Lung(bronchus)	Cell infiltration: minimal, focal, perivascular alveolar

Appendix 9-49(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1101 Female 0 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Spleen	Hematopoiesis,extramedullary: mild

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-50(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1102 Female 0 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Spleen	Hematopoiesis,extramedullary: mild

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-51(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1103 Female 0 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Spleen	Hematopoiesis,extramedullary: mild

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-52(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1104 Female 0 mg/kg Day 45 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-53(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1105 Female 0 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Mineralization,papillary: minimal
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Sciatic nerve, Stomach
Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-54(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1106 Female 0 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-55(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1107 Female 0 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-56(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1108 Female 0 mg/kg Day 43 End of administration period (L4)

Gross pathology:

Stomach	Focus,dark red,glandular stomach: 1 present 6x2mm
Other tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal
Spleen	Hematopoiesis,extramedullary: mild
Stomach	Erosion,glandular stomach: mild

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Sciatic nerve, Skeletal muscle,femoral
Spinal cord,thoracic, Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-57(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1109 Female 0 mg/kg Day 45 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-58(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1110 Female 0 mg/kg Day 46 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-59(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1111 Female 0 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-60(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1112 Female 0 mg/kg Day 49 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-61(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1113 Female 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea
Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-62(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1114 Female 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Pituitary	Cyst: minimal pars distalis

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Ovary
Parathyroid, Pancreas, Salivary gland,submandibular, Sciatic nerve, Spleen
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-63(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1115 Female 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal
Pituitary	Cyst: minimal pars distalis
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Ovary, Parathyroid, Pancreas
Salivary gland,submandibular, Sciatic nerve, Stomach, Skeletal muscle,femoral
Spinal cord,thoracic, Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-64(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1116 Female 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Parathyroid	No sample
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus), Ovary
Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve, Stomach
Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-65(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1117 Female 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-66(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1118 Female 0 mg/kg Day 57 End of recovery period

Gross pathology:

Kidney	Cyst: 1 present, left 1x1x1mm
Other tissues	Not remarkable

Histopathology:

Kidney	Cyst: mild

Appendix 9-67(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1119 Female 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-68(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1120 Female 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-69(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1121 Female 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-70(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1122 Female 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-71(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2101 Female 100 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-72(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2102 Female 100 mg/kg Day 46 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-73(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2103 Female 100 mg/kg Day 45 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-74(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2104 Female 100 mg/kg Day 41 Undelivered

Gross pathology:

All tissues	Not remarkable

Histopathology:

Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-75(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2105 Female 100 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-76(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2106 Female 100 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-77(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2107 Female 100 mg/kg Day 40 All littermates died

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Mineralization,papillary: minimal
Spleen	Hematopoiesis,extramedullary: mild

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Sciatic nerve, Stomach
Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-78(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2108 Female 100 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-79(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2109 Female 100 mg/kg Day 45 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-80(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2110 Female 100 mg/kg Day 45 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-81(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2111 Female 100 mg/kg Day 46 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-82(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2112 Female 100 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-83(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3101 Female 300 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-84(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3102 Female 300 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-85(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3103 Female 300 mg/kg Day 46 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-86(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3104 Female 300 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-87(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3105 Female 300 mg/kg Day 45 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-88(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3106 Female 300 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-89(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3107 Female 300 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-90(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3108 Female 300 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-91(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3109 Female 300 mg/kg Day 46 End of administration period (L4)

Gross pathology:

Stomach	Focus,dark red,glandular stomach: 1 present 1x1mm
Other tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-92(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3110 Female 300 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-93(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3111 Female 300 mg/kg Day 46 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-94(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3112 Female 300 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-95(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4101 Female 1000 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-96(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4102 Female 1000 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Spleen	Hematopoiesis,extramedullary: mild

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-97(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4103 Female 1000 mg/kg Day 42 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Spleen	Hematopoiesis,extramedullary: mild

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-98(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4104 Female 1000 mg/kg Day 45 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-99(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4105 Female 1000 mg/kg Day 45 End of administration period (L4)

Gross pathology:

Stomach	Focus,dark red,glandular stomach: 1 present 1x1mm
Other tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-100(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4106 Female 1000 mg/kg Day 42 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal
Spleen	Hematopoiesis,extramedullary: mild

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Sciatic nerve, Stomach
Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-101(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4107 Female 1000 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-102(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4108 Female 1000 mg/kg Day 46 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-103(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4109 Female 1000 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal
Spleen	Hematopoiesis,extramedullary: mild

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Sciatic nerve, Stomach
Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-104(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4110 Female 1000 mg/kg Day 45 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-105(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4111 Female 1000 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-106(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4112 Female 1000 mg/kg Day 46 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-107(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4113 Female 1000 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea
Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-108(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4114 Female 1000 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Lung(bronchus)	Aggregation,macrophage: minimal
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Sciatic nerve, Stomach
Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-109(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4115 Female 1000 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Sciatic nerve, Stomach
Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-110(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4116 Female 1000 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea
Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-111(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4117 Female 1000 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea
Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-112(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4118 Female 1000 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-113(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4119 Female 1000 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-114(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4120 Female 1000 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-115(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4121 Female 1000 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-116(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4122 Female 1000 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 10-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual estrous cycle in female rats during the pre-mating period (Main group)
Dose (mg/kg): 0

Animal number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)	Count of estrus	Mean duration of cycles	Index of animals with abnormal estrous cycle (%)
1101	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
1102	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
1103	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
1104	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
1105	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
1106	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
1107	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
1108	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
1109	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
1110	D	D	P	E	M	D	D	P	E	M	D	D	P	E	M	3	5.0	
1111	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
1112	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
Total(%)b)																		0/12(0.0)
Mean																3.7	4.1	
S.D.																0.5	0.3	

P: Proestrus E: Estrus M: Metestrus D: Diestrus
a): Day of sampling
b): (No. of animals with abnormal estrous cycle / No. of animals examined)×100

Appendix 10-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual estrous cycle in female rats during the pre-mating period (Main group)
Dose (mg/kg): 100

Animal number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)	Count of estrus	Mean duration of cycles	Index of animals with abnormal estrous cycle (%)
2101	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
2102	E	M	D	P	E	E	M	D	P	E	E	M	D	P	E	4	4.7	
2103	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
2104	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
2105	P	E	M	D	D	P	E	M	D	D	P	E	M	D	D	3	5.0	
2106	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
2107	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
2108	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
2109	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
2110	D	P	E	E	M	D	P	E	E	M	D	P	E	E	M	3	5.0	
2111	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0	
2112	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
Total(%)b)																		0/12(0.0)
Mean																3.6	4.2	
S.D.																0.5	0.4	

P: Proestrus E: Estrus M: Metestrus D: Diestrus
a): Day of sampling
b): (No. of animals with abnormal estrous cycle / No. of animals examined)×100

Appendix 10-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual estrous cycle in female rats during the pre-mating period (Main group)
Dose (mg/kg): 300

Animal number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)	Count of estrus	Mean duration of cycles	Index of animals with abnormal estrous cycle (%)
3101	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
3102	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
3103	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0	
3104	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
3105	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
3106	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
3107	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
3108	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
3109	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0	
3110	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
3111	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0	
3112	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
Total(%)b)																		0/12(0.0)
Mean																3.7	4.0	
S.D.																0.5	0.0	

P: Proestrus E: Estrus M: Metestrus D: Diestrus
a): Day of sampling
b): (No. of animals with abnormal estrous cycle / No. of animals examined)×100

Appendix 10-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual estrous cycle in female rats during the pre-mating period (Main group)
Dose (mg/kg): 1000

Animal number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)	Count of estrus	Mean duration of cycles	Index of animals with abnormal estrous cycle (%)
4101	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
4102	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
4103	D	P	E	M	D	P	E	M	D	P	E	M	D	D	P	3	4.0	
4104	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
4105	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
4106	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
4107	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
4108	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0	
4109	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
4110	D	P	E	M	D	D	P	E	M	D	P	E	E	M	D	3	4.5	
4111	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
4112	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0	
Total(%)b)																		0/12(0.0)
Mean																3.6	4.0	
S.D.																0.5	0.1	

P: Proestrus E: Estrus M: Metestrus D: Diestrus
a): Day of sampling
b): (No. of animals with abnormal estrous cycle / No. of animals examined)×100

Appendix 11-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual mating and fertility of animals
Dose (mg/kg): 0

Pairing number		Copulated or	Days until	Pregnant or
Male	Female	not copulated	copulation	non-pregnant
1001	1101	C	2	P
1002	1102	C	3	P
1003	1103	C	2	P
1004	1104	C	3	P
1005	1105	C	1	P
1006	1106	C	2	P
1007	1107	C	2	P
1008	1108	C	1	P
1009	1109	C	3	P
1010	1110	C	4	P
1011	1111	C	2	P
1012	1112	C	7	P

C: Copulated P: Pregnant

Appendix 11-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual mating and fertility of animals
Dose (mg/kg): 100

Pairing number		Copulated or	Days until	Pregnant or
Male	Female	not copulated	copulation	non-pregnant
2001	2101	C	3	P
2002	2102	C	4	P
2003	2103	C	3	P
2004	2104	C	1	NP
2005	2105	C	2	P
2006	2106	C	2	P
2007	2107	C	1	P
2008	2108	C	1	P
2009	2109	C	3	P
2010	2110	C	3	P
2011	2111	C	4	P
2012	2112	C	2	P

C: Copulated P: Pregnant NP: Non-pregnant

Appendix 11-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual mating and fertility of animals
Dose (mg/kg): 300

Pairing number		Copulated or	Days until	Pregnant or
Male	Female	not copulated	copulation	non-pregnant
3001	3101	C	1	P
3002	3102	C	1	P
3003	3103	C	4	P
3004	3104	C	1	P
3005	3105	C	2	P
3006	3106	C	2	P
3007	3107	C	2	P
3008	3108	C	1	P
3009	3109	C	4	P
3010	3110	C	3	P
3011	3111	C	4	P
3012	3112	C	2	P

C: Copulated P: Pregnant

Appendix 11-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual mating and fertility of animals
Dose (mg/kg): 1000

Pairing number		Copulated or	Days until	Pregnant or
Male	Female	not copulated	copulation	non-pregnant
4001	4101	C	1	P
4002	4102	C	3	P
4003	4103	C	1	P
4004	4104	C	3	P
4005	4105	C	3	P
4006	4106	C	1	P
4007	4107	C	2	P
4008	4108	C	4	P
4009	4109	C	1	P
4010	4110	C	3	P
4011	4111	C	2	P
4012	4112	C	4	P

C: Copulated P: Pregnant

Appendix 12-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Delivery data on dams
Dose (mg/kg): 0

Dam number	Gestation length in days	No. of corpora lutea	No. of implantation sites	Implantation index % a)	Delivery index % b)	No. of stillborns (%)c)	No. of liveborns	External d) abnormalities(%)e)
1101	22	14	13	92.9	100.0	0(0.0)	13	0(0.0)
1102	21	16	15	93.8	93.3	0(0.0)	14	0(0.0)
1103	22	17	15	88.2	100.0	0(0.0)	15	0(0.0)
1104	22	17	16	94.1	87.5	0(0.0)	14	0(0.0)
1105	22	16	15	93.8	86.7	0(0.0)	13	0(0.0)
1106	22	14	13	92.9	92.3	0(0.0)	12	0(0.0)
1107	22	15	15	100.0	86.7	0(0.0)	13	0(0.0)
1108	22	15	15	100.0	100.0	1(6.7)	14	0(0.0)
1109	22	17	16	94.1	100.0	0(0.0)	16	0(0.0)
1110	22	21	14	66.7	100.0	0(0.0)	14	0(0.0)
1111	22	16	16	100.0	93.8	0(0.0)	15	0(0.0)
1112	22	16	15	93.8	100.0	0(0.0)	15	0(0.0)
Total		194	178			1	168	0
Mean	21.9	16.2	14.8	92.5	95.0	(0.6)	14.0	(0.0)
S.D.	0.3	1.9	1.0	8.9	5.7	(1.9)	1.1	(0.0)

a): (No. of implantation sites / No. of corpora lutea)×100
b): (No. of delivered pups / No. of implantation sites)×100
c): (No. of stillborns / No. of delivered pups)×100
d): No. of delivered pups with external abnormalities
e): (No. of delivered pups with external abnormalities / No. of delivered pups)×100

Appendix 12-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Delivery data on dams
Dose (mg/kg): 100

Dam number	Gestation length in days	No. of corpora lutea	No. of implantation sites	Implantation index % a)	Delivery index % b)	No. of stillborns (%)c)	No. of liveborns	External d) abnormalities(%)e)
2101	21	13	13	100.0	100.0	0(0.0)	13	0(0.0)
2102	22	17	15	88.2	100.0	0(0.0)	15	0(0.0)
2103	22	17	15	88.2	93.3	0(0.0)	14	0(0.0)
2104	Non-pregnant							
2105	22	15	14	93.3	92.9	0(0.0)	13	0(0.0)
2106	22	16	14	87.5	92.9	1(7.7)	12	0(0.0)
2107	23	11	2	18.2	100.0	0(0.0)	2	0(0.0)
2108	22	17	16	94.1	93.8	0(0.0)	15	0(0.0)
2109	22	13	13	100.0	100.0	0(0.0)	13	0(0.0)
2110	22	20	16	80.0	75.0	0(0.0)	12	0(0.0)
2111	22	16	15	93.8	100.0	1(6.7)	14	0(0.0)
2112	22	17	17	100.0	94.1	0(0.0)	16	0(0.0)
Total		172	150			2	139	0
Mean	22.0	15.6	13.6	85.8	94.7	(1.3)	12.6	(0.0)
S.D.	0.4	2.5	4.1	23.3	7.3	(2.9)	3.7	(0.0)

a): (No. of implantation sites / No. of corpora lutea)×100
b): (No. of delivered pups / No. of implantation sites)×100
c): (No. of stillborns / No. of delivered pups)×100
d): No. of delivered pups with external abnormalities
e): (No. of delivered pups with external abnormalities / No. of delivered pups)×100

Appendix 12-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Delivery data on dams
Dose (mg/kg): 300

Dam number	Gestation length in days	No. of corpora lutea	No. of implantation sites	Implantation index % a)	Delivery index % b)	No. of stillborns (%)c)	No. of liveborns	External d) abnormalities(%)e)
3101	22	14	13	92.9	84.6	0(0.0)	11	0(0.0)
3102	22	15	15	100.0	100.0	0(0.0)	15	0(0.0)
3103	22	16	16	100.0	100.0	0(0.0)	16	0(0.0)
3104	22	14	13	92.9	100.0	0(0.0)	13	0(0.0)
3105	23	15	14	93.3	85.7	5(41.7)	7	0(0.0)
3106	21	14	13	92.9	100.0	0(0.0)	13	0(0.0)
3107	22	13	13	100.0	100.0	0(0.0)	13	0(0.0)
3108	22	16	16	100.0	93.8	0(0.0)	15	0(0.0)
3109	22	17	14	82.4	100.0	0(0.0)	14	0(0.0)
3110	21	14	14	100.0	100.0	0(0.0)	14	0(0.0)
3111	22	17	14	82.4	100.0	0(0.0)	14	0(0.0)
3112	22	16	15	93.8	100.0	0(0.0)	15	0(0.0)
Total		181	170			5	160	0
Mean	21.9	15.1	14.2	94.2	97.0	(3.5)	13.3	(0.0)
S.D.	0.5	1.3	1.1	6.4	5.8	(12.0)	2.4	(0.0)

a): (No. of implantation sites / No. of corpora lutea)×100
b): (No. of delivered pups / No. of implantation sites)×100
c): (No. of stillborns / No. of delivered pups)×100
d): No. of delivered pups with external abnormalities
e): (No. of delivered pups with external abnormalities / No. of delivered pups)×100

Appendix 12-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Delivery data on dams
Dose (mg/kg): 1000

Dam number	Gestation length in days	No. of corpora lutea	No. of implantation sites	Implantation index % a)	Delivery index % b)	No. of stillborns (%)c)	No. of liveborns	External d) abnormalities(%)e)
4101	22	15	15	100.0	100.0	0(0.0)	15	0(0.0)
4102	21	16	15	93.8	93.3	0(0.0)	14	0(0.0)
4103	21	8	4	50.0	75.0	0(0.0)	3	0(0.0)
4104	22	16	16	100.0	87.5	0(0.0)	14	0(0.0)
4105	22	15	13	86.7	100.0	0(0.0)	13	0(0.0)
4106	21	15	14	93.3	92.9	0(0.0)	13	0(0.0)
4107	22	17	16	94.1	93.8	2(13.3)	13	0(0.0)
4108	22	15	14	93.3	85.7	0(0.0)	12	0(0.0)
4109	22	14	14	100.0	92.9	0(0.0)	13	0(0.0)
4110	22	20	16	80.0	100.0	0(0.0)	16	0(0.0)
4111	22	17	16	94.1	93.8	0(0.0)	15	0(0.0)
4112	22	16	14	87.5	100.0	0(0.0)	14	0(0.0)
Total		184	167			2	155	0
Mean	21.8	15.3	13.9	89.4	92.9	(1.1)	12.9	(0.0)
S.D.	0.5	2.8	3.3	13.8	7.4	(3.8)	3.3	(0.0)

a): (No. of implantation sites / No. of corpora lutea)×100
b): (No. of delivered pups / No. of implantation sites)×100
c): (No. of stillborns / No. of delivered pups)×100
d): No. of delivered pups with external abnormalities
e): (No. of delivered pups with external abnormalities / No. of delivered pups)×100

Appendix 13-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual viability index of pups
Dose (mg/kg): 0

Dam number	No. of live-borns	No. of delivered pups	Live birth index % a)	No. of live pups		Viability index on postnatal day 4 % b)
				Day 0	Day 4	
1101	13	13	100.0	13	13	100.0
1102	14	14	100.0	14	13	92.9
1103	15	15	100.0	15	15	100.0
1104	14	14	100.0	14	14	100.0
1105	13	13	100.0	13	13	100.0
1106	12	12	100.0	12	12	100.0
1107	13	13	100.0	13	13	100.0
1108	14	15	93.3	14	14	100.0
1109	16	16	100.0	16	16	100.0
1110	14	14	100.0	14	14	100.0
1111	15	15	100.0	15	15	100.0
1112	15	15	100.0	15	15	100.0
Total	168	169		168	167	
Mean	14.0	14.1	99.4	14.0	13.9	99.4
S.D.	1.1	1.2	1.9	1.1	1.2	2.0

a): (No. of liveborns / No. of delivered pups)×100
b): (No. of live pups on postnatal day 4 / No. of liveborns)×100

Appendix 13-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual viability index of pups
Dose (mg/kg): 100

Dam number	No. of live-borns	No. of delivered pups	Live birth index % a)	No. of live pups		Viability index on postnatal day 4 % b)
				Day 0	Day 4	
2101	13	13	100.0	13	13	100.0
2102	15	15	100.0	15	15	100.0
2103	14	14	100.0	14	14	100.0
2104	Non-pregnant					
2105	13	13	100.0	13	12	92.3
2106	12	13	92.3	12	12	100.0
2107	2	2	100.0	2	0	0.0
2108	15	15	100.0	15	15	100.0
2109	13	13	100.0	13	13	100.0
2110	12	12	100.0	12	12	100.0
2111	14	15	93.3	14	14	100.0
2112	16	16	100.0	16	16	100.0
Total	139	141		139	136	
Mean	12.6	12.8	98.7	12.6	12.4	90.2
S.D.	3.7	3.8	2.9	3.7	4.3	30.0

a): (No. of liveborns / No. of delivered pups)×100
b): (No. of live pups on postnatal day 4 / No. of liveborns)×100

Appendix 13-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual viability index of pups
Dose (mg/kg): 300

Dam number	No. of live-borns	No. of delivered pups	Live birth index % a)	No. of live pups		Viability index on postnatal day 4 % b)
				Day 0	Day 4	
3101	11	11	100.0	11	11	100.0
3102	15	15	100.0	15	15	100.0
3103	16	16	100.0	16	16	100.0
3104	13	13	100.0	13	13	100.0
3105	7	12	58.3	7	7	100.0
3106	13	13	100.0	13	13	100.0
3107	13	13	100.0	13	13	100.0
3108	15	15	100.0	15	15	100.0
3109	14	14	100.0	14	13	92.9
3110	14	14	100.0	14	14	100.0
3111	14	14	100.0	14	14	100.0
3112	15	15	100.0	15	15	100.0
Total	160	165		160	159	
Mean	13.3	13.8	96.5	13.3	13.3	99.4
S.D.	2.4	1.4	12.0	2.4	2.4	2.0

a): (No. of liveborns / No. of delivered pups)×100
b): (No. of live pups on postnatal day 4 / No. of liveborns)×100

Appendix 13-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual viability index of pups
Dose (mg/kg): 1000

Dam number	No. of live-borns	No. of delivered pups	Live birth index % a)	No. of live pups		Viability index on postnatal day 4 % b)
				Day 0	Day 4	
4101	15	15	100.0	15	15	100.0
4102	14	14	100.0	14	13	92.9
4103	3	3	100.0	3	2	66.7
4104	14	14	100.0	14	14	100.0
4105	13	13	100.0	13	13	100.0
4106	13	13	100.0	13	12	92.3
4107	13	15	86.7	13	13	100.0
4108	12	12	100.0	12	12	100.0
4109	13	13	100.0	13	13	100.0
4110	16	16	100.0	16	16	100.0
4111	15	15	100.0	15	15	100.0
4112	14	14	100.0	14	14	100.0
Total	155	157		155	152	
Mean	12.9	13.1	98.9	12.9	12.7	96.0
S.D.	3.3	3.4	3.8	3.3	3.6	9.7

a): (No. of liveborns / No. of delivered pups)×100
b): (No. of live pups on postnatal day 4 / No. of liveborns)×100

Appendix 14-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual sex ratio of pups
Dose (mg/kg): 0

Dam number	Liveborns		Stillborns		Sex ratio of delivered pups a)	Sex ratio of liveborns b)	Postnatal day 4		Sex ratio of live pups on day 4 c)
	No. of males	No. of females	No. of males	No. of females			No. of males	No. of females	
1101	8	5	0	0	0.62	0.62	8	5	0.62
1102	7	7	0	0	0.50	0.50	7	6	0.54
1103	5	10	0	0	0.33	0.33	5	10	0.33
1104	5	9	0	0	0.36	0.36	5	9	0.36
1105	6	7	0	0	0.46	0.46	6	7	0.46
1106	4	8	0	0	0.33	0.33	4	8	0.33
1107	7	6	0	0	0.54	0.54	7	6	0.54
1108	8	6	0	1	0.53	0.57	8	6	0.57
1109	11	5	0	0	0.69	0.69	11	5	0.69
1110	4	10	0	0	0.29	0.29	4	10	0.29
1111	3	12	0	0	0.20	0.20	3	12	0.20
1112	10	5	0	0	0.67	0.67	10	5	0.67
Total	78	90	0	1			78	89	
Mean	6.5	7.5	0.0	0.1	0.46	0.46	6.5	7.4	0.47
S.D.	2.5	2.3	0.0	0.3	0.16	0.16	2.5	2.4	0.16

a): No. of delivered males / No. of delivered pups
b): No. of liveborn males / No. of liveborns
c): No. of live males on day 4 / No. of live pups on day 4

Appendix 14-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual sex ratio of pups
Dose (mg/kg): 100

Dam number	Liveborns		Stillborns		Sex ratio of delivered pups a)	Sex ratio of liveborns b)	Postnatal day 4		Sex ratio of live pups on day 4 c)
	No. of males	No. of females	No. of males	No. of females			No. of males	No. of females	
2101	4	9	0	0	0.31	0.31	4	9	0.31
2102	6	9	0	0	0.40	0.40	6	9	0.40
2103	3	11	0	0	0.21	0.21	3	11	0.21
2104	Non-pregnant								
2105	9	4	0	0	0.69	0.69	9	3	0.75
2106	6	6	0	1	0.46	0.50	6	6	0.50
2107d)	2	0	0	0	1.00	1.00			
2108	7	8	0	0	0.47	0.47	7	8	0.47
2109	5	8	0	0	0.38	0.38	5	8	0.38
2110	6	6	0	0	0.50	0.50	6	6	0.50
2111	7	7	0	1	0.47	0.50	7	7	0.50
2112	7	9	0	0	0.44	0.44	7	9	0.44
Total	62	77	0	2			60	76	
Mean	5.6	7.0	0.0	0.2	0.48	0.49	6.0	7.6	0.45
S.D.	2.0	3.0	0.0	0.4	0.21	0.21	1.7	2.2	0.14

a): No. of delivered males / No. of delivered pups
b): No. of liveborn males / No. of liveborns
c): No. of live males on day 4 / No. of live pups on day 4
d): All pups died on postnatal day 1.

Appendix 14-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual sex ratio of pups
Dose (mg/kg): 300

Dam number	Liveborns		Stillborns		Sex ratio of delivered pups a)	Sex ratio of liveborns b)	Postnatal day 4		Sex ratio of live pups on day 4 c)
	No. of males	No. of females	No. of males	No. of females			No. of males	No. of females	
3101	3	8	0	0	0.27	0.27	3	8	0.27
3102	6	9	0	0	0.40	0.40	6	9	0.40
3103	10	6	0	0	0.63	0.63	10	6	0.63
3104	7	6	0	0	0.54	0.54	7	6	0.54
3105	3	4	2	3	0.42	0.43	3	4	0.43
3106	5	8	0	0	0.38	0.38	5	8	0.38
3107	6	7	0	0	0.46	0.46	6	7	0.46
3108	7	8	0	0	0.47	0.47	7	8	0.47
3109	8	6	0	0	0.57	0.57	7	6	0.54
3110	9	5	0	0	0.64	0.64	9	5	0.64
3111	5	9	0	0	0.36	0.36	5	9	0.36
3112	8	7	0	0	0.53	0.53	8	7	0.53
Total	77	83	2	3			76	83	
Mean	6.4	6.9	0.2	0.3	0.47	0.47	6.3	6.9	0.47
S.D.	2.2	1.6	0.6	0.9	0.11	0.11	2.1	1.6	0.11

a): No. of delivered males / No. of delivered pups
b): No. of liveborn males / No. of liveborns
c): No. of live males on day 4 / No. of live pups on day 4

Appendix 14-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual sex ratio of pups
Dose (mg/kg): 1000

Dam number	Liveborns		Stillborns		Sex ratio of delivered pups a)	Sex ratio of liveborns b)	Postnatal day 4		Sex ratio of live pups on day 4 c)
	No. of males	No. of females	No. of males	No. of females			No. of males	No. of females	
4101	7	8	0	0	0.47	0.47	7	8	0.47
4102	5	9	0	0	0.36	0.36	5	8	0.38
4103	2	1	0	0	0.67	0.67	2	0	1.00
4104	4	10	0	0	0.29	0.29	4	10	0.29
4105	6	7	0	0	0.46	0.46	6	7	0.46
4106	10	3	0	0	0.77	0.77	10	2	0.83
4107	8	5	2	0	0.67	0.62	8	5	0.62
4108	6	6	0	0	0.50	0.50	6	6	0.50
4109	4	9	0	0	0.31	0.31	4	9	0.31
4110	10	6	0	0	0.63	0.63	10	6	0.63
4111	10	5	0	0	0.67	0.67	10	5	0.67
4112	7	7	0	0	0.50	0.50	7	7	0.50
Total	79	76	2	0			79	73	
Mean	6.6	6.3	0.2	0.0	0.53	0.52	6.6	6.1	0.56
S.D.	2.6	2.6	0.6	0.0	0.16	0.15	2.6	2.8	0.21

a): No. of delivered males / No. of delivered pups
b): No. of liveborn males / No. of liveborns
c): No. of live males on day 4 / No. of live pups on day 4

Appendix 15-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual body weight of pups
Dose (mg/kg): 0

Dam number	Male			Female		
	0	4a)	Gain	0	4a)	Gain
1101	6.9	11.3	4.4	6.5	10.5	4.0
1102	5.8	8.6	2.8	5.5	8.2	2.7
1103	6.9	10.5	3.6	6.4	10.4	4.0
1104	6.8	11.2	4.4	6.5	10.4	3.9
1105	6.7	10.8	4.1	6.2	9.8	3.6
1106	6.8	10.5	3.7	6.4	9.5	3.1
1107	7.1	10.9	3.8	6.8	10.5	3.7
1108	7.0	10.5	3.5	6.0	9.2	3.2
1109	6.3	8.2	1.9	5.9	7.4	1.5
1110	6.5	10.3	3.8	5.9	9.4	3.5
1111	6.9	11.3	4.4	6.4	10.9	4.5
1112	6.6	9.4	2.8	6.2	9.0	2.8
Mean	6.7	10.3	3.6	6.2	9.6	3.4
S.D.	0.4	1.0	0.8	0.4	1.0	0.8

Unit: g
a): Postnatal day

Appendix 15-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual body weight of pups
Dose (mg/kg): 100

Dam number	Male			Female		
	0	4a)	Gain	0	4a)	Gain
2101	6.5	10.3	3.8	6.1	9.3	3.2
2102	7.1	11.1	4.0	6.4	10.6	4.2
2103	6.4	9.4	3.0	6.1	9.3	3.2
2104	Non-pregnant					
2105	7.0	11.3	4.3	6.3	10.0	3.7
2106	7.1	11.5	4.4	6.6	11.2	4.6
2107	7.0	b)		c)		
2108	6.6	10.1	3.5	6.2	9.7	3.5
2109	6.1	9.6	3.5	5.9	9.4	3.5
2110	6.6	11.1	4.5	6.2	10.4	4.2
2111	6.3	9.9	3.6	6.1	9.6	3.5
2112	6.5	10.5	4.0	6.0	9.6	3.6
Mean	6.7	10.5	3.9	6.2	9.9	3.7
S.D.	0.3	0.7	0.5	0.2	0.6	0.5

Unit: g
a): Postnatal day
b): All male pups died.
c): No female pups were born.

Appendix 15-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual body weight of pups
Dose (mg/kg): 300

Dam number	Male			Female		
	0	4a)	Gain	0	4a)	Gain
3101	7.3	12.8	5.5	7.0	12.1	5.1
3102	6.4	9.3	2.9	6.2	8.9	2.7
3103	6.0	9.2	3.2	5.5	8.8	3.3
3104	6.8	10.5	3.7	6.5	10.1	3.6
3105	6.7	13.3	6.6	6.5	12.8	6.3
3106	6.2	9.1	2.9	5.9	8.7	2.8
3107	7.5	10.1	2.6	6.9	9.6	2.7
3108	6.8	9.9	3.1	6.8	9.4	2.6
3109	6.3	10.4	4.1	5.5	9.1	3.6
3110	6.0	9.1	3.1	5.8	8.7	2.9
3111	6.8	10.2	3.4	6.2	9.0	2.8
3112	7.0	10.3	3.3	6.7	10.2	3.5
Mean	6.7	10.4	3.7	6.3	9.8	3.5
S.D.	0.5	1.4	1.2	0.5	1.4	1.1

Unit: g
a): Postnatal day

Appendix 15-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual body weight of pups
Dose (mg/kg): 1000

Dam number	Male			Female		
	0	4a)	Gain	0	4a)	Gain
4101	6.6	9.7	3.1	5.9	8.8	2.9
4102	5.8	7.7	1.9	5.8	7.5	1.7
4103	7.0	9.6	2.6	4.6	b)	
4104	6.7	10.6	3.9	6.6	10.4	3.8
4105	7.1	10.9	3.8	6.5	9.6	3.1
4106	6.5	9.7	3.2	5.3	8.6	3.3
4107	6.7	10.1	3.4	6.2	9.8	3.6
4108	6.9	10.1	3.2	6.6	9.7	3.1
4109	7.6	11.2	3.6	7.2	10.9	3.7
4110	6.6	9.7	3.1	6.1	9.1	3.0
4111	6.5	9.6	3.1	6.3	9.0	2.7
4112	6.4	9.5	3.1	6.2	9.6	3.4
Mean	6.7	9.9	3.2	6.1	9.4	3.1
S.D.	0.4	0.9	0.5	0.7	0.9	0.6

Unit: g
a): Postnatal day
b): All female pups died.

Appendix 16-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual externally for gross abnormalities in dead pups
Dose (mg/kg): 0

Dam number	No. of pups examined Total (Male + Female)	Findings
1101	0	
1102	1 (0 + 1)	NAF
1103	0	
1104	0	
1105	0	
1106	0	
1107	0	
1108	0	
1109	0	
1110	0	
1111	0	
1112	0	

NAF: No abnormal findings

Appendix 16-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual externally for gross abnormalities in dead pups
Dose (mg/kg): 100

Dam number	No. of pups examined Total (Male + Female)	Findings
2101	0	
2102	0	
2103	0	
2104	Non-pregnant	
2105	0	
2106	0	
2107	1 (1 + 0)	NAF
2108	0	
2109	0	
2110	0	
2111	0	
2112	0	

NAF: No abnormal findings

Appendix 16-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual externally for gross abnormalities in dead pups
Dose (mg/kg): 300

Dam number	No. of pups examined Total (Male + Female)	Findings
3101	0	
3102	0	
3103	0	
3104	0	
3105	0	
3106	0	
3107	0	
3108	0	
3109	1 (1 + 0)	NAF
3110	0	
3111	0	
3112	0	

NAF: No abnormal findings

Appendix 16-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual externally for gross abnormalities in dead pups
Dose (mg/kg): 1000

Dam number	No. of pups examined Total (Male + Female)	Findings
4101	0	
4102	1 (0 + 1)	NAF
4103	0	
4104	0	
4105	0	
4106	1 (0 + 1)	NAF
4107	0	
4108	0	
4109	0	
4110	0	
4111	0	
4112	0	

NAF: No abnormal findings

Appendix 17-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual externally for gross abnormalities in pups on postnatal day 4
Dose (mg/kg): 0

Dam number	No. of pups examined Total (Male + Female)	Findings
1101	13 (8 + 5)	NAF
1102	13 (7 + 6)	NAF
1103	15 (5 + 10)	NAF
1104	14 (5 + 9)	NAF
1105	13 (6 + 7)	NAF
1106	12 (4 + 8)	NAF
1107	13 (7 + 6)	NAF
1108	14 (8 + 6)	NAF
1109	16 (11 + 5)	NAF
1110	14 (4 + 10)	NAF
1111	15 (3 + 12)	NAF
1112	15 (10 + 5)	NAF

NAF: No abnormal findings

Appendix 17-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual externally for gross abnormalities in pups on postnatal day 4
Dose (mg/kg): 100

Dam number	No. of pups examined Total (Male + Female)	Findings
2101	13 (4 + 9)	NAF
2102	15 (6 + 9)	NAF
2103	14 (3 + 11)	NAF
2104	Non-pregnant	
2105	12 (9 + 3)	NAF
2106	12 (6 + 6)	NAF
2107a)		
2108	15 (7 + 8)	NAF
2109	13 (5 + 8)	NAF
2110	12 (6 + 6)	NAF
2111	14 (7 + 7)	NAF
2112	16 (7 + 9)	NAF

NAF: No abnormal findings
a): All pups died on postnatal day 1.

Appendix 17-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual externally for gross abnormalities in pups on postnatal day 4
Dose (mg/kg): 300

Dam number	No. of pups examined Total	(Male	+ Female)	Findings
3101	11	3	8	NAF
3102	15	6	9	NAF
3103	16	10	6	NAF
3104	13	7	6	NAF
3105	7	3	4	NAF
3106	13	5	8	NAF
3107	13	6	7	NAF
3108	15	7	8	NAF
3109	13	7	6	NAF
3110	14	9	5	NAF
3111	14	5	9	NAF
3112	15	8	7	NAF

NAF: No abnormal findings

Appendix 17-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of (Z)-hex-3-enyl acetate by oral administration in rats
Individual externally for gross abnormalities in pups on postnatal day 4
Dose (mg/kg): 1000

Dam number	No. of pups examined Total	(Male	+ Female)	Findings
4101	15	7	8	NAF
4102	13	5	8	NAF
4103	2	2	0	NAF
4104	14	4	10	NAF
4105	13	6	7	NAF
4106	12	10	2	NAF
4107	13	8	5	NAF
4108	12	6	6	NAF
4109	13	4	9	NAF
4110	16	10	6	NAF
4111	15	10	5	NAF
4112	14	7	7	NAF

NAF: No abnormal findings

信頼性保証書（1/3）

試験番号　：　R-1100

試験表題　：　酢酸ヘキセニルのラットを用いた経口投与による
反復投与毒性・生殖発生毒性併合試験

本試験は以下に示す基準を遵守して実施されたことを保証致します。

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

なお、調査は下記の通り実施致しました。

2013年 3 月28日
株式会社ボゾリサーチセンター
信頼性保証部門 [redacted]

試験における調査

項　目	担当者	調　査　日	試験責任者及び運営管理者への報告日
試験計画書	[redacted]	2012年　9月　3日	2012年　9月　3日
作業予定表・コンピュータプロトコール		2012年　9月 10日	2012年　9月 11日
調製・保存（被験物質）		2012年　9月 20日	2012年　9月 21日
被験液の濃度確認		2012年　9月 20日	2012年　9月 21日
群分け		2012年　9月 24日	2012年　9月 24日
膣垢検査・体重・摂餌量測定・投与・一般状態の観察		2012年　9月 25日	2012年　9月 25日
詳細な一般状態の観察		2012年　9月 28日	2012年　9月 28日

R-1100

信頼性保証書（2/3）

項　目	担当者	調　査　日	試験責任者及び運営管理者への報告日
交配	[redacted]	2012年 10月 10日	2012年 10月 10日
尿検査（尿量・色調・定性・沈渣）		2012年 10月 30日	2012年 10月 30日
摂水量測定		2012年 10月 31日	2012年 10月 31日
分娩・哺育観察・体重測定		2012年 10月 31日	2012年 10月 31日
機能検査・握力測定・自発運動量測定		2012年 11月 2日	2012年 11月 5日
採血・剖検		2012年 11月 6日	2012年 11月 6日
病理組織学検査（切り出し）		2012年 11月 9日	2012年 11月 9日
被験物質の安定性		2012年 11月 26日	2012年 11月 27日
生データ（被験液の濃度確認、被験物質の安定性）		2013年 1月 28日	2013年 1月 29日
改善確認		2013年 1月 30日	2013年 1月 30日
測定レポート（被験液の濃度確認、被験物質の安定性：案）		2013年 1月 28日	2013年 1月 29日
改善確認		2013年 1月 30日	2013年 1月 30日
生データ（入荷～剖検・病理、飼育関係）		2013年 1月 28日 2013年 1月 29日 2013年 1月 30日 2013年 1月 31日 2013年 2月 1日 2013年 2月 4日	2013年 2月 5日
改善確認		2013年 2月 21日	2013年 2月 22日
図・表・付表		2013年 1月 28日 2013年 1月 29日 2013年 1月 30日 2013年 1月 31日 2013年 2月 4日 2013年 2月 5日	2013年 2月 5日
改善確認		2013年 2月 7日	2013年 2月 7日

R-1100

信頼性保証書（3/3）

項　目	担当者	調　査　日	試験責任者及び運営管理者への報告日
測定レポート（被験液の濃度確認、被験物質の安定性）	[redacted]	2013年　1月 30日	2013年　1月 30日
最終報告書草案		2013年　2月　5日	
		2013年　2月　6日	2013年　2月　6日
改善確認		2013年　2月　6日	2013年　2月　6日
生データ（被験物質関係）		2013年　3月 22日	2013年　3月 22日
最終報告書		2013年　3月 28日	2013年　3月 28日

プロセス調査

項　目	試験番号	担当者	調　査　日	試験責任者及び運営管理者への報告日
動物入荷	B-7293	[redacted]	2012年　8月 20日	2012年　8月 20日
検疫・馴化	B-7293		2012年　8月 20日	2012年　8月 20日
	B-7293		2012年　8月 25日	2012年　8月 27日
尿検査（浸透圧・電解質）	R-1100		2012年 10月 31日	2012年 10月 31日
血液学検査・血液化学検査	B-7321		2012年 10月　4日	
			2012年 10月　5日	2012年 10月　5日
病理組織学検査（包埋・薄切・染色）	B-7279		2012年 10月 10日	2012年 10月 10日
	B-7279		2012年 10月 12日	2012年 10月 12日
	B-7279		2012年 10月 22日	2012年 10月 22日