最　終　報　告　書

（訂正版）

メチル（2-ペンチル-3-オキソ-シクロペンチル）アセテート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

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

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

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

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2.　試験実施概要

2.1　試験番号

R-1106

2.2　試験表題

メチル（2-ペンチル-3-オキソ-シクロペンチル）アセテート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 Methyl (2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats）

2.3　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。

2.4　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

2.5　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

2.6　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

2.7　被験物質

製造者	:	Angene International Limited.
名称	:	メチル（2-ペンチル-3-オキソ-シクロペンチル）アセテート
別名	:	ジヒドロジャスモン酸メチル
CAS 番号	:	24851-98-7
官報公示整理番号	:	3-3309
入手日	:	2012 年 7 月 30 日

2.8　試験日程

試験開始日　：　2012 年 10 月　5 日
被験物質出庫日　：　2012 年 10 月 25 日
動物入荷日　：　2012 年 10 月 10 日
実験開始日（投与開始日）
　：　2012 年 10 月 30 日
交配開始日　：　2012 年 11 月 13 日
分娩開始日　：　2012 年 12 月　5 日
母動物剖検開始日　：　2012 年 12 月 10 日
投与終了剖検日　：　2012 年 12 月 11 日　（雄及び非交配群）
回復開始日　：　2012 年 12 月 11 日
回復終了剖検日　：　2012 年 12 月 25 日
動物試験終了日　：　2012 年 12 月 25 日
実験終了日（病理組織学検査終了日）
　：　2013 年　2 月　8 日
試験終了日　：　2013 年　3 月 28 日

2.9　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]

2.10　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]

2.11　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。

2.12　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

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。

2.13　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。

2.14　試験責任者の記名・なつ印

[redacted]　2013 年 9 月 10 日 [redacted]

3.　要約

メチル（2-ペンチル-3-オキソ-シクロペンチル）アセテートをコーン油で希釈し、100、300 及び 1000 mg/kg/day の投与量で 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）、交配群雌には交配前 14 日間に加え交配期間及び妊娠期間を通して授乳 4 日まで（41~46 日間）、非交配群雌には 42 日間強制経口投与し、反復投与毒性及び生殖発生毒性を検討した。更に、対照群及び 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。なお、対照群には媒体であるコーン油を投与した。

3.1　反復投与毒性

いずれの投与群においても死亡動物はみられず、一般状態、機能検査、握力及び自発運動量には被験物質投与の影響は認められなかった。

1000 mg/kg 投与群において、雌雄で少数例に流涎が散見され、雄で投与初期に一過性の摂餌量低値を伴った体重増加抑制がみられ、交配群雌の妊娠期間中及び非交配群雌の投与期間中に体重増加抑制が認められた。雌雄で摂餌量高値が散見され、雄及び非交配群雌の摂水量及び尿量に高値、非交配群雌の尿浸透圧に低値が認められた。非交配群雌の赤血球数、ヘモグロビン量及びヘマトクリット値に低値、雄の ALP に高値、交配群雌の総コレステロールに高値、グルコースに低値、非交配群雌の ALT、総コレステロール、トリグリセライド及びリン脂質に高値、グルコースに低値が認められた。雄、交配群雌及び非交配群雌で肝臓に重量高値及び小葉中心性肝細胞肥大が、非交配群雌で腎臓に重量高値、交配群雌で腎臓に白色巣及び限局性の尿細管拡張がみられた。

300 mg/kg 投与群において、雄及び交配群雌で肝臓に重量高値及び小葉中心性肝細胞肥大がみられた。

14 日間の投与の休止により投与期間中にみられた変化は、消失するか、頻度及び程度が軽減したことから回復性がみられた。

3.2　生殖発生毒性

1000 mg/kg 投与群で性周期異常、分娩時間の延長傾向、分娩率（着床痕数に対する娩出された総児数の百分率）の低値傾向がみられ、生後 0 日の雌雄体重に低値が認められた。

その他、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雌雄動物における反復投与

毒性に対する無影響量及び無毒性量は雌雄とも 100 mg/kg と判断した。また、雄親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、雌親動物及び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 300 mg/kg と判断した。

4.　緒言

厚生労働省医薬食品局審査管理課化学物質安全対策室の委託により、メチル（2-ペンチル-3-オキソ-シクロペンチル）アセテートのラットを用いた経口投与による反復投与毒性･生殖発生毒性併合試験を実施したので、その成績を報告する。

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

4.1　GLP

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

4.2　毒性試験ガイドライン

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

4.3　動物の福祉

- 「動物の愛護及び管理に関する法律」
  （昭和 48 年 10 月 1 日法律第 105 号、最終改正：平成 23 年 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）

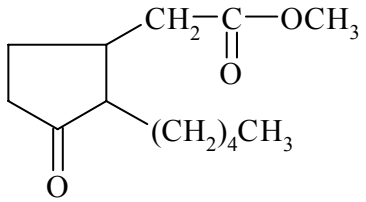
5.　試験材料及び方法

5.1　被験物質及び媒体

5.1.1　被験物質

メチル（2-ペンチル-3-オキソ-シクロペンチル）アセテートは[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-2517、添付資料 1）。

製造者	:	[redacted]
名称	:	メチル（2-ペンチル-3-オキソ-シクロペンチル）アセテート
英語名称	:	Methyl (2-pentyl-3-oxocyclopentyl) acetate
別名	:	ジヒドロジャスモン酸メチル
CAS 番号	:	24851-98-7
官報公示整理番号	:	3-3309
構造式又は示性式	:	



分子式	:	$C_{13}H_{22}O_3$
分子量	:	226.31
常温における性状	:	無色透明液体
沸点	:	307.76°C(760 mmHg)*
引火点	:	130.82°C*
比重（20/20）	:	1.00**
ロット番号	:	024-013-31
純度（GC）	:	98.35%（異性体混合物として）
異性体組成	:	異性体構成比は約 7:1
不純物	:	不明
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。

*　：製造元製品安全データシートに基づく
**：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

5.1.2　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（有効期限）
：　WEN1861（2017 年 7 月 12 日、2017 年 9 月 30 日）、WEK6144（2017 年 10 月 23 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-2517）[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。

5.2　投与液の調製及び保存方法

5.2.1　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。

5.2.2　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。

5.2.3　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：4~9°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。

5.2.4　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 8 日間、その後室温で 24 時間安定であることが株式会社ボゾリサーチセンターで確認されている（試験番号：A-2517、添付資料 3）[1]。

5.2.5　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 99.5~101.5%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-2517）[1]で実施された。分析法の概略を以下に示した。

[測定対象物質]

メチル（2-ペンチル-3-オキソ-シクロペンチル）アセテート

[標準物質]

被験物質から一部分配したものを用いた。

名称	:	メチル（2-ペンチル-3-オキソ-シクロペンチル）アセテート
ロット番号	:	024-013-31
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
特記事項	:	本物質は異性体が存在するため、本測定系ではピーク面積の合計値を用いて算出した。

[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。

測定試料濃度 (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	50	2.5	20	400
60	1	100	2.5	30	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（0.32 mm I.D.×30 m、膜厚 0.25 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 : 2.0 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 : 100°C（Hold 0 分）→280°C（20°C/min、Hold 3 分）
注入量 : 1 μL

5.3 試験動物種及び系統の選択理由

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

5.4　試験動物

Sprague-Dawley 系 SPF ラット〔Crl:CD(SD)、日本チャールス・リバー株式会社、厚木飼育センター〕の雄 62 匹及び雌 83 匹をそれぞれ 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、10、17 及び 20 日の 5 回）、詳細な一般状態の観察（群分け 5 日前の馴化 15 日に 1 回）を実施した。更に、雄について馴化終了日に陰嚢内の精巣の触診及び陰茎亀頭の観察を実施し、雌については腟垢を検疫期間終了後群分け日まで採取して性周期（検疫期間終了後 14 日間）を調べた。その結果、性周期の異常が 2 例（耳標番号：822 及び 869）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 81 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 406~472 g（平均体重：430 g）、雌は 235~282 g（平均体重：256 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。

5.5　飼育条件

動物は、温度 23±3°C（実測値：22~24°C）、相対湿度 50±20%（実測値：50~59 %）、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：908 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、2012-4）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: 120815、120919、121012）をステンレス製給餌器により自由に摂取させた。

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

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

5.6　動物の識別

動物は番号（雄：731~792、雌：793~875）が刻印された耳標を入荷時に装着し、個体識別を行った。群分け後は、1000 の位は群（対照群、低、中及び高用量の順）、100 の位は性別（0 番を雄、1 番を雌）、10 と 1 の位は個体番号を示す 4 桁の動物番号を設定した。各飼育ケージに投与量（群）ごとに色分けしたケージラベルを付け、試験番号、投与経路、投与量、性別、動物番号、耳標番号、剖検予定日（雄及び非交配群の雌）、交尾成立日（交配群の雌雄）及び分娩日（交配群の雌）を明記した。

5.7　投与経路、投与期間及び投与回数並びに回復期間とそれらの選択理由

投与経路は毒性試験法ガイドラインに準じ、経口投与を選択した。投与期間は、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 41~46 日）とした。非交配群の雌については 42 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。

5.8　投与方法

投与方法は、げっ歯類の経口投与に際して一般的な強制経口投与とした。投与容量は 5 mL/kg 体重とし、胃ゾンデを用いて投与液を 08:26~12:24 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、14:51~16:57 の間に投与した。なお、投与時に分娩中で 17:00 までに分娩が終了しなかった個体（動物番号：4101）については、当日の投与は行わなかった。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。

5.9　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。

5.10　投与量の設定根拠

本試験の投与量は、先に実施した「メチル（2-ペンチル-3-オキソ-シクロペンチル）アセテートのラットを用いた 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-R037、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、一般状態及び血液学検査には被験物質投与の影響はみられなかった。しかし、1000 mg/kg 投与群の雌雄で投与初期に摂餌量の低値を伴った一過性の体重減少がみられ、雌で総コレステロールの高値、雌雄で肝臓重量の高値、雄で腎臓重量の高値及び腎臓の陥凹層が認められた。500 mg/kg 投与群では雌で投与初期に摂餌量の低値傾向を伴った一過性の体重減少、雌雄で肝臓重量の高値が認められた。250 mg/kg 投与群では、雌雄ともいずれの検査にも異常はみられなかった。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。

5.11　観察及び検査の方法

試験日の起算は、投与開始日を投与 1 日、投与 1 日から 7 日を投与 1 週、回復開始日（投与 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。

5.11.1　一般状態の観察

全個体について、検疫・馴化期間中は毎日 1 回、投与期間中は毎日 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。

5.11.2　詳細な一般状態の観察、機能検査、握力及び自発運動量の測定

詳細な一般状態の観察は全個体について行った。投与開始前（馴化期間中）に 1 回、また、雄及び非交配群は投与期間中及び回復期間中毎週 1 回、交配群雌は交配前投与期間中毎週 1 回、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、分娩動物は授乳 4 日）にそれぞれ行った。

機能検査、握力測定及び自発運動量の測定は、各群の 5 匹（雄の群内番号 8~12 番、交配群雌の各群の分娩順で動物番号が若い順[注]、非交配群の群内番号 18~22 番）について行った。投与期間中は交配群の雌で授乳 4 日（投与 41~44 日）に、その他は投与期間終了週（投与 6 週、投与 37 日）に、回復期間中は対照群及び高用量群の雌雄で回復期間終了週（回復 2 週、雌雄ともに回復 9 日）に行った。

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

注：交配群雌の検査対象動物を以下に示した。

試験群	動物番号
対 照 群	1101、1102、1103、1105、1110
低用量群	2103、2105、2106、2111、2112
中用量群	3101、3102、3108、3109、3112
高用量群	4101、4103、4104、4106、4110

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。

5.11.3　体重測定

全個体について、馴化 1、3、10、17 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（14:07~17:02 の間）を除き、体重測定は測定日の 07:49~11:37 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 07:39~08:24 の間に測定した。また、妊娠 25 日未分娩動物については、搬出前に体重を測定したが、統計解析の対象から除外した。

5.11.4　摂餌量測定

全個体について、交配群の雄及び非交配群の雌は投与 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 07:49~10:55 の間（投与期間中は投与前）に行った。

5.11.5　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腟垢を採取し、交配前投与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。

5.11.6　交配方法

交配前投与期間終了後、交配群の同じ投与群の雌雄を 1:1 で終夜同居させ、翌朝、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 5 日間であった。

5.11.7　分娩及び哺育観察

1)　母動物の観察

交尾の確認された雌動物は妊娠 21 日から妊娠 25 日の午前まで 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対照群の 1 例（動物番号：1106）と 1000 mg/kg 投与群の 2 例（動物番号：4102 及び 4112）は、イソフルラン麻酔下で採血後、腹大動脈切断により放血致死させ、病理学検査に供した。妊娠の有無を確認した結果、着床が認められなかったため不妊とみなした。

2)　出生児の観察

生後 0 日に出生児数及び死産児数を数え、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。なお、1000 mg/kg 投与群の 1 例（動物番号：4109）における生後 0 日（死産児含む）の性比は、食失により性別判定不能の死産児がいたため算出しなかった。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。

5.11.8　尿検査（摂水量測定を含む）

投与期間終了週（投与 6 週、投与 38~39 日）及び回復期間終了週（回復 2 週、回復 10~11 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）

5.11.9　血液学検査

全例について剖検前日（最終投与日あるいは回復 14 日）から一夜（16~19 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（観察は実施しなかった）。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 日未分娩動物についても採血し同様に検査したが、統計解析の対象から除外した。

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、1110
低用量群	2103、2105、2106、2111、2112
中用量群	3101、3102、3108、3109、3112
高用量群	4101、4103、4104、4106、4110

表 3.血液学検査の項目、測定法及び使用機器など

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

5.11.10　血液化学検査

血液学検査用試料と同時に採取した血液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 日未分娩動物についても同様に検査したが、統計解析の対象から除外した。血清の一部は血中ホルモン測定に備え、約 0.5 mL×3 本をサンプルチューブに分注し、–80°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）		

5.11.11　血中ホルモン測定

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

5.11.12　病理学検査

1)　剖検及び器官重量測定

最終投与翌日及び回復期間終了日に全ての生存動物について、採血した動物は採血後に、その他の動物はイソフルラン麻酔下で、腹大動脈切断により放血致死させ、それぞれ体外表並びに頭部、胸部及び腹部の器官・組織の肉眼検査を行った。妊娠 25 日未分娩動物については、採血して放血致死させた後に剖検を行った。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 日未分娩動物についても同様に器官重量を測定したが、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、交配群の高用量群の雌雄の肝臓及び雌の腎臓、非交配群雌の卵巣に被験物質投与による影響が疑われたため、中及び低用量群並びに回復動物の当該器官・組織の鏡検を行った。また、回復動物の全例の肉眼的異常部位について鏡検を行った。

大脳、小脳（橋を含む）、坐骨神経、脊髄（胸部）、眼球、視神経、<u>ハーダー腺</u>、下垂体、甲状腺、上皮小体、副腎、胸腺、脾臓、顎下リンパ節、腸間膜リンパ節、心臓、<u>胸大動脈</u>、気管、肺（気管支を含む）、<u>舌</u>、<u>喉頭</u>、<u>食道</u>、胃、十二指腸、空腸、回腸（パイエル板を含む）、盲腸、結腸、直腸、顎下腺、舌下腺、肝臓、膵臓、腎臓、膀胱、精巣、卵巣、精巣上体、子宮、腟、前立腺、精嚢（凝固腺を

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

5.12　統計解析

5.12.1　パラメータの算出

以下の式により性周期異常率、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。

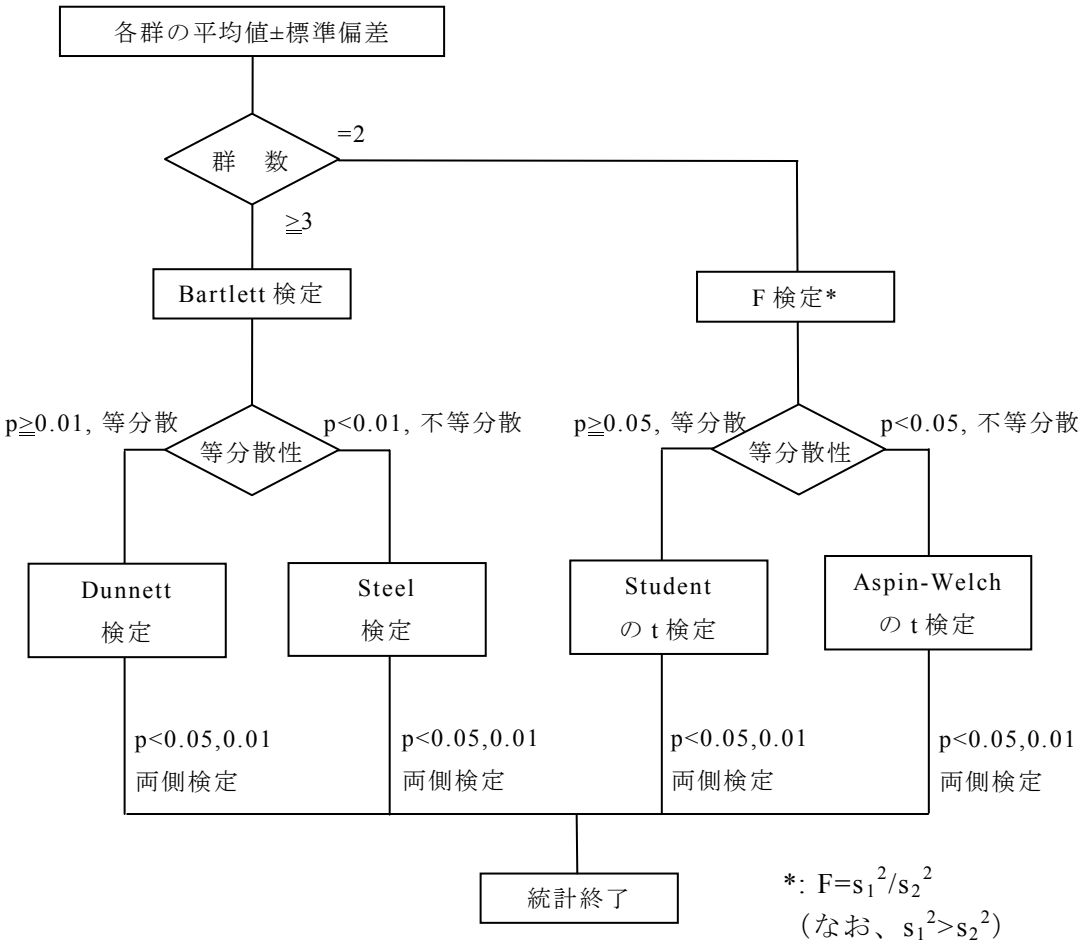
性周期異常率(%) =（性周期異常を示した個体数/観察雌個体数）×100
交尾率(%) =（交尾動物数/同居動物数）×100
授精率(%) =（雌を妊娠させた雄の数/交尾した雄の数）×100
受胎率(%) =（妊娠した雌の数/交尾した雌の数）×100
出産率(%) =（出生児出産雌数/妊娠雌数）×100
妊娠期間(日) = 妊娠 0 日から分娩した日までの日数
着床率(%) =（着床痕数/黄体数）×100
分娩率(%) =（出産児数/着床痕数）×100
死産児率(%) =（死産児数/出産児数）×100
外表異常率(%) =（外表異常児数/出産児数）×100
出生率(%) =（出生児数/出産児数）×100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

5.12.2　検定

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

体重、体重増加量（雄及び非交配群雌：投与 1~42 日及び回復 1~14 日、交配群雌：投与 1~15 日、妊娠 0~20 日及び授乳 0~4 日、出生児：生後 0~4 日）、摂餌量、摂水量、発情期像発現回数、性周期（発情周期）、交尾までに要した日数、妊娠期間、黄体数、着床痕数、生存児数、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]。

6. 試験結果

6.1 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。

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

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

いずれの動物にも異常はみられなかった。

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

雄では、1000 mg/kg 投与群で投与 3、4、5 及び 6 週に流涎が 1 又は 2 例にみられた。

交配群雌では、1000 mg/kg 投与群で妊娠 1、7、14 及び 20 日に流涎が 1 から 5 例にみられた。

非交配群雌では、1000 mg/kg 投与群で投与 3、4、5 及び 6 週に流涎が各 1 例にみられた。

100 及び 300 mg/kg 投与群のいずれの動物にも被験物質投与に関連すると考えられる異常はみられなかった。

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

いずれの動物にも被験物質投与に関連すると考えられる異常はみられなかった。

なお、交配群雌の授乳 4 日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、僅かな低値であり雄及び非交配群雌の立ち上がり回数やその他の詳細な一般状態に異常はみられないことから、偶発的な有意差と判断した。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。

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

1) 投与期間終了週検査

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

2) 回復期間終了週検査

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

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

1)　投与期間終了週測定

雄及び非交配群雌では、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。

交配群雌では、1000 mg/kg 投与群で後肢の握力に対照群と比べ有意な高値が認められたが、雄及び非交配群雌では同様の変化はみられず、後肢のみの変化であり、試験施設の背景データ（720±316、Mean±2S.D.、n=40、2011/04-2013/03）の範囲内であることから、被験物質投与と関連しない偶発的な有意差と考えられた。その他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)　回復期間終了週測定

1000 mg/kg 投与群の雄で対照群と比べ後肢の握力に有意な低値が認められたが、僅かな低値で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、偶発的な有意差と判断した。

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

1)　投与期間終了週測定

雄では、100 mg/kg 投与群で 50-60 分の間の運動量に、1000 mg/kg 投与群で 20-30 分の間の運動量に対照群と比べそれぞれ有意な高値が認められたが、一過性の変動であるか、あるいは明確な用量との相関性はみられず、0-60 分の間の総運動量に異常はないことから、偶発的な有意差と判断した。

交配群雌では、100 mg/kg 投与群で 20-30、30-40 及び 40-50 分の間の運動量に、1000 mg/kg 投与群で 30-40 分の間の運動量と 0-60 分の間の総運動量に対照群と比べそれぞれ有意な低値が認められたが、100 mg/kg 投与群については用量と相関性はみられないこと、1000 mg/kg 投与群の 0-60 分の間の総運動量は試験施設の背景データ（1054±910、Mean±2S.D.、n=40、2011/04-2013/03）の範囲内であることから、いずれも偶発的な有意差と判断した。

非交配群雌では、対照群と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。

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

1)　投与期間

雄では、1000 mg/kg 投与群で投与期間を通じ対照群を下回って推移し、投与期間中の体重増加量に対照群と比べ有意な低値が認められた。100 mg/kg 投与群で投与期間中の体重増加量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。

交配群雌では、1000 mg/kg 投与群で妊娠期間中の体重増加量に対照群と比べ有意な

低値が認められた。

非交配群雌では、1000 mg/kg 投与群で投与期間を通じ対照群を下回って推移し、投与 15 日の体重及び投与期間中の体重増加量に対照群と比べ有意な低値が認められた。

2) 回復期間

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

非交配群雌では、1000 mg/kg 投与群で回復期間中の体重増加量に対照群と比べ有意な高値が認められた。

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

1) 投与期間

雄では、1000 mg/kg 投与群で対照群と比べ投与 2 日（投与開始翌日）の摂餌量に有意な低値、投与 30、36 及び 42 日に有意な高値が認められた。100 mg/kg 投与群で投与 8、15 及び 30 日の摂餌量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。

交配群雌では、1000 mg/kg 投与群で妊娠 7 日及び授乳 2 日の摂餌量に対照群と比べ有意な高値が認められた。

非交配群雌では、1000 mg/kg 投与群で投与 30 及び 36 日の摂餌量に対照群と比べ有意な高値が認められた。

2) 回復期間

雄では、1000 mg/kg 投与群で回復 14 日の摂餌量に対照群と比べ有意な高値が認められたが、わずかな高値であり回復期間中の他の測定時点に有意差はないことから偶発性と判断した。

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

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

1) 投与期間終了週検査

定性項目については、いずれの動物にも異常はみられなかった。

雄では、1000 mg/kg 投与群で摂水量及び尿量に対照群と比べ有意な高値が認められた。

非交配群雌では、1000 mg/kg 投与群で対照群と比べ摂水量、尿量及びカリウムの尿中排泄量に有意な高値、尿浸透圧に有意な低値が認められた。

2) 回復期間終了週検査

定性項目については、いずれの動物にも異常はみられなかった。

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

非交配群雌では、1000 mg/kg 投与群でナトリウム及び塩素の尿中排泄量に対照群と比べ有意な高値が認められたが、いずれも試験施設の背景データ（Na：1.04±0.66、Cl：1.24±0.78、Mean±2S.D.、n=40、2011/04-2013/03）の範囲内であり、投与期間終

了時及び雄には同様の変化はみられないことから、偶発性と判断した。

6.6　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、1000 mg/kg 投与群で白血球分画における大型非染色球比率及び絶対数に対照群と比べ有意な高値が認められたが、白血球に占める割合の少ない分画におけるわずかな変動であり白血球数等の関連項目に異常はないことから偶発性と判断した。

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 1000 mg/kg 投与群で白血球分画における単球比率及び大型非染色球数に有意な高値が認められたが、軽微な変化であり白血球数等の関連項目に異常はないことから偶発性と判断した。

非交配群雌では、1000 mg/kg 投与群で赤血球数、ヘモグロビン量及びヘマトクリット値に対照群と比べ有意な低値が認められた。

2)　回復期間終了時検査

雄では、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低値が認められたが、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。また、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偶発性と判断した。

非交配群雌では、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低値が認められたが、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。

6.7　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、1000 mg/kg 投与群で対照群と比べ尿素窒素及び ALP に有意な高値、塩素に有意な低値が認められた。300 mg/kg 投与群で総ビリルビンに対照群と比べ有意な低値が認められたが、用量に関連しない変化であった。

交配群雌では、1000 mg/kg 投与群で対照群と比べ総コレステロール及び尿素窒素に有意な高値、グルコースに有意な低値が認められた。その他に 1000 mg/kg 投与群で γ-GTP に対照群と比べ有意な高値、300 及び 1000 mg/kg 投与群で総ビリルビンに対照群と比べ有意な低値が認められたが、いずれも軽微な変化であり偶発性と判断した。

非交配群雌では、1000 mg/kg 投与群で対照群と比べ ALT、総コレステロール、トリグリセライド及びリン脂質に有意な高値、グルコース及び塩素に有意な低値が認められた。

2)　回復期間終了時検査

雄では、1000 mg/kg 投与群で LDH に対照群と比べ有意な低値、非交配群雌では、1000 mg/kg 投与群で総たん白質に対照群と比べ有意な高値が認められたが、軽微な変

化であり投与期間終了時検査には同様の変化はみられないことから偶発性と判断した。

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

1)　投与期間終了時検査

雄では、1000 mg/kg 投与群で対照群と比べ剖検時体重に有意な低値、肝臓の絶対及び相対重量、腎臓の相対重量に有意な高値が認められた。300 mg/kg 投与群で肝臓の相対重量に対照群と比べ有意な高値が認められた。他に 1000 mg/kg 投与群で脳及び精巣上体の相対重量に対照群と比べ有意な高値が認められたが、いずれも軽微な相対重量のみの変化であり、偶発的な有意差と判断した。100 mg/kg 投与群で胸腺の絶対及び相対重量に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。

交配群雌では、対照群と比べ 300 及び 1000 mg/kg 投与群で肝臓の絶対及び相対重量に有意な高値、1000 mg/kg 投与群で腎臓の相対重量に有意な高値が認められた。他に 1000 mg/kg 投与群で対照群と比べ甲状腺の相対重量に有意な高値、子宮の絶対重量に有意な低値が認められたが、いずれも軽微な絶対又は相対重量のみの変化であり、偶発的な有意差と判断した。300 mg/kg 投与群で脾臓及び卵巣の相対重量に対照群と比べ有意な高値が認められたが、用量に関連しない変化であった。

非交配群雌では、1000 mg/kg 投与群で対照群と比べ剖検時体重に有意な低値、肝臓及び腎臓の絶対及び相対重量に有意な高値が認められた。他に 1000 mg/kg 投与群で脳、下垂体及び副腎の相対重量に対照群と比べ有意な高値が認められたが、いずれも軽微な相対重量のみの変化であり、偶発的な有意差と判断した。

2)　回復期間終了時検査

雄では、1000 mg/kg 投与群の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。

非交配群雌では、1000 mg/kg 投与群で肝臓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。

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

1)　投与期間終了時検査

交配群雌では、1000 mg/kg 投与群で腎臓に白色巣が 3/10 例にみられ、被験物質投与との関連性が考えられた。

妊娠 25 日未分娩（不妊）であった 1000 mg/kg 投与群の 2 例では肉眼的異常はみられなかった。

その他いくつかの器官/組織に肉眼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偶発性変化と考えられた。

2)　回復期間終了時検査

いくつかの器官/組織に肉眼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偶発性変化と考えられた。

6.10　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

被験物質投与との関連が推察される変化が肝臓及び腎臓にみられた。

肝臓　：　小葉中心性肝細胞肥大（軽微又は軽度）が、300 mg/kg 投与群の雄 1/5 例と交配群雌 3/5 例、1000 mg/kg 投与群の雄 5/5 例、交配群雌 5/7 例及び非交配群雌 5/5 例にみられた。

腎臓　：　限局性の尿細管の拡張（軽微）が、1000 mg/kg 投与群の交配群雌 2/7 例にみられた。

卵巣に萎縮（軽度）が非交配群雌の 1000 mg/kg 投与群で 2/5 例にみられ、この変化は同週齢動物において稀にみられるものの、その出現頻度がやや高いことから被験物質投与との関連を考えて、交配群雌の低及び中用量群並びに回復動物についても検索を行った。しかしながら、交配群雌の 1000 mg/kg 投与群及び回復動物においては同様の変化はみられず、交配群において妊娠・分娩への影響が認められないことから、偶発的変化の可能性が考えられた。

妊娠 25 日未分娩（不妊）であった 1000 mg/kg 投与群の 2 例では、不妊との関連性が疑われる組織学的変化はみられなかった。

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

2)　回復期間終了時検査

肝臓に小葉中心性肝細胞肥大（軽微）が、雄の 1000 mg/kg 投与群で 1/5 例にみられた。

6.11　性周期（Table 11、Appendix 10-1~10-4）

1000 mg/kg 投与群で性周期異常が 3/12 例にみられたが、発情期像発現回数及び平均性周期日数には対照群と各被験物質投与群との間に有意差は認められなかった。

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

交配 5 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。

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

1000 mg/kg 投与群で統計学的な有意差は認められないものの対照群に比して分娩率に低値傾向が認められた。その他、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 1000 mg/kg 投与群の 1 例（動物番号：4101）で分娩時間

の延長傾向がみられたが、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。

6.14　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。

6.15　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。

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

1000 mg/kg 投与群で生後 0 日の雌雄体重に対照群と比べ有意な低値が認められた。その他の生後 0 及び 4 日の雌雄体重並びに生後 0~4 日の間の体重増加量には対照群と各被験物質投与群との間に有意差は認められなかった。

6.17　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。

6.18　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。

7.　考察

メチル(2-ペンチル-3-オキソ-シクロペンチル)アセテートの 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（41~46 日間）、非交配群雌には 42 日間強制経口投与し、反復投与毒性及び生殖発生毒性を検討した。更に、0 及び 1000 mg/kg 投与群の一部の動物については雌雄ともに 42 日間投与した後、14 日間の回復期間を設け、毒性変化の可逆性を検討した。

7.1　反復投与毒性

いずれの投与群においても死亡動物はみられず、一般状態、機能検査、握力及び自発運動量には被験物質投与の影響は認められなかった。

1000 mg/kg 投与群の雌雄に散見された流涎は被験物質投与の影響と判断したが、その他に神経症状はみられず、唾液腺組織に異常はみられないことから、毒性学的意義は低いと考えられた。投与終了とともに流涎は消失し、回復性がみられた。

1000 mg/kg 投与群でみられた雄の投与初期の摂餌量低値を伴った体重増加抑制、交配群雌の妊娠期間中の体重増加抑制、非交配群雌の投与期間中の体重増加抑制は、被験物質投与による影響と考えられた。1000 mg/kg 投与群の雌雄で投与 4 週以降に散見された摂餌量の高値は、流涎の散見と時期が重なることから、被験物質投与との関連性が考えられた。投与期間終了後、雄の体重は対照群と差はみられなくなり、非交配群雌では回復期間中の体重増加量が対照群を上回り、回復性がみられた。

投与期間終了時に 1000 mg/kg 投与群の雄及び非交配群雌で認められた摂水量及び尿量の高値は被験物質投与の毒性影響と判断したが、尿浸透圧の低値は尿量の増加に伴う 2 次的な変化と考えられ、カリウムの尿中排泄量の高値については血中カリウム濃度に変動はみられないことから、毒性学的意義はないと考えられた。回復期間ではこれらの変化はみられず、回復性が認められた。

1000 mg/kg 投与群の非交配群雌で投与終了時に認められた赤血球数、ヘモグロビン量及びヘマトクリット値の低値は、軽微な変化であり他の赤血球系パラメータ及び造血系組織に異常はみられないことから、毒性学的意義は低いと考えられた。回復期間ではこれらの変化はみられず、回復性が認められた。

1000 mg/kg 投与群の雄及び交配群雌で認められた尿素窒素の高値は、明確な用量との相関性はみられず、腎臓組織にも障害性の変化はみられないことから、毒性学的意義は低いと考えられた。1000 mg/kg 投与群の雄及び非交配群雌で認められた塩素の低値は、ナトリウムに異常はなく、腎臓組織にも障害性の変化はみられないことから、毒性学的意義は低いと考えられた。1000 mg/kg 投与群の雄の ALP の高値、交配群雌の総コレステロールの高値、グルコースの低値、非交配群雌の ALT、総コレステロール、トリグリセライド及びリン脂質の高値、グルコースの低値はいずれも肝臓重量及

び組織における変化との関連性が考えられることから、被験物質投与の影響と判断した。回復期間ではこれらの変化はみられず、回復性が認められた。

雄及び交配群雌の 300 及び 1000 mg/kg 投与群、非交配群雌の 1000 mg/kg 投与群で投与期間終了時に認められた肝臓重量高値は被験物質投与の影響と考えられたが、肝臓組織に機能障害を示唆する変化はみられないため、毒性学的意義は低いと判断した。1000 mg/kg 投与群の雄、交配群雌及び非交配群雌で認められた腎臓重量高値、1000 mg/kg 投与群の雄及び非交配群雌で認められた摂水量及び尿量高値、尿浸透圧低値はいずれも弱い変化ではあるものの、総合的に判断して腎臓への影響を示唆する変化と考えられた。しかし、腎臓組織に重量増加を示唆する変化はみられないため、毒性学的意義は低いと判断した。肝臓重量の高値は回復期間終了時にも非交配群雌の 1000 mg/kg 投与群で認められたが、投与期間終了時と比べ程度は減弱し回復性がみられた。

病理学検査では、交配群雌の 1000 mg/kg 投与群で肉眼的に腎臓に白色巣がみられ、組織学的に交配群雌の 1000 mg/kg 投与群で腎臓に限局性の尿細管の拡張が、雄と交配群雌の 300 及び 1000 mg/kg 投与群並びに非交配群雌の 1000 mg/kg 投与群で肝臓に小葉中心性肝細胞肥大がみられ、被験物質投与との関連が推察された。腎臓の変化は交配群雌の高用量群のみにみられた。同用量を投与した非交配群雌にはみられなかった病変は限局性かつ単発性であり、尿細管上皮細胞に壊死や変性などの障害がみられないことから、毒性学的意義は低いものと考えられた。肝臓の変化は重量の増加を伴っていたが、障害性の変化ではないことから、毒性学的意義は低いと判断した。投与終了後の肝臓の変化は非交配群雌では消失し、雄においては 1 例に残存したもののその程度及び頻度は軽減し、雌雄とも回復性がみられた。

7.2　生殖発生毒性

1000 mg/kg 投与群で性周期異常がみられたが、交配成績に異常はないことから、毒性学的意義は低いと考えられた。分娩時間の延長傾向が 1000 mg/kg 投与群の 1/12 例にみられたが、分娩及び哺育状態に異常はみられないことから、毒性学的意義は低いと考えられた。また、同群では分娩率の低値傾向が認められ、被験物質投与が着床後の胎生期における胚・胎児の生存性に影響を及ぼす可能性が示唆された。

その他には、いずれの投与群においても発情期像発現回数、平均性周期日数、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、出産児の外表観察、出生児数及び出生率に被験物質投与の影響は認められず、授乳期間中の哺育状態にも異常が認められないことから、300 mg/kg 投与群では雌雄動物の交尾能、授精能及び受胎能、母動物の妊娠維持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、1000 mg/kg 投与群で生後 0 日の雌雄体重に低値が認められたが、生後 4 日の雌雄体重に異常はないことから、発育への影響は軽度と考えられた。

その他には、いずれの投与群においても生後 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、300 mg/kg 投与群では児の子宮内発生、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、本試験条件下でメチル（2-ペンチル-3-オキソ-シクロペンチル）アセテートを反復経口投与することにより、主な変化として 1000 mg/kg 投与群の雌雄で体重増加抑制、雌で腎臓に限局性の尿細管拡張がみられ、300 mg/kg 以上の投与群の雌雄で肝臓に重量の高値及び小葉中心性肝細胞肥大がみられた。また、1000 mg/kg 投与群で性周期異常例の増加、分娩時間の延長傾向、分娩率の低値傾向、生後 0 日の雌雄体重に低値が認められた。したがって、本被験物質の雌雄動物における反復投与毒性に対する無影響量及び無毒性量は雌雄とも 100 mg/kg と判断した。また、雄親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、雌親動物における無影響量及び無毒性量はいずれも 300 mg/kg、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 300 mg/kg と判断した。

8.　文献

[1] [redacted]メチル（2-ペンチル-3-オキソ-シクロペンチル）アセテートの 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-2517、2012 年）

[2] [redacted] メチル（2-ペンチル-3-オキソ-シクロペンチル）アセテートのラットを用いた 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-R037、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.

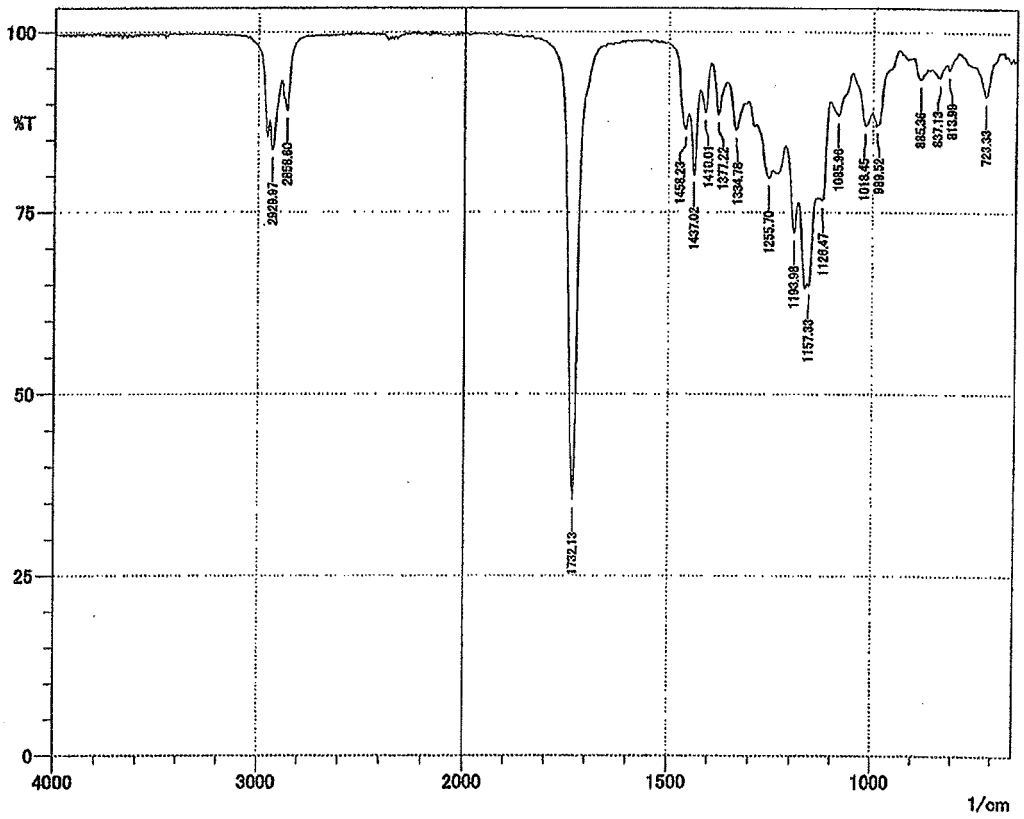
[6] 佐久間昭（1981）：薬効評価－計画と分析–II, pp.23-27, 387-389, 東京大学出版会, 東京.

R-1106
添付資料 1

試験番号：A-2517

試験成績書
［メチル（2-ペンチル-3-オキソ-シクロペンチル）アセテートの特性］

ステージ	：	被験物質の使用前
測定日	：	2012 年 8 月 23 日
被験物質	：	メチル（2-ペンチル-3-オキソ-シクロペンチル）アセテート（ロット番号：024-013-31）
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 9 月 11 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

試験番号：R-1106

試験成績書
[メチル（2-ペンチル-3-オキソ-シクロペンチル）アセテートの安定性]

ステージ	:	投与期間終了後
測定日	:	2012 年 12 月 25 日
被験物質	:	メチル（2-ペンチル-3-オキソ-シクロペンチル）アセテート（ロット番号：024-013-31）
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[1)]と比較するとき、同様な赤外吸収スペクトルである。 1) [redacted] メチル（2-ペンチル-3-オキソ-シクロペンチル）アセテートの 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-2517）
結果	:	特性のスペクトルと同様なスペクトルが得られた。赤外吸収スペクトルは次のページに示す。
判定	:	適
基準	:	「新規化学物質等に係る試験を実施する試験施設に関する基準」（平成 23 年 3 月 31 日：薬食発 0331 第 8 号、平成 23·03·29 製局第 6 号、環保企発第 110331010 号）

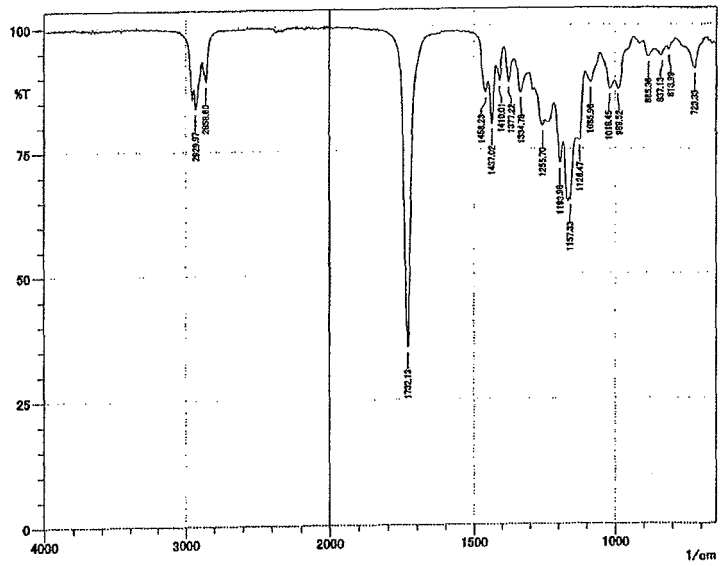
[redacted] 2013 年 2 月 7 日

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

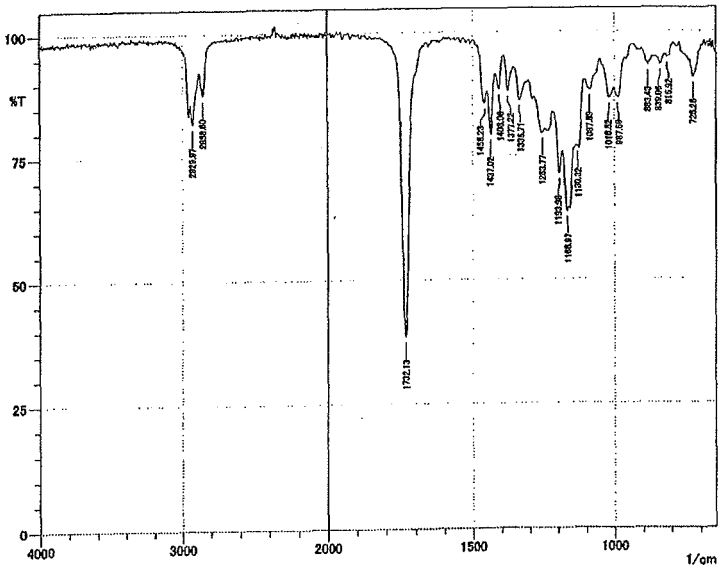
試験番号：R-1106

結果　　：　赤外吸収スペクトル

(特性のスペクトル)



(安定性のスペクトル)



R-1106
添付資料 3

試験番号：A-2517（訂正版）

試験成績書
[被験液中メチル（2-ペンチル-3-オキソ-シクロペンチル）アセテートの安定性]

被験物質　：　メチル（2-ペンチル-3-オキソ-シクロペンチル）アセテート（ロット番号：024-013-31）
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）又は室温保存
保存期間　：　冷所 8 日間＋室温 24 時間保存
評価基準
　安定性　：　残存率｛調製直後の測定濃度の平均値（100）に対する保存後の測定濃度の平均値の割合｝が 100.0±10.0%以内。

結果：

調製濃度 (mg/mL)		測定濃度（mg/mL）	
		調製直後	冷所 8 日間＋室温 24 時間保存後
1.01		1.04	1.02
		1.05	1.01
		1.04	1.00
	平均値	1.04	1.01
	残存率（%）	100	97.1
200		209	203
		206	200
		206	201
	平均値	207	201
	残存率（%）	100	97.1

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 10 月 5 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-1106
添付資料 4

分析結果

試験番号　：　R-1106
測定項目　：　濃度
ステージ　：　初回投与
測定日　：　2012 年 10 月 25 日

測定試料
　被験物質　：　メチル（2-ペンチル-3-オキソ-シクロペンチル）アセテート（ロット番号：024-013-31）
　形態　：　溶液
　媒体　：　コーン油
　調製日　：　2012 年 10 月 25 日

測定対象物質　：　メチル（2-ペンチル-3-オキソ-シクロペンチル）アセテート

評価基準
　濃度　：　表示値に対する割合が 100.0±10%

結果：

表示値 (mg/mL)	測定濃度 (mg/mL)	表示値に対する割合 (%)
20	19.9	99.5
60	59.7	99.5
200	200	100.0

判定　：　適

R-1106
添付資料 5

分析結果

試験番号 : R-1106
測定項目 : 濃度
ステージ : 投与 6 週
測定日 : 2012 年 11 月 29 日

測定試料
被験物質 : メチル（2-ペンチル-3-オキソ-シクロペンチル）アセテート（ロット番号：024-013-31）
形態 : 溶液
媒体 : コーン油
調製日 : 2012 年 11 月 29 日

測定対象物質 : メチル（2-ペンチル-3-オキソ-シクロペンチル）アセテート

評価基準
濃度 : 表示値に対する割合が 100.0±10%

結果：

表示値 (mg/mL)	測定濃度 (mg/mL)	表示値に対する割合 (%)
20	20.3	101.5
60	60.1	100.2
200	199	99.5

判定 : 適

メチル（2-ペンチル-3-オキソ-シクロペンチル）アセテートのラットを用いた
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-R037

被験物質		媒体 a)	メチル（2-ペンチル-3-オキソ-シクロペンチル）アセテート		
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			–	一過性の減少 (投与 4 日、♀)	一過性の減少 (投与 4 日、♂♀)
摂餌量			–	低値傾向 (投与 4 日、♀)	↓（投与 4 日、♂） ↓↓（投与 4 日、♀）
血液学検査			–	–	–
血液化学検査			–	–	総コレステロール：↑（♀）
器官重量	絶対		–	–	肝臓：↑↑（♂♀）
	相対		–	肝臓：↑↑（♂♀）	肝臓：↑↑（♂♀） 腎臓：↑↑（♂）
剖検	生存	–	–	–	腎臓：陥凹巣（♂）
	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)

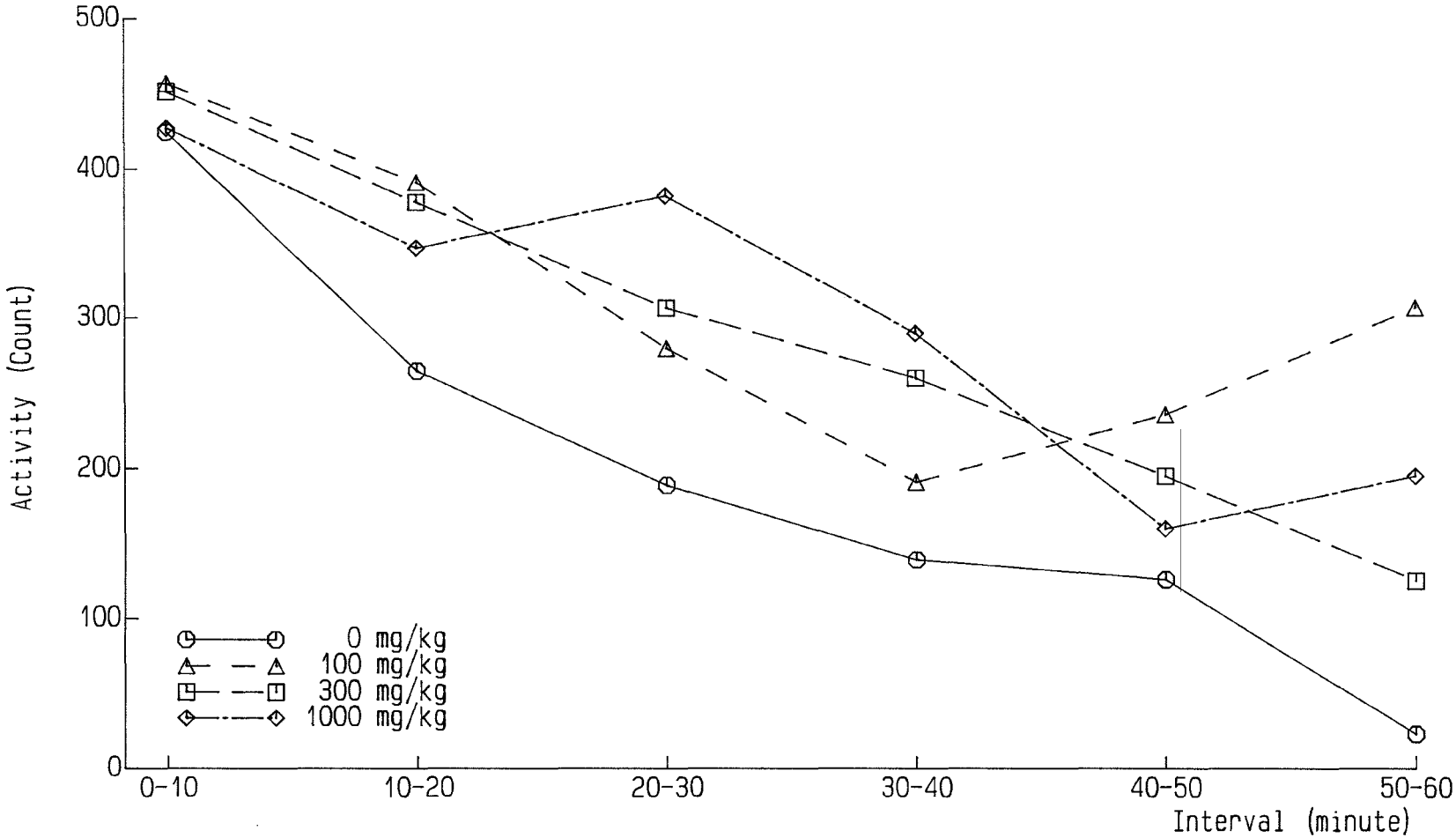


Fig.1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Motor activity of male rats (Week 6 of administration)

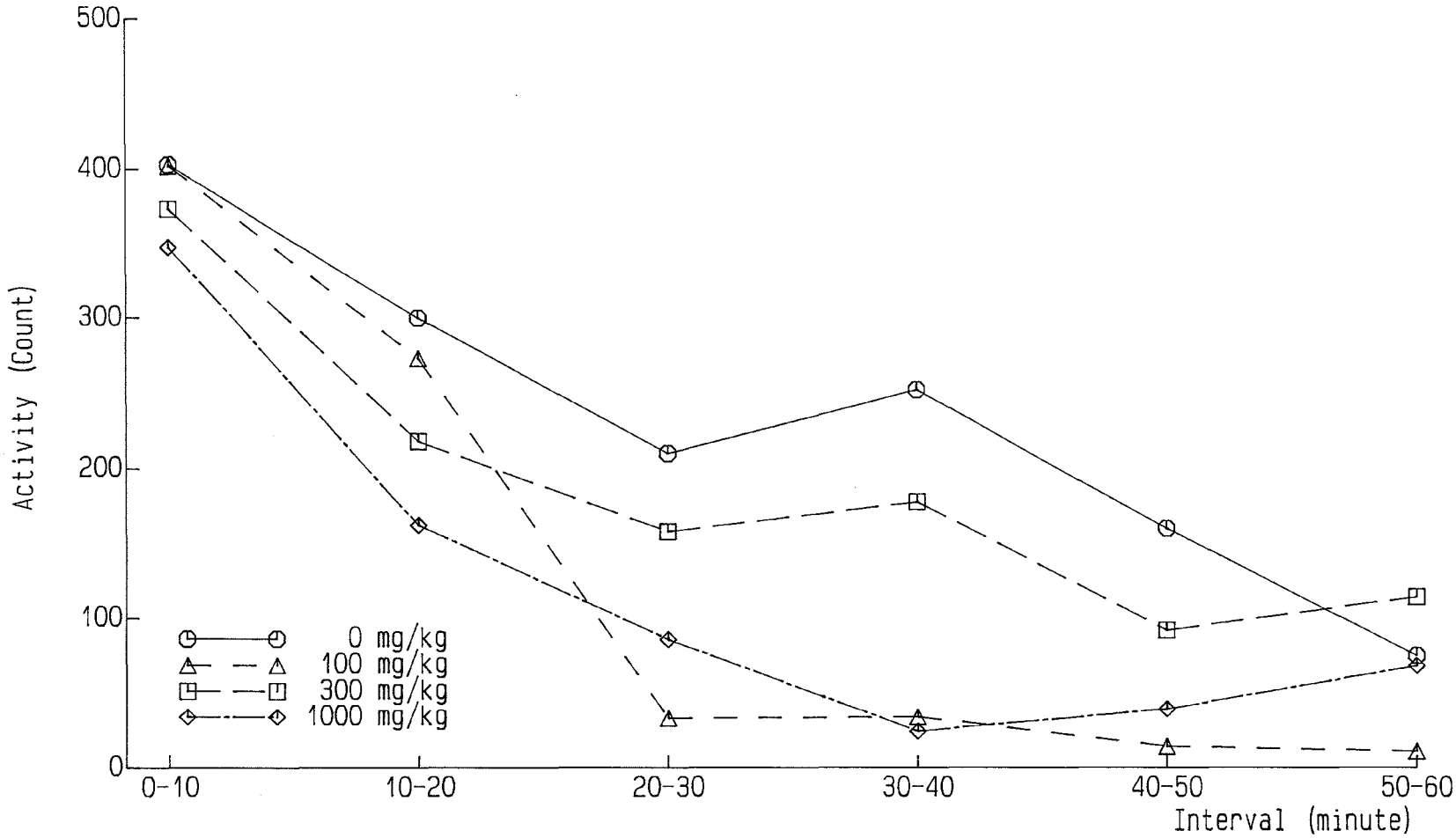


Fig.2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

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

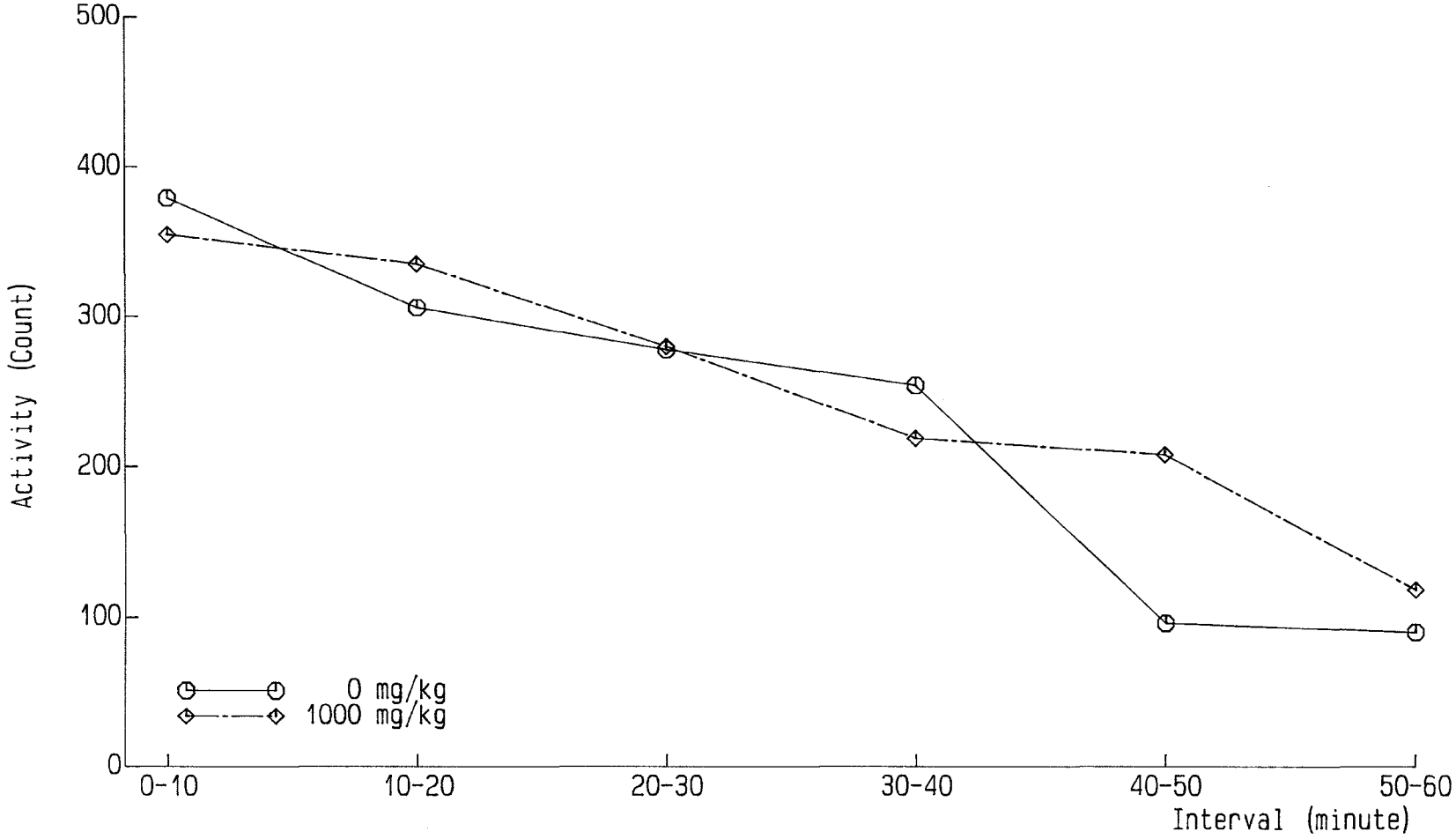


Fig.3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

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

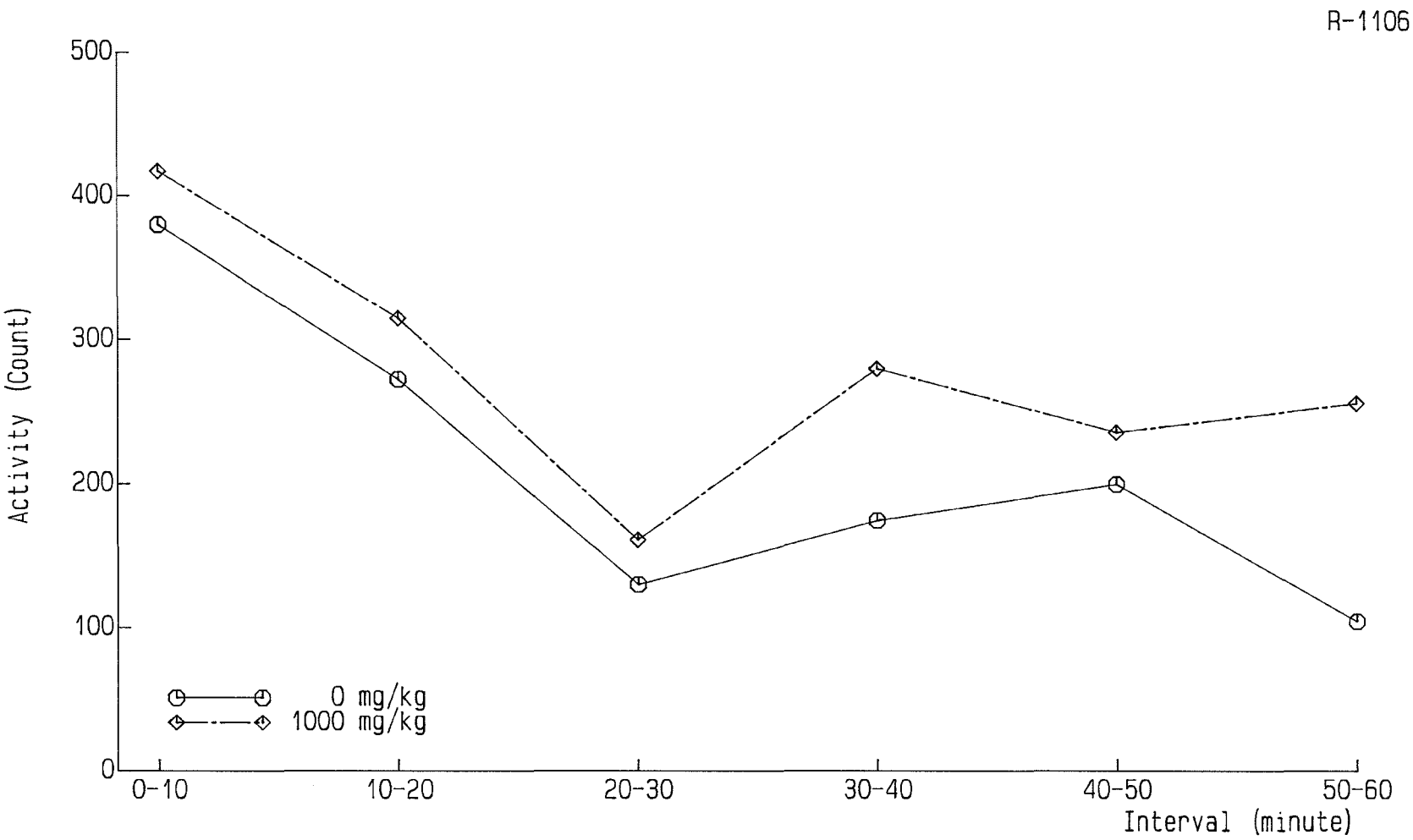


Fig.4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Motor activity of male rats (Week 2 of recovery)

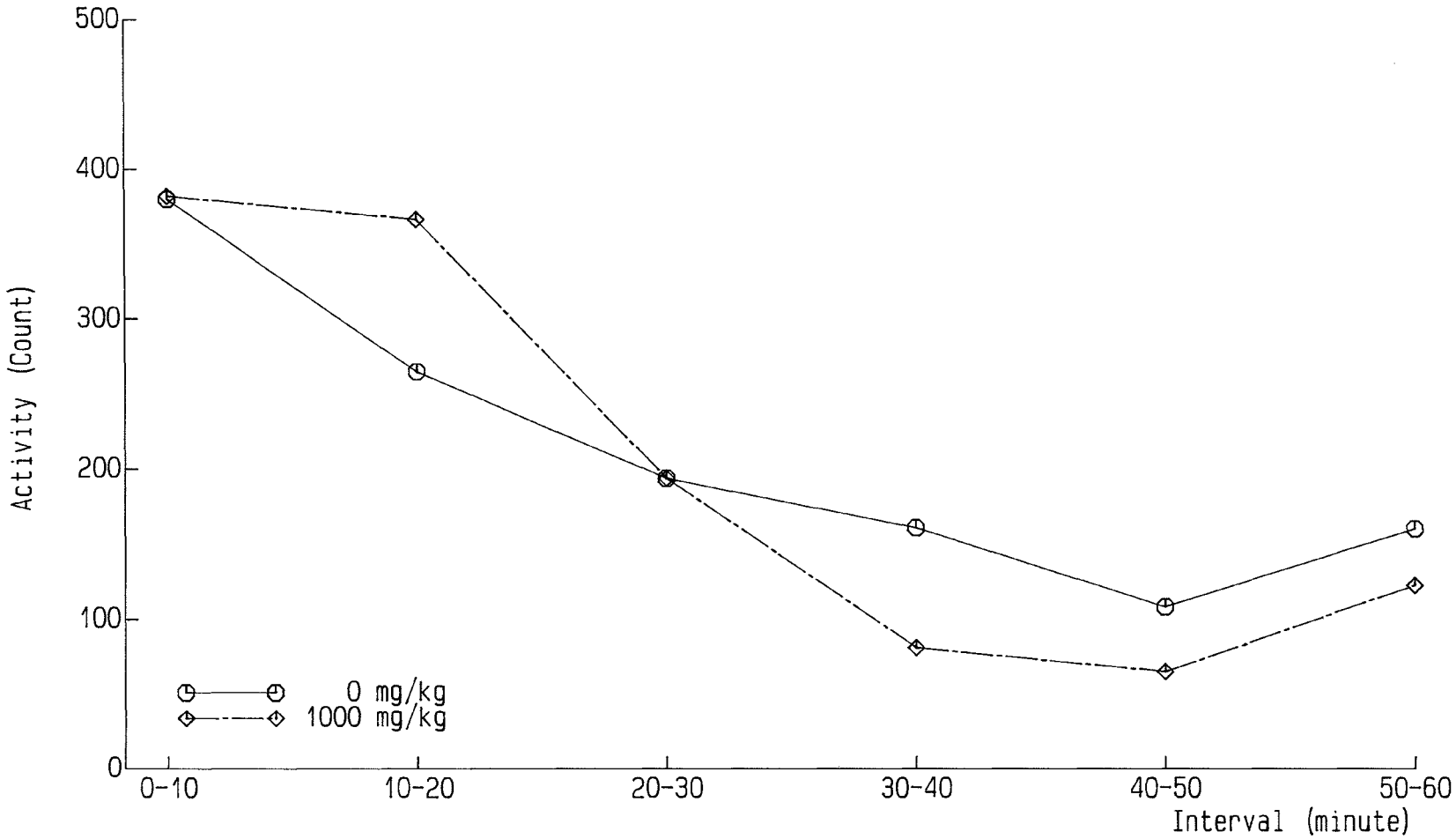


Fig.5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Motor activity of female rats (Week 2 of recovery)

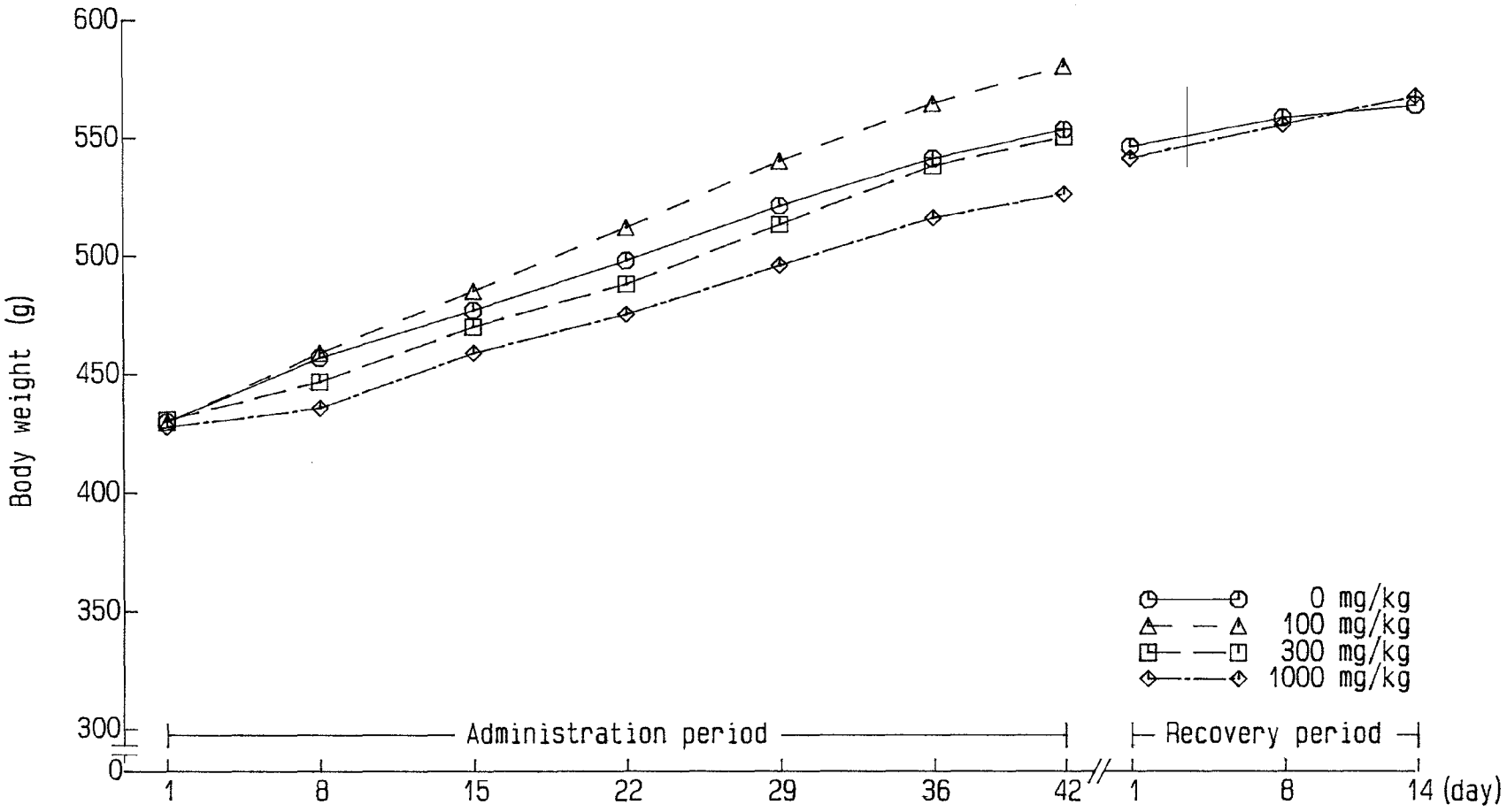


Fig.6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Body weight of male rats

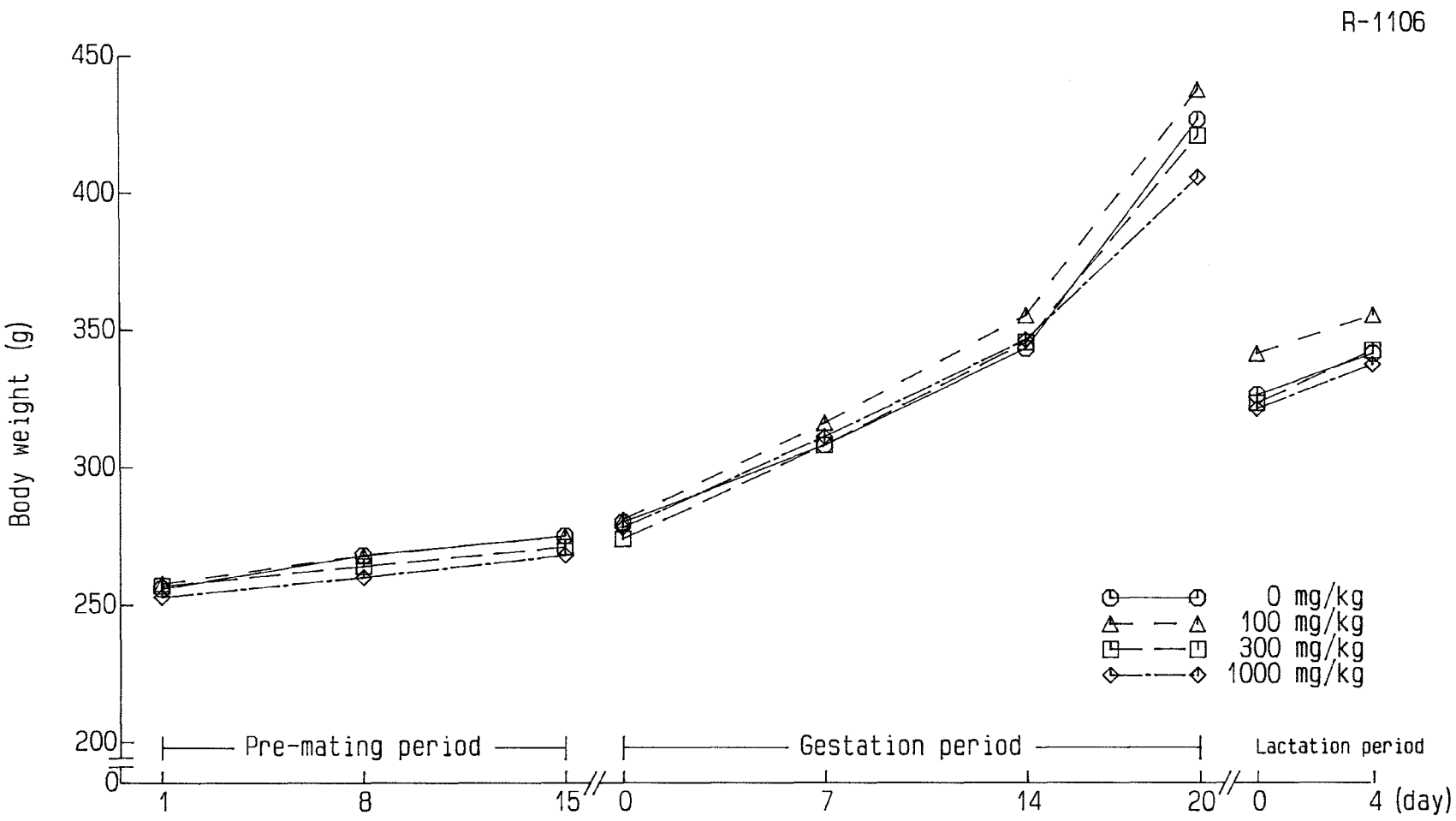


Fig.7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Body weight of female rats (Main group)

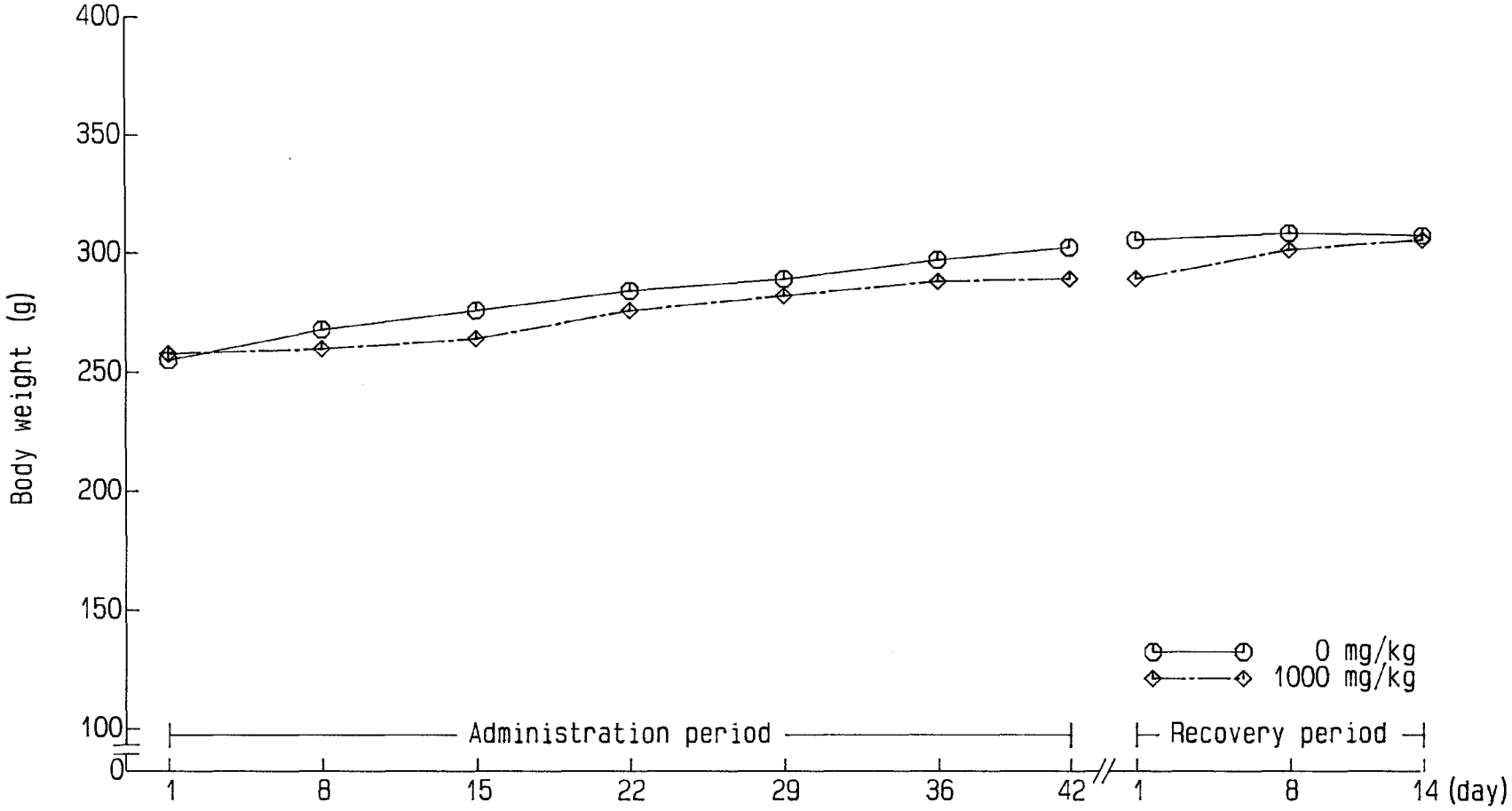


Fig.8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Body weight of female rats (Satellite group)

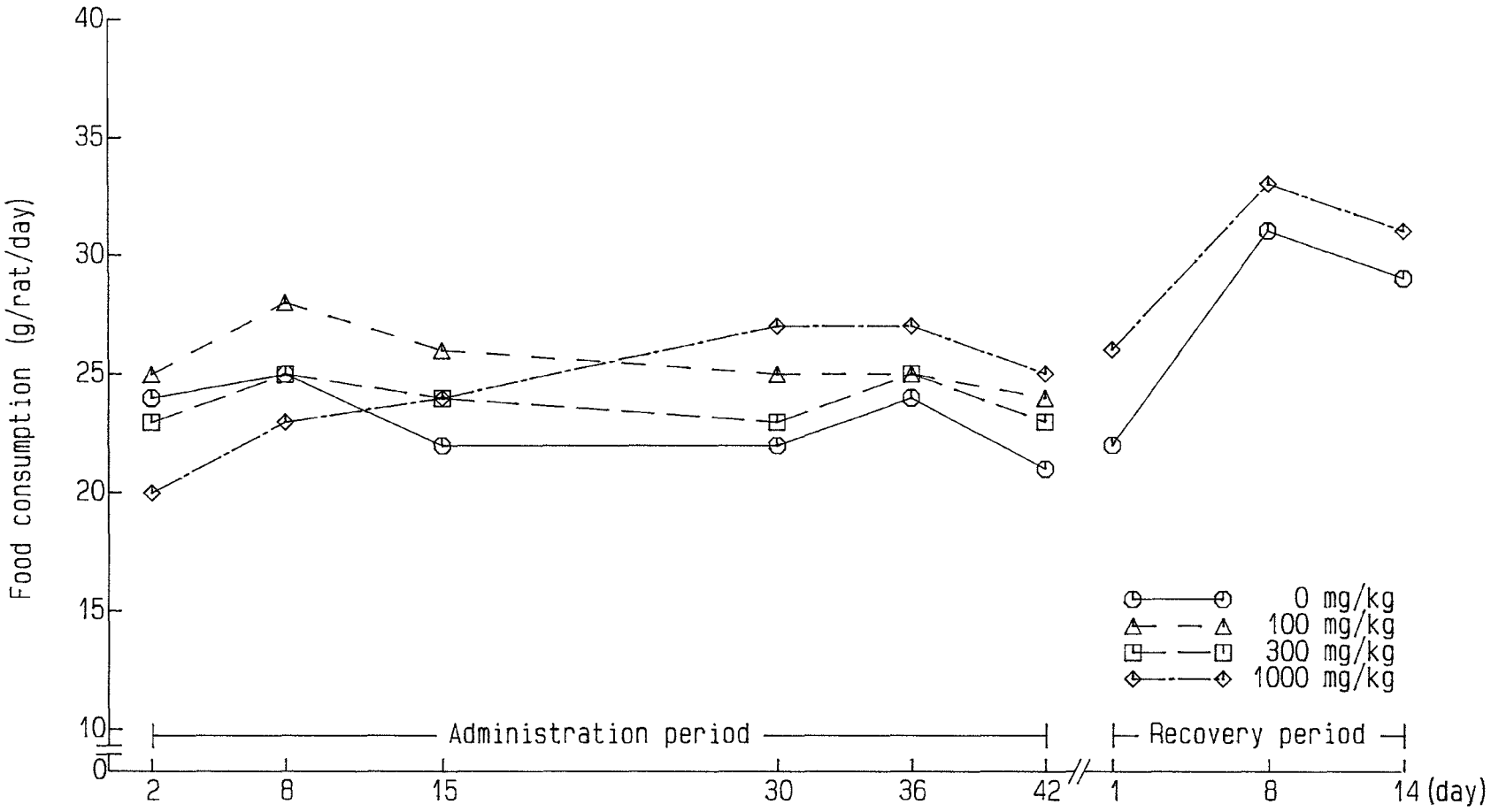


Fig.9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Food consumption of male rats

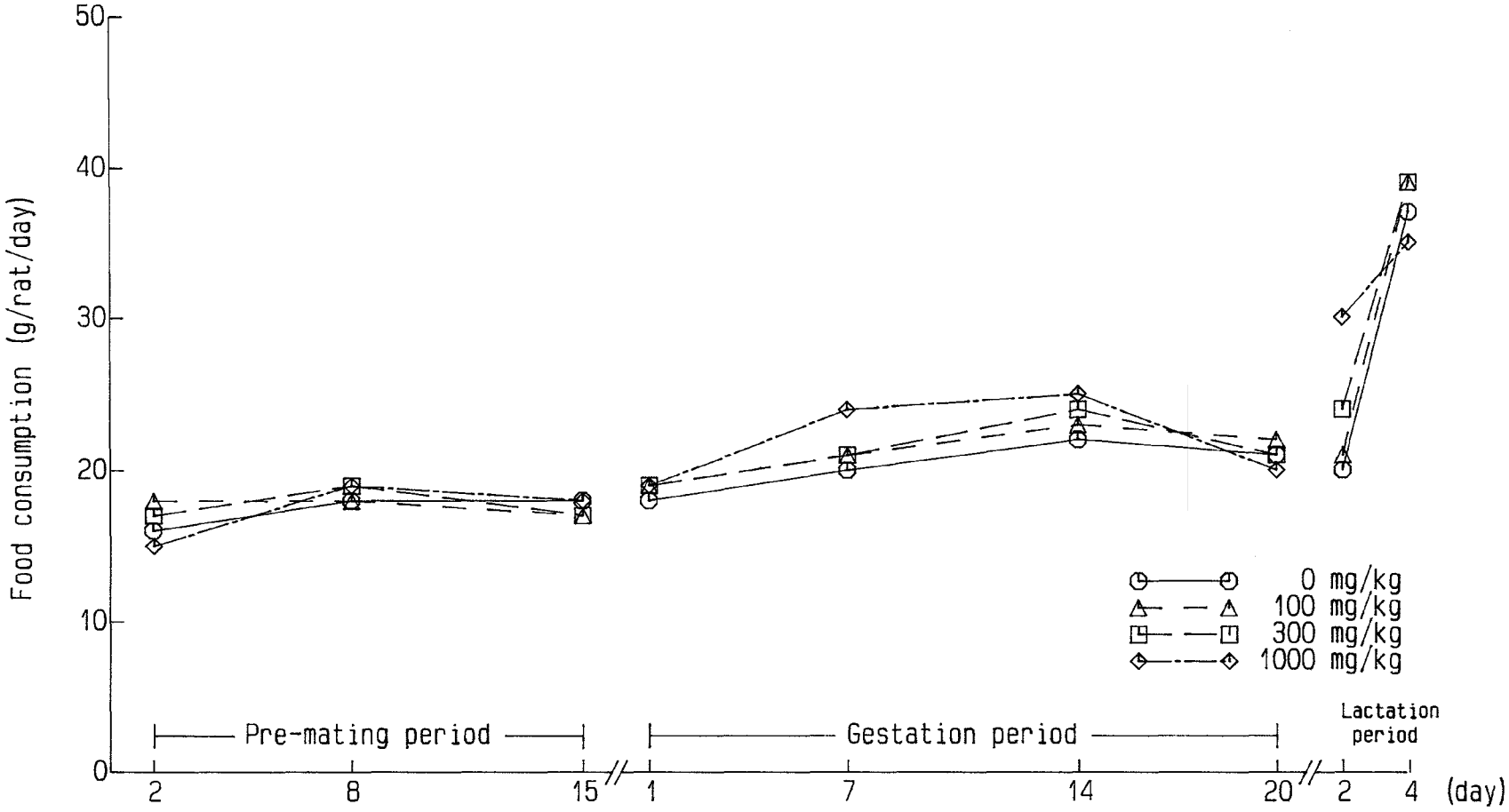


Fig.10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Food consumption of female rats (Main group)

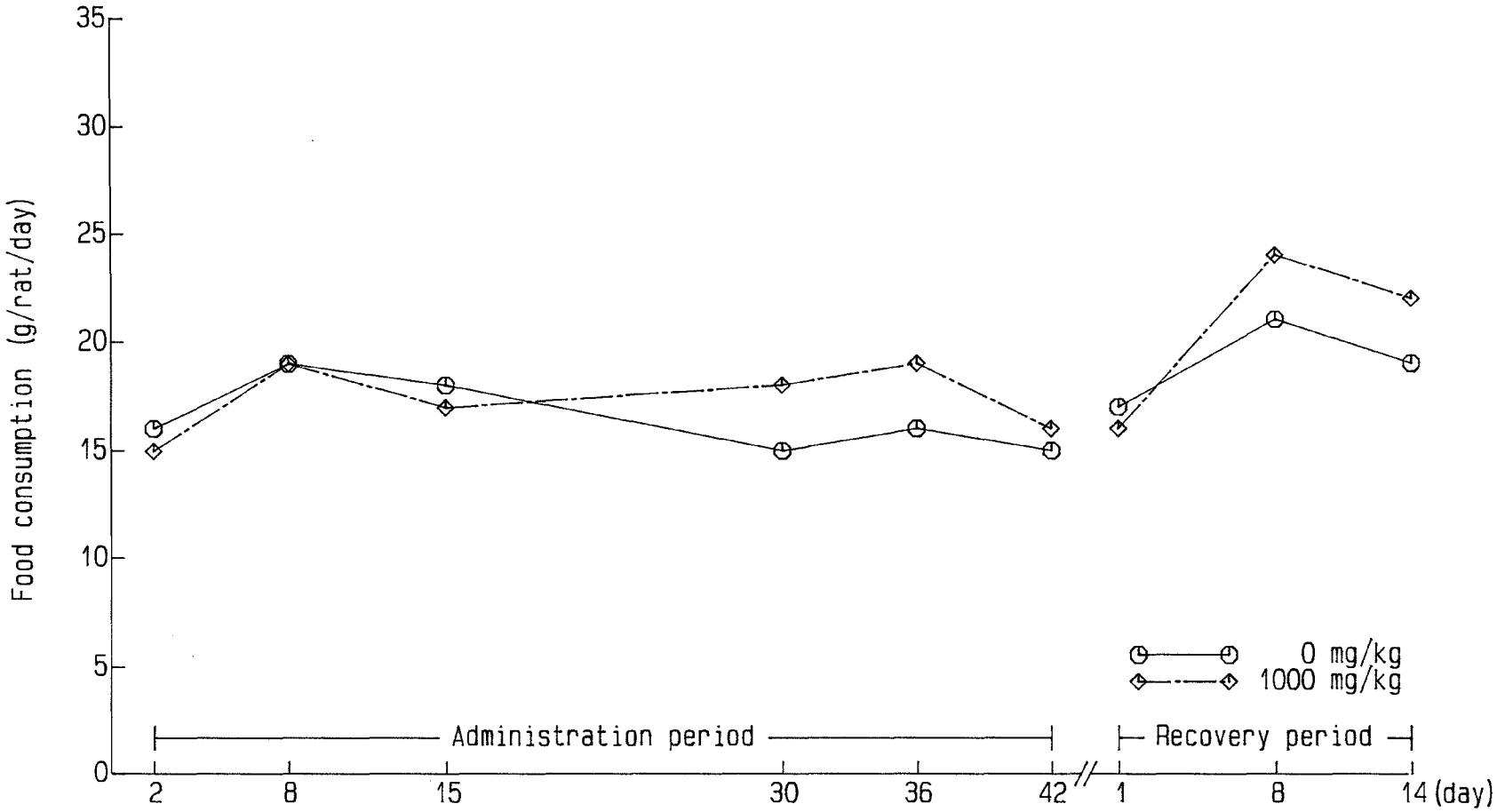


Fig.11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Food consumption of female rats (Satellite group)

Table 1-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	10	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	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	
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	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	
1000	No. of dams	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5	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	1	
	Continuation of delivery	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	

a): Gestation day

Table 1-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	11	11	11	11	11	11
	No. of dams with abnormal findings	0	0	0	0	0	0
100	No. of dams	12	12	12	12	12	12
	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	10	10	10	10	10	10
	No. of dams with abnormal findings	0	0	0	0	0	0

a): Lactation day
b): Day of necropsy

Table 1-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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	11	12	12	10
Posture					
Normal		11	12	12	10
Convulsion					
None		11	12	12	10
Abnormal behavior					
None		11	12	12	10

Table 2-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	11	12	12	10
Posture					
Normal		11	12	12	10
Convulsion					
None		11	12	12	10
Abnormal behavior					
None		11	12	12	10

Table 2-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	11	12	12	10
Posture					
Normal		11	12	12	10
Convulsion					
None		11	12	12	10
Abnormal behavior					
None		11	12	12	10

Table 2-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	11	12	12	10
Posture					
Normal		11	12	12	10
Convulsion					
None		11	12	12	10
Abnormal behavior					
None		11	12	12	10

Table 2-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	11	12	12	10
Posture					
Normal		11	12	12	10
Convulsion					
None		11	12	12	10
Abnormal behavior					
None		11	12	12	10

Table 2-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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	12	12	12
Reactivity to handling					
Easy		12	12	12	12

Table 2-25 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	11	11	11
Soft		0	1	1	1
Reactivity to handling					
Easy		12	12	12	12

Table 2-26 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	11
Slight		0	0	0	1
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	12	12	12
Reactivity to handling					
Easy		12	12	12	12

Table 2-27 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	11
Slight		0	0	0	1
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	12	12	12
Reactivity to handling					
Easy		12	12	12	12

Table 2-28 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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		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	10
Slight		0	0	0	2
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	12	12	12
Reactivity to handling					
Easy		12	12	12	12

Table 2-29 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	11
Slight		0	0	0	1
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	12	12	12
Reactivity to handling					
Easy		12	12	12	12

Table 2-30 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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	11	12	12	10
Ease of removal from cage					
Easy		11	12	12	10
Fur condition					
Normal		11	12	12	10
Skin					
Normal		11	12	12	10
Secretions-Eye, Nose					
Absent		11	12	12	10
Exophthalmos					
Absent		11	12	12	10
Palpebral closure					
Normal		11	12	12	10
Mucosal membranes					
Normal		11	12	12	10
Lacrimation					
Normal		11	12	12	10
Piloerection					
Absent		11	12	12	10
Pupil size					
Normal		11	12	12	10
Salivation					
None		11	12	12	9
Slight		0	0	0	1
Abnormal respiration					
Absent		11	12	12	10
Vocalization					
None		11	12	12	10
Reactivity to handling					
Easy		11	12	12	10

Table 2-33 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	11	12	12	10
Ease of removal from cage					
Easy		11	12	12	10
Fur condition					
Normal		11	12	12	10
Skin					
Normal		11	12	12	10
Secretions-Eye, Nose					
Absent		11	12	12	10
Exophthalmos					
Absent		11	12	12	10
Palpebral closure					
Normal		11	12	12	10
Mucosal membranes					
Normal		11	12	12	10
Lacrimation					
Normal		11	12	12	10
Piloerection					
Absent		11	12	12	10
Pupil size					
Normal		11	12	12	10
Salivation					
None		11	12	12	5
Slight		0	0	0	5
Abnormal respiration					
Absent		11	12	12	10
Vocalization					
None		11	12	12	10
Reactivity to handling					
Easy		11	12	12	10

Table 2-34 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	11	12	12	10
Ease of removal from cage					
Easy		11	12	12	10
Fur condition					
Normal		11	12	12	10
Skin					
Normal		11	12	12	10
Secretions-Eye, Nose					
Absent		11	12	12	10
Exophthalmos					
Absent		11	12	12	10
Palpebral closure					
Normal		11	12	12	10
Mucosal membranes					
Normal		11	12	12	10
Lacrimation					
Normal		11	12	12	10
Piloerection					
Absent		11	12	12	10
Pupil size					
Normal		11	12	12	10
Salivation					
None		11	12	12	6
Slight		0	0	0	4
Abnormal respiration					
Absent		11	12	12	10
Vocalization					
None		11	12	12	10
Reactivity to handling					
Easy		11	12	12	10

Table 2-35 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	11	12	12	10
Ease of removal from cage					
Easy		11	12	12	10
Fur condition					
Normal		11	12	12	10
Skin					
Normal		11	12	12	10
Secretions-Eye, Nose					
Absent		11	12	12	10
Exophthalmos					
Absent		11	12	12	10
Palpebral closure					
Normal		11	12	12	10
Mucosal membranes					
Normal		11	12	12	10
Lacrimation					
Normal		11	12	12	10
Piloerection					
Absent		11	12	12	10
Pupil size					
Normal		11	12	12	10
Salivation					
None		11	12	12	9
Slight		0	0	0	1
Abnormal respiration					
Absent		11	12	12	10
Vocalization					
None		11	12	12	10
Reactivity to handling					
Easy		11	12	12	10

Table 2-36 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	11	12	12	10
Ease of removal from cage					
Easy		11	12	12	10
Fur condition					
Normal		11	12	12	10
Skin					
Normal		11	12	12	10
Secretions-Eye, Nose					
Absent		11	12	12	10
Exophthalmos					
Absent		11	12	12	10
Palpebral closure					
Normal		11	12	12	10
Mucosal membranes					
Normal		11	12	12	10
Lacrimation					
Normal		11	12	12	10
Piloerection					
Absent		11	12	12	10
Pupil size					
Normal		11	12	12	10
Salivation					
None		11	12	12	10
Abnormal respiration					
Absent		11	12	12	10
Vocalization					
None		11	12	12	10
Reactivity to handling					
Easy		11	12	12	10

Table 2-37 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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	9
Slight		0	1
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 Methyl(2-pentyl-3-oxocyclopentyl) 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	9
Slight		0	1
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 Methyl(2-pentyl-3-oxocyclopentyl) 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	9
Slight		0	1
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 Methyl(2-pentyl-3-oxocyclopentyl) 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	9
Slight		0	1
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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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.)		5± 2	5± 2	4± 2	5± 1
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	10	11	9
Small amount		0	2	1	3

No significant difference in any treated groups from control group.

Table 2-48 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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.)		5± 2	4± 2	4± 2	5± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 1	0± 1
Urination					
None		12	10	10	10
Small amount		0	2	2	2

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 Methyl(2-pentyl-3-oxocyclopentyl) 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.)		4± 2	4± 1	3± 2	5± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 1	0± 0
Urination					
None		12	10	9	11
Small amount		0	2	3	1

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 Methyl(2-pentyl-3-oxocyclopentyl) 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					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		5± 1	4± 2	5± 2	4± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		11	10	9	10
Small amount		1	2	3	2

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 Methyl(2-pentyl-3-oxocyclopentyl) 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	4± 1	4± 1	5± 1
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		11	10	10	11
Small amount		1	2	2	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 Methyl(2-pentyl-3-oxocyclopentyl) 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					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		4± 2	3± 1	4± 2	4± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		10	10	11	9
Small amount		2	2	1	3

No significant difference in any treated groups from control group.

Table 2-53 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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.)		7± 3	6± 2	5± 2	5± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	12	12	11
Small amount		0	0	0	1

No significant difference in any treated groups from control group.

Table 2-54 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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.)		7± 3	6± 2	7± 2	7± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	12	11	12
Small amount		0	0	1	0

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 Methyl(2-pentyl-3-oxocyclopentyl) 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	11	12	12	10
Arousal					
Normal		11	12	12	10
Convulsion					
None		11	12	12	10
Abnormal behavior					
None		11	12	12	10
Stereotypy					
None		11	12	12	10
Gait					
Normal		11	12	12	10
Posture					
Normal		11	12	12	10
Grooming					
None		11	12	12	10
Rearing (Mean±S.D.)		7± 2	6± 2	5± 2	6± 1
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		11	12	11	9
Small amount		0	0	1	1

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 Methyl(2-pentyl-3-oxocyclopentyl) 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	11	12	12	10
Arousal					
Normal		11	12	12	10
Convulsion					
None		11	12	12	10
Abnormal behavior					
None		11	12	12	10
Stereotypy					
None		11	12	12	10
Gait					
Normal		11	12	12	10
Posture					
Normal		11	12	12	10
Grooming					
None		11	12	12	10
Rearing (Mean±S.D.)		6± 2	6± 2	6± 2	6± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		11	12	12	10

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 Methyl(2-pentyl-3-oxocyclopentyl) 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	11	12	12	10
Arousal					
Normal		11	12	12	10
Convulsion					
None		11	12	12	10
Abnormal behavior					
None		11	12	12	10
Stereotypy					
None		11	12	12	10
Gait					
Normal		11	12	12	10
Posture					
Normal		11	12	12	10
Grooming					
None		11	12	12	10
Rearing (Mean±S.D.)		6± 2	6± 2	6± 2	5± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		11	12	12	10

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 Methyl(2-pentyl-3-oxocyclopentyl) 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	11	12	12	10
Arousal					
Normal		11	12	12	10
Convulsion					
None		11	12	12	10
Abnormal behavior					
None		11	12	12	10
Stereotypy					
None		11	12	12	10
Gait					
Normal		11	12	12	10
Posture					
Normal		11	12	12	10
Grooming					
None		11	12	12	10
Rearing (Mean±S.D.)		5± 2	5± 2	4± 2	4± 1
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		11	12	12	10

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 Methyl(2-pentyl-3-oxocyclopentyl) 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	11	12	12	10
Arousal					
Normal		11	12	12	10
Convulsion					
None		11	12	12	10
Abnormal behavior					
None		11	12	12	10
Stereotypy					
None		11	12	12	10
Gait					
Normal		11	12	12	10
Posture					
Normal		11	12	12	10
Grooming					
None		11	12	12	10
Rearing (Mean±S.D.)		7± 2	6± 3	6± 2	4± 2*D
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		11	12	12	9
Small amount		0	0	0	1

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

Table 2-60 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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.)		6± 2	6± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	10

No significant difference between treated group and control group.

Table 2-61 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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.)		7± 3	8± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	9
Small amount		0	1

No significant difference between treated group and control group.

Table 2-62 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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.)		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 2-63 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	8± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	10

No significant difference between treated group and control group.

Table 2-64 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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.)		9± 2	8± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	8
Small amount		0	2

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 Methyl(2-pentyl-3-oxocyclopentyl) 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± 3	8± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	10

No significant difference between treated group and control group.

Table 2-66 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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.)		4± 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 Methyl(2-pentyl-3-oxocyclopentyl) 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.)		4± 2	4± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		4	4
Small amount		1	1

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 Methyl(2-pentyl-3-oxocyclopentyl) 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.)		8± 2	8± 3
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		5	5

No significant difference between treated group and control group.

Table 2-69 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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.)		7± 1	8± 1
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		5	5

No significant difference between treated group and control group.

Table 2-70 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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.)		73±30	76±19	83±15	49±13

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 Methyl(2-pentyl-3-oxocyclopentyl) 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.)		50±11	51±18	56±18	48± 9

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 Methyl(2-pentyl-3-oxocyclopentyl) 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±18	51±14

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 Methyl(2-pentyl-3-oxocyclopentyl) 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.)		71±28	63±17

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 Methyl(2-pentyl-3-oxocyclopentyl) 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.)		65±20	65±18

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 Methyl(2-pentyl-3-oxocyclopentyl) 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	1466	939
	S.D.	206	169
100	No.	5	5
	Mean	1407	972
	S.D.	175	94
300	No.	5	5
	Mean	1443	896
	S.D.	179	179
1000	No.	5	5
	Mean	1312	768
	S.D.	148	123

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 Methyl(2-pentyl-3-oxocyclopentyl) 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	1165	707
	S.D.	229	73
100	No.	5	5
	Mean	1212	779
	S.D.	167	145
300	No.	5	5
	Mean	1309	845
	S.D.	135	129
1000	No.	5	5
	Mean	1361	957**
	S.D.	266	71D

No.: No. of animals
**: p<0.01 (Significant difference from control group)
D: Dunnett's test

Table 2-77 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	1029	677
	S.D.	92	137
1000	No.	5	5
	Mean	1122	676
	S.D.	154	174

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 Methyl(2-pentyl-3-oxocyclopentyl) 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	1816	1212
	S.D.	262	85
1000	No.	5	5
	Mean	1759	990**
	S.D.	40	96T

No.: No. of animals
**: p<0.01 (Significant difference from control group)
T: Student's t-test

Table 2-79 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	1302	714
	S.D.	185	163
1000	No.	5	5
	Mean	1414	796
	S.D.	103	58

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

Table 2-80 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	424	265	189	139	126	23	1165
	S.D.	53	163	85	103	111	26	382
100	No.	5	5	5	5	5	5	5
	Mean	456	391	280	191	236	307**	1863
	S.D.	68	55	133	130	155	161D	566
300	No.	5	5	5	5	5	5	5
	Mean	451	378	307	260	195	125	1715
	S.D.	25	40	134	133	146	103	353
1000	No.	5	5	5	5	5	5	5
	Mean	427	347	382*	290	160	195	1802
	S.D.	36	105	31D	141	161	153	432

Unit: Count
No.: No. of animals
*: $p<0.05$; **: $p<0.01$ (Significant difference from control group)
D: Dunnett's test

Table 2-81 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	403	300	210	252	160	75	1401
	S.D.	43	70	102	97	92	87	411
100	No.	5	5	5	5	5	5	5
	Mean	402	273	33*	34*	14*	11	767
	S.D.	24	121	39D	31ST	10ST	9	198
300	No.	5	5	5	5	5	5	5
	Mean	373	218	158	178	92	114	1133
	S.D.	66	143	130	139	110	111	600
1000	No.	5	5	5	5	5	5	5
	Mean	347	162	86	24*	39	68	726*
	S.D.	107	120	73	17ST	62	82	209D

Unit: Count
No.: No. of animals
*: $p<0.05$ (Significant difference from control group)
D: Dunnett's test
ST: Steel's test

Table 2-82 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	379	306	278	254	96	90	1402
	S.D.	16	42	97	135	123	119	330
1000	No.	5	5	5	5	5	5	5
	Mean	355	335	280	219	208	118	1515
	S.D.	59	62	62	134	121	123	471

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 Methyl(2-pentyl-3-oxocyclopentyl) 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	380	272	130	174	199	104	1258
	S.D.	31	127	106	125	148	99	178
1000	No.	5	5	5	5	5	5	5
	Mean	417	315	161	279	235	255	1662
	S.D.	42	100	150	131	100	190	482

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 Methyl(2-pentyl-3-oxocyclopentyl) 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	380	265	194	161	108	160	1268
	S.D.	63	60	139	149	137	121	436
1000	No.	5	5	5	5	5	5	5
	Mean	382	366	194	81	65	122	1210
	S.D.	65	101	133	75	74	118	423

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 Methyl(2-pentyl-3-oxocyclopentyl) 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
	No.	12	12	12	12	12	12	12	12
0	Mean	430	457	477	498	521	541	553	123
	S.D.	19	21	26	30	34	36	35	21
	No.	12	12	12	12	12	12	12	12
100	Mean	430	459	485	512	540	564	580	149*
	S.D.	19	21	25	31	32	33	34	20D
	No.	12	12	12	12	12	12	12	12
300	Mean	431	447	470	488	513	538	550	119
	S.D.	18	23	27	26	30	34	34	21
	No.	12	12	12	12	12	12	12	12
1000	Mean	428	436	459	475	496	516	526	98*
	S.D.	19	24	26	27	31	33	35	26D

Unit: g
No.: No. of animals
*: $p<0.05$ (Significant difference from control group)
D: Dunnett's test

Table 3-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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
	No.	12	12	12	12
0	Mean	256	268	275	19
	S.D.	12	14	12	4
	No.	12	12	12	12
100	Mean	258	268	275	17
	S.D.	15	14	15	9
	No.	12	12	12	12
300	Mean	257	264	271	14
	S.D.	12	13	11	8
	No.	12	12	12	12
1000	Mean	253	260	268	16
	S.D.	9	13	17	15

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 Methyl(2-pentyl-3-oxocyclopentyl) 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
	No.	11	11	11	11	11
0	Mean	280	308	343	426	146
	S.D.	19	19	18	22	12
	No.	12	12	12	12	12
100	Mean	281	316	355	437	156
	S.D.	18	22	25	27	15
	No.	12	12	12	12	12
300	Mean	274	308	345	420	146
	S.D.	16	17	18	23	13
	No.	10	10	10	10	10
1000	Mean	278	311	346	405	127**
	S.D.	13	12	13	14	18D

Unit: g
No.: No. of dams
a): Gestation day
**: p<0.01 (Significant difference from control group)
D: Dunnett's test

Table 3-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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
	No.	11	11	11
0	Mean	326	341	14
	S.D.	27	25	16
	No.	12	12	12
100	Mean	341	355	13
	S.D.	22	24	13
	No.	12	12	12
300	Mean	323	342	19
	S.D.	23	26	13
	No.	10	10	10
1000	Mean	321	337	16
	S.D.	17	16	15

Unit: g
No.: No. of dams
a): Lactation day
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 Methyl(2-pentyl-3-oxocyclopentyl) 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
	No.	10	10	10	10	10	10	10	10
0	Mean	255	268	276	284	289	297	302	47
	S.D.	12	11	9	13	13	11	14	10
	No.	10	10	10	10	10	10	10	10
1000	Mean	258	260	264*	276	282	288	289	31**
	S.D.	11	11	10T	11	13	14	15	14T

Unit: g
No.: No. of animals
*: p<0.05; **: p<0.01 (Significant difference from control group)
T: Student's t-test

Table 3-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	546	558	563	16
	S.D.	28	28	29	9
1000	No.	5	5	5	5
	Mean	541	555	567	27
	S.D.	49	56	53	8

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 Methyl(2-pentyl-3-oxocyclopentyl) 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
	No.	5	5	5	5
0	Mean	305	308	307	2
	S.D.	15	14	11	6
	No.	5	5	5	5
1000	Mean	289	301	305	16**
	S.D.	15	19	18	4T

Unit: g
No.: No. of animals
**: p<0.01 (Significant difference from control group)
T: Student's t-test

Table 4-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	24	25	22	22	24	21
	S.D.	3	2	2	3	2	2
	No.	12	12	12	12	12	12
100	Mean	25	28*	26**	25*	25	24
	S.D.	2	3D	3D	3D	2	3
	No.	12	12	12	12	12	12
300	Mean	23	25	24	23	25	23
	S.D.	3	3	3	3	2	2
	No.	12	12	12	12	12	12
1000	Mean	20**	23	24	27**	27**	25**
	S.D.	2D	4	2	3D	2D	3D

Unit: g/rat/day
No.: No. of animals
*: $p<0.05$; **: $p<0.01$ (Significant difference from control group)
D: Dunnett's test

Table 4-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	18
	S.D.	3	3	2
	No.	12	12	12
100	Mean	18	18	17
	S.D.	3	1	3
	No.	12	12	12
300	Mean	17	19	17
	S.D.	2	3	2
	No.	12	12	12
1000	Mean	15	19	18
	S.D.	3	3	3

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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Food consumption of dams during the gestation period (Main group)

Dose mg/kg		Administration 1	7	14	20a)
	No.	11	11	11	11
0	Mean	18	20	22	21
	S.D.	2	4	4	2
	No.	12	12	12	12
100	Mean	19	21	23	22
	S.D.	3	2	3	3
	No.	12	12	12	12
300	Mean	19	21	24	21
	S.D.	2	3	4	2
	No.	10	10	10	10
1000	Mean	19	24*	25	20
	S.D.	3	3D	3	4

Unit: g/rat/day
No.: No. of dams
a): Gestation day
*: $p<0.05$ (Significant difference from control group)
D: Dunnett's test

Table 4-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Food consumption of dams during the lactation period (Main group)

Dose mg/kg		Administration 2	4a)
	No.	11	11
0	Mean	20	37
	S.D.	6	6
	No.	12	12
100	Mean	21	39
	S.D.	5	6
	No.	12	12
300	Mean	24	39
	S.D.	4	7
	No.	10	10
1000	Mean	30**	35
	S.D.	5D	6

Unit: g/rat/day
No.: No. of dams
a): Lactation day
**: p<0.01 (Significant difference from control group)
D: Dunnett's test

Table 4-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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
	No.	10	10	10	10	10	10
0	Mean	16	19	18	15	16	15
	S.D.	2	2	2	2	1	2
	No.	10	10	10	10	10	10
1000	Mean	15	19	17	18*	19**	16
	S.D.	1	3	3	3T	3AT	2

Unit: g/rat/day
No.: No. of animals
*: $p<0.05$; **: $p<0.01$ (Significant difference from control group)
T: Student's t-test
AT: Aspin-Welch t-test

Table 4-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Food consumption of male rats (Recovery period)

Dose mg/kg		Day of recovery 1	8	14
	No.	5	5	5
0	Mean	22	31	29
	S.D.	2	3	1
	No.	5	5	5
1000	Mean	26	33	31*
	S.D.	3	4	2T

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

Table 4-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	17	21	19
	S.D.	2	1	4
	No.	5	5	5
1000	Mean	16	24	22
	S.D.	1	3	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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Urinalysis of male rats (Week 6 of administration)

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	1	2	1	0	1	0	0	0	1	4	0	0	0	2	0	3	5	0	0	0	0
100	5	0	0	0	1	2	1	0	1	0	1	1	1	2	0	0	1	3	1	0	5	0	0	0	0
300	5	0	0	0	2	2	1	0	0	0	0	0	5	0	0	0	2	3	0	0	5	0	0	0	0
1000	5	0	0	3	1	1	0	0	0	0	0	1	2	1	1	1	3	1	0	0	5	0	0	0	0

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

Table 5-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	3	0	0	0	1	4	0	0	3	2	0	0	0	5	0
100	5	5	0	0	0	0	5	0	0	0	3	2	0	0	0	5	0
300	5	4	1	0	0	0	5	0	0	0	5	0	0	0	0	5	0
1000	5	3	2	0	0	0	5	0	0	0	4	1	0	0	0	5	0

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

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

		URINE SEDIMENT																																
																										CRYSTALLIZATION								
		RBC					WBC					SEC					SREC					Cast			PS					CO				
Dose mg/kg	No.	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	-	+-	+	++	+++	-	+-	+	++	+++
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
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	1	3	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	0	4	1	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	3	2	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 Methyl(2-pentyl-3-oxocyclopentyl) 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	33	8.1	1966	0.78	2.69	1.13
		S.D.	5	2.0	366	0.28	0.75	0.34
100	5	Mean	38	11.3	2122	0.96	3.91	1.41
		S.D.	5	5.5	538	0.39	1.36	0.67
300	5	Mean	41	13.7	1766	0.87	3.98	1.32
		S.D.	9	6.5	410	0.27	1.33	0.45
1000	5	Mean	49**	16.5*	1698	1.11	4.07	1.66
		S.D.	6D	5.2D	330	0.34	1.29	0.53

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

Table 5-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Urinalysis of female rats (Satellite group, Week 6 of administration)

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

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

Table 5-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	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 5-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Urinalysis of female rats (Satellite group, Week 6 of administration)

Dose	No.	URINE SEDIMENT																																
																									CRYSTALLIZATION									
		RBC					WBC					SEC					SREC					Cast			PS					CO				
mg/kg		-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	-	+-	+	++	+++	-	+-	+	++	+++
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	5	0	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	3	2	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 Methyl(2-pentyl-3-oxocyclopentyl) 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	33	6.8	1799	0.51	2.05	0.87
		S.D.	5	1.8	261	0.16	0.28	0.11
1000	5	Mean	54**	19.6**	910**	0.69	2.63*	1.12
		S.D.	6T	4.0T	114T	0.14	0.46T	0.35

*: p<0.05; **: p<0.01 (Significant difference from control group)
T: Student's t-test

Table 5-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	1	2	1	1	1	0	4	0	0	0	1	2	1	1	5	0	0	0	0
1000	5	0	0	0	0	0	0	2	1	2	0	2	2	1	0	0	1	2	2	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 Methyl(2-pentyl-3-oxocyclopentyl) 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	4	1	0	0	4	1	0	0	0	5	0
1000	5	2	3	0	0	0	3	2	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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Urinalysis of male rats (Week 2 of recovery)

		URINE SEDIMENT																																
																									CRYSTALLIZATION									
Dose	No.	RBC					WBC					SEC					SREC					Cast			PS					CO				
mg/kg		-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	-	+-	+	++	+++	-	+-	+	++	+++
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	5	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	4	1	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 Methyl(2-pentyl-3-oxocyclopentyl) 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	39	15.7	1993	1.41	5.03	1.90
		S.D.	6	4.8	335	0.24	1.28	0.28
1000	5	Mean	44	18.1	1905	1.85	5.63	2.31
		S.D.	6	5.5	315	0.56	1.52	0.64

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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Urinalysis of female 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	3	0	0	1	0	1	0	5	0	0	0	0	4	1	0	0	0	5	0	0	0	0
1000	5	0	0	0	0	2	2	1	0	0	3	2	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 Methyl(2-pentyl-3-oxocyclopentyl) 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	5	0	0	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 Methyl(2-pentyl-3-oxocyclopentyl) 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 -	+-	+	++	+++	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	4	1	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 5-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	33	9.6	1987	0.79	2.82	1.01
		S.D.	8	5.4	480	0.13	0.64	0.24
1000	5	Mean	41	16.2	1462	1.11*	3.73	1.47*
		S.D.	9	5.1	220	0.26T	0.66	0.32T

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

Table 6-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	866	15.5	44.5	51.5	17.9	34.8	1.9	102.6	13.6	18.0	277
		S.D.	49	0.3	1.0	2.8	1.0	0.3	0.3	3.7	0.9	1.9	30
100	5	Mean	868	15.2	44.1	50.8	17.5	34.5	2.2	102.4	13.8	17.7	260
		S.D.	34	0.7	2.5	1.4	0.4	0.4	0.4	9.3	1.5	2.0	16
300	5	Mean	872	15.1	43.3	49.8	17.3	34.9	2.3	100.0	14.8	20.0	268
		S.D.	57	0.4	0.9	2.6	0.9	0.4	0.3	9.2	1.6	2.6	25
1000	5	Mean	830	15.2	44.0	53.1	18.3	34.5	2.4	100.9	15.2	19.3	295
		S.D.	13	0.4	1.5	2.2	0.6	0.4	0.4	9.5	1.0	1.2	24

No significant difference in any treated groups from control group.

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

Dose mg/kg	No.		WBC 10E2/μL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/μL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	5	Mean	78.8	73.9	22.0	1.1	0.4	1.8	0.8	57.8	17.8	0.8	0.3	1.5	0.6
		S.D.	12.1	7.0	6.7	0.3	0.1	0.7	0.5	6.3	8.3	0.2	0.1	0.7	0.3
100	5	Mean	104.1	72.2	23.7	0.8	0.4	1.8	1.0	76.7	23.3	0.8	0.5	1.8	1.1
		S.D.	33.3	6.4	6.6	0.3	0.1	0.4	0.5	29.8	4.5	0.3	0.3	0.3	0.6
300	5	Mean	77.6	71.5	24.9	0.8	0.3	1.9	0.7	55.6	19.1	0.6	0.3	1.5	0.6
		S.D.	20.4	3.3	3.2	0.3	0.1	0.8	0.2	15.8	4.5	0.2	0.2	0.7	0.3
1000	5	Mean	90.8	73.3	21.6	0.7	0.4	2.6	1.5*	66.5	19.6	0.7	0.3	2.3	1.4*
		S.D.	6.7	4.0	4.1	0.3	0.1	1.0	0.3D	6.2	4.0	0.3	0.1	0.9	0.3D

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 Methyl(2-pentyl-3-oxocyclopentyl) 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	701	13.0	38.6	55.2	18.6	33.7	7.3	145.4	12.2	14.6	297
		S.D.	18	0.6	2.0	3.2	1.0	0.1	1.4	20.8	0.3	2.4	44
100	5	Mean	684	12.9	38.5	56.5	18.9	33.6	9.2	154.9	12.3	14.6	321
		S.D.	56	0.6	1.9	3.1	0.9	0.4	3.1	15.9	0.6	1.9	40
300	5	Mean	649	12.6	37.0	57.2	19.5	34.1	8.9	133.6	12.0	14.4	319
		S.D.	34	0.7	1.3	1.5	0.3	0.8	3.0	15.1	0.2	1.6	62
1000	5	Mean	699	13.4	38.7	55.5	19.3	34.7*	6.2	148.3	12.2	13.9	256
		S.D.	40	0.4	1.6	2.4	1.0	0.5D	0.9	15.5	0.3	1.4	23

*: $p<0.05$ (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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Hematology of female rats (Lactation day 5)

Dose mg/kg	No.		WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	5	Mean	98.9	54.3	42.3	0.6	0.2	2.1	0.5	53.5	42.0	0.6	0.2	2.2	0.5
		S.D.	8.8	5.9	5.4	0.4	0.0	1.0	0.1	6.2	7.4	0.4	0.0	1.1	0.1
100	5	Mean	106.0	63.4	32.6	0.6	0.3	2.3	0.8	66.7	35.1	0.6	0.3	2.5	0.9
		S.D.	27.4	9.7	9.5	0.2	0.1	0.3	0.3	17.4	14.1	0.2	0.1	0.9	0.5
300	5	Mean	104.8	54.0	42.4	0.4	0.2	2.0	0.9	56.3	44.7	0.4	0.2	2.2	1.0
		S.D.	20.4	7.9	7.8	0.2	0.1	0.5	0.5	12.4	14.1	0.1	0.1	0.7	0.5
1000	5	Mean	85.6	60.3	34.8	0.3	0.2	3.4*	0.9	51.5	30.0	0.3	0.2	2.8	0.8*
		S.D.	10.3	11.3	11.3	0.2	0.1	0.7D	0.3	10.8	11.6	0.1	0.1	0.3	0.2ST

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

Table 6-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	850	15.4	43.5	51.2	18.1	35.4	2.2	101.7	11.8	16.7	197
		S.D.	36	0.6	1.7	0.7	0.2	0.4	0.3	5.1	0.4	2.6	14
1000	5	Mean	785**	14.4*	41.2*	52.5	18.4	35.0	2.3	111.0	11.8	15.7	208
		S.D.	24T	0.4T	1.4T	1.5	0.5	0.3	0.3	10.2	0.6	1.1	30

*: $p<0.05$; **: $p<0.01$ (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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Hematology of female rats (Satellite group, End of administration)

Dose mg/kg	No.		WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	5	Mean	49.6	71.8	24.0	1.3	0.2	2.0	0.6	35.8	11.8	0.6	0.1	1.0	0.3
		S.D.	10.4	7.9	8.3	0.3	0.0	0.8	0.1	8.7	3.8	0.2	0.0	0.5	0.2
1000	5	Mean	48.3	72.6	23.5	0.8	0.2	2.1	0.8	35.4	11.0	0.4	0.1	1.0	0.4
		S.D.	15.9	7.0	7.8	0.4	0.1	0.5	0.4	13.0	5.0	0.3	0.0	0.5	0.3

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 Methyl(2-pentyl-3-oxocyclopentyl) 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	889	15.6	44.3	49.8	17.6	35.3	1.8	95.0	17.5	22.4	294
		S.D.	39	0.4	1.0	1.4	0.6	0.7	0.3	10.8	1.9	3.8	34
1000	5	Mean	888	15.1	44.1	49.7	17.0	34.3*	2.1	113.9*	16.4	20.9	299
		S.D.	25	0.3	0.8	2.0	0.7	0.1AT	0.2	12.8T	2.3	2.8	16

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

Table 6-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Hematology of male rats (End of recovery)

Dose mg/kg	No.		WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	5	Mean	74.3	74.0	21.1	1.5	0.4	2.4	0.5	55.2	15.5	1.1	0.3	1.8	0.4
		S.D.	14.2	6.7	6.7	0.4	0.1	0.6	0.1	13.4	5.4	0.3	0.1	0.7	0.1
1000	5	Mean	71.7	70.3	23.8	1.6	0.4	2.5	1.3	50.8	16.7	1.2	0.3	1.8	1.0
		S.D.	15.9	3.5	4.7	0.6	0.2	0.9	0.7	13.4	2.9	0.4	0.1	0.7	0.7

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 Methyl(2-pentyl-3-oxocyclopentyl) 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	842	15.6	43.5	51.7	18.6	35.9	1.6	109.9	11.9	16.4	195
		S.D.	30	0.4	1.0	1.8	0.8	0.3	0.4	8.9	0.3	2.4	21
1000	5	Mean	864	15.7	44.5	51.6	18.2	35.3*	1.6	116.3	12.3	17.4	196
		S.D.	32	0.6	1.9	1.9	0.6	0.4T	0.4	9.1	0.4	0.9	15

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

Table 6-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Hematology of female rats (End of recovery)

Dose mg/kg	No.		WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	5	Mean	61.4	76.9	18.3	1.5	0.3	2.0	0.9	47.5	10.9	0.9	0.2	1.3	0.6
		S.D.	19.5	6.1	6.1	0.3	0.1	0.4	0.4	15.8	3.6	0.3	0.1	0.6	0.3
1000	5	Mean	58.0	77.6	17.5	1.6	0.3	1.9	1.1	45.2	10.0	1.0	0.1	1.1	0.6
		S.D.	12.4	5.1	5.3	0.3	0.1	0.4	0.4	11.3	2.6	0.4	0.1	0.3	0.3

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 Methyl(2-pentyl-3-oxocyclopentyl) 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	62	30	45	0	363	8.8	52	30	84	0.1	135
		S.D.	6	3	8	0	56	4.7	13	8	13	0.0	20
100	5	Mean	70	32	43	0	463	11.7	49	36	81	0.1	140
		S.D.	8	5	15	0	105	6.0	9	15	14	0.1	14
300	5	Mean	63	27	36	0	438	8.1	38	31	68	0.0*	139
		S.D.	10	3	5	0	77	4.8	5	14	8	0.0ST	10
1000	5	Mean	66	31	40	0	500*	16.9	50	35	85	0.1	132
		S.D.	5	1	5	1	88D	20.4	5	17	9	0.1	8

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

Table 7-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	12	0.31	144	4.4	107	9.9	6.9	5.7	3.1	1.19
		S.D.	1	0.02	1	0.3	1	0.2	0.5	0.3	0.1	0.06
100	5	Mean	13	0.31	144	4.5	106	9.6	6.4	5.6	3.1	1.25
		S.D.	1	0.04	1	0.2	1	0.2	0.2	0.3	0.1	0.14
300	5	Mean	12	0.36	144	4.6	106	10.0	6.4	5.6	3.2	1.28
		S.D.	2	0.02	1	0.2	1	0.4	0.4	0.2	0.2	0.09
1000	5	Mean	14**	0.35	145	4.4	104**	10.0	6.8	5.8	3.2	1.27
		S.D.	1D	0.05	1	0.1	2D	0.3	0.7	0.1	0.0	0.07

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

Table 7-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	73	48	37	0	254	23.1	56	45	117	0.1	132
		S.D.	7	9	8	0	66	33.2	13	20	25	0.0	8
100	5	Mean	89	50	49	0	215	16.0	51	47	101	0.0	123
		S.D.	24	10	11	0	16	6.8	9	26	18	0.1	10
300	5	Mean	85	64	43	0	401	18.8	60	87	118	0.0*	120
		S.D.	13	13	11	0	147	12.0	7	89	20	0.0ST	9
1000	5	Mean	76	64	32	1**	302	34.5	72*	93	139	0.0**	113*
		S.D.	13	7	3	0ST	39	10.9	7D	32	12	0.0ST	9D

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

Table 7-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	0.40	141	3.8	106	9.9	5.9	6.0	3.4	1.37
		S.D.	3	0.05	1	0.2	2	0.3	0.9	0.4	0.3	0.12
100	5	Mean	16	0.40	141	4.3	107	10.3	6.2	5.9	3.4	1.35
		S.D.	1	0.03	1	0.5	2	0.4	0.3	0.2	0.2	0.16
300	5	Mean	14	0.42	140	4.4	105	9.9	6.3	5.7	3.3	1.37
		S.D.	4	0.02	1	0.2	1	0.4	0.6	0.2	0.1	0.10
1000	5	Mean	19*	0.41	143	3.9	104	10.3	5.8	5.7	3.3	1.38
		S.D.	4D	0.04	2	0.3	3	0.4	1.3	0.3	0.1	0.05

*: $p<0.05$ (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 Methyl(2-pentyl-3-oxocyclopentyl) 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	54	23	39	0	262	11.9	61	18	119	0.1	136
		S.D.	5	2	6	0	77	5.7	7	3	8	0.0	7
1000	5	Mean	55	33**	32	0	239	27.0	83**	31**	154*	0.1	115**
		S.D.	8	5AT	5	0	51	25.8	11T	6T	24AT	0.0	8T

*: $p<0.05$; **: $p<0.01$ (Significant difference from control group)
T: Student's t-test
AT: Aspin-Welch t-test

Table 7-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	16	0.37	143	4.3	108	10.2	5.4	6.4	3.8	1.42
		S.D.	3	0.04	1	0.2	1	0.2	0.3	0.2	0.1	0.04
1000	5	Mean	17	0.40	143	4.2	105**	10.2	5.8	6.5	3.8	1.40
		S.D.	2	0.06	1	0.3	1AT	0.2	0.7	0.3	0.3	0.16

**: $p<0.01$ (Significant difference from control group)
AT: Aspin-Welch t-test

Table 7-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	67	31	47	0	344	10.0	53	28	84	0.1	141
		S.D.	10	5	5	0	94	3.7	12	7	13	0.0	6
1000	5	Mean	71	37	40*	0	347	8.8	62	40	95	0.1	139
		S.D.	5	3	3T	0	84	3.7	8	15	7	0.0	6

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

Table 7-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	0.29	144	4.2	106	9.4	5.3	6.1	3.2	1.14
		S.D.	2	0.01	1	0.2	2	0.1	0.3	0.2	0.1	0.05
1000	5	Mean	15	0.28	144	4.3	106	9.6	5.6	6.1	3.3	1.17
		S.D.	1	0.03	1	0.2	2	0.3	0.4	0.2	0.1	0.05

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 Methyl(2-pentyl-3-oxocyclopentyl) 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	82	43	58	0	203	12.7	66	17	123	0.1	139
		S.D.	20	15	16	0	66	5.2	9	4	14	0.0	14
1000	5	Mean	58	28	46	0	162	12.3	76	26	137	0.1	128
		S.D.	5	5	6	0	58	2.3	11	13	19	0.0	5

No significant difference between treated group and control group.

Table 7-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	0.38	143	4.3	109	9.9	5.0	6.4	3.7	1.38
		S.D.	4	0.05	1	0.2	2	0.2	0.5	0.2	0.2	0.07
1000	5	Mean	18	0.37	143	4.5	108	10.0	5.3	6.9*	3.9	1.28
		S.D.	3	0.04	1	0.2	1	0.2	0.4	0.3T	0.1	0.08

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

Table 8-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	540	2.13	14.2	22.7	263	1.60	14.15
		S.D.	41	0.07	1.7	4.2	43	0.16	2.02
	100	No.	12	12	12	12	12	12	12
		Mean	555	2.15	13.3	26.7	363**	1.59	14.65
		S.D.	33	0.07	1.5	4.5	82D	0.14	1.35
	300	No.	12	12	12	12	12	12	12
		Mean	524	2.12	14.0	24.6	304	1.53	15.61
		S.D.	35	0.06	2.3	8.3	73	0.17	1.67
	1000	No.	7	7	7	7	7	7	7
		Mean	489*	2.16	13.2	22.3	284	1.42	17.18**
		S.D.	26D	0.06	1.5	2.5	33	0.09	1.37D
Relative	0	No.		7	7	7	7	7	7
		Mean		0.39	2.6	4.2	49	0.30	2.61
		S.D.		0.03	0.3	0.7	9	0.04	0.22
	100	No.		12	12	12	12	12	12
		Mean		0.39	2.4	4.8	66*	0.29	2.64
		S.D.		0.02	0.3	0.9	15D	0.03	0.21
	300	No.		12	12	12	12	12	12
		Mean		0.41	2.7	4.6	58	0.29	2.97**
		S.D.		0.02	0.3	1.3	14	0.02	0.17D
	1000	No.		7	7	7	7	7	7
		Mean		0.44**	2.7	4.6	58	0.29	3.51**
		S.D.		0.02D	0.2	0.4	6	0.01	0.17D

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

Table 8-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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)
		No.	7	7	7	7	7	7	7
Absolute	0	Mean	0.84	3.44	66	3.25	1355	1.88	1.29
		S.D.	0.10	0.45	10	0.28	132	0.26	0.22
		No.	12	12	12	12	12	12	12
	100	Mean	0.81	3.68	64	3.34	1390	1.86	1.45
		S.D.	0.09	0.26	8	0.27	105	0.18	0.22
		No.	12	12	12	12	12	12	12
	300	Mean	0.80	3.52	66	3.38	1371	1.88	1.29
		S.D.	0.08	0.25	12	0.31	103	0.17	0.19
		No.	7	7	7	7	7	7	7
	1000	Mean	0.78	3.70	63	3.11	1365	1.80	1.29
		S.D.	0.07	0.40	11	0.25	42	0.21	0.22
		No.	7	7	7	7	7	7	7
Relative	0	Mean	0.16	0.64	12	0.60	251	0.35	0.24
		S.D.	0.02	0.06	3	0.03	15	0.04	0.04
		No.	12	12	12	12	12	12	12
	100	Mean	0.15	0.66	12	0.60	252	0.34	0.26
		S.D.	0.02	0.06	2	0.07	28	0.04	0.04
		No.	12	12	12	12	12	12	12
	300	Mean	0.15	0.67	13	0.65	262	0.36	0.25
		S.D.	0.01	0.03	2	0.07	21	0.03	0.03
		No.	7	7	7	7	7	7	7
	1000	Mean	0.16	0.75**	13	0.64	279*	0.37	0.26
		S.D.	0.01	0.05D	2	0.04	12D	0.04	0.05

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

Table 8-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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.	11	11	11	11	11	11	11
		Mean	314	1.99	19.3	16.2	171	1.01	10.35
		S.D.	22	0.06	1.6	3.7	72	0.09	0.74
	100	No.	12	12	12	12	12	12	12
		Mean	325	1.98	17.9	17.6	212	1.00	10.97
		S.D.	22	0.06	3.5	3.0	55	0.08	0.86
	300	No.	12	12	12	12	12	12	12
		Mean	314	2.01	18.3	15.7	174	1.02	11.69**
		S.D.	25	0.07	1.4	2.2	56	0.08	1.01D
	1000	No.	10	10	10	10	10	10	10
		Mean	303	1.99	17.1	19.3	135	0.98	13.66**
		S.D.	13	0.09	2.5	3.7	49	0.07	0.72D
Relative	0	No.		11	11	11	11	11	11
		Mean		0.64	6.2	5.2	54	0.32	3.30
		S.D.		0.04	0.5	1.2	22	0.03	0.14
	100	No.		12	12	12	12	12	12
		Mean		0.61	5.5	5.4	65	0.31	3.38
		S.D.		0.03	1.1	0.8	17	0.03	0.23
	300	No.		12	12	12	12	12	12
		Mean		0.64	5.8	5.0	56	0.33	3.73**
		S.D.		0.04	0.4	0.9	19	0.02	0.22D
	1000	No.		10	10	10	10	10	10
		Mean		0.66	5.6	6.4*	44	0.33	4.51**
		S.D.		0.04	0.7	1.2D	16	0.02	0.21D

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

Table 8-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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.	11	11	11	11	11
		Mean	0.65	2.11	82	97.3	723
		S.D.	0.07	0.32	8	8.5	94
	100	No.	12	12	12	12	12
		Mean	0.74	2.11	85	108.0	724
		S.D.	0.16	0.19	10	18.5	90
	300	No.	12	12	12	12	12
		Mean	0.72	2.23	84	110.3	679
		S.D.	0.09	0.14	11	11.2	108
	1000	No.	10	10	10	10	10
		Mean	0.63	2.35	85	105.2	613*
		S.D.	0.06	0.20	12	12.3	108D
Relative	0	No.	11	11	11	11	11
		Mean	0.21	0.67	26	31.1	232
		S.D.	0.01	0.10	3	2.4	38
	100	No.	12	12	12	12	12
		Mean	0.23	0.65	26	33.2	224
		S.D.	0.04	0.05	3	4.9	34
	300	No.	12	12	12	12	12
		Mean	0.23*	0.71	27	35.2*	216
		S.D.	0.02ST	0.04	4	3.0D	30
	1000	No.	10	10	10	10	10
		Mean	0.21	0.78**	28	34.8	202
		S.D.	0.02	0.08D	4	4.7	34

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

Table 8-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	287	1.95	16.1	16.1	294	0.93	7.19
		S.D.	12	0.05	2.5	1.3	22	0.04	0.67
	1000	No.	5	5	5	5	5	5	5
		Mean	269*	1.97	19.6	17.5	242	0.92	10.65**
		S.D.	8T	0.07	2.6	3.7	77	0.11	1.14T
Relative	0	No.		5	5	5	5	5	5
		Mean		0.68	5.6	5.6	103	0.33	2.50
		S.D.		0.01	1.0	0.4	11	0.02	0.14
	1000	No.		5	5	5	5	5	5
		Mean		0.74*	7.3*	6.5	90	0.34	3.96**
		S.D.		0.04AT	0.8T	1.4	28	0.03	0.34T

*: $p<0.05$; **: $p<0.01$ (Significant difference from control group)
T: Student's t-test
AT: Aspin-Welch t-test

Table 8-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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)
		No.	5	5	5	5	5
Absolute	0	Mean	0.48	1.91	71	91.9	599
		S.D.	0.07	0.16	6	3.6	176
		No.	5	5	5	5	5
	1000	Mean	0.50	2.11*	75	154.7	717
		S.D.	0.09	0.09T	8	176.5	119
		No.	5	5	5	5	5
Relative	0	Mean	0.17	0.67	24	32.1	207
		S.D.	0.02	0.05	2	1.8	52
		No.	5	5	5	5	5
	1000	Mean	0.18	0.78**	28*	56.4	267
		S.D.	0.03	0.02T	3T	62.7	44

*: $p<0.05$; **: $p<0.01$ (Significant difference from control group)
T: Student's t-test

Table 8-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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)
		No.	5	5	5	5	5	5	5
Absolute	0	Mean	531	2.18	14.2	24.1	247	1.62	13.62
		S.D.	26	0.07	1.5	4.0	57	0.23	1.34
		No.	5	5	5	5	5	5	5
	1000	Mean	533	2.20	14.0	25.9	266	1.58	15.11
		S.D.	53	0.05	1.1	3.8	83	0.20	1.86
		No.		5	5	5	5	5	5
Relative	0	Mean		0.41	2.6	4.5	46	0.31	2.56
		S.D.		0.01	0.4	0.7	12	0.05	0.15
		No.		5	5	5	5	5	5
	1000	Mean		0.41	2.6	4.9	49	0.29	2.83
		S.D.		0.04	0.2	0.4	11	0.02	0.25

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 Methyl(2-pentyl-3-oxocyclopentyl) 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)
		No.	5	5	5	5	5	5	5
Absolute	0	Mean	0.85	3.62	61	3.25	1323	2.06	1.51
		S.D.	0.16	0.23	10	0.35	88	0.34	0.13
		No.	5	5	5	5	5	5	5
	1000	Mean	0.89	3.58	66	3.59	1355	2.05	1.50
		S.D.	0.11	0.32	5	0.41	216	0.54	0.31
		No.	5	5	5	5	5	5	5
Relative	0	Mean	0.16	0.68	11	0.61	249	0.39	0.28
		S.D.	0.03	0.03	2	0.09	16	0.06	0.02
		No.	5	5	5	5	5	5	5
	1000	Mean	0.17	0.67	12	0.68	255	0.39	0.28
		S.D.	0.01	0.06	2	0.08	38	0.11	0.05

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 Methyl(2-pentyl-3-oxocyclopentyl) 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)
		No.	5	5	5	5	5	5	5
Absolute	0	Mean	290	1.96	16.8	16.5	296	0.92	7.28
		S.D.	13	0.09	2.1	3.8	52	0.05	0.44
		No.	5	5	5	5	5	5	5
	1000	Mean	285	1.98	17.7	16.8	291	0.96	8.18*
		S.D.	16	0.04	2.8	3.6	80	0.10	0.76T
		No.		5	5	5	5	5	5
Relative	0	Mean		0.67	5.8	5.7	102	0.32	2.51
		S.D.		0.03	0.5	1.6	18	0.02	0.13
		No.		5	5	5	5	5	5
	1000	Mean		0.69	6.2	5.9	103	0.34	2.87**
		S.D.		0.03	0.9	1.1	31	0.02	0.14T

*: $p<0.05$; **: $p<0.01$ (Significant difference from control group)
T: Student's t-test

Table 8-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	0.54	1.90	77	79.3	582
		S.D.	0.05	0.20	14	6.4	180
	1000	No.	5	5	5	5	5
		Mean	0.54	1.98	76	87.9	546
		S.D.	0.05	0.16	9	10.1	134
Relative	0	No.	5	5	5	5	5
		Mean	0.19	0.65	27	27.4	202
		S.D.	0.02	0.05	5	3.0	67
	1000	No.	5	5	5	5	5
		Mean	0.19	0.70	27	30.8	192
		S.D.	0.01	0.05	3	3.5	52

No significant difference between treated group and control group.

R-1106

Table 9-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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
Lung(bronchus)					
Focus,dark red		0	1	0	0
Stomach					
Focus,dark red,glandular stomach		0	0	0	1

M : Male

R-1106

Table 9-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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
Lung(bronchus)			
Focus,dark red		0	2
Ovary			
Cyst,unilateral		0	1
Stomach			
Focus,dark red,glandular stomach		0	1

F : Female

R-1106

Table 9-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:	11	12	12	10
Intestine,ileum(Peyer's patch)					
Diverticulum		1	0	0	0
Kidney					
Focus,white		0	0	0	3
Lung(bronchus)					
Focus,dark red		0	0	1	0
Stomach					
Focus,dark red,glandular stomach		2	0	1	0

F : Female

R-1106

Table 9-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Gross pathological findings (End of recovery period)

Organs	Sex:	M	M
	Dose(mg/kg):	0	1000
Findings	Number:	5	5
Intestine,ileum(Peyer's patch)			
Diverticulum		0	1
Lung(bronchus)			
Focus,dark red		1	0
Stomach			
Focus,dark red,glandular stomach		1	2

M : Male

R-1106

Table 9-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Gross pathological findings (End of recovery period)

Organs	Sex:	F	F
	Dose(mg/kg):	0	1000
Findings	Number:	5	5
Stomach			
Focus,dark red,glandular stomach		0	2

F : Female

R-1106

Table 9-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Gross pathological findings (Undelivered)

Organs	Sex:	F	F
	Dose(mg/kg):	0	1000
Findings	Number:	1	2
Uterus			
Dilatation,lumen		1	0

F : Female

Table 10-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Histopathological findings (End of administration period (D42))

Organs / Findings	Sex:	M	M	M	M
	Dose(mg/kg):	0	100	300	1000
	Number:	7	12	12	7
Adrenal					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Bone+Bone marrow,femoral					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Cerebellum(pons)					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Cerebrum					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Epididymis					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Eye					
Number examined		6	0	0	5
Not remarkable		6	0	0	4
Atrophy,retinal		0	0	0	1
mild		0	0	0	1
Heart					
Number examined		6	0	0	5
Not remarkable		5	0	0	3
Cell infiltration		1	0	0	2
minimal		1	0	0	2
Intestine,duodenum					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Intestine,jejunum					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Intestine,ileum(Peyer's patch)					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Intestine,cecum					
Number examined		6	0	0	5
Not remarkable		5	0	0	5
Cell infiltration		1	0	0	0
minimal		1	0	0	0
Intestine,colon					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Intestine,rectum					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Kidney					
Number examined		6	0	0	5
Not remarkable		2	0	0	1
Regeneration,tubular		4	0	0	4
minimal		4	0	0	4

M : Male

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

Organs / Findings	Sex:	M	M	M	M
	Dose(mg/kg):	0	100	300	1000
	Number:	7	12	12	7
Liver					
Number examined		6	5	5	5
Not remarkable		1	0	3	0
Microgranuloma		5	5	2	4
minimal		5	5	2	4
Hypertrophy,hepatocytic,centrilobular		0	0	1	5
minimal		0	0	1	0
mild		0	0	0	5
Lung(bronchus)					
Number examined		6	0	0	5
Not remarkable		5	0	0	5
Aggregation,alveolar macrophage		1	0	0	0
minimal		1	0	0	0
Lymph node,mesenteric					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Lymph node,submandibular					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Pancreas					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Parathyroid					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Pituitary					
Number examined		6	0	0	5
Not remarkable		5	0	0	5
Cyst,pars distalis		1	0	0	0
minimal		1	0	0	0
Prostate					
Number examined		6	0	0	5
Not remarkable		4	0	0	4
Cell infiltration		2	0	0	1
minimal		2	0	0	1
Salivary gland,submandibular					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Sciatic nerve					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Seminal vesicle(coagulating gland)					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Skeletal muscle,femoral					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Spinal cord,thoracic					
Number examined		6	0	0	5
Not remarkable		6	0	0	5

M : Male

Table 10-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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
Spleen					
Number examined		6	0	0	5
Not remarkable		3	0	0	1
Hematopoiesis,extramedullary		3	0	0	4
minimal		3	0	0	3
mild		0	0	0	1
Stomach					
Number examined		6	0	0	5
Not remarkable		6	0	0	4
Erosion,glandular stomach		0	0	0	1
minimal		0	0	0	1
Testis					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Thymus					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Thyroid					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Trachea					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Urinary bladder					
Number examined		6	0	0	5
Not remarkable		6	0	0	5

M : Male

Table 10-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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
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		5	5
Liver			
Number examined		5	5
Not remarkable		1	0
Microgranuloma		4	4
minimal		4	4
Hypertrophy,hepatocytic,centrilobular		0	5
minimal		0	2
mild		0	3

F : Female

Table 10-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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
Lung(bronchus)			
Number examined		5	5
Not remarkable		5	3
Hemorrhage,focal		0	1
minimal		0	1
Cell infiltration		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	3
Atrophy		0	2
mild		0	2
Cyst,ovarian bursa		0	1
mild		0	1
Pancreas			
Number examined		5	5
Not remarkable		5	5
Parathyroid			
Number examined		5	5
Not remarkable		5	5
Pituitary			
Number examined		5	5
Not remarkable		5	5
Salivary gland,submandibular			
Number examined		5	5
Not remarkable		5	5
Sciatic nerve			
Number examined		5	5
Not remarkable		5	5
Skeletal muscle,femoral			
Number examined		5	5
Not remarkable		5	5
Spinal cord,thoracic			
Number examined		5	5
Not remarkable		5	5
Spleen			
Number examined		5	5
Not remarkable		3	4
Hematopoiesis,extramedullary		2	1
minimal		2	1
Stomach			
Number examined		5	5
Not remarkable		5	4
Erosion,glandular stomach		0	1
minimal		0	1

F : Female

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Table 10-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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
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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Histopathological findings (End of administration period (L4))

Organs / Findings	Sex:	F	F	F	F
	Dose(mg/kg):	0	100	300	1000
	Number:	11	12	12	10
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	4
Dysplasia,retinal		0	0	0	1
minimal		0	0	0	1
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	5	5	5
Not remarkable		3	4	4	2
Dilatation,tubular,focal		0	0	0	2
minimal		0	0	0	2
Regeneration,tubular		2	1	1	2
minimal		2	1	1	2
Liver					
Number examined		5	5	5	5
Not remarkable		3	3	1	0
Microgranuloma		2	2	4	4
minimal		2	2	4	4

F : Female

Table 10-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Histopathological findings (End of administration period (L4))

Organs / Findings	Sex:	F	F	F	F
	Dose(mg/kg):	0	100	300	1000
	Number:	11	12	12	10
Liver (continued)					
Hypertrophy,hepatocytic,centrilobular		0	0	3	5
minimal		0	0	2	0
mild		0	0	1	5
Lung(bronchus)					
Number examined		5	0	0	5
Not remarkable		4	0	0	5
Aggregation,alveolar macrophage		1	0	0	0
mild		1	0	0	0
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	5	5	5
Not remarkable		5	5	5	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
mild		5	0	0	5
Stomach					
Number examined		5	0	0	5
Not remarkable		4	0	0	5
Erosion,glandular stomach		1	0	0	0
minimal		1	0	0	0

F : Female

Table 10-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:	11	12	12	10
Thymus					
Number examined		5	0	0	5
Not remarkable		4	0	0	5
Atrophy		1	0	0	0
minimal		1	0	0	0
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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Histopathological findings (End of recovery period)

Organs	Sex:	M	M
	Dose(mg/kg):	0	1000
Findings	Number:	5	5
Adrenal			
Number examined		0	1
Not remarkable		0	1
Bone+Bone marrow,femoral			
Number examined		0	1
Not remarkable		0	1
Cerebellum(pons)			
Number examined		0	1
Not remarkable		0	1
Cerebrum			
Number examined		0	1
Not remarkable		0	1
Epididymis			
Number examined		0	1
Not remarkable		0	1
Eye			
Number examined		0	1
Not remarkable		0	1
Heart			
Number examined		0	1
Not remarkable		0	1
Intestine,duodenum			
Number examined		0	1
Not remarkable		0	1
Intestine,jejunum			
Number examined		0	1
Not remarkable		0	1
Intestine,ileum(Peyer's patch)			
Number examined		0	2
Not remarkable		0	1
Diverticulum		0	1
mild		0	1
Intestine,cecum			
Number examined		0	1
Not remarkable		0	1
Intestine,colon			
Number examined		0	1
Not remarkable		0	1
Intestine,rectum			
Number examined		0	1
Not remarkable		0	1
Kidney			
Number examined		0	1
Not remarkable		0	1
Liver			
Number examined		5	5
Not remarkable		1	1
Microgranuloma		4	4
minimal		4	4

M : Male

Table 10-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Histopathological findings (End of recovery period)

Organs	Sex:	M	M
	Dose(mg/kg):	0	1000
Findings	Number:	5	5
Liver (continued)			
Hypertrophy,hepatocytic,centrilobular		0	1
minimal		0	1
Lung(bronchus)			
Number examined		1	1
Not remarkable		0	1
Hemorrhage,focal		1	0
minimal		1	0
Lymph node,mesenteric			
Number examined		0	1
Not remarkable		0	1
Lymph node,submandibular			
Number examined		0	1
Not remarkable		0	1
Pancreas			
Number examined		0	1
Not remarkable		0	1
Parathyroid			
Number examined		0	1
Not remarkable		0	1
Pituitary			
Number examined		0	1
Not remarkable		0	1
Prostate			
Number examined		0	1
Cell infiltration		0	1
minimal		0	1
Salivary gland,submandibular			
Number examined		0	1
Not remarkable		0	1
Sciatic nerve			
Number examined		0	1
Not remarkable		0	1
Seminal vesicle(coagulating gland)			
Number examined		0	1
Not remarkable		0	1
Skeletal muscle,femoral			
Number examined		0	1
Not remarkable		0	1
Spinal cord,thoracic			
Number examined		0	1
Not remarkable		0	1
Spleen			
Number examined		0	1
Not remarkable		0	1
Stomach			
Number examined		1	2
Erosion,glandular stomach		1	2
minimal		1	2

M : Male

Table 10-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Histopathological findings (End of recovery period)

Organs	Sex:	M	M
	Dose(mg/kg):	0	1000
Findings	Number:	5	5
Testis			
Number examined		0	1
Not remarkable		0	1
Thymus			
Number examined		0	1
Not remarkable		0	1
Thyroid			
Number examined		0	1
Not remarkable		0	1
Trachea			
Number examined		0	1
Not remarkable		0	1
Urinary bladder			
Number examined		0	1
Not remarkable		0	1

M : Male

Table 10-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Histopathological findings (End of recovery period)

Organs	Sex:	F	F
	Dose(mg/kg):	0	1000
Findings	Number:	5	5
Kidney			
Number examined		5	5
Not remarkable		3	3
Regeneration,tubular		2	2
minimal		2	2
Liver			
Number examined		5	5
Microgranuloma		5	5
minimal		5	5
Ovary			
Number examined		5	5
Not remarkable		5	5
Stomach			
Number examined		0	2
Erosion,glandular stomach		0	2
minimal		0	2

F : Female

Table 10-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Histopathological findings (Undelivered)

Organs / Sex:	F	F
Dose(mg/kg):	0	1000
Findings / Number:	1	2
Adrenal		
Number examined	1	2
Not remarkable	1	2
Bone+Bone marrow,femoral		
Number examined	1	2
Not remarkable	1	2
Cerebellum(pons)		
Number examined	1	2
Not remarkable	1	2
Cerebrum		
Number examined	1	2
Not remarkable	1	2
Eye		
Number examined	1	2
Not remarkable	1	2
Heart		
Number examined	1	2
Not remarkable	1	2
Intestine,duodenum		
Number examined	1	2
Not remarkable	1	2
Intestine,jejunum		
Number examined	1	2
Not remarkable	1	2
Intestine,ileum(Peyer's patch)		
Number examined	1	2
Not remarkable	1	2
Intestine,cecum		
Number examined	1	2
Not remarkable	1	2
Intestine,colon		
Number examined	1	2
Not remarkable	1	2
Intestine,rectum		
Number examined	1	2
Not remarkable	1	2
Kidney		
Number examined	1	2
Not remarkable	1	1
Regeneration,tubular	0	1
minimal	0	1
Liver		
Number examined	1	2
Not remarkable	0	1
Microgranuloma	1	1
minimal	1	1
Lung(bronchus)		
Number examined	1	2
Not remarkable	1	2

F : Female

Table 10-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Histopathological findings (Undelivered)

Organs / Sex:	F	F
Dose(mg/kg):	0	1000
Findings / Number:	1	2
Lymph node,mesenteric		
Number examined	1	2
Not remarkable	1	2
Lymph node,submandibular		
Number examined	1	2
Not remarkable	1	2
Ovary		
Number examined	1	2
Not remarkable	1	2
Pancreas		
Number examined	1	2
Not remarkable	1	2
Parathyroid		
Number examined	1	2
Not remarkable	1	2
Pituitary		
Number examined	1	2
Not remarkable	1	2
Salivary gland,submandibular		
Number examined	1	2
Not remarkable	1	2
Sciatic nerve		
Number examined	1	2
Not remarkable	1	2
Skeletal muscle,femoral		
Number examined	1	2
Not remarkable	1	2
Spinal cord,thoracic		
Number examined	1	2
Not remarkable	1	2
Spleen		
Number examined	1	2
Not remarkable	1	1
Hematopoiesis,extramedullary	0	1
minimal	0	1
Stomach		
Number examined	1	2
Not remarkable	1	2
Thymus		
Number examined	1	2
Not remarkable	1	2
Thyroid		
Number examined	1	2
Not remarkable	1	2
Trachea		
Number examined	1	2
Not remarkable	1	2

F : Female

Table 10-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Histopathological findings (Undelivered)

Organs	Sex:	F	F
	Dose(mg/kg):	0	1000
Findings	Number:	1	2
Urinary bladder			
Number examined		1	2
Not remarkable		1	2
Uterus			
Number examined		1	2
Not remarkable		0	2
Dilatation,lumen		1	0
moderate		1	0
Vagina			
Number examined		1	2
Not remarkable		1	2

F : Female

Table 11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 0	1	2	3	4	Mean±S.D.	Mean duration of cycles Mean±S.D.	Index of animals with abnormal estrous cycle (%)a)
0	12	0	0	0	7	5	3.4±0.5	4.4±0.5	0/12(0.0)
100	12	0	0	0	7	5	3.4±0.5	4.3±0.4	0/12(0.0)
300	12	0	0	0	5	7	3.6±0.5	4.3±0.5	0/12(0.0)
1000	12	0	0	1	3	8	3.6±0.7	4.3±0.6	3/12(25.0)

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 Methyl(2-pentyl-3-oxocyclopentyl) 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	2.4±1.2	12/12(100.0)	11/12(91.7)	12	2.4±1.2	12/12(100.0)	11/12(91.7)
100	12	2.5±1.3	12/12(100.0)	12/12(100.0)	12	2.5±1.3	12/12(100.0)	12/12(100.0)
300	12	2.5±1.2	12/12(100.0)	12/12(100.0)	12	2.5±1.2	12/12(100.0)	12/12(100.0)
1000	12	2.9±1.0	12/12(100.0)	10/12(83.3)	12	2.9±1.0	12/12(100.0)	10/12(83.3)

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 Methyl(2-pentyl-3-oxocyclopentyl) 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	11	11	100.0		179	167			3	156	0
0	Mean				21.9	16.3	15.2	93.5	95.6	(1.9)	14.2	(0.0)
	S.D.				0.3	1.3	1.3	6.7	12.4	(3.2)	2.0	(0.0)
	Total	12	12	100.0		194	185			7	175	0
100	Mean				21.8	16.2	15.4	95.5	98.3	(3.7)	14.6	(0.0)
	S.D.				0.6	1.1	1.2	5.6	3.2	(7.8)	1.7	(0.0)
	Total	12	12	100.0		194	189			2	176	0
300	Mean				21.9	16.2	15.8	97.4	94.6	(1.0)	14.7	(0.0)
	S.D.				0.3	1.3	1.5	3.3	8.5	(2.4)	1.2	(0.0)
	Total	10	10	100.0		157	152			11	124	0
1000	Mean				22.2	15.7	15.2	96.8	88.9	(8.4)	12.4	(0.0)
	S.D.				0.6	1.9	2.0	4.6	11.7	(21.6)	3.8	(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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Day 0	No. of live pups Day 4	Viability index on postnatal day 4 % b)
	Total	11	156	159		11	156	155	
0	Mean		14.2	14.5	98.1		14.2	14.1	99.4
	S.D.		2.0	2.0	3.2		2.0	1.9	1.9
	Total	12	175	182		12	175	167	
100	Mean		14.6	15.2	96.3		14.6	13.9	95.6
	S.D.		1.7	1.5	7.8		1.7	1.8	6.4
	Total	12	176	178		12	176	173	
300	Mean		14.7	14.8	99.0		14.7	14.4	98.2
	S.D.		1.2	1.3	2.4		1.2	1.5	4.7
	Total	10	124	135		10	124	118	
1000	Mean		12.4	13.5	91.6		12.4	11.8	94.3
	S.D.		3.8	2.4	21.6		3.8	3.7	9.6

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 Methyl(2-pentyl-3-oxocyclopentyl) 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)	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	87	69	2	1				87	68	
0	11	Mean	7.9	6.3	0.2	0.1	0.55	0.55	11	7.9	6.2	0.55
		S.D.	2.6	2.1	0.4	0.3	0.18	0.18		2.6	1.9	0.18
		Total	92	83	1	6				87	80	
100	12	Mean	7.7	6.9	0.1	0.5	0.51	0.53	12	7.3	6.7	0.52
		S.D.	2.1	2.5	0.3	1.0	0.14	0.15		2.0	2.1	0.15
		Total	88	88	2	0				86	87	
300	12	Mean	7.3	7.3	0.2	0.0	0.51	0.50	12	7.2	7.3	0.50
		S.D.	2.3	2.3	0.4	0.0	0.15	0.16		2.5	2.3	0.16
		Total	64	60	4	4				60	58	
1000	10	Mean	6.4	6.0	0.4	0.4	0.51	0.49	10	6.0	5.8	0.46
		S.D.	3.2	2.2	1.0	1.0	0.15	0.17		3.3	2.3	0.22

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
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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Body weight of pups

Dose mg/kg		Male 0	Male 4a)	Male Gain	Female 0	Female 4a)	Female Gain
0	No.	11	11	11	11	11	11
	Mean	6.6	9.9	3.3	6.3	9.4	3.1
	S.D.	0.5	1.1	0.7	0.5	1.0	0.6
100	No.	12	12	12	12	12	12
	Mean	6.4	9.9	3.4	6.1	9.4	3.3
	S.D.	0.4	1.1	0.9	0.4	0.9	0.7
300	No.	12	12	12	12	12	12
	Mean	6.3	9.5	3.2	6.0	9.1	3.1
	S.D.	0.3	0.8	0.7	0.2	0.9	0.8
1000	No.	10	9b)	9	10	10	10
	Mean	5.7**	9.0	3.2	5.5*	8.4	2.8
	S.D.	0.7D	1.2	0.6	0.7ST	1.6	1.1

Unit: g
No.: No. of dams
a): Postnatal day
b): All male pups from one dam died.
*: $p<0.05$; **: $p<0.01$ (Significant difference from control group)
D: Dunnett's test
ST: Steel's test

Table 17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	2	0	3
No. of pups with abnormal findings	0	0	0	0
Female				
No. of pups examined	1	0	1	0
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 Methyl(2-pentyl-3-oxocyclopentyl) 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	87	87	86	60
No. of pups with abnormal findings	0	0	0	0
Female				
No. of pups examined	68	80	87	58
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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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	Non-pregnant																							
1107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
1108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
1109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
1110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
1111	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
1112	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	

a): Gestation day
-: No abnormal findings
d: Delivery

Appendix 1-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	cd	d
4102	Non-pregnant																							
4103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
4104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
4105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
4106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d	
4107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
4108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d	
4109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
4110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
4111	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d		
4112	Non-pregnant																							

a): Gestation day
-: No abnormal findings
cd: Continuation of delivery
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 Methyl(2-pentyl-3-oxocyclopentyl) 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	Non-pregnant					
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 Methyl(2-pentyl-3-oxocyclopentyl) 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	-	-	-	-	-	-
2105	-	-	-	-	-	-
2106	-	-	-	-	-	-
2107	-	-	-	-	-	-
2108	-	-	-	-	-	-
2109	-	-	-	-	-	-
2110	-	-	-	-	-	-
2111	-	-	-	-	-	-
2112	-	-	-	-	-	-

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

Appendix 1-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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	Non-pregnant					
4103	-	-	-	-	-	-
4104	-	-	-	-	-	-
4105	-	-	-	-	-	-
4106	-	-	-	-	-	-
4107	-	-	-	-	-	-
4108	-	-	-	-	-	-
4109	-	-	-	-	-	-
4110	-	-	-	-	-	-
4111	-	-	-	-	-	-
4112	Non-pregnant					

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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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
						NP						
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 2-34 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	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 2-35 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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
		NP										NP
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
NP: Non-pregnant

Appendix 2-37 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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
						NP						
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 2-38 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	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 2-39 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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
		NP										NP
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
NP: Non-pregnant

Appendix 2-41 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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
						NP						
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 2-42 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	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 2-43 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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
		NP										NP
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
NP: Non-pregnant

Appendix 2-45 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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
						NP						
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 2-46 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	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 2-47 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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
		NP										NP
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
NP: Non-pregnant

Appendix 2-49 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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
						NP						
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 2-50 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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
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 2-51 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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
		NP										NP
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
NP: Non-pregnant

Appendix 2-53 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-75 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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	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 2-79 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	0	0	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 2-80 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	0	0	1	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-81 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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	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 2-84 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	1
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-85 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-88 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	1
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 2-89 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-90 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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	1	0	0	1
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-93 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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	1
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-97 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 NP	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 2-106 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	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 2-107 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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
		NP										NP
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	1	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
NP: Non-pregnant

Appendix 2-109 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 NP	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 2-110 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	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 2-111 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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
		NP										NP
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)	1		1	1	0	0	0	0	0	1	1	
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
NP: Non-pregnant

Appendix 2-113 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 NP	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 2-114 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	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 2-115 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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
		NP										NP
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		1	1	0	0	0	0	0	1	1	
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
NP: Non-pregnant

Appendix 2-117 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 NP	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 2-118 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	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 2-119 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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
		NP										NP
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	1	
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
NP: Non-pregnant

Appendix 2-121 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 NP	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 2-122 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	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 2-123 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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
		NP										NP
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
NP: Non-pregnant

Appendix 2-125 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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	1	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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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	1	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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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	1	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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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	1	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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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	8	7	5	8	2	5	5	5	4	4	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 2-146 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	5	6	5	6	6	5	5	5	2	2	7	3
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	1	0	0	0	0	1	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-147 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	5	7	7	2	6	2	2	3	5	3	2	4
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 2-148 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	2	5	4	4	3	6	5	4	5	6	6	4
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	1	0	0	1	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 Methyl(2-pentyl-3-oxocyclopentyl) 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	5	5	1	7	4	5	4	6	2	4	7	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 2-150 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	4	5	3	5	4	5	1	4	4	1	7	3
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	1	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 2-151 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	4	5	3	2	4	5	2	3	9	4	4	4
Defecation count	0	0	0	0	0	3	0	0	0	0	0	0
Urination h)	0	0	0	0	1	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 2-152 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	2	5	2	5	5	5	2	5	6	7	4	6
Defecation count	0	0	2	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 2-153 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	6	3	4	5	2	1	6	4	1	6	2	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 2-154 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	5	4	4	4	7	4	3	5	4	2	2	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	1	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 2-155 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	4	5	2	2	5	1	4	4	2	6	3	2
Defecation count	0	0	0	0	0	2	0	0	0	0	0	0
Urination h)	1	1	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 2-156 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	4	7	1	3	8	7	5	5	7	4	5	7
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	1	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-157 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	2	5	5	6	6	4	4	5	5	4
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 2-158 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	3	5	4	7	7	2	4	3	2	2	5	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	1	0	0	0	0	1	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-159 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	6	1	3	5	7	5	4	3	9	4	2	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	1	1	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 2-160 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	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	7	4	6	5	5	2	4	2	6	5	4
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	1	0	1	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-161 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	8	5	3	4	5	5	8	4	3	5	6	6
Defecation count	0	0	0	0	0	0	0	1	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 2-162 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	5	3	3	5	6	5	4	4	5	2	3	7
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	1	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 2-163 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	3	4	3	4	6	6	3	5	7	3	5	3
Defecation count	0	0	0	0	0	0	1	0	0	0	0	0
Urination h)	0	0	0	0	1	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 2-164 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	3	5	2	6	6	5	6	6	7	4	6	4
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	1	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-165 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	6	3	4	2	4	4	5	4	4	5	8	4
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	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 2-166 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	4	1	3	4	4	4	3	5	3	2	4	4
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	1	0	0	0	0	1	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-167 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	5	3	3	0	4	8	2	4	6	3	5	3
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	1	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-168 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	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	4	0	5	8	3	1	3	3	6	5	3
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	1	0	1	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 2-169 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	7	6	2	10	4	7	8	8	3	7	10	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 2-170 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	4	7	8	6	7	8	1	6	7	5	8	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-171 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	6	5	5	6	6	5	8	3	9	3	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	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 Methyl(2-pentyl-3-oxocyclopentyl) 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	6	2	5	3	6	5	3	5	2	3	8
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	1	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-173 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	8	5	0	11	6	8	9	9	5	6	7	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 Methyl(2-pentyl-3-oxocyclopentyl) 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	7	8	3	5	6	7	4	8	7	2	11	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 2-175 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	4	10	6	8	7	9	9	5	9	5	2	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	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 2-176 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	11	8	4	9	5	6	7	7	10	4	6	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-177 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 NP	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	10	3	5	10	7		8	5	6	5	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 2-178 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	9	4	5	7	6	5	6	8	5	10	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 2-179 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	4	3	5	6	3	9	7	2	10	3	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	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 2-180 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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
		NP										NP
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		6	8	8	5	5	6	8	5	6	
Defecation count	0		0	0	0	0	0	0	0	0	0	
Urination h)	0		0	0	1	0	0	0	0	0	0	

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
NP: Non-pregnant

Appendix 2-181 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 NP	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	8	4	3	7	7		6	4	4	8	8	6
Defecation count	0	0	0	0	0		0	0	0	0	0	0
Urination h)	0	0	0	0	0		0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
NP: Non-pregnant

Appendix 2-182 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	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	6	8	6	3	6	7	6	10	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 2-183 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	6	6	7	6	3	7	6	9	3	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 2-184 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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
		NP										NP
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		6	7	6	5	4	6	9	1	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
NP: Non-pregnant

Appendix 2-185 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 NP	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	7	4	5	9	7		8	4	3	6	7	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 2-186 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	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	7	7	8	7	3	6	6	2	11	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 2-187 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	3	5	5	5	10	6	5	6	4	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 2-188 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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
		NP										NP
Arousal a)	0		0	0	0	0	0	0	0	0	0	
Convulsion b)	0		0	0	0	0	0	0	0	0	0	
Abnormal behavior c)	0		0	0	0	0	0	0	0	0	0	
Stereotypy d)	0		0	0	0	0	0	0	0	0	0	
Gait e)	0		0	0	0	0	0	0	0	0	0	
Posture f)	N		N	N	N	N	N	N	N	N	N	
Grooming g)	0		0	0	0	0	0	0	0	0	0	
Rearing	5		3	7	9	3	4	6	6	3	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
NP: Non-pregnant

Appendix 2-189 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 NP	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	4	5	9	4		3	4	3	7	4	5
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 2-190 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	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	5	6	4	3	7	4	4	10	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 2-191 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	5	2	2	3	5	2	6	6	5	6	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 2-192 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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
		NP										NP
Arousal a)	0		0	0	0	0	0	0	0	0	0	
Convulsion b)	0		0	0	0	0	0	0	0	0	0	
Abnormal behavior c)	0		0	0	0	0	0	0	0	0	0	
Stereotypy d)	0		0	0	0	0	0	0	0	0	0	
Gait e)	0		0	0	0	0	0	0	0	0	0	
Posture f)	N		N	N	N	N	N	N	N	N	N	
Grooming g)	0		0	0	0	0	0	0	0	0	0	
Rearing	5		2	3	4	4	3	3	6	4	3	
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
NP: Non-pregnant

Appendix 2-193 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 NP	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	6	9	6	10	6	3	9	7	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
NP: Non-pregnant

Appendix 2-194 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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
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	8	7	6	4	6	3	8	7	4	11	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 2-195 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	7	6	5	5	6	6	5	5	9	8	4	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 2-196 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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
		NP										NP
Arousal a)	0		0	0	0	0	0	0	0	0	0	
Convulsion b)	0		0	0	0	0	0	0	0	0	0	
Abnormal behavior c)	0		0	0	0	0	0	0	0	0	0	
Stereotypy d)	0		0	0	0	0	0	0	0	0	0	
Gait e)	0		0	0	0	0	0	0	0	0	0	
Posture f)	N		N	N	N	N	N	N	N	N	N	
Grooming g)	0		0	0	0	0	0	0	0	0	0	
Rearing	5		5	8	4	4	2	2	6	2	6	
Defecation count	0		0	0	0	0	0	0	0	0	0	
Urination h)	0		0	0	1	0	0	0	0	0	0	

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
NP: Non-pregnant

Appendix 2-197 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	3	6	4	6	3	9	5	4	7	8
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-198 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	6	9	6	5	4	4	4	3	9	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 2-199 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	5	5	10	7	5	12	8	6	5	11
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 Methyl(2-pentyl-3-oxocyclopentyl) 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	6	9	7	9	8	8	6	11	8	7
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	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 2-201 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	5	9	7	7	5	12	7	5	9	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 2-202 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	7	9	9	6	6	6	6	9	8	4
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-203 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	6	11	11	12	5	7	9	8	10	8
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-204 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	5	7	8	12	7	6	6	8	11	7
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-205 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	5	10	10	9	9	10	6	6	10	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 2-206 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	6	8	9	7	9	8	5	10	9	6
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	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 2-207 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	4	7	4	11	7	10	11	6	7	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 2-208 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	10	6	7	6	6	6	7	9	11	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 2-209 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	3	1	7	4
Defecation count	0	0	0	0	0
Urination h)	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 2-210 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	2	6	5	6	5
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 Methyl(2-pentyl-3-oxocyclopentyl) 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	2	2	7	5
Defecation count	0	0	0	0	0
Urination h)	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 2-212 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	1	5	4	3	5
Defecation count	0	0	0	0	0
Urination h)	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 2-213 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	9	8	6	8	11
Defecation count	0	0	0	0	0
Urination h)	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-214 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	5	7	12	8	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 2-215 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	6	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 2-216 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	9	7	9	7	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 Methyl(2-pentyl-3-oxocyclopentyl) 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)	52	65	41	89	117

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 Methyl(2-pentyl-3-oxocyclopentyl) 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)	58	99	93	70	61

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-219 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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)	100	77	72	98	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 2-220 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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)	27	63	54	49	50

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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual manipulative test of female rats (Main group, Lactation day 4)
Dose (mg/kg): 0

Parameter	Animal number (1101-1110)				
	1	2	3	5	10
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	65	57	41	40	49

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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual manipulative test of female rats (Main group, Lactation day 4)
Dose (mg/kg): 100

Parameter	Animal number (2103-2112)				
	3	5	6	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)	30	49	52	45	79

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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual manipulative test of female rats (Main group, Lactation day 4)
Dose (mg/kg): 300

Parameter	Animal number (3101-3112)				
	1	2	8	9	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)	88	47	51	49	47

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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual manipulative test of female rats (Main group, Lactation day 4)
Dose (mg/kg): 1000

Parameter	Animal number (4101-4110)				
	1	3	4	6	10
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	53	41	47	39	60

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 Methyl(2-pentyl-3-oxocyclopentyl) 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)	83	41	78	52	55

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 Methyl(2-pentyl-3-oxocyclopentyl) 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)	27	48	63	59	57

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 Methyl(2-pentyl-3-oxocyclopentyl) 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)	58	58	39	101	100

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 Methyl(2-pentyl-3-oxocyclopentyl) 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)	41	79	50	79	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 Methyl(2-pentyl-3-oxocyclopentyl) 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)	83	46	75	42	81

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 Methyl(2-pentyl-3-oxocyclopentyl) 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)	78	58	75	77	37

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 Methyl(2-pentyl-3-oxocyclopentyl) 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	1456	810
1009	1690	926
1010	1131	756
1011	1536	1025
1012	1515	1178
Mean	1466	939
S.D.	206	169

Appendix 2-232 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	1187	836
2009	1458	1021
2010	1642	1089
2011	1289	940
2012	1460	975
Mean	1407	972
S.D.	175	94

Appendix 2-233 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	1363	891
3009	1260	822
3010	1708	1141
3011	1537	971
3012	1346	657
Mean	1443	896
S.D.	179	179

Appendix 2-234 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	1410	927
4009	1077	637
4010	1352	865
4011	1451	730
4012	1272	682
Mean	1312	768
S.D.	148	123

Appendix 2-235 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	879	667
1102	1162	699
1103	1495	614
1105	1242	798
1110	1049	758
Mean	1165	707
S.D.	229	73

Appendix 2-236 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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
2103	1500	771
2105	1087	566
2106	1203	945
2111	1166	736
2112	1106	876
Mean	1212	779
S.D.	167	145

Appendix 2-237 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	1090	779
3102	1363	815
3108	1362	723
3109	1444	1061
3112	1285	849
Mean	1309	845
S.D.	135	129

Appendix 2-238 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	1222	1031
4103	1165	889
4104	1634	944
4106	1666	1031
4110	1120	891
Mean	1361	957
S.D.	266	71

Appendix 2-239 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	1117	879
1119	1017	728
1120	1110	650
1121	1009	618
1122	891	511
Mean	1029	677
S.D.	92	137

Appendix 2-240 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	1081	544
4119	936	519
4120	1360	954
4121	1151	652
4122	1081	711
Mean	1122	676
S.D.	154	174

Appendix 2-241 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	1857	1121
1009	2026	1317
1010	1372	1254
1011	1832	1241
1012	1995	1128
Mean	1816	1212
S.D.	262	85

Appendix 2-242 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	1817	1082
4009	1775	878
4010	1744	1056
4011	1748	896
4012	1710	1039
Mean	1759	990
S.D.	40	96

Appendix 2-243 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	1241	973
1119	1501	665
1120	1491	767
1121	1186	586
1122	1090	580
Mean	1302	714
S.D.	185	163

Appendix 2-244 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	1461	727
4119	1317	739
4120	1572	848
4121	1378	832
4122	1344	833
Mean	1414	796
S.D.	103	58

Appendix 2-245 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	374	307	175	74	54	2	986
1009	452	405	337	305	111	67	1677
1010	479	226	164	153	282	21	1325
1011	453	383	120	39	185	6	1186
1012	360	2	148	125	0	17	652
Mean	424	265	189	139	126	23	1165
S.D.	53	163	85	103	111	26	382

Unit: Count

Appendix 2-246 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	504	328	132	149	78	50	1241
2009	409	422	250	21	233	391	1726
2010	385	368	222	198	316	405	1894
2011	436	369	309	206	103	251	1674
2012	548	470	488	383	452	439	2780
Mean	456	391	280	191	236	307	1863
S.D.	68	55	133	130	155	161	566

Unit: Count

Appendix 2-247 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	429	380	395	285	211	65	1765
3009	480	370	410	418	344	275	2297
3010	427	368	408	210	19	58	1490
3011	443	330	156	325	326	39	1619
3012	474	441	164	63	74	189	1405
Mean	451	378	307	260	195	125	1715
S.D.	25	40	134	133	146	103	353

Unit: Count

Appendix 2-248 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	441	162	412	150	22	68	1255
4009	440	407	359	429	109	41	1785
4010	447	394	391	428	356	423	2439
4011	363	366	341	300	304	232	1906
4012	446	406	409	145	7	213	1626
Mean	427	347	382	290	160	195	1802
S.D.	36	105	31	141	161	153	432

Unit: Count

Appendix 2-249 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	462	237	174	344	146	8	1371
1102	391	256	131	162	73	25	1038
1103	366	259	110	146	83	4	968
1105	431	395	335	350	204	184	1899
1110	364	355	302	259	294	153	1727
Mean	403	300	210	252	160	75	1401
S.D.	43	70	102	97	92	87	411

Unit: Count

Appendix 2-250 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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)
2103	363	225	0	23	6	4	621
2105	409	138	1	10	13	21	592
2106	423	424	59	26	14	19	965
2111	399	204	19	24	6	7	659
2112	416	373	88	88	30	3	998
Mean	402	273	33	34	14	11	767
S.D.	24	121	39	31	10	9	198

Unit: Count

Appendix 2-251 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	267	76	46	100	30	31	550
3102	437	326	231	308	87	42	1431
3108	359	203	43	151	51	231	1038
3109	390	88	126	2	10	26	642
3112	413	398	345	329	282	238	2005
Mean	373	218	158	178	92	114	1133
S.D.	66	143	130	139	110	111	600

Unit: Count

Appendix 2-252 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	357	5	176	3	10	9	560
4103	390	275	147	24	0	211	1047
4104	393	221	22	26	15	33	710
4106	432	247	16	50	21	23	789
4110	161	64	69	19	149	64	526
Mean	347	162	86	24	39	68	726
S.D.	107	120	73	17	62	82	209

Unit: Count

Appendix 2-253 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	402	346	319	333	302	257	1959
1119	368	339	260	17	4	177	1165
1120	375	299	356	339	38	0	1407
1121	388	303	337	278	18	11	1335
1122	362	241	116	301	120	6	1146
Mean	379	306	278	254	96	90	1402
S.D.	16	42	97	135	123	119	330

Unit: Count

Appendix 2-254 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	408	376	314	269	312	235	1914
4119	260	258	173	0	6	3	700
4120	339	402	327	329	197	1	1595
4121	392	358	281	185	243	256	1715
4122	375	282	303	310	284	97	1651
Mean	355	335	280	219	208	118	1515
S.D.	59	62	62	134	121	123	471

Unit: Count

Appendix 2-255 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	396	387	119	101	41	13	1057
1009	389	333	300	191	38	41	1292
1010	373	141	27	366	335	207	1449
1011	412	370	142	178	258	42	1402
1012	331	128	60	32	322	216	1089
Mean	380	272	130	174	199	104	1258
S.D.	31	127	106	125	148	99	178

Unit: Count

Appendix 2-256 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	445	354	99	179	82	444	1603
4009	382	236	251	279	276	353	1777
4010	473	433	379	416	339	372	2412
4011	373	190	47	401	282	87	1380
4012	414	364	28	121	196	17	1140
Mean	417	315	161	279	235	255	1662
S.D.	42	100	150	131	100	190	482

Unit: Count

Appendix 2-257 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	376	322	324	224	196	299	1741
1119	439	281	183	4	23	80	1010
1120	407	310	338	249	12	20	1336
1121	274	239	16	2	3	132	666
1122	402	175	107	327	308	270	1589
Mean	380	265	194	161	108	160	1268
S.D.	63	60	139	149	137	121	436

Unit: Count

Appendix 2-258 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	320	210	74	5	28	11	648
4119	423	370	271	187	7	37	1295
4120	454	487	375	109	140	232	1797
4121	306	359	189	92	0	63	1009
4122	408	404	60	13	151	265	1301
Mean	382	366	194	81	65	122	1210
S.D.	65	101	133	75	74	118	423

Unit: Count

Appendix 3-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	436	482	502	525	555	581	597	161
1002	413	438	460	481	501	518	534	121
1003	447	472	484	494	514	535	552	105
1004	419	443	462	476	497	517	529	110
1005	451	470	499	522	544	566	573	122
1006	411	429	440	464	480	499	517	106
1007	469	498	528	564	590	612	621	152
1008	406	434	452	466	482	502	518	112
1009	427	448	470	490	516	529	544	117
1010	434	471	501	525	556	583	591	157
1011	421	450	466	477	502	522	533	112
1012	422	444	464	486	509	529	523	101
Mean	430	457	477	498	521	541	553	123
S.D.	19	21	26	30	34	36	35	21

Unit: g

Appendix 3-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	432	452	479	492	519	540	556	124
2002	415	439	460	480	503	523	531	116
2003	439	463	490	530	560	582	609	170
2004	443	474	514	537	564	586	603	160
2005	414	434	460	489	513	531	556	142
2006	438	467	492	519	549	574	585	147
2007	472	499	528	567	593	618	636	164
2008	418	447	462	478	507	532	550	132
2009	419	453	483	509	550	580	589	170
2010	449	493	524	562	592	617	628	179
2011	411	448	464	493	518	543	563	152
2012	411	436	461	492	517	543	548	137
Mean	430	459	485	512	540	564	580	149
S.D.	19	21	25	31	32	33	34	20

Unit: g

Appendix 3-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	416	434	459	468	484	503	521	105
3002	417	428	455	483	513	533	547	130
3003	421	439	465	477	510	537	545	124
3004	420	433	462	488	514	543	565	145
3005	435	460	485	497	518	541	552	117
3006	428	440	446	462	486	527	543	115
3007	406	419	441	462	476	495	505	99
3008	425	435	455	479	496	520	530	105
3009	441	459	479	493	519	538	551	110
3010	431	437	450	471	497	512	516	85
3011	466	501	533	542	580	617	630	164
3012	460	476	507	532	557	584	590	130
Mean	431	447	470	488	513	538	550	119
S.D.	18	23	27	26	30	34	34	21

Unit: g

Appendix 3-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	420	427	449	463	487	517	531	111
4002	407	409	429	444	458	477	487	80
4003	450	458	481	497	514	542	547	97
4004	410	415	437	469	485	506	498	88
4005	418	425	448	453	473	490	505	87
4006	428	451	474	490	515	536	545	117
4007	412	401	431	446	474	494	517	105
4008	443	453	472	487	504	518	535	92
4009	410	435	457	472	493	513	525	115
4010	456	475	513	524	552	571	593	137
4011	457	465	487	510	541	564	565	108
4012	429	421	433	439	454	461	463	34
Mean	428	436	459	475	496	516	526	98
S.D.	19	24	26	27	31	33	35	26

Unit: g

Appendix 3-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	264	273	276	12
1102	246	264	271	25
1103	258	269	274	16
1104	249	265	271	22
1105	246	251	263	17
1106	253	267	268	15
1107	272	289	295	23
1108	278	298	296	18
1109	241	261	268	27
1110	240	247	258	18
1111	263	272	284	21
1112	260	263	276	16
Mean	256	268	275	19
S.D.	12	14	12	4

Unit: g

Appendix 3-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	262	271	275	13
2102	249	258	264	15
2103	261	274	285	24
2104	274	290	299	25
2105	235	244	249	14
2106	236	260	270	34
2107	254	264	268	14
2108	244	247	253	9
2109	282	282	280	-2
2110	262	269	284	22
2111	273	279	288	15
2112	265	273	285	20
Mean	258	268	275	17
S.D.	15	14	15	9

Unit: g

Appendix 3-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	253	264	25
3102	266	253	271	5
3103	257	262	259	2
3104	282	287	293	11
3105	262	266	273	11
3106	255	258	261	6
3107	241	255	258	17
3108	247	245	257	10
3109	258	281	284	26
3110	257	266	276	19
3111	271	278	278	7
3112	251	265	275	24
Mean	257	264	271	14
S.D.	12	13	11	8

Unit: g

Appendix 3-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	255	279	309	54
4102	247	241	250	3
4103	256	267	275	19
4104	255	267	275	20
4105	262	269	266	4
4106	243	260	266	23
4107	247	251	249	2
4108	260	250	254	-6
4109	268	279	286	18
4110	253	257	267	14
4111	236	241	253	17
4112	251	260	271	20
Mean	253	260	268	16
S.D.	9	13	17	15

Unit: g

Appendix 3-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	284	300	337	417	133
1102	269	299	333	408	139
1103	272	295	338	424	152
1104	267	303	338	423	156
1105	261	285	321	396	135
1106	Non-pregnant				
1107	293	324	364	439	146
1108	325	345	373	467	142
1109	280	303	333	412	132
1110	255	285	319	403	148
1111	291	326	359	445	154
1112	280	319	356	454	174
Mean	280	308	343	426	146
S.D.	19	19	18	22	12

Unit: g
a): Gestation day

Appendix 3-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	286	324	367	455	169
2102	271	297	327	410	139
2103	290	329	372	450	160
2104	310	352	405	498	188
2105	245	279	319	396	151
2106	267	298	337	410	143
2107	292	319	349	433	141
2108	265	295	337	427	162
2109	302	344	381	454	152
2110	277	317	355	417	140
2111	280	332	367	448	168
2112	284	311	340	440	156
Mean	281	316	355	437	156
S.D.	18	22	25	27	15

Unit: g
a): Gestation day

Appendix 3-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	256	294	334	411	155
3102	270	310	342	421	151
3103	271	321	352	418	147
3104	311	337	373	462	151
3105	279	299	340	425	146
3106	268	297	320	396	128
3107	260	284	319	380	120
3108	256	290	331	397	141
3109	283	335	373	449	166
3110	278	303	347	413	135
3111	290	320	360	438	148
3112	269	304	349	429	160
Mean	274	308	345	420	146
S.D.	16	17	18	23	13

Unit: g
a): Gestation day

Appendix 3-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	309	324	360	410	101
4102	Non-pregnant				
4103	270	308	350	431	161
4104	273	302	336	392	119
4105	284	302	332	389	105
4106	274	314	347	403	129
4107	274	295	331	396	122
4108	281	326	369	427	146
4109	285	329	356	410	125
4110	267	309	336	400	133
4111	265	297	344	393	128
4112	Non-pregnant				
Mean	278	311	346	405	127
S.D.	13	12	13	14	18

Unit: g
a): Gestation day

Appendix 3-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	308	314	6
1102	316	339	23
1103	321	316	-5
1104	321	358	37
1105	296	319	23
1106	Non-pregnant		
1107	378	366	-12
1108	371	372	1
1109	296	314	18
1110	314	327	13
1111	338	378	40
1112	329	343	14
Mean	326	341	14
S.D.	27	25	16

Unit: g
a): Lactation day

Appendix 3-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	329	370	41
2102	313	333	20
2103	374	370	-4
2104	380	405	25
2105	319	343	24
2106	327	323	-4
2107	321	325	4
2108	352	369	17
2109	358	359	1
2110	352	369	17
2111	329	343	14
2112	343	348	5
Mean	341	355	13
S.D.	22	24	13

Unit: g
a): Lactation day

Appendix 3-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	292	297	5
3102	307	350	43
3103	323	343	20
3104	346	378	32
3105	317	340	23
3106	284	314	30
3107	316	316	0
3108	316	329	13
3109	356	385	29
3110	317	334	17
3111	354	358	4
3112	346	358	12
Mean	323	342	19
S.D.	23	26	13

Unit: g
a): Lactation day

Appendix 3-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	318	331	13
4102	Non-pregnant		
4103	326	359	33
4104	309	339	30
4105	296	323	27
4106	337	349	12
4107	310	331	21
4108	345	365	20
4109	311	312	1
4110	313	332	19
4111	345	329	-16
4112	Non-pregnant		
Mean	321	337	16
S.D.	17	16	15

Unit: g
a): Lactation day

Appendix 3-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	249	260	271	282	287	299	304	55
1114	248	260	272	284	291	295	302	54
1115	249	261	271	270	280	288	287	38
1116	274	283	286	300	307	312	322	48
1117	261	272	274	276	283	291	293	32
1118	274	279	288	304	297	307	315	41
1119	235	250	259	266	270	275	283	48
1120	257	268	276	280	290	298	299	42
1121	255	280	289	298	309	310	322	67
1122	245	264	273	275	276	290	291	46
Mean	255	268	276	284	289	297	302	47
S.D.	12	11	9	13	13	11	14	10

Unit: g

Appendix 3-18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	252	259	266	282	287	297	300	48
4114	256	264	258	277	287	295	290	34
4115	245	253	259	269	282	283	285	40
4116	261	255	257	272	276	267	268	7
4117	262	266	263	276	286	285	286	24
4118	246	249	260	269	271	288	290	44
4119	250	246	253	257	260	270	272	22
4120	263	254	263	272	270	277	278	15
4121	281	282	282	297	304	307	313	32
4122	265	273	283	284	294	306	308	43
Mean	258	260	264	276	282	288	289	31
S.D.	11	11	10	11	13	14	15	14

Unit: g

Appendix 3-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	520	537	543	23
1009	553	562	568	15
1010	592	604	611	19
1011	532	552	555	23
1012	535	536	537	2
Mean	546	558	563	16
S.D.	28	28	29	9

Unit: g

Appendix 3-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	533	545	567	34
4009	533	536	560	27
4010	601	625	624	23
4011	567	590	601	34
4012	470	478	485	15
Mean	541	555	567	27
S.D.	49	56	53	8

Unit: g

Appendix 3-21 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	317	321	315	-2
1119	288	292	290	2
1120	307	304	313	6
1121	323	325	317	-6
1122	291	299	301	10
Mean	305	308	307	2
S.D.	15	14	11	6

Unit: g

Appendix 3-22 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	284	299	300	16
4119	276	278	291	15
4120	276	290	287	11
4121	309	326	330	21
4122	298	314	315	17
Mean	289	301	305	16
S.D.	15	19	18	4

Unit: g

Appendix 4-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	27	26	22	21	25	23
1002	24	26	21	21	23	22
1003	28	25	21	26	24	23
1004	22	25	18	19	24	20
1005	23	23	22	22	25	19
1006	26	22	21	21	22	18
1007	28	31	28	26	28	25
1008	22	25	21	23	20	20
1009	22	23	22	19	21	19
1010	29	28	25	26	26	23
1011	20	23	23	21	24	21
1012	22	25	22	23	24	20
Mean	24	25	22	22	24	21
S.D.	3	2	2	3	2	2

Unit: g/rat/day

Appendix 4-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	24	26	25	24	20	22
2002	25	25	23	23	23	21
2003	28	30	28	26	26	31
2004	27	30	30	27	23	22
2005	23	25	22	22	24	21
2006	27	25	24	26	26	23
2007	26	31	28	24	24	23
2008	25	27	23	26	24	21
2009	21	29	24	28	30	26
2010	27	33	30	31	27	25
2011	26	33	24	23	25	24
2012	23	26	27	25	24	24
Mean	25	28	26	25	25	24
S.D.	2	3	3	3	2	3

Unit: g/rat/day

Appendix 4-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	22	23	24	21	24	23
3002	23	23	23	22	26	24
3003	24	24	23	22	25	19
3004	21	21	25	26	25	25
3005	20	23	25	23	26	22
3006	18	21	21	23	24	23
3007	21	24	24	23	22	21
3008	24	26	19	21	23	24
3009	27	27	25	23	27	24
3010	23	25	21	21	22	21
3011	30	32	30	29	27	26
3012	23	28	26	27	28	27
Mean	23	25	24	23	25	23
S.D.	3	3	3	3	2	2

Unit: g/rat/day

Appendix 4-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	19	24	25	33	29	27
4002	20	22	23	26	30	27
4003	21	26	27	25	24	26
4004	17	19	21	24	24	18
4005	18	24	22	24	24	24
4006	25	26	25	27	27	24
4007	19	14	24	26	27	28
4008	20	23	25	22	25	27
4009	21	28	25	30	27	23
4010	16	24	26	29	30	28
4011	21	27	25	25	28	26
4012	23	24	22	32	26	22
Mean	20	23	24	27	27	25
S.D.	2	4	2	3	2	3

Unit: g/rat/day

Appendix 4-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	14	19	16
1102	15	18	19
1103	13	21	19
1104	15	18	17
1105	16	14	17
1106	20	19	15
1107	10	21	21
1108	20	21	16
1109	19	20	19
1110	16	13	15
1111	20	16	18
1112	17	18	19
Mean	16	18	18
S.D.	3	3	2

Unit: g/rat/day

Appendix 4-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	20	18	14
2102	12	18	17
2103	20	17	18
2104	19	20	20
2105	12	18	17
2106	16	17	18
2107	15	19	13
2108	18	16	16
2109	16	18	11
2110	21	19	22
2111	22	15	18
2112	19	16	19
Mean	18	18	17
S.D.	3	1	3

Unit: g/rat/day

Appendix 4-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	19	21	19
3102	14	15	17
3103	18	21	15
3104	19	22	16
3105	14	20	18
3106	14	17	16
3107	17	18	15
3108	17	13	19
3109	20	20	18
3110	13	18	18
3111	19	24	16
3112	16	19	19
Mean	17	19	17
S.D.	2	3	2

Unit: g/rat/day

Appendix 4-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	19	23	24
4102	17	15	15
4103	9	19	21
4104	19	19	18
4105	17	19	16
4106	14	20	20
4107	15	17	13
4108	15	13	15
4109	15	22	20
4110	8	20	18
4111	16	18	14
4112	15	18	16
Mean	15	19	18
S.D.	3	3	3

Unit: g/rat/day

Appendix 4-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	15	19	19	19
1102	16	22	19	19
1103	17	17	21	20
1104	17	22	22	22
1105	19	15	18	19
1106	Non-pregnant			
1107	18	21	28	23
1108	21	25	31	22
1109	16	20	21	22
1110	17	16	21	21
1111	21	22	22	18
1112	19	26	22	23
Mean	18	20	22	21
S.D.	2	4	4	2

Unit: g/rat/day
a): Gestation day

Appendix 4-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	22	24	23
2102	16	20	23	20
2103	23	23	24	25
2104	20	22	26	28
2105	18	18	25	18
2106	14	20	21	21
2107	18	23	20	20
2108	18	19	22	25
2109	21	25	25	18
2110	19	24	22	21
2111	23	22	24	21
2112	18	17	17	23
Mean	19	21	23	22
S.D.	3	2	3	3

Unit: g/rat/day
a): Gestation day

Appendix 4-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	23	22	20	21
3102	17	23	25	20
3103	22	26	25	22
3104	19	20	21	24
3105	16	16	20	19
3106	15	17	17	15
3107	16	18	25	21
3108	20	20	23	19
3109	20	25	29	23
3110	19	22	27	24
3111	17	21	28	20
3112	19	19	23	20
Mean	19	21	24	21
S.D.	2	3	4	2

Unit: g/rat/day
a): Gestation day

Appendix 4-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	18	25	25	20
4102	Non-pregnant			
4103	16	22	27	16
4104	16	22	23	25
4105	15	22	21	13
4106	18	25	24	22
4107	20	19	21	21
4108	25	29	29	21
4109	21	29	23	20
4110	19	26	29	18
4111	22	24	27	25
4112	Non-pregnant			
Mean	19	24	25	20
S.D.	3	3	3	4

Unit: g/rat/day
a): Gestation day

Appendix 4-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	9	36
1102	19	35
1103	20	26
1104	29	40
1105	21	40
1106	Non-pregnant	
1107	16	34
1108	18	35
1109	19	43
1110	19	33
1111	31	51
1112	24	35
Mean	20	37
S.D.	6	6

Unit: g/rat/day
a): Lactation day

Appendix 4-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	30	52
2102	18	39
2103	18	32
2104	22	40
2105	27	41
2106	17	32
2107	12	33
2108	22	46
2109	16	35
2110	25	45
2111	17	38
2112	25	40
Mean	21	39
S.D.	5	6

Unit: g/rat/day
a): Lactation day

Appendix 4-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	17	27
3102	29	48
3103	19	49
3104	26	41
3105	25	42
3106	26	41
3107	23	30
3108	26	38
3109	25	44
3110	26	34
3111	21	35
3112	20	39
Mean	24	39
S.D.	4	7

Unit: g/rat/day
a): Lactation day

Appendix 4-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	Administration 4a)
4101	27	37
4102	Non-pregnant	
4103	38	33
4104	39	40
4105	27	35
4106	27	34
4107	30	41
4108	30	43
4109	26	22
4110	28	33
4111	25	31
4112	Non-pregnant	
Mean	30	35
S.D.	5	6

Unit: g/rat/day
a): Lactation day

Appendix 4-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	15	20	19	16	17	14
1114	17	17	17	16	14	16
1115	13	22	20	11	14	11
1116	18	17	14	16	14	16
1117	16	17	16	14	15	13
1118	14	19	17	16	18	16
1119	16	17	17	15	15	15
1120	18	20	21	15	17	16
1121	12	23	18	18	16	18
1122	17	19	16	16	16	13
Mean	16	19	18	15	16	15
S.D.	2	2	2	2	1	2

Unit: g/rat/day

Appendix 4-18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	14	24	18	23	21	20
4114	16	22	13	18	23	17
4115	17	21	18	19	18	15
4116	13	18	13	17	14	16
4117	15	19	13	14	15	17
4118	16	16	20	17	17	14
4119	13	18	20	15	21	14
4120	13	14	16	17	17	13
4121	15	21	18	21	22	17
4122	14	20	22	21	21	18
Mean	15	19	17	18	19	16
S.D.	1	3	3	3	3	2

Unit: g/rat/day

Appendix 4-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	20	30	29
1009	22	32	29
1010	25	36	31
1011	20	28	28
1012	23	28	30
Mean	22	31	29
S.D.	2	3	1

Unit: g/rat/day

Appendix 4-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	25	30	31
4009	25	33	32
4010	31	40	32
4011	22	34	33
4012	26	30	29
Mean	26	33	31
S.D.	3	4	2

Unit: g/rat/day

Appendix 4-21 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	17	22	17
1119	16	22	18
1120	20	20	25
1121	16	20	15
1122	15	21	22
Mean	17	21	19
S.D.	2	1	4

Unit: g/rat/day

Appendix 4-22 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	16	24	22
4119	18	19	23
4120	16	22	16
4121	16	26	25
4122	16	27	23
Mean	16	24	22
S.D.	1	3	3

Unit: g/rat/day

Appendix 5-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	6.5	++	+	-	-	+	+-	Y
1009	8.5	+	+	-	+-	-	+-	Y
1010	7.0	++	+++	-	+-	+	+-	Y
1011	7.0	++	+++	-	-	+	+	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 5-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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	34	8.6	1844	0.62	3.03	1.07
1009	32	10.6	1808	1.06	2.98	1.38
1010	41	5.1	2064	0.53	1.69	0.77
1011	29	7.8	2542	1.11	3.58	1.56
1012	31	8.3	1572	0.56	2.17	0.86
Mean	33	8.1	1966	0.78	2.69	1.13
S.D.	5	2.0	366	0.28	0.75	0.34

Appendix 5-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	6.5	++	+	-	-	-	+	Y
2009	7.0	-	+-	-	-	-	+-	Y
2010	7.5	+-	+	-	-	-	+-	Y
2011	8.5	+	++	-	-	-	+-	Y
2012	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 5-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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	4.2	2984	0.56	2.29	0.71
2009	39	19.4	1766	1.47	6.00	2.44
2010	43	12.7	1658	1.07	3.82	1.52
2011	42	9.4	1914	0.56	3.33	0.92
2012	33	10.8	2290	1.12	4.11	1.45
Mean	38	11.3	2122	0.96	3.91	1.41
S.D.	5	5.5	538	0.39	1.36	0.67

Appendix 5-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	7.0	+	+	-	-	-	+-	Y
3010	7.5	+	+	-	-	-	+-	Y
3011	6.5	+	+-	-	+-	-	+-	Y
3012	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 5-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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	27	6.5	2374	0.74	2.77	1.07
3009	41	13.2	1978	0.77	4.73	1.37
3010	45	14.7	1436	0.71	3.81	1.21
3011	50	23.9	1400	1.34	5.84	2.06
3012	42	10.4	1642	0.77	2.73	0.89
Mean	41	13.7	1766	0.87	3.98	1.32
S.D.	9	6.5	410	0.27	1.33	0.45

Appendix 5-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual urinalysis of male rats (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
4008	6.0	++	+	-	+-	-	+-	Y
4009	6.0	+	+-	-	+-	-	+-	Y
4010	6.5	+	+-	-	-	-	+-	Y
4011	7.0	+-	-	-	-	-	+-	Y
4012	6.0	+++	+-	-	-	-	+	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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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	41	15.0	2036	1.41	4.45	2.13
4009	51	18.4	1906	1.36	5.50	2.13
4010	54	16.0	1792	0.93	4.27	1.50
4011	55	23.8	1198	1.24	4.18	1.71
4012	43	9.4	1558	0.60	1.96	0.85
Mean	49	16.5	1698	1.11	4.07	1.66
S.D.	6	5.2	330	0.34	1.29	0.53

Appendix 5-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	6.0	-	-	-	-	-	+-	Y
1119	6.5	-	-	-	-	-	+-	Y
1120	6.5	+-	+-	-	-	-	+-	Y
1121	6.5	-	+-	-	-	-	+-	Y
1122	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 5-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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	36	9.3	1414	0.74	2.34	0.99
1119	29	7.2	1880	0.32	2.22	0.81
1120	39	6.9	1768	0.57	2.09	0.98
1121	29	4.3	2142	0.43	1.62	0.73
1122	30	6.3	1790	0.48	1.96	0.86
Mean	33	6.8	1799	0.51	2.05	0.87
S.D.	5	1.8	261	0.16	0.28	0.11

Appendix 5-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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) Pro-tein	2) Ketone body	3) Glu-cose	4) Occult blood	5) Bili-rubin	6) Urobi-linogen	7) Color
4118	6.5	-	-	-	-	-	+-	Y
4119	6.0	-	+-	-	-	-	+-	Y
4120	5.5	+-	+-	-	-	-	+-	Y
4121	7.5	-	-	-	-	-	+-	Y
4122	6.0	-	+-	-	-	-	+-	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 5-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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	49	24.2	874	0.82	3.05	1.36
4119	57	22.1	820	0.84	2.84	1.46
4120	48	16.8	1080	0.64	2.83	1.08
4121	63	14.3	968	0.51	1.88	0.57
4122	54	20.7	810	0.66	2.55	1.12
Mean	54	19.6	910	0.69	2.63	1.12
S.D.	6	4.0	114	0.14	0.46	0.35

Appendix 5-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual urinalysis of male rats (Week 2 of recovery)
Dose (mg/kg): 0

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
1008	7.5	+	+	-	-	-	+-	Y
1009	8.0	-	+-	-	+-	-	+-	Y
1010	>=9.0	+	+	-	+-	-	+-	Y
1011	8.0	+	++	-	-	+	+	Y
1012	8.5	+	+++	-	+-	-	+-	Y

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL
4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 5-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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	40	14.6	2130	1.40	5.36	1.87
1009	40	23.4	1678	1.68	6.58	2.29
1010	48	16.5	1820	1.62	4.69	2.01
1011	33	13.1	2514	1.15	5.44	1.81
1012	34	10.9	1824	1.20	3.10	1.53
Mean	39	15.7	1993	1.41	5.03	1.90
S.D.	6	4.8	335	0.24	1.28	0.28

Appendix 5-22 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	>=9.0	+	++	-	-	+	+-	Y
4011	>=9.0	+-	+	-	-	-	+-	Y
4012	8.0	+-	+-	-	+-	-	+-	Y

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL
4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 5-23 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual urinalysis of male rats (Week 2 of recovery)
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 5-24 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	39	15.1	1962	1.45	4.95	1.78
4009	36	11.2	2352	1.41	4.49	1.97
4010	47	23.7	2006	2.80	8.00	3.37
4011	47	23.6	1624	1.84	6.27	2.45
4012	49	17.0	1582	1.73	4.44	1.97
Mean	44	18.1	1905	1.85	5.63	2.31
S.D.	6	5.5	315	0.56	1.52	0.64

Appendix 5-25 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual urinalysis of female rats (Week 2 of recovery)
Dose (mg/kg): 0

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
1118	7.5	-	-	-	-	-	+-	Y
1119	6.0	-	-	-	-	-	+-	Y
1120	8.5	-	-	-	-	-	+-	Y
1121	6.0	-	-	-	-	-	+-	Y
1122	6.0	-	+-	-	-	-	+-	Y

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL
4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 5-26 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual urinalysis of female rats (Week 2 of recovery)
Dose (mg/kg): 0

Animal number	URINE SEDIMENT						
						CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
1118	-	-	+-	-	-	-	-
1119	-	-	+-	-	-	-	-
1120	-	-	+-	-	-	+-	-
1121	-	-	+-	-	-	-	-
1122	-	-	+-	-	-	-	-

SEC : Squamous Epithelial Cell
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 Methyl(2-pentyl-3-oxocyclopentyl) 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	47	19.1	1200	0.92	3.75	1.26
1119	29	6.2	2084	0.74	2.10	0.76
1120	31	9.0	2000	0.92	2.96	1.15
1121	31	8.0	2146	0.72	2.92	1.14
1122	27	5.9	2504	0.63	2.36	0.74
Mean	33	9.6	1987	0.79	2.82	1.01
S.D.	8	5.4	480	0.13	0.64	0.24

Appendix 5-28 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	7.5	-	-	-	-	-	+-	Y
4119	7.0	-	-	-	-	-	+-	Y
4120	8.0	+-	+-	-	-	-	+-	Y
4121	7.5	-	-	-	-	-	+-	Y
4122	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 5-29 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual urinalysis of female rats (Week 2 of recovery)
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 5-30 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	45	17.8	1394	1.17	4.11	1.42
4119	34	12.1	1678	1.02	3.40	1.38
4120	31	10.5	1698	0.84	2.78	1.16
4121	53	23.2	1188	1.53	4.50	2.00
4122	43	17.6	1354	0.99	3.86	1.37
Mean	41	16.2	1462	1.11	3.73	1.47
S.D.	9	5.1	220	0.26	0.66	0.32

Appendix 6-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	849	15.2	43.3	51.0	17.9	35.1	2.2	97.7	13.4	18.0	274
1002	952	15.6	45.0	47.3	16.3	34.6	1.7	102.9	14.9	21.1	324
1003	855	15.3	43.6	51.0	17.8	34.9	1.8	107.3	12.6	16.6	278
1004	836	16.0	45.7	54.6	19.1	35.0	2.2	100.4	14.0	18.0	267
1005	837	15.4	44.8	53.5	18.4	34.4	1.7	104.7	13.1	16.3	242
Mean	866	15.5	44.5	51.5	17.9	34.8	1.9	102.6	13.6	18.0	277
S.D.	49	0.3	1.0	2.8	1.0	0.3	0.3	3.7	0.9	1.9	30

Appendix 6-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual hematology of male rats (End of administration)
Dose (mg/kg): 0

Animal number	WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
1001	98.3	62.6	33.1	0.6	0.4	2.7	0.5	61.5	32.6	0.6	0.4	2.6	0.5
1002	65.2	73.6	22.5	1.3	0.3	1.6	0.7	48.0	14.7	0.9	0.2	1.1	0.4
1003	76.5	77.8	18.2	1.4	0.3	1.8	0.5	59.6	13.9	1.0	0.2	1.4	0.4
1004	74.9	74.0	20.7	1.1	0.5	2.0	1.6	55.4	15.5	0.9	0.4	1.5	1.2
1005	79.1	81.3	15.7	0.9	0.5	0.9	0.8	64.3	12.4	0.7	0.4	0.7	0.6
Mean	78.8	73.9	22.0	1.1	0.4	1.8	0.8	57.8	17.8	0.8	0.3	1.5	0.6
S.D.	12.1	7.0	6.7	0.3	0.1	0.7	0.5	6.3	8.3	0.2	0.1	0.7	0.3

LUC: Large unstained cells

Appendix 6-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	909	16.0	46.1	50.7	17.6	34.6	1.9	100.4	12.4	20.5	242
2002	877	15.5	45.6	52.0	17.7	34.1	2.4	92.0	15.4	17.8	284
2003	814	14.1	40.3	49.5	17.3	35.0	2.4	111.3	13.2	16.0	250
2004	867	15.6	45.5	52.5	18.0	34.3	2.8	95.5	12.5	15.7	264
2005	871	14.9	42.9	49.3	17.1	34.7	1.7	112.7	15.3	18.7	261
Mean	868	15.2	44.1	50.8	17.5	34.5	2.2	102.4	13.8	17.7	260
S.D.	34	0.7	2.5	1.4	0.4	0.4	0.4	9.3	1.5	2.0	16

Appendix 6-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual hematology of male rats (End of administration)
Dose (mg/kg): 100

Animal number	WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
2001	87.3	69.6	26.5	0.6	0.4	2.2	0.6	60.8	23.2	0.5	0.4	1.9	0.6
2002	108.4	78.4	16.1	1.2	0.5	2.0	1.8	85.0	17.4	1.3	0.5	2.2	2.0
2003	110.5	71.6	24.5	0.9	0.3	1.4	1.2	79.2	27.1	1.0	0.4	1.6	1.4
2004	62.1	63.2	32.8	0.8	0.3	2.1	0.8	39.3	20.4	0.5	0.2	1.3	0.5
2005	152.4	78.4	18.5	0.5	0.6	1.3	0.8	119.4	28.2	0.8	1.0	1.9	1.2
Mean	104.1	72.2	23.7	0.8	0.4	1.8	1.0	76.7	23.3	0.8	0.5	1.8	1.1
S.D.	33.3	6.4	6.6	0.3	0.1	0.4	0.5	29.8	4.5	0.3	0.3	0.3	0.6

LUC: Large unstained cells

Appendix 6-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	860	15.3	43.9	51.0	17.8	35.0	2.4	92.6	14.5	23.2	249
3002	867	15.4	43.8	50.5	17.7	35.1	2.4	97.1	13.2	16.3	298
3003	832	14.7	41.9	50.4	17.7	35.2	2.2	116.1	13.5	18.7	261
3004	829	14.7	43.0	51.9	17.7	34.1	2.5	98.2	16.6	20.7	240
3005	970	15.4	44.0	45.3	15.8	34.9	1.8	96.1	16.4	21.3	290
Mean	872	15.1	43.3	49.8	17.3	34.9	2.3	100.0	14.8	20.0	268
S.D.	57	0.4	0.9	2.6	0.9	0.4	0.3	9.2	1.6	2.6	25

Appendix 6-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual hematology of male rats (End of administration)
Dose (mg/kg): 300

Animal number	WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
3001	75.8	71.1	24.5	1.0	0.3	2.1	1.0	53.9	18.6	0.8	0.2	1.6	0.7
3002	83.0	68.0	27.1	0.9	0.4	3.0	0.6	56.4	22.5	0.8	0.3	2.5	0.5
3003	108.4	74.4	22.7	0.6	0.4	1.0	0.9	80.7	24.6	0.6	0.5	1.1	1.0
3004	54.1	68.7	29.0	0.4	0.2	1.2	0.5	37.2	15.7	0.2	0.1	0.7	0.3
3005	66.5	75.2	21.0	0.9	0.2	2.1	0.5	50.0	13.9	0.6	0.2	1.4	0.3
Mean	77.6	71.5	24.9	0.8	0.3	1.9	0.7	55.6	19.1	0.6	0.3	1.5	0.6
S.D.	20.4	3.3	3.2	0.3	0.1	0.8	0.2	15.8	4.5	0.2	0.2	0.7	0.3

LUC: Large unstained cells

Appendix 6-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	822	15.2	43.8	53.3	18.5	34.7	2.7	102.7	14.8	17.9	307
4002	849	15.5	44.8	52.8	18.2	34.6	2.5	105.2	16.9	20.1	332
4003	819	15.3	44.9	54.8	18.6	34.0	2.8	93.7	14.5	20.4	276
4004	838	14.5	41.5	49.5	17.3	35.0	1.8	113.5	15.5	19.9	284
4005	822	15.5	45.2	54.9	18.9	34.4	2.4	89.4	14.4	18.0	276
Mean	830	15.2	44.0	53.1	18.3	34.5	2.4	100.9	15.2	19.3	295
S.D.	13	0.4	1.5	2.2	0.6	0.4	0.4	9.5	1.0	1.2	24

Appendix 6-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual hematology of male rats (End of administration)
Dose (mg/kg): 1000

Animal number	WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
4001	82.2	72.6	22.4	0.4	0.4	2.5	1.7	59.7	18.4	0.4	0.3	2.1	1.4
4002	92.9	66.8	28.3	0.6	0.3	2.5	1.6	62.1	26.3	0.5	0.3	2.3	1.5
4003	100.3	75.6	19.9	1.2	0.3	1.8	1.2	75.8	20.0	1.2	0.3	1.8	1.2
4004	87.7	77.1	18.9	0.6	0.4	1.8	1.2	67.6	16.6	0.5	0.3	1.6	1.0
4005	91.0	74.2	18.3	0.9	0.5	4.3	1.8	67.5	16.7	0.8	0.5	3.9	1.7
Mean	90.8	73.3	21.6	0.7	0.4	2.6	1.5	66.5	19.6	0.7	0.3	2.3	1.4
S.D.	6.7	4.0	4.1	0.3	0.1	1.0	0.3	6.2	4.0	0.3	0.1	0.9	0.3

LUC: Large unstained cells

Appendix 6-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	704	12.5	37.1	52.7	17.7	33.6	5.9	172.7	11.8	14.3	349
1102	696	12.7	37.4	53.8	18.2	33.8	7.3	138.2	12.2	16.4	300
1103	709	12.5	37.1	52.4	17.7	33.8	6.1	157.3	12.1	17.5	289
1105	673	13.5	40.2	59.7	20.1	33.7	9.2	141.2	12.7	13.3	317
1106NP	756Z	14.2Z	39.5Z	52.3Z	18.8Z	36.0Z	1.3Z	106.4Z	12.4Z	16.7Z	225Z
1110	722	13.9	41.4	57.3	19.2	33.5	7.9	117.5	12.0	11.5	230
Mean	701	13.0	38.6	55.2	18.6	33.7	7.3	145.4	12.2	14.6	297
S.D.	18	0.6	2.0	3.2	1.0	0.1	1.4	20.8	0.3	2.4	44

NP: Non-pregnant
Z: Data was excluded from statistical analysis.

Appendix 6-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual hematology of female rats (Lactation day 5)
Dose (mg/kg): 0

Animal number	WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
1101	106.5	59.1	37.8	0.4	0.3	1.9	0.5	62.9	40.2	0.5	0.3	2.1	0.5
1102	103.4	45.8	50.4	1.3	0.2	1.7	0.6	47.3	52.1	1.3	0.2	1.8	0.6
1103	100.9	50.8	45.2	0.3	0.2	3.0	0.5	51.3	45.7	0.3	0.2	3.0	0.5
1105	83.8	59.5	38.7	0.3	0.2	0.7	0.5	49.9	32.4	0.3	0.2	0.6	0.5
1106NP	92.6Z	73.5Z	21.5Z	0.9Z	0.6Z	2.3Z	1.3Z	68.0Z	19.9Z	0.9Z	0.6Z	2.1Z	1.2Z
1110	100.0	56.1	39.4	0.7	0.2	3.3	0.4	56.1	39.4	0.7	0.2	3.3	0.4
Mean	98.9	54.3	42.3	0.6	0.2	2.1	0.5	53.5	42.0	0.6	0.2	2.2	0.5
S.D.	8.8	5.9	5.4	0.4	0.0	1.0	0.1	6.2	7.4	0.4	0.0	1.1	0.1

LUC: Large unstained cells
NP: Non-pregnant
Z: Data was excluded from statistical analysis.

Appendix 6-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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
2103	669	12.5	36.7	54.8	18.7	34.1	7.1	143.9	12.4	15.2	300
2105	711	13.3	39.4	55.4	18.7	33.7	8.5	138.4	12.4	15.7	392
2106	709	13.0	38.5	54.3	18.3	33.7	7.2	148.4	11.3	12.0	309
2111	594	12.2	36.8	62.0	20.5	33.1	14.5	171.6	12.5	16.8	311
2112	737	13.7	41.1	55.8	18.5	33.2	8.5	172.3	12.9	13.3	293
Mean	684	12.9	38.5	56.5	18.9	33.6	9.2	154.9	12.3	14.6	321
S.D.	56	0.6	1.9	3.1	0.9	0.4	3.1	15.9	0.6	1.9	40

Appendix 6-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual hematology of female rats (Lactation day 5)
Dose (mg/kg): 100

Animal number	WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
2103	123.6	66.3	30.5	0.3	0.3	1.9	0.6	82.0	37.7	0.4	0.4	2.4	0.8
2105	85.1	75.3	20.8	0.9	0.4	2.1	0.5	64.0	17.7	0.7	0.3	1.8	0.5
2106	78.3	66.1	30.3	0.6	0.1	2.2	0.8	51.7	23.7	0.4	0.1	1.7	0.6
2111	99.1	49.0	46.9	0.4	0.3	2.6	0.7	48.6	46.5	0.4	0.3	2.6	0.7
2112	144.0	60.4	34.7	0.6	0.3	2.7	1.2	87.0	50.0	0.9	0.4	3.9	1.7
Mean	106.0	63.4	32.6	0.6	0.3	2.3	0.8	66.7	35.1	0.6	0.3	2.5	0.9
S.D.	27.4	9.7	9.5	0.2	0.1	0.3	0.3	17.4	14.1	0.2	0.1	0.9	0.5

LUC: Large unstained cells

Appendix 6-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	604	11.6	35.1	58.1	19.2	33.1	11.8	123.6	12.1	16.0	245
3102	642	12.7	37.7	58.8	19.8	33.8	10.3	123.4	12.0	15.5	380
3108	632	12.4	36.5	57.9	19.6	33.9	10.5	149.0	11.8	14.4	263
3109	679	13.3	37.5	55.2	19.6	35.4	4.4	120.9	11.7	14.1	371
3112	687	13.1	38.4	56.0	19.1	34.1	7.4	151.3	12.3	11.8	338
Mean	649	12.6	37.0	57.2	19.5	34.1	8.9	133.6	12.0	14.4	319
S.D.	34	0.7	1.3	1.5	0.3	0.8	3.0	15.1	0.2	1.6	62

Appendix 6-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual hematology of female rats (Lactation day 5)
Dose (mg/kg): 300

Animal number	WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
3101	132.8	46.4	50.5	0.3	0.1	2.2	0.4	61.6	67.1	0.4	0.2	2.9	0.6
3102	79.5	59.0	38.4	0.7	0.2	1.2	0.6	46.9	30.5	0.5	0.1	1.0	0.5
3108	116.1	65.2	31.0	0.1	0.4	2.1	1.2	75.7	36.0	0.2	0.4	2.4	1.4
3109	95.8	50.3	44.5	0.6	0.2	2.7	1.7	48.2	42.7	0.5	0.2	2.6	1.7
3112	99.7	49.0	47.5	0.5	0.3	2.0	0.7	48.9	47.4	0.5	0.3	2.0	0.7
Mean	104.8	54.0	42.4	0.4	0.2	2.0	0.9	56.3	44.7	0.4	0.2	2.2	1.0
S.D.	20.4	7.9	7.8	0.2	0.1	0.5	0.5	12.4	14.1	0.1	0.1	0.7	0.5

LUC: Large unstained cells

Appendix 6-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	653	12.9	37.0	56.6	19.8	34.9	6.8	159.7	12.2	14.2	247
4102NP	804Z	14.8Z	41.6Z	51.8Z	18.5Z	35.7Z	2.0Z	97.7Z	13.5Z	15.6Z	227Z
4103	750	13.9	40.9	54.6	18.5	33.9	5.4	135.5	12.2	13.7	240
4104	725	13.4	38.8	53.6	18.5	34.6	5.3	133.3	12.1	13.9	293
4106	667	13.8	39.5	59.2	20.8	35.1	7.3	144.2	12.8	15.8	239
4110	698	13.1	37.5	53.7	18.8	35.0	6.3	168.8	11.9	11.8	262
4112NP	809Z	14.5Z	41.0Z	50.7Z	17.9Z	35.3Z	2.3Z	91.6Z	12.1Z	12.1Z	254Z
Mean	699	13.4	38.7	55.5	19.3	34.7	6.2	148.3	12.2	13.9	256
S.D.	40	0.4	1.6	2.4	1.0	0.5	0.9	15.5	0.3	1.4	23

NP: Non-pregnant
Z: Data was excluded from statistical analysis.

Appendix 6-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual hematology of female rats (Lactation day 5)
Dose (mg/kg): 1000

Animal number	WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
4101	90.4	74.8	21.3	0.2	0.2	2.5	1.0	67.6	19.3	0.2	0.2	2.3	0.9
4102NP	50.5Z	78.1Z	18.6Z	0.7Z	0.4Z	1.7Z	0.5Z	39.5Z	9.4Z	0.4Z	0.2Z	0.8Z	0.3Z
4103	77.0	67.2	27.2	0.3	0.4	4.1	0.8	51.8	20.9	0.2	0.3	3.2	0.6
4104	91.0	45.0	50.6	0.3	0.1	3.0	0.9	41.0	46.1	0.3	0.1	2.7	0.8
4106	72.5	58.1	35.5	0.7	0.2	4.1	1.4	42.1	25.7	0.5	0.1	2.9	1.0
4110	97.0	56.5	39.3	0.2	0.2	3.1	0.6	54.8	38.1	0.2	0.2	3.0	0.6
4112NP	55.1Z	73.3Z	22.6Z	1.1Z	0.4Z	2.2Z	0.4Z	40.4Z	12.5Z	0.6Z	0.2Z	1.2Z	0.2Z
Mean	85.6	60.3	34.8	0.3	0.2	3.4	0.9	51.5	30.0	0.3	0.2	2.8	0.8
S.D.	10.3	11.3	11.3	0.2	0.1	0.7	0.3	10.8	11.6	0.1	0.1	0.3	0.2

LUC: Large unstained cells
NP: Non-pregnant
Z: Data was excluded from statistical analysis.

Appendix 6-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	865	15.7	44.9	51.9	18.1	34.9	2.2	95.3	11.6	14.6	212
1114	897	16.2	45.6	50.9	18.0	35.4	2.1	103.3	11.5	21.0	209
1115	834	15.3	42.8	51.3	18.3	35.7	2.0	100.6	11.9	15.0	187
1116	801	14.6	41.4	51.6	18.3	35.4	2.7	100.3	11.7	16.4	178
1117	852	15.3	42.8	50.2	18.0	35.8	1.9	109.2	12.4	16.3	199
Mean	850	15.4	43.5	51.2	18.1	35.4	2.2	101.7	11.8	16.7	197
S.D.	36	0.6	1.7	0.7	0.2	0.4	0.3	5.1	0.4	2.6	14

Appendix 6-18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual hematology of female rats (Satellite group, End of administration)
Dose (mg/kg): 0

Animal number	WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
1113	56.5	78.1	18.2	1.3	0.2	1.6	0.7	44.2	10.3	0.7	0.1	0.9	0.4
1114	51.5	65.9	28.6	1.6	0.3	2.9	0.7	34.0	14.8	0.8	0.2	1.5	0.3
1115	62.0	71.5	23.9	1.2	0.2	2.4	0.7	44.3	14.8	0.7	0.1	1.5	0.5
1116	37.5	62.5	35.2	0.9	0.2	0.8	0.4	23.5	13.2	0.4	0.1	0.3	0.1
1117	40.7	81.2	14.2	1.3	0.2	2.5	0.5	33.1	5.8	0.5	0.1	1.0	0.2
Mean	49.6	71.8	24.0	1.3	0.2	2.0	0.6	35.8	11.8	0.6	0.1	1.0	0.3
S.D.	10.4	7.9	8.3	0.3	0.0	0.8	0.1	8.7	3.8	0.2	0.0	0.5	0.2

LUC: Large unstained cells

Appendix 6-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	801	15.0	43.2	53.9	18.8	34.8	2.0	101.9	10.9	15.4	194
4114	776	14.4	41.6	53.6	18.6	34.7	2.1	106.4	12.5	16.1	166
4115	766	14.0	39.9	52.0	18.3	35.2	2.3	103.4	11.7	14.6	211
4116	762	14.1	40.0	52.6	18.6	35.3	2.2	125.0	11.9	17.5	222
4117	819	14.4	41.1	50.2	17.6	35.0	2.8	118.4	11.9	15.0	245
Mean	785	14.4	41.2	52.5	18.4	35.0	2.3	111.0	11.8	15.7	208
S.D.	24	0.4	1.4	1.5	0.5	0.3	0.3	10.2	0.6	1.1	30

Appendix 6-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual hematology of female rats (Satellite group, End of administration)
Dose (mg/kg): 1000

Animal number	WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
4113	58.2	79.3	15.1	1.4	0.2	3.0	0.9	46.2	8.8	0.8	0.1	1.8	0.5
4114	21.7	71.3	25.1	0.5	0.3	2.1	0.8	15.5	5.4	0.1	0.1	0.4	0.2
4115	58.4	66.3	31.0	0.6	0.2	1.5	0.4	38.7	18.1	0.4	0.1	0.9	0.3
4116	45.3	65.7	30.6	1.1	0.1	2.0	0.4	29.8	13.9	0.5	0.1	0.9	0.2
4117	58.0	80.4	15.5	0.5	0.2	2.0	1.3	46.6	9.0	0.3	0.1	1.2	0.8
Mean	48.3	72.6	23.5	0.8	0.2	2.1	0.8	35.4	11.0	0.4	0.1	1.0	0.4
S.D.	15.9	7.0	7.8	0.4	0.1	0.5	0.4	13.0	5.0	0.3	0.0	0.5	0.3

LUC: Large unstained cells

Appendix 6-21 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	896	16.0	44.5	49.6	17.8	36.0	1.7	93.4	17.4	22.7	284
1009	838	15.2	42.6	50.9	18.2	35.7	1.8	113.5	14.5	17.5	286
1010	920	16.1	45.5	49.5	17.5	35.4	1.6	85.7	18.6	28.0	305
1011	863	15.2	44.4	51.4	17.6	34.3	2.3	93.1	17.7	22.8	250
1012	930	15.6	44.4	47.7	16.7	35.0	1.4	89.4	19.5	21.0	343
Mean	889	15.6	44.3	49.8	17.6	35.3	1.8	95.0	17.5	22.4	294
S.D.	39	0.4	1.0	1.4	0.6	0.7	0.3	10.8	1.9	3.8	34

Appendix 6-22 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual hematology of male rats (End of recovery)
Dose (mg/kg): 0

Animal number	WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
1008	93.1	82.8	12.1	1.6	0.6	2.3	0.6	77.1	11.2	1.5	0.5	2.2	0.6
1009	78.5	66.6	28.8	1.0	0.3	2.8	0.4	52.3	22.6	0.8	0.2	2.2	0.3
1010	68.7	78.3	17.5	1.4	0.4	1.9	0.5	53.7	12.0	1.0	0.3	1.3	0.4
1011	76.7	68.4	26.2	1.2	0.3	3.3	0.5	52.5	20.1	0.9	0.2	2.5	0.4
1012	54.4	74.1	21.1	2.1	0.3	1.9	0.5	40.3	11.5	1.1	0.2	1.0	0.3
Mean	74.3	74.0	21.1	1.5	0.4	2.4	0.5	55.2	15.5	1.1	0.3	1.8	0.4
S.D.	14.2	6.7	6.7	0.4	0.1	0.6	0.1	13.4	5.4	0.3	0.1	0.7	0.1

LUC: Large unstained cells

Appendix 6-23 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	880	15.5	44.9	51.0	17.6	34.4	2.3	105.9	15.0	22.4	284
4009	921	14.7	43.1	46.8	16.0	34.2	2.1	114.4	17.0	25.0	283
4010	861	15.0	43.8	50.9	17.5	34.3	2.2	98.9	17.0	20.5	310
4011	870	15.3	44.8	51.5	17.6	34.3	2.0	132.6	13.5	17.9	298
4012	906	15.0	43.9	48.4	16.5	34.1	1.8	117.5	19.6	18.9	319
Mean	888	15.1	44.1	49.7	17.0	34.3	2.1	113.9	16.4	20.9	299
S.D.	25	0.3	0.8	2.0	0.7	0.1	0.2	12.8	2.3	2.8	16

Appendix 6-24 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual hematology of male rats (End of recovery)
Dose (mg/kg): 1000

Animal number	WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
4008	64.3	69.7	24.0	2.6	0.3	2.0	1.4	44.8	15.4	1.7	0.2	1.3	0.9
4009	92.0	75.5	17.7	1.4	0.4	2.7	2.3	69.5	16.3	1.3	0.3	2.5	2.1
4010	64.0	70.8	21.7	1.5	0.5	4.0	1.4	45.3	13.9	0.9	0.3	2.6	0.9
4011	84.6	69.7	25.5	1.5	0.6	2.3	0.5	59.0	21.5	1.3	0.5	1.9	0.5
4012	53.8	65.7	30.3	1.2	0.2	1.7	0.9	35.4	16.3	0.6	0.1	0.9	0.5
Mean	71.7	70.3	23.8	1.6	0.4	2.5	1.3	50.8	16.7	1.2	0.3	1.8	1.0
S.D.	15.9	3.5	4.7	0.6	0.2	0.9	0.7	13.4	2.9	0.4	0.1	0.7	0.7

LUC: Large unstained cells

Appendix 6-25 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	870	15.7	43.9	50.5	18.1	35.8	1.1	115.3	12.5	19.7	162
1119	846	15.5	43.0	50.8	18.3	35.9	2.1	113.1	11.6	13.6	188
1120	870	15.5	43.7	50.2	17.8	35.5	1.9	97.9	12.0	17.5	210
1121	804	15.1	42.1	52.3	18.8	35.9	1.5	119.5	11.8	14.8	208
1122	820	16.2	44.7	54.5	19.8	36.3	1.6	103.7	11.8	16.4	208
Mean	842	15.6	43.5	51.7	18.6	35.9	1.6	109.9	11.9	16.4	195
S.D.	30	0.4	1.0	1.8	0.8	0.3	0.4	8.9	0.3	2.4	21

Appendix 6-26 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual hematology of female rats (End of recovery)
Dose (mg/kg): 0

Animal number	WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
1118	44.9	84.4	11.3	1.6	0.2	1.7	0.7	37.9	5.1	0.7	0.1	0.8	0.3
1119	69.7	77.8	16.6	1.9	0.3	1.9	1.5	54.2	11.6	1.3	0.2	1.3	1.1
1120	74.4	77.1	17.6	1.4	0.4	2.6	1.0	57.4	13.1	1.0	0.3	1.9	0.7
1121	81.3	77.9	17.9	1.2	0.3	2.1	0.6	63.3	14.6	1.0	0.2	1.7	0.5
1122	36.6	67.5	28.1	1.5	0.3	1.7	0.9	24.7	10.3	0.6	0.1	0.6	0.3
Mean	61.4	76.9	18.3	1.5	0.3	2.0	0.9	47.5	10.9	0.9	0.2	1.3	0.6
S.D.	19.5	6.1	6.1	0.3	0.1	0.4	0.4	15.8	3.6	0.3	0.1	0.6	0.3

LUC: Large unstained cells

Appendix 6-27 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	835	15.9	45.1	54.0	19.0	35.2	1.2	108.2	12.8	18.2	210
4119	826	14.9	41.6	50.4	18.1	35.9	2.2	109.9	12.0	17.1	202
4120	876	16.3	46.4	53.0	18.6	35.0	1.4	111.2	12.2	16.1	171
4121	882	15.3	43.7	49.5	17.4	35.1	1.8	128.5	11.9	17.9	192
4122	900	16.2	45.9	51.0	18.0	35.3	1.6	123.6	12.8	17.9	204
Mean	864	15.7	44.5	51.6	18.2	35.3	1.6	116.3	12.3	17.4	196
S.D.	32	0.6	1.9	1.9	0.6	0.4	0.4	9.1	0.4	0.9	15

Appendix 6-28 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual hematology of female rats (End of recovery)
Dose (mg/kg): 1000

Animal number	WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
4118	54.2	70.2	25.5	1.6	0.2	2.1	0.4	38.0	13.8	0.9	0.1	1.1	0.2
4119	51.5	80.4	15.1	1.3	0.2	1.7	1.2	41.5	7.8	0.7	0.1	0.9	0.6
4120	50.3	81.2	14.5	1.3	0.3	1.4	1.3	40.9	7.3	0.7	0.1	0.7	0.6
4121	79.9	81.7	12.5	2.1	0.4	2.0	1.2	65.3	10.0	1.7	0.3	1.6	1.0
4122	54.1	74.4	20.1	1.6	0.2	2.3	1.4	40.2	10.9	0.9	0.1	1.3	0.8
Mean	58.0	77.6	17.5	1.6	0.3	1.9	1.1	45.2	10.0	1.0	0.1	1.1	0.6
S.D.	12.4	5.1	5.3	0.3	0.1	0.4	0.4	11.3	2.6	0.4	0.1	0.3	0.3

LUC: Large unstained cells

Appendix 7-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	63	28	41	0	398	5.7	38	31	71	0.1	126
1002	57	34	44	0	293	5.5	38	42	73	0.1	143
1003	64	28	42	0	333	14.2	66	26	102	0.1	112
1004	71	32	58	0	436	13.7	60	29	89	0.1	131
1005	57	28	39	0	353	4.9	58	22	84	0.1	165
Mean	62	30	45	0	363	8.8	52	30	84	0.1	135
S.D.	6	3	8	0	56	4.7	13	8	13	0.0	20

Appendix 7-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	11	0.29	143	4.0	105	9.7	6.7	5.3	2.9	1.21
1002	11	0.30	144	4.8	108	9.7	6.2	5.9	3.3	1.27
1003	12	0.34	145	4.7	107	9.9	7.2	5.8	3.2	1.23
1004	12	0.30	145	4.5	107	10.0	7.5	5.9	3.1	1.11
1005	12	0.33	145	4.2	107	10.1	6.9	5.8	3.1	1.15
Mean	12	0.31	144	4.4	107	9.9	6.9	5.7	3.1	1.19
S.D.	1	0.02	1	0.3	1	0.2	0.5	0.3	0.1	0.06

Appendix 7-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	80	37	68	0	607	5.8	40	20	68	0.0	117
2002	62	28	34	0	414	11.6	40	20	68	0.1	142
2003	71	29	34	0	371	10.6	49	42	80	0.1	153
2004	62	27	35	0	542	8.8	57	48	98	0.0	137
2005	73	37	43	0	382	21.7	60	50	93	0.1	150
Mean	70	32	43	0	463	11.7	49	36	81	0.1	140
S.D.	8	5	15	0	105	6.0	9	15	14	0.1	14

Appendix 7-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	13	0.35	144	4.4	106	9.6	6.1	5.9	3.1	1.11
2002	12	0.32	146	4.5	108	9.4	6.7	5.6	3.2	1.33
2003	12	0.32	143	4.7	106	9.4	6.2	5.3	3.1	1.41
2004	14	0.28	145	4.3	107	9.9	6.5	5.9	3.1	1.11
2005	12	0.26	143	4.6	105	9.6	6.5	5.3	3.0	1.30
Mean	13	0.31	144	4.5	106	9.6	6.4	5.6	3.1	1.25
S.D.	1	0.04	1	0.2	1	0.2	0.2	0.3	0.1	0.14

Appendix 7-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	70	29	45	0	396	7.2	32	27	61	0.1	150
3002	67	30	38	0	527	16.1	45	30	77	0.0	147
3003	68	28	35	0	447	4.5	38	26	66	0.0	127
3004	62	27	31	0	488	8.6	35	17	59	0.0	129
3005	46	23	33	0	332	4.2	42	54	76	0.0	141
Mean	63	27	36	0	438	8.1	38	31	68	0.0	139
S.D.	10	3	5	0	77	4.8	5	14	8	0.0	10

Appendix 7-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	12	0.35	142	4.7	105	9.4	6.2	5.4	3.0	1.25
3002	12	0.37	145	4.4	106	10.0	6.0	5.5	3.1	1.29
3003	11	0.37	144	4.4	106	9.9	6.3	5.7	3.1	1.19
3004	11	0.37	145	4.6	105	10.1	6.8	5.8	3.2	1.23
3005	15	0.32	145	4.8	106	10.4	6.8	5.8	3.4	1.42
Mean	12	0.36	144	4.6	106	10.0	6.4	5.6	3.2	1.28
S.D.	2	0.02	1	0.2	1	0.4	0.4	0.2	0.2	0.09

Appendix 7-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	63	30	42	0	476	12.5	46	45	79	0.0	133
4002	62	32	44	1	421	7.4	52	44	92	0.1	127
4003	67	32	36	0	421	6.3	56	52	97	0.1	126
4004	65	31	34	1	619	5.2	52	12	78	0.0	146
4005	75	31	46	0	561	53.1	45	22	77	0.1	127
Mean	66	31	40	0	500	16.9	50	35	85	0.1	132
S.D.	5	1	5	1	88	20.4	5	17	9	0.1	8

Appendix 7-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	14	0.32	144	4.4	105	10.0	5.9	5.7	3.2	1.28
4002	13	0.32	145	4.4	104	10.1	7.0	5.8	3.2	1.23
4003	13	0.30	145	4.3	101	10.3	7.2	5.7	3.2	1.28
4004	15	0.41	145	4.2	106	9.6	6.4	5.7	3.3	1.38
4005	15	0.38	144	4.5	104	10.1	7.7	5.9	3.2	1.19
Mean	14	0.35	145	4.4	104	10.0	6.8	5.8	3.2	1.27
S.D.	1	0.05	1	0.1	2	0.3	0.7	0.1	0.0	0.07

Appendix 7-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	77	58	30	0	232	8.4	47	30	98	0.1	140
1102	75	54	36	0	270	13.6	60	73	134	0.1	123
1103	65	50	32	0	180	6.9	77	57	152	0.1	130
1105	80	44	50	0	358	82.2	53	41	109	0.1	127
1106NP	61Z	30Z	43Z	0Z	583Z	6.2Z	50Z	24Z	96Z	0.0Z	199Z
1110	66	34	39	0	232	4.4	45	26	93	0.1	141
Mean	73	48	37	0	254	23.1	56	45	117	0.1	132
S.D.	7	9	8	0	66	33.2	13	20	25	0.0	8

NP: Non-pregnant
Z: Data was excluded from statistical analysis.

Appendix 7-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	14	0.37	143	3.6	106	9.7	6.0	5.7	3.1	1.19
1102	12	0.37	140	3.8	107	9.9	4.7	6.3	3.8	1.52
1103	15	0.48	141	3.7	106	10.3	6.0	6.4	3.7	1.37
1105	17	0.42	140	3.8	103	10.2	7.2	5.8	3.4	1.42
1106NP	18Z	0.41Z	143Z	3.9Z	110Z	9.9Z	3.5Z	5.8Z	3.4Z	1.42Z
1110	10	0.37	140	4.2	108	9.5	5.8	5.6	3.2	1.33
Mean	14	0.40	141	3.8	106	9.9	5.9	6.0	3.4	1.37
S.D.	3	0.05	1	0.2	2	0.3	0.9	0.4	0.3	0.12

NP: Non-pregnant
Z: Data was excluded from statistical analysis.

Appendix 7-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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
2103	64	37	34	0	234	6.5	49	29	91	0.0	139
2105	98	51	43	1	214	18.6	47	36	100	0.1	121
2106	124	56	59	0	190	14.3	47	40	94	0.0	111
2111	87	62	47	0	213	15.6	46	38	89	0.0	121
2112	72	46	60	0	224	25.2	68	93	133	0.1	123
Mean	89	50	49	0	215	16.0	51	47	101	0.0	123
S.D.	24	10	11	0	16	6.8	9	26	18	0.1	10

Appendix 7-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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
2103	15	0.39	142	4.3	106	10.0	6.4	5.8	3.2	1.23
2105	18	0.37	141	3.9	105	10.9	6.4	6.0	3.7	1.61
2106	16	0.44	141	4.4	109	10.0	5.8	5.8	3.3	1.32
2111	15	0.41	142	5.1	109	10.1	6.1	5.8	3.2	1.23
2112	15	0.38	141	3.8	106	10.4	6.4	6.2	3.6	1.38
Mean	16	0.40	141	4.3	107	10.3	6.2	5.9	3.4	1.35
S.D.	1	0.03	1	0.5	2	0.4	0.3	0.2	0.2	0.16

Appendix 7-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	85	65	29	0	398	7.0	49	50	96	0.0	118
3102	106	85	46	1	539	21.5	61	50	115	0.0	120
3108	80	57	47	0	250	8.0	58	61	112	0.0	135
3109	69	62	34	0	558	36.4	64	244	150	0.1	112
3112	84	51	57	0	261	21.3	67	29	118	0.0	115
Mean	85	64	43	0	401	18.8	60	87	118	0.0	120
S.D.	13	13	11	0	147	12.0	7	89	20	0.0	9

Appendix 7-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	9	0.41	140	4.1	104	9.5	5.8	5.6	3.2	1.33
3102	18	0.44	140	4.4	106	10.1	6.6	5.8	3.3	1.32
3108	13	0.41	142	4.4	105	9.7	6.8	5.6	3.2	1.33
3109	14	0.39	140	4.3	104	10.4	6.8	6.0	3.4	1.31
3112	17	0.44	140	4.6	104	9.7	5.6	5.6	3.4	1.55
Mean	14	0.42	140	4.4	105	9.9	6.3	5.7	3.3	1.37
S.D.	4	0.02	1	0.2	1	0.4	0.6	0.2	0.1	0.10

Appendix 7-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	97	69	35	1	286	53.6	65	107	135	0.0	101
4102NP	62Z	46Z	34Z	1Z	591Z	84.5Z	64Z	50Z	135Z	0.0Z	148Z
4103	62	51	36	1	276	28.0	81	129	159	0.0	121
4104	72	66	31	1	365	28.4	66	84	125	0.0	111
4106	78	68	28	1	315	29.3	75	44	139	0.0	109
4110	70	64	31	1	269	33.0	74	102	139	0.0	123
4112NP	50Z	38Z	43Z	0Z	460Z	55.8Z	63Z	38Z	117Z	0.0Z	155Z
Mean	76	64	32	1	302	34.5	72	93	139	0.0	113
S.D.	13	7	3	0	39	10.9	7	32	12	0.0	9

NP: Non-pregnant
Z: Data was excluded from statistical analysis.

Appendix 7-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	25	0.46	140	3.4	99	10.2	6.4	5.5	3.2	1.39
4102NP	28Z	0.46Z	144Z	4.0Z	105Z	10.7Z	5.6Z	6.3Z	3.9Z	1.63Z
4103	19	0.40	143	4.1	103	11.0	7.9	6.2	3.5	1.30
4104	20	0.44	144	3.9	105	9.8	5.0	5.4	3.2	1.45
4106	15	0.36	143	4.1	107	10.2	5.0	5.9	3.4	1.36
4110	17	0.38	143	4.0	105	10.1	4.9	5.7	3.3	1.38
4112NP	26Z	0.43Z	143Z	3.9Z	107Z	10.7Z	4.1Z	6.3Z	3.8Z	1.52Z
Mean	19	0.41	143	3.9	104	10.3	5.8	5.7	3.3	1.38
S.D.	4	0.04	2	0.3	3	0.4	1.3	0.3	0.1	0.05

NP: Non-pregnant
Z: Data was excluded from statistical analysis.

Appendix 7-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	46	22	36	1	198	10.0	64	23	124	0.1	133
1114	56	25	38	0	164	10.1	52	20	113	0.1	146
1115	54	23	37	0	300	22.1	68	17	127	0.1	137
1116	59	24	49	0	302	8.5	64	16	122	0.1	134
1117	53	20	35	0	344	8.9	56	15	107	0.1	128
Mean	54	23	39	0	262	11.9	61	18	119	0.1	136
S.D.	5	2	6	0	77	5.7	7	3	8	0.0	7

Appendix 7-18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	12	0.31	143	4.1	108	10.5	5.4	6.3	3.7	1.42
1114	14	0.34	143	4.3	109	10.0	5.1	6.7	3.9	1.39
1115	17	0.39	142	4.3	108	10.2	5.1	6.6	3.9	1.44
1116	19	0.42	142	4.1	108	10.0	5.8	6.4	3.7	1.37
1117	17	0.37	143	4.7	109	10.3	5.5	6.2	3.7	1.48
Mean	16	0.37	143	4.3	108	10.2	5.4	6.4	3.8	1.42
S.D.	3	0.04	1	0.2	1	0.2	0.3	0.2	0.1	0.04

Appendix 7-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	57	38	40	0	212	45.0	102	36	196	0.1	127
4114	56	36	33	0	316	10.6	76	35	150	0.0	117
4115	68	37	28	1	228	63.5	80	36	147	0.1	104
4116	47	27	29	0	181	7.0	80	25	139	0.1	112
4117	49	28	30	0	257	8.7	77	24	137	0.1	117
Mean	55	33	32	0	239	27.0	83	31	154	0.1	115
S.D.	8	5	5	0	51	25.8	11	6	24	0.0	8

Appendix 7-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	15	0.34	142	4.2	103	10.5	5.8	6.8	4.1	1.52
4114	19	0.43	144	3.8	107	10.1	5.2	6.3	3.8	1.52
4115	20	0.49	144	4.0	105	10.1	5.8	6.3	3.4	1.17
4116	18	0.40	143	4.3	105	10.0	5.2	6.7	3.8	1.31
4117	15	0.35	144	4.5	104	10.5	7.0	6.2	3.7	1.48
Mean	17	0.40	143	4.2	105	10.2	5.8	6.5	3.8	1.40
S.D.	2	0.06	1	0.3	1	0.2	0.7	0.3	0.3	0.16

Appendix 7-21 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	54	28	47	0	255	6.3	51	20	82	0.1	146
1009	62	29	52	0	236	10.4	57	32	90	0.1	147
1010	66	29	53	0	451	7.5	37	28	69	0.1	143
1011	74	30	42	0	404	10.1	52	22	76	0.1	135
1012	80	40	42	0	372	15.9	69	36	102	0.0	133
Mean	67	31	47	0	344	10.0	53	28	84	0.1	141
S.D.	10	5	5	0	94	3.7	12	7	13	0.0	6

Appendix 7-22 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	17	0.31	143	4.6	103	9.3	5.7	5.9	3.2	1.19
1009	15	0.28	143	4.3	105	9.4	5.2	6.1	3.2	1.10
1010	12	0.27	145	4.1	107	9.5	5.1	6.3	3.3	1.10
1011	16	0.29	144	4.0	108	9.4	5.1	5.9	3.1	1.11
1012	15	0.29	145	4.1	106	9.5	5.5	6.1	3.3	1.18
Mean	15	0.29	144	4.2	106	9.4	5.3	6.1	3.2	1.14
S.D.	2	0.01	1	0.2	2	0.1	0.3	0.2	0.1	0.05

Appendix 7-23 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	73	37	44	0	434	6.8	58	30	89	0.1	139
4009	62	34	37	0	253	3.5	72	38	104	0.1	146
4010	70	36	41	0	263	10.3	65	48	95	0.1	141
4011	74	36	39	1	377	10.9	64	61	99	0.0	136
4012	74	41	41	0	409	12.7	51	24	86	0.1	131
Mean	71	37	40	0	347	8.8	62	40	95	0.1	139
S.D.	5	3	3	0	84	3.7	8	15	7	0.0	6

Appendix 7-24 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	17	0.32	143	4.3	105	9.2	5.8	5.9	3.2	1.19
4009	15	0.27	144	4.7	104	9.5	5.8	6.2	3.3	1.14
4010	14	0.25	144	4.2	105	9.5	5.1	6.2	3.4	1.21
4011	15	0.29	144	4.1	105	10.0	5.2	6.3	3.3	1.10
4012	14	0.26	146	4.4	110	9.7	6.1	6.0	3.3	1.22
Mean	15	0.28	144	4.3	106	9.6	5.6	6.1	3.3	1.17
S.D.	1	0.03	1	0.2	2	0.3	0.4	0.2	0.1	0.05

Appendix 7-25 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	107	52	76	0	172	21.9	55	16	110	0.1	119
1119	66	30	45	1	288	9.2	78	16	141	0.1	131
1120	63	25	43	0	259	10.4	64	12	111	0.1	152
1121	73	47	52	0	160	10.9	62	22	120	0.1	145
1122	100	60	74	0	138	11.3	73	18	134	0.1	147
Mean	82	43	58	0	203	12.7	66	17	123	0.1	139
S.D.	20	15	16	0	66	5.2	9	4	14	0.0	14

Appendix 7-26 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	16	0.34	144	4.4	111	9.7	4.5	6.2	3.5	1.30
1119	19	0.35	143	4.1	107	9.9	5.5	6.3	3.6	1.33
1120	18	0.35	142	4.5	108	9.8	5.5	6.2	3.7	1.48
1121	25	0.46	142	4.2	108	10.1	4.8	6.7	3.9	1.39
1122	15	0.40	143	4.5	109	9.8	4.6	6.5	3.8	1.41
Mean	19	0.38	143	4.3	109	9.9	5.0	6.4	3.7	1.38
S.D.	4	0.05	1	0.2	2	0.2	0.5	0.2	0.2	0.07

Appendix 7-27 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	58	27	41	0	131	15.5	68	21	124	0.1	126
4119	66	36	47	0	201	10.1	73	13	123	0.1	123
4120	54	26	48	0	151	10.9	77	25	136	0.1	125
4121	59	27	55	0	237	13.8	94	48	169	0.1	134
4122	53	23	39	0	90	11.2	69	24	132	0.1	133
Mean	58	28	46	0	162	12.3	76	26	137	0.1	128
S.D.	5	5	6	0	58	2.3	11	13	19	0.0	5

Appendix 7-28 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	0.33	143	4.6	109	10.2	5.7	7.1	3.9	1.22
4119	19	0.38	143	4.1	107	9.8	4.9	6.5	3.8	1.41
4120	21	0.42	144	4.5	110	10.0	4.9	6.9	3.9	1.30
4121	22	0.38	142	4.5	107	10.3	5.5	7.3	4.0	1.21
4122	14	0.34	143	4.6	107	9.9	5.3	6.6	3.7	1.28
Mean	18	0.37	143	4.5	108	10.0	5.3	6.9	3.9	1.28
S.D.	3	0.04	1	0.2	1	0.2	0.4	0.3	0.1	0.08

Appendix 8-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	584	2.22	14.3	12.7	15.6	28.3	217
	1002	514	2.11	14.9	10.0	13.3	23.3	261
	1003	523	2.18	14.4	10.0	9.3	19.3	240
	1004	504	2.04	15.0	9.3	6.1	15.4	243
	1005	550	2.05	11.1	13.0	11.2	24.2	347
	1006	500	2.16	13.0	12.8	12.1	24.9	287
	1007	606	2.13	16.6	11.4	12.2	23.6	245
	Mean	540	2.13	14.2	11.3	11.4	22.7	263
	S.D.	41	0.07	1.7	1.6	3.0	4.2	43
Relative	1001		0.38	2.4	2.2	2.7	4.8	37
	1002		0.41	2.9	1.9	2.6	4.5	51
	1003		0.42	2.8	1.9	1.8	3.7	46
	1004		0.40	3.0	1.8	1.2	3.1	48
	1005		0.37	2.0	2.4	2.0	4.4	63
	1006		0.43	2.6	2.6	2.4	5.0	57
	1007		0.35	2.7	1.9	2.0	3.9	40
	Mean		0.39	2.6	2.1	2.1	4.2	49
	S.D.		0.03	0.3	0.3	0.5	0.7	9

Appendix 8-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	1.48	14.20	0.92	1.86	2.03	3.89
	1002	1.58	14.19	0.72	1.72	1.64	3.36
	1003	1.70	12.69	0.84	1.74	1.82	3.56
	1004	1.79	13.15	0.76	1.59	1.52	3.11
	1005	1.42	15.15	0.77	1.44	1.40	2.84
	1006	1.43	11.72	1.01	1.47	1.72	3.19
	1007	1.79	17.95	0.85	1.99	2.14	4.13
	Mean	1.60	14.15	0.84	1.69	1.75	3.44
	S.D.	0.16	2.02	0.10	0.20	0.27	0.45
Relative	1001	0.25	2.43	0.16	0.32	0.35	0.67
	1002	0.31	2.76	0.14	0.33	0.32	0.65
	1003	0.33	2.43	0.16	0.33	0.35	0.68
	1004	0.36	2.61	0.15	0.32	0.30	0.62
	1005	0.26	2.75	0.14	0.26	0.25	0.52
	1006	0.29	2.34	0.20	0.29	0.34	0.64
	1007	0.30	2.96	0.14	0.33	0.35	0.68
	Mean	0.30	2.61	0.16	0.31	0.32	0.64
	S.D.	0.04	0.22	0.02	0.03	0.04	0.06

Appendix 8-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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)
	1001	33	33	66	1.75	1.77	3.52
	1002	27	31	58	1.54	1.55	3.09
	1003	38	41	79	1.75	1.78	3.53
	1004	33	34	67	1.45	1.45	2.90
Absolute	1005	25	25	50	1.61	1.57	3.18
	1006	37	41	78	1.51	1.48	2.99
	1007	30	31	61	1.82	1.75	3.57
	Mean	32	34	66	1.63	1.62	3.25
	S.D.	5	6	10	0.14	0.14	0.28
	1001	6	6	11	0.30	0.30	0.60
	1002	5	6	11	0.30	0.30	0.60
	1003	7	8	15	0.33	0.34	0.67
	1004	7	7	13	0.29	0.29	0.58
Relative	1005	5	5	9	0.29	0.29	0.58
	1006	7	8	16	0.30	0.30	0.60
	1007	5	5	10	0.30	0.29	0.59
	Mean	6	6	12	0.30	0.30	0.60
	S.D.	1	1	3	0.01	0.02	0.03

Appendix 8-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	728	727	1455	1.98	1.37
	1002	692	693	1385	2.01	1.37
	1003	625	627	1252	1.74	1.17
	1004	617	596	1213	1.72	1.18
	1005	643	616	1259	1.49	0.93
	1006	684	649	1333	1.94	1.41
	1007	805	782	1587	2.30	1.61
	Mean	685	670	1355	1.88	1.29
	S.D.	66	67	132	0.26	0.22
Relative	1001	125	124	249	0.34	0.23
	1002	135	135	269	0.39	0.27
	1003	120	120	239	0.33	0.22
	1004	122	118	241	0.34	0.23
	1005	117	112	229	0.27	0.17
	1006	137	130	267	0.39	0.28
	1007	133	129	262	0.38	0.27
	Mean	127	124	251	0.35	0.24
	S.D.	8	8	15	0.04	0.04

Appendix 8-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	542	2.17	12.3	10.8	10.5	21.3	390
	2002	505	2.07	13.3	14.9	13.6	28.5	439
	2003	578	2.22	14.9	13.0	13.9	26.9	503
	2004	581	2.19	14.8	10.3	6.9	17.2	239
	2005	527	2.11	15.2	15.7	13.8	29.5	418
	2006	554	2.17	12.5	13.9	12.3	26.2	308
	2007	606	2.24	12.9	15.2	16.5	31.7	452
	2008	534	2.17	13.7	18.2	15.5	33.7	264
	2009	567	2.15	11.6	11.9	13.6	25.5	277
	2010	606	2.14	12.0	16.2	13.1	29.3	374
	2011	537	2.13	10.9	12.9	14.0	26.9	335
	2012	518	1.99	15.6	11.1	12.4	23.5	359
	Mean	555	2.15	13.3	13.7	13.0	26.7	363
	S.D.	33	0.07	1.5	2.4	2.4	4.5	82
Relative	2001		0.40	2.3	2.0	1.9	3.9	72
	2002		0.41	2.6	3.0	2.7	5.6	87
	2003		0.38	2.6	2.2	2.4	4.7	87
	2004		0.38	2.5	1.8	1.2	3.0	41
	2005		0.40	2.9	3.0	2.6	5.6	79
	2006		0.39	2.3	2.5	2.2	4.7	56
	2007		0.37	2.1	2.5	2.7	5.2	75
	2008		0.41	2.6	3.4	2.9	6.3	49
	2009		0.38	2.0	2.1	2.4	4.5	49
	2010		0.35	2.0	2.7	2.2	4.8	62
	2011		0.40	2.0	2.4	2.6	5.0	62
	2012		0.38	3.0	2.1	2.4	4.5	69
	Mean		0.39	2.4	2.5	2.4	4.8	66
	S.D.		0.02	0.3	0.5	0.5	0.9	15

Appendix 8-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	1.44	12.35	0.82	1.59	1.56	3.15
	2002	1.71	12.55	0.74	1.69	1.87	3.56
	2003	1.70	14.96	1.00	2.02	2.16	4.18
	2004	1.48	16.20	0.74	1.80	1.86	3.66
	2005	1.52	13.56	0.86	2.04	1.89	3.93
	2006	1.62	14.53	0.73	1.72	1.80	3.52
	2007	1.75	15.00	0.75	2.02	1.87	3.89
	2008	1.46	15.04	0.73	1.76	1.82	3.58
	2009	1.52	16.01	0.76	1.75	1.88	3.63
	2010	1.81	15.11	0.92	1.78	1.78	3.56
	2011	1.37	16.57	0.78	1.74	1.81	3.55
	2012	1.68	13.89	0.84	1.95	1.94	3.89
	Mean	1.59	14.65	0.81	1.82	1.85	3.68
	S.D.	0.14	1.35	0.09	0.15	0.14	0.26
Relative	2001	0.27	2.28	0.15	0.29	0.29	0.58
	2002	0.34	2.49	0.15	0.33	0.37	0.70
	2003	0.29	2.59	0.17	0.35	0.37	0.72
	2004	0.25	2.79	0.13	0.31	0.32	0.63
	2005	0.29	2.57	0.16	0.39	0.36	0.75
	2006	0.29	2.62	0.13	0.31	0.32	0.64
	2007	0.29	2.48	0.12	0.33	0.31	0.64
	2008	0.27	2.82	0.14	0.33	0.34	0.67
	2009	0.27	2.82	0.13	0.31	0.33	0.64
	2010	0.30	2.49	0.15	0.29	0.29	0.59
	2011	0.26	3.09	0.15	0.32	0.34	0.66
	2012	0.32	2.68	0.16	0.38	0.37	0.75
	Mean	0.29	2.64	0.15	0.33	0.33	0.66
	S.D.	0.03	0.21	0.02	0.03	0.03	0.06

Appendix 8-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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)
	2001	25	23	48	1.73	1.71	3.44
	2002	29	33	62	1.81	1.72	3.53
	2003	33	34	67	1.87	1.84	3.71
	2004	26	27	53	1.73	1.74	3.47
	2005	33	36	69	1.80	1.80	3.60
	2006	32	30	62	1.59	1.63	3.22
	2007	31	32	63	1.69	1.72	3.41
Absolute	2008	33	35	68	1.54	1.52	3.06
	2009	37	40	77	1.61	1.71	3.32
	2010	31	33	64	1.39	1.40	2.79
	2011	38	37	75	1.50	1.48	2.98
	2012	29	34	63	1.74	1.77	3.51
	Mean	31	33	64	1.67	1.67	3.34
	S.D.	4	5	8	0.14	0.14	0.27
	2001	5	4	9	0.32	0.32	0.63
	2002	6	7	12	0.36	0.34	0.70
	2003	6	6	12	0.32	0.32	0.64
	2004	4	5	9	0.30	0.30	0.60
	2005	6	7	13	0.34	0.34	0.68
	2006	6	5	11	0.29	0.29	0.58
	2007	5	5	10	0.28	0.28	0.56
Relative	2008	6	7	13	0.29	0.28	0.57
	2009	7	7	14	0.28	0.30	0.59
	2010	5	5	11	0.23	0.23	0.46
	2011	7	7	14	0.28	0.28	0.55
	2012	6	7	12	0.34	0.34	0.68
	Mean	6	6	12	0.30	0.30	0.60
	S.D.	1	1	2	0.04	0.03	0.07

Appendix 8-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	649	642	1291	1.49	1.21
	2002	707	724	1431	2.18	1.33
	2003	781	807	1588	1.97	1.98
	2004	644	554	1198	1.76	1.37
	2005	740	722	1462	1.69	1.53
	2006	698	699	1397	1.83	1.34
	2007	676	676	1352	1.86	1.18
	2008	696	656	1352	2.01	1.32
	2009	697	663	1360	1.75	1.63
	2010	655	655	1310	1.88	1.35
	2011	726	683	1409	1.99	1.54
	2012	746	779	1525	1.92	1.63
	Mean	701	688	1390	1.86	1.45
	S.D.	42	66	105	0.18	0.22
Relative	2001	120	118	238	0.27	0.22
	2002	140	143	283	0.43	0.26
	2003	135	140	275	0.34	0.34
	2004	111	95	206	0.30	0.24
	2005	140	137	277	0.32	0.29
	2006	126	126	252	0.33	0.24
	2007	112	112	223	0.31	0.19
	2008	130	123	253	0.38	0.25
	2009	123	117	240	0.31	0.29
	2010	108	108	216	0.31	0.22
	2011	135	127	262	0.37	0.29
	2012	144	150	294	0.37	0.31
	Mean	127	125	252	0.34	0.26
	S.D.	12	16	28	0.04	0.04

Appendix 8-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	507	2.15	15.6	10.5	12.0	22.5	281
	3002	516	2.05	11.5	14.4	8.8	23.2	339
	3003	521	2.17	17.2	9.7	11.2	20.9	260
	3004	536	2.18	12.4	14.3	16.0	30.3	279
	3005	526	2.08	13.4	10.7	9.5	20.2	241
	3006	513	2.04	13.5	8.4	8.9	17.3	442
	3007	481	2.05	12.4	10.9	7.9	18.8	233
	3008	504	2.15	11.9	9.1	7.3	16.4	243
	3009	528	2.12	12.8	12.2	9.5	21.7	443
	3010	489	2.10	12.6	10.2	12.0	22.2	269
	3011	613	2.23	19.0	20.0	19.8	39.8	343
	3012	558	2.10	15.4	22.1	19.5	41.6	275
	Mean	524	2.12	14.0	12.7	11.9	24.6	304
	S.D.	35	0.06	2.3	4.3	4.3	8.3	73
Relative	3001		0.42	3.1	2.1	2.4	4.4	55
	3002		0.40	2.2	2.8	1.7	4.5	66
	3003		0.42	3.3	1.9	2.1	4.0	50
	3004		0.41	2.3	2.7	3.0	5.7	52
	3005		0.40	2.5	2.0	1.8	3.8	46
	3006		0.40	2.6	1.6	1.7	3.4	86
	3007		0.43	2.6	2.3	1.6	3.9	48
	3008		0.43	2.4	1.8	1.4	3.3	48
	3009		0.40	2.4	2.3	1.8	4.1	84
	3010		0.43	2.6	2.1	2.5	4.5	55
	3011		0.36	3.1	3.3	3.2	6.5	56
	3012		0.38	2.8	4.0	3.5	7.5	49
	Mean		0.41	2.7	2.4	2.2	4.6	58
	S.D.		0.02	0.3	0.7	0.7	1.3	14

Appendix 8-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	1.50	15.04	0.74	1.67	1.82	3.49
	3002	1.41	14.40	0.76	1.64	1.72	3.36
	3003	1.59	14.09	0.79	1.73	1.87	3.60
	3004	1.46	15.47	0.74	1.75	1.78	3.53
	3005	1.56	16.60	0.87	1.83	2.06	3.89
	3006	1.74	15.92	0.75	1.87	1.77	3.64
	3007	1.22	14.10	0.63	1.67	1.55	3.22
	3008	1.40	14.83	0.89	1.71	1.60	3.31
	3009	1.53	16.99	0.84	1.79	1.85	3.64
	3010	1.40	13.62	0.80	1.52	1.53	3.05
	3011	1.84	19.52	0.91	1.87	1.92	3.79
	3012	1.65	16.78	0.87	1.97	1.80	3.77
	Mean	1.53	15.61	0.80	1.75	1.77	3.52
	S.D.	0.17	1.67	0.08	0.12	0.15	0.25
Relative	3001	0.30	2.97	0.15	0.33	0.36	0.69
	3002	0.27	2.79	0.15	0.32	0.33	0.65
	3003	0.31	2.70	0.15	0.33	0.36	0.69
	3004	0.27	2.89	0.14	0.33	0.33	0.66
	3005	0.30	3.16	0.17	0.35	0.39	0.74
	3006	0.34	3.10	0.15	0.36	0.35	0.71
	3007	0.25	2.93	0.13	0.35	0.32	0.67
	3008	0.28	2.94	0.18	0.34	0.32	0.66
	3009	0.29	3.22	0.16	0.34	0.35	0.69
	3010	0.29	2.79	0.16	0.31	0.31	0.62
	3011	0.30	3.18	0.15	0.31	0.31	0.62
	3012	0.30	3.01	0.16	0.35	0.32	0.68
	Mean	0.29	2.97	0.15	0.34	0.34	0.67
	S.D.	0.02	0.17	0.01	0.02	0.02	0.03

Appendix 8-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	33	40	73	1.73	1.81	3.54
	3002	28	32	60	1.52	1.49	3.01
	3003	41	43	84	1.81	1.79	3.60
	3004	26	29	55	1.44	1.48	2.92
	3005	24	27	51	1.90	1.93	3.83
	3006	34	38	72	1.56	1.48	3.04
	3007	28	28	56	1.57	1.55	3.12
	3008	32	32	64	1.83	1.85	3.68
	3009	24	27	51	1.85	1.90	3.75
	3010	40	41	81	1.62	1.62	3.24
	3011	36	41	77	1.68	1.64	3.32
	3012	33	35	68	1.71	1.76	3.47
	Mean	32	34	66	1.69	1.69	3.38
	S.D.	6	6	12	0.15	0.17	0.31
Relative	3001	7	8	14	0.34	0.36	0.70
	3002	5	6	12	0.29	0.29	0.58
	3003	8	8	16	0.35	0.34	0.69
	3004	5	5	10	0.27	0.28	0.54
	3005	5	5	10	0.36	0.37	0.73
	3006	7	7	14	0.30	0.29	0.59
	3007	6	6	12	0.33	0.32	0.65
	3008	6	6	13	0.36	0.37	0.73
	3009	5	5	10	0.35	0.36	0.71
	3010	8	8	17	0.33	0.33	0.66
	3011	6	7	13	0.27	0.27	0.54
	3012	6	6	12	0.31	0.32	0.62
	Mean	6	6	13	0.32	0.33	0.65
	S.D.	1	1	2	0.03	0.04	0.07

Appendix 8-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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)
	3001	714	774	1488	1.87	1.04
	3002	662	653	1315	1.80	1.36
	3003	725	733	1458	2.05	1.13
	3004	631	647	1278	1.80	1.56
	3005	739	763	1502	1.99	1.54
	3006	646	616	1262	1.98	1.39
	3007	661	630	1291	1.58	1.08
Absolute	3008	612	576	1188	2.12	1.28
	3009	701	710	1411	1.66	1.51
	3010	684	684	1368	1.85	1.06
	3011	710	704	1414	2.10	1.30
	3012	745	732	1477	1.75	1.18
	Mean	686	685	1371	1.88	1.29
	S.D.	43	62	103	0.17	0.19
	3001	141	153	293	0.37	0.21
	3002	128	127	255	0.35	0.26
	3003	139	141	280	0.39	0.22
	3004	118	121	238	0.34	0.29
	3005	140	145	286	0.38	0.29
	3006	126	120	246	0.39	0.27
	3007	137	131	268	0.33	0.22
Relative	3008	121	114	236	0.42	0.25
	3009	133	134	267	0.31	0.29
	3010	140	140	280	0.38	0.22
	3011	116	115	231	0.34	0.21
	3012	134	131	265	0.31	0.21
	Mean	131	131	262	0.36	0.25
	S.D.	9	12	21	0.03	0.03

Appendix 8-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	502	2.10	13.8	11.7	12.7	24.4	355
	4002	449	2.10	11.5	10.7	9.5	20.2	257
	4003	521	2.24	14.9	13.1	13.5	26.6	287
	4004	483	2.10	12.5	9.6	9.7	19.3	273
	4005	476	2.17	13.2	12.0	9.9	21.9	290
	4006	518	2.20	15.1	11.1	10.8	21.9	267
	4007	477	2.20	11.3	11.8	10.3	22.1	262
	Mean	489	2.16	13.2	11.4	10.9	22.3	284
	S.D.	26	0.06	1.5	1.1	1.6	2.5	33
Relative	4001		0.42	2.7	2.3	2.5	4.9	71
	4002		0.47	2.6	2.4	2.1	4.5	57
	4003		0.43	2.9	2.5	2.6	5.1	55
	4004		0.43	2.6	2.0	2.0	4.0	57
	4005		0.46	2.8	2.5	2.1	4.6	61
	4006		0.42	2.9	2.1	2.1	4.2	52
	4007		0.46	2.4	2.5	2.2	4.6	55
	Mean		0.44	2.7	2.3	2.2	4.6	58
	S.D.		0.02	0.2	0.2	0.2	0.4	6

Appendix 8-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	1.53	18.08	0.84	1.75	1.95	3.70
	4002	1.34	16.41	0.67	1.68	1.68	3.36
	4003	1.49	19.49	0.87	2.17	2.33	4.50
	4004	1.35	15.83	0.80	1.66	1.73	3.39
	4005	1.40	16.62	0.79	1.68	1.79	3.47
	4006	1.51	17.97	0.74	1.89	2.02	3.91
	4007	1.31	15.86	0.74	1.74	1.82	3.56
	Mean	1.42	17.18	0.78	1.80	1.90	3.70
	S.D.	0.09	1.37	0.07	0.18	0.22	0.40
Relative	4001	0.30	3.60	0.17	0.35	0.39	0.74
	4002	0.30	3.65	0.15	0.37	0.37	0.75
	4003	0.29	3.74	0.17	0.42	0.45	0.86
	4004	0.28	3.28	0.17	0.34	0.36	0.70
	4005	0.29	3.49	0.17	0.35	0.38	0.73
	4006	0.29	3.47	0.14	0.36	0.39	0.75
	4007	0.27	3.32	0.16	0.36	0.38	0.75
	Mean	0.29	3.51	0.16	0.36	0.39	0.75
	S.D.	0.01	0.17	0.01	0.03	0.03	0.05

Appendix 8-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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)
	4001	35	35	70	1.43	1.42	2.85
	4002	29	30	59	1.50	1.41	2.91
	4003	43	40	83	1.79	1.77	3.56
	4004	29	30	59	1.61	1.53	3.14
Absolute	4005	30	33	63	1.43	1.49	2.92
	4006	25	28	53	1.66	1.63	3.29
	4007	27	27	54	1.57	1.56	3.13
	Mean	31	32	63	1.57	1.54	3.11
	S.D.	6	5	11	0.13	0.13	0.25
	4001	7	7	14	0.28	0.28	0.57
	4002	6	7	13	0.33	0.31	0.65
	4003	8	8	16	0.34	0.34	0.68
	4004	6	6	12	0.33	0.32	0.65
Relative	4005	6	7	13	0.30	0.31	0.61
	4006	5	5	10	0.32	0.31	0.64
	4007	6	6	11	0.33	0.33	0.66
	Mean	6	7	13	0.32	0.31	0.64
	S.D.	1	1	2	0.02	0.02	0.04

Appendix 8-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	676	664	1340	1.75	1.26
	4002	665	681	1346	1.86	1.18
	4003	704	735	1439	2.11	1.36
	4004	727	671	1398	1.99	1.73
	4005	667	663	1330	1.46	1.23
	4006	672	704	1376	1.66	1.21
	4007	695	632	1327	1.79	1.04
	Mean	687	679	1365	1.80	1.29
	S.D.	23	33	42	0.21	0.22
Relative	4001	135	132	267	0.35	0.25
	4002	148	152	300	0.41	0.26
	4003	135	141	276	0.40	0.26
	4004	151	139	289	0.41	0.36
	4005	140	139	279	0.31	0.26
	4006	130	136	266	0.32	0.23
	4007	146	132	278	0.38	0.22
	Mean	141	139	279	0.37	0.26
	S.D.	8	7	12	0.04	0.05

Appendix 8-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	299	2.02	19.0	6.4	3.8	10.2	85
	1102	308	1.93	20.1	9.7	6.5	16.2	133
	1103	299	2.01	20.2	8.0	6.7	14.7	134
	1104	312	1.99	20.6	10.6	8.9	19.5	202
	1105	299	1.86	19.2	6.7	6.1	12.8	143
	1106NP	340Z	1.91Z	16.9Z	6.4Z	7.4Z	13.8Z	411Z
	1107	335	2.01	20.4	6.7	4.7	11.4	212
	1108	366	2.02	21.1	11.7	8.2	19.9	148
	1109	286	1.98	16.4	11.1	10.1	21.2	115
	1110	305	2.02	20.3	8.7	7.6	16.3	253
	1111	330	2.11	16.5	7.6	8.6	16.2	333
	1112	313	1.99	18.7	10.4	9.3	19.7	128
	Mean	314	1.99	19.3	8.9	7.3	16.2	171
	S.D.	22	0.06	1.6	1.9	2.0	3.7	72
Relative	1101		0.68	6.4	2.1	1.3	3.4	28
	1102		0.63	6.5	3.1	2.1	5.3	43
	1103		0.67	6.8	2.7	2.2	4.9	45
	1104		0.64	6.6	3.4	2.9	6.3	65
	1105		0.62	6.4	2.2	2.0	4.3	48
	1106NP		0.56Z	5.0Z	1.9Z	2.2Z	4.1Z	121Z
	1107		0.60	6.1	2.0	1.4	3.4	63
	1108		0.55	5.8	3.2	2.2	5.4	40
	1109		0.69	5.7	3.9	3.5	7.4	40
	1110		0.66	6.7	2.9	2.5	5.3	83
	1111		0.64	5.0	2.3	2.6	4.9	101
	1112		0.64	6.0	3.3	3.0	6.3	41
	Mean		0.64	6.2	2.8	2.3	5.2	54
	S.D.		0.04	0.5	0.6	0.7	1.2	22

NP: Non-pregnant
Z: Data was excluded from statistical analysis.

Appendix 8-18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	0.92	10.46	0.69	0.98	0.96	1.94
	1102	0.96	9.65	0.64	0.89	0.88	1.77
	1103	0.94	10.12	0.57	0.79	0.80	1.59
	1104	1.17	10.19	0.67	1.21	1.09	2.30
	1105	1.04	10.04	0.63	0.89	0.88	1.77
	1106NP	1.04Z	10.19Z	0.60Z	1.02Z	0.96Z	1.98Z
	1107	0.97	10.83	0.65	1.25	1.21	2.46
	1108	1.09	11.62	0.79	1.06	1.00	2.06
	1109	0.96	9.54	0.55	1.27	1.20	2.47
	1110	0.88	9.34	0.60	1.02	0.97	1.99
	1111	1.12	11.46	0.74	1.29	1.25	2.54
	1112	1.03	10.61	0.66	1.17	1.12	2.29
	Mean	1.01	10.35	0.65	1.07	1.03	2.11
	S.D.	0.09	0.74	0.07	0.17	0.15	0.32
Relative	1101	0.31	3.50	0.23	0.33	0.32	0.65
	1102	0.31	3.13	0.21	0.29	0.29	0.57
	1103	0.31	3.38	0.19	0.26	0.27	0.53
	1104	0.38	3.27	0.21	0.39	0.35	0.74
	1105	0.35	3.36	0.21	0.30	0.29	0.59
	1106NP	0.31Z	3.00Z	0.18Z	0.30Z	0.28Z	0.58Z
	1107	0.29	3.23	0.19	0.37	0.36	0.73
	1108	0.30	3.17	0.22	0.29	0.27	0.56
	1109	0.34	3.34	0.19	0.44	0.42	0.86
	1110	0.29	3.06	0.20	0.33	0.32	0.65
	1111	0.34	3.47	0.22	0.39	0.38	0.77
	1112	0.33	3.39	0.21	0.37	0.36	0.73
	Mean	0.32	3.30	0.21	0.34	0.33	0.67
	S.D.	0.03	0.14	0.01	0.05	0.05	0.10

NP: Non-pregnant
Z: Data was excluded from statistical analysis.

Appendix 8-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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)
	1101	42	43	85	55.2	49.0	104.2	718
	1102	43	47	90	53.9	37.8	91.7	682
	1103	39	40	79	51.3	46.2	97.5	664
	1104	46	48	94	48.7	44.6	93.3	704
	1105	42	39	81	49.8	36.8	86.6	615
	1106NP	33Z	32Z	65Z	41.1Z	35.8Z	76.9Z	3640Z
	1107	31	44	75	50.9	50.4	101.3	787
Absolute	1108	45	50	95	59.8	55.4	115.2	615
	1109	40	42	82	48.1	49.6	97.7	903
	1110	34	37	71	46.3	42.0	88.3	709
	1111	39	41	80	47.4	43.2	90.6	691
	1112	33	40	73	44.9	58.9	103.8	869
	Mean	39	43	82	50.6	46.7	97.3	723
	S.D.	5	4	8	4.3	6.8	8.5	94
	1101	14	14	28	18.5	16.4	34.8	240
	1102	14	15	29	17.5	12.3	29.8	221
	1103	13	13	26	17.2	15.5	32.6	222
	1104	15	15	30	15.6	14.3	29.9	226
	1105	14	13	27	16.7	12.3	29.0	206
	1106NP	10Z	9Z	19Z	12.1Z	10.5Z	22.6Z	1071Z
	1107	9	13	22	15.2	15.0	30.2	235
Relative	1108	12	14	26	16.3	15.1	31.5	168
	1109	14	15	29	16.8	17.3	34.2	316
	1110	11	12	23	15.2	13.8	29.0	232
	1111	12	12	24	14.4	13.1	27.5	209
	1112	11	13	23	14.3	18.8	33.2	278
	Mean	13	14	26	16.2	14.9	31.1	232
	S.D.	2	1	3	1.3	2.0	2.4	38

NP: Non-pregnant
Z: Data was excluded from statistical analysis.

Appendix 8-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	355	2.00	19.1	8.2	7.5	15.7	267
	2102	302	1.85	14.9	10.7	8.6	19.3	183
	2103	350	2.02	18.7	8.8	7.9	16.7	173
	2104	359	2.07	18.5	12.2	9.0	21.2	186
	2105	296	1.92	16.0	4.9	6.5	11.4	275
	2106	304	1.91	16.0	7.1	7.8	14.9	182
	2107	309	2.04	27.0	9.9	8.2	18.1	104
	2108	342	1.98	16.9	11.1	9.0	20.1	307
	2109	330	1.98	21.2	10.8	9.4	20.2	192
	2110	331	1.96	13.8	11.5	9.9	21.4	219
	2111	309	2.03	17.3	8.9	7.5	16.4	213
	2112	314	1.95	15.4	8.9	7.1	16.0	246
	Mean	325	1.98	17.9	9.4	8.2	17.6	212
	S.D.	22	0.06	3.5	2.1	1.0	3.0	55
Relative	2101		0.56	5.4	2.3	2.1	4.4	75
	2102		0.61	4.9	3.5	2.8	6.4	61
	2103		0.58	5.3	2.5	2.3	4.8	49
	2104		0.58	5.2	3.4	2.5	5.9	52
	2105		0.65	5.4	1.7	2.2	3.9	93
	2106		0.63	5.3	2.3	2.6	4.9	60
	2107		0.66	8.7	3.2	2.7	5.9	34
	2108		0.58	4.9	3.2	2.6	5.9	90
	2109		0.60	6.4	3.3	2.8	6.1	58
	2110		0.59	4.2	3.5	3.0	6.5	66
	2111		0.66	5.6	2.9	2.4	5.3	69
	2112		0.62	4.9	2.8	2.3	5.1	78
	Mean		0.61	5.5	2.9	2.5	5.4	65
	S.D.		0.03	1.1	0.6	0.3	0.8	17

Appendix 8-21 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	1.02	12.15	0.59	1.07	1.05	2.12
	2102	0.91	10.77	0.68	1.01	0.96	1.97
	2103	1.06	11.16	0.81	1.15	1.08	2.23
	2104	1.10	11.46	1.03	1.08	1.09	2.17
	2105	1.15	10.63	0.66	1.09	1.14	2.23
	2106	0.88	8.98	0.57	0.86	0.88	1.74
	2107	0.91	10.81	0.59	0.98	0.95	1.93
	2108	1.00	11.48	1.02	1.19	1.20	2.39
	2109	1.02	10.56	0.70	1.10	1.10	2.20
	2110	1.07	11.46	0.69	1.15	1.11	2.26
	2111	0.92	10.24	0.85	0.92	0.93	1.85
	2112	1.01	11.99	0.70	1.10	1.14	2.24
	Mean	1.00	10.97	0.74	1.06	1.05	2.11
	S.D.	0.08	0.86	0.16	0.10	0.10	0.19
Relative	2101	0.29	3.42	0.17	0.30	0.30	0.60
	2102	0.30	3.57	0.23	0.33	0.32	0.65
	2103	0.30	3.19	0.23	0.33	0.31	0.64
	2104	0.31	3.19	0.29	0.30	0.30	0.60
	2105	0.39	3.59	0.22	0.37	0.39	0.75
	2106	0.29	2.95	0.19	0.28	0.29	0.57
	2107	0.29	3.50	0.19	0.32	0.31	0.62
	2108	0.29	3.36	0.30	0.35	0.35	0.70
	2109	0.31	3.20	0.21	0.33	0.33	0.67
	2110	0.32	3.46	0.21	0.35	0.34	0.68
	2111	0.30	3.31	0.28	0.30	0.30	0.60
	2112	0.32	3.82	0.22	0.35	0.36	0.71
	Mean	0.31	3.38	0.23	0.33	0.33	0.65
	S.D.	0.03	0.23	0.04	0.03	0.03	0.05

Appendix 8-22 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	52	98	60.0	45.3	105.3	619
	2102	31	34	65	49.6	43.4	93.0	787
	2103	44	44	88	65.0	57.9	122.9	740
	2104	45	47	92	68.2	71.5	139.7	827
	2105	39	45	84	63.2	63.7	126.9	752
	2106	38	40	78	55.3	42.3	97.6	594
	2107	38	41	79	40.2	41.4	81.6	726
	2108	38	40	78	66.3	56.1	122.4	637
	2109	49	48	97	69.9	53.7	123.6	787
	2110	38	44	82	52.5	46.4	98.9	593
	2111	54	46	100	33.2	52.1	85.3	774
	2112	40	44	84	50.6	48.1	98.7	847
	Mean	42	44	85	56.2	51.8	108.0	724
	S.D.	6	5	10	11.5	9.3	18.5	90
Relative	2101	13	15	28	16.9	12.8	29.7	174
	2102	10	11	22	16.4	14.4	30.8	261
	2103	13	13	25	18.6	16.5	35.1	211
	2104	13	13	26	19.0	19.9	38.9	230
	2105	13	15	28	21.4	21.5	42.9	254
	2106	13	13	26	18.2	13.9	32.1	195
	2107	12	13	26	13.0	13.4	26.4	235
	2108	11	12	23	19.4	16.4	35.8	186
	2109	15	15	29	21.2	16.3	37.5	238
	2110	11	13	25	15.9	14.0	29.9	179
	2111	17	15	32	10.7	16.9	27.6	250
	2112	13	14	27	16.1	15.3	31.4	270
	Mean	13	14	26	17.2	15.9	33.2	224
	S.D.	2	1	3	3.1	2.6	4.9	34

Appendix 8-23 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	283	2.02	19.3	9.3	6.8	16.1	143
	3102	323	2.08	20.5	9.1	7.3	16.4	160
	3103	310	2.07	18.4	10.3	9.1	19.4	129
	3104	350	1.96	19.7	11.9	5.7	17.6	235
	3105	303	2.05	17.7	5.4	7.9	13.3	149
	3106	292	1.95	15.8	9.5	9.8	19.3	95
	3107	294	1.96	15.8	8.5	7.4	15.9	274
	3108	292	1.89	17.9	8.4	5.5	13.9	267
	3109	357	2.03	18.4	6.5	8.3	14.8	143
	3110	298	1.95	17.4	8.0	5.7	13.7	154
	3111	338	2.13	19.2	7.0	7.7	14.7	181
	3112	327	2.07	19.0	6.1	6.7	12.8	153
	Mean	314	2.01	18.3	8.3	7.3	15.7	174
	S.D.	25	0.07	1.4	1.9	1.3	2.2	56
Relative	3101		0.71	6.8	3.3	2.4	5.7	51
	3102		0.64	6.3	2.8	2.3	5.1	50
	3103		0.67	5.9	3.3	2.9	6.3	42
	3104		0.56	5.6	3.4	1.6	5.0	67
	3105		0.68	5.8	1.8	2.6	4.4	49
	3106		0.67	5.4	3.3	3.4	6.6	33
	3107		0.67	5.4	2.9	2.5	5.4	93
	3108		0.65	6.1	2.9	1.9	4.8	91
	3109		0.57	5.2	1.8	2.3	4.1	40
	3110		0.65	5.8	2.7	1.9	4.6	52
	3111		0.63	5.7	2.1	2.3	4.3	54
	3112		0.63	5.8	1.9	2.0	3.9	47
	Mean		0.64	5.8	2.7	2.3	5.0	56
	S.D.		0.04	0.4	0.6	0.5	0.9	19

Appendix 8-24 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	0.99	10.47	0.66	1.15	1.06	2.21
	3102	1.05	11.89	0.76	1.02	1.05	2.07
	3103	0.94	11.62	0.73	1.07	0.96	2.03
	3104	1.20	13.61	0.89	1.18	1.27	2.45
	3105	0.99	11.29	0.72	1.07	1.05	2.12
	3106	0.91	12.34	0.60	1.11	1.05	2.16
	3107	1.06	10.92	0.67	1.07	1.09	2.16
	3108	1.05	11.37	0.80	1.12	1.08	2.20
	3109	1.10	13.00	0.64	1.24	1.22	2.46
	3110	0.94	9.99	0.60	1.15	1.09	2.24
	3111	1.07	11.87	0.76	1.23	1.19	2.42
	3112	0.98	11.95	0.78	1.09	1.15	2.24
	Mean	1.02	11.69	0.72	1.13	1.11	2.23
	S.D.	0.08	1.01	0.09	0.07	0.09	0.14
Relative	3101	0.35	3.70	0.23	0.41	0.37	0.78
	3102	0.33	3.68	0.24	0.32	0.33	0.64
	3103	0.30	3.75	0.24	0.35	0.31	0.65
	3104	0.34	3.89	0.25	0.34	0.36	0.70
	3105	0.33	3.73	0.24	0.35	0.35	0.70
	3106	0.31	4.23	0.21	0.38	0.36	0.74
	3107	0.36	3.71	0.23	0.36	0.37	0.73
	3108	0.36	3.89	0.27	0.38	0.37	0.75
	3109	0.31	3.64	0.18	0.35	0.34	0.69
	3110	0.32	3.35	0.20	0.39	0.37	0.75
	3111	0.32	3.51	0.22	0.36	0.35	0.72
	3112	0.30	3.65	0.24	0.33	0.35	0.69
	Mean	0.33	3.73	0.23	0.36	0.35	0.71
	S.D.	0.02	0.22	0.02	0.03	0.02	0.04

Appendix 8-25 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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)
	3101	42	48	90	42.0	63.7	105.7	619
	3102	40	41	81	48.3	58.7	107.0	787
	3103	42	45	87	68.5	50.9	119.4	592
	3104	47	54	101	71.7	54.8	126.5	588
	3105	32	37	69	57.5	54.0	111.5	760
	3106	41	42	83	46.4	40.2	86.6	530
	3107	48	55	103	68.2	47.2	115.4	666
Absolute	3108	37	42	79	53.8	45.9	99.7	683
	3109	41	44	85	62.9	63.9	126.8	770
	3110	42	46	88	58.1	54.3	112.4	522
	3111	37	38	75	61.8	43.9	105.7	807
	3112	33	35	68	48.9	58.1	107.0	818
	Mean	40	44	84	57.3	53.0	110.3	679
	S.D.	5	6	11	9.6	7.6	11.2	108
	3101	15	17	32	14.8	22.5	37.3	219
	3102	12	13	25	15.0	18.2	33.1	244
	3103	14	15	28	22.1	16.4	38.5	191
	3104	13	15	29	20.5	15.7	36.1	168
	3105	11	12	23	19.0	17.8	36.8	251
	3106	14	14	28	15.9	13.8	29.7	182
	3107	16	19	35	23.2	16.1	39.3	227
Relative	3108	13	14	27	18.4	15.7	34.1	234
	3109	11	12	24	17.6	17.9	35.5	216
	3110	14	15	30	19.5	18.2	37.7	175
	3111	11	11	22	18.3	13.0	31.3	239
	3112	10	11	21	15.0	17.8	32.7	250
	Mean	13	14	27	18.3	16.9	35.2	216
	S.D.	2	2	4	2.8	2.4	3.0	30

Appendix 8-26 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	296	1.99	14.5	8.8	6.7	15.5	115
	4102NP	274Z	2.06Z	17.1Z	8.5Z	7.7Z	16.2Z	205Z
	4103	314	1.95	17.1	11.9	8.8	20.7	245
	4104	301	1.98	15.2	10.9	7.1	18.0	199
	4105	287	1.83	16.3	8.3	6.9	15.2	114
	4106	318	2.13	20.5	9.6	10.8	20.4	118
	4107	297	2.04	20.4	13.6	11.0	24.6	128
	4108	323	1.92	20.3	11.7	11.6	23.3	120
	4109	285	2.11	14.5	10.5	7.4	17.9	97
	4110	299	1.98	17.3	12.6	10.9	23.5	82
	4111	308	1.98	14.8	7.8	6.5	14.3	132
	4112NP	302Z	2.02Z	19.5Z	13.0Z	6.3Z	19.3Z	310Z
	Mean	303	1.99	17.1	10.6	8.8	19.3	135
	S.D.	13	0.09	2.5	1.9	2.1	3.7	49
Relative	4101		0.67	4.9	3.0	2.3	5.2	39
	4102NP		0.75Z	6.2Z	3.1Z	2.8Z	5.9Z	75Z
	4103		0.62	5.4	3.8	2.8	6.6	78
	4104		0.66	5.0	3.6	2.4	6.0	66
	4105		0.64	5.7	2.9	2.4	5.3	40
	4106		0.67	6.4	3.0	3.4	6.4	37
	4107		0.69	6.9	4.6	3.7	8.3	43
	4108		0.59	6.3	3.6	3.6	7.2	37
	4109		0.74	5.1	3.7	2.6	6.3	34
	4110		0.66	5.8	4.2	3.6	7.9	27
	4111		0.64	4.8	2.5	2.1	4.6	43
	4112NP		0.67Z	6.5Z	4.3Z	2.1Z	6.4Z	103Z
	Mean		0.66	5.6	3.5	2.9	6.4	44
	S.D.		0.04	0.7	0.6	0.6	1.2	16

NP: Non-pregnant
Z: Data was excluded from statistical analysis.

Appendix 8-27 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	0.95	13.55	0.60	1.12	1.14	2.26
	4102NP	0.84Z	12.13Z	0.51Z	0.96Z	0.93Z	1.89Z
	4103	1.06	15.21	0.66	1.31	1.28	2.59
	4104	0.96	12.76	0.57	1.01	1.04	2.05
	4105	0.86	12.96	0.59	1.09	1.09	2.18
	4106	1.01	13.43	0.68	1.16	1.12	2.28
	4107	0.94	14.27	0.72	1.24	1.21	2.45
	4108	1.04	14.09	0.65	1.17	1.16	2.33
	4109	1.07	13.10	0.72	1.43	1.32	2.75
	4110	0.96	13.58	0.56	1.14	1.15	2.29
	4111	0.94	13.69	0.57	1.12	1.15	2.27
	4112NP	0.91Z	13.63Z	0.59Z	1.01Z	1.03Z	2.04Z
	Mean	0.98	13.66	0.63	1.18	1.17	2.35
	S.D.	0.07	0.72	0.06	0.12	0.08	0.20
Relative	4101	0.32	4.58	0.20	0.38	0.39	0.76
	4102NP	0.31Z	4.43Z	0.19Z	0.35Z	0.34Z	0.69Z
	4103	0.34	4.84	0.21	0.42	0.41	0.82
	4104	0.32	4.24	0.19	0.34	0.35	0.68
	4105	0.30	4.52	0.21	0.38	0.38	0.76
	4106	0.32	4.22	0.21	0.36	0.35	0.72
	4107	0.32	4.80	0.24	0.42	0.41	0.82
	4108	0.32	4.36	0.20	0.36	0.36	0.72
	4109	0.38	4.60	0.25	0.50	0.46	0.96
	4110	0.32	4.54	0.19	0.38	0.38	0.77
	4111	0.31	4.44	0.19	0.36	0.37	0.74
	4112NP	0.30Z	4.51Z	0.20Z	0.33Z	0.34Z	0.68Z
	Mean	0.33	4.51	0.21	0.39	0.39	0.78
	S.D.	0.02	0.21	0.02	0.05	0.03	0.08

NP: Non-pregnant
Z: Data was excluded from statistical analysis.

Appendix 8-28 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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)
	4101	34	37	71	51.6	44.5	96.1	494
	4102NP	44Z	49Z	93Z	50.0Z	49.0Z	99.0Z	956Z
	4103	43	39	82	49.8	54.1	103.9	721
	4104	39	39	78	47.5	37.5	85.0	537
	4105	50	47	97	46.6	56.1	102.7	580
	4106	43	45	88	48.7	54.7	103.4	709
	4107	46	51	97	45.3	64.4	109.7	524
Absolute	4108	51	47	98	56.7	58.1	114.8	625
	4109	41	47	88	82.1	44.7	126.8	709
	4110	41	48	89	49.9	66.6	116.5	463
	4111	29	33	62	59.8	33.3	93.1	764
	4112NP	33Z	35Z	68Z	54.7Z	44.1Z	98.8Z	620Z
	Mean	42	43	85	53.8	51.4	105.2	613
	S.D.	7	6	12	10.9	11.0	12.3	108
	4101	11	13	24	17.4	15.0	32.5	167
	4102NP	16Z	18Z	34Z	18.2Z	17.9Z	36.1Z	349Z
	4103	14	12	26	15.9	17.2	33.1	230
	4104	13	13	26	15.8	12.5	28.2	178
	4105	17	16	34	16.2	19.5	35.8	202
	4106	14	14	28	15.3	17.2	32.5	223
	4107	15	17	33	15.3	21.7	36.9	176
Relative	4108	16	15	30	17.6	18.0	35.5	193
	4109	14	16	31	28.8	15.7	44.5	249
	4110	14	16	30	16.7	22.3	39.0	155
	4111	9	11	20	19.4	10.8	30.2	248
	4112NP	11Z	12Z	23Z	18.1Z	14.6Z	32.7Z	205Z
	Mean	14	14	28	17.8	17.0	34.8	202
	S.D.	2	2	4	4.1	3.7	4.7	34

NP: Non-pregnant
Z: Data was excluded from statistical analysis.

Appendix 8-29 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	290	1.96	15.7	6.8	7.6	14.4	275
	1114	282	1.93	15.4	9.5	8.0	17.5	282
	1115	277	1.91	20.4	8.3	7.6	15.9	329
	1116	306	2.03	15.4	10.1	7.3	17.4	284
	1117	280	1.90	13.8	7.8	7.7	15.5	299
	Mean	287	1.95	16.1	8.5	7.6	16.1	294
	S.D.	12	0.05	2.5	1.3	0.3	1.3	22
Relative	1113		0.68	5.4	2.3	2.6	5.0	95
	1114		0.68	5.5	3.4	2.8	6.2	100
	1115		0.69	7.4	3.0	2.7	5.7	119
	1116		0.66	5.0	3.3	2.4	5.7	93
	1117		0.68	4.9	2.8	2.8	5.5	107
	Mean		0.68	5.6	3.0	2.7	5.6	103
	S.D.		0.01	1.0	0.4	0.2	0.4	11

Appendix 8-30 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	0.86	7.49	0.58	1.05	1.01	2.06
	1114	0.96	6.54	0.40	0.93	0.83	1.76
	1115	0.96	7.01	0.45	0.88	0.85	1.73
	1116	0.93	8.21	0.48	1.03	0.98	2.01
	1117	0.95	6.72	0.47	1.02	0.99	2.01
	Mean	0.93	7.19	0.48	0.98	0.93	1.91
	S.D.	0.04	0.67	0.07	0.07	0.08	0.16
Relative	1113	0.30	2.58	0.20	0.36	0.35	0.71
	1114	0.34	2.32	0.14	0.33	0.29	0.62
	1115	0.35	2.53	0.16	0.32	0.31	0.62
	1116	0.30	2.68	0.16	0.34	0.32	0.66
	1117	0.34	2.40	0.17	0.36	0.35	0.72
	Mean	0.33	2.50	0.17	0.34	0.32	0.67
	S.D.	0.02	0.14	0.02	0.02	0.03	0.05

Appendix 8-31 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	32	36	68	59.3	37.3	96.6	656
	1114	32	34	66	48.1	45.7	93.8	603
	1115	33	39	72	43.4	44.3	87.7	455
	1116	36	44	80	47.4	41.6	89.0	860
	1117	33	34	67	46.8	45.6	92.4	419
	Mean	33	37	71	49.0	42.9	91.9	599
	S.D.	2	4	6	6.0	3.5	3.6	176
Relative	1113	11	12	23	20.4	12.9	33.3	226
	1114	11	12	23	17.1	16.2	33.3	214
	1115	12	14	26	15.7	16.0	31.7	164
	1116	12	14	26	15.5	13.6	29.1	281
	1117	12	12	24	16.7	16.3	33.0	150
	Mean	12	13	24	17.1	15.0	32.1	207
	S.D.	1	1	2	2.0	1.6	1.8	52

Appendix 8-32 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	279	1.88	23.9	7.9	7.0	14.9	196
	4114	268	2.04	19.7	13.1	10.4	23.5	189
	4115	269	1.99	17.2	7.4	6.9	14.3	261
	4116	257	1.92	18.6	9.7	7.1	16.8	193
	4117	270	2.04	18.5	10.2	7.7	17.9	369
	Mean	269	1.97	19.6	9.7	7.8	17.5	242
	S.D.	8	0.07	2.6	2.3	1.5	3.7	77
Relative	4113		0.67	8.6	2.8	2.5	5.3	70
	4114		0.76	7.4	4.9	3.9	8.8	71
	4115		0.74	6.4	2.8	2.6	5.3	97
	4116		0.75	7.2	3.8	2.8	6.5	75
	4117		0.76	6.9	3.8	2.9	6.6	137
	Mean		0.74	7.3	3.6	2.9	6.5	90
	S.D.		0.04	0.8	0.9	0.6	1.4	28

Appendix 8-33 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	1.10	12.38	0.48	1.13	1.11	2.24
	4114	0.87	10.99	0.41	1.00	1.02	2.02
	4115	0.86	9.45	0.65	1.05	1.05	2.10
	4116	0.91	9.84	0.47	1.06	0.98	2.04
	4117	0.84	10.58	0.49	1.08	1.06	2.14
	Mean	0.92	10.65	0.50	1.06	1.04	2.11
	S.D.	0.11	1.14	0.09	0.05	0.05	0.09
Relative	4113	0.39	4.44	0.17	0.41	0.40	0.80
	4114	0.32	4.10	0.15	0.37	0.38	0.75
	4115	0.32	3.51	0.24	0.39	0.39	0.78
	4116	0.35	3.83	0.18	0.41	0.38	0.79
	4117	0.31	3.92	0.18	0.40	0.39	0.79
	Mean	0.34	3.96	0.18	0.40	0.39	0.78
	S.D.	0.03	0.34	0.03	0.02	0.01	0.02

Appendix 8-34 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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)
	4113	39	44	83	441.8	25.4	467.2	781
	4114	43	40	83	59.4	50.2	109.6	624
	4115	32	35	67	36.7	39.1	75.8	567
Absolute	4116	37	36	73	19.1	20.1	39.2	754
	4117	34	34	68	42.5	39.4	81.9	860
	Mean	37	38	75	119.9	34.8	154.7	717
	S.D.	4	4	8	180.5	12.1	176.5	119
	4113	14	16	30	158.4	9.1	167.5	280
	4114	16	15	31	22.2	18.7	40.9	233
	4115	12	13	25	13.6	14.5	28.2	211
Relative	4116	14	14	28	7.4	7.8	15.3	293
	4117	13	13	25	15.7	14.6	30.3	319
	Mean	14	14	28	43.5	12.9	56.4	267
	S.D.	1	1	3	64.5	4.5	62.7	44

Appendix 8-35 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	512	2.07	16.1	12.6	14.7	27.3	309
	1009	535	2.25	12.0	8.4	10.1	18.5	211
	1010	574	2.22	14.0	14.5	14.1	28.6	215
	1011	529	2.21	14.4	11.3	12.0	23.3	307
	1012	507	2.14	14.4	11.7	11.0	22.7	192
	Mean	531	2.18	14.2	11.7	12.4	24.1	247
	S.D.	26	0.07	1.5	2.2	2.0	4.0	57
Relative	1008		0.40	3.1	2.5	2.9	5.3	60
	1009		0.42	2.2	1.6	1.9	3.5	39
	1010		0.39	2.4	2.5	2.5	5.0	37
	1011		0.42	2.7	2.1	2.3	4.4	58
	1012		0.42	2.8	2.3	2.2	4.5	38
	Mean		0.41	2.6	2.2	2.4	4.5	46
	S.D.		0.01	0.4	0.4	0.4	0.7	12

Appendix 8-36 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	2.03	13.56	1.01	1.73	1.78	3.51
	1009	1.55	13.12	0.78	1.75	1.84	3.59
	1010	1.49	15.71	0.90	1.88	1.95	3.83
	1011	1.54	13.70	0.94	1.94	1.91	3.85
	1012	1.47	12.02	0.61	1.63	1.67	3.30
	Mean	1.62	13.62	0.85	1.79	1.83	3.62
	S.D.	0.23	1.34	0.16	0.12	0.11	0.23
Relative	1008	0.40	2.65	0.20	0.34	0.35	0.69
	1009	0.29	2.45	0.15	0.33	0.34	0.67
	1010	0.26	2.74	0.16	0.33	0.34	0.67
	1011	0.29	2.59	0.18	0.37	0.36	0.73
	1012	0.29	2.37	0.12	0.32	0.33	0.65
	Mean	0.31	2.56	0.16	0.34	0.34	0.68
	S.D.	0.05	0.15	0.03	0.02	0.01	0.03

Appendix 8-37 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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)
	1008	37	36	73	1.80	1.83	3.63
	1009	30	30	60	1.48	1.46	2.94
	1010	34	34	68	1.58	1.54	3.12
Absolute	1011	23	26	49	1.49	1.46	2.95
	1012	30	26	56	1.80	1.82	3.62
	Mean	31	30	61	1.63	1.62	3.25
	S.D.	5	5	10	0.16	0.19	0.35
	1008	7	7	14	0.35	0.36	0.71
	1009	6	6	11	0.28	0.27	0.55
	1010	6	6	12	0.28	0.27	0.54
Relative	1011	4	5	9	0.28	0.28	0.56
	1012	6	5	11	0.36	0.36	0.71
	Mean	6	6	11	0.31	0.31	0.61
	S.D.	1	1	2	0.04	0.05	0.09

Appendix 8-38 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	617	586	1203	1.50	1.47
	1009	643	628	1271	2.13	1.55
	1010	712	704	1416	2.40	1.67
	1011	680	650	1330	2.03	1.31
	1012	707	688	1395	2.24	1.53
	Mean	672	651	1323	2.06	1.51
	S.D.	41	47	88	0.34	0.13
Relative	1008	121	114	235	0.29	0.29
	1009	120	117	238	0.40	0.29
	1010	124	123	247	0.42	0.29
	1011	129	123	251	0.38	0.25
	1012	139	136	275	0.44	0.30
	Mean	127	123	249	0.39	0.28
	S.D.	8	8	16	0.06	0.02

Appendix 8-39 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	536	2.27	15.3	12.0	13.6	25.6	246
	4009	524	2.17	13.4	13.6	9.4	23.0	214
	4010	594	2.23	14.5	14.2	13.8	28.0	358
	4011	561	2.14	14.4	15.0	16.2	31.2	344
	4012	452	2.17	12.4	13.1	8.7	21.8	168
	Mean	533	2.20	14.0	13.6	12.3	25.9	266
	S.D.	53	0.05	1.1	1.1	3.2	3.8	83
Relative	4008		0.42	2.9	2.2	2.5	4.8	46
	4009		0.41	2.6	2.6	1.8	4.4	41
	4010		0.38	2.4	2.4	2.3	4.7	60
	4011		0.38	2.6	2.7	2.9	5.6	61
	4012		0.48	2.7	2.9	1.9	4.8	37
	Mean		0.41	2.6	2.6	2.3	4.9	49
	S.D.		0.04	0.2	0.3	0.4	0.4	11

Appendix 8-40 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	1.52	13.96	0.85	1.83	1.75	3.58
	4009	1.53	16.94	0.88	1.81	1.74	3.55
	4010	1.88	15.99	1.06	2.06	2.05	4.11
	4011	1.63	16.22	0.90	1.64	1.64	3.28
	4012	1.33	12.44	0.76	1.72	1.65	3.37
	Mean	1.58	15.11	0.89	1.81	1.77	3.58
	S.D.	0.20	1.86	0.11	0.16	0.17	0.32
Relative	4008	0.28	2.60	0.16	0.34	0.33	0.67
	4009	0.29	3.23	0.17	0.35	0.33	0.68
	4010	0.32	2.69	0.18	0.35	0.35	0.69
	4011	0.29	2.89	0.16	0.29	0.29	0.58
	4012	0.29	2.75	0.17	0.38	0.37	0.75
	Mean	0.29	2.83	0.17	0.34	0.33	0.67
	S.D.	0.02	0.25	0.01	0.03	0.03	0.06

Appendix 8-41 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	36	37	73	1.75	1.71	3.46
	4009	35	35	70	1.64	1.64	3.28
	4010	29	33	62	2.17	2.13	4.30
	4011	31	30	61	1.69	1.67	3.36
	4012	32	32	64	1.78	1.77	3.55
	Mean	33	33	66	1.81	1.78	3.59
	S.D.	3	3	5	0.21	0.20	0.41
Relative	4008	7	7	14	0.33	0.32	0.65
	4009	7	7	13	0.31	0.31	0.63
	4010	5	6	10	0.37	0.36	0.72
	4011	6	5	11	0.30	0.30	0.60
	4012	7	7	14	0.39	0.39	0.79
	Mean	6	6	12	0.34	0.34	0.68
	S.D.	1	1	2	0.04	0.04	0.08

Appendix 8-42 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	854	831	1685	2.97	1.75
	4009	715	686	1401	1.78	1.35
	4010	635	633	1268	1.93	1.88
	4011	674	649	1323	1.58	1.12
	4012	573	524	1097	1.98	1.42
	Mean	690	665	1355	2.05	1.50
	S.D.	105	111	216	0.54	0.31
Relative	4008	159	155	314	0.55	0.33
	4009	136	131	267	0.34	0.26
	4010	107	107	213	0.32	0.32
	4011	120	116	236	0.28	0.20
	4012	127	116	243	0.44	0.31
	Mean	130	125	255	0.39	0.28
	S.D.	19	19	38	0.11	0.05

Appendix 8-43 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	303	2.05	19.5	6.9	6.1	13.0	335
	1119	279	1.99	14.9	8.0	10.1	18.1	314
	1120	287	1.84	14.9	7.4	6.2	13.6	350
	1121	305	2.01	18.5	8.0	7.5	15.5	241
	1122	277	1.89	16.2	11.6	10.7	22.3	242
	Mean	290	1.96	16.8	8.4	8.1	16.5	296
	S.D.	13	0.09	2.1	1.9	2.2	3.8	52
Relative	1118		0.68	6.4	2.3	2.0	4.3	111
	1119		0.71	5.3	2.9	3.6	6.5	113
	1120		0.64	5.2	2.6	2.2	4.7	122
	1121		0.66	6.1	2.6	2.5	5.1	79
	1122		0.68	5.8	4.2	3.9	8.1	87
	Mean		0.67	5.8	2.9	2.8	5.7	102
	S.D.		0.03	0.5	0.7	0.9	1.6	18

Appendix 8-44 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	0.94	7.17	0.57	1.08	1.08	2.16
	1119	0.84	6.63	0.49	0.89	0.87	1.76
	1120	0.97	7.59	0.61	1.02	1.01	2.03
	1121	0.93	7.77	0.50	0.92	0.94	1.86
	1122	0.91	7.22	0.54	0.84	0.84	1.68
	Mean	0.92	7.28	0.54	0.95	0.95	1.90
	S.D.	0.05	0.44	0.05	0.10	0.10	0.20
Relative	1118	0.31	2.37	0.19	0.36	0.36	0.71
	1119	0.30	2.38	0.18	0.32	0.31	0.63
	1120	0.34	2.64	0.21	0.36	0.35	0.71
	1121	0.30	2.55	0.16	0.30	0.31	0.61
	1122	0.33	2.61	0.19	0.30	0.30	0.61
	Mean	0.32	2.51	0.19	0.33	0.33	0.65
	S.D.	0.02	0.13	0.02	0.03	0.03	0.05

Appendix 8-45 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	44	41	85	38.2	30.3	68.5	434
	1119	34	32	66	42.0	40.8	82.8	585
	1120	32	33	65	52.4	32.7	85.1	872
	1121	34	36	70	45.9	34.4	80.3	428
	1122	49	48	97	36.6	43.3	79.9	591
	Mean	39	38	77	43.0	36.3	79.3	582
	S.D.	7	7	14	6.4	5.5	6.4	180
Relative	1118	15	14	28	12.6	10.0	22.6	143
	1119	12	11	24	15.1	14.6	29.7	210
	1120	11	11	23	18.3	11.4	29.7	304
	1121	11	12	23	15.0	11.3	26.3	140
	1122	18	17	35	13.2	15.6	28.8	213
	Mean	13	13	27	14.8	12.6	27.4	202
	S.D.	3	3	5	2.2	2.4	3.0	67

Appendix 8-46 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	278	1.98	20.3	7.8	6.8	14.6	246
	4119	270	1.97	13.0	6.9	8.0	14.9	396
	4120	273	1.92	18.4	9.2	8.8	18.0	284
	4121	304	2.02	18.5	11.2	11.4	22.6	337
	4122	300	2.02	18.4	7.9	6.1	14.0	190
	Mean	285	1.98	17.7	8.6	8.2	16.8	291
	S.D.	16	0.04	2.8	1.7	2.1	3.6	80
Relative	4118		0.71	7.3	2.8	2.4	5.3	88
	4119		0.73	4.8	2.6	3.0	5.5	147
	4120		0.70	6.7	3.4	3.2	6.6	104
	4121		0.66	6.1	3.7	3.8	7.4	111
	4122		0.67	6.1	2.6	2.0	4.7	63
	Mean		0.69	6.2	3.0	2.9	5.9	103
	S.D.		0.03	0.9	0.5	0.7	1.1	31

Appendix 8-47 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	0.89	8.16	0.56	1.06	1.10	2.16
	4119	0.92	7.56	0.53	0.92	0.89	1.81
	4120	0.86	7.53	0.46	0.91	0.90	1.81
	4121	1.04	9.39	0.60	1.02	1.01	2.03
	4122	1.10	8.28	0.57	1.03	1.07	2.10
	Mean	0.96	8.18	0.54	0.99	0.99	1.98
	S.D.	0.10	0.76	0.05	0.07	0.10	0.16
Relative	4118	0.32	2.94	0.20	0.38	0.40	0.78
	4119	0.34	2.80	0.20	0.34	0.33	0.67
	4120	0.32	2.76	0.17	0.33	0.33	0.66
	4121	0.34	3.09	0.20	0.34	0.33	0.67
	4122	0.37	2.76	0.19	0.34	0.36	0.70
	Mean	0.34	2.87	0.19	0.35	0.35	0.70
	S.D.	0.02	0.14	0.01	0.02	0.03	0.05

Appendix 8-48 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	38	45	83	47.7	48.7	96.4	476
	4119	31	31	62	41.3	45.4	86.7	768
	4120	35	38	73	37.3	37.9	75.2	418
	4121	43	43	86	37.2	44.4	81.6	557
	4122	36	38	74	48.8	50.6	99.4	512
	Mean	37	39	76	42.5	45.4	87.9	546
	S.D.	4	5	9	5.6	4.9	10.1	134
Relative	4118	14	16	30	17.2	17.5	34.7	171
	4119	11	11	23	15.3	16.8	32.1	284
	4120	13	14	27	13.7	13.9	27.5	153
	4121	14	14	28	12.2	14.6	26.8	183
	4122	12	13	25	16.3	16.9	33.1	171
	Mean	13	14	27	14.9	15.9	30.8	192
	S.D.	1	2	3	2.0	1.6	3.5	52

Appendix 9-1(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Parathyroid, Pancreas, Pituitary, Prostate, Salivary gland,submandibular
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral
Seminal vesicle(coagulating gland), Spinal cord,thoracic, Testis, Thymus, Trachea
Thyroid, Urinary bladder

Appendix 9-2(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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

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, Spleen, Stomach
Skeletal muscle,femoral, Seminal vesicle(coagulating 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 Methyl(2-pentyl-3-oxocyclopentyl) 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
Liver	Microgranuloma: minimal
Lung(bronchus)	Aggregation,alveolar macrophage: minimal
Pituitary	Cyst,pars distalis: 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, Parathyroid, Pancreas, Prostate
Salivary gland,submandibular, Sciatic nerve, Spleen, Stomach
Skeletal muscle,femoral, Seminal vesicle(coagulating gland), Spinal cord,thoracic
Testis, Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-4(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Intestine,cecum	Cell infiltration: minimal, lymphocytic
Liver	Microgranuloma: minimal
Prostate	Cell infiltration: minimal, inflammatory ventral
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Sciatic nerve, Stomach, Skeletal muscle,femoral
Seminal vesicle(coagulating gland), Spinal cord,thoracic, Testis, Thymus, Trachea
Thyroid, Urinary bladder

Appendix 9-5(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Kidney	Regeneration,tubular: minimal with hyaline cast
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(coagulating 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 Methyl(2-pentyl-3-oxocyclopentyl) 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:

Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal
Prostate	Cell infiltration: minimal, inflammatory ventral
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Sciatic nerve, Stomach, Skeletal muscle,femoral
Seminal vesicle(coagulating gland), Spinal cord,thoracic, Testis, Thymus, Trachea
Thyroid, Urinary bladder

Appendix 9-7(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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:

Lung(bronchus)	Focus,dark red: 2 present 1x1mm
Other tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Lung(bronchus)	Hemorrhage,focal: minimal alveolar,with hematoidin crystal,inflammatory cell infiltration

Appendix 9-9(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Liver	Microgranuloma: minimal

Appendix 9-10(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Liver	Microgranuloma: minimal

Appendix 9-11(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Following tissues : Not remarkable

Liver

Appendix 9-12(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Stomach	Focus,dark red,glandular stomach: 1 present less than 1x1mm
Other tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Stomach	Erosion,glandular stomach: minimal

Appendix 9-13(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Appendix 9-14(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Liver	Microgranuloma: minimal

Appendix 9-15(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Appendix 9-16(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Lung(bronchus)	Focus,dark red: 1 present 1x1mm
Other tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Appendix 9-17(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Liver	Microgranuloma: minimal

Appendix 9-18(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

All 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 Methyl(2-pentyl-3-oxocyclopentyl) 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:

All 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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:

Liver	Microgranuloma: minimal

Appendix 9-26(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: minimal

Appendix 9-27(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Following tissues : Not remarkable

Liver

Appendix 9-28(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Following tissues : Not remarkable

Liver

Appendix 9-29(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Following tissues : Not remarkable

Liver

Appendix 9-30(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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:

Heart	Cell infiltration: minimal, focal, mononuclear
Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: mild
Prostate	Cell infiltration: minimal, inflammatory ventral
Spleen	Hematopoiesis,extramedullary: mild

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(coagulating gland), Spinal cord,thoracic, Testis, Thymus, Trachea
Thyroid, Urinary bladder

Appendix 9-38(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

All tissues	Not remarkable

Histopathology:

Heart	Cell infiltration: minimal, focal, mononuclear
Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: mild
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(coagulating 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 Methyl(2-pentyl-3-oxocyclopentyl) 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
Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: mild
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(coagulating 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 Methyl(2-pentyl-3-oxocyclopentyl) 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:

Stomach	Focus,dark red,glandular stomach: 3 present 2present:1x1mm,1present:2x1mm
Other tissues	Not remarkable

Histopathology:

Eye	Atrophy,retinal: mild, focal
Liver	Hypertrophy,hepatocytic,centrilobular: mild
Stomach	Erosion,glandular stomach: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, 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, Prostate, Salivary gland,submandibular, Sciatic nerve
Spleen, Skeletal muscle,femoral, Seminal vesicle(coagulating gland)
Spinal cord,thoracic, Testis, Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-41(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: mild
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(coagulating 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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:

Stomach	Focus,dark red,glandular stomach: 1 present 1x1mm
Other tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Stomach	Erosion,glandular stomach: minimal

Appendix 9-45(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Following tissues : Not remarkable

Liver

Appendix 9-46(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Liver	Microgranuloma: minimal

Appendix 9-47(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Intestine,ileum(Peyer's patch)	Diverticulum: 1 present 2x2x10mm,about 32cm above the cecum
Other tissues	Not remarkable

Histopathology:

Intestine,ileum(Peyer's patch)	Diverticulum: mild
Liver	Microgranuloma: minimal

Appendix 9-48(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Stomach	Focus,dark red,glandular stomach: 1 present 3x1mm
Other tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: minimal
Prostate	Cell infiltration: minimal, inflammatory ventral and dorsolateral
Stomach	Erosion,glandular stomach: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Parathyroid
Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve, Spleen
Skeletal muscle,femoral, Seminal vesicle(coagulating gland), Spinal cord,thoracic
Testis, Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-49(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Kidney	Regeneration,tubular: minimal with mononuclear cell infiltration
Liver	Microgranuloma: minimal
Spleen	Hematopoiesis,extramedullary: mild
Thymus	Atrophy: 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, Trachea, Thyroid, Urinary bladder
Uterus, Vagina

Appendix 9-50(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Stomach	Focus,dark red,glandular stomach: 2 present 1x1mm,3x1mm
Other tissues	Not remarkable

Histopathology:

Spleen	Hematopoiesis,extramedullary: mild
Stomach	Erosion,glandular stomach: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-51(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1104 Female 0 mg/kg Day 44 End of administration period (L4)

Gross pathology:

Stomach	Focus,dark red,glandular stomach: 3 present 2present:1x1mm,1present:1x2mm
Other 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 Methyl(2-pentyl-3-oxocyclopentyl) 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	Regeneration,tubular: minimal
Lung(bronchus)	Aggregation,alveolar macrophage: mild
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, 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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1106 Female 0 mg/kg Day 41 Undelivered

Gross pathology:

Uterus	Dilatation,lumen: moderate watery content
Other tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Uterus	Dilatation,lumen: moderate, unilateral

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, Vagina

Appendix 9-55(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1107 Female 0 mg/kg Day 45 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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1108 Female 0 mg/kg Day 47 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-57(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1110 Female 0 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Spleen	Hematopoiesis,extramedullary: mild

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-59(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1111 Female 0 mg/kg Day 45 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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1112 Female 0 mg/kg Day 45 End of administration period (L4)

Gross pathology:

Intestine,ileum(Peyer's patch)	Diverticulum: 1 present 5x5x7mm,32cm above the cecum
Other 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 Methyl(2-pentyl-3-oxocyclopentyl) 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:

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 9-62(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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

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 9-63(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

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 9-64(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

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 9-65(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Ovary

Appendix 9-67(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Kidney, Ovary

Appendix 9-68(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Kidney, Ovary

Appendix 9-69(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Kidney, Ovary

Appendix 9-70(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Ovary

Appendix 9-71(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2101 Female 100 mg/kg Day 47 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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2102 Female 100 mg/kg Day 45 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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2103 Female 100 mg/kg Day 42 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Kidney, Ovary

Appendix 9-74(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2104 Female 100 mg/kg Day 46 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-75(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2105 Female 100 mg/kg Day 42 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Kidney, Liver, Ovary

Appendix 9-76(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2106 Female 100 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Kidney, Liver, Ovary

Appendix 9-77(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2107 Female 100 mg/kg Day 46 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-78(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2108 Female 100 mg/kg Day 45 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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2109 Female 100 mg/kg Day 46 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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2110 Female 100 mg/kg Day 44 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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2111 Female 100 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal

Following tissues : Not remarkable

Liver, Ovary

Appendix 9-82(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2112 Female 100 mg/kg Day 42 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Kidney, Ovary

Appendix 9-83(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3101 Female 300 mg/kg Day 44 End of administration period (L4)

Gross pathology:

Stomach	Focus,dark red,glandular stomach: 1 present 2x1mm
Other tissues	Not remarkable

Histopathology:

Following tissues : Not remarkable

Kidney, Liver, Ovary

Appendix 9-84(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: minimal

Following tissues : Not remarkable

Kidney, Ovary

Appendix 9-85(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3104 Female 300 mg/kg Day 46 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3106 Female 300 mg/kg Day 46 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) 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:

Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: mild

Following tissues : Not remarkable

Kidney, Ovary

Appendix 9-91(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3109 Female 300 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: minimal

Following tissues : Not remarkable

Ovary

Appendix 9-92(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Lung(bronchus)	Focus,dark red: 1 present 2x2mm
Other 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3112 Female 300 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Kidney, Ovary

Appendix 9-95(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4101 Female 1000 mg/kg Day 45 End of administration period (L4)

Gross pathology:

Kidney	Focus,white: 3 present right:2present,left:1present,1x1mm
Other tissues	Not remarkable

Histopathology:

Kidney	Dilatation,tubular,focal: minimal
Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: mild
Spleen	Hematopoiesis,extramedullary: mild

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Sciatic nerve, Stomach
Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-96(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4102 Female 1000 mg/kg Day 41 Undelivered

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 9-97(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4103 Female 1000 mg/kg Day 45 End of administration period (L4)

Gross pathology:

Kidney	Focus,white: 1 present, left 1x1mm
Other tissues	Not remarkable

Histopathology:

Kidney	Dilatation,tubular,focal: minimal Regeneration,tubular: minimal
Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: mild
Spleen	Hematopoiesis,extramedullary: mild

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Sciatic nerve, Stomach
Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-98(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Eye	Dysplasia,retinal: minimal
Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: mild
Spleen	Hematopoiesis,extramedullary: mild

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-99(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4105 Female 1000 mg/kg Day 46 End of administration period (L4)

Gross pathology:

All 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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4106 Female 1000 mg/kg Day 45 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal
Liver	Hypertrophy,hepatocytic,centrilobular: mild
Spleen	Hematopoiesis,extramedullary: mild

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Sciatic nerve, Stomach
Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-101(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4107 Female 1000 mg/kg Day 46 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4109 Female 1000 mg/kg Day 46 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-104(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: mild
Spleen	Hematopoiesis,extramedullary: mild

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-105(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4111 Female 1000 mg/kg Day 45 End of administration period (L4)

Gross pathology:

Kidney	Focus,white: 1 present, right 1x1mm
Other 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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4112 Female 1000 mg/kg Day 42 Undelivered

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 9-107(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Lung(bronchus)	Focus,dark red: 1 present 5x3mm
Ovary	Cyst,unilateral: 1 present, right 10x7x5mm
Other tissues	Not remarkable

Histopathology:

Liver	Hypertrophy,hepatocytic,centrilobular: mild
Lung(bronchus)	Hemorrhage,focal: minimal alveolar,with hematoidin crystal,inflammatory cell infiltration
Ovary	Atrophy: mild, unilateral Cyst,ovarian bursa: mild, unilateral

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, 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Hypertrophy,hepatocytic,centrilobular: mild

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Spleen, 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 Methyl(2-pentyl-3-oxocyclopentyl) 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:

Lung(bronchus)	Focus,dark red: 1 present 1x1mm
Other tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: mild
Lung(bronchus)	Cell infiltration: minimal, inflammatory

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, Spleen, 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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Hypertrophy,hepatocytic,centrilobular: minimal
Ovary	Atrophy: mild, bilateral

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), 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 Methyl(2-pentyl-3-oxocyclopentyl) 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:

Stomach	Focus,dark red,glandular stomach: 1 present 2x2mm
Other tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: minimal
Spleen	Hematopoiesis,extramedullary: minimal
Stomach	Erosion,glandular stomach: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-112(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Ovary

Appendix 9-113(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Stomach	Focus,dark red,glandular stomach: 1 present 1x1mm
Other tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Stomach	Erosion,glandular stomach: minimal

Following tissues : Not remarkable

Kidney, Ovary

Appendix 9-114(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Ovary

Appendix 9-115(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Stomach	Focus,dark red,glandular stomach: 2 present 1x3,1x2mm
Other tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Stomach	Erosion,glandular stomach: minimal

Following tissues : Not remarkable

Kidney, Ovary

Appendix 9-116(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Kidney, Ovary

Appendix 10-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
1102	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
1103	P	E	M	D	D	P	E	M	D	D	P	E	M	D	D	3	5.0	
1104	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
1105	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
1106	M	D	P	E	E	M	D	P	E	E	M	D	P	E	M	3	5.0	
1107	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
1108	M	D	P	E	E	M	D	P	E	E	M	D	P	E	E	3	5.0	
1109	E	M	D	P	E	M	D	P	E	E	M	D	P	E	M	4	4.3	
1110	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
1111	P	E	E	M	D	P	E	E	M	D	P	E	E	M	D	3	5.0	
1112	M	D	P	E	M	D	P	E	E	M	D	P	E	E	M	3	4.5	
Total(%)b)																		0/12(0.0)
Mean																3.4	4.4	
S.D.																0.5	0.5	

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 Methyl(2-pentyl-3-oxocyclopentyl) 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	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0	
2102	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
2103	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
2104	M	D	D	P	E	M	D	D	P	E	M	D	P	E	M	3	4.5	
2105	E	E	M	D	P	E	E	M	D	P	E	E	M	D	P	3	5.0	
2106	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
2107	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0	
2108	D	D	P	E	M	D	D	P	E	M	D	D	P	E	M	3	5.0	
2109	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0	
2110	M	D	P	E	M	D	D	P	E	M	D	P	E	M	D	3	4.5	
2111	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
2112	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																3.4	4.3	
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 Methyl(2-pentyl-3-oxocyclopentyl) 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	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
3102	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
3103	M	D	D	P	E	M	D	D	P	E	M	D	D	P	E	3	5.0	
3104	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0	
3105	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
3106	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0	
3107	E	M	D	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	E	M	D	D	P	E	M	D	D	P	E	M	D	D	P	3	5.0	
3110	P	E	M	D	D	P	E	M	D	D	P	E	M	D	D	3	5.0	
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																3.6	4.3	
S.D.																0.5	0.5	

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 Methyl(2-pentyl-3-oxocyclopentyl) 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 (%)
4101c)	E	M	D	P	E	M	D	D	D	D	D	D	D	D	D	2	4.0	
4102	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
4103	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
4104c)	E	M	D	D	P	E	E	M	D	D	P	E	M	D	D	3	5.5	
4105	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0	
4106	E	M	D	P	E	M	D	P	E	E	M	D	P	E	M	4	4.3	
4107	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
4108c)	M	D	P	E	M	D	D	P	E	E	M	D	D	P	E	3	5.5	
4109	E	M	D	P	E	E	M	D	P	E	M	D	P	E	M	4	4.3	
4110	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
4111	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0	
4112	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
Total(%)b)																		3/12(25.0)
Mean																3.6	4.3	
S.D.																0.7	0.6	

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
c): Abnormal estrous cycle

Appendix 11-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual mating and fertility of animals
Dose (mg/kg): 0

Pairing number Male	Female	Copulated or not copulated	Days until copulation	Pregnant or non-pregnant
1001	1101	C	3	P
1002	1102	C	2	P
1003	1103	C	2	P
1004	1104	C	2	P
1005	1105	C	1	P
1006	1106	C	1	NP
1007	1107	C	3	P
1008	1108	C	5	P
1009	1109	C	3	P
1010	1110	C	1	P
1011	1111	C	3	P
1012	1112	C	3	P

C: Copulated P: Pregnant NP: Non-pregnant

Appendix 11-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual mating and fertility of animals
Dose (mg/kg): 100

Pairing number Male	Female	Copulated or not copulated	Days until copulation	Pregnant or non-pregnant
2001	2101	C	4	P
2002	2102	C	3	P
2003	2103	C	1	P
2004	2104	C	4	P
2005	2105	C	1	P
2006	2106	C	2	P
2007	2107	C	4	P
2008	2108	C	3	P
2009	2109	C	4	P
2010	2110	C	2	P
2011	2111	C	1	P
2012	2112	C	1	P

C: Copulated P: Pregnant

Appendix 11-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual mating and fertility of animals
Dose (mg/kg): 300

Pairing number Male	Female	Copulated or not copulated	Days until copulation	Pregnant or non-pregnant
3001	3101	C	2	P
3002	3102	C	1	P
3003	3103	C	4	P
3004	3104	C	4	P
3005	3105	C	3	P
3006	3106	C	4	P
3007	3107	C	2	P
3008	3108	C	1	P
3009	3109	C	1	P
3010	3110	C	2	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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual mating and fertility of animals
Dose (mg/kg): 1000

Pairing number Male	Female	Copulated or not copulated	Days until copulation	Pregnant or non-pregnant
4001	4101	C	2	P
4002	4102	C	1	NP
4003	4103	C	3	P
4004	4104	C	2	P
4005	4105	C	4	P
4006	4106	C	3	P
4007	4107	C	4	P
4008	4108	C	4	P
4009	4109	C	3	P
4010	4110	C	3	P
4011	4111	C	4	P
4012	4112	C	2	NP

C: Copulated P: Pregnant NP: Non-pregnant

Appendix 12-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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 implan-tation sites	Implan-tation index % a)	Delivery index % b)	No. of stillborns (%)c)	No. of liveborns	External d) abnor-malities(%)e)
1101	21	16	16	100.0	100.0	0(0.0)	16	0(0.0)
1102	22	16	16	100.0	100.0	0(0.0)	16	0(0.0)
1103	22	16	16	100.0	100.0	0(0.0)	16	0(0.0)
1104	22	16	14	87.5	92.9	0(0.0)	13	0(0.0)
1105	22	15	15	100.0	100.0	1(6.7)	14	0(0.0)
1106	Non-pregnant							
1107	22	17	17	100.0	58.8	0(0.0)	10	0(0.0)
1108	22	16	14	87.5	100.0	0(0.0)	14	0(0.0)
1109	22	17	15	88.2	100.0	1(6.7)	14	0(0.0)
1110	22	14	13	92.9	100.0	0(0.0)	13	0(0.0)
1111	22	17	14	82.4	100.0	1(7.1)	13	0(0.0)
1112	22	19	17	89.5	100.0	0(0.0)	17	0(0.0)
Total		179	167			3	156	0
Mean	21.9	16.3	15.2	93.5	95.6	(1.9)	14.2	(0.0)
S.D.	0.3	1.3	1.3	6.7	12.4	(3.2)	2.0	(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 Methyl(2-pentyl-3-oxocyclopentyl) 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 implan-tation sites	Implan-tation index % a)	Delivery index % b)	No. of stillborns (%)c)	No. of liveborns	External d) abnor-malities(%)e)
2101	23	16	16	100.0	100.0	0(0.0)	16	0(0.0)
2102	22	15	15	100.0	100.0	1(6.7)	14	0(0.0)
2103	21	15	14	93.3	92.9	0(0.0)	13	0(0.0)
2104	22	18	18	100.0	100.0	0(0.0)	18	0(0.0)
2105	21	15	15	100.0	100.0	0(0.0)	15	0(0.0)
2106	21	16	14	87.5	100.0	0(0.0)	14	0(0.0)
2107	22	16	16	100.0	100.0	2(12.5)	14	0(0.0)
2108	22	18	15	83.3	93.3	0(0.0)	14	0(0.0)
2109	22	17	16	94.1	100.0	0(0.0)	16	0(0.0)
2110	22	15	14	93.3	92.9	0(0.0)	13	0(0.0)
2111	22	17	16	94.1	100.0	4(25.0)	12	0(0.0)
2112	21	16	16	100.0	100.0	0(0.0)	16	0(0.0)
Total		194	185			7	175	0
Mean	21.8	16.2	15.4	95.5	98.3	(3.7)	14.6	(0.0)
S.D.	0.6	1.1	1.2	5.6	3.2	(7.8)	1.7	(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 Methyl(2-pentyl-3-oxocyclopentyl) 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 implan-tation sites	Implan-tation index % a)	Delivery index % b)	No. of stillborns (%)c)	No. of liveborns	External d) abnor-malities(%)e)
3101	22	16	16	100.0	100.0	1(6.3)	15	0(0.0)
3102	22	17	16	94.1	100.0	0(0.0)	16	0(0.0)
3103	22	18	18	100.0	88.9	0(0.0)	16	0(0.0)
3104	22	15	15	100.0	93.3	0(0.0)	14	0(0.0)
3105	22	17	17	100.0	100.0	1(5.9)	16	0(0.0)
3106	22	17	16	94.1	100.0	0(0.0)	16	0(0.0)
3107	22	18	18	100.0	72.2	0(0.0)	13	0(0.0)
3108	22	15	14	93.3	100.0	0(0.0)	14	0(0.0)
3109	22	17	16	94.1	87.5	0(0.0)	14	0(0.0)
3110	22	14	13	92.9	100.0	0(0.0)	13	0(0.0)
3111	22	15	15	100.0	100.0	0(0.0)	15	0(0.0)
3112	21	15	15	100.0	93.3	0(0.0)	14	0(0.0)
Total		194	189			2	176	0
Mean	21.9	16.2	15.8	97.4	94.6	(1.0)	14.7	(0.0)
S.D.	0.3	1.3	1.5	3.3	8.5	(2.4)	1.2	(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 Methyl(2-pentyl-3-oxocyclopentyl) 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 implan-tation sites	Implan-tation index % a)	Delivery index % b)	No. of stillborns (%)c)	No. of liveborns	External d) abnor-malities(%)e)
4101	23	15	13	86.7	100.0	0(0.0)	13	0(0.0)
4102	Non-pregnant							
4103	22	18	18	100.0	94.4	1(5.9)	16	0(0.0)
4104	23	13	13	100.0	69.2	0(0.0)	9	0(0.0)
4105	22	16	16	100.0	93.8	0(0.0)	15	0(0.0)
4106	22	15	15	100.0	73.3	1(9.1)	10	0(0.0)
4107	22	16	15	93.8	100.0	0(0.0)	15	0(0.0)
4108	22	14	13	92.9	100.0	0(0.0)	13	0(0.0)
4109	23	17	17	100.0	76.5	9(69.2)	4	0(0.0)
4110	22	19	18	94.7	88.9	0(0.0)	16	0(0.0)
4111	21	14	14	100.0	92.9	0(0.0)	13	0(0.0)
4112	Non-pregnant							
Total		157	152			11	124	0
Mean	22.2	15.7	15.2	96.8	88.9	(8.4)	12.4	(0.0)
S.D.	0.6	1.9	2.0	4.6	11.7	(21.6)	3.8	(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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Day 0	No. of live pups Day 4	Viability index on postnatal day 4 % b)
1101	16	16	100.0	16	15	93.8
1102	16	16	100.0	16	16	100.0
1103	16	16	100.0	16	16	100.0
1104	13	13	100.0	13	13	100.0
1105	14	15	93.3	14	14	100.0
1106	Non-pregnant					
1107	10	10	100.0	10	10	100.0
1108	14	14	100.0	14	14	100.0
1109	14	15	93.3	14	14	100.0
1110	13	13	100.0	13	13	100.0
1111	13	14	92.9	13	13	100.0
1112	17	17	100.0	17	17	100.0
Total	156	159		156	155	
Mean	14.2	14.5	98.1	14.2	14.1	99.4
S.D.	2.0	2.0	3.2	2.0	1.9	1.9

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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Day 0	No. of live pups Day 4	Viability index on postnatal day 4 % b)
2101	16	16	100.0	16	15	93.8
2102	14	15	93.3	14	14	100.0
2103	13	13	100.0	13	13	100.0
2104	18	18	100.0	18	18	100.0
2105	15	15	100.0	15	15	100.0
2106	14	14	100.0	14	13	92.9
2107	14	16	87.5	14	13	92.9
2108	14	14	100.0	14	12	85.7
2109	16	16	100.0	16	16	100.0
2110	13	13	100.0	13	13	100.0
2111	12	16	75.0	12	12	100.0
2112	16	16	100.0	16	13	81.3
Total	175	182		175	167	
Mean	14.6	15.2	96.3	14.6	13.9	95.6
S.D.	1.7	1.5	7.8	1.7	1.8	6.4

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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Day 0	No. of live pups Day 4	Viability index on postnatal day 4 % b)
3101	15	16	93.8	15	14	93.3
3102	16	16	100.0	16	16	100.0
3103	16	16	100.0	16	16	100.0
3104	14	14	100.0	14	14	100.0
3105	16	17	94.1	16	16	100.0
3106	16	16	100.0	16	16	100.0
3107	13	13	100.0	13	11	84.6
3108	14	14	100.0	14	14	100.0
3109	14	14	100.0	14	14	100.0
3110	13	13	100.0	13	13	100.0
3111	15	15	100.0	15	15	100.0
3112	14	14	100.0	14	14	100.0
Total	176	178		176	173	
Mean	14.7	14.8	99.0	14.7	14.4	98.2
S.D.	1.2	1.3	2.4	1.2	1.5	4.7

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 Methyl(2-pentyl-3-oxocyclopentyl) 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 Day 0	No. of live pups Day 4	Viability index on postnatal day 4 % b)
4101	13	13	100.0	13	13	100.0
4102	Non-pregnant					
4103	16	17	94.1	16	13	81.3
4104	9	9	100.0	9	9	100.0
4105	15	15	100.0	15	13	86.7
4106	10	11	90.9	10	10	100.0
4107	15	15	100.0	15	15	100.0
4108	13	13	100.0	13	13	100.0
4109	4	13	30.8	4	3	75.0
4110	16	16	100.0	16	16	100.0
4111	13	13	100.0	13	13	100.0
4112	Non-pregnant					
Total	124	135		124	118	
Mean	12.4	13.5	91.6	12.4	11.8	94.3
S.D.	3.8	2.4	21.6	3.8	3.7	9.6

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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual sex ratio of pups
Dose (mg/kg): 0

Dam number	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 males	Postnatal day 4 No. of females	Sex ratio of live pups on day 4 c)
1101	6	10	0	0	0.38	0.38	6	9	0.40
1102	8	8	0	0	0.50	0.50	8	8	0.50
1103	10	6	0	0	0.63	0.63	10	6	0.63
1104	9	4	0	0	0.69	0.69	9	4	0.69
1105	7	7	1	0	0.53	0.50	7	7	0.50
1106	Non-pregnant								
1107	1	9	0	0	0.10	0.10	1	9	0.10
1108	10	4	0	0	0.71	0.71	10	4	0.71
1109	9	5	1	0	0.67	0.64	9	5	0.64
1110	9	4	0	0	0.69	0.69	9	4	0.69
1111	8	5	0	1	0.57	0.62	8	5	0.62
1112	10	7	0	0	0.59	0.59	10	7	0.59
Total	87	69	2	1			87	68	
Mean	7.9	6.3	0.2	0.1	0.55	0.55	7.9	6.2	0.55
S.D.	2.6	2.1	0.4	0.3	0.18	0.18	2.6	1.9	0.18

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 Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual sex ratio of pups
Dose (mg/kg): 100

Dam number	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 males	Postnatal day 4 No. of females	Sex ratio of live pups on day 4 c)
2101	9	7	0	0	0.56	0.56	8	7	0.53
2102	9	5	0	1	0.60	0.64	9	5	0.64
2103	7	6	0	0	0.54	0.54	7	6	0.54
2104	8	10	0	0	0.44	0.44	8	10	0.44
2105	8	7	0	0	0.53	0.53	8	7	0.53
2106	10	4	0	0	0.71	0.71	9	4	0.69
2107	11	3	0	2	0.69	0.79	10	3	0.77
2108	3	11	0	0	0.21	0.21	3	9	0.25
2109	7	9	0	0	0.44	0.44	7	9	0.44
2110	8	5	0	0	0.62	0.62	8	5	0.62
2111	5	7	1	3	0.38	0.42	5	7	0.42
2112	7	9	0	0	0.44	0.44	5	8	0.38
Total	92	83	1	6			87	80	
Mean	7.7	6.9	0.1	0.5	0.51	0.53	7.3	6.7	0.52
S.D.	2.1	2.5	0.3	1.0	0.14	0.15	2.0	2.1	0.15

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 14-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual sex ratio of pups
Dose (mg/kg): 300

Dam number	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 males	Postnatal day 4 No. of females	Sex ratio of live pups on day 4 c)
3101	5	10	1	0	0.38	0.33	4	10	0.29
3102	10	6	0	0	0.63	0.63	10	6	0.63
3103	9	7	0	0	0.56	0.56	9	7	0.56
3104	6	8	0	0	0.43	0.43	6	8	0.43
3105	6	10	1	0	0.41	0.38	6	10	0.38
3106	8	8	0	0	0.50	0.50	8	8	0.50
3107	7	6	0	0	0.54	0.54	6	5	0.55
3108	4	10	0	0	0.29	0.29	4	10	0.29
3109	7	7	0	0	0.50	0.50	7	7	0.50
3110	5	8	0	0	0.38	0.38	5	8	0.38
3111	9	6	0	0	0.60	0.60	9	6	0.60
3112	12	2	0	0	0.86	0.86	12	2	0.86
Total	88	88	2	0			86	87	
Mean	7.3	7.3	0.2	0.0	0.51	0.50	7.2	7.3	0.50
S.D.	2.3	2.3	0.4	0.0	0.15	0.16	2.5	2.3	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 14-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual sex ratio of pups
Dose (mg/kg): 1000

Dam number	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 males	Postnatal day 4 No. of females	Sex ratio of live pups on day 4 c)
4101	4	9	0	0	0.31	0.31	4	9	0.31
4102	Non-pregnant								
4103	10	6	1	0	0.65	0.63	9	4	0.69
4104	3	6	0	0	0.33	0.33	3	6	0.33
4105	8	7	0	0	0.53	0.53	6	7	0.46
4106	7	3	0	1	0.64	0.70	7	3	0.70
4107	6	9	0	0	0.40	0.40	6	9	0.40
4108	6	7	0	0	0.46	0.46	6	7	0.46
4109	1	3	3	3	-d)	0.25	0	3	0.00
4110	12	4	0	0	0.75	0.75	12	4	0.75
4111	7	6	0	0	0.54	0.54	7	6	0.54
4112	Non-pregnant								
Total	64	60	4	4			60	58	
Mean	6.4	6.0	0.4	0.4	0.51	0.49	6.0	5.8	0.46
S.D.	3.2	2.2	1.0	1.0	0.15	0.17	3.3	2.3	0.22

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): Could not be calculated, because there were the stillborns that sex were unclear.

Appendix 15-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual body weight of pups
Dose (mg/kg): 0

Dam number	Male 0	Male 4a)	Male Gain	Female 0	Female 4a)	Female Gain
1101	5.9	8.5	2.6	5.6	8.0	2.4
1102	6.4	9.1	2.7	6.0	8.7	2.7
1103	6.4	9.2	2.8	6.2	8.8	2.6
1104	7.2	11.3	4.1	6.9	10.9	4.0
1105	6.8	9.9	3.1	6.4	9.5	3.1
1106	Non-pregnant					
1107	7.1	11.8	4.7	6.8	10.8	4.0
1108	7.1	11.1	4.0	6.5	9.7	3.2
1109	6.2	9.3	3.1	6.0	9.1	3.1
1110	6.0	9.0	3.0	5.6	8.3	2.7
1111	7.0	10.8	3.8	6.9	10.8	3.9
1112	6.5	9.3	2.8	6.3	9.1	2.8
Mean	6.6	9.9	3.3	6.3	9.4	3.1
S.D.	0.5	1.1	0.7	0.5	1.0	0.6

Unit: g
a): Postnatal day

Appendix 15-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual body weight of pups
Dose (mg/kg): 100

Dam number	Male 0	Male 4a)	Male Gain	Female 0	Female 4a)	Female Gain
2101	6.8	10.7	3.9	6.5	10.2	3.7
2102	6.7	9.2	2.5	6.3	8.6	2.3
2103	6.4	10.3	3.9	6.0	9.4	3.4
2104	6.4	8.9	2.5	6.3	9.1	2.8
2105	5.6	7.6	2.0	5.3	7.4	2.1
2106	5.9	9.5	3.6	5.6	9.1	3.5
2107	6.6	9.5	2.9	6.5	9.5	3.0
2108	6.7	11.2	4.5	6.5	11.1	4.6
2109	6.7	9.6	2.9	6.1	9.1	3.0
2110	6.8	10.8	4.0	6.2	10.3	4.1
2111	6.7	11.6	4.9	6.2	10.0	3.8
2112	5.9	9.3	3.4	5.7	9.1	3.4
Mean	6.4	9.9	3.4	6.1	9.4	3.3
S.D.	0.4	1.1	0.9	0.4	0.9	0.7

Unit: g
a): Postnatal day

Appendix 15-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual body weight of pups
Dose (mg/kg): 300

Dam number	Male 0	Male 4a)	Male Gain	Female 0	Female 4a)	Female Gain
3101	5.9	8.6	2.7	5.6	8.0	2.4
3102	6.4	9.7	3.3	6.1	9.8	3.7
3103	6.1	8.3	2.2	5.7	8.0	2.3
3104	5.9	9.7	3.8	5.9	9.5	3.6
3105	6.1	9.3	3.2	5.9	8.9	3.0
3106	6.5	10.0	3.5	5.9	9.4	3.5
3107	6.2	9.9	3.7	6.1	9.0	2.9
3108	6.6	9.8	3.2	6.3	9.1	2.8
3109	6.6	11.0	4.4	6.1	10.6	4.5
3110	6.3	9.8	3.5	6.2	10.2	4.0
3111	6.7	9.5	2.8	6.3	9.3	3.0
3112	6.3	8.4	2.1	6.0	7.4	1.4
Mean	6.3	9.5	3.2	6.0	9.1	3.1
S.D.	0.3	0.8	0.7	0.2	0.9	0.8

Unit: g
a): Postnatal day

Appendix 15-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) acetate by oral administration in rats
Individual body weight of pups
Dose (mg/kg): 1000

Dam number	Male 0	Male 4a)	Male Gain	Female 0	Female 4a)	Female Gain
4101	6.0	9.2	3.2	6.3	9.4	3.1
4102	Non-pregnant					
4103	5.3	7.2	1.9	5.0	6.7	1.7
4104	6.8	11.2	4.4	6.5	11.2	4.7
4105	5.1	8.3	3.2	5.1	8.6	3.5
4106	6.6	9.7	3.1	6.3	9.5	3.2
4107	5.7	9.1	3.4	5.6	9.0	3.4
4108	6.6	10.0	3.4	5.9	9.1	3.2
4109	4.7	b)		4.9	5.5	0.6
4110	5.1	8.2	3.1	4.6	7.2	2.6
4111	5.5	8.4	2.9	5.1	7.5	2.4
4112	Non-pregnant					
Mean	5.7	9.0	3.2	5.5	8.4	2.8
S.D.	0.7	1.2	0.6	0.7	1.6	1.1

Unit: g
a): Postnatal day
b): All male pups died.

Appendix 16-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	1 (0 + 1)	NAF
1102	0	
1103	0	
1104	0	
1105	0	
1106	Non-pregnant	
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 Methyl(2-pentyl-3-oxocyclopentyl) 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	1 (1 + 0)	NAF
2102	0	
2103	0	
2104	0	
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 Methyl(2-pentyl-3-oxocyclopentyl) 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	1 (0 + 1)	NAF
3108	0	
3109	0	
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 Methyl(2-pentyl-3-oxocyclopentyl) 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	Non-pregnant	
4103	0	
4104	0	
4105	2 (2 + 0)	NAF
4106	0	
4107	0	
4108	0	
4109	1 (1 + 0)	NAF
4110	0	
4111	0	
4112	Non-pregnant	

NAF: No abnormal findings

Appendix 17-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	15 (6 + 9)	NAF
1102	16 (8 + 8)	NAF
1103	16 (10 + 6)	NAF
1104	13 (9 + 4)	NAF
1105	14 (7 + 7)	NAF
1106	Non-pregnant	
1107	10 (1 + 9)	NAF
1108	14 (10 + 4)	NAF
1109	14 (9 + 5)	NAF
1110	13 (9 + 4)	NAF
1111	13 (8 + 5)	NAF
1112	17 (10 + 7)	NAF

NAF: No abnormal findings

Appendix 17-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	15 (8 + 7)	NAF
2102	14 (9 + 5)	NAF
2103	13 (7 + 6)	NAF
2104	18 (8 + 10)	NAF
2105	15 (8 + 7)	NAF
2106	13 (9 + 4)	NAF
2107	13 (10 + 3)	NAF
2108	12 (3 + 9)	NAF
2109	16 (7 + 9)	NAF
2110	13 (8 + 5)	NAF
2111	12 (5 + 7)	NAF
2112	13 (5 + 8)	NAF

NAF: No abnormal findings

Appendix 17-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	14 (4 + 10)	NAF
3102	16 (10 + 6)	NAF
3103	16 (9 + 7)	NAF
3104	14 (6 + 8)	NAF
3105	16 (6 + 10)	NAF
3106	16 (8 + 8)	NAF
3107	11 (6 + 5)	NAF
3108	14 (4 + 10)	NAF
3109	14 (7 + 7)	NAF
3110	13 (5 + 8)	NAF
3111	15 (9 + 6)	NAF
3112	14 (12 + 2)	NAF

NAF: No abnormal findings

Appendix 17-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Methyl(2-pentyl-3-oxocyclopentyl) 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	13 (4 + 9)	NAF
4102	Non-pregnant	
4103	13 (9 + 4)	NAF
4104	9 (3 + 6)	NAF
4105	13 (6 + 7)	NAF
4106	10 (7 + 3)	NAF
4107	15 (6 + 9)	NAF
4108	13 (6 + 7)	NAF
4109	3 (0 + 3)	NAF
4110	16 (12 + 4)	NAF
4111	13 (7 + 6)	NAF
4112	Non-pregnant	

NAF: No abnormal findings