

最終報告書

シクロペンタノンのラットを用いる 反復投与毒性・生殖発生毒性併合試験

厚生労働省医薬・生活衛生局審査管理課 化学物質安全対策室 委託

試験施設

一般財団法人食品薬品安全センター 秦野

〒257-8523 神奈川県秦野市落合 729 番地の 5

TEL 0463-82-4751

試験委託者 厚生労働省医薬・生活衛生局審査管理課 化学物質安全対策室
(東京都千代田区霞が関 1-2-2)

試験番号 R-15-005

被験物質 シクロペンタノン

試験項目 反復投与毒性・生殖発生毒性併合試験

試験開始日 2015年10月21日

実験開始日 2015年10月26日

実験終了日 2016年2月4日

試験終了日 試験責任者の押印日

試験資料保管場所 秦野研究所資料保存施設

保管期間 試験終了後10年間
その後の保管については試験委託者と協議する。

運営管理者 一般財団法人食品薬品安全センター 秦野研究所
所長 

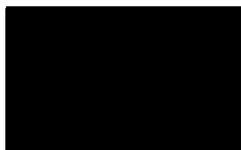
本試験は、「新規化学物質等に係る試験の方法について」(平成23年3月31日付け、薬食発0331第7号厚生労働省医薬食品局長、平成23・03・29製局第5号経済産業省製造産業局長、環境企発第110331009号環境省総合環境政策局長通知)に準拠し、「新規化学物質等に係る試験を実施する試験施設に関する基準」(平成23年3月31日付け、薬食発0331第8号厚生労働省医薬食品局長、平成23・03・29製局第6号経済産業省製造産業局長、環境企発第110331010号環境省総合環境政策局長通知)を遵守して実施した。

2016年3月10日

試験責任者 

試験従事者

試験責任者



試験担当主任者

試験担当者

投与観察

動物飼育管理

(検疫を含む)

尿検査

血液学的検査

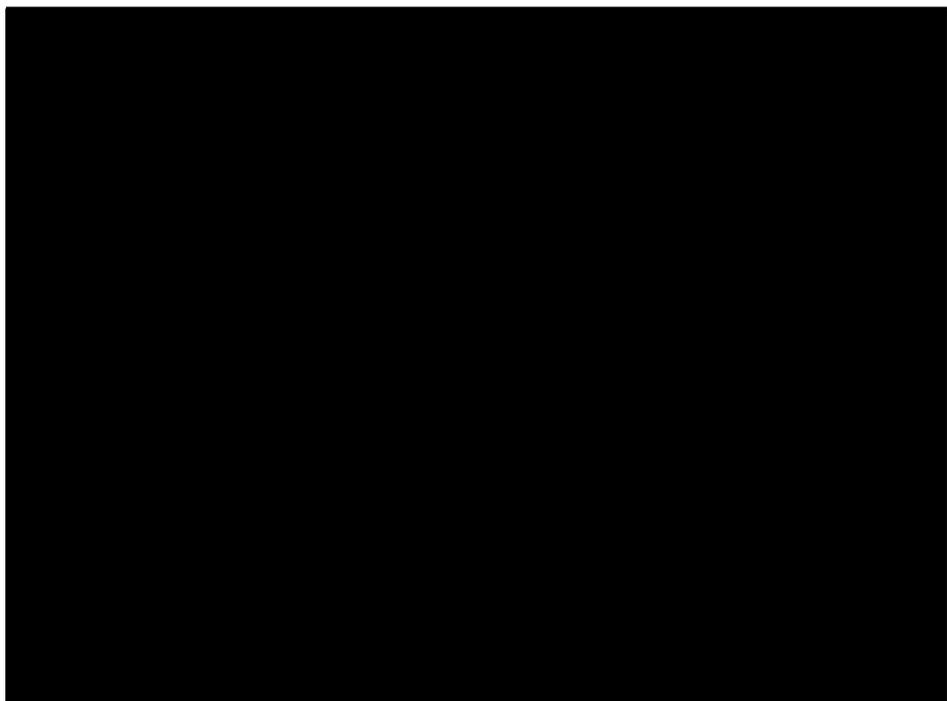
(採血を含む)

血液生化学的検査

病理学的検査

検体調製

化学分析



被験物質管理



目次

要約.....	6
試験目的.....	7
試験ガイドラインとGLP.....	7
動物愛護.....	7
材料と方法.....	7
1. 被験物質.....	7
2. 動物および飼育方法.....	8
3. 投与検体.....	9
1) 調製.....	9
2) 安定性試験.....	9
3) 含量試験.....	9
4. 投与量の設定および投与方法.....	9
5. 検査法.....	10
1) 親動物 (F ₀).....	10
2) 出生児 (F ₁).....	15
6. データの解析法.....	15
予見することができなかつ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つたこと.....	16
試験成績.....	16
1. 親動物.....	16
1) 一般状態.....	16
2) 詳細な症状観察.....	17
3) 体重.....	17
4) 摂餌量.....	17
5) 機能検査.....	17
6) 尿検査.....	17
7) 血液学的検査.....	18
8) 血液生化学的検査.....	18
9) 器官重量.....	18
10) 剖検所見.....	19
11) 病理組織学的検査所見.....	19
2. 生殖能力.....	19
1) 性周期および交配成績.....	19

2) 出産率および妊娠期間.....	19
3) 分娩および哺育状態.....	20
4) 黄体数、着床数および着床率.....	20
3. 出生児.....	20
1) 生存.....	20
2) 体重.....	20
3) 出生児観察.....	20
考察.....	20
文献.....	22
Tables.....	23
Annexes.....	108
Appendices.....	114

(最終ページ:376ページ)

信頼性保証書

要約

シクロペンタノンの反復投与毒性・生殖発生毒性併合試験を化審法ガイドラインに従って実施した。被験物質をトウモロコシ油に希釈して0(媒体のみ)、30、100ならびに300 mg/kgの用量で、各群とも雌雄各12匹のCrI:CD(SD)ラットに強制経口投与した。雄は42日間投与した後に剖検し、雌は交配前14日間および交配期間、妊娠期間を通して哺育4日までの42～46日間投与し、出生児は哺育4日、母動物は哺育5日に剖検した。また、0および300 mg/kgの用量に非交配雌(10匹/群)を設け、42日間投与した後に各5匹を剖検し、残りの各5匹と0および300 mg/kg群の雄5匹は、42日間投与した後に14日間飼育して剖検した。

1. 反復投与毒性および回復性

投与期間中は、300 mg/kg群の雄2例に被験物質の刺激性によると考えられる一過性の流涎が観察された。また、同群においては、雄の体重増加が抑制され、非交配雌の摂餌量が低下した。詳細な症状観察、機能検査、尿検査、器官重量および病理組織学的検査においては、被験物質投与の影響と考えられる変化ならびに所見は認められなかった。

回復観察中は、体重増加抑制および摂餌量の低下はみられなかった。

2. 生殖発生毒性

性周期、交配成績、出産率、妊娠期間、分娩状態、哺育状態、黄体数、着床数および着床率に、被験物質投与の影響は認められなかった。また、出生児の生存率、体重および形態にも被験物質投与の影響は認められなかった。

3. 無毒性量

300 mg/kg群の雄で体重増加抑制、非交配雌で摂餌量の低下が認められたことから、雌雄動物の反復投与毒性に関する無毒性量(NOAE)は100 mg/kg/dayと判断された。また、300 mg/kgまでの用量は、親動物の生殖能力および新生児の発育に影響を及ぼさなかったことから、生殖発生毒性に関する無毒性量は300 mg/kg/dayと判断された。

試験目的

本試験は、ラットにシクロペンタノンを一定期間反復投与したときに現れる一般毒性および生殖発生毒性を明らかにすることを目的とした。

試験ガイドラインと GLP

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

動物愛護

全ての実験操作は、「動物の愛護及び管理に関する法律」(昭和 48 年 10 月 1 日、法律第 105 号、平成 26 年 5 月 30 日 一部改正)、「実験動物の飼養及び保管並びに苦痛の軽減に関する基準」(平成 18 年 4 月 28 日、環境省告示第 88 号、平成 25 年 8 月 30 日 一部改正)および「厚生労働省の所管する実施機関における動物実験等の実施に関する基本指針」(平成 27 年 2 月 20 日、科発 0220 第 1 号)を遵守し、「一般財団法人食品薬品安全センター 動物実験に関する指針(機関内規程)」(平成 2 年 10 月 1 日、平成 27 年 4 月 20 日改定)に基づいて実施した(動物実験承認番号:1150240A)。なお、承認された動物実験計画からの変更はなかった。

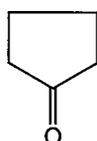
材料と方法

1. 被験物質

- | | |
|------------|---|
| 1) 名称 | シクロペンタノン |
| 2) 英名 | Cyclopentanone |
| 3) 別名 | Adipic Ketone、Ketocyclopentane、Ketopentamethylene |
| 4) 略称 | CPN |
| 5) CAS 番号 | 120-92-3 |
| 6) 分子式 | C ₅ H ₈ O |
| 7) 分子量 | 84.12 |
| 8) 物理化学的性質 | 外観・性状:無色透明な液体、特異臭 |

融点: -51°C
 沸点: 130°C
 引火点: 34°C
 蒸気圧: 1.5kPa/25°C
 比重(20/20): 0.9503
 屈折率(n_{20/D}): 1.4371
 溶解度: 水に難溶、エーテル、アルコール、アセトンに可溶
 オクタノール/水分配係数: 0.24

9) 構造式



- 10) ロット番号 W780E (Annex 1 参照)
- 11) 純度 100.0%(GC)
- 12) 不純物 情報なし
- 13) 安定性 当試験施設において、実験開始前(2015年10月26日)と終了後(2016年1月4日)に目視による性状の確認および赤外吸収スペクトルを測定し、色調や状態、スペクトルに変化がないことを確認した(Annex 2)。測定法はAnnex 3、「1. 原体の安定性試験」に従った。
- 14) 保管条件 冷蔵(実測値: 3~7°C)、遮光、密閉
- 15) 購入元 XXXXXXXXXX
- 16) 被験物質の保管 秦野研究所資料保存施設に 5 g を保管した。

2. 動物および飼育方法

日本チャールス・リバー厚木飼育センター生産の Sprague-Dawley (SD) 系 [CrI:CD(SD)、SPF] ラット、雄 55 匹、雌 83 匹を 8 週齢で購入し、飼育室(8 号室)に収容した。入荷日(検疫 1 日)を含む 15 日間、検疫と馴化を兼ねて飼育した。その間毎日、動物の一般状態を観察し、入荷日および検疫終了日に体重を測定した。検疫・馴化期間中は、赤のフェルトペンで尾に馴化番号を標識し、飼育ケージに試験番号、馴化番号を記入した動物カードを掛けて識別した。また、雌動物については、検疫 3 日から毎日、性周期を観察した。入荷動物の入荷日および検疫終了日の体重は下記の通りであった。

動物入荷日 : 2015 年 10 月 26 日
 入荷時体重 : 雄 266.9~300.1 g、雌 176.7~209.3 g
 検疫終了日 : 2015 年 11 月 9 日
 検疫終了時体重 : 雄 369.0~442.6 g、雌 206.5~284.1 g

検疫、馴化期間中の一般状態に異常(赤色尿)を示した雌 1 匹、体重増加に異常が認められた雌 1 匹、検疫終了日に実施した詳細な症状観察の結果から、脱毛が認められた雄 2 匹および雌 1 匹は、

群分けの対象から除外した。さらに、雌動物については、規則的な発情期の回帰が認められない 8 匹を除外し、投与開始前日に検疫、馴化期間終了時の体重に基づく体重別層化無作為抽出法により群分けした。群分け後は、黒色のフェルトペンで尾に動物番号を標識し、色彩の異なった動物カードに試験番号、動物番号を記入して飼育ケージに掛けた。試験に使用しなかった動物(雄 7 匹、雌 15 匹)は余剰動物とし、他の試験(試験番号 S-15-014)に移管した。

動物は許容温度 21.0～25.0℃、許容湿度 40.0～75.0%、換気設定約 15 回/時間、明暗サイクル 12 時間(7 時～19 時)点灯、12 時間(19 時～7 時)消灯に設定された飼育室内で、金属製金網床ケージ(220w×270d×190h mm、金属製休息板 130w×150d mm 付)に 1 匹ずつ(交配時は 2 匹/ケージとし、金属製休息板を外した)収容し、固型飼料(CE-2、日本クレア)と水道水(秦野市水道局給水)を自由に摂取させて飼育した(剖検前の絶食に関しては剖検の項を参照)。交配雌は、妊娠 18 日から哺育 4 日までラット用プラスチック製繁殖ケージ(350w×400d×180h mm)に 1 匹ずつ収容し、床敷として紙パルプ製チップ(ペパークリーン、日本エスエルシー)を適宜供給した。飼育期間中の動物室の温度は 22.0～25.0℃、湿度は 45.5～69.0%であった。また、供給した飼料、飲料水および床敷の分析結果は、いずれも標準操作手順書に記載の許容範囲内であることを確認した。

3. 投与検体

1) 調製

被験物質を秤量し、媒体(トウモロコシ油、製造元:ナカライテスク、ロット番号:V5M6475)を加え攪拌混和させ、75.0 mg/mL 溶液を調製した。さらに 75.0 mg/mL 溶液を媒体によって希釈し、25.0 ならびに 7.50 mg/mL 溶液を段階的に調製した。調製した検体は、冷蔵(実測値:2～7℃)、遮光、密閉で保管し、安定性の保証期間内に使用した。

2) 安定性試験

7.50 および 75.0 mg/mL の投与検体については、冷蔵(実測値:4℃)、遮光条件下における 8 日間の安定性を確認した(Annex 4)。測定法はAnnex 3、「2. 投与検体中の被験物質濃度測定法」に従った。

3) 含量試験

初回に調製した投与検体(7.50、25.0 および 75.0 mg/mL)について、被験物質含量を測定した。測定法はAnnex 3、「2. 投与検体中の被験物質濃度測定法」に従った。その結果、平均含量は調製濃度の 98.7～100.8%であり、各測定濃度のばらつきも平均値の 99.2～100.4%で規定範囲内にあった(Annex 5)。

4. 投与量の設定および投与方法

本試験の投与量は、「シクロペンタノンのラットを用いる反復投与毒性・生殖発生毒性併合試験(予備試験)」(試験番号 R-15-004)の結果をもとに設定した。なお、予備試験で使用した被験物質は本試験と同じロットを用いた。

予備試験では、0(媒体、トウモロコシ油)、250、500 および 1000 mg/kg のシクロペンタノンを 10 週齢の雌雄各 3 匹の SD 系ラットに 14 日間、反復強制経口投与した結果、1000 mg/kg 群は雌雄とも全例が

投与 5～10 日の間に瀕死状態となり、500 mg/kg 群の雄 1 例も投与 13 日以降に強直性痙攣など重篤な症状を呈した。しかし、250 mg/kg 群では雌の体重に増加抑制傾向がみられたのみであったことから、本試験の最高用量には 300 mg/kg を設定し、以下、公比約 3 で中用量には 100 mg/kg を、低用量には 30 mg/kg を設定した。

本試験では、雄動物は交配前 14 日間、交配期間(最長 14 日間)を通して剖検前日まで(総投与回数 42 回)、雌動物は交配前 14 日間、交配期間(最長 14 日間)、妊娠期間を通して分娩後の哺育 4 日まで(総投与回数 42～46 回)、交尾が確認されなかった雌は剖検前日まで(総投与回数 52 回)、分娩しなかった雌は剖検前日(妊娠 25 日相当日)まで、非交配(サテライト)群の雌は投与 42 日まで、1 日 1 回、1 週 7 回、毎日 9 時～12 時の間(9 時 01 分～11 時 50 分)に投与した。投与容量は 4 mL/kg とし、雌雄とも最新の測定日の体重を基に投与液量を算出した。なお、対照群には媒体であるトウモロコシ油を同様に投与した。投与経路は化審法ガイドラインに拠り、ラット用胃管による強制経口投与とした。

本試験の群構成および動物番号を以下に示した。

群	投与物質	投与量 (mg/kg)	濃度 (mg/mL)	投与容量 (mL/kg)	動物番号	
					雄	雌
対照群	トウモロコシ油 (媒体)	0	0	4	M01001～M01012*	F01001～F01012
低用量群	CPN	30	7.5	4	M02013～M02024	F02013～F02024
中用量群	CPN	100	25	4	M03025～M03036	F03025～F03036
高用量群	CPN	300	75	4	M04037～M04048*	F04037～F04048
対照群 [非交配 (サテライト)群]	トウモロコシ油 (媒体)	0	0	4	-	F05049～F05058*
高用量群 [非交配 (サテライト)群]	CPN	300	75	4	-	F06056～F06065*

* 雄の対照群および高用量群、雌の非交配(サテライト)群の動物番号の大きい各 5 例は回復観察に供した。

5. 検査法

1) 親動物 (F₀)

① 一般状態の観察

全例について、飼育期間中は毎日 1 回、投与期間中は投与前後の毎日 2 回以上観察した。症状が発現した場合は、断続的に観察を継続した。

② 回復および遅発毒性の観察

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

③ 詳細な症状観察

全例について、検疫終了日、投与 8、15、24、30、36 および 42 日(分娩例は哺育 0 日から 4 日の間

に 1 回)、回復期間中は回復 7 および 14 日にスコアリング法による詳細な症状観察を行った。観察は、いずれも 13 時～16 時の間(13 時 10 分～15 時 55 分)に行った。

まず、ケージ越しでの観察を行い、ケージから取り出す際に外表を観察し、作業台上での観察を行った。作業台上では、体位、姿勢、探索行動、立毛、眼裂、振戦、痙攣、呼吸数、歩行、常同行動、奇妙な行動、挙尾反応、身づくろい、発声、排尿、排便、接触に対する反応、撤去反射、耳介反射を観察した。

④機能検査

雄は、各群の動物番号の若い 5 例について、投与 39 日に自発運動測定と握力測定を実施し、投与 42 日に詳細な症状観察に引き続いて刺激に対する感覚運動反応を検査した。分娩例は、投与期間が近接し、分娩から日数が経過した各群の 5 例について、サテライト群の雌は、各群の動物番号の若い 5 例について、投与最終週に自発運動測定、握力測定および刺激に対する感覚運動反応を検査した。なお、投与最終週に実施した握力測定でサテライト群の雌は群間に有意差がみられたため、サテライト群の回復観察例については、回復 14 日にも握力測定を実施した。

(1) 自発運動測定

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

(2) 握力測定

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

(3) 刺激に対する感覚運動反応

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

⑤体重測定

雄およびサテライト群の雌は、投与 1(投与開始日)、4、7、14、21、28、35、42 日、回復 1、7、14 日および剖検日に測定した。交配雌は投与 1、4、7、14 日、妊娠 0(交尾確認日)、7、14、20 日、哺育 0(分娩日)、4 日および剖検日に測定し、未交尾例は投与 21、28、35、42、49 日および剖検日に測定した。

⑥摂餌量測定

雄およびサテライト群の雌は、投与 1～2、7～8、14～15、29～30、35～36、41～42 日、回復 6～7、12～13 日に測定し、サテライト群の雌は投与 21～22 日にも測定した。交配雌は投与 1～2、7～8、14～15 日および妊娠 0～1、7～8、14～15、20～21 日ならびに哺育 3～4 日に測定し、未交尾例は投与 29～30、35～36、41～42、48～49 日に測定した。なお、中用量群の雌 2 例(動物番号 F03035、F03036)については、投与 7～8 日の摂餌量が測定できなかったため、投与 8～9 日の摂餌量を測定し、参考データとした。

⑦尿検査

雄およびサテライト群の雌を検査対象とし、投与 37 日の検査では各群の動物番号が若い 5 例、また、回復 13 日における検査では回復例全例を検査した。

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

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

⑧性周期観察

全例の雌について、検疫 3 日から性周期を観察し、群分け後、投与開始以降も引き続きサテライト群を除く全例の膣スミア標本を作製し、各動物の同居後、交尾が確認されるまで性周期を観察した。また、平均発情回帰日数(個体ごとの発情期から発情期までの平均日数)および投与開始後に 4 あるいは 5 日間隔の性周期がそれ以外の性周期に変化した動物の頻度を群ごとに算出した。なお、規則的に 4~5 日の間で性周期が回帰している動物は正常とみなした。

⑨交配

投与 15 日の 16 時 10 分~16 時 23 分に同群内の雌雄を 1 対 1 で同居させた。なお、対照群の雌 1 例(動物番号 F01006)は、交配相手雄(動物番号 M01006)に歩行異常が認められたため、交尾が確認された雄(動物番号 M01007)と投与 17 日の 15 時 45 分から再同居させた。翌朝より毎朝、膣栓を確認し、同居中の雌の膣スミア標本を作製して鏡検した。膣内に膣栓あるいは膣スミア標本中に精子が確認された動物を交尾成立動物とし、この日を妊娠 0 日と起算して個別飼育に戻した。交配結果および妊娠の成否により、同居開始日から交尾確認日までの日数およびその間に回帰した発情期の回数、交尾率 $[(交尾動物数/交配に用いた動物数) \times 100, \%]$ 、妊娠率 $[(妊娠動物数/交尾した雌動物数) \times 100, \%]$ を算出した。

⑩妊娠・分娩・哺育状態の観察

交尾が確認された全例を自然分娩させた。分娩の確認は、妊娠 21 日相当日から分娩が確認されるまで毎日、午前と午後に行い、15 時までには分娩が完了した例について、その日を哺育 0 日(分娩日)とした。分娩状態の直接観察は観察可能な動物について行い、直接観察できなかった動物についても、分娩後の一般状態および産児の状態から異常の有無を判断した。分娩後は、哺育状態を哺育 1~4 日の間、毎日観察した。分娩例については、妊娠期間(妊娠 0 日から分娩日までの日数)を求めた。また、剖検時に

は、妊娠黄体数と着床数を数え、着床率〔(着床数/妊娠黄体数)×100, %〕を算出した。

⑪採血

雄の投与終了時剖検では各群の動物番号が若い 5 例、回復 15 日における剖検では回復観察に供した全例について採血を行った。また、分娩雌の投与終了時剖検では、投与期間が近接した各群の 5 例について採血を行った。サテライト群の雌の投与終了時剖検では各群の動物番号が若い 5 例、回復 15 日における剖検では回復観察に供した全例について採血を行った。いずれも解剖前 18～24 時間絶食させた後、腹部後大静脈から以下の(1)、(2)、(3)の順に注射筒を換えて採血した。なお、300 mg/kg 群の雌 1 例(動物番号 F06056)では、採血時に呼吸が停止していたため、血液学的検査および血液生化学的検査の測定値については、試験評価の対象から除外した。

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

⑫血液学的検査

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

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

⑬血液生化学的検査

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

項目	測定法	使用機器
総蛋白濃度 (TP)	ビウレット法	自動分析装置 JCA-BM6010(日本電子)
アルブミン濃度 (rALB)	BCG法	同上
グルコース濃度 (Glc)	ヘキソキナーゼ・G-6-PDH法	同上
総コレステロール濃度 (TC)	コレステロールオキシダーゼ・HMMPS法	同上
トリグリセリド濃度 (TG)	GPO・HMMPS法、グリセリン消去法	同上
リン脂質濃度 (PL)	コリンオキシダーゼ・DAOS法	同上
尿素窒素濃度 (BUN)	ウレアーゼ・GODH法、アンモニア消去法	同上
クレアチニン濃度 (cre)	クレアチナーゼ・HMMPS法	同上
γ-グルタミルトランスアミナーゼ活性 (γ-GTP)	IFCC法	同上
アルカリフォスファターゼ活性 (ALP)	GSCC法	同上
アスパラギン酸アミノトランスフェラーゼ活性 (AST)	IFCC法	同上
アラニンアミノトランスフェラーゼ活性 (ALT)	同上	同上
乳酸脱水素酵素活性 (LDH)	JSCC標準化対応法	同上
カルシウム濃度 (Ca)	OCPC法	同上
総ビリルビン濃度 (tbil)	酵素法	同上
無機リン濃度 (IP)	モリブデン酸直接法	同上
胆汁酸濃度 (TBA)	酵素サイクリング法	同上
A/G比	計算 (rALB / (TP - rALB))	同上
ナトリウムイオン濃度 (Na)	イオン電極法	同上
カリウムイオン濃度 (K)	同上	同上
塩素イオン濃度 (Cl)	同上	同上

⑭剖検および器官重量

以下の時期に、採血対象動物はペントバルビタールナトリウム麻酔下で採血した後、これ以外の動物はペントバルビタールナトリウム麻酔下で放血致死させ、引き続き剖検した。

対象動物	解剖時期	屠殺前の絶食
雄		
途中剖検例 (動物番号 M01006)	投与 18 日	実施せず
投与終了時剖検例	投与 42 日の翌日	絶食
回復観察例	回復 15 日	絶食
雌		
分娩例	哺育 4 日の翌日	絶食
未分娩例	妊娠 26 日相当日	実施せず
交尾が確認されなかった例 (未交尾例)	投与 52 日の翌日	実施せず
全哺育児が死亡した例	全哺育児の死亡日	実施せず
非交配群 (投与終了時剖検例)	投与 42 日の翌日	絶食
非交配群 (回復観察例)	回復 15 日	絶食

全例について、脳、甲状腺および上皮小体、胸腺、心臓、肝臓、腎臓、脾臓、副腎、精巣、精巣上体、前立腺 (腹側葉) および精嚢 (凝固腺を含む)、卵巣、子宮の重量を測定し、併せて各器官の比体重値 (相対重量) も算出した。また、全例の脳、脊髄、下垂体、眼球 (ハーダー腺)、顎下腺および舌下腺、気管、甲状腺および上皮小体、胸腺、心臓、肺および気管支、肝臓、腎臓、脾臓、膵臓、副腎、胃、十二指

腸、空腸、回腸、盲腸、結腸、直腸、下顎リンパ節、腸間膜リンパ節、精巣、精巣上部、前立腺(腹側葉)、精嚢および凝固腺、卵巣、子宮、膣、膀胱、大腿骨および大腿骨髄、骨格筋、坐骨神経、および病変部を採取し、保存した。肺/気管支は 15 cm 水柱以下の圧力で、気管内に 10%中性緩衝ホルマリン溶液 5 mL 以下を注入し固定してから摘出して同固定液に保存した。精巣および精巣上部はブアン液に固定(長期保存は 10%中性緩衝ホルマリン溶液)し、その他の器官・組織は 10%中性緩衝ホルマリン溶液に固定した。

なお、途中剖検例、未分娩例、未交尾例および全哺育児が死亡した例の器官重量値は評価対象から除外した。

⑮病理組織学的検査

剖検した動物のうち、雄およびサテライト群の雌の投与終了時剖検では対照群ならびに高用量群の動物番号が若い各 5 例、分娩雌の投与終了時剖検では哺育 5 日に採血した対照群ならびに高用量群の各 5 例について、組織学的検査対象器官のヘマトキシリン・エオジン(HE)標本を作製し、病理組織学的検査を実施した。剖検時に肉眼的異常がみられた器官・組織に関しても病理組織学的検査を実施した。なお、高用量群で被験物質の影響と考えられる変化は認められなかったが、回復終了時の器官重量測定において、雄では甲状腺に、雌では卵巣と副腎に重量の増加が認められたため、病理組織学的検査を実施した。

2) 出生児(F₁)

①出生児の観察

哺育 0 日に生存児数および死亡児数を雌雄別に数えて、性別および外表奇形の有無を観察し、分娩率[(産児数/着床痕数)×100, %]、生児出産率[(出産生児数/着床痕数)×100, %]、出産率[(生児出産雌数/妊娠動物数)×100, %]および出生率[(出産生児数/産児数)×100, %]を算出した。また、哺育 0~4 日まで、毎日、一般状態を観察し、生存児数と死亡児数を雌雄別に数え、新生児生存率[(哺育 4 日の生児数/哺育 0 日の生児数)×100, %]を算出した。生存児については、哺育 0 および 4 日に個別の体重を測定し、腹ごとに雌雄別の平均体重を算出するとともに、哺育 0 日および 4 日における性比[(雄生児数/総生児数)×100, %]を算出した。

②剖検

死亡児は外表奇形の有無を観察して剖検し、10%中性緩衝ホルマリン溶液に固定して保存した。生存児は哺育 4 日に外表奇形の有無を観察してセボフルラン吸入麻酔下に放血致死させて剖検し、内部器官の異常の有無を観察した。

6. データの解析法

交尾率、妊娠率(受胎率)については Fisher の直接確率検定を行った(有意水準:5%)。投与後に性周期が変化した動物はいなかった。被験物質投与群の病理組織学的検査所見のうち、グレード分けしたデータは Mann-Whitney の U 検定により、また陽性グレードの合計値は Fisher の直接確率の片側検定により対照群との間の有意差検定を行った(有意水準:5%)。

その他のデータは、個体ごとに得られた値あるいは litter ごとの平均値を 1 標本とし、サテライト群内あるいはその他の群内で比較した。その際、解析の対象が 2 群の場合には、まず F 検定を行い、有意差が認められなければ Student's-t 検定を行った。F 検定において有意差が認められた場合は、Aspin-Welch 検定を行った。解析の対象が 3 群以上の場合は、先ず、Bartlett の方法により各群の分散の一意性について検定(有意水準:5%)を行った。分散が一意であった場合には、一元配置型の分散分析(有意水準:5%)を行い、群間に有意性が認められた場合は、Dunnett 法により多重比較を行った(有意水準:5%)。一方、いずれかの群で分散が 0 となった場合および分散が一意でなかった場合には、Kruskal-Wallis の順位検定(有意水準:5%)を行い、群間に有意性が認められた場合には、Dunnett 型の検定法により多重比較を行った(有意水準:5%)。

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

試験計画書では、高用量群[非交配(サテライト)群]の雌の動物番号を F06059～F06068 としていたが、試験システムの入力ミスにより同群の雌の動物番号は F06056～F06065 となった。しかし、群番号および各群の動物数に変更はないことから、試験への影響はないと判断し、試験計画書変更書を作成して、試験システム上で付した動物番号を本試験のすべてに適用した。

2015 年 11 月 12 日 11:00～14:28 に受変電設備の定期点検のために停電し、それに伴い動物飼育室内の照明が消え、同日の 11:00～14:39 に空調が停止した。しかし、いずれの動物の一般状態にも上述事象に起因したと考えられる変化は認められず、飼育室の温湿度(23.0～24.5℃、52.0～67.0%)は許容範囲内であったことから、試験への影響はないと判断した。

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

試験成績

1. 親動物

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

投与期間中の雄では、300 mg/kg 群の 2 例に投与後の一過性の流涎が 2 回観察された。その他、歯の欠損が 100 mg/kg 群の 1 例に、頸部の痂皮形成が 100 mg/kg 群の 2 例に観察されたが、いずれも被験物質投与の影響とは考えなかった。なお、対照群の 1 例では、投与 15 日の詳細な症状観察(後述)で発見された歩行異常に加え、下腹部の汚れが投与 16 日以降の一般状態観察でもみられたため、投与 18 日の投与後に安楽死させ、剖検した。回復期間中の雄に一般状態の異常は観察されなかった。

投与期間中の雌では、頸部の痂皮形成が対照群および 300 mg/kg 群の妊娠雌各 1 例に観察されたが、被験物質投与の影響とは考えなかった。非交配雌を含むその他の雌動物には、一般状態の異常は

認められなかった。回復期間中の雌に一般状態の異常は観察されなかった。

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

雄では、投与 15 日の観察で対照群の 1 例に歩行異常と撤去反射の低下が、投与 30 日の観察で対照群の 1 例に常同行動(立ち上がり)が観察された。しかし、雌雄とも、投与期間ならびに回復期間を通して、詳細な症状観察で被験物質投与の影響を示す変化は認められなかった。

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

投与期間中の雄では、300 mg/kg 群に体重増加抑制がみられ、投与 42 日の体重が対照群と比較して有意に低下した。回復期間中の雄では対照群と 300 mg/kg 群との間に有意差は認められなかった。

非交配雌および交配雌ともに、投与期間ならびに回復期間を通して、被験物質投与の影響を示す体重の変化は認められなかった。また、妊娠期および哺育期の体重推移にも被験物質投与の影響は認められなかった。

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

雄では、投与期間および回復期間を通して被験物質投与の影響を示す摂餌量の変化は認められなかった。

交配雌では、交配前、妊娠期および哺育期の摂餌量に被験物質投与の影響は認められなかった。非交配雌では、300 mg/kg 群の投与 7~8 日および投与 35~36 日の摂餌量が対照群と比較して有意に低下したが、回復期間の摂餌量に被験物質投与の影響は認められなかった。

5) 機能検査

① 刺激に対する感覚運動反応 (Table 15~Table 16, Appendix 15-1~Appendix 16-6)

投与最終週に実施したプライエル反応、瞳孔反射、視覚定位、驚愕反応、後肢引込み反射、眼瞼反射、正向反射の検査では、非交配雌を含む雌雄いずれの群の検査対象動物においても異常は認められなかった。

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

雄および分娩雌では、投与最終週に測定した前肢および後肢の握力に、被験物質投与の影響を示す変化は認められなかった。

非交配雌では、投与最終週に測定した 300 mg/kg 群の前肢の握力(平均 1.080 kg)が対照群と比較して有意に増加したが、背景データの範囲(平均±2SD:0.983±0.512 kg)内であったことから、被験物質の影響ではないと判断した。回復終了週に測定した前肢および後肢の握力に、被験物質投与の影響は認められなかった。

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

雄、分娩雌および非交配雌では、投与最終週に実施した自発運動量の測定結果に、被験物質投与の影響を示す変化は認められなかった。

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

雄について実施した投与最終週の尿検査では、300 mg/kg 群の尿量が対照群より増加する傾向にあり、同群の尿比重とカリウムイオン濃度が対照群と比較して有意に低下した。回復 13 日の尿検査では、

300 mg/kg 群のカリウムイオン排泄量が対照群と比較して有意に増加した。

非交配雌の尿検査では、投与最終週および回復 13 日の尿検査で被験物質投与の影響を示す変化は認められなかった。

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

①雄動物

投与終了時の雄では、300 mg/kg 群の白血球数が対照群と比較して有意に低下した。その他、100 mg/kg 群の赤血球数およびヘマトクリット値が、対照群と比較して有意に低下したが、用量に依存した変化ではなかった。

回復終了時の雄では、いずれの検査項目についても被験物質投与の影響を示す変化は認められなかった。

②雌動物

投与終了時の分娩雌では、300 mg/kg 群の単球比率が対照群と比較して有意に増加したが、その差は僅かであり、被験物質投与の影響を示す変化ではないと判断した。

投与終了時の非交配雌では、いずれの検査項目についても被験物質投与の影響を示す変化は認められなかった。

回復終了時の非交配雌では、300 mg/kg 群のヘマトクリット値が対照群と比較して有意に低下した。

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

①雄動物

投与終了時および回復終了時の雄では、いずれの検査項目についても被験物質投与の影響を示す変化は認められなかった。

②雌動物

投与終了時の分娩雌では、いずれの検査項目についても被験物質投与の影響を示す変化は認められなかった。

投与終了時の非交配雌では、300 mg/kg 群の尿素窒素濃度が対照群と比較して有意に低下したが、増加とは逆の変化であったことから、被験物質投与の影響とは考えなかった。

回復終了時の非交配雌では、300 mg/kg 群の塩素イオン濃度が対照群と比較して有意に低下した。

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

①雄動物

投与終了時の雄では、300 mg/kg 群において脳、腎臓、精巣、精囊および副腎の相対重量が対照群と比較して有意に増加したが、これらは解剖時体重の低下に伴う変化であり、被験物質投与が及ぼす器官重量への変化とは考えなかった。

回復終了時の雄では、300 mg/kg 群において甲状腺の絶対重量および相対重量が対照群と比較して有意に増加したが、その他の器官重量に対照群と 300 mg/kg 群との間で有意差は認められなかった。

②雌動物

投与終了時の分娩雌では、300 mg/kg 群において卵巣の相対重量が対照群と比較して有意に増加

した。その他、100 mg/kg 群において脳の絶対重量が対照群と比較して有意に低下したが、用量に依存した変化ではなかった。

投与終了時の非交配雌では、いずれの器官重量にも被験物質投与の影響は認められなかった。

回復終了時の非交配雌では、300 mg/kg 群において卵巣の絶対重量および相対重量が対照群と比較して有意に増加し、左副腎の絶対重量および相対重量と左右を合計した副腎の相対重量が対照群と比較して有意に増加した。

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

投与終了時ならびに回復観察終了時の雄の剖検では、被験物質の投与によると考えられる肉眼的異常は認められなかった。なお、歩行異常がみられ途中解剖した対照群の 1 例では、脾臓の大型化、胸腺の小型化、膀胱の膨満、下腹部の汚れ、右後肢の腫脹、腰部の脊柱管内に出血が観察された。

投与終了時の分娩雌および非交配雌、さらには回復観察終了時の非交配雌の剖検では、被験物質の投与によると考えられる肉眼的異常は認められなかった。また、全哺育児が死亡した例、不妊例および未交尾例についても、被験物質の影響と考えられる肉眼的異常は認められなかった。

11) 病理組織学的検査所見 (Table 33-1~Table 34-3, Appendix 33-1~Appendix 34-3)

投与終了時の雄の病理組織学的検査では、いずれの所見も程度および発生頻度に対照群と 300 mg/kg 群との間に差は認められなかった。なお、途中解剖した対照群の 1 例では、骨髄において白血病細胞が顕著にみられた他、脾臓の赤脾髄、肝臓の類洞、および脊柱管内にも白血病細胞が認められ、その転移性および細胞形態から骨髄性白血病と判断した。

回復観察例の雄では、器官重量測定において甲状腺の重量が増加したが、病理組織学的検査では、被験物質の影響を示す変化は認められなかった。

投与終了時の分娩雌および非交配雌の病理組織学的検査では、いずれの所見も程度および発生頻度に対照群と 300 mg/kg 群との間に差は認められなかった。

回復観察例の非交配雌では、器官重量測定において副腎と卵巣の重量が増加したが、病理組織学的検査では、被験物質の影響を示す変化は認められなかった。

2. 生殖能力

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

4 あるいは 5 日間隔の性周期が投与開始後にそれ以外の性周期に変化した動物は、いずれの投与群にも認められず、平均発情回帰日数にも対照群と各被験物質投与群との間に有意差はなかった。

交配の結果、100 mg/kg 群では交尾が確認されなかった例が 1 組みられ、30 mg/kg 群では不妊が 1 例みられたが、300 mg/kg 群では全例で交尾が確認され、いずれも妊娠した。同居開始日から交尾確認日までの日数およびその間に回帰した発情期の回数に被験物質投与の影響は認められなかった。

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

分娩例の出産率および妊娠期間には、対照群と各被験物質投与との間に有意差は認められなかった。

3) 分娩および哺育状態

300 mg/kg 群の 1 例(動物番号 F04037)では、分娩時間の延長が観察され、分娩が完了した日に全児が死亡した。また、100 mg/kg 群の 1 例(動物番号 F03028)では分娩完了後に児を集めない状況が観察され、哺育 1 日に全児の死亡が確認された。その他の母動物に分娩状態の異常および哺育状態の異常は観察されなかった。

4) 黄体数、着床数および着床率 (Table 37, Appendix 37-1~Appendix 37-4)

黄体数、着床数および着床率に、被験物質投与の影響を示す変化は認められなかった。

3. 出生児

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

産児数、出産生児数、分娩率、生児出産率、出生率、哺育 0 日および哺育 4 日の性比、新生児生存率に被験物質投与の影響は認められなかった。また、哺育 0 日に生存産児の外表奇形は観察されなかった。

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

哺育 0 日および哺育 4 日に測定した出生児体重には、雌雄とも被験物質投与の影響を示す変化は認められなかった。

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

出生児の一般状態に被験物質投与の影響を示す変化はみられなかった。また、死亡児の剖検では、100 mg/kg 群の 1 例に小顎、無眼、口蓋裂および小脳の複合奇形がみられたが、その他の死亡児に異常は認められなかったこと、生存産児に外表奇形は観察されていないことから、自然発生奇形と判断した。哺育 4 日の生存児の剖検では、異常は認められなかった。

考察

シクロペンタノンを 0、30、100 ならびに 300 mg/kg の用量で雌雄ラットに強制経口投与し、雌雄ラットに対する反復投与毒性および回復性、ならびに生殖発生毒性および新生児の発育に及ぼす影響について検討した。

1. 反復投与毒性および回復性

投与期間中の一般状態観察では、300 mg/kg 群の雄 2 例に投与後の流涎がみられたのみで、詳細な症状観察や機能検査においても被験物質投与の影響は認められなかった。14 日間反復投与した予備試験(試験番号 R-15-004)では、1000 mg/kg 群の雌雄全例と 500 mg/kg 群の雄 1 例が瀕死状態となり、これらの例では投与後の流涎が継続してみられた他、流涙、ふらつき歩行、自発運動の低下などの神経症状が観察されている。したがって、シクロペンタノンの 300 mg/kg は、42 日間反復投与しても神経毒性を発症しない投与量と推定される。なお、構造式が類似のシクロペンタンやシクロヘキサンにも、麻

酔作用があることが知られている²⁾。その他、シクロペンタノン³⁾は弱い皮膚刺激性を有する(製品安全データシートより)ことから、本試験で認められた投与後の一過性の流涎は刺激性によるものと推察される。

投与期間中は、300 mg/kg 群の雄において投与 42 日の体重が対照群と比較して有意に低下し、同群の非交配雌において投与 7~8 日および投与 35~36 日の摂餌量が対照群と比較して有意に低下したことから、これらの変化はいずれも被験物質投与の影響と考えられる。なお、予備試験(試験番号 R-15-004)においても、500 mg/kg 群の雄に体重減少がみられ、250 mg/kg 群の雌に体重の増加抑制傾向が認められている。

投与最終週の尿検査では、300 mg/kg 群の雄において尿比重とカリウムイオン濃度が低下した。これは同群の尿量が増加したことに伴う変化で、被験物質の刺激性に関連した飲水量の増加が疑われる。

投与終了時の血液学的検査では、300 mg/kg 群において雄の白血球数(平均 $75.0 \times 100/\mu\text{L}$)が有意に低下したが、背景データ¹⁾の範囲(平均 $\pm 2\text{SD}$: $91.8 \pm 21.8 \times 100/\mu\text{L}$)内であること、回復観察終了時の対照群に比べると投与終了時の対照群の値は高値であることから、偶発的な変化と考えられる。その他、投与終了時の器官重量の測定では、300 mg/kg 群の分娩雌において卵巣の相対重量が有意に増加したが、病理組織学的検査で卵巣に異常は認められていないことから、被験物質投与の影響を示す変化ではないと判断した。

回復観察中は、雌雄の体重推移および摂餌量に被験物質投与の影響はみられなかった。回復 13 日の尿検査では、300 mg/kg 群の雄においてカリウムイオン排泄量が増加したが、投与最終週の尿検査で同様の変化は認められていないことから、被験物質投与の影響ではないと考えられる。また、回復観察終了時の血液学的検査では、300 mg/kg 群において非交配雌のヘマトクリット値が有意に低下したが、その他の検査値や病理組織学的検査で貧血を示す変化が観察されていないことから、被験物質投与の影響ではないと判断した。回復観察終了時の血液生化学的検査では、300 mg/kg 群において非交配雌の塩素イオン濃度(平均 109.7 mEq/L)が有意に低下したが、背景データ¹⁾の範囲(平均 $\pm 2\text{SD}$: 108.4 ± 2.0 mEq/L)内であることから、被験物質の影響ではないと判断した。

回復終了時の器官重量の測定では、300 mg/kg 群の雄において甲状腺の重量(平均 23.3 mg)が対照群と比較して有意に増加したが、背景データ¹⁾の範囲(平均 $\pm 2\text{SD}$: 20.1 ± 5.4 mg)内であり、病理組織学的検査でも異常は認められていないことから、被験物質の影響ではないと判断した。また、同群の非交配雌において卵巣および副腎の絶対重量あるいは相対重量が有意に増加したが、病理組織学的検査で異常は認められていないことから、対照群の値が偶発的に低下したことによるものと推察される。

2. 生殖発生毒性

分娩状態の観察では、300 mg/kg 群と 100 mg/kg 群の各 1 例に異常がみられたが、その他の分娩例に異常は認められなかったこと、妊娠期間に群間の差はなかったことから、被験物質投与の影響を示す変化ではないと判断した。なお、300 mg/kg 群では分娩日の死亡児数が対照群より増加したが、上記 1 例の分娩異常に伴った変化であり、その他の分娩例で死亡児数が増加する傾向はなかったことから、被験物質投与の影響ではないと判断した。

本物質を COBS-CD ラット(25 匹/群)の妊娠 6 日から妊娠 15 日まで強制経口投与した実験³⁾では、300 mg/kg 群で母動物の体重増加抑制と胎児体重の低下が報告されているが、本試験では、妊娠中の体重推移および産児の体重に被験物質投与の影響は認められなかった。試験結果の相違については、一群当たりのサンプル数や投与期間の違いが原因と考えられる。また、被験物質投与群の交配成績、性周期、出産率、黄体数、着床数および着床率に、被験物質投与の影響を示す変化は認められなかったこと、さらに出生児の生存率、体重および形態にも被験物質投与の影響は認められなかったことから、シクロペンタノンの 300 mg/kg までの用量は、親動物の生殖能力および新生児の発育に影響を及ぼさないと考えられる。

3. 無毒性量

300 mg/kg 群の雄で体重増加抑制、非交配雌で摂餌量の低下が認められたことから、雌雄動物の反復投与毒性に関する無毒性量(NOEL)は 100 mg/kg/day と判断された。また、300 mg/kg までの用量は、親動物の生殖能力および新生児の発育に影響を及ぼさなかったことから、生殖発生毒性に関する無毒性量は 300 mg/kg/day と判断された。

文献

- 1) [redacted] ラットを用いる反復経口投与毒性・生殖発生毒性併合試験の背景データ:媒体対照群の比較. 秦野研究所年報 37: 8-25 (2014)
- 2) Fang Z, Sonner J, Laster MJ, Ionescu P, Kandel L, Koblin DD, Eger EI 2nd, Halsey MJ.: Anesthetic and convulsant properties of aromatic compounds and cycloalkanes: implications for mechanisms of narcosis. *Anesth Analg.* 83:1097-1104 (1996)
- 3) Scognamiglio J, Jones L, Letizia CS, Api AM.: Fragrance material review on cyclopentanone. *Food Chem Toxicol.* 50: S608-S612 (2012)

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

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

Group	Number of males and general conditions	Days of recovery														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Control (vehicle: corn oil)	Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	General appearance, No abnormality	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
CPN 300 mg/kg	Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	General appearance, No abnormality	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5

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

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

Group	Number of females and general conditions	Days of recovery														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Control (vehicle: corn oil)	Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	General appearance, No abnormality	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
CPN 300 mg/kg	Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	General appearance, No abnormality	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5

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

Table 3. General conditions in dams during pregnancy

Group	Number of dams and general conditions	Days of pregnancy																											
		0		1		2		3		4		5		6		7		8		9		10		11		12		13	
		Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Control (vehicle: corn oil)	Number of dams	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	
	General appearance, No abnormality	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	
	Neck, Crust formation	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
CPN 30 mg/kg	Number of dams	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	
	General appearance, No abnormality	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	
	Neck, Crust formation	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
CPN 100 mg/kg	Number of dams	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	
	General appearance, No abnormality	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	
	Neck, Crust formation	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
CPN 300 mg/kg	Number of dams	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	
	General appearance, No abnormality	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	
	Neck, Crust formation	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	

Pre: Before administration, Post: after administration.

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

Group	Number of dams and general conditions	Days of pregnancy																			
		14		15		16		17		18		19		20		21		22		23	
		Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Control (vehicle: corn oil)	Number of dams	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	6	6	0	0	
	General appearance, No abnormality	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	6	6	0	0	
	Neck, Crust formation	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	0	0	0	
CPN 30 mg/kg	Number of dams	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	5	5	0	0	
	General appearance, No abnormality	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	5	5	0	0	
	Neck, Crust formation	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
CPN 100 mg/kg	Number of dams	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	5	5	0	0	
	General appearance, No abnormality	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	5	5	0	0	
	Neck, Crust formation	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
CPN 300 mg/kg	Number of dams	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	8	8	1	1	
	General appearance, No abnormality	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	8	8	1	1	
	Neck, Crust formation	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	0	0	0	

Pre: Before administration, Post: after administration.

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

Table 4. General conditions in dams during lactation

Group	Number of dams and general conditions	Days of lactation											
		0		1		2		3		4		5	
		Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Control (vehicle: corn oil)	Number of dams	5	5	12	12	12	12	12	12	12	12	12	12
	General appearance, No abnormality	5	5	12	12	12	12	12	12	12	12	12	12
CPN 30 mg/kg	Number of dams	8	8	11	11	11	11	11	11	11	11	11	11
	General appearance, No abnormality	8	8	11	11	11	11	11	11	11	11	11	11
CPN 100 mg/kg	Number of dams	8	8	11	10	10	10	10	10	10	10	10	10
	General appearance, No abnormality	8	8	11	10	10	10	10	10	10	10	10	10
CPN 300 mg/kg	Number of dams	6	5	11	11	11	11	11	11	11	11	11	11
	General appearance, No abnormality	6	5	11	11	11	11	11	11	11	11	11	11

Pre: Before administration, Post: after administration.

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

Table 5. Detailed clinical observations of male rats

Findings	Group	Initial number of animals	Pre-administration	Days of administration						Days of recovery ^a	
				8	15	24	30	36	42	7	14
[Open-field observations]	Control (vehicle: corn oil)	12	0 ^b	0	1	0 (11)	0 (11)	0 (11)	0 (11)	0	0
Gait (abnormal gait)	CPN 30 mg/kg	12	0	0	0	0	0	0	0		
	CPN 100 mg/kg	12	0	0	0	0	0	0	0		
	CPN 300 mg/kg	12	0	0	0	0	0	0	0	0	0
[Open-field observations]	Control (vehicle: corn oil)	12	0 ^b	0	0	0 (11)	1 (11)	0 (11)	0 (11)	0	0
Stereotypy (rearing)	CPN 30 mg/kg	12	0	0	0	0	0	0	0		
	CPN 100 mg/kg	12	0	0	0	0	0	0	0		
	CPN 300 mg/kg	12	0	0	0	0	0	0	0	0	0
[Open-field observations]	Control (vehicle: corn oil)	12	0 ^b	0	1	0 (11)	0 (11)	0 (11)	0 (11)	0	0
Withdrawal reflex (hyporeflexia)	CPN 30 mg/kg	12	0	0	0	0	0	0	0		
	CPN 100 mg/kg	12	0	0	0	0	0	0	0		
	CPN 300 mg/kg	12	0	0	0	0	0	0	0	0	0

^a the recovery test was performed in 5 animals for each of the 0 and 300 mg/kg groups

^b Values represent number of animals with the findings.

Figures in parentheses indicate number of animals.

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

Table 5 (continued). Detailed clinical observations of male rats

Findings	Group	Initial number of animals	Pre-administration	Days of administration						Days of recovery ^a	
				8	15	24	30	36	42	7	14
[Urination] (frequency/30sec)	Control (vehicle: com oil)	12	1 ^b	2	2	4 (11)	2 (11)	2 (11)	2 (11)	1	0
	CPN 30 mg/kg	12	3	1	1	1	0	0	1		
	CPN 100 mg/kg	12	0	2	2	1	3	3	0		
	CPN 300 mg/kg	12	0	0	1	0	2	1	0	0	2
[Defecation] (frequency/30sec)	Control (vehicle: com oil)	12	0 ^b	0	1	1 (11)	1 (11)	0 (11)	0 (11)	0	0
	CPN 30 mg/kg	12	0	0	0	0	0	0	0		
	CPN 100 mg/kg	12	0	0	0	0	0	0	0		
	CPN 300 mg/kg	12	0	0	0	0	1	0	0	0	0

^a the recovery test was performed in 5 animals for each of the 0 and 300 mg/kg groups

^b Values represent total score of each group.

Figures in parentheses indicate number of animals.

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

Table 6-1. Detailed clinical observations of female rats

Findings	Group	Initial number of animals	Pre-administration	Days of administration						The lactation period	
				8	15	24	30	36	42		49
[Urination] (frequency/30sec)	Control (vehicle: corn oil)	12	1 ^a	0	0	1	1	1			2
	CPN 30 mg/kg	12	2	0	0	1	1	1			1 (11)
	CPN 100 mg/kg	12	0	1	0	0	0	0	0 (1)	0 (1)	1 (11)
	CPN 300 mg/kg	12	0	0	0	0	1	1			3 (11)
[Defecation] (frequency/30sec)	Control (vehicle: corn oil)	12	0 ^a	0	0	0	0	0			1
	CPN 30 mg/kg	12	0	0	0	0	0	0			0 (11)
	CPN 100 mg/kg	12	0	0	0	0	0	0	0 (1)	0 (1)	0 (11)
	CPN 300 mg/kg	12	0	0	0	0	0	0			0 (11)

^a Values represent total score of each group.
 Figures in parentheses indicate number of animals.

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

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

Findings	Group	Initial number of animals	Pre-administration	Days of administration						Days of recovery ^a	
				8	15	24	30	36	42	7	14
[Urination] (frequency/30sec)	Control (vehicle: corn oil)	10	0 ^b	0	0	0	0	0	0	1	1
	CPN 300 mg/kg	10	1	0	0	0	0	0	0	1	0
[Defecation] (frequency/30sec)	Control (vehicle: corn oil)	10	0 ^b	0	0	0	0	0	0	0	0
	CPN 300 mg/kg	10	0	0	0	0	0	0	0	0	0

^a the recovery test was performed in 5 animals for each of the 0 and 300 mg/kg groups

^b Values represent number of animals with the findings.

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

Table 7-1. Body weights of male rats

Group	Control (vehicle: corn oil)		CPN 30 mg/kg		CPN 100 mg/kg		CPN 300 mg/kg	
Number of males	12		12		12		12	
Days of administration								
1	405.4	± 16.4	404.0	± 14.8	402.0	± 15.5	406.7	± 15.7
4	416.4	± 15.4	415.7	± 17.3	415.5	± 17.9	415.9	± 18.2
7	430.0	± 15.8	426.3	± 17.7	427.7	± 19.6	421.7	± 22.2
14	453.1	± 15.5	447.2	± 20.2	453.1	± 20.6	438.1	± 26.6
21	472.8	± 19.5 (11)	467.4	± 24.0	461.4	± 36.2	451.0	± 25.3
28	497.8	± 18.1 (11)	492.0	± 27.7	485.0	± 35.6	469.7	± 28.1
35	516.3	± 18.8 (11)	510.8	± 34.9	505.6	± 35.2	483.7	± 30.9
42	530.5	± 16.2 (11)	525.1	± 38.5	519.5	± 38.9	493.3	± 30.5 *

Each value shows mean (g) ± S.D.

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

Figures in parentheses indicate number of males.

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

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

Group	Control (vehicle: corn oil)	CPN 300 mg/kg
Number of males	5	5
Days of recovery		
1	525.6 ± 20.4	518.5 ± 27.5
7	535.8 ± 20.4	538.7 ± 32.1
14	541.2 ± 21.7	560.1 ± 29.6

Each value shows mean (g) ± S.D.

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

Table 8-1. Body weights of female rats

Group	Control (vehicle: corn oil)	CPN 30 mg/kg	CPN 100 mg/kg	CPN 300 mg/kg
Number of females	12	12	12	12
Days of administration				
1	243.5 ± 13.1	241.4 ± 10.9	243.9 ± 9.4	244.0 ± 9.7
4	250.3 ± 14.6	246.8 ± 13.6	250.5 ± 10.4	249.2 ± 12.3
7	252.0 ± 13.7	250.4 ± 13.4	252.1 ± 11.9	253.1 ± 12.3
14	264.2 ± 18.9	261.2 ± 16.2	265.9 ± 14.6	261.1 ± 12.6

Each value shows mean (g) ± S.D.

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

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

Group	Control (vehicle: corn oil)		CPN 300 mg/kg	
Number of females	10		10	
Days of administration				
1	241.2	± 14.5	241.4	± 10.5
4	252.3	± 15.3	247.9	± 11.8
7	252.3	± 17.2	249.3	± 13.5
14	263.1	± 18.0	253.8	± 11.6
21	271.0	± 23.5	265.2	± 14.2
28	280.1	± 23.6	273.8	± 14.0
35	286.8	± 23.2	277.8	± 12.6
42	294.1	± 23.3	283.3	± 17.0

Each value shows mean (g) ± S.D.

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

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

Group	Control (vehicle: corn oil)		CPN 300 mg/kg	
Number of females	5		5	
Days of recovery				
	1	296.4 ± 33.3	283.6 ± 20.3	
	7	300.9 ± 33.2	288.5 ± 18.3	
	14	304.4 ± 32.4	294.0 ± 23.0	

Each value shows mean (g) ± S.D.

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

Table 9. Body weights of dams during pregnancy

Group	Control (vehicle: corn oil)	CPN 30 mg/kg	CPN 100 mg/kg	CPN 300 mg/kg
Number of dams	12	11	11	12
Days of pregnancy				
0	275.6 ± 21.4	269.5 ± 16.2	274.1 ± 13.0	268.3 ± 15.2
7	313.9 ± 23.6	306.3 ± 19.1	310.1 ± 16.0	306.2 ± 13.9
14	352.5 ± 28.5	344.3 ± 20.9	347.6 ± 19.1	346.1 ± 16.9
20	436.7 ± 35.6	429.5 ± 22.9	428.8 ± 21.5	429.1 ± 21.0

Each value shows mean ± S.D. (g).

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

Table 10. Body weights of dams during lactation

Group	Control (vehicle: corn oil)	CPN 30 mg/kg	CPN 100 mg/kg	CPN 300 mg/kg
Number of dams	12	11	11	12
Days of lactation				
0	339.3 ± 29.8	322.0 ± 28.4	336.1 ± 35.8	329.3 ± 27.3
4	350.0 ± 29.1	337.0 ± 23.9	351.7 ± 17.6 (10)	339.9 ± 16.0 (11)

Each value shows mean ± S.D. (g).

Figures in parentheses indicate number of dams.

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

Table 11-1. Food consumption of male rats

Group	Control (vehicle: corn oil)		CPN 30 mg/kg		CPN 100 mg/kg		CPN 300 mg/kg	
Number of males	12		12		12		12	
Days of administration								
	1	25.6 ± 3.2		27.0 ± 2.4		27.1 ± 3.1		24.7 ± 2.3
	7	24.4 ± 1.9		23.5 ± 2.2		26.2 ± 3.0		24.1 ± 2.9
	14	22.4 ± 2.0		23.3 ± 2.6		23.5 ± 2.7		21.2 ± 2.3
	29	25.6 ± 2.2 (11)		26.8 ± 3.1		25.5 ± 2.5		24.1 ± 1.8
	35	24.8 ± 2.7 (11)		25.7 ± 2.5		24.2 ± 1.8		22.5 ± 3.3
	41	23.8 ± 3.4 (11)		24.8 ± 2.7		26.1 ± 3.2		22.7 ± 2.1

Each value shows mean (g) ± S.D.

Figures in parentheses indicate number of males.

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

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

Group	Control (vehicle: corn oil)		CPN 300 mg/kg	
Number of males	5		5	
Days of recovery				
	6	29.8 ± 2.6	30.6 ± 1.5	
	12	29.6 ± 2.6	32.3 ± 1.5	

Each value shows mean (g) ± S.D.

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

Table 12-1. Food consumption of female rats

Group		Control (vehicle: corn oil)	CPN 30 mg/kg	CPN 100 mg/kg	CPN 300 mg/kg
Number of females		12	12	12	12
Days of administration					
	1	17.8 ± 3.0	17.8 ± 3.6	18.6 ± 2.2	17.7 ± 3.2
	7	18.7 ± 2.9	18.5 ± 2.9	18.3 ± 2.7 (10)	17.5 ± 2.5
	14	16.3 ± 3.0	16.4 ± 2.6	16.2 ± 3.1	15.8 ± 3.7

Each value shows mean (g) ± S.D.

Figures in parentheses indicate number of females.

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

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

Group	Control (vehicle: corn oil)		CPN 300 mg/kg	
Number of females	10		10	
Days of administration				
1	17.9	± 3.0	16.0	± 2.4
7	19.4	± 2.2	16.9	± 1.8 *
14	17.5	± 2.2	16.8	± 1.3
21	17.1	± 2.2	16.1	± 2.9
29	17.2	± 1.9	16.5	± 1.8
35	18.3	± 2.4	16.0	± 2.4 *
41	18.2	± 2.1	16.5	± 2.9

Each value shows mean (g) ± S.D.

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

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

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

Group	Control (vehicle: corn oil)		CPN 300 mg/kg	
Number of females	5		5	
Days of recovery				
	6	20.6 ± 3.4	21.5 ± 2.4	
	12	20.3 ± 2.4	20.0 ± 2.5	

Each value shows mean (g) ± S.D.

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

Table 13. Food consumption in dams during pregnancy

Group	Control (vehicle: corn oil)	CPN 30 mg/kg	CPN 100 mg/kg	CPN 300 mg/kg
Number of dams	12	11	11	12
Days of pregnancy				
0	19.6 ± 3.7	18.2 ± 2.0	18.1 ± 3.0	18.9 ± 1.4
7	25.6 ± 3.6	23.9 ± 2.1	25.1 ± 3.6	24.1 ± 1.7
14	24.5 ± 2.8	24.3 ± 3.0	24.8 ± 2.6	23.0 ± 1.8
20	20.1 ± 3.4	20.1 ± 3.7	23.4 ± 3.4	21.8 ± 3.9

Each value shows mean ± S.D. (g).

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

Table 14. Food consumption in dams during lactation

Group	Control (vehicle: corn oil)	CPN 30 mg/kg	CPN 100 mg/kg	CPN 300 mg/kg
Number of dams	12	11	10	11
Days of lactation	3			
	40.9 ± 7.1	41.5 ± 7.5	39.9 ± 7.8	38.3 ± 8.8

Each value shows mean ± S.D. (g).

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

Table 15. Functional findings of male rats at the last week of the administration period

Group	Control (vehicle: com oil)	CPN 30 mg/kg	CPN 100 mg/kg	CPN 300 mg/kg
<u>Male</u>				
Number of animals	5	5	5	5
Righting reflex	100	100	100	100
Visual placing	100	100	100	100
Pupillary reflex	100	100	100	100
Startle reaction	100	100	100	100
Preyer's reaction	100	100	100	100
Withdrawal reflex	100	100	100	100
Eyelid reflex	100	100	100	100

Values represent % of animals showing normal responses.

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

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

Group	Control (vehicle: com oil)	CPN 30 mg/kg	CPN 100 mg/kg	CPN 300 mg/kg
<u>Female, dam</u>				
Number of animals	5	5	5	5
Righting reflex	100	100	100	100
Visual placing	100	100	100	100
Pupillary reflex	100	100	100	100
Startle reaction	100	100	100	100
Preyer's reaction	100	100	100	100
Withdrawal reflex	100	100	100	100
Eyelid reflex	100	100	100	100
<u>Female, satellite group</u>				
Number of animals	5			5
Righting reflex	100			100
Visual placing	100			100
Pupillary reflex	100			100
Startle reaction	100			100
Preyer's reaction	100			100
Withdrawal reflex	100			100
Eyelid reflex	100			100

Values represent % of animals showing normal responses.

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

Table 17. Assessment of grip strength of male rats at the last week of the administration period

Group	Control (vehicle: com oil)	CPN 30 mg/kg	CPN 100 mg/kg	CPN 300 mg/kg
Number of males	5	5	5	5
Administration period				
Forelimb	1.270 ± 0.161	1.309 ± 0.279	1.181 ± 0.239	1.429 ± 0.219
Hindlimb	0.672 ± 0.068	0.689 ± 0.100	0.689 ± 0.260	0.693 ± 0.126

Each value shows mean (kg) ± S.D.

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

Table 18. Assessment of grip strength of female rats at the last week of the administration period

Group	Control (vehicle: corn oil)	CPN 30 mg/kg	CPN 100 mg/kg	CPN 300 mg/kg
Number of females	5	5	5	5
Administration period				
Forelimb	1.110 ± 0.077	1.117 ± 0.159	1.176 ± 0.097	1.086 ± 0.195
Hindlimb	0.546 ± 0.056	0.516 ± 0.043	0.510 ± 0.087	0.478 ± 0.084

Each value shows mean (kg) ±S.D.

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

Table 19-1. Assessment of grip strength of female rats at the last week of the administration period, satellite group

Group	Control (vehicle: corn oil)	CPN 300 mg/kg
Number of females	5	5
Administration period		
Forelimb	0.931 ± 0.060	1.080 ± 0.057 **
Hindlimb	0.516 ± 0.039	0.507 ± 0.047

Each value shows mean (kg) ±S.D.

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

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

Table 19-2 Assessment of grip strength of female rats at the last week of the administration period, recovery group

Group	Control (vehicle: corn oil)	CPN 300 mg/kg
Number of females	5	5
Administration period		
Forelimb	1.105 ± 0.098	1.061 ± 0.063
Hindlimb	0.538 ± 0.093	0.575 ± 0.080

Each value shows mean (kg) ±S.D.

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

Table 20. Motor activity of male rats at the last week of the administration period

Group	Control (vehicle: corn oil)	CPN 30 mg/kg	CPN 100 mg/kg	CPN 300 mg/kg
Number of males	5	5	5	5
Administration period				
Ambulation (counts)				
5min	1224 ± 204	1159 ± 165	1209 ± 208	1219 ± 351
10min	1164 ± 193	1069 ± 152	1014 ± 314	1107 ± 335
15min	941 ± 201	992 ± 215	1025 ± 149	1012 ± 321
20min	904 ± 194	831 ± 216	829 ± 197	939 ± 308
Total	4233 ± 743	4052 ± 638	4077 ± 824	4277 ± 1249
Rearing (counts)				
5min	29 ± 9	30 ± 8	28 ± 12	31 ± 10
10min	23 ± 5	22 ± 6	15 ± 7	22 ± 8
15min	14 ± 6	18 ± 6	17 ± 5	17 ± 10
20min	9 ± 6	13 ± 6	10 ± 6	14 ± 9
Total	75 ± 17	83 ± 20	70 ± 28	84 ± 34

Each value shows mean±S.D.

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

Table 21. Motor activity of female rats at the last week of the administration period

Group	Control (vehicle: corn oil)	CPN 30 mg/kg	CPN 100 mg/kg	CPN 300 mg/kg
Number of females	5	5	5	5
Administration period				
Ambulation (counts)				
5min	1193 ± 103	1076 ± 232	1304 ± 305	1064 ± 69
10min	977 ± 125	925 ± 280	1190 ± 310	848 ± 214
15min	770 ± 144	704 ± 248	860 ± 215	694 ± 147
20min	679 ± 373	559 ± 314	959 ± 542	475 ± 304
Total	3619 ± 512	3265 ± 949	4312 ± 1180	3081 ± 572
Rearing (counts)				
5min	30 ± 10	30 ± 7	32 ± 16	24 ± 10
10min	19 ± 10	22 ± 12	22 ± 8	14 ± 9
15min	6 ± 5	10 ± 9	6 ± 4	7 ± 7
20min	8 ± 12	7 ± 7	18 ± 16	7 ± 9
Total	63 ± 26	70 ± 26	78 ± 37	53 ± 28

Each value shows mean±S.D.

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

Table 22. Motor activity of female rats at the last week of the administration period, satellite group

Group	Control (vehicle: corn oil)		CPN 300 mg/kg	
Number of females	5		5	
Administration period				
Ambulation (counts)				
5min	1162	± 256	1208	± 136
10min	1178	± 215	1125	± 222
15min	1152	± 295	1041	± 201
20min	1015	± 276	999	± 210
Total	4507	± 971	4373	± 708
Rearing (counts)				
5min	35	± 9	32	± 6
10min	37	± 9	35	± 11
15min	33	± 13	19	± 6
20min	29	± 19	22	± 13
Total	133	± 43	109	± 30

Each value shows mean±S.D.

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

Table 23-1. Urinalysis in male rats

Group	Control (vehicle: com oil)	CPN 30 mg/kg	CPN 100 mg/kg	CPN 300 mg/kg
Number of males	5	5	5	5
pH				
6.0	0	1	0	0
6.5	0	0	1	0
7.0	2	2	3	3
7.5	3	0	0	0
8.0	0	2	0	2
8.5	0	0	1	0
Protein				
- (negative)	0	0	0	0
± (10 ≤ and < 30 mg/dL)	0	1	0	1
+ (30 ≤ and < 100 mg/dL)	4	3	3	4
2+ (100 ≤ and < 300 mg/dL)	1	1	2	0
Glucose				
- (negative)	5	5	5	5
Ketone				
- (negative)	0	0	0	0
± (5 ≤ and < 10 mg/dL)	0	2	0	0
+ (10 ≤ and < 40 mg/dL)	5	3	4	4
2+ (40 ≤ and < 80 mg/dL)	0	0	1	1
Bilirubin				
- (negative)	5	5	5	5
Occult blood				
- (negative)	5	5	5	5
Urobilinogen				
± (normal)	2	2	2	3
+ (2.0 ≤ and < 4.0 mg/dL)	3	3	3	2
Color				
light yellow	5	5	5	5
Turbidity				
- (negative)	4	3	5	5
± (trace)	0	0	0	0
+ (slight)	1	2	0	0
Red Blood cells				
- (not observed)	5	5	5	5
White Blood cells				
- (not observed)	5	5	5	5
Casts				
- (not observed)	5	5	5	5
Cristals				
- (not observed)	0	1	0	1
± (a few)	5	4	5	4
+ (abundant)	0	0	0	0
Epithelial cells				
- (not observed)	5	5	5	5

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

Table 23-1. Urinalysis in male rats

Group	Control (vehicle: corn oil)		CPN 30 mg/kg		CPN 100 mg/kg		CPN 300 mg/kg	
Number of males	5		5		5		5	
Urine volume (mL/24hr)	14.5 ± 3.6		19.1 ± 12.2		16.3 ± 3.4		24.3 ± 6.2	
Specific gravity	1.064 ± 0.012		1.054 ± 0.020		1.055 ± 0.007		1.037 ± 0.006 *	
Electrolyte, density								
Na(mEq/L)	112.7 ± 25.0		103.7 ± 46.0		105.3 ± 33.9		62.4 ± 18.6	
K(mEq/L)	268.76 ± 60.90		233.51 ± 104.00		227.98 ± 35.99		146.16 ± 27.87 *	
Cl(mEq/L)	161.4 ± 36.6		143.3 ± 66.0		141.3 ± 38.1		83.0 ± 19.7	
Electrolyte, gross volume								
Na(mEq/24hr)	1.59 ± 0.25		1.57 ± 0.33		1.66 ± 0.38		1.51 ± 0.51	
K(mEq/24hr)	3.75 ± 0.33		3.56 ± 0.75		3.64 ± 0.45		3.44 ± 0.52	
Cl(mEq/24hr)	2.25 ± 0.24		2.14 ± 0.55		2.23 ± 0.37		2.00 ± 0.55	

Each value shows mean ± S.D.

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

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

Table 23-2. Urinalysis in male rats of the recovery period

Group	Control (vehicle: corn oil)	CPN 300 mg/kg
Number of males	5	5
pH		
7.0	0	1
7.5	2	2
8.0	3	2
Protein		
+ (30 ≤ and < 100 mg/dL)	3	4
2+ (100 ≤ and < 300 mg/dL)	2	1
Glucose		
- (negative)	5	5
Ketone		
- (negative)	0	0
± (5 ≤ and < 10 mg/dL)	3	4
+ (10 ≤ and < 40 mg/dL)	2	1
Bilirubin		
- (negative)	5	5
Occult blood		
- (negative)	5	5
Urobilinogen		
± (normal)	1	3
+ (2.0 ≤ and < 4.0 mg/dL)	4	2
Color		
light yellow	4	5
yellow	1	0
Turbidity		
- (negative)	5	5
Red Blood cells		
- (not observed)	5	5
White Blood cells		
- (not observed)	5	5
Casts		
- (not observed)	5	5
Cristals		
- (not observed)	0	0
± (a few)	5	5
+ (abundant)	0	0
Epithelial cells		
- (not observed)	5	5
± (a few)	0	0
+ (abundant)	0	0

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

Table 23-2. Urinalysis in male rats of the recovery period

Group	Control (vehicle: corn oil)		CPN 300 mg/kg	
Number of males	5		5	
Urine volume (mL/24hr)	16.5 ±	4.6	21.1 ±	3.4
Specific gravity	1.065 ±	0.014	1.055 ±	0.010
Electrolyte, density				
Na(mEq/L)	132.3 ±	55.5	103.5 ±	27.1
K(mEq/L)	283.69 ±	75.71	244.42 ±	42.86
Cl(mEq/L)	166.1 ±	59.0	136.0 ±	31.2
Electrolyte, gross volume				
Na(mEq/24hr)	2.00 ±	0.27	2.15 ±	0.48
K(mEq/24hr)	4.42 ±	0.35	5.05 ±	0.49 *
Cl(mEq/24hr)	2.54 ±	0.20	2.81 ±	0.45

Each value shows mean ± S.D.

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

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

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

Group	Control (vehicle: corn oil)	CPN 300 mg/kg
Number of females	5	5
pH		
6.5	5	3
7.0	0	2
Protein		
- (negative)	0	0
± (10 ≤ and < 30 mg/dL)	1	1
+ (30 ≤ and < 100 mg/dL)	4	4
Glucose		
- (negative)	5	5
Ketone		
- (negative)	1	0
± (5 ≤ and < 10 mg/dL)	3	0
+ (10 ≤ and < 40 mg/dL)	1	4
2+ (40 ≤ and < 80 mg/dL)	0	1
Bilirubin		
- (negative)	5	5
Occult blood		
- (negative)	5	5
Urobilinogen		
± (normal)	2	1
+ (2.0 ≤ and < 4.0 mg/dL)	3	4
Color		
light yellow	4	5
yellow	1	0
Turbidity		
- (negative)	5	5
Red Blood cells		
- (not observed)	5	5
White Blood cells		
- (not observed)	5	5
Casts		
- (not observed)	5	5
Cristals		
- (not observed)	3	1
± (a few)	2	4
Epithelial cells		
- (not observed)	5	5

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

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

Group	Control (vehicle: corn oil)		CPN 300 mg/kg	
Number of females	5		5	
Urine volume (mL/24hr)	9.2 ±	3.5	10.1 ±	4.1
Specific gravity	1.064 ±	0.020	1.051 ±	0.014
Electrolyte, density				
Na(mEq/L)	150.3 ±	63.4	95.7 ±	7.8
K(mEq/L)	286.35 ±	102.18	187.46 ±	70.66
Cl(mEq/L)	185.5 ±	80.7	117.9 ±	35.6
Electrolyte, gross volume				
Na(mEq/24hr)	1.24 ±	0.19	0.94 ±	0.30
K(mEq/24hr)	2.43 ±	0.53	1.89 ±	0.94
Cl(mEq/24hr)	1.55 ±	0.38	1.21 ±	0.68

Each value shows mean ± S.D.

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

Table 24-2. Urinalysis in female rats of the recovery period

Group	Control (vehicle: corn oil)	CPN 300 mg/kg
Number of females	5	5
pH		
6.5	1	2
7.0	1	0
7.5	2	2
8.0	1	0
8.5	0	1
Protein		
- (negative)	2	2
± (10 ≤ and < 30 mg/dL)	1	1
+ (30 ≤ and < 100 mg/dL)	2	2
Glucose		
- (negative)	5	5
Ketone		
- (negative)	4	4
± (5 ≤ and < 10 mg/dL)	1	1
Bilirubin		
- (negative)	5	5
Occult blood		
- (negative)	5	5
Urobilinogen		
± (normal)	3	3
+ (2.0 ≤ and < 4.0 mg/dL)	2	2
Color		
light yellow	5	5
Turbidity		
- (negative)	5	5
Red Blood cells		
- (not observed)	5	5
White Blood cells		
- (not observed)	5	5
Casts		
- (not observed)	5	5
Cristals		
- (not observed)	1	1
± (a few)	4	4
Epithelial cells		
- (not observed)	5	5

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

Table 24-2. Urinalysis in female rats of the recovery period

Group	Control (vehicle: corn oil)		CPN 300 mg/kg	
Number of females	5		5	
Urine volume (mL/24hr)	15.8 ±	7.1	13.2 ±	6.0
Specific gravity	1.047 ±	0.019	1.061 ±	0.016
Electrolyte, density				
Na(mEq/L)	89.0 ±	23.6	122.0 ±	25.5
K(mEq/L)	212.87 ±	100.48	284.23 ±	68.14
Cl(mEq/L)	120.4 ±	55.6	159.3 ±	40.2
Electrolyte, gross volume				
Na(mEq/24hr)	1.36 ±	0.57	1.50 ±	0.28
K(mEq/24hr)	3.15 ±	1.26	3.44 ±	0.47
Cl(mEq/24hr)	1.80 ±	0.75	1.94 ±	0.36

Each value shows mean ± S.D.

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

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

Group		Control (vehicle: corn oil)	CPN 30 mg/kg	CPN 100 mg/kg		CPN 300 mg/kg
Number of males		5	5	5		5
RBC	10000/ μ L	797 \pm 24	758 \pm 28	751 \pm 33	*	808 \pm 28
HGB	g/dL	14.5 \pm 0.6	14.2 \pm 0.3	13.5 \pm 0.4		14.2 \pm 0.9
Hematocrit	%	42.9 \pm 1.4	42.1 \pm 0.9	39.8 \pm 0.6	*	41.7 \pm 2.8
MCV	fL	53.8 \pm 1.3	55.7 \pm 1.6	53.1 \pm 2.2		51.7 \pm 2.7
MCH	pg	18.2 \pm 0.4	18.7 \pm 0.5	17.9 \pm 0.6		17.6 \pm 0.8
MCHC	g/dL	33.7 \pm 0.5	33.6 \pm 0.3	33.8 \pm 0.7		34.0 \pm 0.4
Platelet	10000/ μ L	97.0 \pm 13.6	84.7 \pm 8.2	94.6 \pm 15.8		97.3 \pm 10.9
PT	sec.	16.4 \pm 1.7	14.9 \pm 1.3	14.3 \pm 1.3		17.3 \pm 5.5
APTT	sec.	19.7 \pm 2.9	19.7 \pm 2.1	18.7 \pm 1.2		19.8 \pm 2.3
WBC	100/ μ L	101.0 \pm 6.7	78.4 \pm 10.4	77.8 \pm 13.7		75.0 \pm 21.6 *
Neutrophil	%	18.7 \pm 11.2	19.5 \pm 9.1	17.8 \pm 4.1		22.0 \pm 11.7
Eosinophil	%	1.5 \pm 0.6	1.7 \pm 0.9	1.8 \pm 0.2		1.1 \pm 0.5
Basophil	%	0.0 \pm 0.1	0.0 \pm 0.1	0.0 \pm 0.0		0.0 \pm 0.0
Monocyte	%	4.5 \pm 0.9	4.4 \pm 0.8	3.6 \pm 0.5		5.4 \pm 1.3
Lymphocyte	%	75.3 \pm 11.9	74.4 \pm 9.0	76.8 \pm 4.1		71.4 \pm 11.4
Reticulocyte	%	2.86 \pm 0.43	3.11 \pm 0.40	2.98 \pm 0.26		3.11 \pm 0.26

Each value shows mean \pm S.D.

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

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

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

Group		Control (vehicle: corn oil)	CPN 300 mg/kg
		5	5
	Number of males		
RBC	10000/ μ L	821 \pm 33	802 \pm 28
HGB	g/dL	14.3 \pm 0.7	14.4 \pm 0.3
Hematocrit	%	42.4 \pm 1.3	43.0 \pm 0.7
MCV	fL	51.7 \pm 1.3	53.6 \pm 2.2
MCH	pg	17.4 \pm 0.5	17.9 \pm 0.7
MCHC	g/dL	33.7 \pm 0.7	33.4 \pm 0.5
Platelet	10000/ μ L	100.3 \pm 10.2	104.3 \pm 10.6
PT	sec.	15.8 \pm 1.5	15.3 \pm 2.1
APTT	sec.	17.8 \pm 1.4	19.1 \pm 2.5
WBC	100/ μ L	83.2 \pm 23.5	79.9 \pm 18.1
Neutrophil	%	12.5 \pm 3.8	14.9 \pm 5.8
Eosinophil	%	1.4 \pm 0.4	1.5 \pm 0.5
Basophil	%	0.0 \pm 0.1	0.0 \pm 0.1
Monocyte	%	3.9 \pm 0.4	4.9 \pm 1.7
Lymphocyte	%	82.2 \pm 3.9	78.7 \pm 7.4
Reticulocyte	%	3.23 \pm 0.28	3.43 \pm 0.30

Each value shows mean \pm S.D.

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

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

Group		Control (vehicle: corn oil)	CPN 30 mg/kg	CPN 100 mg/kg	CPN 300 mg/kg
Number of females		5	5	5	5
RBC	10000/ μ L	637 \pm 37	620 \pm 51	620 \pm 25	663 \pm 48
HGB	g/dL	12.4 \pm 0.8	12.3 \pm 1.1	12.3 \pm 0.4	12.5 \pm 0.7
Hematocrit	%	37.8 \pm 3.0	37.7 \pm 2.6	37.5 \pm 1.4	37.9 \pm 1.8
MCV	fL	59.3 \pm 3.4	60.9 \pm 2.0	60.5 \pm 1.4	57.2 \pm 2.7
MCH	pg	19.4 \pm 0.9	19.8 \pm 0.5	19.8 \pm 0.5	18.9 \pm 0.7
MCHC	g/dL	32.8 \pm 0.5	32.6 \pm 0.7	32.8 \pm 0.3	33.1 \pm 0.4
Platelet	10000/ μ L	113.2 \pm 17.0	107.0 \pm 11.5	120.4 \pm 16.4	132.3 \pm 20.3
PT	sec.	13.4 \pm 0.4	12.9 \pm 0.5	12.9 \pm 0.4	13.0 \pm 0.4
APTT	sec.	14.7 \pm 1.9	15.3 \pm 0.8	14.4 \pm 1.2	15.5 \pm 0.6
WBC	100/ μ L	84.8 \pm 14.4	93.4 \pm 34.5	85.2 \pm 12.5	66.8 \pm 20.8
Neutrophil	%	30.6 \pm 3.0	32.0 \pm 8.2	33.8 \pm 8.5	22.1 \pm 5.9
Eosinophil	%	0.9 \pm 0.1	0.8 \pm 0.3	0.7 \pm 0.4	0.6 \pm 0.3
Basophil	%	0.0 \pm 0.0	0.0 \pm 0.0	0.0 \pm 0.1	0.0 \pm 0.1
Monocyte	%	3.6 \pm 1.7	3.0 \pm 0.9	4.0 \pm 0.9	5.8 \pm 1.1 *
Lymphocyte	%	64.9 \pm 3.2	64.2 \pm 8.1	61.5 \pm 8.7	71.5 \pm 5.8
Reticulocyte	%	8.31 \pm 1.43	8.08 \pm 1.35	7.86 \pm 1.05	8.56 \pm 2.47

Each value shows mean \pm S.D.

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

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

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

Group		Control (vehicle: corn oil)	CPN 300 mg/kg
Number of females		5	4
RBC	10000/ μ L	676 \pm 29	726 \pm 65
HGB	g/dL	12.9 \pm 0.5	13.5 \pm 0.7
Hematocrit	%	38.3 \pm 1.8	39.4 \pm 1.6
MCV	fL	56.7 \pm 2.2	54.5 \pm 3.1
MCH	pg	19.0 \pm 0.8	18.7 \pm 1.0
MCHC	g/dL	33.6 \pm 0.5	34.2 \pm 0.4
Platelet	10000/ μ L	85.1 \pm 6.3	95.7 \pm 15.2
PT	sec.	12.3 \pm 0.2	12.0 \pm 0.3
APTT	sec.	13.8 \pm 1.3	15.0 \pm 1.1
WBC	100/ μ L	42.6 \pm 7.7	45.8 \pm 14.3
Neutrophil	%	16.1 \pm 2.0	18.4 \pm 11.1
Eosinophil	%	2.0 \pm 0.7	1.4 \pm 0.3
Basophil	%	0.0 \pm 0.0	0.0 \pm 0.0
Monocyte	%	2.7 \pm 0.8	3.1 \pm 0.2
Lymphocyte	%	79.1 \pm 1.5	77.2 \pm 11.3
Reticulocyte	%	3.44 \pm 0.53	3.16 \pm 0.58

Each value shows mean \pm S.D.

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

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

Group		Control (vehicle: corn oil)	CPN 300 mg/kg
		5	5
Number of females			
RBC	10000/ μ L	768 \pm 49	742 \pm 26
HGB	g/dL	14.0 \pm 0.6	13.4 \pm 0.3
Hematocrit	%	41.8 \pm 1.6	39.8 \pm 0.5 *
MCV	fL	54.5 \pm 1.8	53.7 \pm 1.6
MCH	pg	18.3 \pm 0.6	18.1 \pm 0.5
MCHC	g/dL	33.6 \pm 0.4	33.7 \pm 0.5
Platelet	10000/ μ L	90.2 \pm 14.2	92.5 \pm 3.9
PT	sec.	11.8 \pm 0.6	11.9 \pm 0.5
APTT	sec.	14.4 \pm 2.0	15.3 \pm 1.7
WBC	100/ μ L	47.6 \pm 17.3	46.6 \pm 9.1
Neutrophil	%	17.3 \pm 3.2	20.6 \pm 7.9
Eosinophil	%	2.3 \pm 1.0	1.4 \pm 0.6
Basophil	%	0.0 \pm 0.0	0.0 \pm 0.1
Monocyte	%	3.4 \pm 0.8	3.4 \pm 0.3
Lymphocyte	%	77.0 \pm 3.6	74.5 \pm 7.8
Reticulocyte	%	3.07 \pm 0.45	3.05 \pm 0.35

Each value shows mean \pm S.D.

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

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

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

Group		Control (vehicle: corn oil)	CPN 30 mg/kg	CPN 100 mg/kg	CPN 300 mg/kg
		5	5	5	5
Number of males		5	5	5	5
Total protein	g/dL	5.3 ± 0.2	5.6 ± 0.2	5.5 ± 0.4	5.7 ± 0.2
Albumin	g/dL	3.5 ± 0.0	3.6 ± 0.1	3.5 ± 0.2	3.7 ± 0.1
A/G		1.92 ± 0.19	1.82 ± 0.06	1.80 ± 0.06	1.87 ± 0.18
Glucose	mg/dL	131 ± 15	133 ± 14	132 ± 9	133 ± 6
Total cholesterol	mg/dL	51 ± 12	55 ± 6	55 ± 13	59 ± 8
Triglyceride	mg/dL	50 ± 24	37 ± 9	41 ± 20	25 ± 11
Phospholipid	mg/dL	86 ± 14	88 ± 8	87 ± 18	89 ± 11
AST	U/L	55 ± 9	52 ± 3	51 ± 4	54 ± 10
ALT	U/L	27 ± 3	26 ± 3	25 ± 2	28 ± 5
γ-GTP	U/L	0 ± 0	0 ± 0	0 ± 0	0 ± 0
LDH	U/L	114 ± 73	97 ± 60	92 ± 41	93 ± 59
Bile acid	μmol/L	15.7 ± 17.4	14.4 ± 7.4	11.7 ± 4.3	18.2 ± 10.8
BUN	mg/dL	12.1 ± 1.7	11.9 ± 1.1	13.6 ± 1.0	13.2 ± 1.6
Creatinine	mg/dL	0.28 ± 0.03	0.26 ± 0.03	0.26 ± 0.03	0.26 ± 0.05
Total bilirubin	mg/dL	0.06 ± 0.01	0.07 ± 0.00	0.05 ± 0.01	0.06 ± 0.01
ALP	U/L	477 ± 87	505 ± 98	521 ± 111	400 ± 64
Inorganic phosphorus	mg/dL	5.7 ± 0.1	5.5 ± 0.2	5.6 ± 0.5	5.4 ± 0.5
Ca	mg/dL	9.3 ± 0.2	9.3 ± 0.3	9.2 ± 0.6	9.3 ± 0.4
Na	mEq/L	144.5 ± 0.4	144.3 ± 1.2	145.0 ± 1.0	144.4 ± 1.0
K	mEq/L	3.71 ± 0.06	3.79 ± 0.12	3.81 ± 0.26	3.65 ± 0.14
Cl	mEq/L	110.4 ± 0.9	110.4 ± 1.2	111.7 ± 1.1	110.0 ± 1.1

Each value shows mean ± S.D.

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

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

Group		Control (vehicle: corn oil)	CPN 300 mg/kg
		5	5
Number of males			
Total protein	g/dL	5.7 ± 0.3	5.7 ± 0.3
Albumin	g/dL	3.7 ± 0.2	3.6 ± 0.1
A/G		1.88 ± 0.13	1.73 ± 0.17
Glucose	mg/dL	146 ± 11	141 ± 11
Total cholesterol	mg/dL	70 ± 11	71 ± 23
Triglyceride	mg/dL	45 ± 13	48 ± 14
Phospholipid	mg/dL	102 ± 16	97 ± 19
AST	U/L	64 ± 16	61 ± 11
ALT	U/L	28 ± 8	32 ± 5
γ-GTP	U/L	0 ± 0	0 ± 0
LDH	U/L	111 ± 78	137 ± 144
Bile acid	μmol/L	9.7 ± 1.9	12.8 ± 4.4
BUN	mg/dL	14.4 ± 0.9	13.9 ± 1.8
Creatinine	mg/dL	0.31 ± 0.04	0.29 ± 0.04
Total bilirubin	mg/dL	0.06 ± 0.00	0.06 ± 0.02
ALP	U/L	385 ± 78	409 ± 77
Inorganic phosphorus	mg/dL	5.7 ± 0.5	6.3 ± 0.6
Ca	mg/dL	9.6 ± 0.4	9.6 ± 0.3
Na	mEq/L	144.2 ± 1.1	144.3 ± 0.4
K	mEq/L	3.85 ± 0.17	3.96 ± 0.22
Cl	mEq/L	111.6 ± 1.3	110.5 ± 1.3

Each value shows mean ± S.D.

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

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

Group		Control (vehicle: corn oil)	CPN 30 mg/kg	CPN 100 mg/kg	CPN 300 mg/kg
Number of females		5	5	5	5
Total protein	g/dL	5.6 ± 0.2	5.7 ± 0.2	5.7 ± 0.1	5.9 ± 0.3
Albumin	g/dL	3.8 ± 0.1	3.9 ± 0.2	3.9 ± 0.1	3.8 ± 0.2
A/G		2.22 ± 0.19	2.09 ± 0.20	2.15 ± 0.18	1.90 ± 0.09
Glucose	mg/dL	113 ± 9	110 ± 9	122 ± 2	114 ± 3
Total cholesterol	mg/dL	49 ± 7	53 ± 14	55 ± 9	59 ± 9
Triglyceride	mg/dL	23 ± 7	29 ± 11	28 ± 13	16 ± 4
Phospholipid	mg/dL	94 ± 11	103 ± 23	102 ± 15	100 ± 13
AST	U/L	107 ± 35	88 ± 6	111 ± 49	74 ± 10
ALT	U/L	42 ± 7	40 ± 5	45 ± 14	39 ± 4
γ-GTP	U/L	0 ± 0	0 ± 0	0 ± 0	0 ± 0
LDH	U/L	113 ± 78	163 ± 95	130 ± 57	121 ± 103
Bile acid	μmol/L	21.4 ± 23.6	13.4 ± 7.5	16.3 ± 9.9	22.4 ± 14.5
BUN	mg/dL	13.2 ± 2.5	13.3 ± 2.5	14.4 ± 1.8	15.3 ± 1.6
Creatinine	mg/dL	0.30 ± 0.05	0.33 ± 0.04	0.36 ± 0.08	0.34 ± 0.05
Total bilirubin	mg/dL	0.07 ± 0.01	0.06 ± 0.01	0.06 ± 0.01	0.06 ± 0.01
ALP	U/L	291 ± 86	279 ± 128	229 ± 65	246 ± 91
Inorganic phosphorus	mg/dL	6.5 ± 1.3	6.7 ± 0.7	6.2 ± 0.6	6.0 ± 0.7
Ca	mg/dL	9.6 ± 0.3	9.7 ± 0.3	9.8 ± 0.3	9.6 ± 0.3
Na	mEq/L	142.5 ± 1.3	143.1 ± 1.6	143.3 ± 1.4	144.5 ± 0.6
K	mEq/L	3.67 ± 0.34	3.64 ± 0.12	3.63 ± 0.27	3.87 ± 0.14
Cl	mEq/L	110.5 ± 1.5	111.4 ± 1.4	110.5 ± 2.2	111.4 ± 1.7

Each value shows mean ± S.D.

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

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

Group		Control (vehicle: corn oil)	CPN 300 mg/kg
		5	4
Number of females			
Total protein	g/dL	5.7 ± 0.5	5.9 ± 0.2
Albumin	g/dL	3.9 ± 0.4	4.2 ± 0.2
A/G		2.19 ± 0.15	2.51 ± 0.25
Glucose	mg/dL	104 ± 13	118 ± 18
Total cholesterol	mg/dL	53 ± 12	69 ± 12
Triglyceride	mg/dL	8 ± 3	11 ± 2
Phospholipid	mg/dL	97 ± 21	123 ± 18
AST	U/L	71 ± 12	64 ± 15
ALT	U/L	24 ± 4	24 ± 4
γ-GTP	U/L	0 ± 0	0 ± 1
LDH	U/L	64 ± 32	69 ± 26
Bile acid	μmol/L	14.3 ± 13.1	15.0 ± 10.0
BUN	mg/dL	19.7 ± 2.2	16.2 ± 2.0 *
Creatinine	mg/dL	0.42 ± 0.04	0.40 ± 0.04
Total bilirubin	mg/dL	0.07 ± 0.01	0.08 ± 0.02
ALP	U/L	286 ± 98	311 ± 163
Inorganic phosphorus	mg/dL	5.0 ± 0.4	4.3 ± 0.6
Ca	mg/dL	9.2 ± 0.2	9.3 ± 0.1
Na	mEq/L	143.8 ± 0.9	143.8 ± 0.9
K	mEq/L	3.60 ± 0.28	3.52 ± 0.14
Cl	mEq/L	112.6 ± 0.9	111.6 ± 1.4

Each value shows mean ± S.D.

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

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

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

Group		Control (vehicle: corn oil)	CPN 300 mg/kg
		5	5
Number of females			
Total protein	g/dL	5.9 ± 0.3	6.0 ± 0.2
Albumin	g/dL	3.9 ± 0.3	4.0 ± 0.2
A/G		1.99 ± 0.19	1.99 ± 0.16
Glucose	mg/dL	142 ± 28	147 ± 11
Total cholesterol	mg/dL	78 ± 21	61 ± 10
Triglyceride	mg/dL	22 ± 9	14 ± 8
Phospholipid	mg/dL	128 ± 22	109 ± 14
AST	U/L	80 ± 24	64 ± 7
ALT	U/L	32 ± 13	25 ± 7
γ-GTP	U/L	0 ± 0	0 ± 0
LDH	U/L	90 ± 45	85 ± 51
Bile acid	μmol/L	14.0 ± 7.1	15.3 ± 6.7
BUN	mg/dL	13.0 ± 0.9	15.1 ± 2.8
Creatinine	mg/dL	0.36 ± 0.04	0.38 ± 0.06
Total bilirubin	mg/dL	0.07 ± 0.01	0.07 ± 0.01
ALP	U/L	205 ± 48	231 ± 103
Inorganic phosphorus	mg/dL	5.6 ± 0.9	6.2 ± 0.6
Ca	mg/dL	9.6 ± 0.2	9.6 ± 0.1
Na	mEq/L	144.7 ± 0.9	144.2 ± 0.6
K	mEq/L	3.82 ± 0.17	3.77 ± 0.23
Cl	mEq/L	111.7 ± 0.6	109.7 ± 1.5 *

Each value shows mean ± S.D.

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

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

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

Group	Control (vehicle: com oil)		CPN 30 mg/kg		CPN 100 mg/kg		CPN 300 mg/kg	
		6	12	12	12	7		
Number of males								
Body weight	(g)	508.5 ± 13.7	499.4 ± 37.9	495.4 ± 35.3	448.8 ± 17.1 **			
Brain	(mg)	2028.8 ± 79.7	2058.9 ± 59.3	2015.1 ± 43.4	1992.6 ± 118.7			
	(mg/g)	3.989 ± 0.077	4.140 ± 0.274	4.088 ± 0.323	4.444 ± 0.295 *			
Thymus	(mg)	328.6 ± 65.9	304.7 ± 77.1	303.7 ± 83.0	237.5 ± 43.8			
	(mg/g)	0.647 ± 0.136	0.612 ± 0.163	0.612 ± 0.156	0.529 ± 0.089			
Heart	(mg)	1447.6 ± 155.7	1452.9 ± 118.1	1440.1 ± 83.8	1375.3 ± 128.7			
	(mg/g)	2.846 ± 0.283	2.911 ± 0.133	2.916 ± 0.207	3.063 ± 0.232			
Liver	(mg)	14011.0 ± 782.8	13639.1 ± 1984.9	13988.4 ± 2063.0	12606.4 ± 694.2			
	(mg/g)	27.559 ± 1.476	27.222 ± 2.298	28.140 ± 2.758	28.085 ± 1.035			
Kidney (R)	(mg)	1623.3 ± 91.0	1658.7 ± 133.5	1695.0 ± 151.5	1672.2 ± 150.1			
	(mg/g)	3.191 ± 0.131	3.322 ± 0.111	3.429 ± 0.287	3.721 ± 0.227 **			
Kidney (L)	(mg)	1630.9 ± 83.0	1640.6 ± 126.8	1691.5 ± 157.7	1660.6 ± 119.5			
	(mg/g)	3.207 ± 0.127	3.288 ± 0.172	3.424 ± 0.328	3.699 ± 0.193 **			
Kidneys	(mg)	3254.2 ± 169.3	3299.2 ± 255.1	3386.5 ± 296.6	3332.8 ± 264.6			
	(mg/g)	6.398 ± 0.245	6.610 ± 0.269	6.853 ± 0.587	7.420 ± 0.399 **			
Spleen	(mg)	795.4 ± 131.1	853.1 ± 202.1	822.0 ± 112.5	705.0 ± 102.3			
	(mg/g)	1.563 ± 0.238	1.698 ± 0.292	1.661 ± 0.218	1.575 ± 0.251			
Testis (R)	(mg)	1723.5 ± 168.0	1753.5 ± 151.2	1660.1 ± 85.9	1749.5 ± 169.8			
	(mg/g)	3.390 ± 0.326	3.521 ± 0.308	3.373 ± 0.360	3.898 ± 0.343 *			
Testis (L)	(mg)	1732.1 ± 152.4	1759.4 ± 150.4	1644.0 ± 77.3	1780.2 ± 177.9			
	(mg/g)	3.407 ± 0.285	3.534 ± 0.319	3.339 ± 0.338	3.966 ± 0.359 *			
Testes	(mg)	3455.7 ± 315.6	3513.0 ± 298.1	3304.1 ± 152.8	3529.7 ± 345.4			
	(mg/g)	6.797 ± 0.601	7.055 ± 0.621	6.712 ± 0.688	7.864 ± 0.697 *			
Epididymis (R)	(mg)	657.6 ± 44.6	638.7 ± 40.0	643.2 ± 41.5	650.2 ± 67.7			
	(mg/g)	1.293 ± 0.081	1.284 ± 0.107	1.307 ± 0.154	1.450 ± 0.159			
Epididymis (L)	(mg)	633.4 ± 48.6	630.8 ± 33.5	626.9 ± 34.2	631.4 ± 79.3			
	(mg/g)	1.245 ± 0.080	1.267 ± 0.070	1.274 ± 0.140	1.408 ± 0.181			
Epididymides	(mg)	1291.0 ± 90.3	1269.5 ± 67.1	1270.1 ± 73.0	1281.5 ± 144.2			
	(mg/g)	2.539 ± 0.155	2.551 ± 0.170	2.581 ± 0.291	2.859 ± 0.334			

Each value shows mean ± S.D.

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

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

Table 29-1 (continued). Organ weights of male rats at the end of the administration period

Group		Control (vehicle: com oil)		CPN 30 mg/kg		CPN 100 mg/kg		CPN 300 mg/kg	
Number of males		6		12		12		7	
Body weight	(g)	508.5 ±	13.7	499.4 ±	37.9	495.4 ±	35.3	448.8 ±	17.1 **
Prostate, ventral	(mg)	580.5 ±	167.2	552.9 ±	105.8	622.0 ±	128.9	559.1 ±	106.1
	(mg/g)	1.137 ±	0.307	1.114 ±	0.224	1.259 ±	0.261	1.244 ±	0.216
Seminal vesicles	(mg)	1718.3 ±	164.5	1581.9 ±	297.8	1700.4 ±	180.9	1844.6 ±	163.8
	(mg/g)	3.375 ±	0.259	3.181 ±	0.638	3.464 ±	0.585	4.120 ±	0.454 *
Thyroid gland	(mg)	23.6 ±	3.1	23.3 ±	4.7	22.2 ±	3.1	24.4 ±	2.6
	(mg/g)	0.047 ±	0.006	0.047 ±	0.008	0.045 ±	0.007	0.054 ±	0.007
Adrenal gland (R)	(mg)	25.0 ±	2.9	26.7 ±	3.8	27.0 ±	3.3	28.9 ±	1.8
	(mg/g)	0.049 ±	0.005	0.054 ±	0.007	0.055 ±	0.007	0.064 ±	0.005 **
Adrenal gland (L)	(mg)	26.6 ±	3.0	29.9 ±	4.5	28.5 ±	3.8	30.9 ±	2.3
	(mg/g)	0.052 ±	0.006	0.060 ±	0.008	0.058 ±	0.008	0.069 ±	0.005 **
Adrenal glands	(mg)	51.6 ±	5.6	56.6 ±	8.0	55.4 ±	6.9	59.9 ±	3.7
	(mg/g)	0.101 ±	0.010	0.114 ±	0.015	0.112 ±	0.014	0.134 ±	0.009 **

Each value shows mean ± S.D.

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

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

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

Group		Control (vehicle: corn oil)		CPN 300 mg/kg	
Number of males		5		5	
Body weight	(g)	514.5	± 21.3	526.4	± 32.5
Brain	(mg)	2045.3	± 98.0	2013.4	± 115.5
	(mg/g)	3.985	± 0.316	3.827	± 0.124
Thymus	(mg)	295.7	± 90.1	262.1	± 101.0
	(mg/g)	0.575	± 0.177	0.495	± 0.182
Heart	(mg)	1469.3	± 107.4	1480.8	± 91.0
	(mg/g)	2.856	± 0.171	2.820	± 0.226
Liver	(mg)	13665.6	± 736.9	14627.9	± 1280.3
	(mg/g)	26.568	± 1.202	27.762	± 1.044
Kidney (R)	(mg)	1682.6	± 72.6	1678.1	± 86.9
	(mg/g)	3.271	± 0.083	3.194	± 0.191
Kidney (L)	(mg)	1641.6	± 46.0	1667.2	± 110.1
	(mg/g)	3.193	± 0.083	3.173	± 0.229
Kidneys	(mg)	3324.3	± 106.8	3345.2	± 195.3
	(mg/g)	6.464	± 0.124	6.368	± 0.417
Spleen	(mg)	758.5	± 83.7	805.2	± 106.8
	(mg/g)	1.480	± 0.206	1.529	± 0.170
Testis (R)	(mg)	1748.3	± 204.8	1756.6	± 198.9
	(mg/g)	3.406	± 0.453	3.334	± 0.264
Testis (L)	(mg)	1720.4	± 229.8	1772.9	± 147.3
	(mg/g)	3.352	± 0.502	3.367	± 0.182
Testes	(mg)	3468.7	± 431.2	3529.6	± 340.9
	(mg/g)	6.758	± 0.950	6.701	± 0.430
Epididymis (R)	(mg)	666.9	± 67.7	659.9	± 50.2
	(mg/g)	1.298	± 0.142	1.254	± 0.069
Epididymis (L)	(mg)	679.1	± 56.9	678.0	± 48.2
	(mg/g)	1.323	± 0.139	1.288	± 0.041
Epididymides	(mg)	1346.0	± 120.9	1337.9	± 96.5
	(mg/g)	2.621	± 0.274	2.542	± 0.108

Each value shows mean ± S.D.

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

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

Group		Control (vehicle: corn oil)		CPN 300 mg/kg	
Number of males		5		5	
Body weight	(g)	514.5 ±	21.3	526.4 ±	32.5
Prostate, ventral	(mg)	622.6 ±	258.5	587.2 ±	82.3
	(mg/g)	1.209 ±	0.494	1.126 ±	0.221
Seminal vesicles	(mg)	1589.5 ±	242.9	1929.6 ±	242.6
	(mg/g)	3.099 ±	0.520	3.699 ±	0.705
Thyroid gland	(mg)	18.5 ±	1.2	23.3 ±	3.7 *
	(mg/g)	0.036 ±	0.002	0.044 ±	0.006 *
Adrenal gland (R)	(mg)	21.7 ±	1.8	23.6 ±	3.6
	(mg/g)	0.042 ±	0.004	0.045 ±	0.008
Adrenal gland (L)	(mg)	22.7 ±	2.1	24.7 ±	3.3
	(mg/g)	0.044 ±	0.005	0.047 ±	0.007
Adrenal glands	(mg)	44.4 ±	3.8	48.3 ±	6.7
	(mg/g)	0.086 ±	0.009	0.092 ±	0.015

Each value shows mean ± S.D.

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

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

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

Group		Control (vehicle: corn oil)		CPN 30 mg/kg		CPN 100 mg/kg		CPN 300 mg/kg	
		12		11		10		11	
Number of females									
Body weight	(g)	316.6 ± 22.8		301.2 ± 20.2		315.8 ± 18.0		301.7 ± 14.2	
Brain	(mg)	1931.0 ± 68.0		1900.9 ± 82.8		1832.1 ± 70.0 *		1869.0 ± 87.7	
	(mg/g)	6.127 ± 0.489		6.334 ± 0.446		5.812 ± 0.266		6.207 ± 0.402	
Thymus	(mg)	214.2 ± 56.6		194.3 ± 61.2		212.9 ± 65.0		175.6 ± 44.7	
	(mg/g)	0.679 ± 0.182		0.643 ± 0.185		0.670 ± 0.182		0.584 ± 0.157	
Heart	(mg)	1015.5 ± 64.3		1014.0 ± 51.4		981.4 ± 62.9		994.0 ± 37.0	
	(mg/g)	3.215 ± 0.206		3.373 ± 0.160		3.110 ± 0.155		3.299 ± 0.129	
Liver	(mg)	9993.7 ± 946.5		10050.0 ± 843.3		10202.9 ± 795.8		9943.1 ± 718.0	
	(mg/g)	31.535 ± 1.381		33.383 ± 1.959		32.328 ± 2.127		32.983 ± 2.233	
Kidney (R)	(mg)	1038.0 ± 112.6		1011.9 ± 82.8		974.5 ± 91.0		1058.7 ± 107.7	
	(mg/g)	3.283 ± 0.333		3.370 ± 0.323		3.086 ± 0.238		3.509 ± 0.312	
Kidney (L)	(mg)	1003.4 ± 94.4		997.9 ± 90.5		949.5 ± 92.2		1033.8 ± 76.6	
	(mg/g)	3.174 ± 0.275		3.322 ± 0.327		3.010 ± 0.292		3.429 ± 0.234	
Kidneys	(mg)	2041.4 ± 205.0		2009.8 ± 166.3		1924.0 ± 177.1		2092.5 ± 178.6	
	(mg/g)	6.458 ± 0.601		6.693 ± 0.629		6.096 ± 0.513		6.938 ± 0.522	
Spleen	(mg)	732.8 ± 114.6		691.9 ± 117.7		696.3 ± 84.7		708.4 ± 145.7	
	(mg/g)	2.307 ± 0.257		2.290 ± 0.301		2.206 ± 0.255		2.345 ± 0.449	
Ovary (R)	(mg)	53.1 ± 6.3		55.6 ± 8.8		52.8 ± 11.3		57.7 ± 5.1	
	(mg/g)	0.168 ± 0.024		0.185 ± 0.027		0.167 ± 0.035		0.191 ± 0.015	
Ovary (L)	(mg)	54.1 ± 6.0		53.6 ± 8.9		52.5 ± 6.6		57.9 ± 7.1	
	(mg/g)	0.171 ± 0.019		0.179 ± 0.034		0.166 ± 0.018		0.192 ± 0.024	
Ovaries	(mg)	107.1 ± 5.8		109.2 ± 12.7		105.3 ± 15.4		115.6 ± 8.5	
	(mg/g)	0.340 ± 0.025		0.364 ± 0.048		0.333 ± 0.044		0.383 ± 0.026 *	
Uterus	(mg)	641.9 ± 92.1		689.0 ± 84.5		630.8 ± 82.4		682.5 ± 74.9	
	(mg/g)	2.033 ± 0.292		2.293 ± 0.276		2.003 ± 0.279		2.264 ± 0.242	
Thyroid gland	(mg)	16.4 ± 3.7		16.4 ± 1.7		17.9 ± 3.4		18.9 ± 3.6	
	(mg/g)	0.052 ± 0.013		0.055 ± 0.006		0.057 ± 0.012		0.063 ± 0.011	
Adrenal gland (R)	(mg)	36.0 ± 4.4		33.9 ± 3.6		32.7 ± 3.3		32.9 ± 5.0	
	(mg/g)	0.114 ± 0.013		0.113 ± 0.010		0.104 ± 0.012		0.109 ± 0.016	
Adrenal gland (L)	(mg)	38.5 ± 4.2		37.6 ± 4.2		34.6 ± 2.7		35.9 ± 7.6	
	(mg/g)	0.122 ± 0.012		0.125 ± 0.014		0.110 ± 0.012		0.119 ± 0.024	
Adrenal glands	(mg)	74.4 ± 7.9		71.6 ± 7.7		67.3 ± 5.8		68.8 ± 12.5	
	(mg/g)	0.235 ± 0.022		0.238 ± 0.024		0.214 ± 0.023		0.228 ± 0.039	

Each value shows mean ± S.D.

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

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

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

Group		Control (vehicle: corn oil)		CPN 300 mg/kg	
Number of females		5		5	
Body weight	(g)	281.7 ±	16.9	272.4 ±	12.6
Brain	(mg)	1889.8 ±	90.9	1875.8 ±	61.7
	(mg/g)	6.723 ±	0.407	6.901 ±	0.452
Thymus	(mg)	291.0 ±	66.4	285.0 ±	23.2
	(mg/g)	1.044 ±	0.287	1.050 ±	0.121
Heart	(mg)	909.1 ±	55.1	873.8 ±	80.4
	(mg/g)	3.230 ±	0.151	3.204 ±	0.189
Liver	(mg)	7275.4 ±	631.8	7855.4 ±	741.3
	(mg/g)	25.844 ±	1.929	28.964 ±	3.963
Kidney (R)	(mg)	894.8 ±	78.0	939.6 ±	69.6
	(mg/g)	3.173 ±	0.111	3.452 ±	0.255
Kidney (L)	(mg)	888.8 ±	87.2	924.5 ±	95.7
	(mg/g)	3.151 ±	0.175	3.393 ±	0.292
Kidneys	(mg)	1783.6 ±	163.9	1864.1 ±	164.2
	(mg/g)	6.325 ±	0.282	6.845 ±	0.536
Spleen	(mg)	603.0 ±	78.4	519.8 ±	102.8
	(mg/g)	2.136 ±	0.170	1.901 ±	0.310
Ovary (R)	(mg)	41.4 ±	10.2	47.5 ±	10.3
	(mg/g)	0.146 ±	0.029	0.174 ±	0.033
Ovary (L)	(mg)	46.1 ±	10.4	47.1 ±	8.1
	(mg/g)	0.163 ±	0.030	0.173 ±	0.025
Ovaries	(mg)	87.5 ±	20.3	94.7 ±	18.2
	(mg/g)	0.309 ±	0.057	0.347 ±	0.058
Uterus	(mg)	457.3 ±	86.6	571.3 ±	271.3
	(mg/g)	1.619 ±	0.270	2.085 ±	0.958
Thyroid gland	(mg)	18.4 ±	2.2	18.2 ±	2.5
	(mg/g)	0.066 ±	0.007	0.067 ±	0.010
Adrenal gland (R)	(mg)	32.2 ±	5.3	33.5 ±	3.4
	(mg/g)	0.114 ±	0.013	0.123 ±	0.011
Adrenal gland (L)	(mg)	34.1 ±	5.5	34.1 ±	4.7
	(mg/g)	0.121 ±	0.013	0.125 ±	0.016
Adrenal glands	(mg)	66.3 ±	10.7	67.6 ±	7.9
	(mg/g)	0.234 ±	0.025	0.248 ±	0.027

Each value shows mean ± S.D.

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

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

Group		Control (vehicle: corn oil)		CPN 300 mg/kg	
Number of females		5		5	
Body weight	(g)	285.2 ±	29.9	275.4 ±	18.8
Brain	(mg)	1899.8 ±	69.0	1916.1 ±	85.2
	(mg/g)	6.714 ±	0.693	6.983 ±	0.554
Thymus	(mg)	313.4 ±	88.6	258.0 ±	34.8
	(mg/g)	1.089 ±	0.221	0.941 ±	0.150
Heart	(mg)	958.0 ±	209.0	913.0 ±	34.1
	(mg/g)	3.343 ±	0.465	3.324 ±	0.187
Liver	(mg)	7071.2 ±	1002.8	7271.0 ±	360.5
	(mg/g)	24.723 ±	1.002	26.501 ±	2.230
Kidney (R)	(mg)	943.9 ±	111.9	970.2 ±	87.7
	(mg/g)	3.309 ±	0.127	3.521 ±	0.180
Kidney (L)	(mg)	927.8 ±	121.3	944.0 ±	79.5
	(mg/g)	3.249 ±	0.171	3.429 ±	0.211
Kidneys	(mg)	1871.7 ±	232.4	1914.2 ±	164.8
	(mg/g)	6.558 ±	0.290	6.949 ±	0.379
Spleen	(mg)	495.2 ±	57.2	524.9 ±	54.7
	(mg/g)	1.758 ±	0.319	1.911 ±	0.216
Ovary (R)	(mg)	36.2 ±	4.8	50.8 ±	10.5 *
	(mg/g)	0.127 ±	0.017	0.185 ±	0.038 *
Ovary (L)	(mg)	32.3 ±	6.2	48.2 ±	11.0 *
	(mg/g)	0.113 ±	0.018	0.176 ±	0.047 *
Ovaries	(mg)	68.5 ±	7.6	99.0 ±	20.6 *
	(mg/g)	0.240 ±	0.018	0.361 ±	0.082 *
Uterus	(mg)	746.3 ±	401.6	719.9 ±	295.7
	(mg/g)	2.605 ±	1.374	2.612 ±	1.002
Thyroid gland	(mg)	16.7 ±	4.5	16.4 ±	2.2
	(mg/g)	0.059 ±	0.019	0.060 ±	0.008
Adrenal gland (R)	(mg)	31.8 ±	7.2	35.6 ±	3.6
	(mg/g)	0.110 ±	0.013	0.130 ±	0.014
Adrenal gland (L)	(mg)	30.7 ±	3.7	38.8 ±	5.8 *
	(mg/g)	0.108 ±	0.013	0.141 ±	0.022 *
Adrenal glands	(mg)	62.5 ±	8.1	74.4 ±	9.4
	(mg/g)	0.219 ±	0.008	0.271 ±	0.036 *

Each value shows mean ± S.D.

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

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

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

Findings	Group Dose (mg/kg) Grade	CPN 0		CPN 30		CPN 100		CPN 300	
		-	P	-	P	-	P	-	P
Adipose tissue									
Nodule		5	1	12	0	12	0	7	0
Kidney									
Recessed area		6	0	12	0	12	0	6	1
Liver									
Diaphragmatic nodule		5	1	12	0	12	0	7	0
Pale colored area		5	1	12	0	12	0	7	0

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

Numerals represent the number of animals.

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

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

Findings	Group	CPN		CPN	
	Dose (mg/kg)	0		300	
	Grade	-	P	-	P
Pituitary gland					
Cyst		5	0	4	1
Thymus					
Small		5	0	4	1

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

Numerals represent the number of animals.

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

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

Findings	Group	CPN		CPN		CPN		CPN	
	Dose (mg/kg)	0		30		100		300	
Grade		-	P	-	P	-	P	-	P
Ileum									
Diverticulum		12	0	10	1	10	0	11	0
Stomach									
Dark colored spot/area		11	1	11	0	10	0	11	0
Thickening, mucosa		12	0	11	0	10	0	10	1
Thymus									
Small		12	0	11	0	10	0	10	1

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

Numerals represent the number of animals.

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

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

Findings	Group	CPN		CPN	
	Dose (mg/kg)	0		300	
	Grade	-	P	-	P
All organs and tissues		5		5	

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

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

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

Findings	Group Dose (mg/kg) Grade	CPN		CPN	
		0		300	
		-	P	-	P
Adrenal gland					
Enlargement		4	1	5	0
Malposition		4	1	5	0
Reddish area		4	1	5	0
Liver					
Abnormal lobulation		4	1	5	0
Posterior vena cava					
Malposition		4	1	5	0
Spleen					
Cyst		4	1	5	0

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

Numerals represent the number of animals.

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

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

Findings	Group Dose (mg/kg) Grade	CPN 0						CPN 300							
		-	±	+	2+	3+	P	NE	-	±	+	2+	3+	P	NE
Brain		5							5						
Spinal cord		5							5						
Pituitary gland															
Cyst		4					1		5					0	
Submandibular gland															
Atrophy, acinar cell		4	1	0	0	0			5	0	0	0	0		
Sublingual gland		5							5						
Lymph node, submandibular		5							5						
Thyroid gland															
Cellular infiltration, lymphocyte		5	0	0	0	0			4	1	0	0	0		
Ultimobranchial body		4					1		4					1	
Parathyroid gland		5							5						
Thymus		5							5						
Heart															
Degeneration/fibrosis, myocardial		2	3	0	0	0			3	2	0	0	0		
Trachea		5							5						

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

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

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

Findings	Group Dose (mg/kg) Grade	CFN 0							CFN 300						
		-	±	+	2+	3+	P	NE	-	±	+	2+	3+	P	NE
		Lung													
Accumulation, foam cell		4	1	0	0	0			2	2	1	0	0		
Hemorrhage		4	0	1	0	0			5	0	0	0	0		
Bronchus		5							5						
Liver															
Fatty change, hepatocyte		1	2	1	1	0			1	2	1	1	0		
Microgranuloma		4	1	0	0	0			5	0	0	0	0		
Nodule, hepatodiaphragmatic		4					1		5					0	
Tension lipidosis		4	0	1	0	0			5	0	0	0	0		
Pancreas															
Atrophy, acinar cell		3	2	0	0	0			4	1	0	0	0		
Stomach															
Erosion		5	0	0	0	0			4	1	0	0	0		
Duodenum		5							5						
Jejunum		5							5						

Notes) - : No abnormal changes ±: Very slight + : Slight 2+: Moderate 3+: Marked

P : Non-graded change NE: Not examined

Numerals represent the number of animals.

Not significantly different from control.

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

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

Findings	Group Dose (mg/kg) Grade	CPN 0						CPN 300							
		-	±	+	2+	3+	P	NE	-	±	+	2+	3+	P	NE
		Ileum													
Edema		5	0	0	0	0		4	1	0	0	0			
Cecum		5						5							
Colon		5						5							
Rectum		5						5							
Lymph node, mesenteric		5						5							
Spleen															
Deposit, pigment, brown		0	2	3	0	0		0	1	3	1	0			
Hematopoiesis, extramedullary		0	1	4	0	0		0	1	4	0	0			
Kidney															
Basophilic tubule, cortex		2	3	0	0	0		1	3	1	0	0			
Eosinophilic body		5	0	0	0	0		2	1	2	0	0			
Fibrosis, focal		5	0	0	0	0		4	1	0	0	0			
Hyperplasia, transitional cell		5	0	0	0	0		4	1	0	0	0			
Urinary bladder															
Mineralization		5	0	0	0	0		4	1	0	0	0			

Notes) - : No abnormal changes ±: Very slight + : Slight 2+: Moderate 3+: Marked
P : Non-graded change NE: Not examined

Numerals represent the number of animals.

Not significantly different from control.

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

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

Findings	Group Dose (mg/kg) Grade	CPN 0						CPN 300							
		-	±	+	2+	3+	P	NE	-	±	+	2+	3+	P	NE
		Adrenal gland	5							5					
Testis	5							5							
Epididymis	5							5							
Prostate															
Cellular infiltration, lymphocyte		1	2	2	0	0		4	1	0	0	0	0		
Seminal vesicle	5							5							
Coagulating gland	5							5							
Eyeball															
Dysplasia, retina	5					0		4						1	
Harderian gland															
Cellular infiltration, lymphocyte		4	1	0	0	0		5	0	0	0	0	0		
Sciatic nerve	5							5							
Skeletal muscle	5							5							
Femur	5							5							
Marrow, femur	5							5							

Notes) - : No abnormal changes ±: Very slight + : Slight 2+: Moderate 3+: Marked

P : Non-graded change NE: Not examined

Numerals represent the number of animals.

Not significantly different from control.

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

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

Findings	Group	CPN							CPN						
	Dose (mg/kg)	0							300						
	Grade	-	±	+	2+	3+	P	NE	-	±	+	2+	3+	P	NE
Adipose tissue															
Necrosis, fat		0	0	1	0	0									

Notes) - : No abnormal changes ±: Very slight + : Slight 2+: Moderate 3+: Marked

P : Non-graded change NE: Not examined

Numerals represent the number of animals.

Not significantly different from control.

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

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

Findings	Group Dose (mg/kg) Grade	CPN							CPN						
		0							300						
		-	±	+	2+	3+	P	NE	-	±	+	2+	3+	P	NE
Pituitary gland															
Cyst								0						1	
Thyroid gland															
Cellular infiltration, lymphocyte		4	1	0	0	0		5	0	0	0	0			
Ultimobranchial body		3					2	4						1	
Thymus															
Atrophy								0	1	0	0	0			

Notes) - : No abnormal changes ±: Very slight + : Slight 2+: Moderate 3+: Marked
P : Non-graded change NE: Not examined

Numerals represent the number of animals.

Not significantly different from control.

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

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

Findings	Group Dose (mg/kg) Grade	CPN 0							CPN 30							CPN 300						
		-	±	+	2+	3+	P	NE	-	±	+	2+	3+	P	NE	-	±	+	2+	3+	P	NE
		Brain	5																			
Spinal cord	5																					
Pituitary gland Cyst	4						1														0	
Submandibular gland	5																					
Sublingual gland	5																					
Lymph node, submandibular	5																					
Thyroid gland Ectopic thymic tissue	4						1														0	
Ultimobranchial body	4						1														1	
Parathyroid gland	5																					
Thymus Atrophy	5	0	0	0	0	0									5	0	1	0	0			
Hyperplasia, epithelial tubule/cord	3	2	0	0	0										4	2	0	0	0			
Heart	5																					

Notes) - : No abnormal changes ±: Very slight + : Slight 2+: Moderate 3+: Marked

P : Non-graded change NE: Not examined

Numerals represent the number of animals.

Not significantly different from control.

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

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

Findings	Group Dose (mg/kg) Grade	CPN 0						CPN 30						CPN 300						
		-	±	+	2+	3+	P	NE	-	±	+	2+	3+	P	NE	-	±	+	2+	3+
Trachea		5												5						
Lung																				
Accumulation, foam cell		3	1	1	0	0								4	1	0	0	0		
Metaplasia, osseous		4	1	0	0	0								5	0	0	0	0		
Microgranuloma		5	0	0	0	0								4	1	0	0	0		
Bronchus		5												5						
Liver																				
Necrosis, focal		4	1	0	0	0								5	0	0	0	0		
Pancreas		5												5						
Stomach																				
Edema		5	0	0	0	0								4	0	1	0	0		
Hyperplasia, squamous cell		5	0	0	0	0								4	1	0	0	0		
Duodenum		5												5						
Jejunum		5												5						
Ileum																				
Thinning, muscular layer		5	0	0	0	0		0	0	1	0	0		5	0	0	0	0		

Notes) - : No abnormal changes ±: Very slight + : Slight 2+: Moderate 3+: Marked

P : Non-graded change NE: Not examined

Numerals represent the number of animals.

Not significantly different from control.

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

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

Findings	Group Dose (mg/kg) Grade	CPN 0							CPN 30							CPN 300						
		-	±	+	2+	3+	P	NE	-	±	+	2+	3+	P	NE	-	±	+	2+	3+	P	NE
Cecum		5														5						
Colon		5														5						
Rectum		5														5						
Lymph node, mesenteric		5														5						
Spleen																						
Deposit, pigment, brown		0	1	4	0	0									0	0	4	1	0			
Hematopoiesis, extramedullary		0	0	1	4	0									0	0	3	2	0			
Kidney		5														5						
Urinary bladder		5														5						
Adrenal gland		5														5						
Ovary		5														5						
Uterus		5														5						
Vagina		5														5						

Notes) - : No abnormal changes ±: Very slight + : Slight 2+: Moderate 3+: Marked

P : Non-graded change NE: Not examined

Numerals represent the number of animals.

Not significantly different from control.

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

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

Findings	Group Dose (mg/kg) Grade	CPN 0							CPN 30							CPN 300						
		-	±	+	2+	3+	P	NE	-	±	+	2+	3+	P	NE	-	±	+	2+	3+	P	NE
Eyeball																						
	Dysplasia, retina	4						1										5				0
	Harderian gland	5																5				
	Sciatic nerve	5																5				
	Skeletal muscle	5																5				
	Femur	5																5				
	Marrow, femur	5																5				

Notes) - : No abnormal changes ±: Very slight + : Slight 2+: Moderate 3+: Marked

P : Non-graded change NE: Not examined

Numerals represent the number of animals.

Not significantly different from control.

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

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

Findings	Group Dose (mg/kg) Grade	CPN 0							CPN 300						
		-	±	+	2+	3+	P	NE	-	±	+	2+	3+	P	NE
		Brain	5							5					
Spinal cord	5							5							
Pituitary gland Cyst	4						1	5						0	
Submandibular gland	5							5							
Sublingual gland	5							5							
Lymph node, submandibular	5							5							
Thyroid gland Ultimobranchial body	3						2	3						2	
Parathyroid gland	5							5							
Thymus Hyperplasia, epithelial tubule/cord	4	1	0	0	0			5	0	0	0	0	0		
Heart	5							5							
Trachea	5							5							

Notes) - : No abnormal changes ±: Very slight + : Slight 2+: Moderate 3+: Marked

P : Non-graded change NE: Not examined

Numerals represent the number of animals.

Not significantly different from control.

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

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

Findings	Group Dose (mg/kg) Grade	CPN							CPN						
		0							300						
		-	±	+	2+	3+	P	NE	-	±	+	2+	3+	P	NE
Lung															
Accumulation, foam cell		3	2	0	0	0			3	2	0	0	0		
Metaplasia, osseous		5	0	0	0	0			4	1	0	0	0		
Bronchus															
		5							5						
Liver															
Fatty change, hepatocyte		4	1	0	0	0			3	2	0	0	0		
Pancreas															
Atrophy, acinar cell		4	1	0	0	0			4	1	0	0	0		
Cellular infiltration, lymphocyte		5	0	0	0	0			4	1	0	0	0		
Stomach															
Heterotopic gastric gland		5					0		4					1	
Duodenum															
		5							5						
Jejunum															
		5							5						
Ileum															
		5							5						
Cecum															
		5							5						
Colon															
		5							5						

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

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

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

Findings	Group Dose (mg/kg) Grade	CPN 0							CPN 300						
		-	±	+	2+	3+	P	NE	-	±	+	2+	3+	P	NE
		Rectum	5							5					
Lymph node, mesenteric	5							5							
Spleen															
Deposit, pigment, brown		0	0	2	3	0		0	0	0	4	1			
Hematopoiesis, extramedullary		0	0	5	0	0		0	0	5	0	0			
Kidney															
Basophilic tubule, cortex		4	1	0	0	0		3	2	0	0	0			
Mineralization		5	0	0	0	0		3	1	1	0	0			
Urinary bladder	5							5							
Adrenal gland	5							5							
Ovary															
Luteinized follicle, cystic		5	0	0	0	0		3	1	1	0	0			
Uterus	5							5							
Vagina	5							5							
Eyeball															
Dysplasia, retina		4				1		5					0		

Notes) - : No abnormal changes ±: Very slight + : Slight 2+: Moderate 3+: Marked

P : Non-graded change NE: Not examined

Numerals represent the number of animals.

Not significantly different from control.

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

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

Findings	Group Dose (mg/kg) Grade	CPN 0							CPN 300						
		-	±	+	2+	3+	P	NE	-	±	+	2+	3+	P	NE
		Harderian gland													
Cellular infiltration, lymphocyte		4	1	0	0	0			5	0	0	0	0		
Sciatic nerve		5							5						
Skeletal muscle		5							5						
Femur		5							5						
Marrow, femur		5							5						

Notes) - : No abnormal changes ±: Very slight + : Slight 2+: Moderate 3+: Marked

P : Non-graded change NE: Not examined

Numerals represent the number of animals.

Not significantly different from control.

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

Table 34-3. Histopathological findings of female rats at the end of the recovery period [H.E. staining]

Findings	Group Dose (mg/kg) Grade	CPN 0							CPN 300						
		-	±	+	2+	3+	P	NE	-	±	+	2+	3+	P	NE
		Liver													
Fatty change, hepatocyte		0	1	0	0	0									
Necrosis, focal		0	1	0	0	0									
Spleen															
Deposit, pigment, brown		0	0	0	0	0	1								
Dilatation, cystic		0	1	0	0	0	0								
Hematopoiesis, extramedullary		0	0	0	1	0									
Adrenal gland															
Hypoplasia		4	0	1	0	0		5	0	0	0	0	0		
Mineralization		4	1	0	0	0		5	0	0	0	0	0		
Ovary															
Decreased number, corpus luteum		5	0	0	0	0		4	0	1	0	0			
Luteinized follicle, cystic		4	1	0	0	0		5	0	0	0	0			
Uterus															
		5						5							
Vagina															
		5						5							

Notes) - : No abnormal changes ±: Very slight + : Slight 2+: Moderate 3+: Marked

P : Non-graded change NE: Not examined

Numerals represent the number of animals.

Not significantly different from control.

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

Table 35. Results of observations about estrous cycle

Group	Control (vehicle :corn oil)	CPN 30 mg/kg	CPN 100 mg/kg	CPN 300 mg/kg
Number of animals examined	12	12	12	12
<u>Pre-administration period</u>				
Number of animals showing type of cycle				
4-day cycle	7	6	7	10
4/5-day cycle	3	2	1	0
5-day cycle	2	4	4	2
Mean length of estrous cycle in days; Mean±S.D. (N)	4.3 ± 0.4 (12)	4.4 ± 0.5 (12)	4.4 ± 0.5 (12)	4.2 ± 0.4 (12)
<u>Administration period</u>				
Number of animals showing type of cycle				
4-day cycle	8	8	7	9
4/5-day cycle	1	1	5	2
5-day cycle	3	3	0	1
Mean length of estrous cycle in days; Mean±S.D. (N)	4.3 ± 0.4 (12)	4.3 ± 0.5 (12)	4.2 ± 0.3 (12)	4.2 ± 0.3 (12)
Frequency of animals that show abnormal estrous cycles after the administration	0 / 12	0 / 12	0 / 12	0 / 12
Mean times of vaginal estrus during mating period; Mean±S.D. (N)	1.0 ± 0.0 (12)	1.0 ± 0.0 (12)	1.0 ± 0.0 (11)	1.0 ± 0.0 (12)

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

Table 36. Results of observations about reproductive performance

Group	Control (vehicle: corn oil)	CPN 30 mg/kg	CPN 100 mg/kg	CPN 300 mg/kg
Number of mated pairs [A]	12	12	12	12
Number of copulated pairs [B]	12	12	11	12
Copulation index [(B/A)×100,%]	100.0	100.0	91.7	100.0
Number of pregnant females [C]	12	11	11	12
Fertility index [(C/B)×100,%]	100.0	91.7	100.0	100.0
Pairing days until copulation ; Mean±S.D.(N)	2.9 ± 1.2 (12)	3.0 ± 1.1 (12)	2.7 ± 1.1 (11)	2.3 ± 1.2 (12)

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

Table 37. Observation of offspring (F₁)

Group	Control (vehicle: corn oil)	CPN 30 mg/kg	CPN 100 mg/kg	CPN 300 mg/kg
Number of dams	12	11	11	12
Gestation length (days)				
Mean ± S.D. per dam	21.9 ± 0.3	22.2 ± 0.4	22.2 ± 0.4	22.3 ± 0.6
Number of corpora lutea				
Total	192	181	181	200
Mean ± S.D. per dam	16.0 ± 1.9	16.5 ± 1.8	16.5 ± 1.8	16.7 ± 1.2
Number of implantation scars				
Total	187	175	171	193
Mean ± S.D. per dam	15.6 ± 1.8	15.9 ± 1.4	15.5 ± 1.6	16.1 ± 1.2
Implantation index (%) ^{a)}	97.5 ± 3.1	96.9 ± 3.8	94.7 ± 5.0	96.6 ± 4.5
Delivery index (dams,%) ^{b)}	100.0	100.0	100.0	91.7
Number of offspring at birth				
Total	175	167	154	185
Mean ± S.D. per dam	14.6 ± 1.6	15.2 ± 1.6	14.0 ± 1.9	15.4 ± 1.4
Number of live offspring at birth				
Male	87	73	75	75
Female	84	85	71	91
Total	171	158	146	166
Mean ± S.D. per dam	14.3 ± 1.8	14.4 ± 2.0	13.3 ± 2.8	13.8 ± 4.6
Sex ratio ^{c)}				
Mean ± S.D. per dam	0.51 ± 0.09	0.46 ± 0.13	0.53 ± 0.14	0.45 ± 0.13 (11)
Number of dead offspring				
Total	4	9	8	19
Mean ± S.D. per dam	0.3 ± 0.9	0.8 ± 1.5	0.7 ± 1.8	1.6 ± 4.0
Delivery index (offspring) ^{d)}				
Mean% ± S.D. per dam	93.9 ± 6.9	95.4 ± 5.9	90.1 ± 8.9	95.8 ± 4.7
Birth index ^{e)}				
Mean% ± S.D. per dam	91.7 ± 7.9	90.2 ± 8.6	85.4 ± 16.3	85.9 ± 27.7
Live birth index ^{f)}				
Mean% ± S.D. per dam	97.7 ± 6.3	94.8 ± 9.6	94.4 ± 13.8	89.1 ± 28.7
Number of offspring on day 4				
Male	86	73	70	73
Female	82	85	69	91
Sex ratio ^{c)}				
Mean ± S.D. per dam	0.51 ± 0.10	0.46 ± 0.13	0.51 ± 0.13 (10)	0.45 ± 0.13 (11)
Viability index ^{g)}				
Mean% ± S.D. per dam	98.2 ± 3.3	100.0 ± 0.0	90.9 ± 30.2	98.7 ± 2.8 (11)
Number of external abnormalities ^{h)}	0	0	0	0
Mean% ± S.D. per dam	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0 (11)

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

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

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

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

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

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

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

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

Figures in parentheses indicate number of dams.

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

Table 38. Body weights of offspring (F₁) before weaning

Group		Control (vehicle: corn oil)	CPN 30 mg/kg	CPN 100 mg/kg	CPN 300 mg/kg
Number of dams		12	11	11	11
Male					
Days after birth	0	6.8 ± 0.3	6.7 ± 0.4	6.7 ± 0.5	6.4 ± 0.4
	4	10.9 ± 0.5	10.8 ± 1.0	11.3 ± 1.0 (10)	10.3 ± 0.8
Number of dams		12	11	11	11
Female					
Days after birth	0	6.3 ± 0.3	6.3 ± 0.3	6.3 ± 0.3	6.2 ± 0.4
	4	10.3 ± 0.5	10.2 ± 0.8	10.6 ± 0.9 (10)	9.8 ± 0.7

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

Figures in parentheses indicate number of dams.

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

Table 39. General conditions in offspring (F₁) before weaning

Group	Number of offspring and general conditions	Days after birth				
		0	1	2	3	4
Control (vehicle: corn oil)	Number of offspring	171	171	170	168	168
	General appearance, No abnormality	171	170	168	168	168
	General appearance, Death		1	2		
CPN 30 mg/kg	Number of offspring	158	158	158	158	158
	General appearance, No abnormality	158	158	158	158	158
	General appearance, Death					
CPN 100 mg/kg	Number of offspring	146	146	139	139	139
	General appearance, No abnormality	146	139	139	139	139
	General appearance, Death		7			
CPN 300 mg/kg	Number of offspring	166	166	164	164	164
	General appearance, No abnormality	166	164	164	164	164
	General appearance, Death		2			

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

Table 40. Morphological observations of offspring (F₁)

Group	Control (vehicle: corn oil)	CPN 30 mg/kg	CPN 100 mg/kg	CPN 300 mg/kg
Dead pups				
Number of dead pups ^{a)}	7	9	15	21
Number of missing pups	2	0	0	5
Number of dead pups examined	5 (1)	9 (4)	15 (7)	16 (11)
Number of dead pups with external changes	0	0	1	0
Micrognathia			1	
Anophthalmia			1	
Cleft palate			1	
Number of dead pups with visceral changes	0	0	1	0
Micrencephaly			1	
Live pups				
Number of live pups examined (postnatal day 0)	171	158	146	166
Number of live pups with external changes	0	0	0	0
Number of live pups examined (postnatal day 4)	168	158	139	164
Number of live pups with external changes	0	0	0	0
Number of live pups with visceral changes	0	0	0	0

^{a)} including missing pups

Parenthesis indicates the number of offspring not examined because of their autolysis.

Annex 1



試験成績書

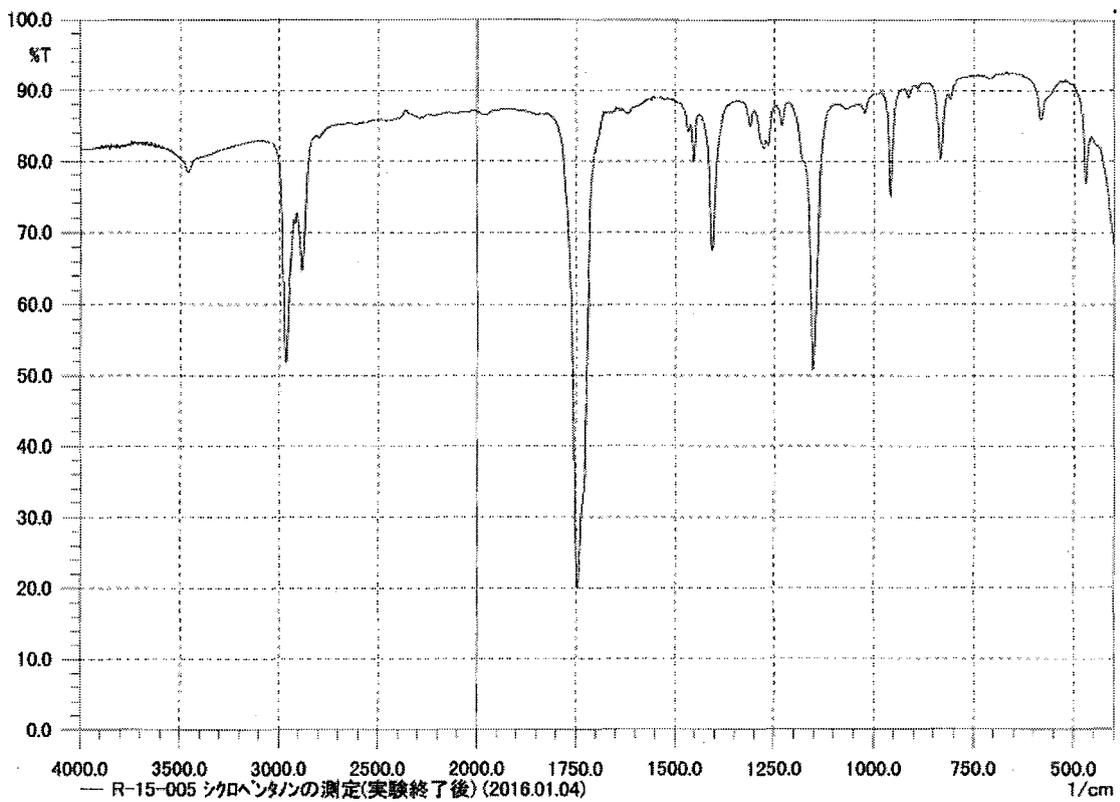
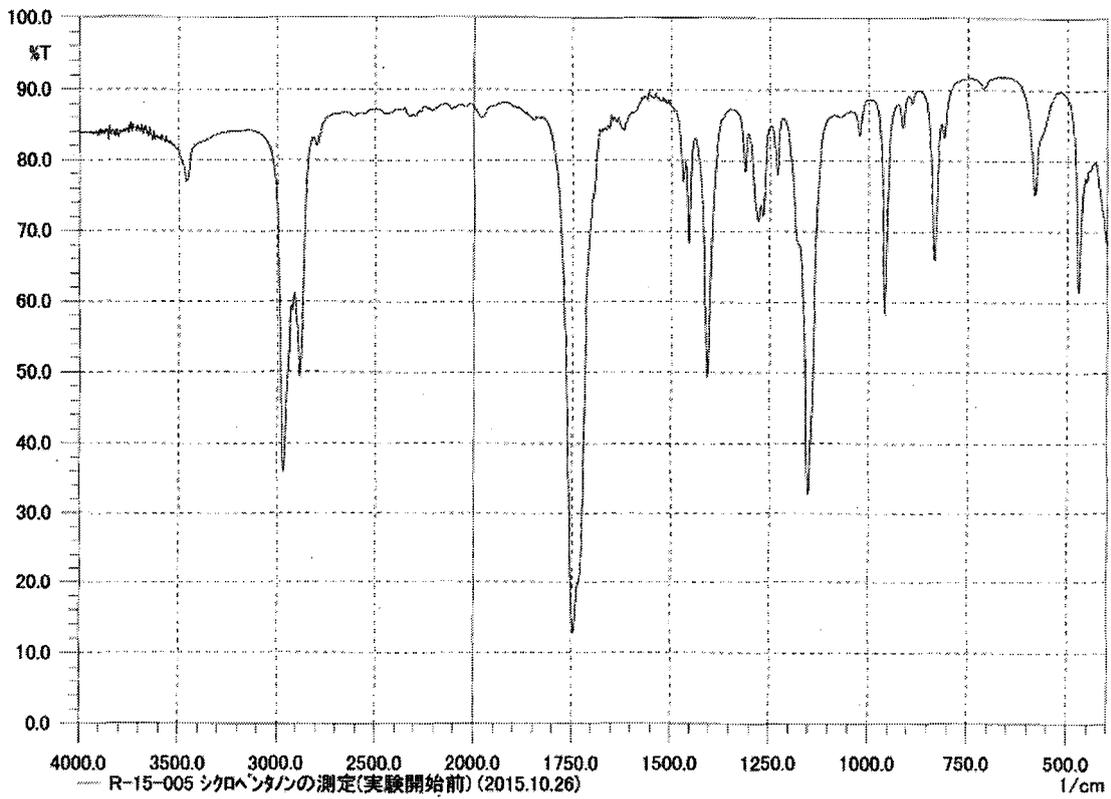
2015年09月01日

東京化成工業株式会社 品質保証
 〒103-0023
 東京都中央区日本橋本町4丁目10番
 TEL: 03(5640)8860 FAX: 03(5640)8861

製品名: Cyclopentanone			
製品コード: C0510 CAS番号: 120-92-3	等級: GR	製品ロット: W780E	判定: 合格
項目	結果	規格値	
純度(GC)	100.0 %	99.0 %以上	
比重 (20/20)	0.9503	0.9490 ~ 0.9520	
屈折率 n _{20/D}	1.4371	1.4350 ~ 1.4380	

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

Annex 2



Annex 3

1. 原体の安定性試験

- 1) 試薬等
赤外分光用臭化カリウム液体セル(以下、窓板) 島津製作所
- 2) 機器
フーリエ変換赤外分光光度計 (FTIR-8300) 島津製作所
- 3) 試験方法
実験開始前および実験終了後に以下の項目について確認する。
 - ① 性状
目視により被験物質の色調および性状を観察し、比較する。
 - ② 確認試験(赤外吸収スペクトル)
被験物質 1~3 滴を 2 枚の臭化カリウムの窓板の間にはさみ、これを $4000\sim 400\text{ cm}^{-1}$ の範囲で赤外吸収スペクトルを測定し(液膜法)、得られたスペクトルを比較する。
 - ③ 安定性の判断基準
判定の目安は、実験開始前と実験終了後で被験物質の色調や性状に変化がなく、かつ、赤外吸収スペクトルに変化がないこと。

2. 投与検体中の被験物質濃度測定法

- 2) 試薬等
2-プロパノール(HPLC 用、以下、2-PrOH) 和光純薬工業
- 3) 機器
電子天秤 (R200D および MSA1203S100DE) ザルトリウス
ガスクロマトグラフ 島津製作所
構成: GC-17A(ガスクロマトグラフ)、AOC-20i(オートインジェクタ)、C-R7A(データ処理装置)
- 4) 投与検体中の被験物質濃度測定法
 - ① 標準溶液の調製被験物質約 50 mg を精密に量り採り、2-PrOH に溶かし正確に 10 mL とする。この液 1 mL を正確に採り、2-PrOH を加えて正確に 100 mL とし、標準原液(約 $50\text{ }\mu\text{g/mL}$)とする。この液 1、1、3 および 5 mL を正確に採り、それぞれ 2-PrOH を加えて正確に 50、20、20 および 10 mL として標準溶液(約 1、2.5、7.5 および $25\text{ }\mu\text{g/mL}$ 、St 1~4)とする。標準原液および標準溶液は測定日ごとに被験物質を秤量し、各 $n=1$ で調製する。
 - ② 試料溶液の調製
 - (1) 約 7.5 mg/mL 溶液
投与検体 1 mL を正確に採り、2-PrOH を加えて正確に 50 mL とする。さらに、この液 1 mL を正確に採り、2-PrOH を加えて正確に 50 mL として試料溶液とする(約 $3\text{ }\mu\text{g/mL}$ 、希釈率 2500)。試料溶液の調製は投与検体の採取から $n=3$ とする。
 - (2) 約 25 mg/mL 溶液
投与検体 1 mL を正確に採り、2-PrOH を加えて正確に 50 mL とする。この液 1 mL を正確に採り、2-PrOH を加えて正確に 50 mL として試料溶液とする(約 $10\text{ }\mu\text{g/mL}$ 、希釈率 2500)。試料溶液の調製は投与検体の採取から $n=3$ とする。
 - (3) 約 75 mg/mL 溶液
投与検体 1 mL を正確に採り、2-PrOH を加えて正確に 100 mL とする。この液 1 mL を正確に採り、2-PrOH を加えて正確に 100 mL として試料溶液とする(約 $7.5\text{ }\mu\text{g/mL}$ 、希釈率 10000)。試料溶液の調製は投与検体の採取から $n=3$ とする。

Annex 3 (continued)

③ 被験物質の濃度測定

標準溶液 (St 1~4) および試料溶液をそれぞれ下記の試験条件でガスクロマトグラフィーにより試験を行う。標準溶液は各濃度 3 回ずつ、試料溶液はそれぞれ 1 回ずつ測定し、標準溶液から作成した検量線を用いて試料溶液中の被験物質濃度を求め、これに希釈率を乗じて投与検体中の被験物質濃度を算出する。検量線の作成はデータ処理装置の定量計算機能を用いる。また、安定性試験開始日と含量試験の測定の際、投与検体の媒体 (n=1、トウモロコシ油を 2-PrOH で 2500 倍に希釈する) を 1 回測定し、被験物質に相当するピークがないことを確認する。

試験条件

検出器	水素炎イオン化検出器 (FID)
カラム	InertCap 624 (内径 0.32 mm、長さ 30 m、膜厚 1.80 μ m)、 ジーエルサイエンス
キャリアガス	ヘリウム (He、70 kPa)
カラム温度	50°C (0.5min)、15°C/min、200°C (240°C)*
*: 媒体を含む試料溶液を測定する場合	
注入口温度	220°C
検出器温度	250°C
注入量	1 μ L
注入方式	スプリットレス (サンプリング時間 1分)
オートインジェクタ洗浄溶媒 2-PrOH	

システム適合性

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

④ 数値の取り扱い

- (1) 投与検体の調製濃度は、四捨五入して有効数字 3 桁で表示する。
- (2) 標準原液および標準溶液の濃度は、切り捨てて、有効数字 4 桁で表示する。
- (3) 試験結果における測定濃度 (mg/mL) およびその平均は四捨五入して有効数字 3 桁で表示する。
- (4) 含量 (%)、平均含量 (%)、残存率 (%)、平均残存率 (%) およびばらつき (%) は四捨五入して、小数第 1 位まで表示する。
- (5) システム適合性における偏差% は四捨五入して、小数第 1 位まで表示する。

Annex 4

安定性試験結果

試験番号: R-15-005

被験物質: シクロペンタン

調製年月日: 2015年10月27日

ロット番号: W780E

測定年月日: A 2015年10月27日(調製直後)

媒体: トウモロコシ油

B 2015年11月4日(保管後8日)

保管条件: 冷蔵、遮光

調製濃度 (mg/mL)	A				B				
	試料 番号	測定濃度 (mg/mL)	含量 ^{a)} (%)	ばらつき ^{b)} (%)	試料 番号	測定濃度 (mg/mL)	含量 ^{a)} (%)	ばらつき ^{b)} (%)	残存率 ^{c)} (%)
7.50	1	7.58	101.1	100.7	7	7.74	103.2	101.4	102.8
	2	7.50	100.0	99.6	8	7.57	100.9	99.2	100.5
	3	7.52	100.3	99.9	9	7.59	101.2	99.5	100.8
	平均	7.53	100.5		平均	7.63	101.8		101.4
75.0	4	74.4	99.2	99.9	10	74.4	99.2	99.9	99.9
	5	73.8	98.4	99.1	11	74.8	99.7	100.4	100.4
	6	75.2	100.3	100.9	12	74.3	99.1	99.7	99.7
	平均	74.5	99.3		平均	74.5	99.3		100.0

a): 各測定時の測定濃度 / 調製濃度×100、b): 各測定時の測定濃度 / 各測定時の平均測定濃度×100、c): 各測定時の測定濃度 / 調製直後の平均測定濃度×100

安定性の判定基準(溶液)

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

Annex 5

試験番号： R - 15 - 005

含量試験結果

被験物質：シクロペンタン

ロット番号：W780E

媒 体：トウモロコシ油

調製年月日：2015年11月9日

測定年月日：2015年11月9日

試料番号	調製濃度 (A) (mg/mL)	測定濃度 (B) (mg/mL)	平均測定濃度 (C) (mg/mL)	含量 B/A×100 (%)	平均含量 (%)	ばらつき B/C×100 (%)
13	7.50	7.56	7.56	100.8	100.8	100.0
14		7.56		100.8		100.0
15		7.57		100.9		100.1
16	25.0	24.5	24.7	98.0	98.7	99.2
17		24.8		99.2		100.4
18		24.7		98.8		100.0
19	75.0	74.8	75.1	99.7	100.1	99.6
20		75.1		100.1		100.0
21		75.3		100.4		100.3

含量の判定基準(溶液)

平均含量(%)が調製濃度の90.0~110.0%、また、各測定濃度(mg/mL)のばらつきがそれぞれ平均値の90.0~110.0%以内とする

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

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

Control (vehicle: corn oil)

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

-: General appearance, No abnormality.

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

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

CPN 300 mg/kg

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

-: General appearance, No abnormality.

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

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

Control (vehicle: corn oil)

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

-: General appearance, No abnormality.

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

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

CPN 300 mg/kg

Female No.	Days of recovery														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
F06061	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F06062	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F06063	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F06064	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F06065	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
-	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5

-: General appearance, No abnormality.

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

Appendix 3-1. General conditions in dams during pregnancy

Control (vehicle: corn oil)

Dam No.	Days of pregnancy																											
	0		1		2		3		4		5		6		7		8		9		10		11		12		13	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F01001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01002	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01003	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01004	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01005	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01006	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01007	a	a	a	a	a	a	a	a	a	a	a	a	a	a	a	a	a	a	a	a	a	a	a	a	a	a	a	a
F01008	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01009	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01010	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01011	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Number of dams	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
-	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
a	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

>: Excluded from analysis (not pregnant)

Pre: Before administration, Post: after administration.

-: General appearance, No abnormality.

a: Neck, Crust formation.

Appendix 3-1 (continued). General conditions in dams during pregnancy

Control (vehicle: corn oil)

Dam No.	Days of pregnancy																										
	14		15		16		17		18		19		20		21		22		23		24		25		26		
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	
F01001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01002	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01003	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01004	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01005	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01006	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01007	a	a	a	a	a	a	a	a	a	a	a	a	a	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01008	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01009	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01010	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01011	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F01012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Number of dams	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	6	6	0	0	0	0	0	0	0	0	0	0
-	11	11	11	11	11	11	11	11	11	11	11	11	11	12	12	12	12	6	6	0	0	0	0	0	0	0	0
a	1	1	1	1	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0

>: Excluded from analysis (not pregnant)

Pre: Before administration, Post: after administration.

-: General appearance, No abnormality.

a: Neck, Crust formation.

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

Appendix 3-2. General conditions in dams during pregnancy

CPN 30 mg/kg

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

>: Excluded from analysis (not pregnant)
 Pre: Before administration, Post: after administration.
 -: General appearance, No abnormality.
 a: Neck, Crust formation.

Appendix 3-2 (continued). General conditions in dams during pregnancy

CPN 30 mg/kg

Dam No.	Days of pregnancy																										
	14		15		16		17		18		19		20		21		22		23		24		25		26		
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	
F02013	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
F02014	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
F02015	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
F02016	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
F02017	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
F02018	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
F02019	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
F02020	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
F02021	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
F02022	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
F02023	>	>	>	>	>	>	>	>	>	>	>	>	>	>	>	>	>	>	>	>	>	>	>	>	>	>	>
F02024	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Number of dams	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	5	5	0	0	0	0	0	0	0	0	
-	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	5	5	0	0	0	0	0	0	0	0	
a	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	

>: Excluded from analysis (not pregnant)
 Pre: Before administration, Post: after administration.
 -: General appearance, No abnormality.
 a: Neck, Crust formation.

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

Appendix 3-3. General conditions in dams during pregnancy

CPN 100 mg/kg

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

>: Excluded from analysis (not pregnant)

Pre: Before administration, Post: after administration.

-: General appearance, No abnormality.

a: Neck, Crust formation.

Appendix 3-3 (continued). General conditions in dams during pregnancy

CPN 100 mg/kg

Dam No.	Days of pregnancy																											
	14		15		16		17		18		19		20		21		22		23		24		25		26			
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F03025	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03026	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03027	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03028	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03029	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03030	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03031	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03032	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03033	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03035	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F03036	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Number of dams	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	5	5	0	0	0	0	0	0	0	0	0	0
-	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	5	5	0	0	0	0	0	0	0	0	0	
a	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	

>: Excluded from analysis (not pregnant)

Pre: Before administration, Post: after administration.

-: General appearance, No abnormality.

a: Neck, Crust formation.

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

Appendix 3-4. General conditions in dams during pregnancy

CPN 300 mg/kg

Dam No.	Days of pregnancy																											
	0		1		2		3		4		5		6		7		8		9		10		11		12		13	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F04037	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04038	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04039	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04040	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04041	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04042	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04043	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04044	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04045	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04046	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04047	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04048	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Number of dams	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
-	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
a	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

>: Excluded from analysis (not pregnant)

Pre: Before administration, Post: after administration.

-: General appearance, No abnormality.

a: Neck, Crust formation.

Appendix 3-4 (continued). General conditions in dams during pregnancy

CPN 300 mg/kg

Dam No.	Days of pregnancy																											
	14		15		16		17		18		19		20		21		22		23		24		25		26			
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F04037	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04038	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04039	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04040	a	a	a	a	a	a	a	a	a	a	a	a	a	a	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04041	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04042	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04043	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04044	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04045	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04046	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04047	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F04048	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Number of dams	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	8	8	1	1	0	0	0	0	0	0	0	0
-	11	11	11	11	11	11	11	11	11	11	11	11	11	11	12	12	8	8	1	1	0	0	0	0	0	0	0	0
a	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0

>: Excluded from analysis (not pregnant)

Pre: Before administration, Post: after administration.

-: General appearance, No abnormality.

a: Neck, Crust formation.

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

Appendix 4-1. General conditions in dams during lactation

Control (vehicle: corn oil)

Dam No.	Days of lactation											
	0		1		2		3		4		5	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F01001	#	#	-	-	-	-	-	-	-	-	-	-
F01002	#	#	-	-	-	-	-	-	-	-	-	-
F01003	-	-	-	-	-	-	-	-	-	-	-	-
F01004	#	#	-	-	-	-	-	-	-	-	-	-
F01005	-	-	-	-	-	-	-	-	-	-	-	-
F01006	#	#	-	-	-	-	-	-	-	-	-	-
F01007	-	-	-	-	-	-	-	-	-	-	-	-
F01008	-	-	-	-	-	-	-	-	-	-	-	-
F01009	#	#	-	-	-	-	-	-	-	-	-	-
F01010	#	#	-	-	-	-	-	-	-	-	-	-
F01011	-	-	-	-	-	-	-	-	-	-	-	-
F01012	#	#	-	-	-	-	-	-	-	-	-	-
Number of dams	5	5	12	12	12	12	12	12	12	12	12	12
-	5	5	12	12	12	12	12	12	12	12	12	12

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

Pre: Before administration, Post: after administration.

-: General appearance, No abnormality.

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

Appendix 4-2. General conditions in dams during lactation

CPN 30 mg/kg

Dam No.	Days of lactation											
	0		1		2		3		4		5	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F02013	-	-	-	-	-	-	-	-	-	-	-	-
F02014	#	#	-	-	-	-	-	-	-	-	-	-
F02015	-	-	-	-	-	-	-	-	-	-	-	-
F02016	#	#	-	-	-	-	-	-	-	-	-	-
F02017	-	-	-	-	-	-	-	-	-	-	-	-
F02018	-	-	-	-	-	-	-	-	-	-	-	-
F02019	-	-	-	-	-	-	-	-	-	-	-	-
F02020	-	-	-	-	-	-	-	-	-	-	-	-
F02021	-	-	-	-	-	-	-	-	-	-	-	-
F02022	#	#	-	-	-	-	-	-	-	-	-	-
F02024	-	-	-	-	-	-	-	-	-	-	-	-
Number of dams	8	8	11	11	11	11	11	11	11	11	11	11
-	8	8	11	11	11	11	11	11	11	11	11	11

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

Pre: Before administration, Post: after administration.

-: General appearance, No abnormality.

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

Appendix 4-3. General conditions in dams during lactation

CPN 100 mg/kg

Dam No.	Days of lactation											
	0		1		2		3		4		5	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F03025	-	-	-	-	-	-	-	-	-	-	-	-
F03026	-	-	-	-	-	-	-	-	-	-	-	-
F03027	-	-	-	-	-	-	-	-	-	-	-	-
F03028	-	-	-	Total litter loss on day 1 of lactation								
F03029	-	-	-	-	-	-	-	-	-	-	-	-
F03030	#	#	-	-	-	-	-	-	-	-	-	-
F03031	#	#	-	-	-	-	-	-	-	-	-	-
F03032	-	-	-	-	-	-	-	-	-	-	-	-
F03033	-	-	-	-	-	-	-	-	-	-	-	-
F03035	#	#	-	-	-	-	-	-	-	-	-	-
F03036	-	-	-	-	-	-	-	-	-	-	-	-
Number of dams	8	8	11	10	10	10	10	10	10	10	10	10
-	8	8	11	10	10	10	10	10	10	10	10	10

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

Pre: Before administration, Post: after administration.

-: General appearance, No abnormality.

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

Appendix 4-4. General conditions in dams during lactation

CPN 300 mg/kg

Dam No.	Days of lactation											
	0		1		2		3		4		5	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F04037	-	Total litter loss on day 0 of lactation										
F04038	#	#	-	-	-	-	-	-	-	-	-	-
F04039	-	-	-	-	-	-	-	-	-	-	-	-
F04040	-	-	-	-	-	-	-	-	-	-	-	-
F04041	#	#	-	-	-	-	-	-	-	-	-	-
F04042	-	-	-	-	-	-	-	-	-	-	-	-
F04043	#	#	-	-	-	-	-	-	-	-	-	-
F04044	#	#	-	-	-	-	-	-	-	-	-	-
F04045	#	#	-	-	-	-	-	-	-	-	-	-
F04046	-	-	-	-	-	-	-	-	-	-	-	-
F04047	-	-	-	-	-	-	-	-	-	-	-	-
F04048	#	#	-	-	-	-	-	-	-	-	-	-
Number of dams	6	5	11	11	11	11	11	11	11	11	11	11
-	6	5	11	11	11	11	11	11	11	11	11	11

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

Pre: Before administration, Post: after administration.

-: General appearance, No abnormality.

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

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

Control (vehicle: corn oil)

Male No.	Open-field observations																														
	Gait										Stereotypy						Withdrawal reflex														
	Pre ^a	T8 ^b	T15	T24	T30	T36	T42	R7 ^c	R14	Pre	T8	T15	T24	T30	T36	T42	R7	R14	Pre	T8	T15	T24	T30	T36	T42	R7	R14				
M01001	2	2	2	2	2	2	2			2	2	2	2	2	2				2	2	2	2	2	2							
M01002	2	2	2	2	2	2	2			2	2	2	2	2	2				2	2	2	2	2	2							
M01003	2	2	2	2	2	2	2			2	2	2	2	2	2				2	2	2	2	2	2							
M01004	2	2	2	2	2	2	2			2	2	2	2	2	2				2	2	2	2	2	2							
M01005	2	2	2	2	2	2	2			2	2	2	2	3	2	2			2	2	2	2	2	2							
M01006	2	2	1	Sacrificed on day 18 of administration								2	2	2	Sacrificed on day 18 of administration								2	2	1	Sacrificed on day 18 of administration					
M01007	2	2	2	2	2	2	2			2	2	2	2	2	2				2	2	2	2	2	2							
M01008	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2			
M01009	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2			
M01010	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2			
M01011	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2			
M01012	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2			
Total score	1:0	1:0	1:1	1:0	1:0	1:0	1:0	1:0	1:0	3:0	3:0	3:0	3:0	3:1	3:0	3:0	3:0	3:0	1:0	1:0	1:1	1:0	1:0	1:0	1:0	1:0	1:0				
(N)	(12)	(12)	(12)	(11)	(11)	(11)	(11)	(5)	(5)	(12)	(12)	(12)	(11)	(11)	(11)	(11)	(5)	(5)	(12)	(12)	(12)	(11)	(11)	(11)	(11)	(5)	(5)				

^a pre-administration; ^b day 8 of administration; ^c day 7 of recovery

Gait [2, normal; 1, abnormal gait]

Stereotypy [2, not observed; 3, observed (rearing)]

Withdrawal reflex [2, normal; 1, hyporeflexia]

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

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

Appendix 5-1-1 (continued). Detailed clinical observations of male rats

Control (vehicle: corn oil)

Male No.	Open-field observations																	
	Urination									Defecation								
	Pre ^a	T8 ^b	T15	T24	T30	T36	T42	R7 ^c	R14	Pre	T8	T15	T24	T30	T36	T42	R7	R14
M01001	0	0	0	2	2	1	1			0	0	0	0	0	0	0		
M01002	0	1	0	0	0	0	0			0	0	0	0	0	0	0		
M01003	0	0	0	1	0	0	1			0	0	0	0	0	0	0		
M01004	0	0	0	0	0	1	0			0	0	0	0	0	0	0		
M01005	0	0	1	1	0	0	0			0	0	0	0	0	0	0		
M01006	0	0	0	Sacrificed on day 18 of administration							0	0	0	Sacrificed on day 18 of administration				
M01007	0	0	0	0	0	0	0			0	0	0	0	0	0	0		
M01008	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M01009	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
M01010	0	1	1	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0
M01011	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M01012	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Total score	1	2	2	4	2	2	2	1	0	0	0	1	1	1	0	0	0	0
(N)	(12)	(12)	(12)	(11)	(11)	(11)	(11)	(5)	(5)	(12)	(12)	(12)	(11)	(11)	(11)	(11)	(5)	(5)

^a pre-administration; ^b day 8 of administration; ^c day 7 of recovery

Urination [frequency/30sec]

Defecation [frequency/30sec]

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

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

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

CPN 30 mg/kg

Male No.	Open-field observations																							
	Gait							Stereotypy							Withdrawal reflex									
	Pre ^a	T8 ^b	T15	T24	T30	T36	T42	Pre	T8	T15	T24	T30	T36	T42	Pre	T8	T15	T24	T30	T36	T42			
M02013	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2		
M02014	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2		
M02015	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2		
M02016	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2		
M02017	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2		
M02018	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2		
M02019	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2		
M02020	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2		
M02021	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2		
M02022	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2		
M02023	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2		
M02024	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2		
Total score	1:0	1:0	1:0	1:0	1:0	1:0	1:0	3:0	3:0	3:0	3:0	3:0	3:0	3:0	1:0	1:0	1:0	1:0	1:0	1:0	1:0	1:0		
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)		

^a pre-administration; ^b day 8 of administration

Gait [2, normal; 1, abnormal gait]

Stereotypy [2, not observed; 3, observed (rearing)]

Withdrawal reflex [2, normal; 1, hyporeflexia]

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

Combined repeat dose and reproductive/developmental toxicity screening test of Cyclopentanone by oral administration in rats
Appendix 5-1-2 (continued). Detailed clinical observations of male rats

CPN 30 mg/kg

Male No.	Open-field observations													
	Urination							Defecation						
	Pre ^a	T8 ^b	T15	T24	T30	T36	T42	Pre	T8	T15	T24	T30	T36	T42
M02013	1	0	0	0	0	0	0	0	0	0	0	0	0	0
M02014	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M02015	0	0	0	0	0	0	1	0	0	0	0	0	0	0
M02016	0	1	0	0	0	0	0	0	0	0	0	0	0	0
M02017	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M02018	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M02019	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M02020	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M02021	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M02022	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M02023	1	0	0	0	0	0	0	0	0	0	0	0	0	0
M02024	1	0	1	1	0	0	0	0	0	0	0	0	0	0
Total score	3	1	1	1	0	0	1	0	0	0	0	0	0	0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)

^a pre-administration; ^b day 8 of administration

Urination [frequency/30sec]

Defecation [frequency/30sec]

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

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

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

CPN 100 mg/kg

Male No.	Open-field observations																				
	Gait							Stereotypy							Withdrawal reflex						
	Pre ^a	T8 ^b	T15	T24	T30	T36	T42	Pre	T8	T15	T24	T30	T36	T42	Pre	T8	T15	T24	T30	T36	T42
M03025	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
M03026	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
M03027	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
M03028	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
M03029	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
M03030	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
M03031	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
M03032	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
M03033	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
M03034	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
M03035	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
M03036	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Total score	1:0	1:0	1:0	1:0	1:0	1:0	1:0	3:0	3:0	3:0	3:0	3:0	3:0	3:0	1:0	1:0	1:0	1:0	1:0	1:0	1:0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)

^a pre-administration; ^b day 8 of administration

Gait [2, normal; 1, abnormal gait]

Stereotypy [2, not observed; 3, observed (rearing)]

Withdrawal reflex [2, normal; 1, hyporeflexia]

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

Combined repeat dose and reproductive/developmental toxicity screening test of Cyclopentanone by oral administration in rats
Appendix 5-1-3 (continued). Detailed clinical observations of male rats

CPN 100 mg/kg

Male No.	Open-field observations													
	Urination							Defecation						
	Pre ^a	T8 ^b	T15	T24	T30	T36	T42	Pre	T8	T15	T24	T30	T36	T42
M03025	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M03026	0	1	1	1	1	1	0	0	0	0	0	0	0	0
M03027	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M03028	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M03029	0	0	0	0	0	1	0	0	0	0	0	0	0	0
M03030	0	1	0	0	0	0	0	0	0	0	0	0	0	0
M03031	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M03032	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M03033	0	0	1	0	2	1	0	0	0	0	0	0	0	0
M03034	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M03035	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M03036	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Total score	0	2	2	1	3	3	0	0	0	0	0	0	0	0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)

^a pre-administration; ^b day 8 of administration

Urination [frequency/30sec]

Defecation [frequency/30sec]

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

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

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

CPN 300 mg/kg

Male No.	Open-field observations																													
	Gait										Stereotypy										Withdrawal reflex									
	Pre ^a	T8 ^b	T15	T24	T30	T36	T42	R7 ^c	R14	Pre	T8	T15	T24	T30	T36	T42	R7	R14	Pre	T8	T15	T24	T30	T36	T42	R7	R14			
M04037	2	2	2	2	2	2	2			2	2	2	2	2	2	2			2	2	2	2	2	2	2					
M04038	2	2	2	2	2	2	2			2	2	2	2	2	2	2			2	2	2	2	2	2	2					
M04039	2	2	2	2	2	2	2			2	2	2	2	2	2	2			2	2	2	2	2	2	2					
M04040	2	2	2	2	2	2	2			2	2	2	2	2	2	2			2	2	2	2	2	2	2					
M04041	2	2	2	2	2	2	2			2	2	2	2	2	2	2			2	2	2	2	2	2	2					
M04042	2	2	2	2	2	2	2			2	2	2	2	2	2	2			2	2	2	2	2	2	2					
M04043	2	2	2	2	2	2	2			2	2	2	2	2	2	2			2	2	2	2	2	2	2					
M04044	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2			
M04045	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2			
M04046	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2			
M04047	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2			
M04048	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2			
Total score	1:0	1:0	1:0	1:0	1:0	1:0	1:0	1:0	1:0	3:0	3:0	3:0	3:0	3:0	3:0	3:0	3:0	3:0	3:0	1:0	1:0	1:0	1:0	1:0	1:0	1:0				
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(5)	(5)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(5)	(5)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(5)	(5)			

^a pre-administration; ^b day 8 of administration; ^c day 7 of recovery

Gait [2, normal; 1, abnormal gait]

Stereotypy [2, not observed; 3, observed (rearing)]

Withdrawal reflex [2, normal; 1, hyporeflexia]

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

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

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

CPN 300 mg/kg

Male No.	Open-field observations ^{c)}																	
	Urination									Defecation								
	Pre ^a	T8 ^b	T15	T24	T30	T36	T42	R7 ^c	R14	Pre	T8	T15	T24	T30	T36	T42	R7	R14
M04037	0	0	0	0	0	0	0			0	0	0	0	0	0	0		
M04038	0	0	0	0	0	0	0			0	0	0	0	0	0	0		
M04039	0	0	0	0	0	0	0			0	0	0	0	0	0	0		
M04040	0	0	1	0	1	0	0			0	0	0	0	1	0	0		
M04041	0	0	0	0	0	0	0			0	0	0	0	0	0	0		
M04042	0	0	0	0	0	0	0			0	0	0	0	0	0	0		
M04043	0	0	0	0	0	0	0			0	0	0	0	0	0	0		
M04044	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M04045	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
M04046	0	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0	0	0
M04047	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M04048	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Total score	0	0	1	0	2	1	0	0	2	0	0	0	0	1	0	0	0	0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(5)	(5)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(5)	(5)

^a pre-administration; ^b day 8 of administration; ^c day 7 of recovery

Urination [frequency/30sec]

Defecation [frequency/30sec]

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

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

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

Control (vehicle: corn oil)

Male No.	Open-field observations																	
	Urination									Defecation								
	Pre ^a	T8 ^b	T15	T24	T30	T36	T42	T49	L ^c	Pre ^a	T8 ^b	T15	T24	T30	T36	T42	T49	L ^c
F01001	0	0	0	0	0	0			1	0	0	0	0	0	0			0
F01002	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F01003	0	0	0	0	0	0			1	0	0	0	0	0	0			1
F01004	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F01005	0	0	0	0	1	0			0	0	0	0	0	0	0			0
F01006	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F01007	0	0	0	1	0	1			0	0	0	0	0	0	0			0
F01008	1	0	0	0	0	0			0	0	0	0	0	0	0			0
F01009	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F01010	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F01011	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F01012	0	0	0	0	0	0			0	0	0	0	0	0	0			0
Total score	1	0	0	1	1	1			2	0	0	0	0	0	0			1
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(0)	(0)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(0)	(0)	(12)

^a pre-administration; ^b day 8 of administration; ^c lactation period

Urination [frequency/30sec]

Defecation [frequency/30sec]

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

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

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

CPN 30 mg/kg

Male No.	Open-field observations																	
	Urination									Defecation								
	Pre ^a	T8 ^b	T15	T24	T30	T36	T42	T49	L ^c	Pre ^a	T8 ^b	T15	T24	T30	T36	T42	T49	L ^c
F02013	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F02014	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F02015	0	0	0	1	0	0			0	0	0	0	0	0	0			0
F02016	1	0	0	0	0	0			1	0	0	0	0	0	0			0
F02017	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F02018	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F02019	0	0	0	0	0	1			0	0	0	0	0	0	0			0
F02020	1	0	0	0	1	0			0	0	0	0	0	0	0			0
F02021	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F02022	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F02023	0	0	0	0	0	0			Not pregnant	0	0	0	0	0	0			Not pregnant
F02024	0	0	0	0	0	0			0	0	0	0	0	0	0			0
Total score	2	0	0	1	1	1			1	0	0	0	0	0	0			0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(0)	(0)	(11)	(12)	(12)	(12)	(12)	(12)	(12)	(0)	(0)	(11)

^a pre-administration; ^b day 8 of administration; ^c lactation period

Urination [frequency/30sec]

Defecation [frequency/30sec]

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

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

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

CPN 100 mg/kg

Male No.	Open-field observations																	
	Urination									Defecation								
	Pre ^a	T8 ^b	T15	T24	T30	T36	T42	T49	L ^c	Pre ^a	T8 ^b	T15	T24	T30	T36	T42	T49	L ^c
F03025	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F03026	0	1	0	0	0	0			0	0	0	0	0	0	0			0
F03027	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F03028	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F03029	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F03030	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F03031	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F03032	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F03033	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F03034	0	0	0	0	0	0	0	0	Not copulated	0	0	0	0	0	0	0	0	Not copulated
F03035	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F03036	0	0	0	0	0	0			1	0	0	0	0	0	0			0
Total score	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(1)	(1)	(11)	(12)	(12)	(12)	(12)	(12)	(12)	(1)	(1)	(11)

^a pre-administration; ^b day 8 of administration; ^c lactation period

Urination [frequency/30sec]

Defecation [frequency/30sec]

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

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

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

CPN 300 mg/kg

Male No.	Open-field observations																	
	Urination									Defecation								
	Pre ^a	T8 ^b	T15	T24	T30	T36	T42	T49	L ^c	Pre ^a	T8 ^b	T15	T24	T30	T36	T42	T49	L ^c
F04037	0	0	0	0	0	0			#	0	0	0	0	0	0			#
F04038	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F04039	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F04040	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F04041	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F04042	0	0	0	0	0	0			1	0	0	0	0	0	0			0
F04043	0	0	0	0	0	0			1	0	0	0	0	0	0			0
F04044	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F04045	0	0	0	0	0	0			1	0	0	0	0	0	0			0
F04046	0	0	0	0	1	1			0	0	0	0	0	0	0			0
F04047	0	0	0	0	0	0			0	0	0	0	0	0	0			0
F04048	0	0	0	0	0	0			0	0	0	0	0	0	0			0
Total score	0	0	0	0	1	1			3	0	0	0	0	0	0			0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(0)	(0)	(11)	(12)	(12)	(12)	(12)	(12)	(12)	(0)	(0)	(11)

^a pre-administration; ^b day 8 of administration; ^c lactation period

Urination [frequency/30sec]

Defecation [frequency/30sec]

Total litter loss on day 0 of lactation

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

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

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

Control (vehicle: corn oil)

Female No.	Open-field observations																		
	Urination									Defecation									
	Pre ^a	T8 ^b	T15	T24	T30	T36	T42	R7 ^c	R14	Pre	T8	T15	T24	T30	T36	T42	R7 ^c	R14	
F05049	0	0	0	0	0	0	0			0	0	0	0	0	0	0			
F05050	0	0	0	0	0	0	0			0	0	0	0	0	0	0			
F05051	0	0	0	0	0	0	0			0	0	0	0	0	0	0			
F05052	0	0	0	0	0	0	0			0	0	0	0	0	0	0			
F05053	0	0	0	0	0	0	0			0	0	0	0	0	0	0			
F05054	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
F05055	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
F05056	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	
F05057	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	
F05058	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Total score	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	
(N)	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(5)	(5)	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(5)	(5)	

^a pre-administration; ^b day 8 of administration; ^c day 7 of recovery

Urination [frequency/30sec]

Defecation [frequency/30sec]

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

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

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

CPN 300 mg/kg

Female No.	Open-field observations																	
	Urination									Defecation								
	Pre ^a	T8 ^b	T15	T24	T30	T36	T42	R7 ^c	R14	Pre	T8	T15	T24	T30	T36	T42	R7	R14
F06056	0	0	0	0	0	0	0			0	0	0	0	0	0	0		
F06057	0	0	0	0	0	0	0			0	0	0	0	0	0	0		
F06058	0	0	0	0	0	0	0			0	0	0	0	0	0	0		
F06059	0	0	0	0	0	0	0			0	0	0	0	0	0	0		
F06060	0	0	0	0	0	0	0			0	0	0	0	0	0	0		
F06061	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F06062	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F06063	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
F06064	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F06065	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Total score	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
(N)	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(5)	(5)	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(5)	(5)

^a pre-administration; ^b day 8 of administration; ^c day 7 of recovery

Urination [frequency/30sec]

Defecation [frequency/30sec]

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

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

Appendix 7-1-1. Body weights of male rats

Control (vehicle: corn oil)

Male No.	Days of administration							
	1	4	7	14	21	28	35	42
M01001	399.3	409.9	427.0	447.5	468.6	509.0	537.1	539.1
M01002	423.1	431.4	445.7	468.4	491.1	519.9	544.5	552.5
M01003	403.0	406.7	425.7	446.8	472.3	490.0	502.3	521.9
M01004	409.1	426.3	449.3	470.5	493.0	511.9	530.1	540.8
M01005	393.4	408.5	423.5	452.2	473.7	493.7	515.0	518.7
M01006	413.7	417.1	433.1	458.4	Sacrificed on day 18 of administration			
M01007	412.4	424.7	425.5	443.2	465.4	487.0	514.2	526.6
M01008	368.7	385.4	397.2	427.2	433.1	472.0	485.6	501.9
M01009	410.0	418.5	427.5	443.1	459.3	485.7	503.5	527.8
M01010	422.9	427.9	441.2	460.4	475.9	493.9	514.1	540.1
M01011	422.9	441.2	452.2	482.1	506.3	531.9	536.9	553.0
M01012	386.8	399.3	411.5	437.7	462.4	481.1	496.4	513.4
Number of males	12	12	12	12	11	11	11	11
Mean	405.4	416.4	430.0	453.1	472.8	497.8	516.3	530.5
S.D.	16.4	15.4	15.8	15.5	19.5	18.1	18.8	16.2

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

Appendix 7-1-2. Body weights of male rats

CPN 30 mg/kg

Male No.	Days of administration							
	1	4	7	14	21	28	35	42
M02013	394.8	408.8	421.2	427.1	456.7	477.8	492.0	500.1
M02014	395.0	410.3	417.5	442.0	464.9	487.1	500.3	507.9
M02015	399.8	404.8	414.5	433.4	444.5	475.1	493.4	502.5
M02016	417.4	422.5	432.2	452.1	474.0	498.3	518.7	524.9
M02017	411.4	427.6	435.5	455.5	476.1	490.7	511.6	520.9
M02018	410.1	411.8	425.2	443.5	474.1	494.0	507.0	523.6
M02019	394.4	408.5	416.3	449.2	453.3	482.4	506.5	530.1
M02020	425.6	449.1	461.4	488.8	525.8	552.6	584.7	602.8
M02021	378.9	382.6	391.2	410.0	426.4	436.2	438.5	449.8
M02022	425.4	432.9	438.0	456.4	472.4	507.1	527.2	541.2
M02023	387.3	401.9	418.5	438.8	460.6	484.3	500.3	519.7
M02024	408.3	427.9	444.2	469.7	480.4	518.6	548.9	578.2
Number of males	12	12	12	12	12	12	12	12
Mean	404.0	415.7	426.3	447.2	467.4	492.0	510.8	525.1
S.D.	14.8	17.3	17.7	20.2	24.0	27.7	34.9	38.5
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	DU

NS: Not significantly different from the control group.

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

DU: Analysis by Dunnett's test.

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

Appendix 7-1-3. Body weights of male rats

CPN 100 mg/kg

Male No.	Days of administration							
	1	4	7	14	21	28	35	42
M03025	427.4	435.9	445.6	469.6	492.3	515.4	533.5	545.3
M03026	400.9	413.1	430.2	453.0	460.5	479.5	497.9	505.0
M03027	374.8	385.2	391.8	416.9	378.3	410.5	434.6	442.0
M03028	400.8	421.2	437.9	467.7	477.4	500.0	519.4	528.9
M03029	417.2	441.7	458.0	486.5	508.7	534.4	549.3	566.1
M03030	403.6	418.4	434.7	460.3	473.8	494.1	514.5	531.0
M03031	418.7	431.7	439.4	466.8	489.2	519.4	541.8	557.0
M03032	414.1	431.1	445.8	470.4	494.2	518.3	547.8	574.2
M03033	392.7	403.4	416.6	444.7	455.3	475.8	492.4	508.2
M03034	384.0	390.2	403.4	432.5	432.5	454.4	483.9	506.6
M03035	389.0	404.4	411.2	432.2	436.3	457.3	468.0	474.0
M03036	401.0	409.5	417.2	436.6	438.3	460.6	484.4	495.4
Number of males	12	12	12	12	12	12	12	12
Mean	402.0	415.5	427.7	453.1	461.4	485.0	505.6	519.5
S.D.	15.5	17.9	19.6	20.6	36.2	35.6	35.2	38.9
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	DU

NS: Not significantly different from the control group.

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

DU: Analysis by Dunnett's test.

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

Appendix 7-1-4. Body weights of male rats

CPN 300 mg/kg

Male No.	Days of administration							
	1	4	7	14	21	28	35	42
M04037	403.8	411.2	418.5	443.9	460.2	476.4	486.7	489.3
M04038	400.7	409.5	413.7	425.0	436.1	460.5	472.8	484.5
M04039	412.9	413.7	419.8	423.5	440.1	450.0	458.1	461.4
M04040	406.7	421.0	426.4	440.5	456.4	475.1	490.1	493.1
M04041	418.2	413.9	414.5	427.3	433.1	452.9	460.2	469.0
M04042	410.4	416.8	427.4	436.1	450.3	469.9	484.3	493.0
M04043	386.6	394.9	394.5	402.8	413.4	422.5	435.1	447.9
M04044	419.8	435.4	445.8	469.4	465.1	487.8	513.6	527.5
M04045	435.4	452.4	465.3	486.8	496.4	517.8	530.2	543.6
M04046	396.6	416.9	422.7	445.6	461.8	477.5	498.3	507.8
M04047	376.0	379.8	378.5	393.6	414.0	434.8	445.7	466.4
M04048	413.6	424.7	433.5	462.7	484.5	511.4	529.0	536.5
Number of males	12	12	12	12	12	12	12	12
Mean	406.7	415.9	421.7	438.1	451.0	469.7	483.7	493.3
S.D.	15.7	18.2	22.2	26.6	25.3	28.1	30.9	30.5
Significance	NS	NS	NS	NS	NS	NS	NS	*
Statistical method	AN	AN	AN	AN	AN	AN	AN	DU

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

NS: Not significantly different from the control group.

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

DU: Analysis by Dunnett's test.

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

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

Control (vehicle: corn oil)

Male No.	Days of recovery		
	1	7	14
M01008	500.2	507.9	514.8
M01009	519.2	529.0	529.8
M01010	536.6	544.0	548.2
M01011	553.8	563.7	572.9
M01012	518.0	534.4	540.4
Number of males	5	5	5
Mean	525.6	535.8	541.2
S.D.	20.4	20.4	21.7

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

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

CPN 300 mg/kg

Male No.	Days of recovery		
	1	7	14
M04044	527.3	561.4	580.4
M04045	540.8	566.5	590.3
M04046	511.6	519.5	541.5
M04047	474.0	491.6	518.5
M04048	538.9	554.5	569.9
Number of males	5	5	5
Mean	518.5	538.7	560.1
S.D.	27.5	32.1	29.6
Significance	NS	NS	NS
Statistical method	TT	TT	TT

NS: Not significantly different from the control group.

TT: Analysis by Student's t-test.

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

Appendix 8-1-1. Body weights of female rats

Control (vehicle: corn oil)

Female No.	Days of administration								
	1	4	7	14	21	28	35	42	49
F01001	239.0	253.9	256.6	264.5					
F01002	231.9	237.4	234.7	248.7					
F01003	257.6	269.7	264.2	280.5					
F01004	273.9	278.4	278.3	294.2					
F01005	246.9	256.1	260.4	264.9					
F01006	235.9	244.1	242.1	263.1					
F01007	243.1	245.4	257.2	276.7					
F01008	244.7	248.9	251.0	263.1					
F01009	234.8	236.1	242.5	252.2					
F01010	253.4	264.0	263.8	287.4					
F01011	229.8	231.5	236.5	226.2					
F01012	230.5	238.3	236.2	249.4					
Number of females	12	12	12	12					
Mean	243.5	250.3	252.0	264.2					
S.D.	13.1	14.6	13.7	18.9					

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

Appendix 8-1-2. Body weights of female rats

CPN 30 mg/kg

Female No.	Days of administration								
	1	4	7	14	21	28	35	42	49
F02013	237.9	239.9	244.5	253.6					
F02014	229.6	238.6	241.9	254.8					
F02015	248.7	257.3	257.7	274.9					
F02016	234.3	239.8	240.3	241.9					
F02017	260.7	269.2	270.1	277.3					
F02018	261.6	273.4	274.4	298.3					
F02019	230.7	232.0	228.9	241.2					
F02020	237.8	235.0	255.7	256.1					
F02021	240.9	246.1	248.2	258.8					
F02022	236.0	244.6	256.9	259.4					
F02023	246.5	251.6	250.9	268.3					
F02024	231.7	233.9	235.5	250.3					
Number of females	12	12	12	12					
Mean	241.4	246.8	250.4	261.2					
S.D.	10.9	13.6	13.4	16.2					
Significance	NS	NS	NS	NS					
Statistical method	AN	AN	AN	AN					

NS: Not significantly different from the control group.

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

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

Appendix 8-1-3. Body weights of female rats

CPN 100 mg/kg

Female No.	Days of administration								
	1	4	7	14	21	28	35	42	49
F03025	245.6	255.7	253.0	278.7					
F03026	250.8	258.8	255.3	273.9					
F03027	258.0	268.7	268.0	281.1					
F03028	233.8	236.3	243.4	250.2					
F03029	247.9	246.9	247.5	260.9					
F03030	238.2	249.3	251.4	256.3					
F03031	258.8	259.8	272.4	288.4					
F03032	232.6	235.0	233.8	246.5					
F03033	235.1	245.7	252.0	260.9					
F03034	233.6	240.4	236.1	247.6	282.8	311.5	294.9	295.0	307.5
F03035	242.4	249.9	247.4	263.6					
F03036	249.9	259.8	265.4	282.7					
Number of females	12	12	12	12					
Mean	243.9	250.5	252.1	265.9					
S.D.	9.4	10.4	11.9	14.6					
Significance	NS	NS	NS	NS	---	---	---	---	---
Statistical method	AN	AN	AN	AN	NA	NA	NA	NA	NA

NS: Not significantly different from the control group.

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

NA: Not analyzed.

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

Appendix 8-1-4. Body weights of female rats

CPN 300 mg/kg

Female No.	Days of administration								
	1	4	7	14	21	28	35	42	49
F04037	226.6	225.4	236.9	250.8					
F04038	244.8	246.9	239.3	254.8					
F04039	232.2	246.9	247.0	254.1					
F04040	244.5	240.7	255.8	267.5					
F04041	253.9	261.7	268.5	279.3					
F04042	255.4	257.6	262.8	258.9					
F04043	251.8	254.9	253.1	259.4					
F04044	239.1	240.9	237.1	238.5					
F04045	251.5	266.5	273.2	285.2					
F04046	237.5	248.0	249.0	256.0					
F04047	255.0	264.5	265.2	268.7					
F04048	235.7	236.4	248.8	259.4					
Number of females	12	12	12	12					
Mean	244.0	249.2	253.1	261.1					
S.D.	9.7	12.3	12.3	12.6					
Significance	NS	NS	NS	NS					
Statistical method	AN	AN	AN	AN					

NS: Not significantly different from the control group.

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

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

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

Control (vehicle: corn oil)

Female No.	Days of administration							
	1	4	7	14	21	28	35	42
F05049	258.1	268.2	266.9	270.3	284.5	295.0	300.3	307.3
F05050	253.0	258.0	254.0	268.8	277.5	285.7	283.1	299.3
F05051	236.9	255.4	256.4	272.3	274.9	289.1	303.0	310.8
F05052	227.7	246.9	245.5	257.5	252.6	270.2	280.2	283.9
F05053	236.9	244.3	238.8	249.9	259.8	260.3	265.8	271.2
F05054	262.1	274.7	276.9	290.0	311.5	321.4	327.4	331.8
F05055	219.6	228.1	226.3	229.6	227.4	240.3	250.1	252.1
F05056	241.8	260.1	263.6	275.2	280.7	291.1	301.7	306.4
F05057	225.4	229.1	228.1	242.4	252.7	255.4	261.8	275.0
F05058	250.4	258.4	266.9	274.6	288.2	292.8	294.7	303.6
Number of females	10	10	10	10	10	10	10	10
Mean	241.2	252.3	252.3	263.1	271.0	280.1	286.8	294.1
S.D.	14.5	15.3	17.2	18.0	23.5	23.6	23.2	23.3

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

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

CPN 300 mg/kg

Female No.	Days of administration							
	1	4	7	14	21	28	35	42
F06056	229.7	242.2	244.1	243.6	258.2	266.3	265.9	262.0
F06057	245.0	253.4	256.2	256.9	269.3	282.4	287.1	280.5
F06058	252.4	261.3	241.7	246.3	256.0	277.5	286.9	300.6
F06059	243.6	253.9	258.0	261.1	273.8	277.6	283.9	285.6
F06060	240.4	243.5	252.0	263.4	274.7	274.4	284.7	289.9
F06061	235.8	233.8	240.6	250.6	255.2	260.9	271.8	278.5
F06062	243.1	248.0	257.6	262.8	284.1	293.3	288.3	306.2
F06063	221.2	227.9	218.9	230.2	236.5	245.5	250.6	252.5
F06064	257.1	266.8	266.4	269.4	280.1	289.6	288.2	299.6
F06065	245.9	247.8	257.8	253.8	264.4	270.3	270.9	278.0
Number of females	10	10	10	10	10	10	10	10
Mean	241.4	247.9	249.3	253.8	265.2	273.8	277.8	283.3
S.D.	10.5	11.8	13.5	11.6	14.2	14.0	12.6	17.0
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	TT	TT	TT	TT	TT	TT	TT	TT

NS: Not significantly different from the control group.

TT: Analysis by Student's t-test.

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

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

Control (vehicle: corn oil)

Female No.	Days of recovery		
	1	7	14
F05054	339.6	346.4	351.3
F05055	255.7	255.6	267.2
F05056	313.4	311.6	320.0
F05057	271.9	288.3	286.0
F05058	301.2	302.7	297.6
Number of females	5	5	5
Mean	296.4	300.9	304.4
S.D.	33.3	33.2	32.4

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

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

CPN 300 mg/kg

Female No.	Days of recovery		
	1	7	14
F06061	276.8	278.3	288.3
F06062	306.4	306.8	316.5
F06063	259.9	267.0	262.5
F06064	303.1	308.4	316.8
F06065	272.0	282.0	285.9
Number of females	5	5	5
Mean	283.6	288.5	294.0
S.D.	20.3	18.3	23.0
Significance	NS	NS	NS
Statistical method	TT	TT	TT

NS: Not significantly different from the control group.

TT: Analysis by Student's t-test.

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

Appendix 9-1. Body weights of dams during pregnancy

Control (vehicle: corn oil)

Dam No.	Days of pregnancy				
	0	7	14	20	26
F01001	274.1	314.1	344.6	418.1	
F01002	257.4	298.5	345.7	421.8	
F01003	305.4	347.7	392.1	490.3	
F01004	302.0	345.2	386.6	478.5	
F01005	281.6	328.3	383.5	481.4	
F01006	275.5	299.6	327.9	405.2	
F01007	272.2	307.8	344.2	428.8	
F01008	280.3	314.4	351.2	435.3	
F01009	256.2	296.9	330.2	414.1	
F01010	307.5	347.5	389.8	475.2	
F01011	241.3	277.6	312.8	382.1	
F01012	253.6	289.3	321.2	409.4	
Number of dams	12	12	12	12	
Mean	275.6	313.9	352.5	436.7	
S.D.	21.4	23.6	28.5	35.6	

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

Appendix 9-2. Body weights of dams during pregnancy

CPN 30 mg/kg

Dam No.	Days of pregnancy				
	0	7	14	20	26
F02013	252.3	291.6	333.1	411.5	
F02014	259.8	294.5	332.9	418.8	
F02015	290.9	332.1	370.7	448.0	
F02016	253.5	290.3	323.5	404.8	
F02017	286.9	322.4	357.3	442.1	
F02018	300.6	347.3	389.7	481.0	
F02019	258.5	292.4	323.7	417.8	
F02020	265.7	297.8	346.8	443.3	
F02021	264.4	305.3	340.9	420.7	
F02022	261.0	295.0	326.3	404.8	
F02023	> 271.3 >	304.5 >	312.7 >	331.0 >	337.8
F02024	270.6	300.8	342.3	432.0	
Number of dams	11	11	11	11	
Mean	269.5	306.3	344.3	429.5	
S.D.	16.2	19.1	20.9	22.9	
Significance	NS	NS	NS	NS	---
Statistical method	AN	AN	AN	AN	NA

>: Excluded from analysis (not pregnant)

NS: Not significantly different from the control group.

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

NA: Not analyzed.

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

Appendix 9-3. Body weights of dams during pregnancy

CPN 100 mg/kg

Dam No.	Days of pregnancy				
	0	7	14	20	26
F03025	279.4	319.5	364.7	447.1	
F03026	292.4	318.8	355.7	436.7	
F03027	289.7	322.1	351.3	446.2	
F03028	258.8	281.7	313.5	389.1	
F03029	269.0	302.1	342.8	423.6	
F03030	271.4	298.5	345.2	433.9	
F03031	286.1	331.6	377.2	452.3	
F03032	260.6	300.5	334.8	412.1	
F03033	254.4	291.7	322.0	402.3	
F03035	269.2	316.5	348.8	419.6	
F03036	283.6	328.1	367.6	454.4	
Number of dams	11	11	11	11	
Mean	274.1	310.1	347.6	428.8	
S.D.	13.0	16.0	19.1	21.5	
Significance	NS	NS	NS	NS	
Statistical method	AN	AN	AN	AN	

NS: Not significantly different from the control group.

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

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

Appendix 9-4. Body weights of dams during pregnancy

CPN 300 mg/kg

Dam No.	Days of pregnancy				
	0	7	14	20	26
F04037	251.4	294.7	322.0	414.3	
F04038	262.8	306.9	346.5	428.4	
F04039	252.8	299.1	343.8	420.4	
F04040	267.1	295.8	335.3	418.2	
F04041	288.4	327.9	378.3	459.1	
F04042	277.7	308.0	346.3	430.1	
F04043	274.6	308.1	348.2	430.4	
F04044	245.3	288.9	327.6	403.3	
F04045	287.5	325.0	362.8	448.7	
F04046	260.1	307.7	351.9	428.8	
F04047	289.6	325.0	364.9	468.4	
F04048	262.7	287.2	326.1	398.7	
Number of dams	12	12	12	12	
Mean	268.3	306.2	346.1	429.1	
S.D.	15.2	13.9	16.9	21.0	
Significance	NS	NS	NS	NS	
Statistical method	AN	AN	AN	AN	

NS: Not significantly different from the control group.

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

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

Appendix 10-1. Body weights of dams during lactation

Control (vehicle: corn oil)

Dam No.	Days of lactation	
	0	4
F01001	320.8	328.3
F01002	340.8	343.2
F01003	366.6	396.7
F01004	386.6	391.8
F01005	360.7	364.3
F01006	336.4	322.8
F01007	303.5	335.0
F01008	317.0	355.8
F01009	328.4	329.7
F01010	389.1	385.1
F01011	310.8	305.9
F01012	311.3	341.7
Number of dams	12	12
Mean	339.3	350.0
S.D.	29.8	29.1

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

Appendix 10-2. Body weights of dams during lactation

CPN 30 mg/kg

Dam No.	Days of lactation	
	0	4
F02013	311.0	317.6
F02014	310.8	321.2
F02015	359.1	364.6
F02016	298.4	319.5
F02017	283.8	328.0
F02018	374.6	396.9
F02019	297.6	330.3
F02020	327.1	337.3
F02021	307.3	327.5
F02022	351.1	322.7
F02024	321.5	341.6
Number of dams	11	11
Mean	322.0	337.0
S.D.	28.4	23.9
Significance	NS	NS
Statistical method	AN	AN

NS: Not significantly different from the control group.

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

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

Appendix 10-3. Body weights of dams during lactation

CPN 100 mg/kg

Dam No.	Days of lactation	
	0	4
F03025	324.7	327.4
F03026	331.8	356.5
F03027	341.3	368.5
F03028	265.1	Total litter loss on day 1 of lactation
F03029	342.9	345.8
F03030	338.5	342.6
F03031	390.5	374.4
F03032	317.5	346.8
F03033	301.5	329.0
F03035	354.9	347.7
F03036	388.2	378.5
Number of dams	11	10
Mean	336.1	351.7
S.D.	35.8	17.6
Significance	NS	NS
Statistical method	AN	AN

NS: Not significantly different from the control group.

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

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

Appendix 10-4. Body weights of dams during lactation

CPN 300 mg/kg

Dam No.	Days of lactation	
	0	4
F04037	266.6	Total litter loss on day 0 of lactation
F04038	351.0	348.1
F04039	323.3	346.5
F04040	303.3	324.9
F04041	373.2	354.5
F04042	322.6	343.5
F04043	339.2	335.6
F04044	325.2	339.6
F04045	353.7	317.7
F04046	339.1	362.7
F04047	340.2	353.9
F04048	314.7	312.2
Number of dams	12	11
Mean	329.3	339.9
S.D.	27.3	16.0
Significance	NS	NS
Statistical method	AN	AN

NS: Not significantly different from the control group.

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

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

Appendix 11-1-1. Food consumption of male rats

Control (vehicle: corn oil)

Male No.	Days of administration					
	1	7	14	29	35	41
M01001	23.2	25.7	21.9	27.0	27.7	18.9
M01002	23.6	22.3	23.1	25.6	23.3	23.8
M01003	23.3	22.6	19.8	25.1	23.3	21.4
M01004	29.7	26.6	24.6	27.9	27.0	27.4
M01005	29.1	25.8	20.9	25.0	25.2	25.7
M01006	22.2	24.6	21.1	Sacrificed on day 18 of administration		
M01007	23.7	23.3	22.1	26.0	22.5	23.1
M01008	22.3	21.3	19.6	24.5	21.3	22.2
M01009	27.5	24.3	23.5	29.4	25.6	30.0
M01010	31.8	27.8	26.3	26.3	30.3	27.5
M01011	26.4	24.8	23.4	22.9	24.2	21.6
M01012	24.5	23.2	23.0	21.7	22.4	20.5
Number of males	12	12	12	11	11	11
Mean	25.6	24.4	22.4	25.6	24.8	23.8
S.D.	3.2	1.9	2.0	2.2	2.7	3.4

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

Appendix 11-1-2. Food consumption of male rats

CPN 30 mg/kg

Male No.	Days of administration					
	1	7	14	29	35	41
M02013	25.2	22.9	22.0	27.1	24.9	22.0
M02014	28.0	24.9	26.2	28.2	27.7	25.5
M02015	25.0	22.9	21.6	25.2	26.4	21.6
M02016	28.1	21.0	19.7	23.6	24.4	23.4
M02017	27.6	22.0	22.6	27.3	26.4	26.5
M02018	26.0	23.3	24.3	27.7	24.7	25.8
M02019	22.2	23.5	24.4	27.2	26.6	26.2
M02020	28.2	27.4	28.0	32.3	29.8	30.9
M02021	24.8	19.2	19.5	20.0	19.7	20.9
M02022	29.0	24.5	25.3	29.5	25.3	25.2
M02023	27.8	25.1	24.4	25.0	24.6	24.3
M02024	31.5	25.3	22.1	28.1	27.6	25.6
Number of males	12	12	12	12	12	12
Mean	27.0	23.5	23.3	26.8	25.7	24.8
S.D.	2.4	2.2	2.6	3.1	2.5	2.7
Significance	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	DU	DU

NS: Not significantly different from the control group.

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

DU: Analysis by Dunnett's test.

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

Appendix 11-1-3. Food consumption of male rats

CPN 100 mg/kg

Male No.	Days of administration					
	1	7	14	29	35	41
M03025	25.7	24.8	23.1	23.6	24.6	24.9
M03026	23.5	23.2	25.3	26.4	21.4	22.1
M03027	25.3	21.9	20.7	25.5	23.1	23.8
M03028	28.9	30.1	22.9	26.5	25.2	27.2
M03029	34.8	32.6	28.2	28.8	26.2	32.4
M03030	26.8	27.4	22.8	25.6	25.0	28.2
M03031	28.6	27.2	28.0	27.8	25.9	26.9
M03032	24.9	26.0	20.6	26.2	25.8	27.8
M03033	23.5	23.6	22.6	24.5	22.7	24.8
M03034	25.6	26.3	25.3	27.6	23.7	29.9
M03035	27.6	27.6	20.1	19.2	21.0	22.0
M03036	29.5	23.9	22.5	24.5	25.7	23.5
Number of males	12	12	12	12	12	12
Mean	27.1	26.2	23.5	25.5	24.2	26.1
S.D.	3.1	3.0	2.7	2.5	1.8	3.2
Significance	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	DU	DU

NS: Not significantly different from the control group.

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

DU: Analysis by Dunnett's test.

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

Appendix 11-1-4. Food consumption of male rats

CPN 300 mg/kg

Male No.	Days of administration					
	1	7	14	29	35	41
M04037	26.0	21.3	20.8	23.6	20.5	21.3
M04038	26.8	30.4	25.4	27.3	24.1	25.4
M04039	26.4	23.1	18.2	21.9	21.2	21.6
M04040	25.8	24.3	21.1	24.4	23.1	20.1
M04041	22.5	21.9	18.9	23.1	20.7	25.9
M04042	23.8	25.0	20.8	23.2	18.7	19.4
M04043	21.9	19.1	17.0	21.6	18.3	20.8
M04044	27.6	24.8	22.6	24.4	23.3	24.2
M04045	28.0	26.0	23.2	23.2	25.9	22.7
M04046	22.5	25.2	22.9	25.9	19.2	24.6
M04047	21.5	22.5	21.7	23.8	27.4	22.5
M04048	23.9	25.7	22.2	27.2	27.8	24.3
Number of males	12	12	12	12	12	12
Mean	24.7	24.1	21.2	24.1	22.5	22.7
S.D.	2.3	2.9	2.3	1.8	3.3	2.1
Significance	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	DU	DU

NS: Not significantly different from the control group.

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

DU: Analysis by Dunnett's test.

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

Appendix 11-2-1. Food consumption of male rats at the recovery period

Control (vehicle: corn oil)

Male No.	Days of recovery	
	6	12
M01008	25.6	27.2
M01009	29.2	30.2
M01010	31.9	33.5
M01011	30.4	27.2
M01012	31.9	29.9
Number of males	5	5
Mean	29.8	29.6
S.D.	2.6	2.6

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

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

CPN 300 mg/kg

Male No.	Days of recovery	
	6	12
M04044	32.7	34.6
M04045	31.4	31.8
M04046	29.5	31.3
M04047	30.3	30.9
M04048	28.9	32.7
Number of males	5	5
Mean	30.6	32.3
S.D.	1.5	1.5
Significance	NS	NS
Statistical method	TT	TT

NS: Not significantly different from the control group.

TT: Analysis by Student's t-test.

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

Appendix 12-1-1. Food consumption of female rats

Control (vehicle: corn oil)

Female No.	Days of administration						
	1	7	14	29	35	41	48
F01001	18.0	19.2	18.7				
F01002	18.6	18.9	10.3				
F01003	22.8	20.9	13.9				
F01004	16.3	22.2	15.3				
F01005	12.2	22.1	21.5				
F01006	17.3	19.2	16.4				
F01007	20.9	15.1	18.0				
F01008	18.8	17.8	14.4				
F01009	16.7	15.5	18.6				
F01010	20.4	20.4	15.9				
F01011	18.3	12.8	13.9				
F01012	13.0	19.8	18.5				
Number of females	12	12	12				
Mean	17.8	18.7	16.3				
S.D.	3.0	2.9	3.0				

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

Appendix 12-1-2. Food consumption of female rats

CPN 30 mg/kg

Female No.	Days of administration						
	1	7	14	29	35	41	48
F02013	17.3	11.9	18.0				
F02014	18.8	17.6	14.0				
F02015	19.2	22.5	14.1				
F02016	10.0	16.3	16.5				
F02017	16.3	20.7	17.0				
F02018	15.5	21.1	19.4				
F02019	21.9	17.4	12.9				
F02020	22.0	17.3	20.4				
F02021	15.0	20.2	18.8				
F02022	20.8	21.2	18.2				
F02023	21.7	19.3	13.9				
F02024	15.6	16.4	13.6				
Number of females	12	12	12				
Mean	17.8	18.5	16.4				
S.D.	3.6	2.9	2.6				
Significance	NS	NS	NS				
Statistical method	AN	AN	AN				

NS: Not significantly different from the control group.

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

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

Appendix 12-1-3. Food consumption of female rats

CPN 100 mg/kg

Female No.	Days of administration						
	1	7	14	29	35	41	48
F03025	14.5	20.5	21.3				
F03026	18.2	19.9	11.6				
F03027	20.0	22.4	12.6				
F03028	19.3	18.9	14.7				
F03029	19.3	12.5	17.2				
F03030	15.5	17.5	16.9				
F03031	20.7	16.8	18.1				
F03032	15.2	17.3	11.6				
F03033	20.7	17.8	18.4				
F03034	19.9	19.4	15.1	26.6	16.8	21.4	22.7
F03035	19.4	(18.7) #	18.5				
F03036	20.2	(15.4) #	18.0				
Number of females	12	10	12				
Mean	18.6	18.3	16.2				
S.D.	2.2	2.7	3.1				
Significance	NS	NS	NS	---	---	---	---
Statistical method	AN	AN	AN	NA	NA	NA	NA

NS: Not significantly different from the control group.

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

NA: Not analyzed.

#: Reference data by a measurement error

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

Appendix 12-1-4. Food consumption of female rats

CPN 300 mg/kg

Female No.	Days of administration						
	1	7	14	29	35	41	48
F04037	18.5	14.5	17.5				
F04038	17.3	18.3	11.4				
F04039	16.8	18.9	13.7				
F04040	16.8	13.3	15.9				
F04041	21.7	14.3	16.8				
F04042	12.4	18.6	18.8				
F04043	21.8	17.4	9.8				
F04044	14.3	17.0	10.3				
F04045	18.7	21.3	21.2				
F04046	21.2	20.5	18.5				
F04047	13.2	19.6	17.6				
F04048	19.7	15.9	18.0				
Number of females	12	12	12				
Mean	17.7	17.5	15.8				
S.D.	3.2	2.5	3.7				
Significance	NS	NS	NS				
Statistical method	AN	AN	AN				

NS: Not significantly different from the control group.

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

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

Appendix 12-2-1. Food consumption of female rats, satellite group

Control (vehicle: corn oil)

Female No.	Days of administration						
	1	7	14	21	29	35	41
F05049	16.7	22.7	18.3	16.9	17.3	21.6	18.6
F05050	17.8	18.7	13.1	16.5	17.0	16.3	20.4
F05051	20.9	18.5	18.9	18.5	20.0	21.4	18.5
F05052	19.5	18.9	19.0	17.2	17.8	17.7	16.8
F05053	11.8	19.6	16.5	12.1	14.0	16.9	15.0
F05054	16.6	20.6	19.5	17.3	15.3	18.7	16.5
F05055	14.7	14.7	16.5	15.5	16.7	15.9	15.7
F05056	22.0	20.2	20.4	19.7	20.0	20.8	20.6
F05057	19.7	18.2	14.9	16.9	17.7	15.0	19.9
F05058	19.1	22.1	17.4	19.9	16.4	18.8	19.9
Number of females	10	10	10	10	10	10	10
Mean	17.9	19.4	17.5	17.1	17.2	18.3	18.2
S.D.	3.0	2.2	2.2	2.2	1.9	2.4	2.1

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

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

CPN 300 mg/kg

Female No.	Days of administration						
	1	7	14	21	29	35	41
F06056	13.5	17.8	16.8	14.7	15.3	17.1	13.2
F06057	14.9	18.5	18.5	15.4	15.7	18.8	14.4
F06058	14.6	17.6	15.0	17.6	17.8	14.0	18.8
F06059	18.2	17.3	16.9	16.4	16.2	15.6	14.0
F06060	18.2	14.7	16.2	18.6	19.7	13.1	17.5
F06061	17.4	12.9	16.8	18.0	16.8	16.7	16.2
F06062	17.8	18.1	15.8	18.3	14.5	14.5	21.2
F06063	13.1	16.6	17.4	9.7	17.1	12.6	12.5
F06064	13.0	18.7	19.3	13.1	13.7	18.3	17.6
F06065	19.4	16.3	15.5	18.8	18.0	19.2	19.2
Number of females	10	10	10	10	10	10	10
Mean	16.0	16.9	16.8	16.1	16.5	16.0	16.5
S.D.	2.4	1.8	1.3	2.9	1.8	2.4	2.9
Significance	NS	*	NS	NS	NS	*	NS
Statistical method	TT	TT	TT	TT	TT	TT	TT

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

NS: Not significantly different from the control group.

TT: Analysis by Student's t-test.

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

Appendix 12-3-1. Food consumption of female rats at the recovery period

Control (vehicle: corn oil)

Female No.	Days of recovery	
	6	12
F05054	23.5	23.7
F05055	18.2	17.8
F05056	19.3	21.5
F05057	24.8	18.6
F05058	17.2	20.1
Number of females	5	5
Mean	20.6	20.3
S.D.	3.4	2.4

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

Appendix 12-3-2. Food consumption of female rats at the recovery period

CPN 300 mg/kg

Female No.	Days of recovery	
	6	12
F06061	17.6	18.9
F06062	23.2	18.8
F06063	21.4	17.7
F06064	23.6	24.2
F06065	21.9	20.3
Number of females	5	5
Mean	21.5	20.0
S.D.	2.4	2.5
Significance	NS	NS
Statistical method	TT	TT

NS: Not significantly different from the control group.

TT: Analysis by Student's t-test.

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

Appendix 13-1. Food consumption in dams during pregnancy

Control (vehicle: corn oil)

Dam No.	Days of pregnancy			
	0	7	14	20
F01001	19.9	24.2	21.8	21.5
F01002	18.9	25.1	26.1	16.8
F01003	26.8	29.8	28.2	27.0
F01004	21.2	26.4	26.6	22.4
F01005	21.8	31.8	28.3	17.6
F01006	17.9	18.9	21.9	17.9
F01007	18.0	24.3	22.0	17.9
F01008	19.0	26.4	25.7	23.2
F01009	10.9	28.0	21.8	19.3
F01010	20.8	28.1	27.7	19.5
F01011	17.5	21.9	22.5	14.7
F01012	22.1	22.8	21.3	22.9
Number of dams	12	12	12	12
Mean	19.6	25.6	24.5	20.1
S.D.	3.7	3.6	2.8	3.4

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

Appendix 13-2. Food consumption in dams during pregnancy

CPN 30 mg/kg

Dam No.	Days of pregnancy			
	0	7	14	20
F02013	16.6	21.8	20.3	19.9
F02014	17.7	25.3	27.3	22.6
F02015	23.6	23.9	24.9	20.1
F02016	19.5	23.6	21.9	19.5
F02017	17.8	22.1	21.2	10.7
F02018	18.1	24.5	25.4	23.1
F02019	17.2	20.9	24.2	21.0
F02020	16.4	27.4	29.3	23.5
F02021	18.3	27.1	28.1	16.6
F02022	16.5	21.9	21.1	23.1
F02023	> 21.3	> 23.2	> 14.0	> 16.1
F02024	19.0	24.1	23.3	21.4
Number of dams	11	11	11	11
Mean	18.2	23.9	24.3	20.1
S.D.	2.0	2.1	3.0	3.7
Significance	NS	NS	NS	NS
Statistical method	KW	AN	AN	AN

>: Excluded from analysis (not pregnant)

NS: Not significantly different from the control group.

KW: Analysis by Kruskal-Wallis' test (one-way layout).

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

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

Appendix 13-3. Food consumption in dams during pregnancy

CPN 100 mg/kg

Dam No.	Days of pregnancy			
	0	7	14	20
F03025	17.1	26.7	23.8	21.4
F03026	19.2	26.3	26.5	25.3
F03027	16.7	23.3	24.9	21.7
F03028	13.3	18.1	22.5	17.7
F03029	17.6	22.5	21.4	21.5
F03030	16.7	24.6	24.4	18.8
F03031	25.1	31.1	30.3	26.8
F03032	20.2	24.9	26.2	27.4
F03033	17.4	24.9	23.2	23.8
F03035	19.8	23.3	22.4	26.5
F03036	15.6	30.1	27.7	26.8
Number of dams	11	11	11	11
Mean	18.1	25.1	24.8	23.4
S.D.	3.0	3.6	2.6	3.4
Significance	NS	NS	NS	NS
Statistical method	KW	AN	AN	AN

NS: Not significantly different from the control group.

KW: Analysis by Kruskal-Wallis' test (one-way layout).

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

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

Appendix 13-4. Food consumption in dams during pregnancy

CPN 300 mg/kg

Dam No.	Days of pregnancy			
	0	7	14	20
F04037	19.9	21.2	20.2	13.9
F04038	19.3	24.7	23.0	19.9
F04039	18.3	23.5	21.9	28.0
F04040	19.0	24.5	23.6	24.4
F04041	20.6	27.8	25.3	24.5
F04042	18.5	25.5	24.5	19.1
F04043	16.3	24.3	23.2	20.0
F04044	21.2	22.0	24.7	18.0
F04045	18.9	24.3	23.2	26.3
F04046	19.7	25.4	25.0	23.9
F04047	17.6	22.8	20.6	22.9
F04048	17.2	23.5	20.2	20.8
Number of dams	12	12	12	12
Mean	18.9	24.1	23.0	21.8
S.D.	1.4	1.7	1.8	3.9
Significance	NS	NS	NS	NS
Statistical method	KW	AN	AN	AN

NS: Not significantly different from the control group.

KW: Analysis by Kruskal-Wallis' test (one-way layout).

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

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

Appendix 14-1. Food consumption in dams during lactation

Control (vehicle: corn oil)

Dam No.	Days of lactation
	3
F01001	30.9
F01002	39.0
F01003	53.3
F01004	46.6
F01005	38.2
F01006	32.1
F01007	44.9
F01008	46.8
F01009	39.3
F01010	35.2
F01011	35.2
F01012	49.0
Number of dams	12
Mean	40.9
S.D.	7.1

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

Appendix 14-2. Food consumption in dams during lactation

CPN 30 mg/kg

Dam No.	Days of lactation
	3
F02013	37.2
F02014	33.5
F02015	46.4
F02016	47.5
F02017	34.9
F02018	41.6
F02019	53.8
F02020	44.8
F02021	40.7
F02022	28.3
F02024	47.3
Number of dams	11
Mean	41.5
S.D.	7.5
Significance	NS
Statistical method	AN

NS: Not significantly different from the control group.

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

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

Appendix 14-3. Food consumption in dams during lactation

CPN 100 mg/kg

Dam No.	Days of lactation
	3
F03025	30.2
F03026	49.5
F03027	44.3
F03029	45.0
F03030	39.6
F03031	36.1
F03032	53.4
F03033	35.9
F03035	34.1
F03036	31.3
Number of dams	10
Mean	39.9
S.D.	7.8
Significance	NS
Statistical method	AN

NS: Not significantly different from the control group.

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

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

Appendix 14-4. Food consumption in dams during lactation

CPN 300 mg/kg

Dam No.	Days of lactation
	3
F04038	31.9
F04039	46.8
F04040	42.2
F04041	33.9
F04042	38.4
F04043	37.2
F04044	50.7
F04045	17.7
F04046	43.9
F04047	41.6
F04048	36.6
Number of dams	11
Mean	38.3
S.D.	8.8
Significance	NS
Statistical method	AN

NS: Not significantly different from the control group.

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

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

Appendix 15-1. Functional findings of male rats at the last week of the administration period

Control (vehicle: corn oil)

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

2 or +, normal

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

Appendix 15-2. Functional findings of male rats at the last week of the administration period

CPN 30 mg/kg

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

2 or +, normal

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

Appendix 15-3. Functional findings of male rats at the last week of the administration period

CPN 100 mg/kg

Male No.	Righting reflex	Visual placing	Pupillary reflex	Startle reaction	Preyer's reaction	Withdrawal reflex	Eyelid reflex
M03025	2	2	2	2	+	+	+
M03026	2	2	2	2	+	+	+
M03027	2	2	2	2	+	+	+
M03028	2	2	2	2	+	+	+
M03029	2	2	2	2	+	+	+
Total	2: 5	2: 5	2: 5	2: 5	+: 5	+: 5	+: 5

2 or +, normal

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

Appendix 15-4. Functional findings of male rats at the last week of the administration period

CPN 300 mg/kg

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

2 or +, normal

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

Appendix 16-1. Functional findings of female rats at the last week of the administration period

Control (vehicle: corn oil)

Female, dam

Female No.	Righting reflex	Visual placing	Pupillary reflex	Startle reaction	Preyer's reaction	Withdrawal reflex	Eyelid reflex
F01001	2	2	2	2	+	+	+
F01005	2	2	2	2	+	+	+
F01006	2	2	2	2	+	+	+
F01007	2	2	2	2	+	+	+
F01012	2	2	2	2	+	+	+
Total	2: 5	2: 5	2: 5	2: 5	+: 5	+: 5	+: 5

2 or +, normal

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

Appendix 16-2. Functional findings of female rats at the last week of the administration period

CPN 30 mg/kg

Female, dam

Female No.	Righting reflex	Visual placing	Pupillary reflex	Startle reaction	Preyer's reaction	Withdrawal reflex	Eyelid reflex
F02013	2	2	2	2	+	+	+
F02016	2	2	2	2	+	+	+
F02018	2	2	2	2	+	+	+
F02020	2	2	2	2	+	+	+
F02022	2	2	2	2	+	+	+
Total	2: 5	2: 5	2: 5	2: 5	+: 5	+: 5	+: 5

2 or +, normal

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

Appendix 16-3. Functional findings of female rats at the last week of the administration period

CPN 100 mg/kg

Female, dam

Female No.	Righting reflex	Visual placing	Pupillary reflex	Startle reaction	Preyer's reaction	Withdrawal reflex	Eyelid reflex
F03029	2	2	2	2	+	+	+
F03031	2	2	2	2	+	+	+
F03033	2	2	2	2	+	+	+
F03035	2	2	2	2	+	+	+
F03036	2	2	2	2	+	+	+
Total	2: 5	2: 5	2: 5	2: 5	+: 5	+: 5	+: 5

2 or +, normal

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

Appendix 16-4. Functional findings of female rats at the last week of the administration period

CPN 300 mg/kg

Female, dam

Female No.	Righting reflex	Visual placing	Pupillary reflex	Startle reaction	Preyer's reaction	Withdrawal reflex	Eyelid reflex
F04039	2	2	2	2	+	+	+
F04040	2	2	2	2	+	+	+
F04041	2	2	2	2	+	+	+
F04045	2	2	2	2	+	+	+
F04048	2	2	2	2	+	+	+
Total	2:5	2:5	2:5	2:5	+:5	+:5	+:5

2 or +, normal

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

Appendix 16-5. Functional findings of female rats at the last week of the administration period

Control (vehicle: corn oil)

Female, satellite group

Female No.	Righting reflex	Visual placing	Pupillary reflex	Startle reaction	Preyer's reaction	Withdrawal reflex	Eyelid reflex
F05049	2	2	2	2	+	+	+
F05050	2	2	2	2	+	+	+
F05051	2	2	2	2	+	+	+
F05052	2	2	2	2	+	+	+
F05053	2	2	2	2	+	+	+
Total	2: 5	2: 5	2: 5	2: 5	+: 5	+: 5	+: 5

2 or +, normal

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

Appendix 16-6. Functional findings of female rats at the last week of the administration period

CPN 300 mg/kg

Female, satellite group

Female No.	Righting reflex	Visual placing	Pupillary reflex	Startle reaction	Preyer's reaction	Withdrawal reflex	Eyelid reflex
F06056	2	2	2	2	+	+	+
F06057	2	2	2	2	+	+	+
F06058	2	2	2	2	+	+	+
F06059	2	2	2	2	+	+	+
F06060	2	2	2	2	+	+	+
Total	2: 5	2: 5	2: 5	2: 5	+: 5	+: 5	+: 5

2 or +, normal

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

Appendix 17-1. Assessment of grip strength of male rats at the last week of the administration period

Control (vehicle: corn oil)

Male No.	Administration period	
	Forelimb	Hindlimb
	(kg)	(kg)
M01001	1.177	0.562
M01002	1.380	0.729
M01003	1.036	0.661
M01004	1.429	0.724
M01005	1.329	0.685
Number of males	5	5
Mean	1.270	0.672
S.D.	0.161	0.068

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

Appendix 17-2. Assessment of grip strength of male rats at the last week of the administration period

CPN 30 mg/kg

Male No.	Administration period	
	Forelimb	Hindlimb
	(kg)	(kg)
M02013	1.343	0.597
M02014	0.987	0.722
M02015	1.320	0.712
M02016	1.737	0.827
M02017	1.157	0.585
Number of males	5	5
Mean	1.309	0.689
S.D.	0.279	0.100

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

Appendix 17-3. Assessment of grip strength of male rats at the last week of the administration period

CPN 100 mg/kg

Male No.	Administration period	
	Forelimb	Hindlimb
	(kg)	(kg)
M03025	0.828	0.610
M03026	1.209	0.597
M03027	1.500	1.148
M03028	1.161	0.500
M03029	1.208	0.588
Number of males	5	5
Mean	1.181	0.689
S.D.	0.239	0.260

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

Appendix 17-4. Assessment of grip strength of male rats at the last week of the administration period

CPN 300 mg/kg

Male No.	Administration period	
	Forelimb	Hindlimb
	(kg)	(kg)
M04037	1.428	0.603
M04038	1.398	0.879
M04039	1.450	0.595
M04040	1.743	0.768
M04041	1.125	0.618
Number of males	5	5
Mean	1.429	0.693
S.D.	0.219	0.126

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

Appendix 18-1. Assessment of grip strength of female rats at the last week of the administration period

Control (vehicle: corn oil)

Female No.	Administration period	
	Forelimb	Hindlimb
	(kg)	(kg)
F01001	1.168	0.594
F01005	1.167	0.452
F01006	1.049	0.582
F01007	1.007	0.545
F01012	1.161	0.558
Number of females	5	5
Mean	1.110	0.546
S.D.	0.077	0.056

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

Appendix 18-2. Assessment of grip strength of female rats at the last week of the administration period

CPN 30 mg/kg

Female No.	Administration period	
	Forelimb	Hindlimb
	(kg)	(kg)
F02013	1.035	0.527
F02016	1.253	0.545
F02018	1.162	0.483
F02020	1.255	0.564
F02022	0.882	0.461
Number of females	5	5
Mean	1.117	0.516
S.D.	0.159	0.043

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

Appendix 18-3. Assessment of grip strength of female rats at the last week of the administration period

CPN 100 mg/kg

Female No.	Administration period	
	Forelimb	Hindlimb
	(kg)	(kg)
F03029	1.215	0.431
F03031	1.114	0.623
F03033	1.164	0.544
F03035	1.068	0.413
F03036	1.320	0.537
Number of females	5	5
Mean	1.176	0.510
S.D.	0.097	0.087

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

Appendix 18-4. Assessment of grip strength of female rats at the last week of the administration period

CPN 300 mg/kg

Female No.	Administration period	
	Forelimb	Hindlimb
	(kg)	(kg)
F04039	1.142	0.536
F04040	1.270	0.585
F04041	1.146	0.473
F04045	0.753	0.378
F04048	1.121	0.419
Number of females	5	5
Mean	1.086	0.478
S.D.	0.195	0.084

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

Appendix 19-1-1. Assessment of grip strength of female rats at the last week of the administration period, satellite group

Control (vehicle: corn oil)

Female No.	Administration period	
	Forelimb	Hindlimb
	(kg)	(kg)
F05049	1.030	0.527
F05050	0.902	0.519
F05051	0.932	0.544
F05052	0.869	0.543
F05053	0.923	0.449
Number of females	5	5
Mean	0.931	0.516
S.D.	0.060	0.039

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

Appendix 19-1-2. Assessment of grip strength of female rats at the last week of the administration period, satellite group

CPN 300 mg/kg

Female No.	Administration period	
	Forelimb	Hindlimb
	(kg)	(kg)
F06056	0.980	0.441
F06057	1.109	0.472
F06058	1.111	0.536
F06059	1.094	0.537
F06060	1.108	0.547
Number of females	5	5
Mean	1.080 **	0.507
S.D.	0.057	0.047

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

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

Appendix 19-2-1. Assessment of grip strength of female rats at the last week of the administration period, recovery group

Control (vehicle: corn oil)

Female No.	Administration period	
	Forelimb	Hindlimb
	(kg)	(kg)
F05054	1.208	0.621
F05055	1.137	0.559
F05056	1.120	0.509
F05057	1.116	0.607
F05058	0.943	0.392
Number of females	5	5
Mean	1.105	0.538
S.D.	0.098	0.093

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

Appendix 19-2-2. Assessment of grip strength of female rats at the last week of the administration period, recovery group

CPN 300 mg/kg

Female No.	Administration period	
	Forelimb	Hindlimb
	(kg)	(kg)
F06061	1.035	0.682
F06062	1.006	0.511
F06063	1.144	0.499
F06064	1.111	0.635
F06065	1.008	0.548
Number of females	5	5
Mean	1.061	0.575
S.D.	0.063	0.080

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

Appendix 20-1. Motor activity of male rats at the last week of the administration period

Control (vehicle: corn oil)

Male No.	Administration period									
	Ambulation (counts)					Rearing (counts)				
	5min	10min	15min	20min	Total	5min	10min	15min	20min	Total
M01001	1369	1152	1008	1083	4612	39	16	11	15	81
M01002	1067	1030	871	771	3739	21	21	10	3	55
M01003	1053	1172	870	697	3792	20	22	15	6	63
M01004	1510	1479	1246	1134	5369	38	30	24	7	99
M01005	1122	985	709	837	3653	27	27	9	16	79
Number of males	5	5	5	5	5	5	5	5	5	5
Mean	1224	1164	941	904	4233	29	23	14	9	75
S.D.	204	193	201	194	743	9	5	6	6	17

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

Appendix 20-2. Motor activity of male rats at the last week of the administration period

CPN 30 mg/kg

Male No.	Administration period									
	Ambulation (counts)					Rearing (counts)				
	5min	10min	15min	20min	Total	5min	10min	15min	20min	Total
M02013	1150	1138	1057	918	4263	32	23	26	13	94
M02014	1094	943	1047	1022	4106	31	14	19	16	80
M02015	1267	1222	1242	749	4480	29	28	21	14	92
M02016	1357	1170	962	976	4465	40	26	15	18	99
M02017	928	873	653	491	2945	18	17	11	3	49
Number of males	5	5	5	5	5	5	5	5	5	5
Mean	1159	1069	992	831	4052	30	22	18	13	83
S.D.	165	152	215	216	638	8	6	6	6	20

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

Appendix 20-3. Motor activity of male rats at the last week of the administration period

CPN 100 mg/kg

Male No.	Administration period									
	Ambulation (counts)					Rearing (counts)				
	5min	10min	15min	20min	Total	5min	10min	15min	20min	Total
M03025	1257	1000	1111	860	4228	30	14	13	8	65
M03026	1447	1381	1182	1017	5027	39	21	16	12	88
M03027	1132	850	810	816	3608	30	13	24	15	82
M03028	1312	1247	1083	945	4587	33	24	20	15	92
M03029	896	593	939	505	2933	7	5	11	1	24
Number of males	5	5	5	5	5	5	5	5	5	5
Mean	1209	1014	1025	829	4077	28	15	17	10	70
S.D.	208	314	149	197	824	12	7	5	6	28

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

Appendix 20-4. Motor activity of male rats at the last week of the administration period

CPN 300 mg/kg

Male No.	Administration period									
	Ambulation (counts)					Rearing (counts)				
	5min	10min	15min	20min	Total	5min	10min	15min	20min	Total
M04037	1226	1122	1108	1176	4632	39	30	22	28	119
M04038	1783	1670	1496	1325	6274	21	12	7	9	49
M04039	1088	1028	962	846	3924	42	31	23	9	105
M04040	1172	888	631	558	3249	19	16	5	7	47
M04041	825	827	863	792	3307	33	23	27	18	101
Number of males	5	5	5	5	5	5	5	5	5	5
Mean	1219	1107	1012	939	4277	31	22	17	14	84
S.D.	351	335	321	308	1249	10	8	10	9	34

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

Appendix 21-1. Motor activity of female rats at the last week of the administration period

Control (vehicle: corn oil)

Female No.	Administration period									
	Ambulation (counts)					Rearing (counts)				
	5min	10min	15min	20min	Total	5min	10min	15min	20min	Total
F01001	1284	1037	584	350	3255	38	20	6	0	64
F01005	1147	1115	678	1188	4128	38	36	5	27	106
F01006	1274	971	958	954	4157	35	13	2	12	62
F01007	1223	987	804	521	3535	25	13	2	0	40
F01012	1037	777	825	381	3020	16	12	13	3	44
Number of females	5	5	5	5	5	5	5	5	5	5
Mean	1193	977	770	679	3619	30	19	6	8	63
S.D.	103	125	144	373	512	10	10	5	12	26

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

Appendix 21-2. Motor activity of female rats at the last week of the administration period

CPN 30 mg/kg

Female No.	Administration period									
	Ambulation (counts)					Rearing (counts)				
	5min	10min	15min	20min	Total	5min	10min	15min	20min	Total
F02013	1181	949	794	1068	3992	35	16	10	20	81
F02016	866	582	551	286	2285	19	7	8	3	37
F02018	1182	1019	767	544	3512	30	24	1	6	61
F02020	803	755	380	316	2254	28	26	7	4	65
F02022	1348	1322	1030	580	4280	38	39	26	3	106
Number of females	5	5	5	5	5	5	5	5	5	5
Mean	1076	925	704	559	3265	30	22	10	7	70
S.D.	232	280	248	314	949	7	12	9	7	26

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

Appendix 21-3. Motor activity of female rats at the last week of the administration period

CPN 100 mg/kg

Female No.	Administration period									
	Ambulation (counts)					Rearing (counts)				
	5min	10min	15min	20min	Total	5min	10min	15min	20min	Total
F03029	1406	1127	963	1182	4678	60	32	12	38	142
F03031	1012	996	703	1234	3945	18	14	1	32	65
F03033	1783	1737	1192	1418	6130	26	17	7	6	56
F03035	1113	1063	729	916	3821	28	30	2	13	73
F03036	1205	1025	713	43	2986	30	16	6	0	52
Number of females	5	5	5	5	5	5	5	5	5	5
Mean	1304	1190	860	959	4312	32	22	6	18	78
S.D.	305	310	215	542	1180	16	8	4	16	37

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

Appendix 21-4. Motor activity of female rats at the last week of the administration period

CPN 300 mg/kg

Female No.	Administration period									
	Ambulation (counts)					Rearing (counts)				
	5min	10min	15min	20min	Total	5min	10min	15min	20min	Total
F04039	1112	835	832	309	3088	28	16	15	2	61
F04040	1145	1149	722	669	3685	37	22	4	10	73
F04041	980	914	827	891	3612	22	24	14	22	82
F04045	1075	783	589	126	2573	10	3	1	0	14
F04048	1009	559	498	380	2446	23	7	3	2	35
Number of females	5	5	5	5	5	5	5	5	5	5
Mean	1064	848	694	475	3081	24	14	7	7	53
S.D.	69	214	147	304	572	10	9	7	9	28

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

Appendix 22-1. Motor activity of female rats at the last week of the administration period, satellite group

Control (vehicle: corn oil)

Female No.	Administration period									
	Ambulation (counts)					Rearing (counts)				
	5min	10min	15min	20min	Total	5min	10min	15min	20min	Total
F05049	1192	1109	1221	1246	4768	46	47	47	56	196
F05050	1444	1394	1423	1281	5542	44	32	45	33	154
F05051	1159	1273	1241	749	4422	29	41	30	6	106
F05052	749	839	645	695	2928	30	40	22	31	123
F05053	1264	1276	1229	1104	4873	26	23	19	18	86
Number of females	5	5	5	5	5	5	5	5	5	5
Mean	1162	1178	1152	1015	4507	35	37	33	29	133
S.D.	256	215	295	276	971	9	9	13	19	43

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

Appendix 22-2. Motor activity of female rats at the last week of the administration period, satellite group

CPN 300 mg/kg

Female No.	Administration period									
	Ambulation (counts)					Rearing (counts)				
	5min	10min	15min	20min	Total	5min	10min	15min	20min	Total
F06056	1170	1032	1093	915	4210	26	36	29	25	116
F06057	1373	1321	1252	1214	5160	36	37	14	12	99
F06058	1288	1345	1059	1234	4926	41	51	22	44	158
F06059	1196	1122	1094	794	4206	27	32	16	11	86
F06060	1011	807	707	836	3361	30	21	15	20	86
Number of females	5	5	5	5	5	5	5	5	5	5
Mean	1208	1125	1041	999	4373	32	35	19	22	109
S.D.	136	222	201	210	708	6	11	6	13	30

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

Appendix 23-1-1. Urinalysis in male rats

Control (vehicle: corn oil)

Male No.	Quality									Urinary sediments				
	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen	Color	Turbidity	Red blood cells	White blood cells	Casts	Crystals	Epithelial cells
M01001	7.5	+	-	+	-	-	+	light yellow	-	-	-	-	±	-
M01002	7.5	+	-	+	-	-	+	light yellow	-	-	-	-	±	-
M01003	7.0	2+	-	+	-	-	+	light yellow	+	-	-	-	±	-
M01004	7.5	+	-	+	-	-	±	light yellow	-	-	-	-	±	-
M01005	7.0	+	-	+	-	-	±	light yellow	-	-	-	-	±	-
Protein,	-: negative; ±: 10 ≤ and < 30 mg/dL; +: 30 ≤ and < 100 mg/dL; 2+: 100 ≤ and < 300 mg/dL; 3+: 300 ≤ and < 600 mg/dL; 4+: 600 mg/dL ≤													
Glucose,	-: negative; ±: 30 ≤ and < 70 mg/dL; +: 70 ≤ and < 150 mg/dL; 2+: 150 ≤ and < 300 mg/dL; 3+: 300 ≤ and < 1,000 mg/dL; 4+: 1,000 mg/dL ≤													
Ketone,	-: negative; ±: (5 ≤ and < 10 mg/dL; +: 10 ≤ and < 40 mg/dL; 2+: 40 ≤ and < 80 mg/dL; 3+: 80 ≤ and < 150 mg/dL; 4+: 150 mg/dL ≤													
Bilirubin,	-: negative; +: 0.5 ≤ and < 2.0 mg/dL; 2+: 2.0 ≤ and < 6.0 mg/dL; 3+: 6.0 ≤ and < 10.0 mg/dL; 4+: 10.0 mg/dL ≤													
Occult blood,	-: negative; ±: 0.03 ≤ and < 0.06 mg/dL; +: 0.06 ≤ and < 0.20 mg/dL; 2+: 0.20 ≤ and < 1.00 mg/dL; 3+: 1.00 mg/dL ≤													
Urobilinogen,	±: normal; +: 2.0 ≤ and < 4.0 mg/dL; 2+: 4.0 ≤ and < 8.0 mg/dL; 3+: 8.0 ≤ and < 12.0 mg/dL; 4+: 12.0 mg/dL ≤													
Turbidity,	-: negative; ±: trace; +: slight; 2+: moderate; 3+: marked													
Red Blood cells,	-: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≥ 300/3 visual field													
White Blood cells,	-: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≥ 300/3 visual field													
Casts,	-: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≥ 300/3 visual field													
Crystals,	-: not observed; ±: a few; +: abundant													
Epithelial cells,	-: not observed; ±: a few; +: abundant													

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

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

Control (vehicle: corn oil)

Male No.	Urine volume mL/24hr	S.G.	Electrolyte, density			Electrolyte, gross volume		
			Na mEq/L	K mEq/L	Cl mEq/L	Na mEq/24hr	K mEq/24hr	Cl mEq/24hr
M01001	12.3	1.072	129.3	332.12 #	185.2	1.59	4.09	2.28
M01002	13.7	1.063	86.5	236.60	136.1	1.19	3.24	1.86
M01003	13.4	1.066	136.0	296.98	188.9	1.82	3.98	2.53
M01004	12.3	1.074	127.2	299.16	187.4	1.56	3.68	2.31
M01005	20.9	1.043	84.6	178.94	109.3	1.77	3.74	2.28
Number of males	5	5	5	5	5	5	5	5
Mean	14.5	1.064	112.7	268.76	161.4	1.59	3.75	2.25
S.D.	3.6	0.012	25.0	60.90	36.6	0.25	0.33	0.24

S.G.: Specific gravity

#: The specimen was diluted to two folds with distilled water.

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

Appendix 23-1-2. Urinalysis in male rats

CPN 30 mg/kg

Male No.	Quality									Urinary sediments				
	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen	Color	Turbidity	Red blood cells	White blood cells	Casts	Crystals	Epithelial cells
M02013	6.0	+	-	±	-	-	±	light yellow	+	-	-	-	-	-
M02014	8.0	±	-	±	-	-	±	light yellow	-	-	-	-	±	-
M02015	7.0	+	-	+	-	-	+	light yellow	-	-	-	-	±	-
M02016	8.0	+	-	+	-	-	+	light yellow	-	-	-	-	±	-
M02017	7.0	2+	-	+	-	-	+	light yellow	+	-	-	-	±	-

Protein, -: negative; ±: 10 ≤ and < 30 mg/dL; +: 30 ≤ and < 100 mg/dL; 2+: 100 ≤ and < 300 mg/dL; 3+: 300 ≤ and < 600 mg/dL; 4+: 600 mg/dL ≤

Glucose, -: negative; ±: 30 ≤ and < 70 mg/dL; +: 70 ≤ and < 150 mg/dL; 2+: 150 ≤ and < 300 mg/dL; 3+: 300 ≤ and < 1,000 mg/dL; 4+: 1,000 mg/dL ≤

Ketone, -: negative; ±: (5 ≤ and < 10 mg/dL; +: 10 ≤ and < 40 mg/dL; 2+: 40 ≤ and < 80 mg/dL; 3+: 80 ≤ and < 150 mg/dL; 4+: 150 mg/dL ≤

Bilirubin, -: negative; +: 0.5 ≤ and < 2.0 mg/dL; 2+: 2.0 ≤ and < 6.0 mg/dL; 3+: 6.0 ≤ and < 10.0 mg/dL; 4+: 10.0 mg/dL ≤

Occult blood, -: negative; ±: 0.03 ≤ and < 0.06 mg/dL; +: 0.06 ≤ and < 0.20 mg/dL; 2+: 0.20 ≤ and < 1.00 mg/dL; 3+: 1.00 mg/dL ≤

Urobilinogen, ±: normal; +: 2.0 ≤ and < 4.0 mg/dL; 2+: 4.0 ≤ and < 8.0 mg/dL; 3+: 8.0 ≤ and < 12.0 mg/dL; 4+: 12.0 mg/dL ≤

Turbidity, -: negative; ±: trace; +: slight; 2+: moderate; 3+: marked

Red Blood cells, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≥ 300/3 visual field

White Blood cells, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≥ 300/3 visual field

Casts, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≥ 300/3 visual field

Crystals, -: not observed; ±: a few; +: abundant

Epithelial cells, -: not observed; ±: a few; +: abundant

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

Appendix 23-1-2 (continued). Urinalysis in male rats

CPN 30 mg/kg

Male No.	Urine volume mL/24hr	S.G.	Electrolyte, density			Electrolyte, gross volume		
			Na mEq/L	K mEq/L	Cl mEq/L	Na mEq/24hr	K mEq/24hr	Cl mEq/24hr
M02013	13.0	1.052	95.5	201.54	128.4	1.24	2.62	1.67
M02014	40.9	1.020	28.8	70.74	35.4	1.18	2.89	1.45
M02015	15.0	1.063	115.8	276.81	165.2	1.74	4.15	2.48
M02016	14.3	1.064	131.3	274.53	190.5	1.88	3.93	2.72
M02017	12.2	1.071	147.0	343.92 #	196.8	1.79	4.20	2.40
Number of males	5	5	5	5	5	5	5	5
Mean	19.1	1.054	103.7	233.51	143.3	1.57	3.56	2.14
S.D.	12.2	0.020	46.0	104.00	66.0	0.33	0.75	0.55
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	KW	DU	AN	DU	AN	AN	AN	AN

S.G.: Specific gravity

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

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

KW: Analysis by Kruskal-Wallis' test (one-way layout).

#: The specimen was diluted to two folds with distilled water.

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

Appendix 23-1-3. Urinalysis in male rats

CPN 100 mg/kg

Male No.	Quality									Urinary sediments				
	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen	Color	Turbidity	Red blood cells	White blood cells	Casts	Crystals	Epithelial cells
M03025	8.5	+	-	+	-	-	±	light yellow	-	-	-	-	±	-
M03026	7.0	2+	-	2+	-	-	+	light yellow	-	-	-	-	±	-
M03027	6.5	+	-	+	-	-	±	light yellow	-	-	-	-	±	-
M03028	7.0	+	-	+	-	-	+	light yellow	-	-	-	-	±	-
M03029	7.0	2+	-	+	-	-	+	light yellow	-	-	-	-	±	-

Protein, -: negative; ±: 10 ≤ and < 30 mg/dL; +: 30 ≤ and < 100 mg/dL; 2+: 100 ≤ and < 300 mg/dL; 3+: 300 ≤ and < 600 mg/dL; 4+: 600 mg/dL ≤
 Glucose, -: negative; ±: 30 ≤ and < 70 mg/dL; +: 70 ≤ and < 150 mg/dL; 2+: 150 ≤ and < 300 mg/dL; 3+: 300 ≤ and < 1,000 mg/dL; 4+: 1,000 mg/dL ≤
 Ketone, -: negative; ±: 5 ≤ and < 10 mg/dL; +: 10 ≤ and < 40 mg/dL; 2+: 40 ≤ and < 80 mg/dL; 3+: 80 ≤ and < 150 mg/dL; 4+: 150 mg/dL ≤
 Bilirubin, -: negative; +: 0.5 ≤ and < 2.0 mg/dL; 2+: 2.0 ≤ and < 6.0 mg/dL; 3+: 6.0 ≤ and < 10.0 mg/dL; 4+: 10.0 mg/dL ≤
 Occult blood, -: negative; ±: 0.03 ≤ and < 0.06 mg/dL; +: 0.06 ≤ and < 0.20 mg/dL; 2+: 0.20 ≤ and < 1.00 mg/dL; 3+: 1.00 mg/dL ≤
 Urobilinogen, ±: normal; +: 2.0 ≤ and < 4.0 mg/dL; 2+: 4.0 ≤ and < 8.0 mg/dL; 3+: 8.0 ≤ and < 12.0 mg/dL; 4+: 12.0 mg/dL ≤
 Turbidity, -: negative; ±: trace; +: slight; 2+: moderate; 3+: marked
 Red Blood cells, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≥ 300/3 visual field
 White Blood cells, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≥ 300/3 visual field
 Casts, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≥ 300/3 visual field
 Crystals, -: not observed; ±: a few; +: abundant
 Epithelial cells, -: not observed; ±: a few; +: abundant

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

Appendix 23-1-3 (continued). Urinalysis in male rats

CPN 100 mg/kg

Male No.	Urine volume mL/24hr	S.G.	Electrolyte, density			Electrolyte, gross volume		
			Na mEq/L	K mEq/L	Cl mEq/L	Na mEq/24hr	K mEq/24hr	Cl mEq/24hr
M03025	15.7	1.059	121.7	249.66	157.2	1.91	3.92	2.47
M03026	14.0	1.054	84.4	218.28	124.8	1.18	3.06	1.75
M03027	16.6	1.048	80.9	201.51	118.2	1.34	3.35	1.96
M03028	13.2	1.066	157.8	278.89	200.3	2.08	3.68	2.64
M03029	21.9	1.049	81.8	191.57	105.8	1.79	4.20	2.32
Number of males	5	5	5	5	5	5	5	5
Mean	16.3	1.055	105.3	227.98	141.3	1.66	3.64	2.23
S.D.	3.4	0.007	33.9	35.99	38.1	0.38	0.45	0.37
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	KW	DU	AN	DU	AN	AN	AN	AN

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

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

KW: Analysis by Kruskal-Wallis' test (one-way layout).

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

Appendix 23-1-4. Urinalysis in male rats

CPN 300 mg/kg

Male No.	Quality									Urinary sediments				
	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen	Color	Turbidity	Red blood cells	White blood cells	Casts	Crystals	Epithelial cells
M04037	8.0	±	-	+	-	-	±	light yellow	-	-	-	-	-	-
M04038	7.0	+	-	+	-	-	+	light yellow	-	-	-	-	±	-
M04039	7.0	+	-	2+	-	-	+	light yellow	-	-	-	-	±	-
M04040	8.0	+	-	+	-	-	±	light yellow	-	-	-	-	±	-
M04041	7.0	+	-	+	-	-	±	light yellow	-	-	-	-	±	-
Protein,	-: negative; ±: 10 ≤ and < 30 mg/dL; +: 30 ≤ and < 100 mg/dL; 2+: 100 ≤ and < 300 mg/dL; 3+: 300 ≤ and < 600 mg/dL; 4+: 600 mg/dL ≤													
Glucose,	-: negative; ±: 30 ≤ and < 70 mg/dL; +: 70 ≤ and < 150 mg/dL; 2+: 150 ≤ and < 300 mg/dL; 3+: 300 ≤ and < 1,000 mg/dL; 4+: 1,000 mg/dL ≤													
Ketone,	-: negative; ±(5 ≤ and < 10 mg/dL; +: 10 ≤ and < 40 mg/dL; 2+: 40 ≤ and < 80 mg/dL; 3+: 80 ≤ and < 150 mg/dL; 4+: 150 mg/dL ≤													
Bilirubin,	-: negative; +: 0.5 ≤ and < 2.0 mg/dL; 2+: 2.0 ≤ and < 6.0 mg/dL; 3+: 6.0 ≤ and < 10.0 mg/dL; 4+: 10.0 mg/dL ≤													
Occult blood,	-: negative; ±: 0.03 ≤ and < 0.06 mg/dL; +: 0.06 ≤ and < 0.20 mg/dL; 2+: 0.20 ≤ and < 1.00 mg/dL; 3+: 1.00 mg/dL ≤													
Urobilinogen,	±: normal; +: 2.0 ≤ and < 4.0 mg/dL; 2+: 4.0 ≤ and < 8.0 mg/dL; 3+: 8.0 ≤ and < 12.0 mg/dL; 4+: 12.0 mg/dL ≤													
Turbidity,	-: negative; ±: trace; +: slight; 2+: moderate; 3+: marked													
Red Blood cells,	-: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≥ 300/3 visual field													
White Blood cells,	-: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≥ 300/3 visual field													
Casts,	-: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≥ 300/3 visual field													
Crystals,	-: not observed; ±: a few; +: abundant													
Epithelial cells,	-: not observed; ±: a few; +: abundant													

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

Appendix 23-1-4 (continued). Urinalysis in male rats

CPN 300 mg/kg

Male No.	Urine volume mL/24hr	S.G.	Electrolyte, density			Electrolyte, gross volume		
			Na mEq/L	K mEq/L	Cl mEq/L	Na mEq/24hr	K mEq/24hr	Cl mEq/24hr
M04037	33.6	1.029	56.1	111.49	67.2	1.88	3.75	2.26
M04038	22.2	1.042	94.8	182.94	114.6	2.10	4.06	2.54
M04039	16.5	1.044	49.5	162.50	65.7	0.82	2.68	1.08
M04040	25.6	1.033	60.3	129.33	82.3	1.54	3.31	2.11
M04041	23.5	1.036	51.2	144.54	85.4	1.20	3.40	2.01
Number of males	5	5	5	5	5	5	5	5
Mean	24.3	1.037	62.4	146.16	83.0	1.51	3.44	2.00
S.D.	6.2	0.006	18.6	27.87	19.7	0.51	0.52	0.55
Significance	NS	*	NS	*	NS	NS	NS	NS
Statistical method	KW	DU	AN	DU	AN	AN	AN	AN

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

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

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

KW: Analysis by Kruskal-Wallis' test (one-way layout).

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

Appendix 23-2-1. Urinalysis in male rats of the recovery period

Control (vehicle: corn oil)

Male No.	Quality										Urinary sediments				
	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen	Color	Turbidity	Red blood cells	White blood cells	Casts	Crystals	Epithelial cells	
M01008	8.0	2+	-	+	-	-	+	light yellow	-	-	-	-	±	-	
M01009	7.5	+	-	±	-	-	+	light yellow	-	-	-	-	±	-	
M01010	7.5	+	-	±	-	-	+	light yellow	-	-	-	-	±	-	
M01011	8.0	2+	-	+	-	-	+	yellow	-	-	-	-	±	-	
M01012	8.0	+	-	±	-	-	±	light yellow	-	-	-	-	±	-	

Protein, -: negative; ±: 10 ≤ and < 30 mg/dL; +: 30 ≤ and < 100 mg/dL; 2+: 100 ≤ and < 300 mg/dL; 3+: 300 ≤ and < 600 mg/dL; 4+: 600 mg/dL ≤

Glucose, -: negative; ±: 30 ≤ and < 70 mg/dL; +: 70 ≤ and < 150 mg/dL; 2+: 150 ≤ and < 300 mg/dL; 3+: 300 ≤ and < 1,000 mg/dL; 4+: 1,000 mg/dL ≤

Ketone, -: negative; ±: (5 ≤ and < 10 mg/dL; +: 10 ≤ and < 40 mg/dL; 2+: 40 ≤ and < 80 mg/dL; 3+: 80 ≤ and < 150 mg/dL; 4+: 150 mg/dL ≤

Bilirubin, -: negative; +: 0.5 ≤ and < 2.0 mg/dL; 2+: 2.0 ≤ and < 6.0 mg/dL; 3+: 6.0 ≤ and < 10.0 mg/dL; 4+: 10.0 mg/dL ≤

Occult blood, -: negative; ±: 0.03 ≤ and < 0.06 mg/dL; +: 0.06 ≤ and < 0.20 mg/dL; 2+: 0.20 ≤ and < 1.00 mg/dL; 3+: 1.00 mg/dL ≤

Urobilinogen, ±: normal; +: 2.0 ≤ and < 4.0 mg/dL; 2+: 4.0 ≤ and < 8.0 mg/dL; 3+: 8.0 ≤ and < 12.0 mg/dL; 4+: 12.0 mg/dL ≤

Turbidity, -: negative; ±: trace; +: slight; 2+: moderate; 3+: marked

Red Blood cells, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≥ 300/3 visual field

White Blood cells, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≥ 300/3 visual field

Casts, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≥ 300/3 visual field

Crystals, -: not observed; ±: a few; +: abundant

Epithelial cells, -: not observed; ±: a few; +: abundant

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

Appendix 23-2-1 (continued). Urinalysis in male rats of the recovery period

Control (vehicle: corn oil)

Male No.	Urine volume mL/24hr	S.G.	Electrolyte, density			Electrolyte, gross volume		
			Na mEq/L	K mEq/L	Cl mEq/L	Na mEq/24hr	K mEq/24hr	Cl mEq/24hr
M01008	10.9	1.080	223.4	371.50 #	250.4	2.44	4.05	2.73
M01009	22.7	1.048	87.5	209.77	111.9	1.99	4.76	2.54
M01010	18.6	1.057	92.7	232.69	127.9	1.72	4.33	2.38
M01011	13.4	1.080	143.4	359.08 #	204.6	1.92	4.81	2.74
M01012	16.9	1.059	114.4	245.39	135.5	1.93	4.15	2.29
Number of males	5	5	5	5	5	5	5	5
Mean	16.5	1.065	132.3	283.69	166.1	2.00	4.42	2.54
S.D.	4.6	0.014	55.5	75.71	59.0	0.27	0.35	0.20

S.G.: Specific gravity

#: The specimen was diluted to two folds with distilled water.

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

Appendix 23-2-2. Urinalysis in male rats of the recovery period

CPN 300 mg/kg

Male No.	Quality									Urinary sediments				
	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen	Color	Turbidity	Red blood cells	White blood cells	Casts	Crystals	Epithelial cells
M04044	7.0	+	-	±	-	-	+	light yellow	-	-	-	-	±	-
M04045	8.0	2+	-	±	-	-	±	light yellow	-	-	-	-	±	-
M04046	7.5	+	-	±	-	-	±	light yellow	-	-	-	-	±	-
M04047	7.5	+	-	+	-	-	+	light yellow	-	-	-	-	±	-
M04048	8.0	+	-	±	-	-	±	light yellow	-	-	-	-	±	-

Protein, -: negative; ±: 10 ≤ and < 30 mg/dL; +: 30 ≤ and < 100 mg/dL; 2+: 100 ≤ and < 300 mg/dL; 3+: 300 ≤ and < 600 mg/dL; 4+: 600 mg/dL ≤
 Glucose, -: negative; ±: 30 ≤ and < 70 mg/dL; +: 70 ≤ and < 150 mg/dL; 2+: 150 ≤ and < 300 mg/dL; 3+: 300 ≤ and < 1,000 mg/dL; 4+: 1,000 mg/dL ≤
 Ketone, -: negative; ±: (5 ≤ and < 10 mg/dL; +: 10 ≤ and < 40 mg/dL; 2+: 40 ≤ and < 80 mg/dL; 3+: 80 ≤ and < 150 mg/dL; 4+: 150 mg/dL ≤
 Bilirubin, -: negative; +: 0.5 ≤ and < 2.0 mg/dL; 2+: 2.0 ≤ and < 6.0 mg/dL; 3+: 6.0 ≤ and < 10.0 mg/dL; 4+: 10.0 mg/dL ≤
 Occult blood, -: negative; ±: 0.03 ≤ and < 0.06 mg/dL; +: 0.06 ≤ and < 0.20 mg/dL; 2+: 0.20 ≤ and < 1.00 mg/dL; 3+: 1.00 mg/dL ≤
 Urobilinogen, ±: normal; +: 2.0 ≤ and < 4.0 mg/dL; 2+: 4.0 ≤ and < 8.0 mg/dL; 3+: 8.0 ≤ and < 12.0 mg/dL; 4+: 12.0 mg/dL ≤
 Turbidity, -: negative; ±: trace; +: slight; 2+: moderate; 3+: marked
 Red Blood cells, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≥ 300/3 visual field
 White Blood cells, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≥ 300/3 visual field
 Casts, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≥ 300/3 visual field
 Crystals, -: not observed; ±: a few; +: abundant
 Epithelial cells, -: not observed; ±: a few; +: abundant

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

Appendix 23-2-2 (continued). Urinalysis in male rats of the recovery period

CPN 300 mg/kg

Male No.	Urine volume mL/24hr	S.G.	Electrolyte, density			Electrolyte, gross volume		
			Na mEq/L	K mEq/L	Cl mEq/L	Na mEq/24hr	K mEq/24hr	Cl mEq/24hr
M04044	26.0	1.047	86.4	199.15	109.8	2.25	5.18	2.85
M04045	22.9	1.044	79.3	201.94	101.0	1.82	4.62	2.31
M04046	20.2	1.058	129.2	267.98	157.7	2.61	5.41	3.19
M04047	18.8	1.067	136.5	297.50	175.0	2.57	5.59	3.29
M04048	17.5	1.060	86.1	255.51	136.4	1.51	4.47	2.39
Number of males	5	5	5	5	5	5	5	5
Mean	21.1	1.055	103.5	244.42	136.0	2.15	5.05	2.81
S.D.	3.4	0.010	27.1	42.86	31.2	0.48	0.49	0.45
Significance	NS	NS	NS	NS	NS	NS	*	NS
Statistical method	TT	TT	TT	TT	TT	TT	TT	TT

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

NS: Not significantly different from the control group.

TT: Analysis by Student's t-test.

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

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

Control (vehicle: corn oil)

Female No.	Quality									Urinary sediments				
	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen	Color	Turbidity	Red blood cells	White blood cells	Casts	Crystals	Epithelial cells
F05049	6.5	+	-	±	-	-	+	yellow	-	-	-	-	-	-
F05050	6.5	+	-	±	-	-	±	light yellow	-	-	-	-	±	-
F05051	6.5	+	-	±	-	-	+	light yellow	-	-	-	-	±	-
F05052	6.5	+	-	+	-	-	+	light yellow	-	-	-	-	-	-
F05053	6.5	±	-	-	-	-	±	light yellow	-	-	-	-	-	-
Protein,	-: negative; ±: 10 ≤ and < 30 mg/dL; +: 30 ≤ and < 100 mg/dL; 2+: 100 ≤ and < 300 mg/dL; 3+: 300 ≤ and < 600 mg/dL; 4+: 600 mg/dL ≤													
Glucose,	-: negative; ±: 30 ≤ and < 70 mg/dL; +: 70 ≤ and < 150 mg/dL; 2+: 150 ≤ and < 300 mg/dL; 3+: 300 ≤ and < 1,000 mg/dL; 4+: 1,000 mg/dL ≤													
Ketone,	-: negative; ±(5 ≤ and < 10 mg/dL; +: 10 ≤ and < 40 mg/dL; 2+: 40 ≤ and < 80 mg/dL; 3+: 80 ≤ and < 150 mg/dL; 4+: 150 mg/dL ≤													
Bilirubin,	-: negative; +: 0.5 ≤ and < 2.0 mg/dL; 2+: 2.0 ≤ and < 6.0 mg/dL; 3+: 6.0 ≤ and < 10.0 mg/dL; 4+: 10.0 mg/dL ≤													
Occult blood,	-: negative; ±: 0.03 ≤ and < 0.06 mg/dL; +: 0.06 ≤ and < 0.20 mg/dL; 2+: 0.20 ≤ and < 1.00 mg/dL; 3+: 1.00 mg/dL ≤													
Urobilinogen,	±: normal; +: 2.0 ≤ and < 4.0 mg/dL; 2+: 4.0 ≤ and < 8.0 mg/dL; 3+: 8.0 ≤ and < 12.0 mg/dL; 4+: 12.0 mg/dL ≤													
Turbidity,	-: negative; ±: trace; +: slight; 2+: moderate; 3+: marked													
Red Blood cells,	-: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≥ 300/3 visual field													
White Blood cells,	-: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≥ 300/3 visual field													
Casts,	-: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≥ 300/3 visual field													
Crystals,	-: not observed; ±: a few; +: abundant													
Epithelial cells,	-: not observed; ±: a few; +: abundant													

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

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

Control (vehicle: corn oil)

Female No.	Urine volume mL/24hr	S.G.	Electrolyte, density			Electrolyte, gross volume		
			Na mEq/L	K mEq/L	Cl mEq/L	Na mEq/24hr	K mEq/24hr	Cl mEq/24hr
F05049	5.6	1.092	253.6	442.54 #	310.5	1.42	2.48	1.74
F05050	14.7	1.038	82.7	178.34	106.2	1.22	2.62	1.56
F05051	8.8	1.071	154.1	316.08 #	213.1	1.36	2.78	1.88
F05052	10.0	1.059	125.5	277.23	167.7	1.26	2.77	1.68
F05053	6.9	1.061	135.7	217.57	130.1	0.94	1.50	0.90
Number of females	5	5	5	5	5	5	5	5
Mean	9.2	1.064	150.3	286.35	185.5	1.24	2.43	1.55
S.D.	3.5	0.020	63.4	102.18	80.7	0.19	0.53	0.38

S.G.: Specific gravity

#: The specimen was diluted to two folds with distilled water.

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

Appendix 24-1-2. Urinalysis in female rats, satellite group

CPN 300 mg/kg

Female No.	Quality									Urinary sediments				
	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen	Color	Turbidity	Red blood cells	White blood cells	Casts	Crystals	Epithelial cells
F06056	6.5	±	-	+	-	-	±	light yellow	-	-	-	-	-	-
F06057	7.0	+	-	+	-	-	+	light yellow	-	-	-	-	±	-
F06058	7.0	+	-	+	-	-	+	light yellow	-	-	-	-	±	-
F06059	6.5	+	-	2+	-	-	+	light yellow	-	-	-	-	±	-
F06060	6.5	+	-	+	-	-	+	light yellow	-	-	-	-	±	-
Protein,	-: negative; ±: 10 ≤ and < 30 mg/dL; +: 30 ≤ and < 100 mg/dL; 2+: 100 ≤ and < 300 mg/dL; 3+: 300 ≤ and < 600 mg/dL; 4+: 600 mg/dL ≤													
Glucose,	-: negative; ±: 30 ≤ and < 70 mg/dL; +: 70 ≤ and < 150 mg/dL; 2+: 150 ≤ and < 300 mg/dL; 3+: 300 ≤ and < 1,000 mg/dL; 4+: 1,000 mg/dL ≤													
Ketone,	-: negative; ±: 5 ≤ and < 10 mg/dL; +: 10 ≤ and < 40 mg/dL; 2+: 40 ≤ and < 80 mg/dL; 3+: 80 ≤ and < 150 mg/dL; 4+: 150 mg/dL ≤													
Bilirubin,	-: negative; +: 0.5 ≤ and < 2.0 mg/dL; 2+: 2.0 ≤ and < 6.0 mg/dL; 3+: 6.0 ≤ and < 10.0 mg/dL; 4+: 10.0 mg/dL ≤													
Occult blood,	-: negative; ±: 0.03 ≤ and < 0.06 mg/dL; +: 0.06 ≤ and < 0.20 mg/dL; 2+: 0.20 ≤ and < 1.00 mg/dL; 3+: 1.00 mg/dL ≤													
Urobilinogen,	±: normal; +: 2.0 ≤ and < 4.0 mg/dL; 2+: 4.0 ≤ and < 8.0 mg/dL; 3+: 8.0 ≤ and < 12.0 mg/dL; 4+: 12.0 mg/dL ≤													
Turbidity,	-: negative; ±: trace; +: slight; 2+: moderate; 3+: marked													
Red Blood cells,	-: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≥ 300/3 visual field													
White Blood cells,	-: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≥ 300/3 visual field													
Casts,	-: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≥ 300/3 visual field													
Crystals,	-: not observed; ±: a few; +: abundant													
Epithelial cells,	-: not observed; ±: a few; +: abundant													

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

Appendix 24-1-2 (continued). Urinalysis in female rats, satellite group

CPN 300 mg/kg

Female No.	Urine volume mL/24hr	S.G.	Electrolyte, density			Electrolyte, gross volume		
			Na mEq/L	K mEq/L	Cl mEq/L	Na mEq/24hr	K mEq/24hr	Cl mEq/24hr
F06056	13.8	1.038	88.2	132.10	80.6	1.22	1.82	1.11
F06057	7.0	1.064	99.2	239.48	121.9	0.69	1.68	0.85
F06058	15.2	1.046	86.4	212.74	153.2	1.31	3.23	2.33
F06059	6.4	1.040	102.7	94.89	82.1	0.66	0.61	0.53
F06060	8.2	1.067	102.1	258.11	151.6	0.84	2.12	1.24
Number of females	5	5	5	5	5	5	5	5
Mean	10.1	1.051	95.7	187.46	117.9	0.94	1.89	1.21
S.D.	4.1	0.014	7.8	70.66	35.6	0.30	0.94	0.68
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	TT	TT	AW	TT	TT	TT	TT	TT

NS: Not significantly different from the control group.

TT: Analysis by Student's t-test.

AW: Analysis by Aspin-Welch t-test.

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

Appendix 24-2-1. Urinalysis in female rats of the recovery period

Control (vehicle: corn oil)

Female No.	Quality									Urinary sediments				
	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen	Color	Turbidity	Red blood cells	White blood cells	Casts	Crystals	Epithelial cells
F05054	7.0	+	-	-	-	-	+	light yellow	-	-	-	-	±	-
F05055	7.5	-	-	-	-	-	±	light yellow	-	-	-	-	±	-
F05056	7.5	-	-	-	-	-	±	light yellow	-	-	-	-	±	-
F05057	6.5	+	-	±	-	-	+	light yellow	-	-	-	-	±	-
F05058	8.0	±	-	-	-	-	±	light yellow	-	-	-	-	-	-
Protein,	-: negative; ±: 10 ≤ and < 30 mg/dL; +: 30 ≤ and < 100 mg/dL; 2+: 100 ≤ and < 300 mg/dL; 3+: 300 ≤ and < 600 mg/dL; 4+: 600 mg/dL ≤													
Glucose,	-: negative; ±: 30 ≤ and < 70 mg/dL; +: 70 ≤ and < 150 mg/dL; 2+: 150 ≤ and < 300 mg/dL; 3+: 300 ≤ and < 1,000 mg/dL; 4+: 1,000 mg/dL ≤													
Ketone,	-: negative; ±: 5 ≤ and < 10 mg/dL; +: 10 ≤ and < 40 mg/dL; 2+: 40 ≤ and < 80 mg/dL; 3+: 80 ≤ and < 150 mg/dL; 4+: 150 mg/dL ≤													
Bilirubin,	-: negative; +: 0.5 ≤ and < 2.0 mg/dL; 2+: 2.0 ≤ and < 6.0 mg/dL; 3+: 6.0 ≤ and < 10.0 mg/dL; 4+: 10.0 mg/dL ≤													
Occult blood,	-: negative; ±: 0.03 ≤ and < 0.06 mg/dL; +: 0.06 ≤ and < 0.20 mg/dL; 2+: 0.20 ≤ and < 1.00 mg/dL; 3+: 1.00 mg/dL ≤													
Urobilinogen,	±: normal; +: 2.0 ≤ and < 4.0 mg/dL; 2+: 4.0 ≤ and < 8.0 mg/dL; 3+: 8.0 ≤ and < 12.0 mg/dL; 4+: 12.0 mg/dL ≤													
Turbidity,	-: negative; ±: trace; +: slight; 2+: moderate; 3+: marked													
Red Blood cells,	-: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≥ 300/3 visual field													
White Blood cells,	-: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≥ 300/3 visual field													
Casts,	-: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≥ 300/3 visual field													
Crystals,	-: not observed; ±: a few; +: abundant													
Epithelial cells,	-: not observed; ±: a few; +: abundant													

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

Appendix 24-2-1 (continued). Urinalysis in female rats of the recovery period

Control (vehicle: corn oil)

Female No.	Urine volume mL/24hr	S.G.	Electrolyte, density			Electrolyte, gross volume		
			Na mEq/L	K mEq/L	Cl mEq/L	Na mEq/24hr	K mEq/24hr	Cl mEq/24hr
F05054	15.2	1.046	104.8	213.34	131.6	1.59	3.24	2.00
F05055	21.0	1.039	92.9	190.83	112.3	1.95	4.01	2.36
F05056	24.8	1.034	68.6	167.57	93.7	1.70	4.16	2.32
F05057	8.8	1.080	117.2	379.74 #	207.0	1.03	3.34	1.82
F05058	9.0	1.038	61.5	112.88	57.5	0.55	1.02	0.52
Number of females	5	5	5	5	5	5	5	5
Mean	15.8	1.047	89.0	212.87	120.4	1.36	3.15	1.80
S.D.	7.1	0.019	23.6	100.48	55.6	0.57	1.26	0.75

S.G.: Specific gravity

#: The specimen was diluted to two folds with distilled water.

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

Appendix 24-2-2. Urinalysis in female rats of the recovery period

CPN 300 mg/kg

Female No.	Quality									Urinary sediments				
	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen	Color	Turbidity	Red blood cells	White blood cells	Casts	Crystals	Epithelial cells
F06061	7.5	-	-	-	-	-	±	light yellow	-	-	-	-	-	-
F06062	6.5	-	-	-	-	-	±	light yellow	-	-	-	-	±	-
F06063	6.5	±	-	-	-	-	±	light yellow	-	-	-	-	±	-
F06064	8.5	+	-	-	-	-	+	light yellow	-	-	-	-	±	-
F06065	7.5	+	-	±	-	-	+	light yellow	-	-	-	-	±	-

Protein, -: negative; ±: 10 ≤ and < 30 mg/dL; +: 30 ≤ and < 100 mg/dL; 2+: 100 ≤ and < 300 mg/dL; 3+: 300 ≤ and < 600 mg/dL; 4+: 600 mg/dL ≤
 Glucose, -: negative; ±: 30 ≤ and < 70 mg/dL; +: 70 ≤ and < 150 mg/dL; 2+: 150 ≤ and < 300 mg/dL; 3+: 300 ≤ and < 1,000 mg/dL; 4+: 1,000 mg/dL ≤
 Ketone, -: negative; ±: 5 ≤ and < 10 mg/dL; +: 10 ≤ and < 40 mg/dL; 2+: 40 ≤ and < 80 mg/dL; 3+: 80 ≤ and < 150 mg/dL; 4+: 150 mg/dL ≤
 Bilirubin, -: negative; +: 0.5 ≤ and < 2.0 mg/dL; 2+: 2.0 ≤ and < 6.0 mg/dL; 3+: 6.0 ≤ and < 10.0 mg/dL; 4+: 10.0 mg/dL ≤
 Occult blood, -: negative; ±: 0.03 ≤ and < 0.06 mg/dL; +: 0.06 ≤ and < 0.20 mg/dL; 2+: 0.20 ≤ and < 1.00 mg/dL; 3+: 1.00 mg/dL ≤
 Urobilinogen, ±: normal; +: 2.0 ≤ and < 4.0 mg/dL; 2+: 4.0 ≤ and < 8.0 mg/dL; 3+: 8.0 ≤ and < 12.0 mg/dL; 4+: 12.0 mg/dL ≤
 Turbidity, -: negative; ±: trace; +: slight; 2+: moderate; 3+: marked
 Red Blood cells, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≥300/3 visual field
 White Blood cells, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≥300/3 visual field
 Casts, -: not observed; ±: 1-9/3 visual field; +: 10-99/3 visual field; 2+: 100-299/3 visual field; 3+: ≥300/3 visual field
 Crystals, -: not observed; ±: a few; +: abundant
 Epithelial cells, -: not observed; ±: a few; +: abundant

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

Appendix 24-2-2 (continued). Urinalysis in female rats of the recovery period

CPN 300 mg/kg

Female No.	Urine volume mL/24hr	S.G.	Electrolyte, density			Electrolyte, gross volume		
			Na mEq/L	K mEq/L	Cl mEq/L	Na mEq/24hr	K mEq/24hr	Cl mEq/24hr
F06061	23.5	1.035	82.3	174.67	99.1	1.93	4.10	2.33
F06062	9.4	1.073	135.9	345.16 #	209.5	1.28	3.24	1.97
F06063	8.7	1.073	150.8	337.18 #	172.5	1.31	2.93	1.50
F06064	13.5	1.061	120.4	277.42	166.3	1.63	3.75	2.25
F06065	11.1	1.065	120.7	286.73	149.2	1.34	3.18	1.66
Number of females	5	5	5	5	5	5	5	5
Mean	13.2	1.061	122.0	284.23	159.3	1.50	3.44	1.94
S.D.	6.0	0.016	25.5	68.14	40.2	0.28	0.47	0.36
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	TT	TT	TT	TT	TT	TT	TT	TT

S.G.: Specific gravity

NS: Not significantly different from the control group.

TT: Analysis by Student's t-test.

#: The specimen was diluted to two folds with distilled water.

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

Appendix 25-1-1. Hematological findings of male rats at the end of the administration period

Control (vehicle: corn oil)

Male No.	RBC 10000/ μ L	HGB g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelet 10000/ μ L	PT sec.	APTT sec.	WBC 100/ μ L	Neutrophil %	Eosinophil %	Basophil %	Monocyte %	Lymphocyte %	Reticulocyte %
M01001	783	14.5	43.8	55.9	18.5	33.1	106.7	17.1	23.9	93.8	10.8	1.6	0.1	4.9	82.6	2.45
M01002	783	14.0	41.3	52.7	17.9	33.9	103.1	18.5	18.9	110.7	15.8	1.6	0.1	5.2	77.3	3.48
M01003	775	14.1	41.7	53.8	18.2	33.8	78.1	14.2	15.7	104.5	11.1	0.6	0.0	3.0	85.3	2.90
M01004	814	14.4	43.1	52.9	17.7	33.4	109.6	15.2	19.8	99.0	17.9	1.3	0.0	4.7	76.1	2.99
M01005	831	15.4	44.7	53.8	18.5	34.5	87.4	16.9	20.3	97.0	37.9	2.3	0.0	4.7	55.1	2.46
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	797	14.5	42.9	53.8	18.2	33.7	97.0	16.4	19.7	101.0	18.7	1.5	0.0	4.5	75.3	2.86
S.D.	24	0.6	1.4	1.3	0.4	0.5	13.6	1.7	2.9	6.7	11.2	0.6	0.1	0.9	11.9	0.43

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

Appendix 25-1-2. Hematological findings of male rats at the end of the administration period

CPN 30 mg/kg

Male No.	RBC 10000/ μ L	HGB g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelet 10000/ μ L	PT sec.	APTT sec.	WBC 100/ μ L	Neutrophil %	Eosinophil %	Basophil %	Monocyte %	Lymphocyte %	Reticulocyte %
M02013	771	14.5	42.6	55.3	18.8	34.0	78.8	13.0	16.7	88.8	11.5	0.9	0.1	5.1	82.4	3.19
M02014	754	13.8	40.8	54.1	18.3	33.8	81.0	14.5	18.5	83.8	19.3	1.7	0.0	4.8	74.2	3.73
M02015	713	13.8	41.5	58.2	19.4	33.3	82.6	16.3	22.0	70.5	31.1	0.7	0.0	3.8	64.4	3.12
M02016	764	14.4	42.9	56.2	18.8	33.6	99.2	15.7	20.4	84.5	9.8	2.4	0.1	3.4	84.3	2.81
M02017	786	14.3	42.9	54.6	18.2	33.3	82.1	15.0	20.9	64.3	25.6	2.6	0.0	5.1	66.7	2.71
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	758	14.2	42.1	55.7	18.7	33.6	84.7	14.9	19.7	78.4	19.5	1.7	0.0	4.4	74.4	3.11
S.D.	28	0.3	0.9	1.6	0.5	0.3	8.2	1.3	2.1	10.4	9.1	0.9	0.1	0.8	9.0	0.40
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	AN	DT	DU	DU	AN	AN	KW	AN	DU	AN	AN	AN	AN	AN	AN

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

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

DT: Analysis by Dunnett type mean rank test.

KW: Analysis by Kruskal-Wallis' test (one-way layout).

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

Appendix 25-1-3. Hematological findings of male rats at the end of the administration period

CPN 100 mg/kg

Male No.	RBC 10000/ μ L	HGB g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelet 10000/ μ L	PT sec.	APTT sec.	WBC 100/ μ L	Neutrophil %	Eosinophil %	Basophil %	Monocyte %	Lymphocyte %	Reticulocyte %
M03025	739	13.5	39.9	54.0	18.3	33.8	78.0	14.0	18.2	89.0	14.2	1.8	0.0	4.2	79.8	2.97
M03026	735	13.3	40.4	55.0	18.1	32.9	98.4	13.6	19.2	67.9	19.0	1.8	0.0	3.5	75.7	2.97
M03027	711	13.1	39.1	55.0	18.4	33.5	78.4	16.3	19.0	59.6	15.7	1.5	0.0	3.9	78.9	2.57
M03028	788	14.1	40.5	51.4	17.9	34.8	105.6	12.8	16.9	91.4	24.5	2.0	0.0	3.5	70.0	3.16
M03029	781	13.3	39.3	50.3	17.0	33.8	112.6	14.7	20.2	81.1	15.7	1.8	0.0	3.0	79.5	3.24
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	751	13.5	39.8	53.1	17.9	33.8	94.6	14.3	18.7	77.8	17.8	1.8	0.0	3.6	76.8	2.98
S.D.	33	0.4	0.6	2.2	0.6	0.7	15.8	1.3	1.2	13.7	4.1	0.2	0.0	0.5	4.1	0.26
Significance	*	NS	*	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	AN	DT	DU	DU	AN	AN	KW	AN	DU	AN	AN	AN	AN	AN	AN

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

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

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

DT: Analysis by Dunnett type mean rank test.

KW: Analysis by Kruskal-Wallis' test (one-way layout).

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

Appendix 25-1-4. Hematological findings of male rats at the end of the administration period

CPN 300 mg/kg

Male No.	RBC 10000/ μ L	HGB g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelet 10000/ μ L	PT sec.	APTT sec.	WBC 100/ μ L	Neutrophil %	Eosinophil %	Basophil %	Monocyte %	Lymphocyte %	Reticulocyte %
M04037	794	14.3	41.6	52.4	18.0	34.4	102.6	12.7	17.3	99.3	14.3	0.5	0.1	4.4	80.7	2.97
M04038	804	14.9	44.2	55.0	18.5	33.7	82.1	16.1	21.4	86.4	17.4	0.7	0.0	5.7	76.2	3.24
M04039	805	13.2	38.3	47.6	16.4	34.5	108.5	26.5	20.4	45.6	12.8	1.5	0.0	5.9	79.8	2.73
M04040	854	15.1	44.7	52.3	17.7	33.8	103.4	17.9	22.3	83.1	24.4	1.6	0.0	7.1	66.9	3.31
M04041	781	13.4	39.8	51.0	17.2	33.7	89.7	13.4	17.6	60.5	41.3	1.3	0.0	3.8	53.6	3.32
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	808	14.2	41.7	51.7	17.6	34.0	97.3	17.3	19.8	75.0	22.0	1.1	0.0	5.4	71.4	3.11
S.D.	28	0.9	2.8	2.7	0.8	0.4	10.9	5.5	2.3	21.6	11.7	0.5	0.0	1.3	11.4	0.26
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	*	NS	NS	NS	NS	NS	NS
Statistical method	DU	AN	DT	DU	DU	AN	AN	KW	AN	DU	AN	AN	AN	AN	AN	AN

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

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

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

DT: Analysis by Dunnett type mean rank test.

KW: Analysis by Kruskal-Wallis' test (one-way layout).

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

Appendix 25-2-1. Hematological findings of male rats at the end of the recovery period

Control (vehicle: corn oil)

Male No.	RBC 10000/ μ L	HGB g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelet 10000/ μ L	PT sec.	APTT sec.	WBC 100/ μ L	Neutrophil %	Eosinophil %	Basophil %	Monocyte %	Lymphocyte %	Reticulocyte %
M01008	782	13.6	41.7	53.3	17.4	32.6	85.5	13.5	17.8	98.9	17.8	1.2	0.1	4.3	76.6	2.92
M01009	819	14.4	42.7	52.1	17.6	33.7	109.5	16.8	16.7	114.4	7.4	1.7	0.1	3.6	87.2	3.44
M01010	861	14.4	42.9	49.8	16.7	33.6	99.1	15.8	16.2	65.7	13.3	1.2	0.0	4.4	81.1	3.01
M01011	796	13.7	40.6	51.0	17.2	33.7	110.2	15.6	18.4	79.7	10.9	1.9	0.0	3.6	83.6	3.59
M01012	846	15.3	44.1	52.1	18.1	34.7	97.3	17.4	19.7	57.2	13.2	1.0	0.0	3.5	82.3	3.21
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	821	14.3	42.4	51.7	17.4	33.7	100.3	15.8	17.8	83.2	12.5	1.4	0.0	3.9	82.2	3.23
S.D.	33	0.7	1.3	1.3	0.5	0.7	10.2	1.5	1.4	23.5	3.8	0.4	0.1	0.4	3.9	0.28

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

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

CPN 300 mg/kg

Male No.	RBC 10000/ μ L	HGB g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelet 10000/ μ L	PT sec.	APTT sec.	WBC 100/ μ L	Neutrophil %	Eosinophil %	Basophil %	Monocyte %	Lymphocyte %	Reticulocyte %
M04044	793	14.2	42.1	53.1	17.9	33.7	95.0	18.0	21.6	69.8	19.6	1.3	0.0	6.3	72.8	3.86
M04045	852	14.5	42.8	50.2	17.0	33.9	117.6	16.5	19.0	100.9	10.1	1.5	0.0	3.7	84.7	3.15
M04046	784	14.8	43.9	56.0	18.9	33.7	110.2	13.7	15.8	96.5	8.5	1.1	0.1	2.7	87.6	3.60
M04047	790	14.2	43.0	54.4	18.0	33.0	92.2	15.3	21.5	58.8	21.8	1.2	0.0	6.6	70.4	3.27
M04048	792	14.2	43.2	54.5	17.9	32.9	106.6	12.8	17.8	73.4	14.3	2.3	0.1	5.2	78.1	3.25
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	802	14.4	43.0	53.6	17.9	33.4	104.3	15.3	19.1	79.9	14.9	1.5	0.0	4.9	78.7	3.43
S.D.	28	0.3	0.7	2.2	0.7	0.5	10.6	2.1	2.5	18.1	5.8	0.5	0.1	1.7	7.4	0.30
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT

NS: Not significantly different from the control group.

TT: Analysis by Student's t-test.

AW: Analysis by Aspin-Welch t-test.

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

Appendix 26-1-1. Hematological findings of female rats at the end of the administration period

Control (vehicle: corn oil)

Female No.	RBC 10000/ μ L	HGB g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelet 10000/ μ L	PT sec.	APTT sec.	WBC 100/ μ L	Neutrophil %	Eosinophil %	Basophil %	Monocyte %	Lymphocyte %	Reticulocyte %
F01001	647	11.7	35.2	54.4	18.1	33.2	112.3	13.4	13.7	73.4	29.7	1.0	0.0	4.0	65.3	7.92
F01005	676	13.0	39.9	59.0	19.2	32.6	91.4	12.9	12.0	83.6	25.9	1.0	0.0	3.6	69.5	6.80
F01006	576	11.3	34.0	59.0	19.6	33.2	113.1	13.4	15.6	108.5	31.3	0.8	0.0	3.8	64.1	7.90
F01007	648	12.8	39.2	60.5	19.8	32.7	139.1	13.7	16.7	73.0	33.0	1.0	0.0	5.6	60.4	8.26
F01012	639	13.1	40.8	63.8	20.5	32.1	110.1	13.8	15.7	85.7	33.3	0.7	0.0	0.9	65.1	10.68
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	637	12.4	37.8	59.3	19.4	32.8	113.2	13.4	14.7	84.8	30.6	0.9	0.0	3.6	64.9	8.31
S.D.	37	0.8	3.0	3.4	0.9	0.5	17.0	0.4	1.9	14.4	3.0	0.1	0.0	1.7	3.2	1.43

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

Appendix 26-1-2. Hematological findings of female rats at the end of the administration period

CPN 30 mg/kg

Female No.	RBC 10000/ μ L	HGB g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelet 10000/ μ L	PT sec.	APTT sec.	WBC 100/ μ L	Neutrophil %	Eosinophil %	Basophil %	Monocyte %	Lymphocyte %	Reticulocyte %
F02013	681	13.5	40.7	59.8	19.8	33.2	97.0	13.1	15.8	110.2	22.3	1.1	0.0	4.1	72.5	7.13
F02016	550	10.6	33.6	61.1	19.3	31.5	119.7	13.0	15.7	50.3	26.2	0.4	0.0	1.6	71.8	9.86
F02018	651	12.6	38.0	58.4	19.4	33.2	117.1	12.6	14.5	120.3	42.9	0.9	0.0	2.7	53.5	6.47
F02020	594	12.2	37.9	63.8	20.5	32.2	94.1	13.6	16.0	62.3	36.4	0.5	0.0	3.4	59.7	8.84
F02022	625	12.6	38.3	61.3	20.2	32.9	107.1	12.2	14.3	123.9	32.3	0.9	0.0	3.4	63.4	8.10
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	620	12.3	37.7	60.9	19.8	32.6	107.0	12.9	15.3	93.4	32.0	0.8	0.0	3.0	64.2	8.08
S.D.	51	1.1	2.6	2.0	0.5	0.7	11.5	0.5	0.8	34.5	8.2	0.3	0.0	0.9	8.1	1.35
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN

NS: Not significantly different from the control group.

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

DU: Analysis by Dunnett's test.

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

Appendix 26-1-3. Hematological findings of female rats at the end of the administration period

CPN 100 mg/kg

Female No.	RBC 10000/ μ L	HGB g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelet 10000/ μ L	PT sec.	APTT sec.	WBC 100/ μ L	Neutrophil %	Eosinophil %	Basophil %	Monocyte %	Lymphocyte %	Reticulocyte %
F03029	604	11.8	35.6	58.9	19.5	33.1	120.8	12.9	13.9	86.5	25.5	0.2	0.0	2.7	71.6	8.65
F03031	601	12.2	37.1	61.7	20.3	32.9	104.4	13.0	16.4	65.8	27.7	1.2	0.2	4.9	66.0	8.13
F03033	600	12.2	37.2	62.0	20.3	32.8	104.1	12.5	14.5	97.7	35.3	0.5	0.0	3.6	60.6	7.37
F03035	647	12.4	38.3	59.2	19.2	32.4	132.0	12.6	13.8	94.0	33.1	0.9	0.0	4.7	61.3	6.29
F03036	648	12.8	39.3	60.6	19.8	32.6	140.8	13.6	13.3	82.1	47.3	0.6	0.0	4.0	48.1	8.87
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	620	12.3	37.5	60.5	19.8	32.8	120.4	12.9	14.4	85.2	33.8	0.7	0.0	4.0	61.5	7.86
S.D.	25	0.4	1.4	1.4	0.5	0.3	16.4	0.4	1.2	12.5	8.5	0.4	0.1	0.9	8.7	1.05
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN

NS: Not significantly different from the control group.

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

DU: Analysis by Dunnett's test.

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

Appendix 26-1-4. Hematological findings of female rats at the end of the administration period

CPN 300 mg/kg

Female No.	RBC 10000/ μ L	HGB g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelet 10000/ μ L	PT sec.	APTT sec.	WBC 100/ μ L	Neutrophil %	Eosinophil %	Basophil %	Monocyte %	Lymphocyte %	Reticulocyte %
F04039	668	12.8	38.2	57.2	19.2	33.5	135.3	13.4	14.7	103.5	18.6	0.3	0.0	5.2	75.9	6.43
F04040	735	13.1	38.9	52.9	17.8	33.7	116.5	13.4	16.2	58.9	13.4	0.5	0.2	6.8	79.1	6.00
F04041	667	12.8	39.2	58.8	19.2	32.7	114.1	12.6	15.8	55.1	25.8	0.5	0.0	6.9	66.8	8.16
F04045	606	11.4	34.7	57.3	18.8	32.9	164.7	12.7	15.2	53.5	24.8	0.6	0.0	4.5	70.1	10.93
F04048	639	12.6	38.3	59.9	19.7	32.9	131.1	13.0	15.8	62.9	27.8	1.0	0.0	5.4	65.8	11.30
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	663	12.5	37.9	57.2	18.9	33.1	132.3	13.0	15.5	66.8	22.1	0.6	0.0	5.8	71.5	8.56
S.D.	48	0.7	1.8	2.7	0.7	0.4	20.3	0.4	0.6	20.8	5.9	0.3	0.1	1.1	5.8	2.47
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	*	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN

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

NS: Not significantly different from the control group.

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

DU: Analysis by Dunnett's test.

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

Appendix 26-2-1. Hematological findings of female rats at the end of the administration period, satellite group

Control (vehicle: corn oil)

Female No.	RBC 10000/ μ L	HGB g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelet 10000/ μ L	PT sec.	APTT sec.	WBC 100/ μ L	Neutrophil %	Eosinophil %	Basophil %	Monocyte %	Lymphocyte %	Reticulocyte %
F05049	636	12.1	35.3	55.5	19.0	34.3	82.0	12.1	11.7 §	33.4	14.1	3.3	0.0	3.6	79.0	2.98
F05050	683	12.8	38.7	56.7	18.7	33.1	87.9	12.3	14.7	38.1	17.3	1.8	0.0	1.6	79.3	4.17
F05051	677	13.0	38.7	57.2	19.2	33.6	75.4	12.6	13.6	43.4	17.1	1.8	0.0	3.2	77.9	3.25
F05052	669	13.6	40.1	59.9	20.3	33.9	90.6	12.2	15.1	54.0	14.0	1.7	0.0	2.8	81.5	3.80
F05053	717	12.9	38.7	54.0	18.0	33.3	89.5	12.1	13.9	44.3	18.2	1.4	0.0	2.5	77.9	2.99
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	676	12.9	38.3	56.7	19.0	33.6	85.1	12.3	13.8	42.6	16.1	2.0	0.0	2.7	79.1	3.44
S.D.	29	0.5	1.8	2.2	0.8	0.5	6.3	0.2	1.3	7.7	2.0	0.7	0.0	0.8	1.5	0.53

§: Remeasurement (the sharp variation of the light scattering was not detected in the reaction in the first measurement.)

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

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

CPN 300 mg/kg

Female No.	RBC 10000/ μ L	HGB g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelet 10000/ μ L	PT sec.	APTT sec.	WBC 100/ μ L	Neutrophil %	Eosinophil %	Basophil %	Monocyte %	Lymphocyte %	Reticulocyte %
F06056	697 a	12.9 a	38.0 a	54.5 a	18.5 a	33.9 a	84.8 a	12.3 a	13.1 a	49.7 a	19.0 a	0.8 a	0.2 a	5.8 a	74.2 a	2.69 a
F06057	740	13.1	38.6	52.2	17.7	33.9	98.2	11.8	15.6	50.2	9.1	1.6	0.0	3.2	86.1	2.75
F06058	669	13.0	38.5	57.5	19.4	33.8	81.3	11.9	13.4	58.1	15.0	1.0	0.0	2.8	81.2	3.24
F06059	812	14.5	41.8	51.5	17.9	34.7	115.9	12.5	15.5	49.8	14.9	1.2	0.0	3.2	80.7	2.69
F06060	684	13.4	38.8	56.7	19.6	34.5	87.2	11.9	15.4	25.2	34.5	1.6	0.0	3.2	60.7	3.94
Number of females	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
Mean	726	13.5	39.4	54.5	18.7	34.2	95.7	12.0	15.0	45.8	18.4	1.4	0.0	3.1	77.2	3.16
S.D.	65	0.7	1.6	3.1	1.0	0.4	15.2	0.3	1.1	14.3	11.1	0.3	0.0	0.2	11.3	0.58
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	AW	TT	TT	TT	AW	TT

NS: Not significantly different from the control group.

TT: Analysis by Student's t-test.

AW: Analysis by Aspin-Welch t-test.

a, Excluded from data analysis (anesthetic death).

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

Appendix 26-3-1. Hematological findings of female rats at the end of the recovery period

Control (vehicle: corn oil)

Female No.	RBC 10000/ μ L	HGB g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelet 10000/ μ L	PT sec.	APTT sec.	WBC 100/ μ L	Neutrophil %	Eosinophil %	Basophil %	Monocyte %	Lymphocyte %	Reticulocyte %
F05054	840	14.9	44.3	52.7	17.7	33.6	91.2	11.0	11.4	44.9	12.7	2.0	0.0	2.4	82.9	3.42
F05055	735	13.4	40.6	55.2	18.2	33.0	95.7	12.2	16.9	76.6	20.6	1.7	0.0	4.3	73.4	3.50
F05056	718	13.6	40.4	56.3	18.9	33.7	83.5	11.4	15.0	41.0	17.3	2.9	0.0	3.7	76.1	3.17
F05057	755	14.3	42.1	55.8	18.9	34.0	71.3	12.6	14.8	45.2	19.9	1.1	0.0	3.8	75.2	2.81
F05058	790	13.9	41.5	52.5	17.6	33.5	109.4	11.6	13.7	30.3	16.2	3.6	0.0	2.6	77.6	2.43
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	768	14.0	41.8	54.5	18.3	33.6	90.2	11.8	14.4	47.6	17.3	2.3	0.0	3.4	77.0	3.07
S.D.	49	0.6	1.6	1.8	0.6	0.4	14.2	0.6	2.0	17.3	3.2	1.0	0.0	0.8	3.6	0.45

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

Appendix 26-3-2. Hematological findings of female rats at the end of the recovery period

CPN 300 mg/kg

Female No.	RBC 10000/ μ L	HGB g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelet 10000/ μ L	PT sec.	APTT sec.	WBC 100/ μ L	Neutrophil %	Eosinophil %	Basophil %	Monocyte %	Lymphocyte %	Reticulocyte %
F06061	754	13.5	40.2	53.3	17.9	33.6	88.9	11.7	12.6	47.7	23.4	1.0	0.0	3.1	72.5	3.58
F06062	747	13.8	40.1	53.7	18.5	34.4	92.9	12.6	16.0	36.8	15.8	1.1	0.0	3.8	79.3	2.96
F06063	762	13.6	40.1	52.6	17.8	33.9	96.8	11.5	16.6	49.9	9.8	2.2	0.0	3.4	84.6	2.61
F06064	748	13.1	39.1	52.3	17.5	33.5	95.7	12.1	14.6	59.5	30.4	2.0	0.2	3.5	63.9	3.14
F06065	697	13.0	39.3	56.4	18.7	33.1	88.2	11.6	16.7	39.3	23.6	0.8	0.0	3.3	72.3	2.97
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	742	13.4	39.8	53.7	18.1	33.7	92.5	11.9	15.3	46.6	20.6	1.4	0.0	3.4	74.5	3.05
S.D.	26	0.3	0.5	1.6	0.5	0.5	3.9	0.5	1.7	9.1	7.9	0.6	0.1	0.3	7.8	0.35
Significance	NS	NS	*	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	TT	TT	TT	TT	TT	TT	AW	TT	TT	TT	TT	TT	TT	AW	TT	TT

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

NS: Not significantly different from the control group.

TT: Analysis by Student's t-test.

AW: Analysis by Aspin-Welch t-test.

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

Appendix 27-1-1. Biochemical findings of male rats at the end of the administration period

Control (vehicle: corn oil)

Male No.	Total protein g/dL	Albumin g/dL	A/G	Glucose mg/dL	Total cholesterol mg/dL	Triglyceride mg/dL	Phospholipid mg/dL	AST U/L	ALT U/L	γ-GTP U/L	LDH U/L	Bile acid μmol/L	BUN mg/dL	Creatinine mg/dL	Total bilirubin mg/dL	ALP U/L
M01001	5.1	3.5	2.19	132	31	32	62	66	28	0	98	8.7	14.2	0.31	0.04	351
M01002	5.4	3.5	1.84	125	56	39	88	54	32	0	230	46.7	12.1	0.32	0.06	454
M01003	5.3	3.5	1.94	155	59	93	99	42	25	0	133	9.8	10.4	0.24	0.06	591
M01004	5.6	3.5	1.67	116	52	45	86	51	23	0	65	8.4	10.4	0.27	0.05	482
M01005	5.3	3.5	1.94	128	59	41	93	60	27	0	46	4.8	13.5	0.28	0.07	505
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	5.3	3.5	1.92	131	51	50	86	55	27	0	114	15.7	12.1	0.28	0.06	477
S.D.	0.2	0.0	0.19	15	12	24	14	9	3	0	73	17.4	1.7	0.03	0.01	87

Control (vehicle: corn oil)

Male No.	Inorganic				
	phosphorus mg/dL	Ca mg/dL	Na mEq/L	K mEq/L	Cl mEq/L
M01001	5.5	9.0	143.9	3.69	111.2
M01002	5.7	9.2	144.7	3.67	111.0
M01003	5.7	9.3	144.5	3.82	109.6
M01004	5.8	9.4	145.1	3.70	109.3
M01005	5.8	9.4	144.4	3.69	110.8
Number of males	5	5	5	5	5
Mean	5.7	9.3	144.5	3.71	110.4
S.D.	0.1	0.2	0.4	0.06	0.9

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

Appendix 27-1-2. Biochemical findings of male rats at the end of the administration period

CPN 30 mg/kg

Male No.	Total protein g/dL	Albumin g/dL	A/G	Glucose mg/dL	Total cholesterol mg/dL	Triglyceride mg/dL	Phospholipid mg/dL	AST U/L	ALT U/L	γ-GTP U/L	LDH U/L	Bile acid μmol/L	BUN mg/dL	Creatinine mg/dL	Total bilirubin mg/dL	ALP U/L
M02013	5.7	3.7	1.85	150	50	46	84	54	28	0	103	7.5	11.1	0.23	0.07	624
M02014	5.8	3.7	1.76	138	61	40	98	54	30	0	56	7.4	12.6	0.30	0.07	406
M02015	5.5	3.5	1.75	113	47	22	77	50	23	0	191	23.4	10.7	0.24	0.06	427
M02016	5.2	3.4	1.89	137	60	35	87	54	27	0	102	13.2	11.5	0.28	0.07	591
M02017	5.7	3.7	1.85	126	55	40	92	47	22	0	35	20.7	13.4	0.25	0.07	479
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	5.6	3.6	1.82	133	55	37	88	52	26	0	97	14.4	11.9	0.26	0.07	505
S.D.	0.2	0.1	0.06	14	6	9	8	3	3	0	60	7.4	1.1	0.03	0.00	98
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN

NS: Not significantly different from the control group.

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

KW: Analysis by Kruskal-Wallis' test (one-way layout).

CPN 30 mg/kg

Male No.	Inorganic				
	phosphorus mg/dL	Ca mg/dL	Na mEq/L	K mEq/L	Cl mEq/L
M02013	5.2	9.4	143.8	3.63	109.6
M02014	5.4	9.4	142.9	3.85	108.9
M02015	5.5	9.0	146.1	3.82	111.5
M02016	5.7	8.9	144.4	3.72	111.5
M02017	5.6	9.6	144.4	3.93	110.7
Number of males	5	5	5	5	5
Mean	5.5	9.3	144.3	3.79	110.4
S.D.	0.2	0.3	1.2	0.12	1.2
Significance	NS	NS	NS	NS	NS
Statistical method	KW	AN	AN	AN	AN

NS: Not significantly different from the control group.

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

KW: Analysis by Kruskal-Wallis' test (one-way layout).

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

Appendix 27-1-3. Biochemical findings of male rats at the end of the administration period

CPN 100 mg/kg

Male No.	Total protein g/dL	Albumin g/dL	A/G	Glucose mg/dL	Total cholesterol mg/dL	Triglyceride mg/dL	Phospholipid mg/dL	AST U/L	ALT U/L	γ-GTP U/L	LDH U/L	Bile acid μmol/L	BUN mg/dL	Creatinine mg/dL	Total bilirubin mg/dL	ALP U/L
M03025	5.3	3.4	1.79	144	54	26	83	50	27	0	133	10.7	14.9	0.30	0.06	607
M03026	5.7	3.6	1.71	132	61	38	94	47	25	0	83	13.3	12.3	0.26	0.06	453
M03027	4.9	3.2	1.88	125	34	19	57	57	27	0	42	6.4	13.0	0.26	0.04	357
M03028	5.6	3.6	1.80	136	65	55	101	50	22	0	136	10.0	14.4	0.27	0.06	590
M03029	5.9	3.8	1.81	123	62	66	99	52	24	0	66	18.1	13.5	0.22	0.05	597
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	5.5	3.5	1.80	132	55	41	87	51	25	0	92	11.7	13.6	0.26	0.05	521
S.D.	0.4	0.2	0.06	9	13	20	18	4	2	0	41	4.3	1.0	0.03	0.01	111
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN

NS: Not significantly different from the control group.

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

KW: Analysis by Kruskal-Wallis' test (one-way layout).

CPN 100 mg/kg

Male No.	Inorganic phosphorus mg/dL	Ca mg/dL	Na mEq/L	K mEq/L	Cl mEq/L
M03025	4.9	9.1	144.3	3.43	110.6
M03026	5.2	9.2	144.2	3.86	111.0
M03027	6.2	8.3	144.3	4.12	112.9
M03028	5.8	9.5	145.6	3.94	113.0
M03029	6.0	10.0	146.4	3.68	111.1
Number of males	5	5	5	5	5
Mean	5.6	9.2	145.0	3.81	111.7
S.D.	0.5	0.6	1.0	0.26	1.1
Significance	NS	NS	NS	NS	NS
Statistical method	KW	AN	AN	AN	AN

NS: Not significantly different from the control group.

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

KW: Analysis by Kruskal-Wallis' test (one-way layout).

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

Appendix 27-1-4. Biochemical findings of male rats at the end of the administration period

CPN 300 mg/kg

Male No.	Total protein g/dL	Albumin g/dL	A/G	Glucose mg/dL	Total cholesterol mg/dL	Triglyceride mg/dL	Phospholipid mg/dL	AST U/L	ALT U/L	γ-GTP U/L	LDH U/L	Bile acid μmol/L	BUN mg/dL	Creatinine mg/dL	Total bilirubin mg/dL	ALP U/L
M04037	5.8	3.6	1.64	133	69	35	100	43	26	0	191	16.4	14.2	0.26	0.06	399
M04038	5.7	3.7	1.85	141	63	37	100	68	37	0	106	34.0	14.1	0.28	0.07	307
M04039	5.3	3.6	2.12	135	50	18	76	51	24	0	47	11.0	12.4	0.22	0.05	465
M04040	5.9	3.8	1.81	125	51	25	80	49	25	0	57	23.3	10.8	0.20	0.08	454
M04041	5.6	3.7	1.95	132	61	10	87	60	26	0	63	6.5	14.7	0.33	0.06	375
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	5.7	3.7	1.87	133	59	25	89	54	28	0	93	18.2	13.2	0.26	0.06	400
S.D.	0.2	0.1	0.18	6	8	11	11	10	5	0	59	10.8	1.6	0.05	0.01	64
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN	AN

NS: Not significantly different from the control group.

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

KW: Analysis by Kruskal-Wallis' test (one-way layout).

CPN 300 mg/kg

Male No.	Inorganic phosphorus mg/dL	Ca mg/dL	Na mEq/L	K mEq/L	Cl mEq/L
M04037	4.9	9.9	144.0	3.61	109.7
M04038	5.0	9.1	145.1	3.52	110.3
M04039	5.7	9.2	144.3	3.85	111.9
M04040	6.0	9.3	145.6	3.75	109.1
M04041	5.5	8.8	143.1	3.53	109.2
Number of males	5	5	5	5	5
Mean	5.4	9.3	144.4	3.65	110.0
S.D.	0.5	0.4	1.0	0.14	1.1
Significance	NS	NS	NS	NS	NS
Statistical method	KW	AN	AN	AN	AN

NS: Not significantly different from the control group.

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

KW: Analysis by Kruskal-Wallis' test (one-way layout).

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

Appendix 27-2-1. Biochemical findings of male rats at the end of the recovery period

Control (vehicle: corn oil)

Male No.	Total protein g/dL	Albumin g/dL	A/G	Glucose mg/dL	Total cholesterol mg/dL	Triglyceride mg/dL	Phospholipid mg/dL	AST U/L	ALT U/L	γ -GTP U/L	LDH U/L	Bile acid μ mol/L	BUN mg/dL	Creatinine mg/dL	Total bilirubin mg/dL	ALP U/L
M01008	5.4	3.6	2.00	138	64	35	88	55	23	0	67	10.0	13.6	0.36	0.06	434
M01009	6.1	3.9	1.77	154	89	53	128	56	25	0	72	6.5	14.5	0.28	0.06	370
M01010	5.6	3.7	1.95	132	61	28	88	57	30	0	107	10.7	13.6	0.32	0.05	334
M01011	5.9	3.9	1.95	144	70	53	105	58	21	0	63	9.8	14.4	0.32	0.06	296
M01012	5.7	3.6	1.71	160	68	56	103	93	42	0	248	11.3	15.7	0.27	0.06	491
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	5.7	3.7	1.88	146	70	45	102	64	28	0	111	9.7	14.4	0.31	0.06	385
S.D.	0.3	0.2	0.13	11	11	13	16	16	8	0	78	1.9	0.9	0.04	0.00	78

Control (vehicle: corn oil)

Male No.	Inorganic phosphorus mg/dL	Ca mg/dL	Na mEq/L	K mEq/L	Cl mEq/L
M01008	5.3	9.0	143.3	3.90	111.5
M01009	5.4	10.1	144.2	3.61	112.5
M01010	6.4	9.4	144.9	3.97	112.7
M01011	5.6	9.7	142.9	4.01	109.5
M01012	6.0	9.6	145.5	3.74	111.7
Number of males	5	5	5	5	5
Mean	5.7	9.6	144.2	3.85	111.6
S.D.	0.5	0.4	1.1	0.17	1.3

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

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

CPN 300 mg/kg

Male No.	Total protein g/dL	Albumin g/dL	A/G	Glucose mg/dL	Total cholesterol mg/dL	Triglyceride mg/dL	Phospholipid mg/dL	AST U/L	ALT U/L	γ-GTP U/L	LDH U/L	Bile acid μmol/L	BUN mg/dL	Creatinine mg/dL	Total bilirubin mg/dL	ALP U/L
M04044	5.5	3.5	1.75	154	41	66	71	67	29	0	110	15.9	14.1	0.31	0.06	335
M04045	6.1	3.6	1.44	148	89	40	113	75	38	0	391	14.5	17.0	0.31	0.08	515
M04046	5.9	3.8	1.81	131	95	29	113	49	25	0	40	15.8	12.4	0.32	0.07	447
M04047	5.5	3.5	1.75	128	56	52	84	62	35	0	62	12.5	12.7	0.24	0.04	411
M04048	5.5	3.6	1.89	142	75	51	106	51	34	0	83	5.4	13.4	0.25	0.05	336
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	5.7	3.6	1.73	141	71	48	97	61	32	0	137	12.8	13.9	0.29	0.06	409
S.D.	0.3	0.1	0.17	11	23	14	19	11	5	0	144	4.4	1.8	0.04	0.02	77
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT

NS: Not significantly different from the control group.

TT: Analysis by Student's t-test.

AW: Analysis by Aspin-Welch t-test.

CPN 300 mg/kg

Male No.	Inorganic phosphorus mg/dL	Ca mg/dL	Na mEq/L	K mEq/L	Cl mEq/L
M04044	7.0	9.3	143.8	3.91	109.2
M04045	6.5	9.9	144.3	4.30	112.3
M04046	6.2	9.7	144.3	4.03	109.8
M04047	6.1	9.4	144.8	3.71	110.0
M04048	5.5	9.8	144.5	3.85	111.3
Number of males	5	5	5	5	5
Mean	6.3	9.6	144.3	3.96	110.5
S.D.	0.6	0.3	0.4	0.22	1.3
Significance	NS	NS	NS	NS	NS
Statistical method	TT	TT	TT	TT	TT

NS: Not significantly different from the control group.

TT: Analysis by Student's t-test.

AW: Analysis by Aspin-Welch t-test.

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

Appendix 28-1-1. Biochemical findings of female rats at the end of the administration period

Control (vehicle: corn oil)

Female No.	Total protein g/dL	Albumin g/dL	A/G	Glucose mg/dL	Total cholesterol mg/dL	Triglyceride mg/dL	Phospholipid mg/dL	AST U/L	ALT U/L	γ-GTP U/L	LDH U/L	Bile acid μmol/L	BUN mg/dL	Creatinine mg/dL	Total bilirubin mg/dL	ALP U/L
F01001	5.2	3.7	2.47	120	44	25	82	167	43	0	77	9.9	9.8	0.29	0.07	212
F01005	5.7	3.9	2.17	114	54	23	99	81	33	0	191	63.3	12.8	0.28	0.07	239
F01006	5.6	3.9	2.29	124	59	29	108	108	38	0	205	6.4	13.3	0.24	0.06	236
F01007	5.6	3.7	1.95	102	44	28	85	94	45	0	45	12.9	13.5	0.32	0.06	390
F01012	5.8	4.0	2.22	107	46	12	95	86	51	0	49	14.4	16.8	0.38	0.08	380
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	5.6	3.8	2.22	113	49	23	94	107	42	0	113	21.4	13.2	0.30	0.07	291
S.D.	0.2	0.1	0.19	9	7	7	11	35	7	0	78	23.6	2.5	0.05	0.01	86

Control (vehicle: corn oil)

Female No.	Inorganic				
	phosphorus mg/dL	Ca mg/dL	Na mEq/L	K mEq/L	Cl mEq/L
F01001	6.9	9.4	142.3	3.62	112.6
F01005	8.5	10.1	144.0	3.65	109.8
F01006	6.2	9.5	142.3	3.17	109.7
F01007	6.0	9.4	140.6	4.11	109.0
F01012	5.1	9.6	143.1	3.82	111.3
Number of females	5	5	5	5	5
Mean	6.5	9.6	142.5	3.67	110.5
S.D.	1.3	0.3	1.3	0.34	1.5

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

Appendix 28-1-2. Biochemical findings of female rats at the end of the administration period

CPN 30 mg/kg

Female No.	Total protein g/dL	Albumin g/dL	A/G	Glucose mg/dL	Total cholesterol mg/dL	Triglyceride mg/dL	Phospholipid mg/dL	AST U/L	ALT U/L	γ-GTP U/L	LDH U/L	Bile acid μmol/L	BUN mg/dL	Creatinine mg/dL	Total bilirubin mg/dL	ALP U/L
F02013	5.8	4.0	2.22	125	36	41	77	78	37	0	99	6.4	12.9	0.28	0.06	381
F02016	5.9	4.0	2.11	111	68	35	125	90	42	0	219	25.5	16.7	0.32	0.06	162
F02018	5.8	4.0	2.22	108	66	35	123	89	38	0	145	11.0	9.7	0.36	0.07	250
F02020	5.5	3.5	1.75	108	43	14	82	94	48	0	296	8.6	13.7	0.32	0.04	441
F02022	5.7	3.9	2.17	100	52	22	108	91	36	0	58	15.3	13.6	0.38	0.07	159
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	5.7	3.9	2.09	110	53	29	103	88	40	0	163	13.4	13.3	0.33	0.06	279
S.D.	0.2	0.2	0.20	9	14	11	23	6	5	0	95	7.5	2.5	0.04	0.01	128
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	KW	AN	AN	AN	KW	AN	AN	AN	AN	AN	AN	AN	AN

NS: Not significantly different from the control group.

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

KW: Analysis by Kruskal-Wallis' test (one-way layout).

CPN 30 mg/kg

Female No.	Inorganic phosphorus mg/dL	Ca mg/dL	Na mEq/L	K mEq/L	Cl mEq/L
F02013	7.0	9.9	140.5	3.78	110.2
F02016	7.5	10.2	143.9	3.44	111.4
F02018	5.5	9.3	143.1 §	3.68	110.6
F02020	6.6	9.7	144.6	3.64	113.7
F02022	6.8	9.5	143.4	3.67	111.0
Number of females	5	5	5	5	5
Mean	6.7	9.7	143.1	3.64	111.4
S.D.	0.7	0.3	1.6	0.12	1.4
Significance	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN

NS: Not significantly different from the control group.

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

KW: Analysis by Kruskal-Wallis' test (one-way layout).

§: Remeasurement (the difference between two measured values exceeded the permissible limit.)

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

Appendix 28-1-3. Biochemical findings of female rats at the end of the administration period

CPN 100 mg/kg

Female No.	Total protein g/dL	Albumin g/dL	A/G	Glucose mg/dL	Total cholesterol mg/dL	Triglyceride mg/dL	Phospholipid mg/dL	AST U/L	ALT U/L	γ-GTP U/L	LDH U/L	Bile acid μmol/L	BUN mg/dL	Creatinine mg/dL	Total bilirubin mg/dL	ALP U/L
F03029	5.6	3.9	2.29	123	70	49	126	193	69	1	175	28.2	13.5	0.29	0.06	251
F03031	5.9	4.0	2.11	120	53	30	96	93	42	0	45	9.9	16.3	0.32	0.06	145
F03033	5.6	3.9	2.29	121	45	19	87	118	44	0	104	23.9	14.9	0.49	0.07	278
F03035	5.7	3.7	1.85	120	51	20	98	81	35	0	142	3.9	15.4	0.38	0.05	179
F03036	5.8	4.0	2.22	124	55	22	101	72	35	0	186	15.8	11.7	0.33	0.07	294
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	5.7	3.9	2.15	122	55	28	102	111	45	0	130	16.3	14.4	0.36	0.06	229
S.D.	0.1	0.1	0.18	2	9	13	15	49	14	0	57	9.9	1.8	0.08	0.01	65
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	KW	AN	AN	AN	KW	AN	AN	AN	AN	AN	AN	AN	AN

NS: Not significantly different from the control group.

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

KW: Analysis by Kruskal-Wallis' test (one-way layout).

CPN 100 mg/kg

Female No.	Inorganic phosphorus mg/dL	Ca mg/dL	Na mEq/L	K mEq/L	Cl mEq/L
F03029	5.3	9.8	141.9	3.35	108.9
F03031	6.5	10.2	141.7	4.08	107.9
F03033	6.6	9.4	144.1	3.60	111.0
F03035	6.8	10.0	144.7	3.55	113.5
F03036	5.9	9.6	144.1	3.58	111.4
Number of females	5	5	5	5	5
Mean	6.2	9.8	143.3	3.63	110.5
S.D.	0.6	0.3	1.4	0.27	2.2
Significance	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN

NS: Not significantly different from the control group.

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

KW: Analysis by Kruskal-Wallis' test (one-way layout).

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

Appendix 28-1-4. Biochemical findings of female rats at the end of the administration period

CPN 300 mg/kg

Female No.	Total protein g/dL	Albumin g/dL	A/G	Glucose mg/dL	Total cholesterol mg/dL	Triglyceride mg/dL	Phospholipid mg/dL	AST U/L	ALT U/L	γ-GTP U/L	LDH U/L	Bile acid μmol/L	BUN mg/dL	Creatinine mg/dL	Total bilirubin mg/dL	ALP U/L
F04039	5.8	3.7	1.76	119	60	20	102	69	43	0	41	15.1	16.3	0.32	0.06	405
F04040	6.0	4.0	2.00	113	59	16	103	76	43	0	74	43.7	16.9	0.26	0.07	233
F04041	6.0	3.9	1.86	110	70	19	115	64	38	0	72	27.1	15.1	0.36	0.05	204
F04045	5.3	3.5	1.94	114	61	14	98	90	35	0	299	4.9	12.7	0.39	0.05	175
F04048	6.2	4.1	1.95	114	46	11	80	71	36	0	118	21.0	15.5	0.38	0.06	215
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	5.9	3.8	1.90	114	59	16	100	74	39	0	121	22.4	15.3	0.34	0.06	246
S.D.	0.3	0.2	0.09	3	9	4	13	10	4	0	103	14.5	1.6	0.05	0.01	91
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	KW	AN	AN	AN	KW	AN	AN	AN	AN	AN	AN	AN	AN

NS: Not significantly different from the control group.

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

KW: Analysis by Kruskal-Wallis' test (one-way layout).

CPN 300 mg/kg

Female No.	Inorganic				
	phosphorus mg/dL	Ca mg/dL	Na mEq/L	K mEq/L	Cl mEq/L
F04039	7.0	9.5	144.7	4.10	110.4
F04040	5.8	9.8	144.3	3.85	111.3
F04041	5.5	9.9	145.3	3.87	112.7
F04045	6.3	9.2	144.6	3.83	113.3
F04048	5.4	9.8	143.8	3.70	109.2
Number of females	5	5	5	5	5
Mean	6.0	9.6	144.5	3.87	111.4
S.D.	0.7	0.3	0.6	0.14	1.7
Significance	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN

NS: Not significantly different from the control group.

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

KW: Analysis by Kruskal-Wallis' test (one-way layout).

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

Appendix 28-2-1. Biochemical findings of female rats at the end of the administration period, satellite group

Control (vehicle: corn oil)

Female No.	Total protein g/dL	Albumin g/dL	A/G	Glucose mg/dL	Total cholesterol mg/dL	Triglyceride mg/dL	Phospholipid mg/dL	AST U/L	ALT U/L	γ-GTP U/L	LDH U/L	Bile acid μmol/L	BUN mg/dL	Creatinine mg/dL	Total bilirubin mg/dL	ALP U/L
F05049	5.0	3.4	2.13	89	38	7	69	62	19	0	70	3.7	21.6	0.36	0.06	215
F05050	6.3	4.3	2.15	125	70	8	124	82	28	0	56	37.0	16.9	0.46	0.08	355
F05051	5.4	3.6	2.00	102	48	6	84	67	21	0	116	8.6	18.9	0.42	0.06	328
F05052	6.1	4.3	2.39	108	53	13	107	59	26	0	47	13.1	18.9	0.43	0.06	152
F05053	5.6	3.9	2.29	98	55	7	99	86	27	0	32	9.2	22.3	0.44	0.07	379
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	5.7	3.9	2.19	104	53	8	97	71	24	0	64	14.3	19.7	0.42	0.07	286
S.D.	0.5	0.4	0.15	13	12	3	21	12	4	0	32	13.1	2.2	0.04	0.01	98

Control (vehicle: corn oil)

Female No.	Inorganic				
	phosphorus mg/dL	Ca mg/dL	Na mEq/L	K mEq/L	Cl mEq/L
F05049	5.4	9.1	143.4	3.42	113.1
F05050	4.9	9.0	143.0	4.00	111.6
F05051	5.4	9.0	144.6	3.26	113.9
F05052	4.5	9.4	144.9	3.65	112.1
F05053	5.0	9.3	142.9	3.66	112.5
Number of females	5	5	5	5	5
Mean	5.0	9.2	143.8	3.60	112.6
S.D.	0.4	0.2	0.9	0.28	0.9

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

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

CPN 300 mg/kg

Female No.	Total protein g/dL	Albumin g/dL	A/G	Glucose mg/dL	Total cholesterol mg/dL	Triglyceride mg/dL	Phospholipid mg/dL	AST U/L	ALT U/L	γ-GTP U/L	LDH U/L	Bile acid μmol/L	BUN mg/dL	Creatinine mg/dL	Total bilirubin mg/dL	ALP U/L
F06056	6.0 a	4.1 a	2.16 a	79 a	65 a	10 a	129 a	96 a	32 a	0 a	264 a	17.8 a	14.8 a	0.42 a	0.11 a	231 a
F06057	5.8	4.3	2.87	144	66	10	117	63	29	0	107	5.2	14.0	0.35	0.06	172
F06058	5.6	3.9	2.29	105	57	9	105	85	27	1	49	24.9	17.1	0.42	0.10	539
F06059	6.1	4.3	2.39	105	68	12	122	52	21	0	53	7.7	15.2	0.37	0.08	312
F06060	5.9	4.2	2.47	119	85	12	148	57	20	0	67	22.2	18.6	0.44	0.07	221
Number of females	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
Mean	5.9	4.2	2.51	118	69	11	123	64	24	0	69	15.0	16.2	0.40	0.08	311
S.D.	0.2	0.2	0.25	18	12	2	18	15	4	1	26	10.0	2.0	0.04	0.02	163
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	*	NS	NS	NS
Statistical method	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT

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

NS: Not significantly different from the control group.

TT: Analysis by Student's t-test.

a, Excluded from data analysis (anesthetic death).

CPN 300 mg/kg

Female No.	Inorganic				
	phosphorus mg/dL	Ca mg/dL	Na mEq/L	K mEq/L	Cl mEq/L
F06056	6.7 a	9.5 a	140.3 a	12.28 a,#	110.5 a
F06057	4.3	9.2	144.2	3.32	111.7
F06058	5.2	9.4	144.0	3.61	111.0
F06059	3.9	9.3	142.4	3.52	110.2
F06060	3.8	9.3	144.5	3.64	113.5
Number of females	4	4	4	4	4
Mean	4.3	9.3	143.8	3.52	111.6
S.D.	0.6	0.1	0.9	0.14	1.4
Significance	NS	NS	NS	NS	NS
Statistical method	TT	TT	TT	TT	TT

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

NS: Not significantly different from the control group.

TT: Analysis by Student's t-test.

a, Excluded from data analysis (anesthetic death).

#, The specimen was diluted to two folds with distilled water.

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

Appendix 28-3-1. Biochemical findings of female rats at the end of the recovery period

Control (vehicle: corn oil)

Female No.	Total protein g/dL	Albumin g/dL	A/G	Glucose mg/dL	Total cholesterol mg/dL	Triglyceride mg/dL	Phospholipid mg/dL	AST U/L	ALT U/L	γ-GTP U/L	LDH U/L	Bile acid μmol/L	BUN mg/dL	Creatinine mg/dL	Total bilirubin mg/dL	ALP U/L
F05054	6.2	4.2	2.10	185	113	35	164	91	41	1	105	23.8	13.4	0.43	0.05	142
F05055	5.6	3.7	1.95	118	58	26	107	72	25	0	62	5.9	12.4	0.32	0.07	246
F05056	6.2	4.2	2.10	155	74	23	133	117	50	0	158	16.7	13.8	0.36	0.08	249
F05057	5.6	3.5	1.67	118	74	12	123	62	25	0	40	15.3	13.7	0.34	0.07	220
F05058	5.9	4.0	2.11	134	71	15	114	59	19	0	83	8.2	11.6	0.33	0.07	169
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	5.9	3.9	1.99	142	78	22	128	80	32	0	90	14.0	13.0	0.36	0.07	205
S.D.	0.3	0.3	0.19	28	21	9	22	24	13	0	45	7.1	0.9	0.04	0.01	48

Control (vehicle: corn oil)

Female No.	Inorganic phosphorus mg/dL	Ca mg/dL	Na mEq/L	K mEq/L	Cl mEq/L
F05054	4.4	9.7	144.5	3.97	111.9
F05055	6.5	9.4	144.5	3.72	111.6
F05056	5.0	9.9	145.2	3.66	111.0
F05057	5.7	9.4	143.4	4.03	112.5
F05058	6.3	9.5	145.8	3.73	111.4
Number of females	5	5	5	5	5
Mean	5.6	9.6	144.7	3.82	111.7
S.D.	0.9	0.2	0.9	0.17	0.6

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

Appendix 28-3-2. Biochemical findings of female rats at the end of the recovery period

CPN 300 mg/kg

Female No.	Total protein g/dL	Albumin g/dL	A/G	Glucose mg/dL	Total cholesterol mg/dL	Triglyceride mg/dL	Phospholipid mg/dL	AST U/L	ALT U/L	γ -GTP U/L	LDH U/L	Bile acid μ mol/L	BUN mg/dL	Creatinine mg/dL	Total bilirubin mg/dL	ALP U/L
F06061	5.7	3.9	2.17	164	65	27	121	63	19	0	44	11.8	20.0	0.47	0.07	401
F06062	5.9	3.8	1.81	139	50	10	97	59	25	0	147	16.2	13.4	0.31	0.08	207
F06063	5.9	4.0	2.11	140	61	12	110	59	20	0	39	9.1	13.1	0.37	0.05	185
F06064	6.0	3.9	1.86	153	53	8	93	64	24	0	62	12.9	13.9	0.40	0.08	237
F06065	6.3	4.2	2.00	138	74	12	123	77	37	0	131	26.3	15.2	0.37	0.07	126
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	6.0	4.0	1.99	147	61	14	109	64	25	0	85	15.3	15.1	0.38	0.07	231
S.D.	0.2	0.2	0.16	11	10	8	14	7	7	0	51	6.7	2.8	0.06	0.01	103
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	TT	TT	TT	TT	TT	TT	TT	AW	TT	TT	TT	TT	TT	TT	TT	TT

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

NS: Not significantly different from the control group.

TT: Analysis by Student's t-test.

AW: Analysis by Aspin-Welch t-test.

CPN 300 mg/kg

Female No.	Inorganic				
	phosphorus mg/dL	Ca mg/dL	Na mEq/L	K mEq/L	Cl mEq/L
F06061	5.3	9.6	144.5	3.61	112.1
F06062	6.2	9.5	144.7	4.07	109.5
F06063	6.3	9.6	143.7	3.95	109.8
F06064	6.0	9.5	143.3	3.72	107.9
F06065	7.1	9.8	144.7	3.51	109.3
Number of females	5	5	5	5	5
Mean	6.2	9.6	144.2	3.77	109.7
S.D.	0.6	0.1	0.6	0.23	1.5
Significance	NS	NS	NS	NS	*
Statistical method	TT	TT	TT	TT	TT

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

NS: Not significantly different from the control group.

TT: Analysis by Student's t-test.

AW: Analysis by Aspin-Welch t-test.

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

Appendix 29-1-1. Organ weights of male rats at the end of the administration period

Control (vehicle: corn oil)

Male No.	Body weight (g)	Brain		Thymus		Heart		Liver		Kidney (R)		Kidney (L)		Kidneys		Spleen	
		(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
M01001	514.6	2094.8	4.071	312.6	0.607	1684.7	3.274	14875.7	28.907	1628.1	3.164	1625.9	3.160	3254.0	6.323	631.9	1.228
M01002	528.6	2136.9	4.043	339.1	0.642	1369.7	2.591	13928.3	26.349	1682.3	3.183	1714.8	3.244	3397.1	6.427	1000.3	1.892
M01003	497.1	1978.9	3.981	454.6	0.915	1316.9	2.649	14432.3	29.033	1511.6	3.041	1521.3	3.060	3032.9	6.101	876.2	1.763
M01004	514.8	2060.5	4.003	276.3	0.537	1486.3	2.887	13637.7	26.491	1693.4	3.289	1625.7	3.158	3319.1	6.447	804.5	1.563
M01005	490.9	1958.9	3.990	280.4	0.571	1276.1	2.600	12688.4	25.847	1511.3	3.079	1563.1	3.184	3074.4	6.263	698.4	1.423
M01006	421.8 a	1933.4 a	4.584 a	229.6 a	0.544 a	1306.7 a	3.098 a	14628.5 a	34.681 a	1741.3 a	4.128 a	1613.4 a	3.825 a	3354.7 a	7.953 a	1308.9 a	3.103 a
M01007	504.9	1943.0	3.848	308.3	0.611	1551.9	3.074	14503.8	28.726	1712.8	3.392	1734.7	3.436	3447.5	6.828	761.1	1.507
Number of males	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
Mean	508.5	2028.8	3.989	328.6	0.647	1447.6	2.846	14011.0	27.559	1623.3	3.191	1630.9	3.207	3254.2	6.398	795.4	1.563
S.D.	13.7	79.7	0.077	65.9	0.136	155.7	0.283	782.8	1.476	91.0	0.131	83.0	0.127	169.3	0.245	131.1	0.238

a, Excluded from data analysis (sacrificed during the administration period).

Appendix 29-1-1 (continued). Organ weights of male rats at the end of the administration period

Control (vehicle: corn oil)

Male No.	Testis (R)		Testis (L)		Testes		Epididymis (R)		Epididymis (L)		Epididymides	
	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
M01001	1475.9	2.868	1562.7	3.037	3038.6	5.905	623.8	1.212	625.6	1.216	1249.4	2.428
M01002	1900.8	3.596	1938.2	3.667	3839.0	7.263	720.7	1.363	691.5	1.308	1412.2	2.672
M01003	1599.6	3.218	1561.9	3.142	3161.5	6.360	665.3	1.338	615.4	1.238	1280.7	2.576
M01004	1702.7	3.307	1696.0	3.294	3398.7	6.602	610.9	1.187	602.1	1.170	1213.0	2.356
M01005	1762.3	3.590	1804.3	3.675	3566.6	7.265	626.7	1.277	573.4	1.168	1200.1	2.445
M01006	1724.0 a	4.087 a	1705.9 a	4.044 a	3429.9 a	8.132 a	535.3 a	1.269 a	556.3 a	1.319 a	1091.6 a	2.588 a
M01007	1899.9	3.763	1829.7	3.624	3729.6	7.387	698.0	1.382	692.4	1.371	1390.4	2.754
Number of males	6	6	6	6	6	6	6	6	6	6	6	6
Mean	1723.5	3.390	1732.1	3.407	3455.7	6.797	657.6	1.293	633.4	1.245	1291.0	2.539
S.D.	168.0	0.326	152.4	0.285	315.6	0.601	44.6	0.081	48.6	0.080	90.3	0.155

a, Excluded from data analysis (sacrificed during the administration period).

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

Appendix 29-1-1 (continued). Organ weights of male rats at the end of the administration period

Control (vehicle: corn oil)

Male No.	Body weight (g)	Prostate, ventral		Seminal vesicles		Thyroid gland		Adrenal gland (R)		Adrenal gland (L)		Adrenal glands	
		(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
M01001	514.6	608.1	1.182	1766.7	3.433	21.9	0.043	29.0	0.056	28.2	0.055	57.2	0.111
M01002	528.6	724.2	1.370	1850.1	3.500	25.2	0.048	23.9	0.045	25.5	0.048	49.4	0.093
M01003	497.1	328.1	0.660	1727.6	3.475	26.2	0.053	23.2	0.047	25.7	0.052	48.9	0.098
M01004	514.8	793.6	1.542	1894.4	3.680	27.0	0.052	28.3	0.055	31.4	0.061	59.7	0.116
M01005	490.9	498.7	1.016	1441.5	2.936	22.6	0.046	22.8	0.046	22.3	0.045	45.1	0.092
M01006	421.8 a	627.2 a	1.487 a	1637.7 a	3.883 a	17.7 a	0.042 a	32.8 a	0.078 a	30.4 a	0.072 a	63.2 a	0.150 a
M01007	504.9	530.0	1.050	1629.5	3.227	18.9	0.037	22.6	0.045	26.4	0.052	49.0	0.097
Number of males	6	6	6	6	6	6	6	6	6	6	6	6	6
Mean	508.5	580.5	1.137	1718.3	3.375	23.6	0.047	25.0	0.049	26.6	0.052	51.6	0.101
S.D.	13.7	167.2	0.307	164.5	0.259	3.1	0.006	2.9	0.005	3.0	0.006	5.6	0.010

a, Excluded from data analysis (sacrificed during the administration period).

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

Appendix 29-1-2. Organ weights of male rats at the end of the administration period

Male No.	Body	Brain		Thymus		Heart		Liver		Kidney (R)		Kidney (L)		Kidneys		Spleen	
	weight (g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
M02013	478.7	2109.9	4.408	257.8	0.539	1376.7	2.876	12875.9	26.898	1598.8	3.340	1568.5	3.277	3167.3	6.616	853.6	1.783
M02014	482.0	2120.9	4.400	279.5	0.580	1435.9	2.979	13548.3	28.109	1580.3	3.279	1525.6	3.165	3105.9	6.444	887.1	1.840
M02015	476.9	2095.0	4.393	180.4	0.378	1342.1	2.814	12269.0	25.727	1663.5	3.488	1603.4	3.362	3266.9	6.850	697.1	1.462
M02016	498.0	2089.3	4.195	312.1	0.627	1437.3	2.886	11454.3	23.001	1625.3	3.264	1618.9	3.251	3244.2	6.514	776.5	1.559
M02017	495.3	2069.4	4.178	230.2	0.465	1458.3	2.944	14461.6	29.198	1751.0	3.535	1853.4	3.742	3604.4	7.277	741.3	1.497
M02018	495.2	2036.6	4.113	287.4	0.580	1373.7	2.774	13215.8	26.688	1693.8	3.420	1677.9	3.388	3371.7	6.809	805.1	1.626
M02019	506.4	1975.1	3.900	295.0	0.583	1353.3	2.672	13292.7	26.249	1609.6	3.179	1573.1	3.106	3182.7	6.285	926.0	1.829
M02020	575.4	2127.9	3.698	312.5	0.543	1646.8	2.862	18502.5	32.156	1911.3	3.322	1845.4	3.207	3756.7	6.529	1433.5	2.491
M02021	423.5	1937.1	4.574	417.4	0.986	1339.4	3.163	10922.1	25.790	1353.5	3.196	1407.9	3.324	2761.4	6.520	719.1	1.698
M02022	520.6	2021.8	3.884	380.4	0.731	1533.0	2.945	15338.3	29.463	1699.0	3.264	1626.4	3.124	3325.4	6.388	815.3	1.566
M02023	492.4	2035.3	4.133	256.6	0.521	1437.0	2.918	13162.8	26.732	1640.1	3.331	1650.5	3.352	3290.6	6.683	661.1	1.343
M02024	548.8	2088.7	3.806	447.3	0.815	1700.8	3.099	14625.7	26.650	1777.9	3.240	1735.6	3.163	3513.5	6.402	921.6	1.679
Number of males	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
Mean	499.4	2058.9	4.140	304.7	0.612	1452.9	2.911	13639.1	27.222	1658.7	3.322	1640.6	3.288	3299.2	6.610	853.1	1.698
S.D.	37.9	59.3	0.274	77.1	0.163	118.1	0.133	1984.9	2.298	133.5	0.111	126.8	0.172	255.1	0.269	202.1	0.292
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DT	KW	DT	AN	AN	AN	AN	KW	AN	AN	DT	AN	DU	AN	DT	AN	AN

NS: Not significantly different from the control group.

DT: Analysis by Dunnett type mean rank test.

KW: Analysis by Kruskal-Wallis' test (one-way layout).

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

DU: Analysis by Dunnett's test.

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

Appendix 29-1-2 (continued). Organ weights of male rats at the end of the administration period

CPN 30 mg/kg

Male No.	Testis (R)		Testis (L)		Testes		Epididymis (R)		Epididymis (L)		Epididymides	
	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
M02013	1764.2	3.685	1722.3	3.598	3486.5	7.283	657.2	1.373	645.8	1.349	1303.0	2.722
M02014	1507.9	3.128	1505.0	3.122	3012.9	6.251	683.5	1.418	641.9	1.332	1325.4	2.750
M02015	1865.2	3.911	1814.1	3.804	3679.3	7.715	706.3	1.481	635.7	1.333	1342.0	2.814
M02016	1747.0	3.508	1795.7	3.606	3542.7	7.114	632.1	1.269	622.5	1.250	1254.6	2.519
M02017	1694.1	3.420	1703.4	3.439	3397.5	6.859	637.4	1.287	616.2	1.244	1253.6	2.531
M02018	1773.4	3.581	1761.5	3.557	3534.9	7.138	608.5	1.229	628.1	1.268	1236.6	2.497
M02019	1560.0	3.081	1601.0	3.162	3161.0	6.242	628.6	1.241	651.6	1.287	1280.2	2.528
M02020	1716.1	2.982	1690.0	2.937	3406.1	5.920	609.9	1.060	627.3	1.090	1237.2	2.150
M02021	1625.4	3.838	1654.1	3.906	3279.5	7.744	553.8	1.308	551.3	1.302	1105.1	2.609
M02022	1973.2	3.790	2052.6	3.943	4025.8	7.733	637.4	1.224	674.7	1.296	1312.1	2.520
M02023	1799.7	3.655	1857.8	3.773	3657.5	7.428	631.9	1.283	599.2	1.217	1231.1	2.500
M02024	2016.3	3.674	1955.7	3.564	3972.0	7.238	678.2	1.236	675.3	1.231	1353.5	2.466
Number of males	12	12	12	12	12	12	12	12	12	12	12	12
Mean	1753.5	3.521	1759.4	3.534	3513.0	7.055	638.7	1.284	630.8	1.267	1269.5	2.551
S.D.	151.2	0.308	150.4	0.319	298.1	0.621	40.0	0.107	33.5	0.070	67.1	0.170
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	DU	AN	DU	AN	DU	AN	AN	KW	KW	AN	AN

NS: Not significantly different from the control group.

DT: Analysis by Dunnett type mean rank test.

KW: Analysis by Kruskal-Wallis' test (one-way layout).

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

DU: Analysis by Dunnett's test.

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

Appendix 29-1-2 (continued). Organ weights of male rats at the end of the administration period

CPN 30 mg/kg

Male No.	Body weight (g)	Prostate, ventral		Seminal vesicles		Thyroid gland		Adrenal gland (R)		Adrenal gland (L)		Adrenal glands	
		(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
M02013	478.7	687.5	1.436	1660.0	3.468	18.7	0.039	26.6	0.056	27.3	0.057	53.9	0.113
M02014	482.0	688.7	1.429	1722.8	3.574	26.6	0.055	21.9	0.045	23.7	0.049	45.6	0.095
M02015	476.9	540.1	1.133	1815.9	3.808	23.6	0.049	24.4	0.051	27.2	0.057	51.6	0.108
M02016	498.0	563.0	1.131	1335.3	2.681	15.7	0.032	23.2	0.047	30.3	0.061	53.5	0.107
M02017	495.3	468.9	0.947	1774.3	3.582	27.5	0.056	28.7	0.058	31.8	0.064	60.5	0.122
M02018	495.2	563.1	1.137	1685.8	3.404	23.3	0.047	31.9	0.064	34.7	0.070	66.6	0.134
M02019	506.4	525.5	1.038	1615.2	3.190	20.3	0.040	21.8	0.043	22.2	0.044	44.0	0.087
M02020	575.4	329.3	0.572	1423.5	2.474	24.9	0.043	29.8	0.052	31.5	0.055	61.3	0.107
M02021	423.5	443.1	1.046	1093.1	2.581	15.8	0.037	23.1	0.055	26.9	0.064	50.0	0.118
M02022	520.6	594.7	1.142	1149.1	2.207	30.8	0.059	27.2	0.052	32.6	0.063	59.8	0.115
M02023	492.4	557.2	1.132	2158.5	4.384	26.0	0.053	32.9	0.067	35.7	0.073	68.6	0.139
M02024	548.8	673.2	1.227	1549.7	2.824	26.2	0.048	28.9	0.053	35.1	0.064	64.0	0.117
Number of males	12	12	12	12	12	12	12	12	12	12	12	12	12
Mean	499.4	552.9	1.114	1581.9	3.181	23.3	0.047	26.7	0.054	29.9	0.060	56.6	0.114
S.D.	37.9	105.8	0.224	297.8	0.638	4.7	0.008	3.8	0.007	4.5	0.008	8.0	0.015
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DT	AN	AN	AN	DU	AN	AN	AN	DU	AN	DU	AN	DU

NS: Not significantly different from the control group.

DT: Analysis by Dunnett type mean rank test.

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

DU: Analysis by Dunnett's test.

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

Appendix 29-1-3. Organ weights of male rats at the end of the administration period

CPN 100 mg/kg

Male No.	Body	Brain		Thymus		Heart		Liver		Kidney (R)		Kidney (L)		Kidneys		Spleen	
	weight (g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
M03025	515.2	2067.8	4.014	383.5	0.744	1532.2	2.974	14202.4	27.567	1646.1	3.195	1637.3	3.178	3283.4	6.373	947.6	1.839
M03026	484.4	2016.8	4.164	225.7	0.466	1324.1	2.733	14085.5	29.078	1663.7	3.435	1574.1	3.250	3237.8	6.684	901.0	1.860
M03027	422.9	2036.9	4.817	263.5	0.623	1319.7	3.121	9986.5	23.614	1573.1	3.720	1524.9	3.606	3098.0	7.326	812.6	1.921
M03028	504.5	2018.2	4.000	324.7	0.644	1578.9	3.130	13403.4	26.568	1582.6	3.137	1515.0	3.003	3097.6	6.140	789.6	1.565
M03029	536.6	2087.4	3.890	240.1	0.447	1433.8	2.672	18403.2	34.296	1886.5	3.516	1868.0	3.481	3754.5	6.997	897.1	1.672
M03030	508.6	1966.1	3.866	233.3	0.459	1518.4	2.985	15778.6	31.024	2010.2	3.952	2043.2	4.017	4053.4	7.970	903.5	1.776
M03031	526.8	1963.2	3.727	382.5	0.726	1419.0	2.694	14514.0	27.551	1705.9	3.238	1735.0	3.293	3440.9	6.532	803.1	1.524
M03032	548.1	1998.2	3.646	449.0	0.819	1406.4	2.566	14681.1	26.785	1709.7	3.119	1640.3	2.993	3350.0	6.112	885.8	1.616
M03033	485.6	2003.4	4.126	222.8	0.459	1397.0	2.877	14496.1	29.852	1793.7	3.694	1758.1	3.620	3551.8	7.314	719.1	1.481
M03034	483.1	2007.7	4.156	317.0	0.656	1483.8	3.071	13980.4	28.939	1537.0	3.182	1521.4	3.149	3058.4	6.331	888.1	1.838
M03035	458.6	2064.6	4.502	396.7	0.865	1363.4	2.973	12021.1	26.213	1477.9	3.223	1724.6	3.761	3202.5	6.983	782.9	1.707
M03036	470.0	1950.4	4.150	206.0	0.438	1504.5	3.201	12308.4	26.188	1753.4	3.731	1756.5	3.737	3509.9	7.468	534.0	1.136
Number of males	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
Mean	495.4	2015.1	4.088	303.7	0.612	1440.1	2.916	13988.4	28.140	1695.0	3.429	1691.5	3.424	3386.5	6.853	822.0	1.661
S.D.	35.3	43.4	0.323	83.0	0.156	83.8	0.207	2063.0	2.758	151.5	0.287	157.7	0.328	296.6	0.587	112.5	0.218
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DT	KW	DT	AN	AN	AN	AN	KW	AN	AN	DT	AN	DU	AN	DT	AN	AN

NS: Not significantly different from the control group.

DT: Analysis by Dunnett type mean rank test.

KW: Analysis by Kruskal-Wallis' test (one-way layout).

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

DU: Analysis by Dunnett's test.

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

Appendix 29-1-3 (continued). Organ weights of male rats at the end of the administration period

CPN 100 mg/kg

Male No.	Testis (R)		Testis (L)		Testes		Epididymis (R)		Epididymis (L)		Epididymides	
	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
M03025	1625.8	3.156	1666.9	3.235	3292.7	6.391	649.8	1.261	655.3	1.272	1305.1	2.533
M03026	1615.3	3.335	1617.5	3.339	3232.8	6.674	600.9	1.241	622.4	1.285	1223.3	2.525
M03027	1706.1	4.034	1673.1	3.956	3379.2	7.991	662.4	1.566	656.2	1.552	1318.6	3.118
M03028	1733.3	3.436	1658.7	3.288	3392.0	6.723	662.5	1.313	654.4	1.297	1316.9	2.610
M03029	1442.9	2.689	1427.8	2.661	2870.7	5.350	656.5	1.223	636.1	1.185	1292.6	2.409
M03030	1666.8	3.277	1674.2	3.292	3341.0	6.569	651.8	1.282	603.8	1.187	1255.6	2.469
M03031	1690.6	3.209	1642.6	3.118	3333.2	6.327	635.5	1.206	629.8	1.196	1265.3	2.402
M03032	1680.2	3.065	1674.7	3.055	3354.9	6.121	554.6	1.012	546.9	0.998	1101.5	2.010
M03033	1580.4	3.255	1689.3	3.479	3269.7	6.733	671.9	1.384	633.6	1.305	1305.5	2.688
M03034	1705.1	3.529	1582.7	3.276	3287.8	6.806	614.0	1.271	601.2	1.244	1215.2	2.515
M03035	1766.5	3.852	1720.2	3.751	3486.7	7.603	723.5	1.578	675.1	1.472	1398.6	3.050
M03036	1707.6	3.633	1700.7	3.619	3408.3	7.252	634.8	1.351	607.7	1.293	1242.5	2.644
Number of males	12	12	12	12	12	12	12	12	12	12	12	12
Mean	1660.1	3.373	1644.0	3.339	3304.1	6.712	643.2	1.307	626.9	1.274	1270.1	2.581
S.D.	85.9	0.360	77.3	0.338	152.8	0.688	41.5	0.154	34.2	0.140	73.0	0.291
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	DU	AN	DU	AN	DU	AN	AN	KW	KW	AN	AN

NS: Not significantly different from the control group.

DT: Analysis by Dunnett type mean rank test.

KW: Analysis by Kruskal-Wallis' test (one-way layout).

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

DU: Analysis by Dunnett's test.

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

Appendix 29-1-3 (continued). Organ weights of male rats at the end of the administration period

CPN 100 mg/kg

Male No.	Body weight (g)	Prostate, ventral		Seminal vesicles		Thyroid gland		Adrenal gland (R)		Adrenal gland (L)		Adrenal glands	
		(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
M03025	515.2	406.5	0.789	1621.5	3.147	25.1	0.049	27.5	0.053	29.2	0.057	56.7	0.110
M03026	484.4	678.2	1.400	1777.4	3.669	22.4	0.046	26.7	0.055	29.9	0.062	56.6	0.117
M03027	422.9	527.3	1.247	2102.5	4.972	22.5	0.053	25.0	0.059	27.0	0.064	52.0	0.123
M03028	504.5	715.9	1.419	1777.1	3.522	28.3	0.056	21.9	0.043	21.8	0.043	43.7	0.087
M03029	536.6	709.1	1.321	1666.9	3.106	22.7	0.042	32.7	0.061	32.5	0.061	65.2	0.122
M03030	508.6	531.4	1.045	1673.2	3.290	23.2	0.046	30.0	0.059	33.3	0.065	63.3	0.124
M03031	526.8	661.9	1.256	1667.1	3.165	21.9	0.042	22.6	0.043	26.4	0.050	49.0	0.093
M03032	548.1	669.7	1.222	1467.2	2.677	18.9	0.034	29.6	0.054	28.5	0.052	58.1	0.106
M03033	485.6	458.4	0.944	1937.0	3.989	21.6	0.044	24.1	0.050	24.5	0.050	48.6	0.100
M03034	483.1	882.7	1.827	1469.8	3.042	24.3	0.050	30.2	0.063	34.9	0.072	65.1	0.135
M03035	458.6	590.8	1.288	1652.2	3.603	17.4	0.038	24.9	0.054	25.2	0.055	50.1	0.109
M03036	470.0	631.7	1.344	1592.9	3.389	17.6	0.037	28.3	0.060	28.3	0.060	56.6	0.120
Number of males	12	12	12	12	12	12	12	12	12	12	12	12	12
Mean	495.4	622.0	1.259	1700.4	3.464	22.2	0.045	27.0	0.055	28.5	0.058	55.4	0.112
S.D.	35.3	128.9	0.261	180.9	0.585	3.1	0.007	3.3	0.007	3.8	0.008	6.9	0.014
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DT	AN	AN	AN	DU	AN	AN	AN	DU	AN	DU	AN	DU

NS: Not significantly different from the control group.

DT: Analysis by Dunnett type mean rank test.

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

DU: Analysis by Dunnett's test.

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

Appendix 29-1-4. Organ weights of male rats at the end of the administration period

CPN 300 mg/kg																	
Male No.	Body weight (g)	Brain		Thymus		Heart		Liver		Kidney (R)		Kidney (L)		Kidneys		Spleen	
		(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
M04037	457.8	2010.7	4.392	253.2	0.553	1342.2	2.932	13864.9	30.286	1671.1	3.650	1589.7	3.472	3260.8	7.123	688.3	1.503
M04038	452.4	1852.9	4.096	278.5	0.616	1341.3	2.965	12756.6	28.198	1595.8	3.527	1632.3	3.608	3228.1	7.135	716.9	1.585
M04039	436.8	2185.6	5.004	217.7	0.498	1318.0	3.017	12141.3	27.796	1681.0	3.848	1688.9	3.867	3369.9	7.715	630.0	1.442
M04040	468.8	2060.8	4.396	186.6	0.398	1662.9	3.547	12766.3	27.232	1946.0	4.151	1879.4	4.009	3825.4	8.160	830.2	1.771
M04041	438.1	1854.0	4.232	226.2	0.516	1356.7	3.097	12323.2	28.129	1580.1	3.607	1534.8	3.503	3114.9	7.110	685.3	1.564
M04042	465.8	2034.6	4.368	305.8	0.657	1313.4	2.820	12755.7	27.384	1755.9	3.770	1736.4	3.728	3492.3	7.497	550.1	1.181
M04043	422.1	1949.4	4.618	194.8	0.462	1292.3	3.062	11636.5	27.568	1475.2	3.495	1562.9	3.703	3038.1	7.198	834.1	1.976
Number of males	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7
Mean	448.8	1992.6	4.444	237.5	0.529	1375.3	3.063	12606.4	28.085	1672.2	3.721	1660.6	3.699	3332.8	7.420	705.0	1.575
S.D.	17.1	118.7	0.295	43.8	0.089	128.7	0.232	694.2	1.035	150.1	0.227	119.5	0.193	264.6	0.399	102.3	0.251
Significance	**	NS	*	NS	NS	NS	NS	NS	NS	NS	**	NS	**	NS	**	NS	NS
Statistical method	DT	KW	DT	AN	AN	AN	AN	KW	AN	AN	DT	AN	DU	AN	DT	AN	AN

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

NS: Not significantly different from the control group.

DT: Analysis by Dunnett type mean rank test.

KW: Analysis by Kruskal-Wallis' test (one-way layout).

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

DU: Analysis by Dunnett's test.

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

Appendix 29-1-4 (continued). Organ weights of male rats at the end of the administration period

CPN 300 mg/kg

Male No.	Testis (R)		Testis (L)		Testes		Epididymis (R)		Epididymis (L)		Epididymides	
	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
M04037	1769.4	3.865	1766.9	3.860	3536.3	7.725	618.0	1.350	633.0	1.383	1251.0	2.733
M04038	1801.3	3.982	1820.6	4.024	3621.9	8.006	700.6	1.549	633.7	1.401	1334.3	2.949
M04039	1744.3	3.993	1850.3	4.236	3594.6	8.229	693.3	1.587	678.8	1.554	1372.1	3.141
M04040	2046.9	4.366	2097.8	4.475	4144.7	8.841	734.8	1.567	751.6	1.603	1486.4	3.171
M04041	1486.9	3.394	1521.9	3.474	3008.8	6.868	557.1	1.272	534.9	1.221	1092.0	2.493
M04042	1638.4	3.517	1661.6	3.567	3300.0	7.085	574.5	1.233	527.3	1.132	1101.8	2.365
M04043	1759.0	4.167	1742.3	4.128	3501.3	8.295	672.8	1.594	660.3	1.564	1333.1	3.158
Number of males	7	7	7	7	7	7	7	7	7	7	7	7
Mean	1749.5	3.898	1780.2	3.966	3529.7	7.864	650.2	1.450	631.4	1.408	1281.5	2.859
S.D.	169.8	0.343	177.9	0.359	345.4	0.697	67.7	0.159	79.3	0.181	144.2	0.334
Significance	NS	*	NS	*	NS	*	NS	NS	NS	NS	NS	NS
Statistical method	AN	DU	AN	DU	AN	DU	AN	AN	KW	KW	AN	AN

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

NS: Not significantly different from the control group.

DT: Analysis by Dunnett type mean rank test.

KW: Analysis by Kruskal-Wallis' test (one-way layout).

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

DU: Analysis by Dunnett's test.

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

Appendix 29-1-4 (continued). Organ weights of male rats at the end of the administration period

CPN 300 mg/kg

Male No.	Body weight (g)	Prostate, ventral		Seminal vesicles		Thyroid gland		Adrenal gland (R)		Adrenal gland (L)		Adrenal glands	
		(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
M04037	457.8	552.9	1.208	1848.7	4.038	27.4	0.060	26.2	0.057	27.3	0.060	53.5	0.117
M04038	452.4	443.8	0.981	2039.7	4.509	24.5	0.054	29.5	0.065	31.5	0.070	61.0	0.135
M04039	436.8	535.4	1.226	1738.2	3.979	25.4	0.058	31.4	0.072	31.7	0.073	63.1	0.144
M04040	468.8	559.5	1.193	1813.5	3.868	18.8	0.040	29.7	0.063	34.8	0.074	64.5	0.138
M04041	438.1	486.9	1.111	1973.2	4.504	24.7	0.056	30.2	0.069	30.5	0.070	60.7	0.139
M04042	465.8	779.3	1.673	1554.6	3.337	25.1	0.054	28.2	0.061	31.0	0.067	59.2	0.127
M04043	422.1	555.8	1.317	1944.0	4.606	24.6	0.058	27.2	0.064	29.8	0.071	57.0	0.135
Number of males	7	7	7	7	7	7	7	7	7	7	7	7	7
Mean	448.8	559.1	1.244	1844.6	4.120	24.4	0.054	28.9	0.064	30.9	0.069	59.9	0.134
S.D.	17.1	106.1	0.216	163.8	0.454	2.6	0.007	1.8	0.005	2.3	0.005	3.7	0.009
Significance	**	NS	NS	NS	*	NS	NS	NS	**	NS	**	NS	**
Statistical method	DT	AN	AN	AN	DU	AN	AN	AN	DU	AN	DU	AN	DU

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

NS: Not significantly different from the control group.

DT: Analysis by Dunnett type mean rank test.

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

DU: Analysis by Dunnett's test.

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

Appendix 29-2-1. Organ weights of male rats at the end of the recovery period

Control (vehicle: corn oil)

Male No.	Body weight (g)	Brain		Thymus		Heart		Liver		Kidney (R)		Kidney (L)		Kidneys		Spleen	
		(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
M01008	490.5	2059.7	4.199	400.9	0.817	1401.6	2.857	12737.9	25.969	1665.6	3.396	1591.1	3.244	3256.7	6.640	827.7	1.687
M01009	501.9	2116.3	4.217	238.5	0.475	1543.0	3.074	14391.4	28.674	1604.6	3.197	1592.0	3.172	3196.6	6.369	734.4	1.463
M01010	519.4	2135.8	4.112	206.5	0.398	1379.9	2.657	13577.8	26.141	1659.8	3.196	1667.6	3.211	3327.4	6.406	715.9	1.378
M01011	546.9	1888.4	3.453	384.5	0.703	1622.0	2.966	14416.8	26.361	1801.7	3.294	1674.6	3.062	3476.3	6.356	655.2	1.198
M01012	513.9	2026.2	3.943	248.1	0.483	1400.1	2.724	13204.3	25.694	1681.5	3.272	1682.9	3.275	3364.4	6.547	859.2	1.672
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	514.5	2045.3	3.985	295.7	0.575	1469.3	2.856	13665.6	26.568	1682.6	3.271	1641.6	3.193	3324.3	6.464	758.5	1.480
S.D.	21.3	98.0	0.316	90.1	0.177	107.4	0.171	736.9	1.202	72.6	0.083	46.0	0.083	106.8	0.124	83.7	0.206

Appendix 29-2-1 (continued). Organ weights of male rats at the end of the recovery period

Control (vehicle: corn oil)

Male No.	Testis (R)		Testis (L)		Testes		Epididymis (R)		Epididymis (L)		Epididymides	
	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
M01008	1896.1	3.866	1928.4	3.931	3824.5	7.797	659.1	1.344	687.0	1.401	1346.1	2.744
M01009	1539.3	3.067	1506.1	3.001	3045.4	6.068	671.9	1.339	723.1	1.441	1395.0	2.779
M01010	2020.9	3.891	2007.4	3.865	4028.3	7.756	775.0	1.492	742.6	1.430	1517.6	2.922
M01011	1590.0	2.907	1588.9	2.905	3178.9	5.813	636.6	1.164	632.8	1.157	1269.4	2.321
M01012	1695.4	3.299	1571.0	3.057	3266.4	6.356	591.9	1.152	610.1	1.187	1202.0	2.339
Number of males	5	5	5	5	5	5	5	5	5	5	5	5
Mean	1748.3	3.406	1720.4	3.352	3468.7	6.758	666.9	1.298	679.1	1.323	1346.0	2.621
S.D.	204.8	0.453	229.8	0.502	431.2	0.950	67.7	0.142	56.9	0.139	120.9	0.274

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

Appendix 29-2-1 (continued). Organ weights of male rats at the end of the recovery period

Control (vehicle: corn oil)

Male No.	Body weight (g)	Prostate, ventral		Seminal vesicles		Thyroid gland		Adrenal gland (R)		Adrenal gland (L)		Adrenal glands	
		(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
M01008	490.5	464.4	0.947	1437.5	2.931	17.5	0.036	21.2	0.043	22.8	0.046	44.0	0.090
M01009	501.9	440.4	0.877	1752.8	3.492	19.2	0.038	24.0	0.048	24.9	0.050	48.9	0.097
M01010	519.4	1044.2	2.010	1805.0	3.475	16.8	0.032	19.1	0.037	19.6	0.038	38.7	0.075
M01011	546.9	463.6	0.848	1237.2	2.262	19.4	0.035	22.1	0.040	21.8	0.040	43.9	0.080
M01012	513.9	700.4	1.363	1714.8	3.337	19.5	0.038	22.2	0.043	24.2	0.047	46.4	0.090
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	514.5	622.6	1.209	1589.5	3.099	18.5	0.036	21.7	0.042	22.7	0.044	44.4	0.086
S.D.	21.3	258.5	0.494	242.9	0.520	1.2	0.002	1.8	0.004	2.1	0.005	3.8	0.009

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

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

CPN 300 mg/kg

Male No.	Body weight (g)	Brain		Thymus		Heart		Liver		Kidney (R)		Kidney (L)		Kidneys		Spleen	
		(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
M04044	545.0	2162.5	3.968	405.6	0.744	1339.3	2.457	15206.4	27.902	1680.6	3.084	1620.2	2.973	3300.8	6.057	777.0	1.426
M04045	558.6	2063.4	3.694	223.5	0.400	1552.6	2.779	16361.4	29.290	1644.2	2.943	1630.6	2.919	3274.8	5.863	958.4	1.716
M04046	507.9	1901.4	3.744	312.4	0.615	1527.4	3.007	14242.7	28.042	1614.6	3.179	1614.2	3.178	3228.8	6.357	865.8	1.705
M04047	478.9	1891.4	3.949	139.0	0.290	1439.8	3.006	12885.8	26.907	1624.2	3.392	1607.2	3.356	3231.4	6.748	696.6	1.455
M04048	541.6	2048.3	3.782	230.2	0.425	1545.0	2.853	14443.3	26.668	1826.8	3.373	1863.6	3.441	3690.4	6.814	728.3	1.345
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	526.4	2013.4	3.827	262.1	0.495	1480.8	2.820	14627.9	27.762	1678.1	3.194	1667.2	3.173	3345.2	6.368	805.2	1.529
S.D.	32.5	115.5	0.124	101.0	0.182	91.0	0.226	1280.3	1.044	86.9	0.191	110.1	0.229	195.3	0.417	106.8	0.170
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT

NS: Not significantly different from the control group.

TT: Analysis by Student's t-test.

AW: Analysis by Aspin-Welch t-test.

Appendix 29-2-2 (continued). Organ weights of male rats at the end of the recovery period

CPN 300 mg/kg

Male No.	Testis (R)		Testis (L)		Testes		Epididymis (R)		Epididymis (L)		Epididymides	
	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
M04044	1677.3	3.078	1734.4	3.182	3411.7	6.260	709.1	1.301	731.2	1.342	1440.3	2.643
M04045	2038.4	3.649	1917.4	3.433	3955.8	7.082	704.8	1.262	717.1	1.284	1421.9	2.545
M04046	1818.3	3.580	1842.4	3.627	3660.7	7.208	669.4	1.318	665.0	1.309	1334.4	2.627
M04047	1494.5	3.121	1536.5	3.208	3031.0	6.329	598.4	1.250	609.8	1.273	1208.2	2.523
M04048	1754.6	3.240	1834.0	3.386	3588.6	6.626	617.9	1.141	666.7	1.231	1284.6	2.372
Number of males	5	5	5	5	5	5	5	5	5	5	5	5
Mean	1756.6	3.334	1772.9	3.367	3529.6	6.701	659.9	1.254	678.0	1.288	1337.9	2.542
S.D.	198.9	0.264	147.3	0.182	340.9	0.430	50.2	0.069	48.2	0.041	96.5	0.108
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	AW	TT

NS: Not significantly different from the control group.

TT: Analysis by Student's t-test.

AW: Analysis by Aspin-Welch t-test.

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

Appendix 29-2-2 (continued). Organ weights of male rats at the end of the recovery period

CPN 300 mg/kg

Male No.	Body weight (g)	Prostate, ventral		Seminal vesicles		Thyroid gland		Adrenal gland (R)		Adrenal gland (L)		Adrenal glands	
		(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
M04044	545.0	519.6	0.953	1932.2	3.545	28.8	0.053	19.9	0.037	21.3	0.039	41.2	0.076
M04045	558.6	486.4	0.871	1694.3	3.033	24.6	0.044	23.1	0.041	26.2	0.047	49.3	0.088
M04046	507.9	611.1	1.203	1926.6	3.793	19.1	0.038	20.6	0.041	21.0	0.041	41.6	0.082
M04047	478.9	685.4	1.431	2323.3	4.851	21.8	0.046	27.9	0.058	26.4	0.055	54.3	0.113
M04048	541.6	633.5	1.170	1771.4	3.271	22.0	0.041	26.7	0.049	28.5	0.053	55.2	0.102
Number of males	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	526.4	587.2	1.126	1929.6	3.699	23.3	0.044	23.6	0.045	24.7	0.047	48.3	0.092
S.D.	32.5	82.3	0.221	242.6	0.705	3.7	0.006	3.6	0.008	3.3	0.007	6.7	0.015
Significance	NS	NS	NS	NS	NS	*	*	NS	NS	NS	NS	NS	NS
Statistical method	TT	AW	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT

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

NS: Not significantly different from the control group.

TT: Analysis by Student's t-test.

AW: Analysis by Aspin-Welch t-test.

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

Appendix 30-1-1. Organ weights of female rats at the end of the administration period

Control (vehicle: corn oil)

Female No.	Body weight (g)	Brain		Thymus		Heart		Liver		Kidney (R)		Kidney (L)		Kidneys		Spleen	
		(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
F01001	302.8	1888.4	6.236	196.8	0.650	892.9	2.949	8794.0	29.042	870.0	2.873	869.3	2.871	1739.3	5.744	695.7	2.298
F01002	310.9	1826.5	5.875	212.8	0.684	980.4	3.153	9368.0	30.132	1102.3	3.546	1034.2	3.326	2136.5	6.872	645.6	2.077
F01003	348.6	1915.5	5.495	162.5	0.466	1069.9	3.069	11303.8	32.426	1188.1	3.408	1138.7	3.266	2326.8	6.675	926.4	2.657
F01004	341.8	1902.3	5.566	178.4	0.522	1063.0	3.110	11328.8	33.145	1127.1	3.298	1136.2	3.324	2263.3	6.622	780.2	2.283
F01005	335.5	1933.1	5.762	329.7	0.983	1135.3	3.384	11150.3	33.235	1064.8	3.174	1025.6	3.057	2090.4	6.231	857.3	2.555
F01006	296.4	2055.2	6.934	305.0	1.029	1005.7	3.393	9546.1	32.207	973.1	3.283	981.0	3.310	1954.1	6.593	576.4	1.945
F01007	303.6	1948.3	6.417	201.3	0.663	945.7	3.115	9531.8	31.396	936.0	3.083	911.7	3.003	1847.7	6.086	606.7	1.998
F01008	320.1	1847.6	5.772	155.1	0.485	1075.0	3.358	10375.6	32.414	1154.8	3.608	1055.4	3.297	2210.2	6.905	795.7	2.486
F01009	295.0	1957.1	6.634	146.3	0.496	987.3	3.347	9717.6	32.941	1151.7	3.904	1081.0	3.664	2232.7	7.568	595.4	2.018
F01010	352.5	2047.5	5.809	247.9	0.703	1016.1	2.883	10710.9	30.386	1038.5	2.946	989.9	2.808	2028.4	5.754	857.7	2.433
F01011	283.5	1933.0	6.818	216.8	0.765	1018.9	3.594	8693.7	30.666	992.7	3.502	968.0	3.414	1960.7	6.916	755.5	2.665
F01012	309.0	1917.7	6.206	217.7	0.705	995.6	3.222	9404.0	30.434	857.2	2.774	849.8	2.750	1707.0	5.524	700.5	2.267
Number of females	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
Mean	316.6	1931.0	6.127	214.2	0.679	1015.5	3.215	9993.7	31.535	1038.0	3.283	1003.4	3.174	2041.4	6.458	732.8	2.307
S.D.	22.8	68.0	0.489	56.6	0.182	64.3	0.206	946.5	1.381	112.6	0.333	94.4	0.275	205.0	0.601	114.6	0.257

Appendix 30-1-1 (continued). Organ weights of female rats at the end of the administration period

Control (vehicle: corn oil)

Female No.	Ovary (R)		Ovary (L)		Ovaries		Uterus		Thyroid gland		Adrenal gland (R)		Adrenal gland (L)		Adrenal glands	
	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
F01001	50.6	0.167	61.5	0.203	112.1	0.370	529.5	1.749	15.4	0.051	34.0	0.112	39.2	0.129	73.2	0.242
F01002	43.0	0.138	58.9	0.189	101.9	0.328	638.6	2.054	19.2	0.062	34.7	0.112	37.0	0.119	71.7	0.231
F01003	53.9	0.155	58.4	0.168	112.3	0.322	667.9	1.916	13.5	0.039	42.4	0.122	44.7	0.128	87.1	0.250
F01004	56.5	0.165	61.3	0.179	117.8	0.345	887.6	2.597	20.9	0.061	34.4	0.101	45.4	0.133	79.8	0.233
F01005	49.7	0.148	56.5	0.168	106.2	0.317	627.1	1.869	14.8	0.044	39.3	0.117	37.7	0.112	77.0	0.230
F01006	47.4	0.160	57.3	0.193	104.7	0.353	653.2	2.204	17.2	0.058	42.3	0.143	41.2	0.139	83.5	0.282
F01007	59.4	0.196	49.7	0.164	109.1	0.359	580.3	1.911	13.8	0.045	33.2	0.109	36.1	0.119	69.3	0.228
F01008	65.1	0.203	47.7	0.149	112.8	0.352	607.5	1.898	11.3	0.035	41.4	0.129	41.3	0.129	82.7	0.258
F01009	51.2	0.174	55.3	0.187	106.5	0.361	685.2	2.323	24.9	0.084	29.9	0.101	30.3	0.103	60.2	0.204
F01010	46.0	0.130	52.6	0.149	98.6	0.280	578.3	1.641	13.8	0.039	36.8	0.104	37.2	0.106	74.0	0.210
F01011	55.8	0.197	43.9	0.155	99.7	0.352	685.9	2.419	15.5	0.055	32.1	0.113	37.2	0.131	69.3	0.244
F01012	58.1	0.188	45.8	0.148	103.9	0.336	561.6	1.817	16.9	0.055	31.1	0.101	34.3	0.111	65.4	0.212
Number of females	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
Mean	53.1	0.168	54.1	0.171	107.1	0.340	641.9	2.033	16.4	0.052	36.0	0.114	38.5	0.122	74.4	0.235
S.D.	6.3	0.024	6.0	0.019	5.8	0.025	92.1	0.292	3.7	0.013	4.4	0.013	4.2	0.012	7.9	0.022

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

Appendix 30-1-2. Organ weights of female rats at the end of the administration period

CPN 30 mg/kg

Female No.	Body weight (g)	Brain		Thymus		Heart		Liver		Kidney (R)		Kidney (L)		Kidneys		Spleen	
		(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
F02013	296.4	1833.4	6.186	179.5	0.606	955.6	3.224	10578.1	35.689	986.8	3.329	988.3	3.334	1975.1	6.664	696.9	2.351
F02014	285.6	1829.9	6.407	160.8	0.563	979.9	3.431	9798.5	34.308	1051.7	3.682	972.3	3.404	2024.0	7.087	667.2	2.336
F02015	325.2	1994.2	6.132	98.0	0.301	1081.0	3.324	11100.6	34.135	967.4	2.975	1024.7	3.151	1992.1	6.126	905.7	2.785
F02016	279.2	1942.3	6.957	161.2	0.577	1048.2	3.754	9694.2	34.721	963.6	3.451	953.0	3.413	1916.6	6.865	632.2	2.264
F02017	287.0	2027.8	7.066	104.5	0.364	938.1	3.269	10099.9	35.191	1030.5	3.591	1070.5	3.730	2101.0	7.321	500.4	1.744
F02018	348.9	1884.3	5.401	288.2	0.826	1093.0	3.133	11458.2	32.841	1053.4	3.019	1012.9	2.903	2066.3	5.922	791.7	2.269
F02019	292.1	1813.1	6.207	250.4	0.857	1012.6	3.467	9924.0	33.975	1061.9	3.635	957.7	3.279	2019.6	6.914	675.0	2.311
F02020	310.2	1974.3	6.365	262.2	0.845	1066.4	3.438	10691.2	34.466	1067.7	3.442	1080.7	3.484	2148.4	6.926	807.7	2.604
F02021	293.4	1817.5	6.195	211.2	0.720	994.3	3.389	9175.2	31.272	976.6	3.329	1001.3	3.413	1977.9	6.741	633.0	2.157
F02022	294.7	1819.0	6.172	198.3	0.673	984.5	3.341	8685.1	29.471	824.8	2.799	783.0	2.657	1607.8	5.456	547.3	1.857
F02023	337.8 a	1964.0 a	5.814 a	412.9 a	1.222 a	1039.0 a	3.076 a	11855.5 a	35.096 a	1096.1 a	3.245 a	1074.1 a	3.180 a	2170.2 a	6.425 a	696.2 a	2.061 a
F02024	300.0	1974.4	6.581	222.8	0.743	1000.4	3.335	9344.6	31.149	1146.4	3.821	1132.9	3.776	2279.3	7.598	754.3	2.514
Number of females	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
Mean	301.2	1900.9	6.334	194.3	0.643	1014.0	3.373	10050.0	33.383	1011.9	3.370	997.9	3.322	2009.8	6.693	691.9	2.290
S.D.	20.2	82.8	0.446	61.2	0.185	51.4	0.160	843.3	1.959	82.8	0.323	90.5	0.327	166.3	0.629	117.7	0.301
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	DU	DU	AN	AN	AN	DU	AN	AN	AN	DU	AN	DU	AN	DU	AN	AN

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

NS: Not significantly different from the control group.

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

DU: Analysis by Dunnett's test.

KW: Analysis by Kruskal-Wallis' test (one-way layout).

DT: Analysis by Dunnett type mean rank test.

a, Excluded from data analysis (not pregnant).

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

Appendix 30-1-2 (continued). Organ weights of female rats at the end of the administration period

Female No.	Ovary (R)		Ovary (L)		Ovaries		Uterus		Thyroid gland		Adrenal gland (R)		Adrenal gland (L)		Adrenal glands	
	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
F02013	50.8	0.171	65.5	0.221	116.3	0.392	664.6	2.242	15.8	0.053	36.4	0.123	40.2	0.136	76.6	0.258
F02014	68.0	0.238	60.9	0.213	128.9	0.451	710.6	2.488	14.8	0.052	35.1	0.123	41.7	0.146	76.8	0.269
F02015	61.5	0.189	50.0	0.154	111.5	0.343	880.9	2.709	18.8	0.058	36.3	0.112	38.3	0.118	74.6	0.229
F02016	47.3	0.169	44.8	0.160	92.1	0.330	635.1	2.275	16.8	0.060	31.3	0.112	35.2	0.126	66.5	0.238
F02017	50.6	0.176	51.2	0.178	101.8	0.355	723.1	2.520	18.3	0.064	36.2	0.126	41.1	0.143	77.3	0.269
F02018	68.6	0.197	42.2	0.121	110.8	0.318	643.7	1.845	16.3	0.047	38.4	0.110	42.5	0.122	80.9	0.232
F02019	49.0	0.168	59.9	0.205	108.9	0.373	583.0	1.996	16.8	0.058	26.7	0.091	28.1	0.096	54.8	0.188
F02020	48.3	0.156	51.3	0.165	99.6	0.321	652.9	2.105	17.8	0.057	36.5	0.118	39.8	0.128	76.3	0.246
F02021	67.7	0.231	59.8	0.204	127.5	0.435	750.2	2.557	13.1	0.045	30.7	0.105	35.0	0.119	65.7	0.224
F02022	49.9	0.169	40.0	0.136	89.9	0.305	595.8	2.022	17.3	0.059	30.2	0.102	34.7	0.118	64.9	0.220
F02023	37.7 a	0.112 a	42.1 a	0.125 a	79.8 a	0.236 a	440.7 a	1.305 a	17.3 a	0.051 a	25.3 a	0.075 a	29.9 a	0.089 a	55.2 a	0.163 a
F02024	50.2	0.167	63.9	0.213	114.1	0.380	738.7	2.462	14.9	0.050	35.4	0.118	37.5	0.125	72.9	0.243
Number of females	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
Mean	55.6	0.185	53.6	0.179	109.2	0.364	689.0	2.293	16.4	0.055	33.9	0.113	37.6	0.125	71.6	0.238
S.D.	8.8	0.027	8.9	0.034	12.7	0.048	84.5	0.276	1.7	0.006	3.6	0.010	4.2	0.014	7.7	0.024
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	KW	DU	AN	DU	AN	AN	AN	AN	DT	AN	AN	AN

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

NS: Not significantly different from the control group.

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

DU: Analysis by Dunnett's test.

KW: Analysis by Kruskal-Wallis' test (one-way layout).

DT: Analysis by Dunnett type mean rank test.

a, Excluded from data analysis (not pregnant).

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

Appendix 30-1-3. Organ weights of female rats at the end of the administration period

CPN 100 mg/kg																	
Female No.	Body weight (g)	Brain (mg)		Thymus (mg)		Heart (mg)		Liver (mg)		Kidney (R) (mg)		Kidney (L) (mg)		Kidneys (mg)		Spleen (mg)	
F03025	301.7	1827.6	6.058	112.3	0.372	1027.3	3.405	8739.2	28.967	820.8	2.721	802.5	2.660	1623.3	5.381	543.2	1.800
F03026	318.4	1879.9	5.904	198.8	0.624	1014.0	3.185	11600.3	36.433	1016.1	3.191	999.9	3.140	2016.0	6.332	794.1	2.494
F03027	326.4	1785.0	5.469	145.2	0.445	944.7	2.894	10527.0	32.252	1094.1	3.352	981.2	3.006	2075.3	6.358	802.0	2.457
F03028	260.6 b	1792.1 b	6.877 b	85.8 b	0.329 b	872.6 b	3.348 b	9148.9 b	35.107 b	974.1 b	3.738 b	972.5 b	3.732 b	1946.6 b	7.470 b	491.3 b	1.885 b
F03029	314.4	1930.6	6.141	219.4	0.698	1000.8	3.183	10538.0	33.518	964.2	3.067	946.6	3.011	1910.8	6.078	650.6	2.069
F03030	311.5	1851.7	5.944	214.4	0.688	898.1	2.883	10361.0	33.262	946.0	3.037	954.0	3.063	1900.0	6.100	795.3	2.553
F03031	338.7	1838.7	5.429	357.3	1.055	1031.7	3.046	10608.6	31.322	1045.8	3.088	987.1	2.914	2032.9	6.002	697.8	2.060
F03032	303.3	1741.2	5.741	218.0	0.719	947.0	3.122	10097.6	33.292	1079.3	3.559	1131.7	3.731	2211.0	7.290	719.4	2.372
F03033	283.1	1740.2	6.147	190.6	0.673	870.1	3.073	9118.2	32.208	844.3	2.982	847.9	2.995	1692.2	5.977	616.1	2.176
F03034	314.1 c	2088.5 c	6.649 c	407.6 c	1.298 c	944.8 c	3.008 c	11600.8 c	36.933 c	1108.2 c	3.528 c	1147.8 c	3.654 c	2256.0 c	7.182 c	503.6 c	1.603 c
F03035	315.9	1789.4	5.664	219.4	0.695	1019.9	3.229	10289.8	32.573	947.5	2.999	872.9	2.763	1820.4	5.763	684.5	2.167
F03036	344.6	1936.5	5.620	253.2	0.735	1060.2	3.077	10149.7	29.454	987.2	2.865	970.9	2.817	1958.1	5.682	659.8	1.915
Number of females	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
Mean	315.8	1832.1	5.812	212.9	0.670	981.4	3.110	10202.9	32.328	974.5	3.086	949.5	3.010	1924.0	6.096	696.3	2.206
S.D.	18.0	70.0	0.266	65.0	0.182	62.9	0.155	795.8	2.127	91.0	0.238	92.2	0.292	177.1	0.513	84.7	0.255
Significance	NS	*	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	DU	DU	AN	AN	AN	DU	AN	AN	AN	DU	AN	DU	AN	DU	AN	AN

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

NS: Not significantly different from the control group.

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

DU: Analysis by Dunnett's test.

KW: Analysis by Kruskal-Wallis' test (one-way layout).

DT: Analysis by Dunnett type mean rank test.

b, Excluded from data analysis (total litter loss).

c, Excluded from data analysis (not copulated).

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

Appendix 30-1-3 (continued). Organ weights of female rats at the end of the administration period

CPN 100 mg/kg

Female No.	Ovary (R)		Ovary (L)		Ovaries		Uterus		Thyroid gland		Adrenal gland (R)		Adrenal gland (L)		Adrenal glands	
	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
F03025	52.8	0.175	52.0	0.172	104.8	0.347	593.8	1.968	14.8	0.049	29.6	0.098	31.2	0.103	60.8	0.202
F03026	60.8	0.191	45.4	0.143	106.2	0.334	664.1	2.086	15.6	0.049	31.2	0.098	33.8	0.106	65.0	0.204
F03027	61.7	0.189	53.9	0.165	115.6	0.354	525.1	1.609	14.0	0.043	31.0	0.095	32.4	0.099	63.4	0.194
F03028	53.6 b	0.206 b	60.2 b	0.231 b	113.8 b	0.437 b	2787.2 b	10.695 b	13.7 b	0.053 b	32.9 b	0.126 b	34.6 b	0.133 b	67.5 b	0.259 b
F03029	58.6	0.186	60.3	0.192	118.9	0.378	767.3	2.441	22.5	0.072	34.5	0.110	38.0	0.121	72.5	0.231
F03030	51.3	0.165	50.4	0.162	101.7	0.326	746.2	2.396	14.9	0.048	31.4	0.101	34.1	0.109	65.5	0.210
F03031	44.4	0.131	62.3	0.184	106.7	0.315	676.6	1.998	22.2	0.066	30.5	0.090	32.1	0.095	62.6	0.185
F03032	50.1	0.165	53.7	0.177	103.8	0.342	554.4	1.828	17.5	0.058	28.5	0.094	32.6	0.107	61.1	0.201
F03033	29.5	0.104	39.8	0.141	69.3	0.245	588.3	2.078	22.3	0.079	36.4	0.129	38.8	0.137	75.2	0.266
F03034	52.1 c	0.166 c	43.9 c	0.140 c	96.0 c	0.306 c	2864.2 c	9.119 c	15.5 c	0.049 c	40.4 c	0.129 c	42.3 c	0.135 c	82.7 c	0.263 c
F03035	70.7	0.224	56.4	0.179	127.1	0.402	636.8	2.016	19.0	0.060	36.7	0.116	35.1	0.111	71.8	0.227
F03036	47.9	0.139	50.9	0.148	98.8	0.287	554.9	1.610	15.8	0.046	37.6	0.109	37.7	0.109	75.3	0.219
Number of females	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
Mean	52.8	0.167	52.5	0.166	105.3	0.333	630.8	2.003	17.9	0.057	32.7	0.104	34.6	0.110	67.3	0.214
S.D.	11.3	0.035	6.6	0.018	15.4	0.044	82.4	0.279	3.4	0.012	3.3	0.012	2.7	0.012	5.8	0.023
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	KW	DU	AN	DU	AN	AN	AN	AN	DT	AN	AN	AN

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

NS: Not significantly different from the control group.

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

DU: Analysis by Dunnett's test.

KW: Analysis by Kruskal-Wallis' test (one-way layout).

DT: Analysis by Dunnett type mean rank test.

b, Excluded from data analysis (total litter loss).

c, Excluded from data analysis (not copulated).

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

Appendix 30-1-4. Organ weights of female rats at the end of the administration period

CPN 300 mg/kg

Female No.	Body weight (g)	Brain		Thymus		Heart		Liver		Kidney (R)		Kidney (L)		Kidneys		Spleen	
		(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
F04037	266.4 b	1769.7 b	6.643 b	64.6 b	0.242 b	864.7 b	3.246 b	12347.5 b	46.349 b	1056.5 b	3.966 b	988.8 b	3.712 b	2045.3 b	7.678 b	395.8 b	1.486 b
F04038	310.7	1825.7	5.876	206.2	0.664	959.6	3.089	9612.5	30.938	1056.9	3.402	1006.4	3.239	2063.3	6.641	620.5	1.997
F04039	305.5	1865.3	6.106	163.3	0.535	991.0	3.244	9429.3	30.865	1022.9	3.348	1092.2	3.575	2115.1	6.923	697.6	2.283
F04040	279.2	1878.7	6.729	255.9	0.917	951.2	3.407	9756.7	34.945	961.3	3.443	949.3	3.400	1910.6	6.843	564.9	2.023
F04041	322.3	1902.2	5.902	156.1	0.484	981.2	3.044	9762.7	30.291	964.0	2.991	968.9	3.006	1932.9	5.997	633.6	1.966
F04042	301.7	2052.8	6.804	153.7	0.509	1028.4	3.409	9647.1	31.976	1202.1	3.984	1079.4	3.578	2281.5	7.562	576.5	1.911
F04043	299.1	1826.0	6.105	89.7	0.300	1005.5	3.362	10865.7	36.328	1095.1	3.661	1080.0	3.611	2175.1	7.272	919.8	3.075
F04044	295.9	1930.8	6.525	192.6	0.651	1002.6	3.388	10003.1	33.806	1084.2	3.664	1080.4	3.651	2164.6	7.315	695.0	2.349
F04045	299.9	1770.8	5.905	184.0	0.614	982.0	3.274	9675.4	32.262	929.3	3.099	915.6	3.053	1844.9	6.152	609.7	2.033
F04046	309.8	1732.5	5.592	217.9	0.703	1017.3	3.284	11429.3	36.893	1189.3	3.839	1140.3	3.681	2329.6	7.520	977.9	3.157
F04047	317.9	1939.3	6.100	181.2	0.570	1071.3	3.370	10386.7	32.673	1211.3	3.810	1105.2	3.477	2316.5	7.287	871.7	2.742
F04048	276.6	1835.4	6.636	130.9	0.473	944.4	3.414	8805.2	31.834	929.7	3.361	954.2	3.450	1883.9	6.811	625.4	2.261
Number of females	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
Mean	301.7	1869.0	6.207	175.6	0.584	994.0	3.299	9943.1	32.983	1058.7	3.509	1033.8	3.429	2092.5	6.938	708.4	2.345
S.D.	14.2	87.7	0.402	44.7	0.157	37.0	0.129	718.0	2.233	107.7	0.312	76.6	0.234	178.6	0.522	145.7	0.449
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	DU	DU	AN	AN	AN	DU	AN	AN	AN	DU	AN	DU	AN	DU	AN	AN

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

NS: Not significantly different from the control group.

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

DU: Analysis by Dunnett's test.

KW: Analysis by Kruskal-Wallis' test (one-way layout).

DT: Analysis by Dunnett type mean rank test.

b, Excluded from data analysis (total litter loss).

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

Appendix 30-1-4 (continued). Organ weights of female rats at the end of the administration period

CPN 300 mg/kg

Female No.	Ovary (R)		Ovary (L)		Ovaries		Uterus		Thyroid gland		Adrenal gland (R)		Adrenal gland (L)		Adrenal glands	
	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
F04037	68.9 b	0.259 b	36.9 b	0.139 b	105.8 b	0.397 b	3463.2 b	13.000 b	16.0 b	0.060 b	46.6 b	0.175 b	48.6 b	0.182 b	95.2 b	0.357 b
F04038	55.3	0.178	53.7	0.173	109.0	0.351	733.9	2.362	16.9	0.054	34.7	0.112	34.9	0.112	69.6	0.224
F04039	65.2	0.213	50.3	0.165	115.5	0.378	627.0	2.052	18.5	0.061	33.8	0.111	40.3	0.132	74.1	0.243
F04040	57.5	0.206	66.6	0.239	124.1	0.444	611.2	2.189	12.3	0.044	28.3	0.101	29.3	0.105	57.6	0.206
F04041	65.5	0.203	69.3	0.215	134.8	0.418	732.7	2.273	25.5	0.079	29.0	0.090	31.8	0.099	60.8	0.189
F04042	54.3	0.180	58.5	0.194	112.8	0.374	626.5	2.077	20.9	0.069	32.4	0.107	33.2	0.110	65.6	0.217
F04043	58.5	0.196	53.6	0.179	112.1	0.375	860.6	2.877	18.3	0.061	37.3	0.125	38.7	0.129	76.0	0.254
F04044	47.6	0.161	64.2	0.217	111.8	0.378	665.4	2.249	15.9	0.054	31.6	0.107	33.4	0.113	65.0	0.220
F04045	54.8	0.183	57.7	0.192	112.5	0.375	728.6	2.429	16.8	0.056	30.6	0.102	33.8	0.113	64.4	0.215
F04046	58.5	0.189	61.8	0.199	120.3	0.388	635.9	2.053	19.3	0.062	45.5	0.147	56.5	0.182	102.0	0.329
F04047	61.0	0.192	54.7	0.172	115.7	0.364	653.4	2.055	21.8	0.069	29.8	0.094	29.8	0.094	59.6	0.187
F04048	56.5	0.204	46.0	0.166	102.5	0.371	632.6	2.287	21.9	0.079	28.7	0.104	33.0	0.119	61.7	0.223
Number of females	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
Mean	57.7	0.191	57.9	0.192	115.6	0.383	682.5	2.264	18.9	0.063	32.9	0.109	35.9	0.119	68.8	0.228
S.D.	5.1	0.015	7.1	0.024	8.5	0.026	74.9	0.242	3.6	0.011	5.0	0.016	7.6	0.024	12.5	0.039
Significance	NS	NS	NS	NS	NS	*	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	KW	DU	AN	DU	AN	AN	AN	AN	DT	AN	AN	AN

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

NS: Not significantly different from the control group.

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

DU: Analysis by Dunnett's test.

KW: Analysis by Kruskal-Wallis' test (one-way layout).

DT: Analysis by Dunnett type mean rank test.

b, Excluded from data analysis (total litter loss).

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

Appendix 30-2-1. Organ weights of female rats at the end of the administration period, satellite group

Control (vehicle: corn oil)

Female No.	Body weight (g)	Brain		Thymus		Heart		Liver		Kidney (R)		Kidney (L)		Kidneys		Spleen	
		(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
F05049	300.0	1818.2	6.061	269.5	0.898	920.6	3.069	7262.1	24.207	970.2	3.234	975.5	3.252	1945.7	6.486	714.0	2.380
F05050	284.7	1902.1	6.681	249.2	0.875	979.6	3.441	8052.9	28.286	939.2	3.299	957.0	3.361	1896.2	6.660	569.3	2.000
F05051	294.7	2041.4	6.927	231.9	0.787	924.1	3.136	7382.7	25.052	935.3	3.174	898.6	3.049	1833.9	6.223	654.4	2.221
F05052	268.5	1827.7	6.807	399.4	1.488	892.7	3.325	7387.7	27.515	847.9	3.158	854.5	3.182	1702.4	6.340	527.6	1.965
F05053	260.4	1859.5	7.141	305.0	1.171	828.3	3.181	6291.7	24.162	781.5	3.001	758.5	2.913	1540.0	5.914	549.9	2.112
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	281.7	1889.8	6.723	291.0	1.044	909.1	3.230	7275.4	25.844	894.8	3.173	888.8	3.151	1783.6	6.325	603.0	2.136
S.D.	16.9	90.9	0.407	66.4	0.287	55.1	0.151	631.8	1.929	78.0	0.111	87.2	0.175	163.9	0.282	78.4	0.170

Appendix 30-2-1 (continued). Organ weights of female rats at the end of the administration period, satellite group

Control (vehicle: corn oil)

Female No.	Ovary (R)		Ovary (L)		Ovaries		Uterus		Thyroid gland		Adrenal gland (R)		Adrenal gland (L)		Adrenal glands	
	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
F05049	58.0	0.193	63.3	0.211	121.3	0.404	430.8	1.436	18.9	0.063	38.6	0.129	42.0	0.140	80.6	0.269
F05050	37.0	0.130	36.1	0.127	73.1	0.257	489.2	1.718	21.3	0.075	34.4	0.121	35.8	0.126	70.2	0.247
F05051	43.8	0.149	47.4	0.161	91.2	0.309	555.6	1.885	18.2	0.062	34.3	0.116	35.1	0.119	69.4	0.235
F05052	31.5	0.117	41.2	0.153	72.7	0.271	486.7	1.813	15.2	0.057	28.0	0.104	29.5	0.110	57.5	0.214
F05053	36.8	0.141	42.3	0.162	79.1	0.304	324.0	1.244	18.4	0.071	25.6	0.098	28.3	0.109	53.9	0.207
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	41.4	0.146	46.1	0.163	87.5	0.309	457.3	1.619	18.4	0.066	32.2	0.114	34.1	0.121	66.3	0.234
S.D.	10.2	0.029	10.4	0.030	20.3	0.057	86.6	0.270	2.2	0.007	5.3	0.013	5.5	0.013	10.7	0.025

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

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

CPN 300 mg/kg

Female No.	Body weight (g)		Brain (mg/g)		Thymus (mg/g)		Heart (mg/g)		Liver (mg/g)		Kidney (R) (mg/g)		Kidney (L) (mg/g)		Kidneys (mg/g)		Spleen (mg/g)	
	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
F06056	253.1	1882.2	7.437	318.9	1.260	816.1	3.224	8944.3	35.339	951.9	3.761	901.4	3.561	1853.3	7.322	444.2	1.755	
F06057	271.4	1953.3	7.197	269.1	0.992	810.5	2.986	8191.5	30.182	943.9	3.478	939.3	3.461	1883.2	6.939	401.5	1.479	
F06058	288.1	1809.8	6.282	297.9	1.034	1009.1	3.503	7707.7	26.754	1043.8	3.623	1077.0	3.738	2120.8	7.361	654.3	2.271	
F06059	273.0	1818.6	6.662	262.2	0.960	858.8	3.146	7392.7	27.079	856.1	3.136	819.2	3.001	1675.3	6.137	512.4	1.877	
F06060	276.5	1914.9	6.925	277.0	1.002	874.4	3.162	7040.9	25.464	902.2	3.263	885.5	3.203	1787.7	6.465	586.5	2.121	
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	272.4	1875.8	6.901	285.0	1.050	873.8	3.204	7855.4	28.964	939.6	3.452	924.5	3.393	1864.1	6.845	519.8	1.901	
S.D.	12.6	61.7	0.452	23.2	0.121	80.4	0.189	741.3	3.963	69.6	0.255	95.7	0.292	164.2	0.536	102.8	0.310	
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT

NS: Not significantly different from the control group.

TT: Analysis by Student's t-test.

AW: Analysis by Aspin-Welch t-test.

Appendix 30-2-2 (continued). Organ weights of female rats at the end of the administration period, satellite group

CPN 300 mg/kg

Female No.	Ovary (R)		Ovary (L)		Ovaries		Uterus		Thyroid gland		Adrenal gland (R)		Adrenal gland (L)		Adrenal glands	
	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
F06056	44.7	0.177	46.7	0.185	91.4	0.361	349.0	1.379	18.5	0.073	31.2	0.123	31.5	0.124	62.7	0.248
F06057	40.9	0.151	41.4	0.153	82.3	0.303	467.4	1.722	21.4	0.079	38.3	0.141	39.9	0.147	78.2	0.288
F06058	64.0	0.222	60.9	0.211	124.9	0.434	523.3	1.816	18.2	0.063	35.8	0.124	38.2	0.133	74.0	0.257
F06059	50.3	0.184	45.5	0.167	95.8	0.351	474.0	1.736	14.4	0.053	30.2	0.111	32.2	0.118	62.4	0.229
F06060	37.8	0.137	41.1	0.149	78.9	0.285	1042.9	3.772	18.5	0.067	32.0	0.116	28.7	0.104	60.7	0.220
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	47.5	0.174	47.1	0.173	94.7	0.347	571.3	2.085	18.2	0.067	33.5	0.123	34.1	0.125	67.6	0.248
S.D.	10.3	0.033	8.1	0.025	18.2	0.058	271.3	0.958	2.5	0.010	3.4	0.011	4.7	0.016	7.9	0.027
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	TT	TT	TT	TT	TT	TT	AW	AW	TT	TT	TT	TT	TT	TT	TT	TT

NS: Not significantly different from the control group.

TT: Analysis by Student's t-test.

AW: Analysis by Aspin-Welch t-test.

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

Appendix 30-3-1. Organ weights of female rats at the end of the recovery period

Control (vehicle: corn oil)

Female No.	Body weight (g)	Brain		Thymus		Heart		Liver		Kidney (R)		Kidney (L)		Kidneys		Spleen	
		(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
F05054	325.8	1964.4	6.029	424.6	1.303	1318.5	4.047	8401.9	25.789	1123.8	3.449	1110.1	3.407	2233.9	6.857	448.9	1.378
F05055	245.9	1933.3	7.862	256.7	1.044	832.1	3.384	5883.9	23.928	814.4	3.312	769.1	3.128	1583.5	6.440	531.0	2.159
F05056	299.1	1907.7	6.378	389.5	1.302	919.7	3.075	7707.0	25.767	935.3	3.127	907.5	3.034	1842.8	6.161	559.8	1.872
F05057	271.2	1783.2	6.575	275.8	1.017	923.8	3.406	6422.3	23.681	922.4	3.401	929.0	3.426	1851.4	6.827	512.9	1.891
F05058	283.9	1910.2	6.728	220.6	0.777	795.7	2.803	6940.8	24.448	923.8	3.254	923.3	3.252	1847.1	6.506	423.3	1.491
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	285.2	1899.8	6.714	313.4	1.089	958.0	3.343	7071.2	24.723	943.9	3.309	927.8	3.249	1871.7	6.558	495.2	1.758
S.D.	29.9	69.0	0.693	88.6	0.221	209.0	0.465	1002.8	1.002	111.9	0.127	121.3	0.171	232.4	0.290	57.2	0.319

Appendix 30-3-1 (continued). Organ weights of female rats at the end of the recovery period

Control (vehicle: corn oil)

Female No.	Ovary (R)		Ovary (L)		Ovaries		Uterus		Thyroid gland		Adrenal gland (R)		Adrenal gland (L)		Adrenal glands	
	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
F05054	36.9	0.113	34.2	0.105	71.1	0.218	820.7	2.519	16.0	0.049	43.4	0.133	27.9	0.086	71.3	0.219
F05055	33.8	0.137	22.0	0.089	55.8	0.227	518.0	2.107	16.9	0.069	24.1	0.098	26.2	0.107	50.3	0.205
F05056	37.1	0.124	36.6	0.122	73.7	0.246	562.2	1.880	9.7	0.032	32.5	0.109	35.4	0.118	67.9	0.227
F05057	30.1	0.111	37.3	0.138	67.4	0.249	417.1	1.538	21.7	0.080	29.3	0.108	31.2	0.115	60.5	0.223
F05058	43.1	0.152	31.4	0.111	74.5	0.262	1413.6	4.979	19.0	0.067	29.6	0.104	33.0	0.116	62.6	0.221
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	36.2	0.127	32.3	0.113	68.5	0.240	746.3	2.605	16.7	0.059	31.8	0.110	30.7	0.108	62.5	0.219
S.D.	4.8	0.017	6.2	0.018	7.6	0.018	401.6	1.374	4.5	0.019	7.2	0.013	3.7	0.013	8.1	0.008

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

Appendix 30-3-2. Organ weights of female rats at the end of the recovery period

CPN 300 mg/kg

Female No.	Body weight (g)	Brain		Thymus		Heart		Liver		Kidney (R)		Kidney (L)		Kidneys		Spleen	
		(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
F06061	267.1	1817.5	6.805	229.7	0.860	900.8	3.373	7181.2	26.886	1005.3	3.764	1003.3	3.756	2008.6	7.520	566.4	2.121
F06062	297.2	1845.6	6.210	230.9	0.777	899.1	3.025	6953.4	23.396	1015.3	3.416	984.6	3.313	1999.9	6.729	462.5	1.556
F06063	250.5	1916.1	7.649	286.8	1.145	869.7	3.472	7025.8	28.047	824.8	3.293	805.7	3.216	1630.5	6.509	471.3	1.881
F06064	290.9	2003.0	6.886	303.8	1.044	951.5	3.271	7334.8	25.214	1048.6	3.605	974.4	3.350	2023.0	6.954	581.0	1.997
F06065	271.4	1998.4	7.363	238.8	0.880	944.0	3.478	7859.9	28.961	956.8	3.525	952.2	3.508	1909.0	7.034	543.2	2.001
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	275.4	1916.1	6.983	258.0	0.941	913.0	3.324	7271.0	26.501	970.2	3.521	944.0	3.429	1914.2	6.949	524.9	1.911
S.D.	18.8	85.2	0.554	34.8	0.150	34.1	0.187	360.5	2.230	87.7	0.180	79.5	0.211	164.8	0.379	54.7	0.216
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	TT	TT	TT	TT	TT	AW	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT	TT

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

NS: Not significantly different from the control group.

TT: Analysis by Student's t-test.

AW: Analysis by Aspin-Welch t-test.

Appendix 30-3-2 (continued). Organ weights of female rats at the end of the recovery period

CPN 300 mg/kg

Female No.	Ovary (R)		Ovary (L)		Ovaries		Uterus		Thyroid gland		Adrenal gland (R)		Adrenal gland (L)		Adrenal glands	
	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)	(mg)	(mg/g)
F06061	51.7	0.194	50.2	0.188	101.9	0.382	734.8	2.751	19.8	0.074	33.7	0.126	37.3	0.140	71.0	0.266
F06062	54.0	0.182	45.0	0.151	99.0	0.333	385.0	1.295	16.4	0.055	33.2	0.112	34.9	0.117	68.1	0.229
F06063	53.5	0.214	60.9	0.243	114.4	0.457	523.5	2.090	13.8	0.055	32.3	0.129	33.6	0.134	65.9	0.263
F06064	61.6	0.212	53.6	0.184	115.2	0.396	1159.1	3.985	15.6	0.054	37.8	0.130	40.0	0.138	77.8	0.267
F06065	33.2	0.122	31.4	0.116	64.6	0.238	797.3	2.938	16.6	0.061	40.9	0.151	48.2	0.178	89.1	0.328
Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	50.8	0.185	48.2	0.176	99.0	0.361	719.9	2.612	16.4	0.060	35.6	0.130	38.8	0.141	74.4	0.271
S.D.	10.5	0.038	11.0	0.047	20.6	0.082	295.7	1.002	2.2	0.008	3.6	0.014	5.8	0.022	9.4	0.036
Significance	*	*	*	*	*	*	NS	NS	NS	NS	NS	NS	*	*	NS	*
Statistical method	TT	TT	TT	TT	TT	AW	TT	TT	TT	TT	TT	TT	TT	TT	TT	AW

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

NS: Not significantly different from the control group.

TT: Analysis by Student's t-test.

AW: Analysis by Aspin-Welch t-test.

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

Appendix 31-1. Macroscopic findings of male rats at the end of the administration period

Animal No.	Fate	Organs	Findings	Notes
M01001		Liver/	Pale colored area	Between right and left medial lobes
M01002		Liver/	Diaphragmatic nodule	
M01003		All organs/	Within normal limits	
M01004		Adipose tissue/	Nodule	Yellowish, Around pancreas
M01005		All organs/	Within normal limits	
M01006	S	Hindlimb/ Skin/ Spleen/ Thymus/ Urinary bladder/ Vertebral canal/	Swelling Soiled fur Enlargement Small Distention Hemorrhage	Right Perineal area Lumbar region
M01007		All organs/	Within normal limits	

S: Sacrificed during dosing period

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

Appendix 31-1 (continued). Macroscopic findings of male rats at the end of the administration period

Animal No.	Organs	Findings	Notes
M02013	All organs/	Within normal limits	
M02014	All organs/	Within normal limits	
M02015	All organs/	Within normal limits	
M02016	All organs/	Within normal limits	
M02017	All organs/	Within normal limits	
M02018	All organs/	Within normal limits	
M02019	All organs/	Within normal limits	
M02020	All organs/	Within normal limits	
M02021	All organs/	Within normal limits	
M02022	All organs/	Within normal limits	
M02023	All organs/	Within normal limits	
M02024	All organs/	Within normal limits	

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

Appendix 31-1 (continued). Macroscopic findings of male rats at the end of the administration period

Animal No.	Organs	Findings	Notes
M03025	All organs/	Within normal limits	
M03026	All organs/	Within normal limits	
M03027	All organs/	Within normal limits	
M03028	All organs/	Within normal limits	
M03029	All organs/	Within normal limits	
M03030	All organs/	Within normal limits	
M03031	All organs/	Within normal limits	
M03032	All organs/	Within normal limits	
M03033	All organs/	Within normal limits	
M03034	All organs/	Within normal limits	
M03035	All organs/	Within normal limits	
M03036	All organs/	Within normal limits	

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

Appendix 31-1 (continued). Macroscopic findings of male rats at the end of the administration period

Animal No.	Organs	Findings	Notes
M04037	All organs/	Within normal limits	
M04038	All organs/	Within normal limits	
M04039	Kidney/	Recessed area	Left
M04040	All organs/	Within normal limits	
M04041	All organs/	Within normal limits	
M04042	All organs/	Within normal limits	
M04043	All organs/	Within normal limits	

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

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

Animal No.	Organs	Findings	Notes
M01008	All organs/	Within normal limits	
M01009	All organs/	Within normal limits	
M01010	All organs/	Within normal limits	
M01011	All organs/	Within normal limits	
M01012	All organs/	Within normal limits	

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

Appendix 31-2 (continued). Macroscopic findings of male rats at the end of the recovery period

Animal No.	Organs	Findings	Notes
M04044	All organs/	Within normal limits	
M04045	All organs/	Within normal limits	
M04046	All organs/	Within normal limits	
M04047	Thymus/	Small	
M04048	Pituitary gland/	Cyst	

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

Appendix 32-1. Macroscopic findings of female rats at the end of the administration period

Animal No.	Organs	Findings	Notes
F01001	All organs/	Within normal limits	
F01002	All organs/	Within normal limits	
F01003	All organs/	Within normal limits	
F01004	All organs/	Within normal limits	
F01005	All organs/	Within normal limits	
F01006	All organs/	Within normal limits	
F01007	All organs/	Within normal limits	
F01008	All organs/	Within normal limits	
F01009	All organs/	Within normal limits	
F01010	All organs/	Within normal limits	
F01011	All organs/	Within normal limits	
F01012	Stomach/	Dark colored spot/area	Mucosa, Glandular stomach

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

Appendix 32-1 (continued). Macroscopic findings of female rats at the end of the administration period

Animal No.	Fate	Organs	Findings	Notes
F02013		All organs/	Within normal limits	
F02014		All organs/	Within normal limits	
F02015		All organs/	Within normal limits	
F02016		All organs/	Within normal limits	
F02017		All organs/	Within normal limits	
F02018		All organs/	Within normal limits	
F02019		All organs/	Within normal limits	
F02020		Ileum/	Diverticulum	
F02021		All organs/	Within normal limits	
F02022		All organs/	Within normal limits	
F02023	NP	Vagina/	Dilatation	Partial
F02024		All organs/	Within normal limits	

NP: Not pregnant

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

Appendix 32-1 (continued). Macroscopic findings of female rats at the end of the administration period

Animal No.	Fate	Organs	Findings	Notes
F03025		All organs/	Within normal limits	
F03026		All organs/	Within normal limits	
F03027		All organs/	Within normal limits	
F03028	TL	Skin/ Thymus/	Soiled fur Small	Perineal area
F03029		All organs/	Within normal limits	
F03030		All organs/	Within normal limits	
F03031		All organs/	Within normal limits	
F03032		All organs/	Within normal limits	
F03033		All organs/	Within normal limits	
F03034	NC	All organs/	Within normal limits	
F03035		All organs/	Within normal limits	
F03036		All organs/	Within normal limits	

TL: total litter loss NC: Not copulated

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

Appendix 32-1 (continued). Macroscopic findings of female rats at the end of the administration period

Animal No.	Fate	Organs	Findings	Notes
F04037	TL	Heart/ Liver/ Stomach/ Thymus/	Whitish spot Whitish area Thickening, mucosa Small	Apex Right medial lobe Forestomach
F04038		All organs/	Within normal limits	
F04039		All organs/	Within normal limits	
F04040		All organs/	Within normal limits	
F04041		All organs/	Within normal limits	
F04042		All organs/	Within normal limits	
F04043		Thymus/	Small	
F04044		All organs/	Within normal limits	
F04045		Stomach/	Thickening, mucosa	Forestomach
F04046		All organs/	Within normal limits	
F04047		All organs/	Within normal limits	
F04048		All organs/	Within normal limits	

TL: total litter loss

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

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

Animal No.	Organs	Findings	Notes
F05049	All organs/	Within normal limits	
F05050	All organs/	Within normal limits	
F05051	All organs/	Within normal limits	
F05052	All organs/	Within normal limits	
F05053	All organs/	Within normal limits	

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

Appendix 32-2 (continued). Macroscopic findings of female rats at the end of the administration period, satellite group

Animal No.	Organs	Findings	Notes
F06056	All organs/	Within normal limits	
F06057	All organs/	Within normal limits	
F06058	All organs/	Within normal limits	
F06059	All organs/	Within normal limits	
F06060	All organs/	Within normal limits	

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

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

Animal No.	Organs	Findings	Notes
F05054	Adrenal gland/ Liver/ Posterior vena cava/ Spleen/	Enlargement Malposition Reddish area Abnormal lobulation Malposition Cyst	Right Left Left Caudate lobe Left side
F05055	All organs/	Within normal limits	
F05056	All organs/	Within normal limits	
F05057	All organs/	Within normal limits	
F05058	All organs/	Within normal limits	

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

Appendix 32-3 (continued). Macroscopic findings of female rats at the end of the recovery period

Animal No.	Organs	Findings	Notes
F06061	All organs/	Within normal limits	
F06062	All organs/	Within normal limits	
F06063	All organs/	Within normal limits	
F06064	All organs/	Within normal limits	
F06065	All organs/	Within normal limits	

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

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

Animal No.	Organs	Findings	Notes
M01001	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Cyst P	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Degeneration/fibrosis, myocardial ±	Focal
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Fatty change, hepatocyte + Tension lipidosis +	Periportal
	Pancreas /	Atrophy, acinar cell ±	Focal
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown + Hematopoiesis, extramedullary +	
	Kidney /	Within normal limits	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Testis /	Within normal limits	
	Epididymis /	Within normal limits	
	Prostate /	Cellular infiltration, lymphocyte ±	Interstitial
	Seminal vesicle /	Within normal limits	
Coagulating gland /	Within normal limits		

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

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

Animal No.	Organs	Findings	Notes
M01001	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	
M01002	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Degeneration/fibrosis, myocardial ±	Focal
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Fatty change, hepatocyte ± Nodule, hepatodiaphragmatic P	Periportal With focal fibrosis
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown ± Hematopoiesis, extramedullary +	
	Kidney /	Within normal limits	

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

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

Animal No.	Organs	Findings	Notes
M01002	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Testis /	Within normal limits	
	Epididymis /	Within normal limits	
	Prostate /	Cellular infiltration, lymphocyte +	Interstitial
	Seminal vesicle /	Within normal limits	
	Coagulating gland /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	
M01003	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Atrophy, acinar cell ±	Focal
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Degeneration/fibrosis, myocardial ±	Focal
	Trachea /	Within normal limits	
	Lung /	Hemorrhage +	Alveolus, Focal, With inflammatory cell infiltration
	Bronchus /	Within normal limits	
	Liver /	Fatty change, hepatocyte 2+	Periportal
	Pancreas /	Atrophy, acinar cell ±	Focal
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
Ileum /	Within normal limits		
Cecum /	Within normal limits		

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

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

Animal No.	Organs	Findings	Notes
M01003	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown + Hematopoiesis, extramedullary +	
	Kidney /	Basophilic tubule, cortex ±	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Testis /	Within normal limits	
	Epididymis /	Within normal limits	
	Prostate /	Cellular infiltration, lymphocyte ±	Interstitial
	Seminal vesicle /	Within normal limits	
	Coagulating gland /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
Femur /	Within normal limits		
Marrow, femur /	Within normal limits		
M01004	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Ultimobranchial body P	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Fatty change, hepatocyte ±	Periportal

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

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

Animal No.	Organs	Findings	Notes
M01004	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown + Hematopoiesis, extramedullary +	
	Kidney /	Basophilic tubule, cortex ±	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Testis /	Within normal limits	
	Epididymis /	Within normal limits	
	Prostate /	Within normal limits	
	Seminal vesicle /	Within normal limits	
	Coagulating gland /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
Marrow, femur /	Within normal limits		
Adipose tissue /	Necrosis, fat +		
M01005	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
Thyroid gland /	Within normal limits		

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

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

Animal No.	Fate	Organs	Findings	Notes
M01005		Parathyroid gland /	Within normal limits	
		Thymus /	Within normal limits	
		Heart /	Within normal limits	
		Trachea /	Within normal limits	
		Lung /	Accumulation, foam cell ±	Alveolus
		Bronchus /	Within normal limits	
		Liver /	Microgranuloma ±	
		Pancreas /	Within normal limits	
		Stomach /	Within normal limits	
		Duodenum /	Within normal limits	
		Jejunum /	Within normal limits	
		Ileum /	Within normal limits	
		Cecum /	Within normal limits	
		Colon /	Within normal limits	
		Rectum /	Within normal limits	
		Lymph node, mesenteric /	Within normal limits	
		Spleen /	Deposit, pigment, brown ± Hematopoiesis, extramedullary ±	
		Kidney /	Basophilic tubule, cortex ±	
		Urinary bladder /	Within normal limits	
		Adrenal gland /	Within normal limits	
		Testis /	Within normal limits	
		Epididymis /	Within normal limits	
		Prostate /	Cellular infiltration, lymphocyte +	Interstitial
		Seminal vesicle /	Within normal limits	
		Coagulating gland /	Within normal limits	
		Eyeball /	Within normal limits	
		Harderian gland /	Cellular infiltration, lymphocyte ±	Interstitial
Sciatic nerve /	Within normal limits			
Skeletal muscle /	Within normal limits			
Femur /	Within normal limits			
Marrow, femur /	Within normal limits			
M01006	S	Thymus /	Atrophy ±	

S: Sacrificed during dosing period

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

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

Animal No.	Fate	Organs	Findings	Notes
M01006	S	Liver / Spleen /	Leukemic cell + Deposit, pigment, brown ± Increase, red pulp + Leukemic cell 2+	Sinusoid Red pulp
		Urinary bladder / Sciatic nerve / Skeletal muscle / Femur / Marrow, femur / Hematopoietic system / Hindlimb /	Within normal limits Within normal limits Within normal limits Leukemic cell + Leukemic cell 3+ Leukemia, myeloid P Abscess ±	Periosteum, Muscular layer Hair follicle, With edema, Foot Muscular layer, Periosteum, Around tibia
		Marrow, others / Vertebral canal /	Leukemic cell 3+ Leukemic cell +	Vertebra, Tibia, Fibula Dura mater, Periosteum, Muscular layer

S: Sacrificed during dosing period

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

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

Animal No.	Organs	Findings	Notes
M04037	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Degeneration/fibrosis, myocardial ±	Focal
	Trachea /	Within normal limits	
	Lung /	Accumulation, foam cell +	Alveolus
	Bronchus /	Within normal limits	
	Liver /	Fatty change, hepatocyte +	Periportal
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Edema ±	Lamina propria, With lymphangiectasis
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown 2+ Hematopoiesis, extramedullary +	
	Kidney /	Basophilic tubule, cortex ± Eosinophilic body ±	Proximal tubule Submucosa, Focal
	Urinary bladder /	Mineralization ±	
	Adrenal gland /	Within normal limits	
	Testis /	Within normal limits	
	Epididymis /	Within normal limits	
	Prostate /	Within normal limits	
Seminal vesicle /	Within normal limits		
Coagulating gland /	Within normal limits		

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

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

Animal No.	Organs	Findings	Notes
M04037	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	
M04038	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Ultimobranchial body P	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Degeneration/fibrosis, myocardial ±	Focal
	Trachea /	Within normal limits	
	Lung /	Accumulation, foam cell ±	Alveolus
	Bronchus /	Within normal limits	
	Liver /	Fatty change, hepatocyte ±	Periportal
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
Spleen /	Deposit, pigment, brown + Hematopoiesis, extramedullary +		
Kidney /	Basophilic tubule, cortex ± Eosinophilic body +	Proximal tubule	

Continued

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

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

Animal No.	Organs	Findings	Notes
M04038	Kidney /	Hyperplasia, transitional cell ±	Renal pelvis
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Testis /	Within normal limits	
	Epididymis /	Within normal limits	
	Prostate /	Within normal limits	
	Seminal vesicle /	Within normal limits	
	Coagulating gland /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
Marrow, femur /	Within normal limits		
M04039	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Cellular infiltration, lymphocyte ±	Periarterial, Focal
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Fatty change, hepatocyte ±	Periportal
	Pancreas /	Atrophy, acinar cell ±	Focal
	Stomach /	Erosion ±	Limiting ridge
	Duodenum /	Within normal limits	
Jejunum /	Within normal limits		
Ileum /	Within normal limits		

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

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

Animal No.	Organs	Findings	Notes
M04039	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown ± Hematopoiesis, extramedullary ±	
	Kidney /	Fibrosis, focal ±	Subcapsule
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Testis /	Within normal limits	
	Epididymis /	Within normal limits	
	Prostate /	Within normal limits	
	Seminal vesicle /	Within normal limits	
	Coagulating gland /	Within normal limits	
	Eyeball /	Dysplasia, retina P	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
Femur /	Within normal limits		
Marrow, femur /	Within normal limits		
M04040	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Accumulation, foam cell ±	Alveolus
	Bronchus /	Within normal limits	

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

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

Animal No.	Organs	Findings	Notes
M04040	Liver /	Fatty change, hepatocyte 2+	Periportal
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown + Hematopoiesis, extramedullary +	
	Kidney /	Basophilic tubule, cortex +	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Testis /	Within normal limits	
	Epididymis /	Within normal limits	
	Prostate /	Within normal limits	
	Seminal vesicle /	Within normal limits	
	Coagulating gland /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
Sciatic nerve /	Within normal limits		
Skeletal muscle /	Within normal limits		
Femur /	Within normal limits		
Marrow, femur /	Within normal limits		
M04041	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	

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

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

Animal No.	Organs	Findings	Notes
M04041	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Within normal limits	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown + Hematopoiesis, extramedullary +	
	Kidney /	Basophilic tubule, cortex ± Eosinophilic body +	Proximal tubule
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Testis /	Within normal limits	
	Epididymis /	Within normal limits	
	Prostate /	Cellular infiltration, lymphocyte ±	Interstitial
	Seminal vesicle /	Within normal limits	
	Coagulating gland /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
Skeletal muscle /	Within normal limits		
Femur /	Within normal limits		
Marrow, femur /	Within normal limits		

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

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

Animal No.	Organs	Findings	Notes
M01008	Thyroid gland /	Within normal limits	
M01009	Thyroid gland /	Ultimobranchial body P	
M01010	Thyroid gland /	Cellular infiltration, lymphocyte ± Ultimobranchial body P	Interstitial, Focal
M01011	Thyroid gland /	Within normal limits	
M01012	Thyroid gland /	Within normal limits	

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

Appendix 33-2 (continued). Histopathological findings of male rats at the end of the recovery period [H.E. staining]

Animal No.	Organs	Findings	Notes
M04044	Thyroid gland /	Ultimobranchial body P	
M04045	Thyroid gland /	Within normal limits	
M04046	Thyroid gland /	Within normal limits	
M04047	Thyroid gland / Thymus /	Within normal limits Atrophy ±	
M04048	Pituitary gland / Thyroid gland /	Cyst P Within normal limits	

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

Appendix 34-1. Histopathological findings of female rats at the end of the administration period, satellite group [H.E. staining]

Animal No.	Organs	Findings	Notes
F01001	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Accumulation, foam cell +	Alveolus
	Bronchus /	Within normal limits	
	Liver /	Within normal limits	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown ± Hematopoiesis, extramedullary 2+	
	Kidney /	Within normal limits	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
Ovary /	Within normal limits		
Uterus /	Within normal limits		
Vagina /	Within normal limits		
Eyeball /	Within normal limits		
Harderian gland /	Within normal limits		
Sciatic nerve /	Within normal limits		

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

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

Animal No.	Organs	Findings	Notes
F01001	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	
F01005	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Cyst P	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Ectopic thymic tissue P	
		Ultimobranchial body P	
	Parathyroid gland /	Within normal limits	
	Thymus /	Hyperplasia, epithelial tubule/cord ±	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Metaplasia, osseous ±	Focal
	Bronchus /	Within normal limits	
	Liver /	Within normal limits	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown + Hematopoiesis, extramedullary 2+	
	Kidney /	Within normal limits	
Urinary bladder /	Within normal limits		
Adrenal gland /	Within normal limits		
Ovary /	Within normal limits		

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

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

Animal No.	Organs	Findings	Notes
F01005	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Dysplasia, retina P	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	
F01006	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Hyperplasia, epithelial tubule/cord ±	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Within normal limits	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
Rectum /	Within normal limits		
Lymph node, mesenteric /	Within normal limits		
Spleen /	Deposit, pigment, brown + Hematopoiesis, extramedullary 2+		

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

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

Animal No.	Organs	Findings	Notes
F01006	Kidney /	Within normal limits	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
Marrow, femur /	Within normal limits		
F01007	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Accumulation, foam cell ±	Alveolus
	Bronchus /	Within normal limits	
	Liver /	Within normal limits	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
Cecum /	Within normal limits		
Colon /	Within normal limits		

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

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

Animal No.	Organs	Findings	Notes
F01007	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown + Hematopoiesis, extramedullary +	
	Kidney /	Within normal limits	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
Marrow, femur /	Within normal limits		
F01012	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Necrosis, focal ±	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
Duodenum /	Within normal limits		

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

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

Animal No.	Organs	Findings	Notes
F01012	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown + Hematopoiesis, extramedullary 2+	
	Kidney /	Within normal limits	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	

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

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

Animal No.	Fate	Organs	Findings	Notes
F02020		Ileum /	Thinning, muscular layer +	Focal, Diverticulum area
F02023	NP	Vagina /	Dilatation, cystic P Mucinous degeneration 3+	With cell debris Mucosa

NP: Not pregnant

Combined repeat dose and reproductive/developmental toxicity screening test of Cyclopentanone by oral administration in rats
 Appendix 34-1 (continued). Histopathological findings of female rats at the end of the administration period [H.E. staining]

Animal No.	Fate	Organs	Findings	Notes
F03028	TL	Thymus /	Atrophy 2+	

TL: total litter loss

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

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

Animal No.	Organs	Findings	Notes
F04039	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
Marrow, femur /	Within normal limits		
F04040	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Hyperplasia, epithelial tubule/cord ±	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Accumulation, foam cell ± Microgranuloma ±	Alveolus
	Bronchus /	Within normal limits	
	Liver /	Within normal limits	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
Colon /	Within normal limits		

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

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

Animal No.	Organs	Findings	Notes
F04040	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown + Hematopoiesis, extramedullary +	
	Kidney /	Within normal limits	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
Marrow, femur /	Within normal limits		
F04041	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Within normal limits	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
Duodenum /	Within normal limits		

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

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

Animal No.	Organs	Findings	Notes
F04041	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown + Hematopoiesis, extramedullary +	
	Kidney /	Within normal limits	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
Femur /	Within normal limits		
Marrow, femur /	Within normal limits		
F04043	Thymus /	Atrophy +	
F04045	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Hyperplasia, epithelial tubule/cord ±	
	Heart /	Within normal limits	
Trachea /	Within normal limits		

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

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

Animal No.	Organs	Findings	Notes
F04045	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Within normal limits	
	Pancreas /	Within normal limits	
	Stomach /	Edema + Hyperplasia, squamous cell ±	Lamina propria/submucosa, Forestomach Forestomach
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown + Hematopoiesis, extramedullary 2+	
	Kidney /	Within normal limits	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
Femur /	Within normal limits		
Marrow, femur /	Within normal limits		
F04048	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	

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

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

Animal No.	Organs	Findings	Notes
F04048	Thyroid gland /	Ultimobranchial body P	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Within normal limits	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown 2+	
		Hematopoiesis, extramedullary 2+	
	Kidney /	Within normal limits	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	

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

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

Animal No.	Organs	Findings	Notes
F05049	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Ultimobranchial body P	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Accumulation, foam cell ±	Alveolus
	Bronchus /	Within normal limits	
	Liver /	Within normal limits	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown + Hematopoiesis, extramedullary +	
	Kidney /	Within normal limits	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
Eyeball /	Within normal limits		
Harderian gland /	Within normal limits		
Sciatic nerve /	Within normal limits		

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

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

Animal No.	Organs	Findings	Notes
F05049	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	
F05050	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Hyperplasia, epithelial tubule/cord ±	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Within normal limits	
	Pancreas /	Atrophy, acinar cell ±	Focal
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown 2+ Hematopoiesis, extramedullary +	
Kidney /	Within normal limits		
Urinary bladder /	Within normal limits		
Adrenal gland /	Within normal limits		
Ovary /	Within normal limits		
Uterus /	Within normal limits		

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

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

Animal No.	Organs	Findings	Notes
F05050	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	
F05051	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Cyst P	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Accumulation, foam cell ±	Alveolus
	Bronchus /	Within normal limits	
	Liver /	Fatty change, hepatocyte ±	Periportal
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
Rectum /	Within normal limits		
Lymph node, mesenteric /	Within normal limits		
Spleen /	Deposit, pigment, brown 2+		
	Hematopoiesis, extramedullary +		
Kidney /	Within normal limits		

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

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

Animal No.	Organs	Findings	Notes
F05051	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Cellular infiltration, lymphocyte ±	Interstitial
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
Marrow, femur /	Within normal limits		
F05052	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Within normal limits	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
Ileum /	Within normal limits		
Cecum /	Within normal limits		
Colon /	Within normal limits		
Rectum /	Within normal limits		

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

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

Animal No.	Organs	Findings	Notes
F05052	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown 2+	
		Hematopoiesis, extramedullary +	
	Kidney /	Within normal limits	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Dysplasia, retina P	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
Femur /	Within normal limits		
Marrow, femur /	Within normal limits		
F05053	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Ultimobranchial body P	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Within normal limits	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
Jejunum /	Within normal limits		

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

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

Animal No.	Organs	Findings	Notes
F05053	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown + Hematopoiesis, extramedullary +	
	Kidney /	Basophilic tubule, cortex ±	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	

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

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

Animal No.	Organs	Findings	Notes
F06056	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Metaplasia, osseous ±	Focal
	Bronchus /	Within normal limits	
	Liver /	Within normal limits	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown 2+ Hematopoiesis, extramedullary +	
	Kidney /	Basophilic tubule, cortex ±	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
Eyeball /	Within normal limits		
Harderian gland /	Within normal limits		
Sciatic nerve /	Within normal limits		

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

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

Animal No.	Organs	Findings	Notes
F06057	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur / Marrow, femur /	Within normal limits Within normal limits	
F06058	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Within normal limits	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Within normal limits	
	Pancreas /	Within normal limits	
	Stomach /	Heterotopic gastric gland P	Submucosa, Forestomach
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
Rectum /	Within normal limits		
Lymph node, mesenteric /	Within normal limits		
Spleen /	Deposit, pigment, brown 2+		

Continued

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

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

Animal No.	Organs	Findings	Notes
F06058	Spleen /	Hematopoiesis, extramedullary +	
	Kidney /	Within normal limits	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Luteinized follicle, cystic +	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	
F06059	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Ultimobranchial body P	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Within normal limits	
	Bronchus /	Within normal limits	
	Liver /	Within normal limits	
	Pancreas /	Within normal limits	
	Stomach /	Within normal limits	
	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
Ileum /	Within normal limits		
Cecum /	Within normal limits		

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

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

Animal No.	Organs	Findings	Notes
F06059	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown 2+ Hematopoiesis, extramedullary +	
	Kidney /	Mineralization ±	Cortico-medullary junction
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Luteinized follicle, cystic ±	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
Marrow, femur /	Within normal limits		
F06060	Brain /	Within normal limits	
	Spinal cord /	Within normal limits	
	Pituitary gland /	Within normal limits	
	Submandibular gland /	Within normal limits	
	Sublingual gland /	Within normal limits	
	Lymph node, submandibular /	Within normal limits	
	Thyroid gland /	Ultimobranchial body P	
	Parathyroid gland /	Within normal limits	
	Thymus /	Within normal limits	
	Heart /	Within normal limits	
	Trachea /	Within normal limits	
	Lung /	Accumulation, foam cell ±	Alveolus
	Bronchus /	Within normal limits	
	Liver /	Fatty change, hepatocyte ±	Periportal
	Pancreas /	Within normal limits	
Stomach /	Within normal limits		

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

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

Animal No.	Organs	Findings	Notes
F06060	Duodenum /	Within normal limits	
	Jejunum /	Within normal limits	
	Ileum /	Within normal limits	
	Cecum /	Within normal limits	
	Colon /	Within normal limits	
	Rectum /	Within normal limits	
	Lymph node, mesenteric /	Within normal limits	
	Spleen /	Deposit, pigment, brown 2+	
		Hematopoiesis, extramedullary +	
	Kidney /	Within normal limits	
	Urinary bladder /	Within normal limits	
	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
	Eyeball /	Within normal limits	
	Harderian gland /	Within normal limits	
	Sciatic nerve /	Within normal limits	
	Skeletal muscle /	Within normal limits	
	Femur /	Within normal limits	
	Marrow, femur /	Within normal limits	

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

Appendix 34-3. Histopathological findings of female rats at the end of the recovery period [H.E. staining]

Animal No.	Organs	Findings	Notes
F05054	Liver /	Fatty change, hepatocyte ±	Periportal
	Spleen /	Necrosis, focal ± Deposit, pigment, brown 3+	
	Adrenal gland /	Dilatation, cystic ± Hematopoiesis, extramedullary 2+	Artery, Capsule
	Ovary /	Hypoplasia +	Cortex, Unilateral
	Uterus /	Mineralization ±	
	Vagina /	Within normal limits	
F05055	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
F05056	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
F05057	Adrenal gland /	Within normal limits	
	Ovary /	Within normal limits	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	
F05058	Adrenal gland /	Within normal limits	
	Ovary /	Luteinized follicle, cystic ±	
	Uterus /	Within normal limits	
	Vagina /	Within normal limits	

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

Appendix 34-3 (continued). Histopathological findings of female rats at the end of the recovery period [H.E. staining]

Animal No.	Organs	Findings	Notes
F06061	Adrenal gland / Ovary / Uterus / Vagina /	Within normal limits Within normal limits Within normal limits Within normal limits	
F06062	Adrenal gland / Ovary / Uterus / Vagina /	Within normal limits Within normal limits Within normal limits Within normal limits	
F06063	Adrenal gland / Ovary / Uterus / Vagina /	Within normal limits Within normal limits Within normal limits Within normal limits	
F06064	Adrenal gland / Ovary / Uterus / Vagina /	Within normal limits Within normal limits Within normal limits Within normal limits	
F06065	Adrenal gland / Ovary / Uterus / Vagina /	Within normal limits Decreased number, corpus luteum + Within normal limits Within normal limits	

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

Appendix 35-1. Results of observations about estrous cycle

Control (vehicle :corn oil)

Animal no.	Pre-mating period						Mating period	Times of vaginal estrus observed
	Pre-administration period			Administration period				
	Stage	Type	Mean length (days)	Type	Mean length (days)	Stage		
F01001	DDPEDDDDPEDDDDDE	5-day	5.0	DDPEDDDDPEDDDDDEDD	4-day	4.0	P PL	1
F01002	DDDEDDDEDDPEDD	4-day	4.0	DEDDDEDDPEDDDE	4-day	4.0	DD D PL	1
F01003	DDPEDDDDPEDDPEDD	4-day	4.0	PEDDDDPEDDPEDDDE	4-day	4.0	DD P PL	1
F01004	DPEDDDDPEDDPEDDP	4-day	4.0	EDDDPEDDPEEDDDDE	4/5-day	4.3	DD P PL	1
F01005	DDDEDDDEDDPEDDDD	4-day	4.0	EDDDDEDDDEDDDEED	4-day	4.0	D P PL	1
F01006	DDPEDDDDPEDDPEDD	4-day	4.0	PEDDDEDDPEDDPEDD	4-day	4.0	P PL	1
F01007	DDDDPEDDDDPEDDDEED	4/5-day	4.3	DPEDDDDPEDDPEDDP	4-day	4.0	PL	1
F01008	DDPEDDDDPEDDPEDD	4-day	4.0	PEDDDDPEDDPEDDPE	4-day	4.0	DD P PL	1
F01009	EDDDDDPEDDDDPEDDDD	5-day	5.0	PEDDDDPEDDDEEDDD	5-day	5.0	D P PL	1
F01010	DDPEDDDEDDPEDD	4-day	4.0	PEDDDDPEDDPEDDPE	4-day	4.0	DD P PL	1
F01011	DDDDPEDDDEDDDEED	4/5-day	4.3	DPEDDDDPEDDPPED	5-day	5.0	D P PL	1
F01012	EDDDDEDDDDDEDDDD	4/5-day	4.6	EDDDPEDDPEEDDDP	5-day	5.0	PL	1
Mean			4.3			4.3		1.0
S.D.			0.4			0.4		0.0
(N)			(12)			(12)		(12)

D, diestrus; P, proestrus; E, estrus; PL, vaginal plug; SP, sperm positive

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

Appendix 35-2. Results of observations about estrous cycle

CPN 30 mg/kg

Animal no.	Pre-mating period						Mating period		Times of vaginal estrus observed
	Pre-administration period			Administration period			Stage		
	Stage	Type	Mean length (days)	Type	Mean length (days)				
F02013	E D D D P E D D D P E D D D	5-day	5.0	P E D D D P E D D D E D D D	4/5-day	4.5	P PL	1	
F02014	D D E D D D P E D D D P E D	5-day	5.0	D D P E D D D E E D D D P E	5-day	5.0	D D D P PL	1	
F02015	D D P E D D P E D D P E D D	4-day	4.0	P E D D P E D D P E D D P E	4-day	4.0	D D P PL	1	
F02016	D E D D D E D D D E D D D D	4/5-day	4.3	E D D P E D D P E D D P E D	4-day	4.0	D P PL	1	
F02017	D D E D D D E D D D E D D D	4-day	4.0	E D D D E D D D E D D D E D	4-day	4.0	D P PL	1	
F02018	D D D P E D D D P E D D D P	5-day	5.0	E D D D P E D D D P E D D D	5-day	5.0	P PL	1	
F02019	D D D E D D P E D D D E D D	4-day	4.0	P E D D P E D D P E D D P E	4-day	4.0	D D P PL	1	
F02020	P E D D D P E D D D P E D D	5-day	5.0	D P E D D D P E D D D P E D	5-day	5.0	D D PL	1	
F02021	D P E D D P E D D P E D D P	4-day	4.0	E D D P E D D P E D D P E D	4-day	4.0	D P PL	1	
F02022	E D D D E D D P E D D P E	4/5-day	4.3	D D P E D D P E D D P E D D	4-day	4.0	P PL	1	
F02023	D D D E D D D E D D D E D D	4-day	4.0	D E D D D E D D P E D D D E	4-day	4.0	PL	1	
F02024	D D P E D D D E D D P E D D	4-day	4.0	P E D D P E D D P E D D D E	4-day	4.0	D D P PL	1	
Mean			4.4			4.3		1.0	
S.D.			0.5			0.5		0.0	
(N)			(12)			(12)		(12)	

D, diestrus; P, proestrus; E, estrus; PL, vaginal plug; SP, sperm positive

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

Appendix 35-3. Results of observations about estrous cycle

CPN 100 mg/kg

Animal no.	Pre-mating period						Mating period		Times of vaginal estrus observed
	Pre-administration period			Administration period			Stage		
	Stage	Type	Mean length (days)	Type	Mean length (days)				
F03025	D D D P E D D D P E D D D P	5-day	5.0	E D D P E D D D E D D D P	4/5-day	4.5	E PL	1	
F03026	D D P E D D P E D D P E D D	4-day	4.0	P E D D P E D D P E D D P E	4-day	4.0	D D P PL	1	
F03027	D D P E D D D P E D D D P E	5-day	5.0	D D D P E D D D P E D D D E	4/5-day	4.6	D D D PL	1	
F03028	D P E D D D P E D D P E E D	5-day	5.0	D D E E D D D E D D D P E D	4/5-day	4.5	D D P PL	1	
F03029	P E D D D E E D D D E D D D	4/5-day	4.5	D E D D D P E D D D E D D D	4/5-day	4.5	P PL	1	
F03030	D D E D D P E D D P E D D P	4-day	4.0	E D D P E D D P E D D P E D	4-day	4.0	D P PL	1	
F03031	E D D P E D D P E D D P E D	4-day	4.0	D P E D D P E D D P E D D P	4-day	4.0	PL	1	
F03032	D D P E D D P E D D P E D D	4-day	4.0	D E D D P E D D P E D D P E	4-day	4.0	D D P PL	1	
F03033	P E D D P E D D P E D D P E	4-day	4.0	D D P E D D P E D D P E D D	4-day	4.0	P PL	1	
F03034	D D P E D D P E D D P E D D	4-day	4.0	P E D D P E D D P E D D P E	4-day	4.0	D D D D D D D D D D D D	Not copulated	
F03035	E D D D P E D D D P E D D D	5-day	5.0	E E D D D E E D D D E D D D	4/5-day	4.5	P PL	1	
F03036	P E D D P E D D P E D D P E	4-day	4.0	D D P E D D P E D D P E D D	4-day	4.0	P PL	1	
Mean			4.4			4.2		1.0	
S.D.			0.5			0.3		0.0	
(N)			(12)			(12)		(11)	

D, diestrus; P, proestrus; E, estrus; PL, vaginal plug; SP, sperm positive

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

Appendix 35-4. Results of observations about estrous cycle

CPN 300 mg/kg

Animal no.	Pre-mating period						Mating period	Times of vaginal estrus observed
	Pre-administration period			Administration period				
	Stage	Type	Mean length (days)	Type	Mean length (days)	Stage		
F04037	E D D P E D D P E D D P E D	4-day	4.0	D P E D D P E E D D P E D D	4/5-day	4.5	P PL	1
F04038	D D P E D D P E D D P E D D	4-day	4.0	P E D D D E D D P E D D P E	4-day	4.0	D D P PL	1
F04039	D D D E D D D E E D D D P E	5-day	5.0	D D D P E D D D P E D D D P	5-day	5.0	PL	1
F04040	E D D D E D D D E D D D E D	4-day	4.0	D P E D D P E D D P E D D P	4-day	4.0	PL	1
F04041	E D D P E D D D E D D P E D	4-day	4.0	D P E D D P E D D P E D D P	4-day	4.0	PL	1
F04042	D D E D D P E D D P E D D P	4-day	4.0	E D D P E D D P E D D P E D	4-day	4.0	D P PL	1
F04043	D D D E D D P E D D P E D D	4-day	4.0	P E D D P E D D P E D D P E	4-day	4.0	D D P PL	1
F04044	D P E D D P E D D P E D D P	4-day	4.0	E D D P E D D P E D D D P E	4/5-day	4.3	D D P PL	1
F04045	D E D D D E D D D E D D P E	4-day	4.0	D D P E D D P E D D D E D D	4-day	4.0	P PL	1
F04046	D E D D D E D D P E D D P E	4-day	4.0	D D P E D D P E D D D E D D	4-day	4.0	D PL	1
F04047	D D E D D P E D D P E D D P	4-day	4.0	E D D P E D D P E D D P E D	4-day	4.0	D P PL	1
F04048	P E D D P E E D D D P E D D	5-day	5.0	D D E D D P E D D P E D D P	4-day	4.0	PL	1
Mean			4.2			4.2		1.0
S.D.			0.4			0.3		0.0
(N)			(12)			(12)		(12)

D, diestrus; P, proestrus; E, estrus; PL, vaginal plug; SP, sperm positive

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

Appendix 36-1. Results of observations about reproductive performance

Control (vehicle: corn oil)

Male no.	Female no.	Copulation	Conception	Pairing days until copulation
M01001	F01001	+	+	2
M01002	F01002	+	+	4
M01003	F01003	+	+	4
M01004	F01004	+	+	4
M01005	F01005	+	+	3
M01007	F01006	+	+	2
M01007	F01007	+	+	1
M01008	F01008	+	+	4
M01009	F01009	+	+	3
M01010	F01010	+	+	4
M01011	F01011	+	+	3
M01012	F01012	+	+	1
Total		+: 12, -: 0	+: 12, -: 0	
Mean				2.9
S.D.				1.2
(N)				(12)

+, confirmed

-, not confirmed

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

Appendix 36-2. Results of observations about reproductive performance

CPN 30 mg/kg

Male no.	Female no.	Copulation	Conception	Pairing days until copulation
M02013	F02013	+	+	2
M02014	F02014	+	+	5
M02015	F02015	+	+	4
M02016	F02016	+	+	3
M02017	F02017	+	+	3
M02018	F02018	+	+	2
M02019	F02019	+	+	4
M02020	F02020	+	+	3
M02021	F02021	+	+	3
M02022	F02022	+	+	2
M02023	F02023	+	-	1
M02024	F02024	+	+	4
Total		+: 12, -: 0	+: 11, -: 1	
Mean				3.0
S.D.				1.1
(N)				(12)

+, confirmed

-, not confirmed

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

Appendix 36-3. Results of observations about reproductive performance

CPN 100 mg/kg

Male no.	Female no.	Copulation	Conception	Pairing days until copulation
M03025	F03025	+	+	2
M03026	F03026	+	+	4
M03027	F03027	+	+	4
M03028	F03028	+	+	4
M03029	F03029	+	+	2
M03030	F03030	+	+	3
M03031	F03031	+	+	1
M03032	F03032	+	+	4
M03033	F03033	+	+	2
M03034	F03034	-		Not copulated
M03035	F03035	+	+	2
M03036	F03036	+	+	2
Total		+: 11, -: 1	+: 11, -: 0	
Mean				2.7
S.D.				1.1
(N)				(11)

+, confirmed

-, not confirmed

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

Appendix 36-4. Results of observations about reproductive performance

CPN 300 mg/kg

Male no.	Female no.	Copulation	Conception	Pairing days until copulation
M04037	F04037	+	+	2
M04038	F04038	+	+	4
M04039	F04039	+	+	1
M04040	F04040	+	+	1
M04041	F04041	+	+	1
M04042	F04042	+	+	3
M04043	F04043	+	+	4
M04044	F04044	+	+	4
M04045	F04045	+	+	2
M04046	F04046	+	+	2
M04047	F04047	+	+	3
M04048	F04048	+	+	1
Total		+: 12, -: 0	+: 12, -: 0	
Mean				2.3
S.D.				1.2
(N)				(12)

+, confirmed

-, not confirmed

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

Appendix 37-1. Observation of offspring (F₁)

Control (vehicle: corn oil)																				
Dam No.	Gestation length (days)	Number of corpora lutea	Number of implantation scars	Implantation index (%)	Delivery index (%)	Number of offspring at birth					Delivery index (%)	Birth index (%)	Live birth index (%)	Number of live offspring			External abnormalities ^{b)}			
						Number of offspring	Live			Sex ratio				Dead offspring	4 days	Sex ratio	Viability index (%)	(Number)	%	
							Male	Female	Total											
																				Male
F01001	22	15	14	93.3	+	14	5	6	11	0.45	3	100.0	78.6	78.6	5	6	0.45	100.0	0	0.0
F01002	22	13	13	100.0	+	13	7	6	13	0.54	0	100.0	100.0	100.0	6	6	0.50	92.3	0	0.0
F01003	22	19	18	94.7	+	17	7	9	16	0.44	1	94.4	88.9	94.1	7	9	0.44	100.0	0	0.0
F01004	22	18	18	100.0	+	16	9	7	16	0.56	0	88.9	88.9	100.0	9	7	0.56	100.0	0	0.0
F01005	22	18	17	94.4	+	17	8	9	17	0.47	0	100.0	100.0	100.0	8	9	0.47	100.0	0	0.0
F01006	21	13	13	100.0	+	13	8	5	13	0.62	0	100.0	100.0	100.0	8	5	0.62	100.0	0	0.0
F01007	22	17	17	100.0	+	16	7	9	16	0.44	0	94.1	94.1	100.0	7	9	0.44	100.0	0	0.0
F01008	22	16	16	100.0	+	15	8	7	15	0.53	0	93.8	93.8	100.0	8	6	0.57	93.3	0	0.0
F01009	22	16	16	100.0	+	13	4	9	13	0.31	0	81.3	81.3	100.0	4	9	0.31	100.0	0	0.0
F01010	22	15	15	100.0	+	14	8	6	14	0.57	0	93.3	93.3	100.0	8	6	0.57	100.0	0	0.0
F01011	22	17	16	94.1	+	13	8	5	13	0.62	0	81.3	81.3	100.0	8	4	0.67	92.3	0	0.0
F01012	22	15	14	93.3	+	14	8	6	14	0.57	0	100.0	100.0	100.0	8	6	0.57	100.0	0	0.0
Number of dams	12	12	12	12	12 ^{a)}	12			12	12	12	12	12	12			12	12	12	12
Total		192	187			175	87	84	171		4				86	82			0	
Mean	21.9	16.0	15.6	97.5		14.6	7.3	7.0	14.3	0.51	0.3	93.9	91.7	97.7	7.2	6.8	0.51	98.2		0.0
S.D.	0.3	1.9	1.8	3.1		1.6	1.4	1.6	1.8	0.09	0.9	6.9	7.9	6.3	1.5	1.7	0.10	3.3		0.0
%					100.0															

+: Dams with live offspring, -: dams without live offspring

a): Number of dams with live offspring.

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

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

Appendix 37-2. Observation of offspring (F₁)

CPN 30 mg/kg																					
Dam No.	Gestation length (days)	Number of corpora lutea	Number of implantation scars	Implantation index (%)	Delivery index (%)	Number of offspring at birth					Sex ratio	Dead offspring	Delivery index (%)	Birth index (%)	Live birth index (%)	Number of live offspring				External abnormalities ^{b)}	
						Number of offspring	Live			Viability index (%)						Sex ratio	4 days	External abnormalities ^{b)}			
							Male	Female	Total									(Number)	%		
																				External abnormalities ^{b)}	
F02013	23	17	17	100.0	+	15	6	9	15	0.40	0	88.2	88.2	100.0	6	9	0.40	100.0	0	0.0	
F02014	22	17	16	94.1	+	16	9	6	15	0.60	1	100.0	93.8	93.8	9	6	0.60	100.0	0	0.0	
F02015	22	18	17	94.4	+	15	7	8	15	0.47	0	88.2	88.2	100.0	7	8	0.47	100.0	0	0.0	
F02016	22	17	16	94.1	+	16	7	7	14	0.50	2	100.0	87.5	87.5	7	7	0.50	100.0	0	0.0	
F02017	23	17	16	94.1	+	16	6	5	11	0.55	5	100.0	68.8	68.8	6	5	0.55	100.0	0	0.0	
F02018	22	19	17	89.5	+	16	7	9	16	0.44	0	94.1	94.1	100.0	7	9	0.44	100.0	0	0.0	
F02019	22	17	17	100.0	+	17	11	6	17	0.65	0	100.0	100.0	100.0	11	6	0.65	100.0	0	0.0	
F02020	22	17	17	100.0	+	16	7	9	16	0.44	0	94.1	94.1	100.0	7	9	0.44	100.0	0	0.0	
F02021	22	14	14	100.0	+	14	2	11	13	0.15	1	100.0	92.9	92.9	2	11	0.15	100.0	0	0.0	
F02022	22	13	13	100.0	+	11	5	6	11	0.45	0	84.6	84.6	100.0	5	6	0.45	100.0	0	0.0	
F02023	Not pregnant																				
F02024	22	15	15	100.0	+	15	6	9	15	0.40	0	100.0	100.0	100.0	6	9	0.40	100.0	0	0.0	
Number of dams	11	11	11	11	11 ^{a)}	11			11	11	11	11	11	11			11	11	11	11	
Total		181	175			167	73	85	158		9				73	85			0		
Mean	22.2	16.5	15.9	96.9		15.2	6.6	7.7	14.4	0.46	0.8	95.4	90.2	94.8	6.6	7.7	0.46	100.0		0.0	
S.D.	0.4	1.8	1.4	3.8		1.6	2.2	1.8	2.0	0.13	1.5	5.9	8.6	9.6	2.2	1.8	0.13	0.0		0.0	
%					100.0																
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN	KW	AN	KW	AN	KW	KW	AN	AN	AN	AN	KW	AN	

+: Dams with live offspring - -: dams without live offspring

a): Number of dams with live offspring

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

NS: Not significantly different from the control group.

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

KW: Analysis by Kruskal-Wallis' test (one-way layout).

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

Appendix 37-3. Observation of offspring (F₁)

CPN 100 mg/kg																				
Dam No.	Gestation length (days)	Number of corpora lutea	Number of implantation scars	Implantation index (%)	Delivery index (%)	Number of offspring at birth						Delivery index (%)	Birth index (%)	Live birth index (%)	Number of live offspring			External abnormalities ^{b)}		
						Number of offspring	Sex ratio			Dead offspring	4 days				Sex ratio	Viability index (%)	(Number)	%		
							Live													
							Male	Female	Total											
F03025	23	15	15	100.0	+	14	5	9	14	0.36	0	93.3	93.3	100.0	5	9	0.36	100.0	0	0.0
F03026	22	19	17	89.5	+	16	7	9	16	0.44	0	94.1	94.1	100.0	7	9	0.44	100.0	0	0.0
F03027	22	19	18	94.7	+	17	8	8	16	0.50	1	94.4	88.9	94.1	8	8	0.50	100.0	0	0.0
F03028	23	17	15	88.2	+	13	5	2	7	0.71	6	86.7	46.7	53.8	0	0		0.0	0	0.0
F03029	22	19	18	94.7	+	15	10	5	15	0.67	0	83.3	83.3	100.0	10	5	0.67	100.0	0	0.0
F03030	22	15	15	100.0	+	15	7	8	15	0.47	0	100.0	100.0	100.0	7	8	0.47	100.0	0	0.0
F03031	22	15	15	100.0	+	11	4	6	10	0.40	1	73.3	66.7	90.9	4	6	0.40	100.0	0	0.0
F03032	22	15	15	100.0	+	15	6	9	15	0.40	0	100.0	100.0	100.0	6	9	0.40	100.0	0	0.0
F03033	22	15	14	93.3	+	14	9	5	14	0.64	0	100.0	100.0	100.0	9	5	0.64	100.0	0	0.0
F03035	22	17	16	94.1	+	13	6	7	13	0.46	0	81.3	81.3	100.0	6	7	0.46	100.0	0	0.0
F03036	22	15	13	86.7	+	11	8	3	11	0.73	0	84.6	84.6	100.0	8	3	0.73	100.0	0	0.0
Number of dams	11	11	11	11	11 ^{a)}	11			11	11	11	11	11	11			10	11	11	11
Total			181	171		154	75	71	146		8				70	69			0	
Mean	22.2	16.5	15.5	94.7		14.0	6.8	6.5	13.3	0.53	0.7	90.1	85.4	94.4	6.4	6.3	0.51	90.9		0.0
S.D.	0.4	1.8	1.6	5.0		1.9	1.8	2.5	2.8	0.14	1.8	8.9	16.3	13.8	2.7	2.9	0.13	30.2		0.0
%					100.0															
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN	KW	AN	KW	AN	KW	KW	AN	AN	AN	KW		AN

+: Dams with live offspring. -: dams without live offspring.

a): Number of dams with live offspring.

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

NS: Not significantly different from the control group.

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

KW: Analysis by Kruskal-Wallis' test (one-way layout).

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

Appendix 37-4. Observation of offspring (F₁)

Dam No.	Gestation length (days)	Number of corpora lutea	Number of implantation scars	Implantation index (%)	Delivery index (dams) (%)	Number of offspring at birth						Delivery index (offspring) (%)	Birth index (%)	Live birth index (%)	Number of live offspring			External abnormalities ^{b)}		
						Number of offspring	Sex ratio			Dead offspring	4 days				Sex ratio	Viability index (%)	(Number)	%		
							Live				Male								Female	Viability index (%)
							Male	Female	Total											
F04037	24	16	16	100.0	—	14	0	0	0	0.71	14	87.5	0.0	0.0	10	4	0.71	100.0	0	0.0
F04038	22	16	15	93.8	+	14	10	4	14	0.31	0	93.3	93.3	100.0	4	9	0.31	100.0	0	0.0
F04039	22	15	14	93.3	+	13	4	9	13	0.41	0	92.9	92.9	100.0	7	10	0.41	100.0	0	0.0
F04040	22	17	17	100.0	+	17	7	10	17	0.36	2	100.0	87.5	87.5	5	9	0.36	100.0	0	0.0
F04041	22	18	16	88.9	+	16	5	9	14	0.31	0	100.0	100.0	100.0	4	11	0.27	93.8	0	0.0
F04042	23	17	16	94.1	+	16	5	11	16	0.44	0	88.9	88.9	100.0	7	9	0.44	100.0	0	0.0
F04043	22	18	18	100.0	+	16	7	9	16	0.50	0	93.3	93.3	100.0	7	7	0.50	100.0	0	0.0
F04044	22	15	15	100.0	+	14	7	7	14	0.56	0	100.0	100.0	100.0	9	7	0.56	100.0	0	0.0
F04045	22	18	16	88.9	+	16	9	7	16	0.53	0	93.8	93.8	100.0	8	7	0.53	100.0	0	0.0
F04046	22	16	16	100.0	+	15	8	7	15	0.33	0	100.0	100.0	100.0	6	12	0.33	100.0	0	0.0
F04047	22	18	18	100.0	+	18	6	12	18	0.54	3	100.0	81.3	81.3	6	6	0.50	92.3	0	0.0
F04048	22	16	16	100.0	+	16	7	6	13						6	6	0.50	92.3	0	0.0
Number of dams	12	12	12	12	11 ^{a)}	12			12	11	12	12	12	12			11	11	11	11
Total		200	193			185	75	91	166		19				73	91			0	
Mean	22.3	16.7	16.1	96.6		15.4	6.3	7.6	13.8	0.45	1.6	95.8	85.9	89.1	6.6	8.3	0.45	98.7		0.0
S.D.	0.6	1.2	1.2	4.5		1.4	2.6	3.3	4.6	0.13	4.0	4.7	27.7	28.7	1.9	2.3	0.13	2.8		0.0
%					91.7															
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	AN	AN	AN	AN	AN	AN	AN	AN	KW	AN	KW	AN	KW	KW	AN	AN	AN	KW	AN	AN

+: Dams with live offspring. -: dams without live offspring

a): Number of dams with live offspring

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

NS: Not significantly different from the control group.

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

KW: Analysis by Kruskal-Wallis' test (one-way layout).

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

Appendix 38-1. Body weights of offspring (F₁) before weaning

Control (vehicle: corn oil)

Dam No.	Days after birth							
	Male body weight				Female body weight			
	0		4		0		4	
F01001	6.7	(5)	11.0	(5)	6.4	(6)	10.9	(6)
F01002	7.0	(7)	10.9	(6)	6.8	(6)	11.1	(6)
F01003	6.6	(7)	11.1	(7)	6.3	(9)	10.6	(9)
F01004	6.8	(9)	10.9	(9)	6.7	(7)	10.7	(7)
F01005	6.7	(8)	11.2	(8)	5.9	(9)	9.9	(9)
F01006	6.1	(8)	10.0	(8)	5.7	(5)	9.5	(5)
F01007	6.8	(7)	10.9	(7)	6.1	(9)	10.0	(9)
F01008	6.5	(8)	10.6	(8)	6.2	(7)	10.2	(6)
F01009	7.1	(4)	11.6	(4)	6.6	(9)	10.6	(9)
F01010	7.4	(8)	11.5	(8)	6.5	(6)	10.6	(6)
F01011	6.5	(8)	10.4	(8)	6.1	(5)	10.0	(4)
F01012	7.1	(8)	10.6	(8)	6.7	(6)	9.9	(6)
Number of dams	12		12		12		12	
Mean	6.8		10.9		6.3		10.3	
S.D.	0.3		0.5		0.3		0.5	

Each value shows mean per dam (g).

Figures in parentheses indicate number of offspring.

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

Appendix 38-2. Body weights of offspring (F₁) before weaning

CPN 30 mg/kg

Dam No.	Days after birth							
	Male body weight				Female body weight			
	0		4		0		4	
F02013	7.0	(6)	11.2	(6)	6.4	(9)	10.3	(9)
F02014	6.5	(9)	9.7	(9)	6.6	(6)	9.7	(6)
F02015	6.9	(7)	11.1	(7)	6.6	(8)	9.8	(8)
F02016	6.7	(7)	9.9	(7)	6.2	(7)	9.4	(7)
F02017	6.5	(6)	10.2	(6)	6.0	(5)	9.6	(5)
F02018	6.4	(7)	10.7	(7)	6.0	(9)	10.3	(9)
F02019	6.2	(11)	10.3	(11)	5.7	(6)	9.1	(6)
F02020	6.4	(7)	10.3	(7)	6.2	(9)	10.1	(9)
F02021	7.5	(2)	12.8	(2)	6.9	(11)	11.6	(11)
F02022	6.7	(5)	12.5	(5)	6.3	(6)	11.7	(6)
F02023	Not pregnant							
F02024	6.7	(6)	10.3	(6)	6.4	(9)	10.1	(9)
Number of dams	11		11		11		11	
Mean	6.7		10.8		6.3		10.2	
S.D.	0.4		1.0		0.3		0.8	
Significance	NS		NS		NS		NS	
Statistical method	AN		AN		AN		AN	

Each value shows mean per dam (g).

Figures in parentheses indicate number of offspring.

NS: Not significantly different from the control group.

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

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

Appendix 38-3. Body weights of offspring (F₁) before weaning

CPN 100 mg/kg

Dam No.	Days after birth							
	Male body weight				Female body weight			
	0		4		0		4	
F03025	7.1	(5)	10.3	(5)	6.6	(9)	9.7	(9)
F03026	6.7	(7)	11.2	(7)	6.1	(9)	10.1	(9)
F03027	5.9	(8)	10.4	(8)	5.7	(8)	9.7	(8)
F03028	6.1	(5)	#		6.3	(2)	#	
F03029	6.6	(10)	11.1	(10)	6.3	(5)	11.0	(5)
F03030	6.9	(7)	10.3	(7)	6.9	(8)	10.0	(8)
F03031	7.3	(4)	13.2	(4)	6.6	(6)	12.3	(6)
F03032	6.2	(6)	11.4	(6)	5.9	(9)	10.6	(9)
F03033	6.5	(9)	10.5	(9)	6.3	(5)	9.8	(5)
F03035	6.8	(6)	12.3	(6)	6.6	(7)	11.8	(7)
F03036	7.3	(8)	11.9	(8)	6.5	(3)	10.7	(3)
Number of dams	11		10		11		10	
Mean	6.7		11.3		6.3		10.6	
S.D.	0.5		1.0		0.3		0.9	
Significance	NS		NS		NS		NS	
Statistical method	AN		AN		AN		AN	

#: Total litter loss on day 1 of lactation

Each value shows mean per dam (g).

Figures in parentheses indicate number of offspring.

NS: Not significantly different from the control group.

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

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

Appendix 38-4. Body weights of offspring (F₁) before weaning

CPN 300 mg/kg

Dam No.	Days after birth							
	Male body weight				Female body weight			
	0		4		0		4	
F04038	6.7	(10)	9.8	(10)	6.5	(4)	9.4	(4)
F04039	7.0	(4)	12.1	(4)	6.6	(9)	11.4	(9)
F04040	6.5	(7)	9.4	(7)	6.0	(10)	8.7	(10)
F04041	6.1	(5)	10.1	(5)	6.2	(9)	9.5	(9)
F04042	5.8	(5)	9.6	(4)	6.0	(11)	9.9	(11)
F04043	6.9	(7)	10.3	(7)	6.9	(9)	9.9	(9)
F04044	6.9	(7)	11.1	(7)	6.5	(7)	10.9	(7)
F04045	6.2	(9)	9.4	(9)	6.1	(7)	9.5	(7)
F04046	6.0	(8)	10.5	(8)	5.4	(7)	9.8	(7)
F04047	6.0	(6)	10.0	(6)	5.9	(12)	9.3	(12)
F04048	6.5	(7)	10.6	(6)	6.0	(6)	9.7	(6)
Number of dams	11		11		11		11	
Mean	6.4		10.3		6.2		9.8	
S.D.	0.4		0.8		0.4		0.7	
Significance	NS		NS		NS		NS	
Statistical method	AN		AN		AN		AN	

Each value shows mean per dam (g).

Figures in parentheses indicate number of offspring.

NS: Not significantly different from the control group.

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

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

Appendix 39-1. General conditions in offspring (F₁) before weaning

Control (vehicle: corn oil)

Dam No.	Number of offspring and general conditions	Days after birth				
		0	1	2	3	4
F01001	Number of offspring	11	11	11	11	11
	General appearance, No abnormality	11	11	11	11	11
F01002	Number of offspring	13	13	13	12	12
	General appearance, No abnormality	13	13	12	12	12
	General appearance, Death	0	0	1	0	0
F01003	Number of offspring	16	16	16	16	16
	General appearance, No abnormality	16	16	16	16	16
F01004	Number of offspring	16	16	16	16	16
	General appearance, No abnormality	16	16	16	16	16
F01005	Number of offspring	17	17	17	17	17
	General appearance, No abnormality	17	17	17	17	17
F01006	Number of offspring	13	13	13	13	13
	General appearance, No abnormality	13	13	13	13	13
F01007	Number of offspring	16	16	16	16	16
	General appearance, No abnormality	16	16	16	16	16
F01008	Number of offspring	15	15	15	14	14
	General appearance, No abnormality	15	15	14	14	14
	General appearance, Death	0	0	1	0	0
F01009	Number of offspring	13	13	13	13	13
	General appearance, No abnormality	13	13	13	13	13
F01010	Number of offspring	14	14	14	14	14
	General appearance, No abnormality	14	14	14	14	14
F01011	Number of offspring	13	13	12	12	12
	General appearance, No abnormality	13	12	12	12	12
	General appearance, Death	0	1	0	0	0
F01012	Number of offspring	14	14	14	14	14
	General appearance, No abnormality	14	14	14	14	14
Number of offspring		171	171	170	168	168
General appearance, No abnormality		171	170	168	168	168
General appearance, Death			1	2		

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

Appendix 39-2. General conditions in offspring (F₁) before weaning

CPN 30 mg/kg						
Dam No.	Number of offspring and general conditions	Days after birth				
		0	1	2	3	4
F02013	Number of offspring	15	15	15	15	15
	General appearance, No abnormality	15	15	15	15	15
F02014	Number of offspring	15	15	15	15	15
	General appearance, No abnormality	15	15	15	15	15
F02015	Number of offspring	15	15	15	15	15
	General appearance, No abnormality	15	15	15	15	15
F02016	Number of offspring	14	14	14	14	14
	General appearance, No abnormality	14	14	14	14	14
F02017	Number of offspring	11	11	11	11	11
	General appearance, No abnormality	11	11	11	11	11
F02018	Number of offspring	16	16	16	16	16
	General appearance, No abnormality	16	16	16	16	16
F02019	Number of offspring	17	17	17	17	17
	General appearance, No abnormality	17	17	17	17	17
F02020	Number of offspring	16	16	16	16	16
	General appearance, No abnormality	16	16	16	16	16
F02021	Number of offspring	13	13	13	13	13
	General appearance, No abnormality	13	13	13	13	13
F02022	Number of offspring	11	11	11	11	11
	General appearance, No abnormality	11	11	11	11	11
F02023	Not pregnant					
F02024	Number of offspring	15	15	15	15	15
	General appearance, No abnormality	15	15	15	15	15
Number of offspring		158	158	158	158	158
General appearance, No abnormality		158	158	158	158	158
General appearance, Death						

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

Appendix 39-3. General conditions in offspring (F₁) before weaning

CPN 100 mg/kg		Days after birth				
Dam No.	Number of offspring and general conditions	0	1	2	3	4
		F03025	Number of offspring	14	14	14
	General appearance, No abnormality	14	14	14	14	14
F03026	Number of offspring	16	16	16	16	16
	General appearance, No abnormality	16	16	16	16	16
F03027	Number of offspring	16	16	16	16	16
	General appearance, No abnormality	16	16	16	16	16
F03028	Number of offspring	7	7	0	0	0
	General appearance, No abnormality	7	0	0	0	0
	General appearance, Death	0	7	0	0	0
F03029	Number of offspring	15	15	15	15	15
	General appearance, No abnormality	15	15	15	15	15
F03030	Number of offspring	15	15	15	15	15
	General appearance, No abnormality	15	15	15	15	15
F03031	Number of offspring	10	10	10	10	10
	General appearance, No abnormality	10	10	10	10	10
F03032	Number of offspring	15	15	15	15	15
	General appearance, No abnormality	15	15	15	15	15
F03033	Number of offspring	14	14	14	14	14
	General appearance, No abnormality	14	14	14	14	14
F03035	Number of offspring	13	13	13	13	13
	General appearance, No abnormality	13	13	13	13	13
F03036	Number of offspring	11	11	11	11	11
	General appearance, No abnormality	11	11	11	11	11
	Number of offspring	146	146	139	139	139
	General appearance, No abnormality	146	139	139	139	139
	General appearance, Death		7			

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

Appendix 39-4. General conditions in offspring (F₁) before weaning

CPN 300 mg/kg

Dam No.	Number of offspring and general conditions	Days after birth				
		0	1	2	3	4
F04038	Number of offspring	14	14	14	14	14
	General appearance, No abnormality	14	14	14	14	14
F04039	Number of offspring	13	13	13	13	13
	General appearance, No abnormality	13	13	13	13	13
F04040	Number of offspring	17	17	17	17	17
	General appearance, No abnormality	17	17	17	17	17
F04041	Number of offspring	14	14	14	14	14
	General appearance, No abnormality	14	14	14	14	14
F04042	Number of offspring	16	16	15	15	15
	General appearance, No abnormality	16	15	15	15	15
	General appearance, Death	0	1	0	0	0
F04043	Number of offspring	16	16	16	16	16
	General appearance, No abnormality	16	16	16	16	16
F04044	Number of offspring	14	14	14	14	14
	General appearance, No abnormality	14	14	14	14	14
F04045	Number of offspring	16	16	16	16	16
	General appearance, No abnormality	16	16	16	16	16
F04046	Number of offspring	15	15	15	15	15
	General appearance, No abnormality	15	15	15	15	15
F04047	Number of offspring	18	18	18	18	18
	General appearance, No abnormality	18	18	18	18	18
F04048	Number of offspring	13	13	12	12	12
	General appearance, No abnormality	13	12	12	12	12
	General appearance, Death	0	1	0	0	0
	Number of offspring	166	166	164	164	164
	General appearance, No abnormality	166	164	164	164	164
	General appearance, Death		2			

信頼性保証書

表題 シクロペンタノンのラットを用いる反復投与毒性・生殖発生毒性併合試験

試験番号 R-15-005

この試験に関する信頼性保証部門による査察および監査状況等は下記のとおりであった。

査察・監査項目	査察・監査年月日	運営管理者および試験責任者への報告年月日
試験計画書	2015年10月21日	2015年10月21日
試験計画書変更書		
R-15-005-No.1	2015年11月11日	2015年11月11日
R-15-005-No.2	2015年11月25日	2015年11月25日
動物の受入れおよび検疫	2015年10月26日	2015年10月26日
原体の安定性(実験開始前)	2015年10月26日	2015年10月26日
投与検体中の安定性 (安定性試験開始日)	2015年10月27日	2015年10月28日
性周期観察	2015年10月28日	2015年10月28日
群分け、検体調製および含量試験	2015年11月9日	2015年11月9日
体重測定、給餌量測定、投与および 一般状態の観察	2015年11月10日	2015年11月10日
詳細な症状観察	2015年11月17日	2015年11月18日
交尾確認	2015年11月25日	2015年11月25日
尿検査	2015年12月16、17日	2015年12月17日
分娩状態および哺育状態の観察	2015年12月18日	2015年12月18日
機能検査	2015年12月18、21日	2015年12月21日
出生児剖検、採血、雄および母動物剖 検、血液学的検査、血液生化学的検査、 器官重量測定および固定	2015年12月22日	2015年12月22日
病理組織学検査(標本作製:包埋)	2016年1月5日	2016年1月5日
報告書草案および生データ	2016年2月10日	2016年2月10日
最終報告書	2016年3月9日	2016年3月9日

試験は、「新規化学物質等に係る試験を実施する試験施設に関する基準」(平成23年3月31日、薬食発0331第8号、平成23・03・29製局第6号、環企発第110331010号)を遵守して実施され、また、この報告書は試験に使用された方法および手順を正確に記載し、記載された結果は試験の生データを正確に反映していることを保証する。

2016年3月9日

一般財団法人食品薬品安全センター 秦野研究所
信頼性保証部門責任者