B-6355

原本

最終報告書

試験名：4-ヒドロキシジフェニルメタンのラットを用いた２週間回復性観察を含む28日間反復経口投与毒性試験

試験番号：B-6355

試験期間：2008年7月3日-2009年8月7日

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

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

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

1. GLP陳述書

試験番号　　：　　B-6355

試験表題　　：　　4-ヒドロキシジフェニルメタンのラットを用いた
2週間回復性観察を含む28日間反復経口投与毒性試験

試験は以下のGLP基準を遵守して実施したものです。

- 「新規化学物質等に係る試験を実施する試験施設に関する基準について」
（平成15年11月21日：薬食発第1121003号、平成15･11･17製局第3号、環保企発第031121004号、平成17年4月1日 最終改正）

[redacted]　2009 年 8 月 7 日 [redacted]

試験責任者
株式会社ボゾリサーチセンター　御殿場研究所

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信頼性保証書

3. 試験実施概要

3.1 試験計画書

試験番号　：　B-6355
試験表題　：　4-ヒドロキシジフェニルメタンのラットを用いた
2週間回復性観察を含む28日間反復経口投与毒性試験

3.2 試験目的

被験物質をラットに28日間反復経口投与し、その影響を明らかにするとともに、その後2週間の回復期間を設けて障害の可逆性を調べることを目的とした。なお、本試験は株式会社ボゾリサーチセンター動物実験委員会の承認を受けている。

3.3 試験委託者

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

3.4 試験受託者

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

3.5 試験実施施設

株式会社ボゾリサーチセンター
1) 動物試験及び病理標本観察
株式会社ボゾリサーチセンター　御殿場研究所
〒412-0039　静岡県御殿場市かまど 1284
2) 病理標本作製
株式会社ボゾリサーチセンター　東京研究所
〒156-0042　東京都世田谷区羽根木 1-3-11

3.6 試験日程

試験開始日	：	2008年　7月　3日
被験物質入手日	：	2008年　1月　24日
動物入荷日	：	2008年　7月　7日
投与（実験）開始日	：	2008年　7月　15日
投与期間終了日	：	2008年　8月　11日
投与期間終了剖検日	：	2008年　8月　12日
回復期間終了剖検日	：	2008年　8月　26日

病理学検査終了日（実験終了日）
：　2008 年 11 月 20 日
試験終了日　：　2009 年　8 月　7 日

3.7　試験責任者

株式会社ボゾリサーチセンター　御殿場研究所　研究部

[redacted]

3.8　試験担当者

被験物質保存責任者：
動物試験主担当者　：
臨床検査責任者　：
病理検査責任者　：

化学分析責任者　：
統計解析責任者　：

3.9　試験従事者

検疫・馴化　：

群分け　：
被験液調製　：
被験液分析　：
投与　：

一般状態の観察　：

[redacted]

詳細な一般状態の観察・機能検査・握力・自発運動量の測定
：

体重・摂餌量測定　：

[redacted]

尿検査（摂水量測定を含む）
：

[redacted]

採血・血液学検査・血液化学検査
：[redacted]

剖検（器官重量及び確認・整形者含む）
：[redacted]

病理組織検査　：

統計解析　：

3.10　試験成績の信頼性に影響を及ぼしたと思われる環境要因

飼育条件（相対湿度）において2008年8月9日に14時00分~16時00分の間に107号室で停電により、試験計画書の範囲（50±20%）の上限を逸脱したが、一時的な変動であり、動物に異常は認められず、試験の信頼性に及ぼす影響はないと判断した。その他には本試験に関して、試験成績の信頼性に影響を及ぼしたと思われる環境要因はなかった。

3.11　資料保存

試験計画書及び試験計画書変更書（原本）、記録文書、生データ、報告書類（最終報告書の原本を含む）並びに標本（被験物質保存サンプルを含む）は株式会社ボゾリサーチセンター御殿場研究所の資料保存施設に保存する。なお、その期間は最終報告書提出後10年間とする。期間終了後の保存については、厚生労働省 医薬食品局 審査管理課　化学物質安全対策室と株式会社ボゾリサーチセンター間で協議し、その処置を決定する。ただし、長期保存に耐えられない生体試料（尿、血漿、血清）については、試験終了時に廃棄する。

3.12　試験責任者の記名・捺印

[redacted]　2009年 8月 7日 [redacted]

株式会社ボゾリサーチセンター　御殿場研究所

4. 要約

Sprague-Dawley 系 SPF ラット〔Crl:CD(SD)〕を用いて、4-ヒドロキシジフェニルメタンの反復投与による毒性並びにその可逆性を検討した。投与量は 0（0.5w/v%メチルセルロース水溶液：対照群）、30、150 及び 750 mg/kg/day とし、28 日間反復強制経口投与した。1 群の動物数は対照群及び 750 mg/kg 投与群で雌雄各 12 匹、30 及び 150 mg/kg 投与群で雌雄各 6 匹とした。このうち、対照群及び 750 mg/kg 投与群の雌雄各 6 匹については、28 日間投与後 2 週間休薬させた。

投与及び回復期間を通じて死亡動物はみられなかった。また、握力、機能検査及び血液学検査では、被験物質投与の影響は認められなかった。

一般状態では、投与 5 日以降に 750 mg/kg 投与群の雌雄で流涎が散見された。

詳細な一般状態では、手に持っての観察において投与 2 週以降に 750 mg/kg 投与群の雌雄で流涎が散見された。また、オープンフィールド内観察において投与 1 週に 750 mg/kg 投与群の雄で立ち上がり回数の低値が認められた。

自発運動量では、750 mg/kg 投与群の雌雄で測定開始後 0~10 分の測定で低値が認められた。

体重では、750 mg/kg 投与群の雄で投与 4 日以降および投与期間中の体重増加量に低値が認められた。

摂餌量では、750 mg/kg 投与群の雌雄で投与初期に低値が認められた。

尿検査では、750 mg/kg 投与群の雌雄で尿量の高値と浸透圧の低値が、また、雄で摂水量の高値が認められた。

血液化学検査では、750 mg/kg 投与群の雄で ALT の高値と総コレステロール、グルコース及び塩素の低値が、雌でトリグリセライドの高値が認められた。

病理学検査では、器官重量において肝臓で 750 mg/kg 投与群の雌雄で相対重量の高値がみられ、組織学的にも 150 mg/kg 投与群の雄及び 750 mg/kg 投与群の雌雄で小葉中心性の肝細胞肥大が認められた。また、胃において肉眼的に 750 mg/kg 投与群の雌雄で前胃の壁肥厚と雄で境界縁の肥厚が、組織学的には 150 mg/kg 以上の雌雄で前胃の角化亢進及び境界縁の扁平上皮過形成が、750 mg/kg 投与群の雌雄で前胃の扁平上皮過形成が認められた。更に、盲腸において肉眼的に 150 mg/kg 投与群の雌と 750 mg/kg 投与群の雌雄で拡張が認められた。

投与期間中でみられた変化は休薬により消失あるいは程度又は発現頻度の軽減がみられ、回復性が認められた。

以上の結果、4-ヒドロキシジフェニルメタンの本試験条件下における無影響量は病理学検査で肝臓、胃あるいは盲腸で被験物質投与の影響が認められたことから、雌雄とも 30 mg/kg/day と推定された。また、みられた変化はいずれも可逆性が認められた。

5. 緒言

厚生労働省 医薬食品局 審査管理課 化学物質安全対策室の依頼により、4-ヒドロキシジフェニルメタンをラットに28日間反復経口投与し、その影響を明らかにするとともに、2 週間休薬し、障害の可逆性を調べたのでその成績を報告する。なお、遵守した基準及び準拠したガイドラインなどは以下の通りである。

1) GLP

- 「新規化学物質等に係る試験を実施する試験施設に関する基準について」
  （平成15年11月21日：薬食発第1121003号、平成15･11･17製局第3号、環保企発第031121004号、平成17年4月1日 最終改正）

2) 毒性試験ガイドライン

- 「新規化学物質等に係る試験の方法について」
  （平成15年11月21日：薬食発第1121002号、平成15･11･13製局第2号、環保企発第031121002号、平成18年11月20日 最終改正）
- 「OECD Guideline for Testing of Chemicals 407」
  （OECD 理事会：1995年7月27日）

3) 動物の福祉

- 「動物の愛護及び管理に関する法律」
  （昭和48年10月1日法律第105号、平成17年6月22日 最終改正）
- 「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）
- 「動物実験の適正な実施に向けたガイドライン」
  （日本学術会議、平成18年6月1日）

6. 試験材料及び方法

6.1 被験物質及び媒体

6.1.1 被験物質

被験物質は東京化成工業株式会社より購入した。当試験に使用した被験物質のロット番号、純度等は次の通りである。また、試験成績を添付資料 1 に示した。

名称	:	4-ヒドロキシジフェニルメタン
英名	:	4-Hydroxydiphenylmethane
別名	:	4-ベンジルフェノール
CAS 番号	:	101-53-1
示性式	:	$HOC_6H_4CH_2C_6H_5$
ロット番号	:	UJSVE
純度	:	99.8%（GC 法）
入手量	:	500 g
性状	:	白色小針状結晶
融点	:	83°C
安定性	:	動物試験終了後、被験物質の分析を試験受託者で HPLC 法により実施し安定であることを確認した。（添付資料 2）
保存方法	:	冷蔵（冷蔵庫内、実測値：3~9°C）、遮光、防湿
保存場所	:	御殿場研究所　被験物質保存室及び第 1 研究棟被験物質調製室
取扱い上の注意	:	マスク、手袋を着用する。 取扱い場所及び周囲の火気を厳禁し、高温物及び強酸化剤との接触を避ける。
返却	:	被験物質約 1g を保存試料として保存した。分析用に小分けした被験物質の残量は廃棄した。また、投与期間中の安定性を確認するため、投与後の残量は全て 4-ヒドロキシジフェニルメタン（Lot No. UJSVE）の安定性試験（試験番号；A-2165）へ移管した。

6.1.2 媒体

名称	:	メチルセルロース 400cP
ロット番号	:	EWM1974
メーカー	:	和光純薬工業株式会社
保存方法	:	室温
保存場所	:	御殿場研究所　第 1 研究棟被験物質調製室

6.2 投与液の調製

6.2.1 媒体の調製

調製方法 : メチルセルロース 400cP を注射用水（株式会社大塚製薬工場、ロット番号；8B74）に溶解し、0.5w/v%メチルセルロース水溶液とした。

保存方法 : 冷所（冷蔵庫内、実測値；4~8°C）に保存し、調製後 8 日以内に使用した。

6.2.2 被験液の調製

濃度ごとに必要量の被験物質を正確に採取し、0.5w/v%メチルセルロース水溶液に懸濁して 6 mg/mL 液（低用量群液）、30 mg/mL 液（中用量群液）及び 150 mg/mL 液（高用量群液）を調製した。被験液は週 1 回以上の頻度で調製し、調製後 8 日以内に使用した。

6.2.3 投与液の保存方法

投与液は 1 日の必要分ずつ褐色瓶に分注し、使用時まで冷所（冷蔵庫内、実測値：4~8°C）に保存した。

6.2.4 投与液の安定性

本被験物質の 0.5 及び 200 mg/mL 懸濁液（媒体：0.5w/v%メチルセルロース水溶液）は、冷所（冷蔵庫内、1~10°C）で 8 日間、その後室温で 24 時間安定であることを株式会社ボゾリサーチセンター御殿場研究所で確認した（試験番号：A-2110、添付資料 3）。

6.2.5 投与液の濃度・均一性確認

投与 1 週と第 4 週の投与に用いる各濃度の被験液について、その濃度・均一性を株式会社ボゾリサーチセンター 御殿場研究所で HPLC 法を用いて確認した。その結果、表示値に対する濃度の割合は 96.0~107.3%（許容範囲：表示値に対する割合；100±10%）、均一性は 1.3~7.6%（許容値：CV10%以内）であり、いずれも許容範囲内であった（添付資料 4 及び 5）。分析法の概略を次に示す。

1 濃度当たりの採取本数及び採取量 : 3 本（上、中及び下層から採取）、1 本につき 10 mL

測定対象物質 : 4-ヒドロキシジフェニルメタン

測定対象標準物質

名称 : 4-ヒドロキシジフェニルメタン

ロット番号 : UJSVE

保存方法 : 冷蔵（冷蔵庫内、実測値：4~6°C）、遮光、防湿で保存

測定条件

HPLC 条件

カラム　　：　L-column ODS（4.6 mm I.D.×150 mm、5 μm、財団法人 化学物質評価研究機構）

カラム恒温槽設定温度

：　40°C

HPLC 移動相　：

試薬名	混合比*
Milli-Q 水	50%
アセトニトリル	50%

*：HPLC システムで混合。

流速　　：　1.0 mL/min

オートサンプラー設定温度

：　4°C

注入量　　：　20 μL

検出　　：　UV（測定波長 227 nm）

注入順序　：

注入順序	注入回数	注入内容
1	3	標準溶液（システム適合性用）
2	3	標準溶液（定量用）
3	1	測定実測試料（6 mg/mL-上層）
4	1	測定実測試料（6 mg/mL-中層）
5	1	測定実測試料（6 mg/mL-下層）
6	1	測定実測試料（30 mg/mL-上層）
7	1	測定実測試料（30 mg/mL-中層）
8	1	測定実測試料（30 mg/mL-下層）
9	1	測定実測試料（150 mg/mL-上層）
10	1	測定実測試料（150 mg/mL-中層）
11	1	測定実測試料（150 mg/mL-下層）

なお、標準溶液及び測定実測試料の測定は 24 時間以内に実施すること（バリデーション試験で、オートサンプラー内における 24 時間保存後の安定性が確認されている）。

6.3　試験動物種及び系統の選択理由

毒性試験法ガイドラインによりラットを用いた試験が必要とされている。この試験に使用される系統のラットは特性がよく知られ、背景資料が豊富であることから選択した。

6.4　試験動物及び群分け

Sprague-Dawley系SPFラット〔Crl:CD(SD)、日本チャールス・リバー株式会社、厚木飼育センター〕雌雄各 47 匹[注)] を 5 週齢で入手し、当所で 8 日間検疫・馴化飼育し、一般状態の観察（1 回/日）、体重測定（3 回）及び詳細な一般状態の観察（1 回）を行

い、体重増加量、詳細な一般状態の観察及び一般状態に異常がみられず健康と思われる雌雄各 36 匹（主群として雌雄各 24 匹、回復群として雌雄各 12 匹）を選び、6 週齢で試験に供した。投与開始日の体重範囲は、雄で 200~220 g、雌で 140~167 gであった。動物は、検疫・馴化期間中の体重増加量により選別後、群分け当日（投与開始の 3 日前）の体重に基づいて層別化し、各群の平均体重ができるだけ均等となるよう各群を構成した。個体の割付けはコンピュータを用いたブロック配置法及び無作為抽出法の組合せ（ブロック配置法で必要な群を構成し、試験群及び群内の個体番号を無作為に割当てる）により行った。また、余剰動物は投与開始日に試験系から除外した。

注）：試験計画書に従い、注文匹数は雌雄各 45 匹であったが、実際には雌雄各 47 匹が納入された。

6.5　飼育条件

動物は温度 21~25°C、相対湿度 47~72%、換気回数 1 時間 10~15 回、照明 1 日 12 時間（07:00~19:00）の動物飼育室（雄 107 号室、雌 108 号室）で、ブラケット式金属製網ケージ（W 250×D 350×H 200 mm：日本ケージ株式会社）で個別飼育し、毎日 1 回の飼育室内の清掃を実施した。固形飼料 CRF-1（オリエンタル酵母工業株式会社、ロット番号：080305、080509）及び御殿場市営水道水を給水瓶により自由に摂取させた。

6.6　飼料及び飲料水中の混入物質

飼料中の混入物質に関しては使用全ロットについて財団法人日本食品分析センターあるいは Eurofins Scientific Analytics で分析を行い、また、飲料水については東芝機械環境センター株式会社で水道法に準拠する水質検査を定期的に（年 4 回）行った。これらの分析成績書を入手し、試験成績に影響がないことを確認した後、写しを保存した。

6.7　動物の識別及びケージへの表示

動物は入荷時に耳標を装着して個体識別した。入荷から群分け前までの間は試験番号、性別及び耳標番号を明記したケージラベルをつけた。群分け後は、性別及び用量ごと（対照群、低、中及び高用量群の順）に 4 桁の番号をつけた。この場合、1000 の位は群、100 の位は性（0 番を雄、1 番を雌）、10 と 1 の位は個体番号とした。各飼育ケージには、群分け前まで使用したケージラベルの裏に用量（群）ごとに色分けしたラベルをつけ、試験番号、投与経路、投与量、性、動物番号、耳標番号及び剖検予定日を明記した。ただし、詳細な一般状態の観察、機能検査、握力及び自発運動量測定中は、観察者に対して投与の情報を制限するため、ケージラベルを裏返して試験番号、性別及び耳標番号のみを表示した。

6.8　投与経路、投与期間、投与回数及び回復期間とそれらの選択理由

毒性試験法ガイドラインに準じ、投与経路は経口を選択し、投与期間は 28 日間とした。投与回数は反復投与試験で一般的に行われている 1 日 1 回（7 回/週）とした。回

復期間は障害の可逆性を検討するのに適当と考えられる2週間（14日間）とし、この間投与を行わなかった。

6.9　投与方法

投与容量は 5 mL/kg 体重とし、胃ゾンデを用いて強制経口投与した（08:00~12:20の間）。対照群には媒体（0.5w/v%メチルセルロース水溶液）を同様に投与した。個体ごとの投与液量は最新の体重を基準に算出した。

6.10　投与量及びその設定根拠並びに群構成

4-ヒドロキシジフェニルメタンの0（0.5w/v%メチルセルロース水溶液）、100、300及び1000 mg/kg/dayを1群雌雄各5匹のラットに14日間反復経口投与した結果[1)]、主な変化としては、1000 mg/kg投与群の雄1例で死亡が、血液学検査において白血球数の高値が300 mg/kg投与群の雌と1000 mg/kg投与群の雌雄、また、血液化学検査においてALT活性の高値と総コレステロールの低値が1000 mg/kg投与群の雄で、更に、病理学検査で肝臓の絶対及び相対重量において高値が1000 mg/kg投与群の雌で、剖検所見において300及び1000 mg/kg投与群の雌雄で盲腸拡張が、1000 mg/kg投与群の雌で腺胃の壁肥厚が認められた。以上のことから、本試験における投与量は、750 mg/kgを高用量とし、公比5で除して、150及び30 mg/kgの3用量を設定した。群構成表を次の表1.に示した。

表 1.群構成表

試験群	投与量 (mg/kg)	濃　度 (mg/mL)	投与容量 (mL/kg)	性	主　群		回　復　群	
					動物数	動物番号	動物数	動物番号
対照群	0	0	5	雄 雌	6 6	1001~1006 1101~1106	6 6	1007~1012 1107~1112
低用量群	30	6	5	雄 雌	6 6	2001~2006 2101~2106	- -	- -
中用量群	150	30	5	雄 雌	6 6	3001~3006 3101~3106	- -	- -
高用量群	750	150	5	雄 雌	6 6	4001~4006 4101~4106	6 6	4007~4012 4107~4112

6.11　観察及び検査の方法

それぞれ記載された時期に観察及び検査を実施した。試験日の起算に関しては下記の通りである。

投与1日（day 1 of administration）　：投与開始日
投与1週（week 1 of administration）　：投与1から投与7日
回復1日（day 1 of recovery）　：回復開始日（投与期間終了の翌日）
回復1週（week 1 of recovery）　：回復1から回復7日

6.11.1　　一般状態の観察

全個体について投与期間中は毎日3回、投与前と投与直後及び約2時間後（ただし、土曜及び休日は投与前と投与直後の2回）、回復期間中は毎日1回、体外表、栄養状態、姿勢、行動及び排泄物などの一般状態を観察した。

6.11.2　　詳細な一般状態の観察、機能検査、握力及び自発運動量の測定

詳細な一般状態の観察は、全ての動物について投与開始前に1回、また、投与期間中及び回復期間中は毎週1回実施した。また、機能検査、握力及び自発運動量の測定は、全個体について投与4週（雄を投与25日、雌を投与26日）及び回復2週（回復11日）に行った。なお、観察及び検査は投与の情報を制限（ブラインド化）し、動物をランダムに配置した状態で行った。

投与開始前（検疫・馴化期間中）の詳細な一般状態の観察において異常は認められなかった。

6.11.2.1　　詳細な一般状態の観察

1)　ホームケージ内観察

姿勢、痙攣、異常行動

2)　手に持っての観察

ケージからの取り出しやすさ、被毛・皮膚の状態、眼・鼻の分泌物、眼球（眼球突出、眼瞼閉鎖状態）、可視粘膜、自律神経機能（流涙、立毛、瞳孔径、流涎、異常呼吸）、ハンドリングに対する反応

3)　オープンフィールド内観察

覚醒状態、痙攣、異常行動、常同行動、歩行、姿勢、身繕い、立ち上がり回数、排泄物（排糞数、排尿）

6.11.2.2　　機能検査

聴覚反応、接近反応、接触反応、痛覚反応、瞳孔反射、空中正向反射、着地開脚幅

6.11.2.3　　握力測定

CPUゲージMODEL-9502A（アイコーエンジニアリング株式会社）を用いて前肢及び後肢の握力を測定した。

6.11.2.4　　自発運動量の測定

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

6.11.3　　体重測定

全個体について、投与 1、4、7、10、14、17、21、24 及び 28 日の投与前に、回復期間中は回復 1、3、7、10 及び 14 日に測定した。測定は 08:26~10:58 の間に行った。更に、全投与期間中及び回復期間中の体重増加量を算出した。剖検日には相対器官重量算出のため、前日から約 16 時間絶食させた後の体重を測定した（08:09~08:31）。

6.11.4　　摂餌量測定

全個体について、投与期間中は投与 1、4、7、10、14、17、21、24 及び 28 日の投与前に、回復期間中は回復 3、7、10 及び 14 日に測定した。測定は 08:38~11:28 の間に行った。なお、投与期間中の投与開始日は前日からの 1 日量、それ以降は 3~4 日間の累積量、回復期間中の回復 1 週は回復 1 から 3 日及び回復 3 から 7 日までの 2 ないし 4 日間の累積摂取量を、その後は 3 から 4 日ごとに 3 ないし 4 日間の累積摂取量を測定し、1 匹 1 日量を算出した。

6.11.5　　尿検査

投与 4 週及び回復 2 週に行った。

投与 4 週（投与 23 日の投与後）は検査当日の全個体について、回復 2 週（回復 9 日）は回復群の全個体について、それぞれ採尿器をセットしたケージに収容し、絶食・自由摂水下で4時間尿を、次いで自由摂食・自由摂水下でその後の20時間尿を採取し、表 2.に記載した項目及び方法により検査した。また、摂水量は、採尿ケージに収容した状態で前日からの 1 日当たりの摂水量を、給水瓶を用いて測定した。

表 2. 尿検査の項目、測定法及び使用機器など

1）4 時間尿についての検査	
検査項目	測定方法
pH	オーションスティックス-7EA試験紙[a)]（アークレイ株式会社）
たん白質	オーションスティックス-7EA試験紙[a)]（アークレイ株式会社）
ケトン体	オーションスティックス-7EA試験紙[a)]（アークレイ株式会社）
グルコース	オーションスティックス-7EA試験紙[a)]（アークレイ株式会社）
潜血	オーションスティックス-7EA試験紙[a)]（アークレイ株式会社）
ビリルビン	オーションスティックス-7EA試験紙[a)]（アークレイ株式会社）
ウロビリノーゲン	オーションスティックス-7EA試験紙[a)]（アークレイ株式会社）
色調	肉眼観察
沈渣	鏡検法
尿量（4 時間量）[注)]	目盛付スピッツ管を用いた容量測定（単位：mL）
2）20 時間尿についての検査	
検査項目	測定方法
尿量（20 時間量）[注)]	メスシリンダーを用いた容量測定（単位：mL）
浸透圧	氷点降下法[b)]（単位：mOsm/kg）
使用測定機器 [a)]：AUTION™ MINI AM-4290（アークレイ株式会社） [b)]：自動浸透圧測定装置　オートアンドスタットOM-6030（アークレイ株式会社）	

注）：4 時間の尿量と 20 時間の尿量を合計して 24 時間の尿量（mL/24h）を算出した。

6.11.6　　血液学検査

投与期間及び回復期間終了の翌日の計画剖検時に、前日から一夜（約 16~20 時間）絶食させた全個体について、エーテル麻酔下で開腹し、腹大動脈から EDTA-2K 加採血瓶（SB-41：シスメックス株式会社）に血液（約 1 mL）を採取した。得られた血液について表 3.1）に記載した項目及び方法により検査した。更に、血液（約 0.9 mL）を 3.8%クエン酸ナトリウム溶液加試験管（血液 9 容に対し 1 容の割合）に採取し、遠心分離（設定：約 3,000 rpm、約 1,600×g、約 10 分間）により得られた血漿について表 3.2）に記載した項目及び方法により検査した。なお、鏡検による確認に備え、全個体について May-Grünwald-Giemsa 染色法による血液塗抹標本を作製したが、鏡検による確認は不要と判断し、鏡検は実施しなかった。

表 3. 血液学検査の項目、測定法及び使用機器など

1）EDTA-2K 加血液についての検査		
検査項目	測定方法	単位
赤血球数（RBC）	2 角度レーザーフローサイトメトリー法[a)]	$10^4/\mu L$
ヘモグロビン量（HGB）	シアンメトヘモグロビン変法[a)]	g/dL
ヘマトクリット値（HCT）	赤血球数及び平均赤血球容積から算出[a)]	%
平均赤血球容積（MCV）	2 角度レーザーフローサイトメトリー法[a)]	fL
平均赤血球血色素量（MCH）	赤血球数及びヘモグロビン量から算出[a)]	pg
平均赤血球血色素濃度（MCHC）	ヘモグロビン量及びヘマトクリット値から算出[a)]	g/dL
網赤血球率（Reticul.）	RNA染色によるレーザーフローサイトメトリー法[a)]	%
血小板数（PLT）	2 角度レーザーフローサイトメトリー法[a)]	$10^4/\mu L$
白血球数（WBC）	2 角度レーザーフローサイトメトリー法[a)]	$10^2/\mu L$
白血球百分率[注)]	ペルオキシダーゼ染色によるフローサイトメトリー法	%·
	+2 角度レーザーフローサイトメトリー法[a)]	$10^2/\mu L$
2）クエン酸ナトリウム加血液から分離した血漿についての検査		
検査項目	測定方法	単位
プロトロンビン時間（PT）	クロット法[b)]	s
活性化部分トロンボプラスチン時間（APTT）	クロット法[b)]	s
フィブリノーゲン量（FIB）	トロンボプラスチン法[b)]	mg/dL
使用測定機器 [a)]：総合血液学検査装置アドヴィア 120（Siemens Medical Solutions Diagnostics, New York, USA） [b)]：血液凝固自動測定装置　ACL 100（Instrumentation Laboratory）		

注）：リンパ球（LYMP）、好中球（NEUT）、好酸球（EOS）、好塩基球（BASO）、単球（MONO）及び大型非染色球（LUC）。また、白血球百分率と白血球数から各分画の実数を算出した。

6.11.7　　血液化学検査

血液学検査用試料と同時に採取した血液を凝固促進剤入り試験管（ベノジェクト II-オートセップ：テルモ株式会社）に取り、遠心分離（設定：約 3,000 rpm、約 1,600×g、約 10 分間）し、得られた血清について、表 4.1）に記載した項目及び方法により検査した。また、ヘパリン加試験管（血液 1 mL 当たり約 20 単位のヘパリン）に採取した血液を遠心分離（設定：約 3,000 rpm、約 1,600×g、約 10 分間）し、得られた血漿について表 4.2）に記載した項目及び方法により検査した。

表 4. 血液化学検査の項目、測定法及び使用機器など

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

6.11.8　　病理学検査

6.11.8.1　　剖検

全ての計画剖検動物については、採血後腹大動脈切断により放血致死させ、体外表・頭部・胸部・腹部を含む全身の器官・組織の肉眼による詳細な病理解剖を行い、結果を記録した。

6.11.8.2　　器官重量測定

全ての計画剖検動物については、次に示す器官の重量（絶対重量）を測定するとともに、絶対重量と剖検時の体重から体重 100 g 当たりの相対重量を算出した。

なお、*印を付した両側性の器官については左右別々に測定し、その合計値で評価した。

脳、副腎*、胸腺、脾臓、心臓、肝臓、腎臓*、精巣*、精巣上体*、卵巣*、子宮

6.11.8.3　　病理組織学検査

全ての個体について次に示す器官・組織を採取し、リン酸緩衝 10vol%ホルマリン液で固定した。ただし、肺はリン酸緩衝 10vol%ホルマリン液を注入後、眼球及び視神経はリン酸緩衝液で調製した 3vol %グルタルアルデヒド・2.5vol%ホルマリン液で固定後、精巣及び精巣上体はブアン液で固定した後、それぞれ、リン酸緩衝 10vol%ホルマリン液で保存し、パラフィン包埋した。その後、切片としてヘマトキシリン・エオジン染色標本を作製し、対照群及び高用量群（肉眼的異常部位については全例）について鏡検した。なお、被験物質投与の影響が疑われた雌雄の肝臓及び胃については低及び中用量群並びに回復群の全個体についても鏡検した。さらに、*で示した両側性器官については両側を摘出したが、鏡検は片側のみ行った。

大脳、小脳、脊髄（胸部）、坐骨神経、眼球*、下垂体、甲状腺*、上皮小体*、副腎*、胸腺、脾臓、顎下リンパ節、腸間膜リンパ節、心臓、気管、肺（気管支を含む）、胃、十二指腸、空腸、回腸（パイエル板を含む）、盲腸、結腸、直腸、肝臓、腎臓*、膀胱、精巣*、精巣上体*、前立腺、卵巣*、子宮、胸骨（骨髄を含む）、大腿骨（骨髄を含む）及び大腿部骨格筋

他に、ハーダー腺*、視神経*、胸大動脈、舌、食道、顎下腺*、舌下腺*、膵臓、腟、精嚢、乳腺（鼠径部）、皮膚（鼠径部）、個体識別部位（耳介）及び喉頭を摘出して保存した。

6.12　統計解析

オープンフィールド内観察の定量的項目、機能検査における定量的項目、握力測定、自発運動量の測定、体重（体重増加量を含む）、摂餌量、摂水量、尿検査の定量的項目、血液学検査、血液化学検査及び器官重量データについて、対照群と各投与群との間で統計解析を行った。先ず、Bartlett検定により分散性の検定を行った（有意水準：両側 1%）。分散が等しい場合はDunnett法を用いて、非等分散の場合はDunnett型のmean rank testを用いて、対照群と各投与群との間で検定を行った（有意水準：両側 5 及び 1%）。なお、回復群については、F検定により各群の分散の均一性の検定（有意水準：片側 5%）を行った。その結果、等分散性が認められた場合には対照群と被験物質投与群との平均値の差についてStudentのt検定（有意水準：両側 5 及び 1%）を、等分散性が認められなかった場合にはAspin-Welchのt検定（有意水準：両側 5 及び 1%）を行った[2) ~6)]。

7. 試験結果

7.1 一般状態

成績を Table 1-1~1-3 及び Appendix 1~10 に示した。

1) 投与期間

750 mg/kg 投与群の雌雄において、投与 5 日以降で流涎が散見された。

2) 回復期間

いずれの動物においても、回復期間を通じて異常は認められなかった。

7.2 詳細な一般状態、機能検査、握力及び自発運動量

7.2.1 詳細な一般状態

成績を Table 2-1~2-18 及び Appendix 11~70 に示した。

1) 投与期間

(1) 投与 1 週

オープンフィールド内観察において 750 mg/kg 投与群の雄で立ち上がり回数の有意な低値が認められた。

(2) 投与 2 週

手に持っての観察において、750 mg/kg 投与群の雄 3 例と雌 1 例で軽度な流涎が認められた。

(3) 投与 3 週

手に持っての観察において、750 mg/kg 投与群の雄 4 例と雌 5 例で軽度な流涎が認められた。

(4) 投与 4 週

手に持っての観察において、750 mg/kg 投与群の雄 1 例と雌 2 例で軽度な流涎が認められた。

2) 回復期間

いずれの検査項目においても異常はなく、750 mg/kg 投与群の雌雄とも対照群との間に有意差は認められなかった。

7.2.2 機能検査

成績を Table 2-19、2-20 及び Appendix 71~76 に示した。

1) 投与 4 週

いずれの検査項目においても異常はなく、各被験物質投与群の雌雄とも対照群との間に有意差は認められなかった。

2) 回復 2 週

いずれの検査項目においても異常はなく、750 mg/kg 投与群の雌雄とも対照群との間に有意差は認められなかった。

7.2.3 握力

成績を Table 2-21、2-22 及び Appendix 77~82 に示した。

1) 投与 4 週

各被験物質投与群の雌雄とも対照群との間に有意差は認められなかった。

2) 回復 2 週

750 mg/kg 投与群の雌雄とも対照群との間に有意差は認められなかった。

7.2.4 自発運動量

成績を Fig. 1~4、Table 2-23、2-24 及び Appendix 83~88 に示した。

1) 投与 4 週

750 mg/kg 投与群の雌雄で測定開始後 0~10 分の測定に有意な低値が認められた。その他には、30 mg/kg 投与群の雌で測定開始後 20~30 分の測定と 150 mg/kg 投与群の雄で測定開始後 10~20 分の測定に有意な低値が認められたが、いずれも測定開始後 0~10 分の測定を含む他の測定時期と 0~60 分の測定では変化が認められていない一過性の変化であることから、偶発性の変化と判断した。

2) 回復 2 週

750 mg/kg 投与群の雌で測定開始後 40~50 分の測定に有意な低値が認められたが、測定開始後 0~10 分の測定を含む他の測定時期と 0~60 分の測定では変化が認められていない一過性の変化であることから、偶発性の変化と判断した。

7.3 体重

成績を Fig.5、Table 3-1、3-2 及び Appendix 89~94 に示した。

1) 投与期間

750 mg/kg 投与群の雄で投与 4 日以降に有意な低値が、更に、投与期間中の体重増加量にも有意な低値が認められた。

2) 回復期間

750 mg/kg 投与群の雌雄とも対照群と同様に推移し有意差は認められなかった。

7.4 摂餌量

成績を Fig.6、Table 4-1、4-2 及び Appendix 95~100 に示した。

1) 投与期間

750 mg/kg 投与群の雌雄で投与 4 日に有意な低値が認められた。

2) 回復期間

750 mg/kg 投与群の雌雄とも対照群と同様に推移し有意差は認められなかった。

7.5　尿検査（摂水量含む）

成績を Table 5-1~5-8 及び Appendix 101~118 に示した。

1)　投与 4 週

750 mg/kg 投与群の雌雄で尿量の有意な高値と浸透圧の有意な低値が、雄で摂水量の有意な高値が認められた。

2)　回復 2 週

750 mg/kg 投与群の雌雄とも定性的項目に異常は認められず、尿量、摂水量及び浸透圧においても対照群との間に有意差は認められなかった。

7.6　血液学検査

成績を Table 6-1~6-6 及び Appendix 119~136 に示した。

1)　投与期間終了時

750 mg/kg 投与群の雄で白血球百分率と白血球数からの各分画の実数において好中球数の有意な高値が認められたが、白血球数及び白血球百分率には変化がないことから偶発性と判断した。

2)　回復期間終了時

750 mg/kg 投与群の雄で網赤血球率の有意な高値が認められたが、投与期間終了時に認められていないことから偶発性と判断した。

7.7　血液化学検査

成績を Table 7-1~7-4 及び Appendix 137~148 に示した。

1)　投与期間終了時

750 mg/kg 投与群の雄で ALT の有意な高値と総コレステロール、グルコース及び塩素の有意な低値が、雌でトリグリセライドの有意な高値が認められた。その他には、30 及び 150 mg/kg 投与群の雌でカリウムの有意な高値が認められたが、高用量群には同様な変化は認められていないことから偶発性と判断した。また、750 mg/kg 投与群の雄で A/G 比率の有意な高値が認められたが、総たん白質とアルブミン等には変化がみられていないことから偶発性と判断した。

2)　回復期間終了時

750 mg/kg 投与群の雌で ALT とナトリウムの有意な低値が認められたが、いずれの変化も投与期間終了時にみられていないことから偶発性と判断した。

7.8　器官重量

成績を Table 8-1~8-8 及び Appendix 149~172 に示した。

1)　投与期間終了時

被験物質投与によると考えられる変化が肝臓に認められた。

肝臓　：　750 mg/kg 投与群の雌雄で相対重量の有意な高値が認められた。

上記のほか、剖検時体重の有意な低値が 750 mg/kg 投与群の雄で認められた。

以下に示す変化については、その出現状況からいずれも被験物質投与との関連性のない変化（主として剖検時体重の低値に起因）と判断した。

腎臓 : 750 mg/kg 投与群の雄で相対重量の有意な高値が認められた。

脳 : 750 mg/kg 投与群の雄で相対重量の有意な高値が認められた。

心臓 : 各被験物質投与群の雄で絶対重量の有意な低値が認められた。

2) 回復期間終了時

いずれの器官においても、雌雄とも 750 mg/kg 投与群と対照群の間に有意差は認められなかった。

7.9 剖検所見

成績を Table 9-1、9-2 及び Appendix 173~244 に示した。

1) 投与期間終了時

被験物質投与によると考えられる変化が盲腸及び胃に認められた。

盲腸 : 150 mg/kg 投与群の雌 1 例、750 mg/kg 投与群の雌雄各 5 例で拡張が認められた。

胃 : 750 mg/kg 投与群の雄 4 例と雌 5 例で前胃の壁肥厚が、750 mg/kg 投与群の雄 2 例で境界縁の肥厚が認められた。

以下に示す所見についてはその出現状況などから、いずれも偶発性の変化と判断した。

精巣上体 : 750 mg/kg 投与群の 1 例で一部黄色巣が認められた。

2) 回復期間終了時

被験物質投与によると考えられる変化が胃に認められた。

胃 : 750 mg/kg 投与群の雄 1 例で前胃の壁肥厚が、750 mg/kg 投与群の雌 2 例で境界縁の肥厚が認められた。

7.10 病理組織学検査

成績を Table 10-1~10-4 及び Appendix 173~244 に示した。

1) 投与期間終了時

被験物質投与によると考えられる変化が肝臓及び胃で認められた。

肝臓 : 150 mg/kg 投与群の雄 3 例、750 mg/kg 投与群の雄全例と雌 2 例で軽微あるいは軽度な小葉中心性の肝細胞肥大が認められた。

胃 : 剖検において前胃の壁肥厚あるいは境界縁の肥厚がみ

られた 750 mg/kg 投与群の雄 6 例と雌 5 例を含み次の所見が認められた。150 mg/kg 投与群の雄 3 例と雌 1 例、750 mg/kg 投与群の雌雄各全例で軽微あるいは軽度な前胃の角化亢進が、750 mg/kg 投与群の雄 5 例と雌 4 例で軽微あるいは軽度な前胃の扁平上皮過形成が、150 mg/kg 投与群の雄 5 例と雌 1 例、750 mg/kg 投与群の雌雄各全例で軽微あるいは軽度な境界縁の扁平上皮過形成が認められた。

以下に示す所見については、その出現状況あるいは病理組織学的性状からいずれも偶発性の変化と判断した。なお、剖検時に盲腸で拡張が認められた 150 mg/kg 投与群の雌 1 例と 750 mg/kg 投与群の雌雄各 5 例については病理組織学検査において剖検所見に関連する異常は認められなかった。

胸骨（骨髄を含む）：　対照群の雄 1 例と雌 2 例、750 mg/kg 投与群の雄 2 例と雌 3 例で軽微な軟骨粘液変性が認められた。

精巣上体：　剖検において一部黄色巣がみられた 750 mg/kg 投与群の 1 例で軽度な精子肉芽腫が認められた。

心臓：　対照群の雌 1 例で軽微な心筋炎が認められた。

腎臓：　対照群の雄 4 例と雌 1 例、750 mg/kg 投与群の雌雄各 4 例で軽微あるいは軽度な再生尿細管が、750 mg/kg 投与群の雌 1 例で軽微な硝子円柱が、対照群の雌 1 例で軽度な限局性の繊維化が認められた。

肝臓：　対照群の雌雄各 5 例、30 mg/kg 投与群の雄 1 例と雌 4 例、150 mg/kg 投与群の雄 1 例と雌 3 例、750 mg/kg 投与群の雌雄各 2 例で軽微あるいは軽度な小葉辺縁性の肝細胞空胞化が、対照群の雄 4 例と雌 2 例、30 mg/kg 投与群の雄 3 例と雌 4 例、150 mg/kg 投与群の雄 1 例と雌 3 例、750 mg/kg 投与群の雄 4 例と雌 2 例で軽微あるいは軽度な微小肉芽腫が認められた。

肺：　750 mg/kg 投与群の雄 1 例で軽微な動脈壁の鉱質沈着が、対照群の雌 1 例に軽微な限局性の出血が、対照群の雄 1 例で軽微な肺胞貪食細胞の出現が、対照群の雄 1 例で軽微な限局性の肺炎が認められた。

上皮小体：　750 mg/kg 投与群の雄 1 例で軽微なリンパ球の細胞浸潤が認められた。

前立腺：　対照群の 4 例、750 mg/kg 投与群の 2 例で軽微あるいは軽度な間質性の細胞浸潤が認められた。

大腿部骨格筋：　対照群の雌雄各 1 例、750 mg/kg 投与群の雌雄各 1 例で筋繊維の変性が、対照群の雄 1 例で軽微な間質性の

細胞浸潤が認められた。

脾臓　：　対照群の雄 4 例、750 mg/kg 投与群の雄 3 例で軽微な髄外造血が認められた。

甲状腺　：　対照群の雄 1 例で異所性胸腺が、750 mg/kg 投与群の雄 2 例で鰓後体遺残が認められた。

2)　回復期間終了時

被験物質投与によると考えられる変化が肝臓及び胃に認められた。

肝臓　：　750 mg/kg 投与群の雄 2 例で軽微な小葉中心性肝細胞肥大が認められた。

胃　：　剖検において前胃の壁肥厚がみられた 750 mg/kg 投与群の雄 1 例では、軽微な前胃の角化亢進、軽度な前胃の扁平上皮過形成と軽微な境界縁の扁平上皮過形成が認められた。また、剖検において境界縁の肥厚がみられた 750 mg/kg 投与群の雌 2 例では、軽微な境界縁の扁平上皮過形成と前胃の軽微な扁平上皮過形成と軽微な角化亢進が認められた。

以下に示す所見については、その出現状況あるいは病理組織学的性状からいずれも偶発性の変化と判断した。

肝臓　：　対照群の雄 2 例と雌 3 例、750 mg/kg 投与群の雄 1 例と雌 4 例で軽微あるいは軽度な小葉辺縁性の肝細胞空胞化が、対照群の雄 4 例と雌 5 例、750 mg/kg 投与群の雄 4 例と雌 3 例で軽微な微小肉芽腫が認められた。

8. 考察

Sprague-Dawley系SPFラット〔Crl:CD(SD)〕に4-ヒドロキシジフェニルメタンを0（0.5w/v%メチルセルロース水溶液：対照群）、30、150及び750 mg/kg/dayの用量で28日間反復強制経口投与し、その毒性を検討するとともに、対照群及び750 mg/kg投与群はその後2週間休薬させ、変化の可逆性について検討した。

投与及び回復期間を通じて死亡動物はみられなかった。また、一般状態では、750 mg/kg投与群の雌雄で投与5日以降に流涎が散見されたが、一過性の変化であった。

詳細な一般状態では、手に持っての観察において750 mg/kg投与群の雌雄で投与2週以降において流涎が散見された。また、オープンフィールド内観察において750 mg/kg投与群の雄で投与1週に立ち上がり回数の低値が認められた。これらの変化は休薬により消失し、回復性が認められた。

機能検査及び握力では、被験物質投与の影響は認められなかった。

自発運動量では、750 mg/kg投与群の雌雄で測定開始後0~10分の測定に低値が認められた。この変化は休薬により消失し、回復性が認められた。

体重では、750 mg/kg投与群の雄で投与4日以降と投与期間中の体重増加量に低値が認められた。この変化は休薬により消失し、回復性が認められた。

摂餌量では、750 mg/kg投与群の雌雄で投与初期（投与4日）に低値が認められ、被験物質投与の影響が疑われた。

尿検査では、750 mg/kg投与群の雌雄で尿量の高値と浸透圧の低値が、また、雄で摂水量の高値が認められた。これらの変化は休薬により消失し、回復性が認められた。

血液学検査では、被験物質投与の影響は認められなかった。

血液化学検査では、750 mg/kg投与群の雄でALTの高値が、雌でトリグリセライドの高値が認められ、被験物質投与による肝臓への影響が疑われた。また、750 mg/kg投与群の雄で総コレステロール、グルコースの低値が認められ、被験物質投与による体重低下との関連が疑われた。更に、750 mg/kg投与群の雄で塩素の低値が認められた。これらの変化は休薬により消失し、回復性が認められた。

病理学検査では、肝臓、胃及び盲腸に被験物質投与の影響が認められた。肝臓において750 mg/kg投与群の雌雄で相対重量の高値が認められ、組織学的には150 mg/kg投与群の雄と750 mg/kg投与群の雌雄で小葉中心性の肝細胞肥大が認められた。また、胃において肉眼的に750 mg/kg投与群の雌雄で前胃の壁肥厚が、雄で境界縁の肥厚が、組織学的には150 mg/kg以上の投与群の雌雄で前胃の角化亢進及び境界縁の扁平上皮過形成が、750 mg/kg投与群の雌雄で前胃の扁平上皮過形成が認められた。更に、盲腸において肉眼的に150 mg/kg投与群の雌と750 mg/kg投与群の雌雄で拡張が認められた。これらの変化は休薬後ほぼ消失したが、肉眼的に胃において前胃の壁肥厚あるいは境界縁の肥厚が雌雄で、組織学的には肝臓で小葉中心性の肝細胞肥大が雄で、胃において前胃の角化亢進と扁平上皮過形成、境界縁の扁平上皮過形成が雌雄で認めら

れた。しかし、いずれも程度あるいは発現頻度が軽減し、回復性が認められた。

以上の結果、4-ヒドロキシジフェニルメタンの本試験条件下における無影響量は病理学検査で肝臓、胃あるいは盲腸で被験物質投与の影響が認められたことから、雌雄とも 30 mg/kg/day と推定された。また、みられた変化はいずれも可逆性が認められた。

9. 文献

1) [redacted]4-ヒドロキシジフェニルメタンのラットを用いた14日間反復経口投与毒性試験（予備試験）（株式会社ボゾリサーチセンター、試験番号：C-B406、2008年）
2) Snedecor GW, Cochran WG. Statistical methods.8th ed. Ames: Iowa State University Press;1989.
3) Dunnett CW. A multiple comparison procedure for comparing several treatments with a control.J Am Stat Assoc 1955; 50:1096-121.
4) Dunnett CW. New tables for multiple comparisons with a control. Biometrics 1964; 20:482-91.
5) 佐久間昭（1977）：薬効評価－計画と解析－I 東京大学出版会, 東京.
6) 佐久間昭（1981）：薬効評価－計画と解析－II 東京大学出版会, 東京.

B-6355
添付資料　1

試験成績書

2008年01月22日

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

製品名: 4-Benzylphenol				[redacted]
製品コード: H0239	等級: EP	製品ロット: UJSVE	判定: 合格	

項目	結果	規格値
純度(GC)	99.8 %	98.0 %以上
融点	84.3 deg-C	83.0 ～ 86.0 deg-C
メタノール溶状	澄明	ほとんど澄明以内

B-6355
添付資料　2

4-ヒドロキシジフェニルメタンの安定性試験成績書

安定性試験番号　：　A-2165
試験実施施設　：　株式会社ボゾリサーチセンター　御殿場研究所
測定日　：　2008年10月16日
測定方法　：　HPLC

被験物質　：　4-ヒドロキシジフェニルメタン（Lot No. UJSVE）
使用試験番号　：　B-6355
測定対象物質　：　4-ヒドロキシジフェニルメタン

保存・使用期間　：　2008年1月24日（入手日）～2008年10月16日（最終使用日）

判定基準　：　4-ヒドロキシジフェニルメタン（Lot No. UJSVE）の純度が、東京化成工業株式会社より発行されている成績書の規格値（95.0%以上）を満たすこと。

結果

4-ヒドロキシジフェニルメタンのピーク面積 (μV·sec)	総類縁物質の合計ピーク面積 (μV·sec)	総類縁物質 (%)	純度 (%)
37332044	104211	0.3	99.7
37791826	109174	0.3	99.7
37003261	99493	0.3	99.7

判定　：　測定結果は全て純度99.7%であり、規格値を満たした。

試験責任者　：　[redacted]　2008年11月25日

B-6355
添付資料　3（1/2）

被験液中 4-ヒドロキシジフェニルメタン安定性・均一性試験成績書

試験番号	:	A-2110
試験実施施設	:	株式会社ボゾリサーチセンター　御殿場研究所
測定日（ステージ）	:	2008 年　4 月 15 日（調製直後） 2008 年　4 月 24 日（冷所 8 日間+室温 24 時間）
測定方法	:	HPLC
被験物質	:	4-ヒドロキシジフェニルメタン（Lot No. UJSVE）
媒体	:	0.5 w/v%メチルセルロース溶液
調製濃度	:	0.500 及び 200 mg/mL
調製形態	:	懸濁液
調製日	:	2008 年　4 月 15 日
保存条件	:	褐色ガラス瓶に入れ、冷所（冷蔵庫内、許容値：1～10℃）及び室温
測定対象物質	:	4-ヒドロキシジフェニルメタン
評価基準		
安定性	:	残存率（初期値に対する保存後の濃度の平均値）が 100 ±10%以内。
均一性	:	変動係数（CV）が 10%以下。
判定	:	本被験液は冷所 8 日間+室温 24 時間安定であり、かつ均一であることが確認された。
結果	:	次ページを参照
試験責任者	:	[redacted]　2008 年 4 月 24 日

結果　　：

調製濃度 (mg/mL)	採取層	測定濃度 (mg/mL)	
		調製直後	冷所 8 日間 +室温 24 時間
0.500	上層	0.484	0.477
	中層	0.489	0.478
	下層	0.483	0.476
平均値		0.485	0.477
標準偏差		0.003	0.001
残存率(%)		100	98.4
CV(%)		0.6	0.2
200	上層	198	203
	中層	204	206
	下層	203	202
平均値		202	204
標準偏差		3	2
残存率(%)		100	101.0
CV(%)		1.5	1.0

平均値及び標準偏差は Empower を用いて算出した。

B-6355
添付資料　4

4-ヒドロキシジフェニルメタンの被験液中濃度・均一性測定成績書

試　験　番　号　：　B-6355
測定実施施設　：　株式会社ボゾリサーチセンター　御殿場研究所
ス　テ　ー　ジ　：　投与1週
測　定　年　月　日　：　2008年7月11日及び2008年7月12日
測　定　方　法　：　HPLC

被　験　液
　被　験　物　質　：　4-ヒドロキシジフェニルメタン（Lot No. UJSVE）
　媒　　体　：　0.5% MC 水溶液
　表　示　値　：　6、30及び150 mg/mL
　調　製　形　態　：　懸濁
　調製年月日　：　2008年7月11日

判　定　基　準　：　濃度許容範囲；表示値に対する割合；100±10%
　　均一性許容範囲；CV10%以内

結　　果　：

表示値 (mg/mL)	測定濃度 (mg/mL)	平均値±標準偏差	表示値に対する割合 (%)	CV (%)
6	5.93 6.11 6.07	6.04 ± 0.10	100.7	1.7
30	26.3 29.7 30.4	28.8 ± 2.2	96.0	7.6
150	163 162 158	161 ± 3	107.3	1.9

平均値及び標準偏差はEmpowerを用いて算出した。

判　　定　：　適

化学分析責任者　：　[redacted]　2008年7月15日

B-6355
添付資料　5

4-ヒドロキシジフェニルメタンの被験液中濃度・均一性測定成績書

試　験　番　号　：　B-6355
測定実施施設　：　株式会社ボゾリサーチセンター　御殿場研究所
ス　テ　ー　ジ　：　投与4週
測　定　年　月　日　：　2008年8月5日
測　定　方　法　：　HPLC

被　験　液
　被　験　物　質　：　4-ヒドロキシジフェニルメタン（Lot No. UJSVE）
　媒　　体　：　0.5% MC 水溶液
　表　示　値　：　6、30及び150 mg/mL
　調　製　形　態　：　懸濁
　調製年月日　：　2008年8月5日

判　定　基　準　：　濃度許容範囲；表示値に対する割合；100±10%
　　均一性許容範囲；CV10%以内

結　　果　：

表示値 (mg/mL)	測定濃度 (mg/mL)	平均値±標準偏差	表示値に対する割合 (%)	CV (%)
6	5.85 6.02 5.93	5.94 ± 0.08	99.0	1.3
30	29.9 30.6 30.0	30.2 ± 0.4	100.7	1.3
150	141 143 149	144 ± 4	96.0	2.8

平均値及び標準偏差はEmpowerを用いて算出した。

判　　定　：　適

化学分析責任者　：　[redacted]　2008年 8月 8日

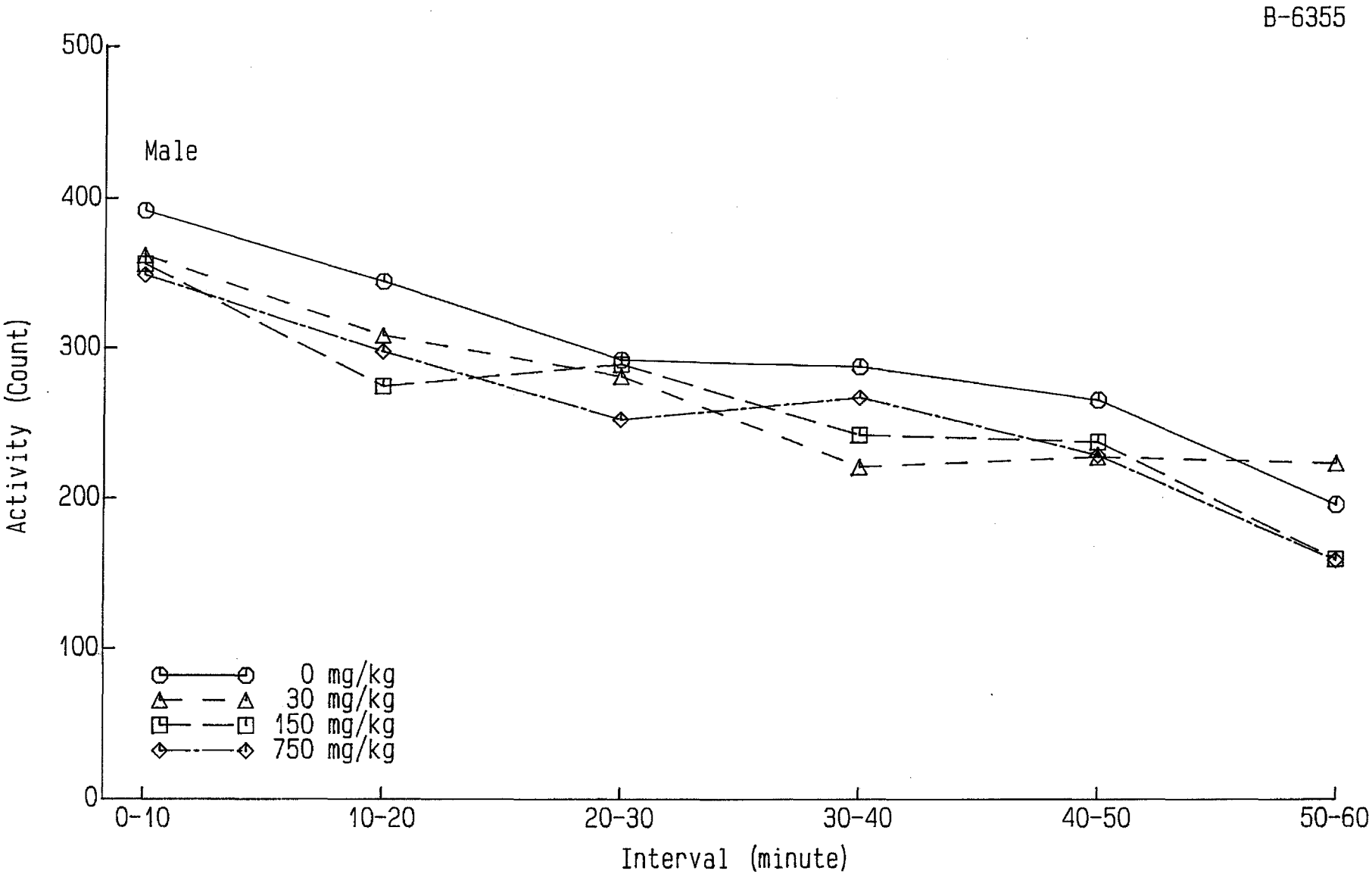

Fig.1 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

——— Motor activity (Week 4 of administration period)———

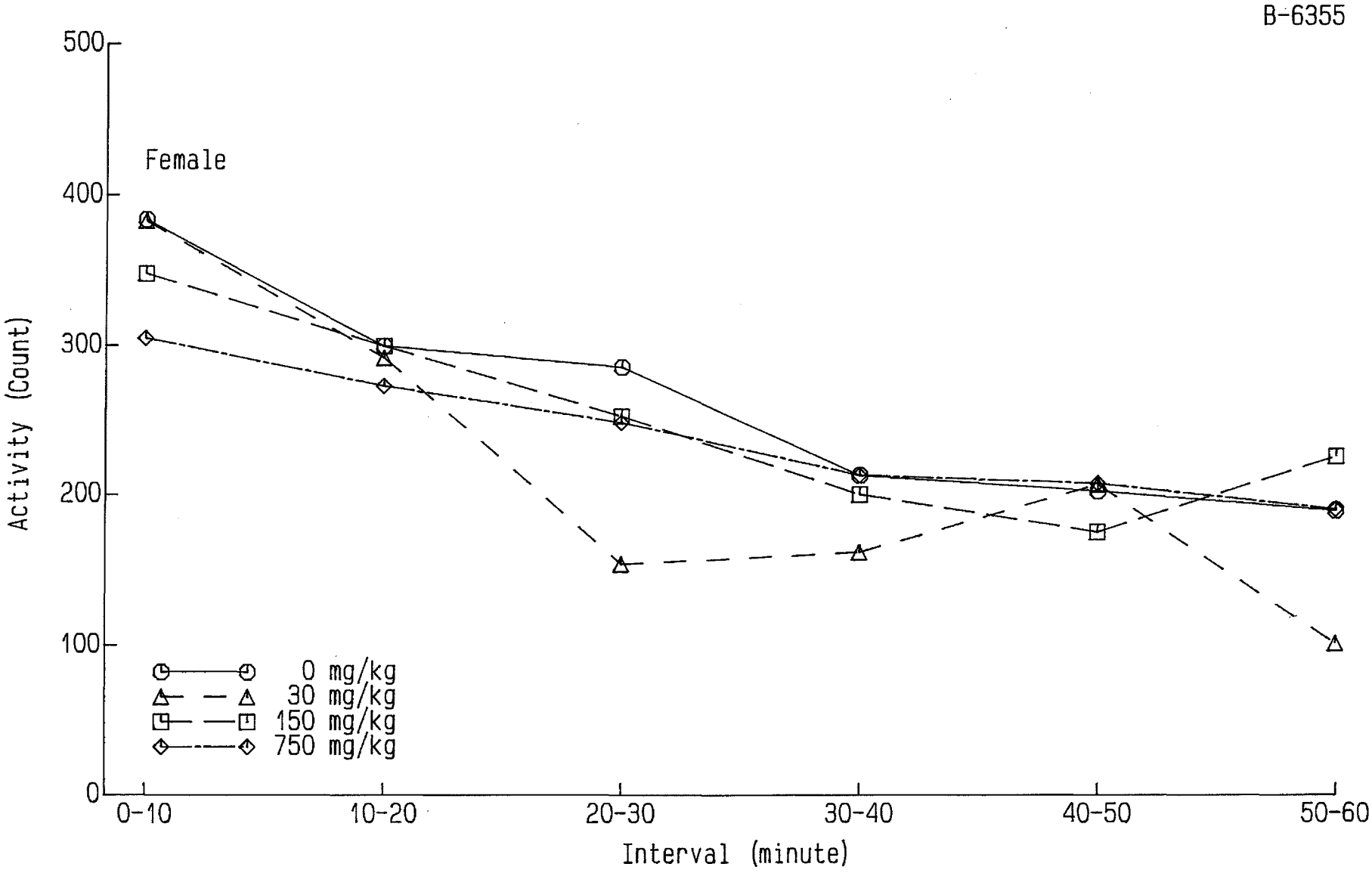

Fig.2 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

——— Motor activity (Week 4 of administration period)———

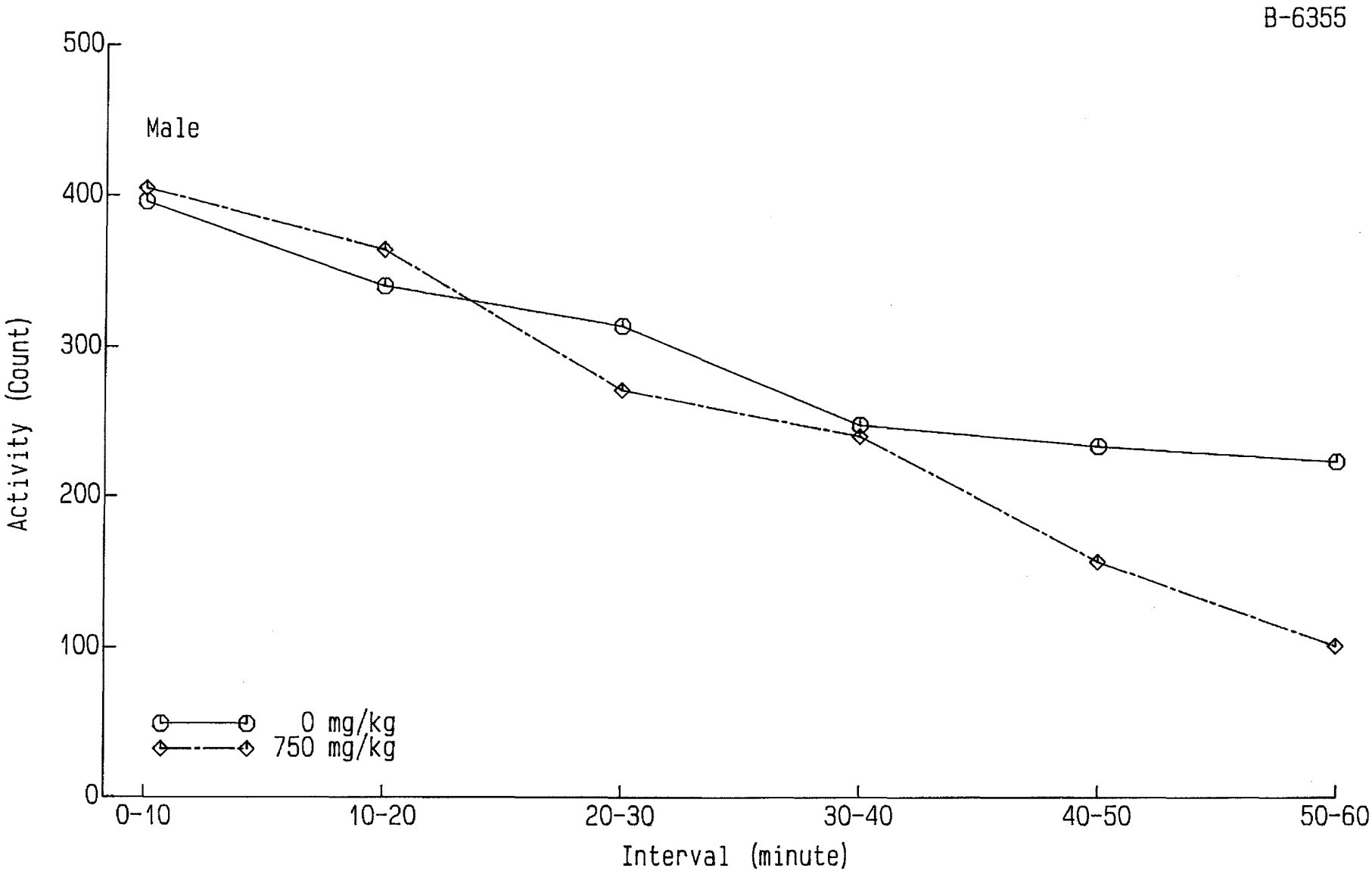

Fig.3 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

——— Motor activity (Week 2 of recovery period)———

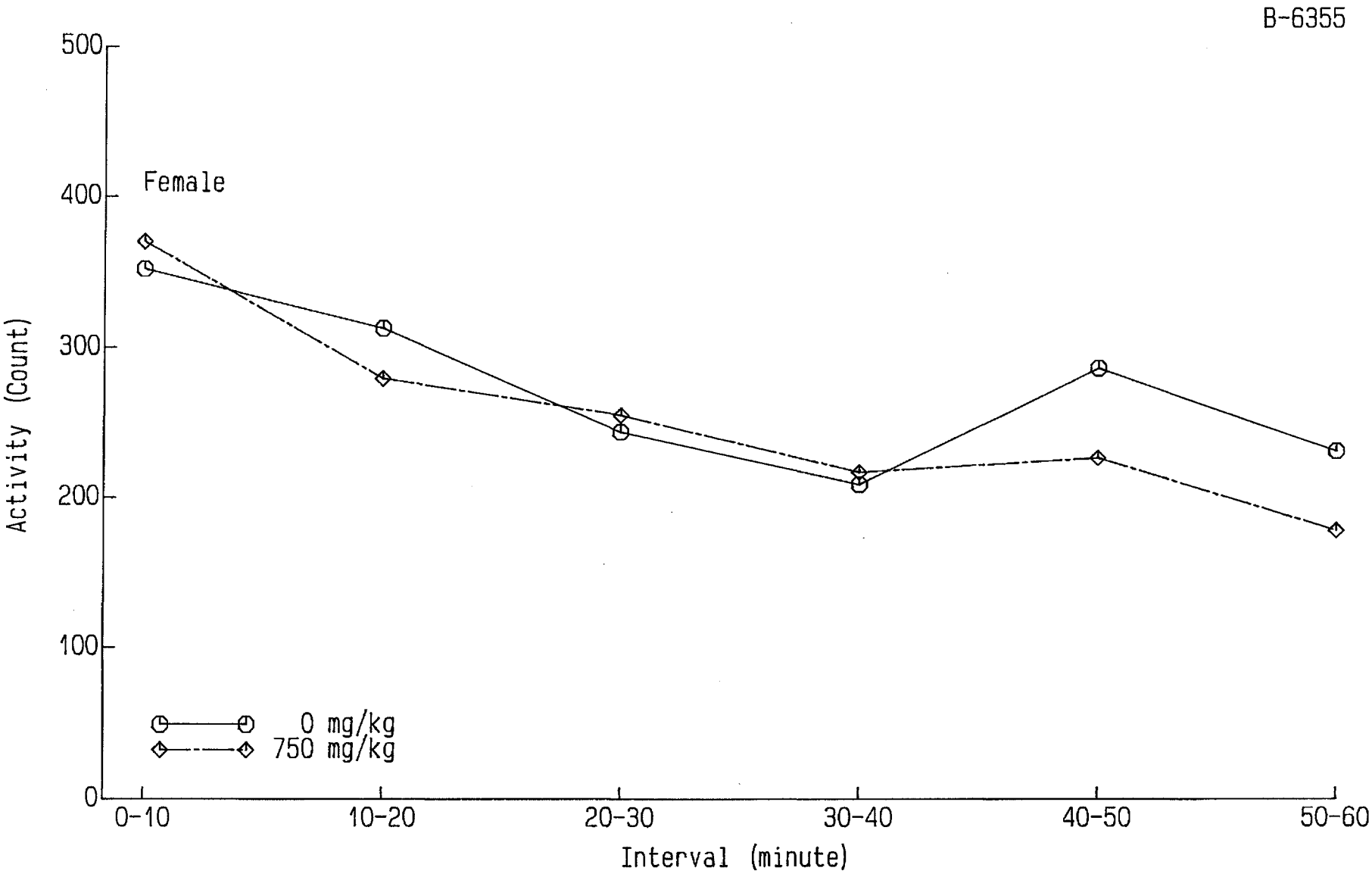

Fig.4 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

——— Motor activity (Week 2 of recovery period)———

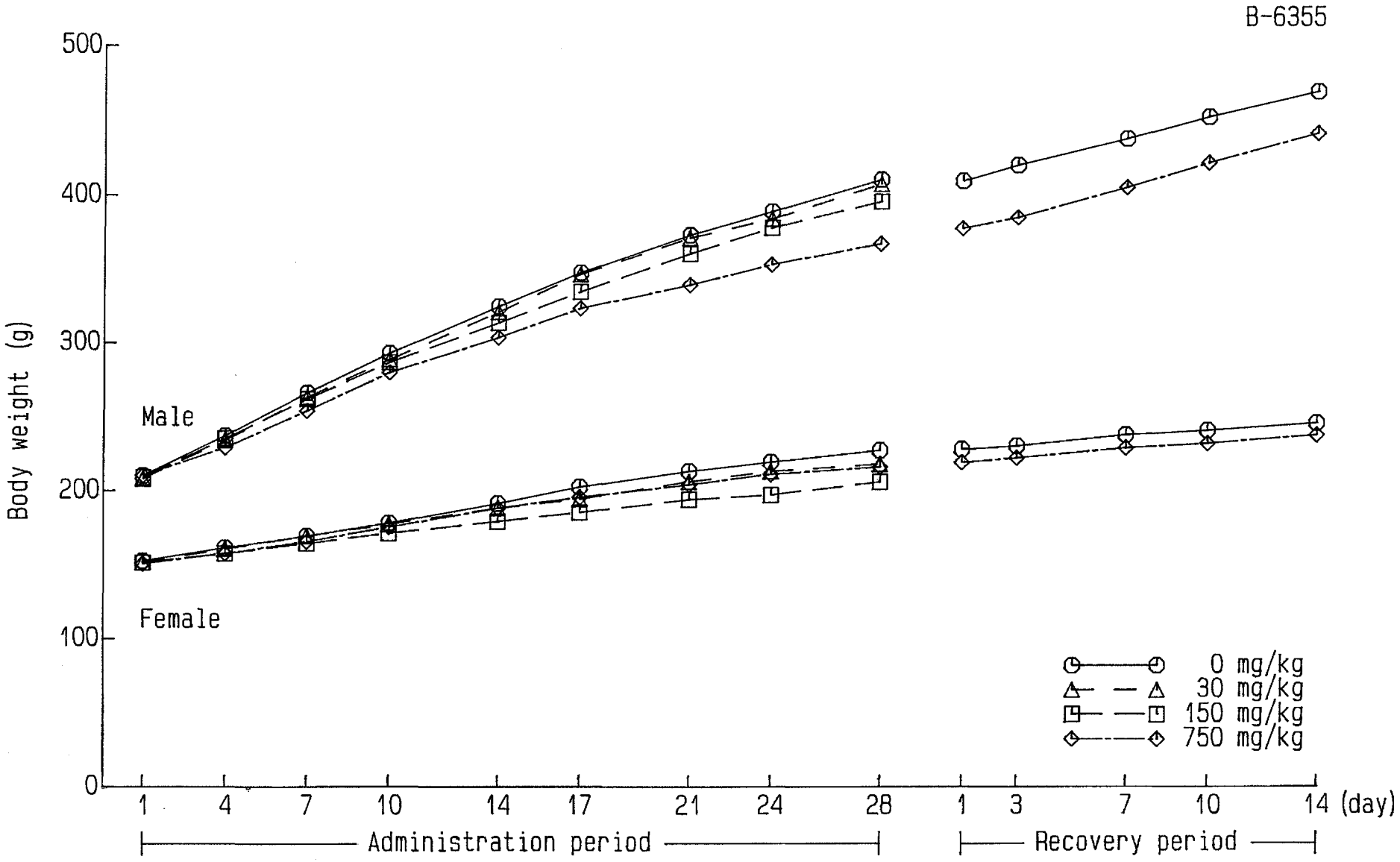

Fig.5 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

——— Body weight ———

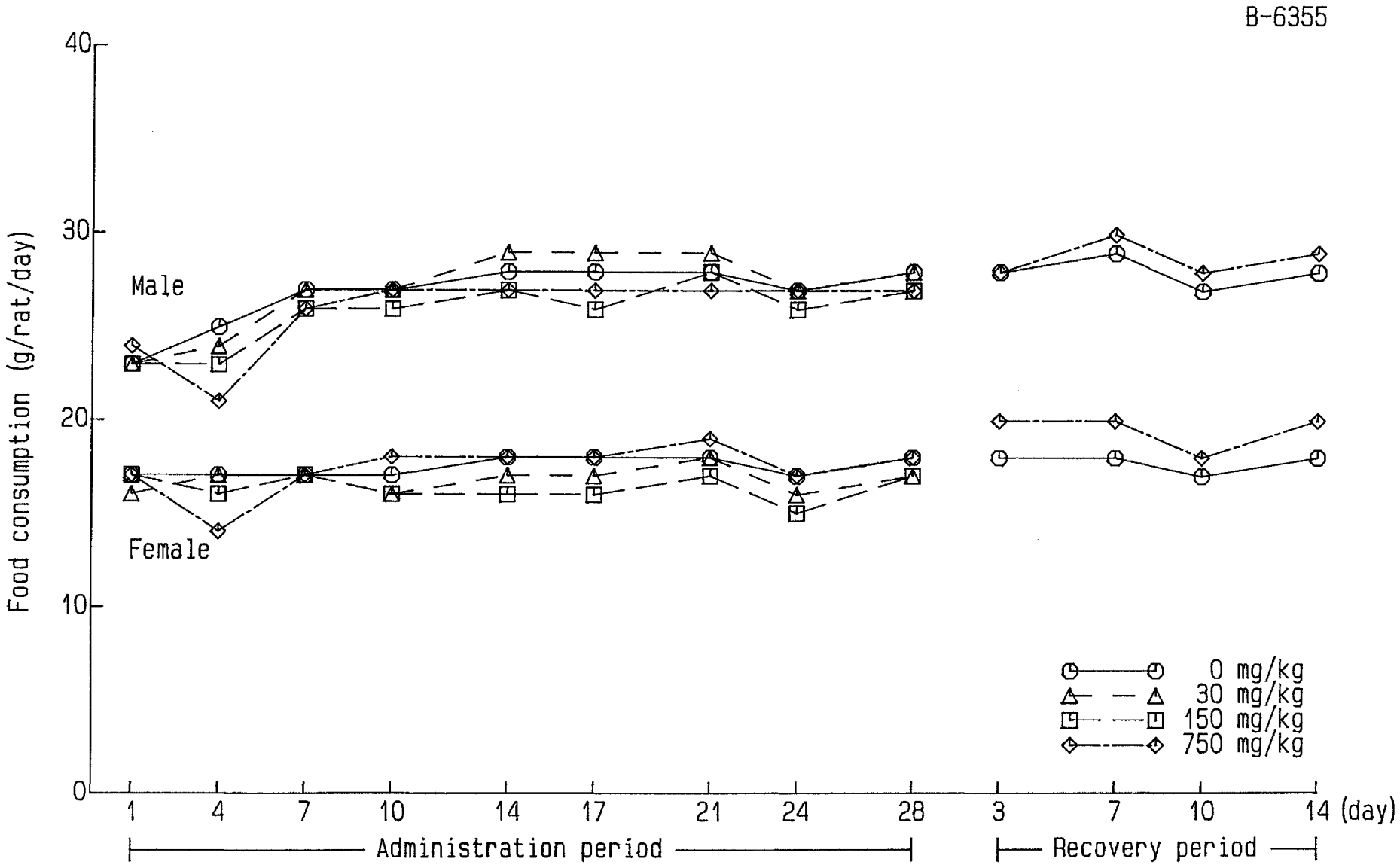

Fig.6 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

——— Food consumption ———

Table 1-1 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Clinical signs (Administration period)

Sex	Dose mg/kg	Findings	Day of administration													
			1	2	3	4	5	6	7	8	9	10	11	12	13	14
Male	0	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12
		No abnormality	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	30	No. of animals	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	150	No. of animals	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	750	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12
		No abnormality	12	12	12	12	11	10	12	9	11	12	12	12	12	12
		Salivation	0	0	0	0	1	2	0	3	1	0	0	0	0	0
Female	0	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12
		No abnormality	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	30	No. of animals	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	150	No. of animals	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	750	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12
		No abnormality	12	12	12	12	10	11	11	9	12	10	10	9	8	12
		Salivation	0	0	0	0	2	1	1	3	0	2	2	3	4	0

Table 1-2 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Clinical signs (Administration period)

Sex	Dose mg/kg	Findings	Day of administration													
			15	16	17	18	19	20	21	22	23	24	25	26	27	28
Male	0	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12
		No abnormality	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	30	No. of animals	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	150	No. of animals	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	750	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12
		No abnormality	10	11	10	10	10	12	11	11	10	10	10	10	9	10
		Salivation	2	1	2	2	2	0	1	1	2	2	2	2	3	2
Female	0	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12
		No abnormality	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	30	No. of animals	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	150	No. of animals	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	750	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12
		No abnormality	10	10	9	10	8	9	11	10	10	10	10	9	8	9
		Salivation	2	2	3	2	4	3	1	2	2	2	2	3	4	3

Table 1-3 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Clinical signs (Recovery period)

Sex	Dose mg/kg	Findings	Day of recovery													
			1	2	3	4	5	6	7	8	9	10	11	12	13	14
Male	0	No. of animals	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	750	No. of animals	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	6	6	6	6	6	6	6	6	6	6	6	6	6	6
Female	0	No. of animals	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	750	No. of animals	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	6	6	6	6	6	6	6	6	6	6	6	6	6	6

Table 2-1 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Detailed clinical signs : home cage observations (Week 1 of administration period)

	Sex	Male				Female			
	Dose (mg/kg)	0	30	150	750	0	30	150	750
Parameter	No. of animals	12	6	6	12	12	6	6	12
Posture									
Normal		12	6	6	12	12	6	6	12
Convulsion									
None		12	6	6	12	12	6	6	12
Abnormal behavior									
None		12	6	6	12	12	6	6	12

Table 2-2 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Detailed clinical signs : home cage observations (Week 2 of administration period)

	Sex	Male				Female			
	Dose (mg/kg)	0	30	150	750	0	30	150	750
Parameter	No. of animals	12	6	6	12	12	6	6	12
Posture									
Normal		12	6	6	12	12	6	6	12
Convulsion									
None		12	6	6	12	12	6	6	12
Abnormal behavior									
None		12	6	6	12	12	6	6	12

Table 2-3 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Detailed clinical signs : home cage observations (Week 3 of administration period)

	Sex	Male				Female			
	Dose (mg/kg)	0	30	150	750	0	30	150	750
Parameter	No. of animals	12	6	6	12	12	6	6	12
Posture									
Normal		12	6	6	12	12	6	6	12
Convulsion									
None		12	6	6	12	12	6	6	12
Abnormal behavior									
None		12	6	6	12	12	6	6	12

Table 2-4 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Detailed clinical signs : home cage observations (Week 4 of administration period)

	Sex	Male				Female			
	Dose (mg/kg)	0	30	150	750	0	30	150	750
Parameter	No. of animals	12	6	6	12	12	6	6	12
Posture									
Normal		12	6	6	12	12	6	6	12
Convulsion									
None		12	6	6	12	12	6	6	12
Abnormal behavior									
None		12	6	6	12	12	6	6	12

Table 2-5 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Detailed clinical signs : home cage observations (Week 1 of recovery period)

	Sex	Male		Female	
	Dose (mg/kg)	0	750	0	750
Parameter	No. of animals	6	6	6	6
Posture					
Normal		6	6	6	6
Convulsion					
None		6	6	6	6
Abnormal behavior					
None		6	6	6	6

Table 2-6 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Detailed clinical signs : home cage observations (Week 2 of recovery period)

	Sex	Male		Female	
	Dose (mg/kg)	0	750	0	750
Parameter	No. of animals	6	6	6	6
Posture					
Normal		6	6	6	6
Convulsion					
None		6	6	6	6
Abnormal behavior					
None		6	6	6	6

Table 2-7 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Detailed clinical signs : in-the-hand observations (Week 1 of administration period)

	Sex	Male				Female			
	Dose (mg/kg)	0	30	150	750	0	30	150	750
Parameter	No. of animals	12	6	6	12	12	6	6	12
Ease of removal from cage									
Easy		12	6	6	12	12	6	6	12
Fur condition									
Normal		12	6	6	12	12	6	6	12
Skin									
Normal		12	6	6	12	12	6	6	12
Secretions-Eye, Nose									
Absent		12	6	6	12	12	6	6	12
Exophthalmos									
Absent		12	6	6	12	12	6	6	12
Palpebral closure									
Normal		12	6	6	12	12	6	6	12
Mucosal membranes									
Normal		12	6	6	12	12	6	6	12
Lacrimation									
Normal		12	6	6	12	12	6	6	12
Piloerection									
Absent		12	6	6	12	12	6	6	12
Pupil size									
Normal		12	6	6	12	12	6	6	12
Salivation									
None		12	6	6	12	12	6	6	12
Abnormal respiration									
Absent		12	6	6	12	12	6	6	12
Reactivity to handling									
Easy		12	6	6	12	12	6	6	12

Table 2-8 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Detailed clinical signs : in-the-hand observations (Week 2 of administration period)

	Sex	Male				Female			
	Dose (mg/kg)	0	30	150	750	0	30	150	750
Parameter	No. of animals	12	6	6	12	12	6	6	12
Ease of removal from cage									
Easy		12	6	6	12	12	6	6	12
Fur condition									
Normal		12	6	6	12	12	6	6	12
Skin									
Normal		12	6	6	12	12	6	6	12
Secretions-Eye, Nose									
Absent		12	6	6	12	12	6	6	12
Exophthalmos									
Absent		12	6	6	12	12	6	6	12
Palpebral closure									
Normal		12	6	6	12	12	6	6	12
Mucosal membranes									
Normal		12	6	6	12	12	6	6	12
Lacrimation									
Normal		12	6	6	12	12	6	6	12
Piloerection									
Absent		12	6	6	12	12	6	6	12
Pupil size									
Normal		12	6	6	12	12	6	6	12
Salivation									
None		12	6	6	9	12	6	6	11
Slight		0	0	0	3	0	0	0	1
Abnormal respiration									
Absent		12	6	6	12	12	6	6	12
Reactivity to handling									
Easy		12	6	6	12	12	6	6	12

Table 2-9 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Detailed clinical signs : in-the-hand observations (Week 3 of administration period)

	Sex	Male				Female			
	Dose (mg/kg)	0	30	150	750	0	30	150	750
Parameter	No. of animals	12	6	6	12	12	6	6	12
Ease of removal from cage									
Easy		12	6	6	12	12	6	6	12
Fur condition									
Normal		12	6	6	12	12	6	6	12
Skin									
Normal		12	6	6	12	12	6	6	12
Secretions-Eye, Nose									
Absent		12	6	6	12	12	6	6	12
Exophthalmos									
Absent		12	6	6	12	12	6	6	12
Palpebral closure									
Normal		12	6	6	12	12	6	6	12
Mucosal membranes									
Normal		12	6	6	12	12	6	6	12
Lacrimation									
Normal		12	6	6	12	12	6	6	12
Piloerection									
Absent		12	6	6	12	12	6	6	12
Pupil size									
Normal		12	6	6	12	12	6	6	12
Salivation									
None		12	6	6	8	12	6	6	7
Slight		0	0	0	4	0	0	0	5
Abnormal respiration									
Absent		12	6	6	12	12	6	6	12
Reactivity to handling									
Easy		12	6	6	12	12	6	6	12

Table 2-10 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Detailed clinical signs : in-the-hand observations (Week 4 of administration period)

	Sex	Male				Female			
	Dose (mg/kg)	0	30	150	750	0	30	150	750
Parameter	No. of animals	12	6	6	12	12	6	6	12
Ease of removal from cage									
Easy		12	6	6	12	12	6	6	12
Fur condition									
Normal		12	6	6	12	12	6	6	12
Skin									
Normal		12	6	6	12	12	6	6	12
Secretions-Eye, Nose									
Absent		12	6	6	12	12	6	6	12
Exophthalmos									
Absent		12	6	6	12	12	6	6	12
Palpebral closure									
Normal		12	6	6	12	12	6	6	12
Mucosal membranes									
Normal		12	6	6	12	12	6	6	12
Lacrimation									
Normal		12	6	6	12	12	6	6	12
Piloerection									
Absent		12	6	6	12	12	6	6	12
Pupil size									
Normal		12	6	6	12	12	6	6	12
Salivation									
None		12	6	6	11	12	6	6	10
Slight		0	0	0	1	0	0	0	2
Abnormal respiration									
Absent		12	6	6	12	12	6	6	12
Reactivity to handling									
Easy		12	6	6	12	12	6	6	12

Table 2-11 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks •

Detailed clinical signs : in-the-hand observations (Week 1 of recovery period)

	Sex	Male		Female	
	Dose (mg/kg)	0	750	0	750
Parameter	No. of animals	6	6	6	6
Ease of removal from cage					
Easy		6	6	6	6
Fur condition					
Normal		6	6	6	6
Skin					
Normal		6	6	6	6
Secretions-Eye, Nose					
Absent		6	6	6	6
Exophthalmos					
Absent		6	6	6	6
Palpebral closure					
Normal		6	6	6	6
Mucosal membranes					
Normal		6	6	6	6
Lacrimation					
Normal		6	6	6	6
Piloerection					
Absent		6	6	6	6
Pupil size					
Normal		6	6	6	6
Salivation					
None		6	6	6	6
Abnormal respiration					
Absent		6	6	6	6
Reactivity to handling					
Easy		6	6	6	6

Table 2-12 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Detailed clinical signs : in-the-hand observations (Week 2 of recovery period)

	Sex	Male		Female	
	Dose (mg/kg)	0	750	0	750
Parameter	No. of animals	6	6	6	6
Ease of removal from cage					
Easy		6	6	6	6
Fur condition					
Normal		6	6	6	6
Skin					
Normal		6	6	6	6
Secretions-Eye, Nose					
Absent		6	6	6	6
Exophthalmos					
Absent		6	6	6	6
Palpebral closure					
Normal		6	6	6	6
Mucosal membranes					
Normal		6	6	6	6
Lacrimation					
Normal		6	6	6	6
Piloerection					
Absent		6	6	6	6
Pupil size					
Normal		6	6	6	6
Salivation					
None		6	6	6	6
Abnormal respiration					
Absent		6	6	6	6
Reactivity to handling					
Easy		6	6	6	6

Table 2-13 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Detailed clinical signs : open field observation (Week 1 of administration period)

	Sex	Male				Female			
	Dose (mg/kg)	0	30	150	750	0	30	150	750
Parameter	No. of animals	12	6	6	12	12	6	6	12
Arousal									
Normal		12	6	6	12	12	6	6	12
Convulsion									
None		12	6	6	12	12	6	6	12
Abnormal behavior									
None		12	6	6	12	12	6	6	12
Stereotypy									
None		12	6	6	12	12	6	6	12
Gait									
Normal		12	6	6	12	12	6	6	12
Posture									
Normal		12	6	6	12	12	6	6	12
Grooming									
None		12	6	6	12	12	6	6	12
Rearing count (Mean±S.D.)		7± 2	6± 4	6± 3	4± 2*D	6± 3	5± 3	6± 1	4± 2
Defecation count (Mean±S.D.)		0± 0	0± 1	0± 1	1± 1	0± 0	0± 0	0± 0	0± 0
Urination									
None		11	4	4	7	12	6	5	12
Small amount		1	2	2	1	0	0	1	0
Moderate amount		0	0	0	4	0	0	0	0

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

Table 2-14 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Detailed clinical signs : open field observation (Week 2 of administration period)

	Sex	Male				Female			
	Dose (mg/kg)	0	30	150	750	0	30	150	750
Parameter	No. of animals	12	6	6	12	12	6	6	12
Arousal									
Normal		12	6	6	12	12	6	6	12
Convulsion									
None		12	6	6	12	12	6	6	12
Abnormal behavior									
None		12	6	6	12	12	6	6	12
Stereotypy									
None		12	6	6	12	12	6	6	12
Gait									
Normal		12	6	6	12	12	6	6	12
Posture									
Normal		12	6	6	12	12	6	6	12
Grooming									
None		12	6	6	12	12	6	6	12
Rearing count (Mean±S.D.)		4± 2	3± 2	3± 2	3± 2	5± 3	4± 2	5± 2	3± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 1	1± 2	0± 0	0± 0	0± 0	0± 0
Urination									
None		12	6	5	8	12	6	6	12
Small amount		0	0	1	4	0	0	0	0

No significant difference in any treated groups from control group.

Table 2-15 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Detailed clinical signs : open field observation (Week 3 of administration period)

	Sex	Male				Female			
	Dose (mg/kg)	0	30	150	750	0	30	150	750
Parameter	No. of animals	12	6	6	12	12	6	6	12
Arousal									
Normal		12	6	6	12	12	6	6	12
Convulsion									
None		12	6	6	12	12	6	6	12
Abnormal behavior									
None		12	6	6	12	12	6	6	12
Stereotypy									
None		12	6	6	12	12	6	6	12
Gait									
Normal		12	6	6	12	12	6	6	12
Posture									
Normal		12	6	6	12	12	6	6	12
Grooming									
None		12	6	6	12	12	6	6	12
Rearing count (Mean±S.D.)		6± 3	4± 2	5± 1	4± 2	8± 3	8± 2	9± 3	7± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	1± 1	0± 1	0± 0	0± 0	0± 0	0± 0
Urination									
None		10	5	6	9	12	6	6	12
Small amount		2	1	0	2	0	0	0	0
Moderate amount		0	0	0	1	0	0	0	0

No significant difference in any treated groups from control group.

Table 2-16 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Detailed clinical signs : open field observation (Week 4 of administration period)

	Sex	Male				Female			
	Dose (mg/kg)	0	30	150	750	0	30	150	750
Parameter	No. of animals	12	6	6	12	12	6	6	12
Arousal									
Normal		12	6	6	12	12	6	6	12
Convulsion									
None		12	6	6	12	12	6	6	12
Abnormal behavior									
None		12	6	6	12	12	6	6	12
Stereotypy									
None		12	6	6	12	12	6	6	12
Gait									
Normal		12	6	6	12	12	6	6	12
Posture									
Normal		12	6	5	12	12	6	6	12
Flattened		0	0	1	0	0	0	0	0
Grooming									
None		12	6	6	12	12	6	6	12
Rearing count (Mean±S.D.)		6± 2	5± 3	6± 1	4± 2	9± 4	9± 2	10± 3	6± 3
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 1	0± 0	0± 0	0± 0	0± 0
Urination									
None		12	5	5	10	11	6	6	11
Small amount		0	1	1	1	1	0	0	1
Moderate amount		0	0	0	1	0	0	0	0

No significant difference in any treated groups from control group.

Table 2-17 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Detailed clinical signs : open field observation (Week 1 of recovery period)

	Sex	Male		Female	
	Dose (mg/kg)	0	750	0	750
Parameter	No. of animals	6	6	6	6
Arousal					
Normal		6	6	6	6
Convulsion					
None		6	6	6	6
Abnormal behavior					
None		6	6	6	6
Stereotypy					
None		6	6	6	6
Gait					
Normal		6	6	6	6
Posture					
Normal		6	6	6	6
Grooming					
None		6	6	6	6
Rearing count (Mean±S.D.)		6± 2	6± 3	8± 2	9± 2
Defecation count (Mean±S.D.)		0± 0	1± 1	0± 0	0± 0
Urination					
None		5	4	6	6
Small amount		1	2	0	0

No significant difference between treated group and control group.

Table 2-18 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Detailed clinical signs : open field observation (Week 2 of recovery period)

	Sex	Male		Female	
	Dose (mg/kg)	0	750	0	750
Parameter	No. of animals	6	6	6	6
Arousal					
Normal		6	6	6	6
Convulsion					
None		6	6	6	6
Abnormal behavior					
None		6	6	6	6
Stereotypy					
None		6	6	6	6
Gait					
Normal		6	6	6	6
Posture					
Normal		6	6	6	6
Grooming					
None		6	6	6	6
Rearing count (Mean±S.D.)		6± 1	5± 3	9± 3	9± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		6	5	6	6
Moderate amount		0	1	0	0

No significant difference between treated group and control group.

Table 2-19 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Manipulative test (Week 4 of administration period)

	Sex	Male				Female			
	Dose (mg/kg)	0	30	150	750	0	30	150	750
Parameter	No. of animals	12	6	6	12	12	6	6	12
Auditory response Normal		12	6	6	12	12	6	6	12
Approach response Normal		12	6	6	12	12	6	6	12
Touch response Normal		12	6	6	12	12	6	6	12
Tail pinch response Normal		12	6	6	12	12	6	6	12
Pupillary reflex Pass, both		12	6	6	12	12	6	6	12
Aerial righting reflex (Total score: Mean±S.D.)		0± 0	0± 0	0± 0	0± 0	0± 0	0± 0	0± 0	0± 0
Landing foot splay (mm: Mean±S.D.)		71±14	62± 9	64± 7	62±13	58±19	58± 3	48±12	47±10

No significant difference in any treated groups from control group.

Table 2-20 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Manipulative test (Week 2 of recovery period)

	Sex	Male		Female	
	Dose (mg/kg)	0	750	0	750
Parameter	No. of animals	6	6	6	6
Auditory response Normal		6	6	6	6
Approach response Normal		6	6	6	6
Touch response Normal		6	6	6	6
Tail pinch response Normal		6	6	6	6
Pupillary reflex Pass, both		6	6	6	6
Aerial righting reflex (Total score: Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Landing foot splay (mm: Mean±S.D.)		84±16	97±11	68±18	65±16

No significant difference between treated group and control group.

Table 2-21 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Grip strength (Week 4 of administration period)

Sex	Dose mg/kg		Fore limb g	Hind limb g
Male	0	No.	12	12
		Mean	976	473
		S.D.	197	100
	30	No.	6	6
		Mean	764	429
		S.D.	147	91
	150	No.	6	6
		Mean	899	492
		S.D.	161	123
	750	No.	12	12
		Mean	963	425
		S.D.	239	91
Female	0	No.	12	12
		Mean	786	324
		S.D.	142	95
	30	No.	6	6
		Mean	817	304
		S.D.	130	52
	150	No.	6	6
		Mean	767	330
		S.D.	57	71
	750	No.	12	12
		Mean	831	360
		S.D.	156	92

No significant difference in any treated groups from control group.

Table 2-22 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Grip strength (Week 2 of recovery period)

Sex	Dose mg/kg		Fore limb g	Hind limb g
Male	0	No.	6	6
		Mean	1319	621
		S.D.	287	135
	750	No.	6	6
		Mean	1319	511
		S.D.	211	98
Female	0	No.	6	6
		Mean	768	420
		S.D.	187	100
	750	No.	6	6
		Mean	965	385
		S.D.	130	83

No significant difference between treated group and control group.

Table 2-23 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Motor activity (Week 4 of administration period)

Sex	Dose mg/kg		Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
Male	0	No.	12	12	12	12	12	12	12
		Mean	392	345	293	289	267	198	1785
		S.D.	45	40	74	91	110	108	365
	30	No.	6	6	6	6	6	6	6
		Mean	362	309	282	222	229	225	1627
		S.D.	45	35	49	108	116	119	326
	150	No.	6	6	6	6	6	6	6
		Mean	356	275*	290	243	239	162	1563
		S.D.	46	29DT	61	79	67	124	152
	750	No.	12	12	12	12	12	12	12
		Mean	349*	298	253	268	230	161	1559
		S.D.	36D	94	87	59	84	116	292
Female	0	No.	12	12	12	12	12	12	12
		Mean	384	300	286	214	204	191	1579
		S.D.	58	53	85	110	116	87	333
	30	No.	6	6	6	6	6	6	6
		Mean	383	292	155**	163	208	102	1302
		S.D.	31	37	87D	105	116	78	176
	150	No.	6	6	6	6	6	6	6
		Mean	348	300	253	201	177	227	1506
		S.D.	49	57	72	117	124	115	409
	750	No.	12	12	12	12	12	12	12
		Mean	305*	273	249	214	209	192	1442
		S.D.	87D	63	47	62	93	65	164

Unit : Count
* : $p<0.05$; ** : $p<0.01$ (Significant difference from control group)
D : Dunnett's test
DT : Dunnett-type rank test

Table 2-24 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Motor activity (Week 2 of recovery period)

Sex	Dose mg/kg		Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
Male	0	No.	6	6	6	6	6	6	6
		Mean	396	341	315	249	235	225	1761
		S.D.	36	41	56	75	122	152	379
	750	No.	6	6	6	6	6	6	6
		Mean	405	365	272	241	158	102	1542
		S.D.	37	37	56	89	104	100	335
Female	0	No.	6	6	6	6	6	6	6
		Mean	352	313	245	210	288	233	1642
		S.D.	46	64	48	68	43	139	273
	750	No.	6	6	6	6	6	6	6
		Mean	370	280	256	218	228*	180	1531
		S.D.	34	39	69	119	46T	105	194

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

Table 3-1 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Body weight (Administration period)

Sex	Dose mg/kg		Day of administration 1	4	7	10	14	17	21	24	28	Gain 1-28
Male	0	No.	12	12	12	12	12	12	12	12	12	12
		Mean	210	237	266	293	325	348	374	390	412	202
		S.D.	7	7	10	12	15	17	21	21	24	20
	30	No.	6	6	6	6	6	6	6	6	6	6
		Mean	208	234	263	289	321	347	372	385	409	202
		S.D.	5	7	7	7	8	8	11	11	14	12
	150	No.	6	6	6	6	6	6	6	6	6	6
		Mean	209	235	262	287	314	335	361	379	397	188
		S.D.	5	6	8	10	13	17	19	21	21	18
	750	No.	12	12	12	12	12	12	12	12	12	12
		Mean	210	229*	254*	280*	304**	324**	340**	354**	368**	158**
		S.D.	6	7D	11D	12D	16D	18D	24D	26D	29D	27D
Female	0	No.	12	12	12	12	12	12	12	12	12	12
		Mean	153	162	170	179	192	203	214	220	228	74
		S.D.	7	8	11	13	15	16	19	16	18	16
	30	No.	6	6	6	6	6	6	6	6	6	6
		Mean	152	161	170	178	189	195	207	214	219	68
		S.D.	8	9	10	11	12	12	10	12	13	6
	150	No.	6	6	6	6	6	6	6	6	6	6
		Mean	152	158	165	172	180	186	195	198	207	55
		S.D.	8	10	13	15	20	21	21	21	20	18
	750	No.	12	12	12	12	12	12	12	12	12	12
		Mean	151	158	166	176	189	196	205	212	217	66
		S.D.	8	13	16	16	19	21	23	25	27	20

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

Table 3-2 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Body weight (Recovery period)

Sex	Dose mg/kg		Day of recovery 1	3	7	10	14	Gain 1-14
Male	0	No.	6	6	6	6	6	6
		Mean	411	422	440	455	472	61
		S.D.	29	34	35	42	42	15
	750	No.	6	6	6	6	6	6
		Mean	379	386	407	424	444	66
		S.D.	35	39	43	46	50	17
Female	0	No.	6	6	6	6	6	6
		Mean	229	231	239	242	247	18
		S.D.	16	19	19	18	20	7
	750	No.	6	6	6	6	6	6
		Mean	220	223	230	233	239	19
		S.D.	21	23	25	26	31	11

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

Table 4-1 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Food consumption (Administration period)

Sex	Dose mg/kg		Day of administration 1	4	7	10	14	17	21	24	28
	0	No.	12	12	12	12	12	12	12	12	12
		Mean	23	25	27	27	28	28	28	27	28
		S.D.	1	1	2	1	1	1	2	1	2
Male	30	No.	6	6	6	6	6	6	6	6	6
		Mean	23	24	27	27	29	29	29	27	28
		S.D.	2	2	1	1	1	2	2	2	2
	150	No.	6	6	6	6	6	6	6	6	6
		Mean	23	23	26	26	27	26	28	26	27
		S.D.	1	1	1	1	1	2	2	2	2
	750	No.	12	12	12	12	12	12	12	12	12
		Mean	24	21**	26	27	27	27	27	27	27
		S.D.	2	2D	2	2	3	2	3	3	3
	0	No.	12	12	12	12	12	12	12	12	12
		Mean	17	17	17	17	18	18	18	17	18
		S.D.	1	1	2	1	2	1	2	1	2
Female	30	No.	6	6	6	6	6	6	6	6	6
		Mean	16	17	17	16	17	17	18	16	17
		S.D.	2	1	1	2	2	1	1	2	1
	150	No.	6	6	6	6	6	6	6	6	6
		Mean	17	16	17	16	16	16	17	15	17
		S.D.	2	2	2	2	2	2	2	2	2
	750	No.	12	12	12	12	12	12	12	12	12
		Mean	17	14*	17	18	18	18	19	17	18
		S.D.	2	3DT	2	2	3	3	2	2	3

Unit : g/rat/day
* : $p<0.05$; ** : $p<0.01$ (Significant difference from control group)
D : Dunnett's test
DT : Dunnett-type rank test

Table 4-2 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Food consumption (Recovery period)

Sex	Dose mg/kg		Day of recovery 3	7	10	14
Male	0	No.	6	6	6	6
		Mean	28	29	27	28
		S.D.	2	2	4	2
	750	No.	6	6	6	6
		Mean	28	30	28	29
		S.D.	3	3	4	3
Female	0	No.	6	6	6	6
		Mean	18	18	17	18
		S.D.	2	2	2	2
	750	No.	6	6	6	6
		Mean	20	20	18	20
		S.D.	3	2	1	3

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

Table 5-1 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Urinalysis (Week 4 of administration period)

Sex	Dose mg/kg	No.	pH									1) Protein						2) Ketone body						3) Glucose					
			5.0	5.5	6.0	6.5	7.0	7.5	8.0	8.5	9.0	-	+-	+	++	+++	++++	-	+-	+	++	+++	++++	-	+-	+	++	+++	++++
Male	0	12	0	0	0	0	0	0	1	7	4	1	6	5	0	0	0	6	3	3	0	0	0	12	0	0	0	0	0
	30	6	0	0	0	0	0	0	0	6	0	2	2	2	0	0	0	4	0	2	0	0	0	6	0	0	0	0	0
	150	6	0	0	0	0	0	1	0	3	2	0	3	3	0	0	0	1	4	1	0	0	0	6	0	0	0	0	0
	750	12	0	0	0	1	1	1	4	5	0	6	5	1	0	0	0	11	1	0	0	0	0	12	0	0	0	0	0
Female	0	12	0	0	0	0	2	0	1	6	3	10	1	1	0	0	0	11	0	1	0	0	0	12	0	0	0	0	0
	30	6	0	0	0	0	0	1	0	3	2	4	2	0	0	0	0	3	3	0	0	0	0	6	0	0	0	0	0
	150	6	0	0	0	2	1	0	2	0	1	3	3	0	0	0	0	3	3	0	0	0	0	6	0	0	0	0	0
	750	12	0	0	0	1	3	5	2	1	0	12	0	0	0	0	0	12	0	0	0	0	0	12	0	0	0	0	0

1) - : <10 mg/dL +- : 10 - 25 mg/dL + : 26 - 85 mg/dL ++ : 86 - 250 mg/dL +++ : 251 - 600 mg/dL ++++ : >600 mg/dL
2) - : <5 mg/dL +- : 5 - 7.5 mg/dL + : 7.6 - 30 mg/dL ++ : 31 - 70 mg/dL +++ : 71 - 125 mg/dL ++++ : >125 mg/dL
3) - : <30 mg/dL +- : 30 - 60 mg/dL + : 61 - 125 mg/dL ++ : 126 - 250 mg/dL +++ : 251 - 750 mg/dL ++++ : >750 mg/dL

Table 5-2 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Urinalysis (Week 4 of administration period)

Sex	Dose mg/kg	No.	4) Occult blood					5) Bilirubin					6) Urobilinogen					7) Color		
			-	+-	+	++	+++	-	+	++	+++	++++	+-	+	++	+++	++++	LY	Y	DY
Male	0	12	11	0	0	1	0	12	0	0	0	0	11	1	0	0	0	0	12	0
	30	6	6	0	0	0	0	6	0	0	0	0	5	1	0	0	0	0	6	0
	150	6	6	0	0	0	0	6	0	0	0	0	6	0	0	0	0	0	6	0
	750	12	12	0	0	0	0	12	0	0	0	0	12	0	0	0	0	0	12	0
Female	0	12	12	0	0	0	0	12	0	0	0	0	11	1	0	0	0	0	12	0
	30	6	5	1	0	0	0	6	0	0	0	0	6	0	0	0	0	0	6	0
	150	6	6	0	0	0	0	6	0	0	0	0	5	1	0	0	0	0	6	0
	750	12	12	0	0	0	0	12	0	0	0	0	12	0	0	0	0	0	12	0

4) - : <0.03 mg/dL +- : 0.03 - 0.05 mg/dL + : 0.06 - 0.15 mg/dL ++ : 0.16 - 0.75 mg/dL +++ : >0.75 mg/dL
5) - : <0.5 mg/dL + : 0.5 - 1.5 mg/dL ++ : 1.6 - 5.0 mg/dL +++ : 5.1 - 10.0 mg/dL ++++ : >10.0 mg/dL
6) +- : <2.0 mg/dL + : 2.0 - 3.5 mg/dL ++ : 3.6 - 7.0 mg/dL +++ : 7.1 - 12.0 mg/dL ++++ : >12.0 mg/dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Table 5-3 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Urinalysis (Week 4 of administration period)

Sex	Dose mg/kg	No.	URINE SEDIMENT																															
			RBC					WBC					SEC					SREC					Cast			CRYSTALLIZATION PS						CRYSTALLIZATION CO				
			-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	-	+-	+	++	+++	-	+-	+	++	+++
Male	0	12	12	0	0	0	0	12	0	0	0	0	0	11	1	0	0	12	0	0	0	0	12	0	0	11	1	0	0	0	12	0	0	0	0
	30	6	6	0	0	0	0	5	1	0	0	0	0	6	0	0	0	6	0	0	0	0	6	0	0	6	0	0	0	0	6	0	0	0	0
	150	6	6	0	0	0	0	6	0	0	0	0	0	5	1	0	0	6	0	0	0	0	6	0	0	6	0	0	0	0	6	0	0	0	0
	750	12	12	0	0	0	0	12	0	0	0	0	0	12	0	0	0	11	1	0	0	0	12	0	0	9	3	0	0	0	12	0	0	0	0
Female	0	12	12	0	0	0	0	11	1	0	0	0	0	12	0	0	0	12	0	0	0	0	12	0	0	9	3	0	0	0	11	1	0	0	0
	30	6	6	0	0	0	0	5	1	0	0	0	0	6	0	0	0	6	0	0	0	0	6	0	0	5	1	0	0	0	6	0	0	0	0
	150	6	6	0	0	0	0	6	0	0	0	0	0	6	0	0	0	6	0	0	0	0	6	0	0	5	1	0	0	0	6	0	0	0	0
	750	12	12	0	0	0	0	12	0	0	0	0	0	12	0	0	0	12	0	0	0	0	12	0	0	6	6	0	0	0	12	0	0	0	0

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

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

Table 5-4 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Water intake and urinalysis (Week 4 of administration period)

Sex	Dose mg/kg	No.		Water intake mL/24h	Urine volume mL/24h	Osmolality mOsm/kg
Male	0	12	Mean	37	10.8	2019
			S.D.	10	4.4	360
	30	6	Mean	35	12.1	2005
			S.D.	8	3.6	364
	150	6	Mean	41	13.1	1709
			S.D.	10	3.2	321
	750	12	Mean	57**	18.2**	1227**
			S.D.	11D	6.3D	245D
Female	0	12	Mean	32	6.3	2081
			S.D.	8	2.4	401
	30	6	Mean	29	6.5	2326
			S.D.	10	2.6	536
	150	6	Mean	31	4.5	2211
			S.D.	9	3.1	549
	750	12	Mean	41	12.7**	1224**
			S.D.	9	6.1D	275D

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

Table 5-5 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Urinalysis (Week 2 of recovery period)

Sex	Dose mg/kg	No.	pH									1) Protein						2) Ketone body						3) Glucose					
			5.0	5.5	6.0	6.5	7.0	7.5	8.0	8.5	9.0	-	+-	+	++	+++	++++	-	+-	+	++	+++	++++	-	+-	+	++	+++	++++
Male	0	6	0	0	0	0	0	0	0	4	2	0	1	5	0	0	0	3	2	1	0	0	0	6	0	0	0	0	0
	750	6	0	0	0	0	0	0	1	5	0	0	1	5	0	0	0	0	3	3	0	0	0	6	0	0	0	0	0
Female	0	6	0	0	0	0	0	2	0	2	2	3	3	0	0	0	0	5	1	0	0	0	0	6	0	0	0	0	0
	750	6	0	0	0	0	0	0	0	5	1	1	4	1	0	0	0	3	3	0	0	0	0	6	0	0	0	0	0

1) - : <10 mg/dL +- : 10 - 25 mg/dL + : 26 - 85 mg/dL ++ : 86 - 250 mg/dL +++ : 251 - 600 mg/dL ++++ : >600 mg/dL

2) - : <5 mg/dL +- : 5 - 7.5 mg/dL + : 7.6 - 30 mg/dL ++ : 31 - 70 mg/dL +++ : 71 - 125 mg/dL ++++ : >125 mg/dL

3) - : <30 mg/dL +- : 30 - 60 mg/dL + : 61 - 125 mg/dL ++ : 126 - 250 mg/dL +++ : 251 - 750 mg/dL ++++ : >750 mg/dL

Table 5-6 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Urinalysis (Week 2 of recovery period)

Sex	Dose mg/kg	No.	4) Occult blood					5) Bilirubin					6) Urobilinogen					7) Color		
			-	+-	+	++	+++	-	+	++	+++	++++	+-	+	++	+++	++++	LY	Y	DY
Male	0	6	6	0	0	0	0	6	0	0	0	0	6	0	0	0	0	0	6	0
	750	6	6	0	0	0	0	6	0	0	0	0	5	1	0	0	0	0	6	0
Female	0	6	6	0	0	0	0	6	0	0	0	0	6	0	0	0	0	0	6	0
	750	6	6	0	0	0	0	6	0	0	0	0	6	0	0	0	0	0	6	0

4) - : <0.03 mg/dL +- : 0.03 - 0.05 mg/dL + : 0.06 - 0.15 mg/dL ++ : 0.16 - 0.75 mg/dL +++ : >0.75 mg/dL
5) - : <0.5 mg/dL + : 0.5 - 1.5 mg/dL ++ : 1.6 - 5.0 mg/dL +++ : 5.1 - 10.0 mg/dL ++++ : >10.0 mg/dL
6) +- : <2.0 mg/dL + : 2.0 - 3.5 mg/dL ++ : 3.6 - 7.0 mg/dL +++ : 7.1 - 12.0 mg/dL ++++ : >12.0 mg/dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Table 5-7 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Urinalysis (Week 2 of recovery period)

Sex	Dose mg/kg	No.	URINE SEDIMENT																																	
			RBC					WBC					SEC					SREC					Cast			CRYSTALLIZATION PS						CRYSTALLIZATION CO					
			-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	-	+-	+	++	+++	-	+-	+	++	+++
Male	0	6	6	0	0	0	0	6	0	0	0	0	0	6	0	0	0	6	0	0	0	0	6	0	0	5	1	0	0	0	6	0	0	0	0
	750	6	6	0	0	0	0	6	0	0	0	0	0	6	0	0	0	6	0	0	0	0	6	0	0	4	2	0	0	0	6	0	0	0	0
Female	0	6	6	0	0	0	0	6	0	0	0	0	0	5	1	0	0	6	0	0	0	0	6	0	0	6	0	0	0	0	6	0	0	0	0
	750	6	6	0	0	0	0	6	0	0	0	0	0	6	0	0	0	6	0	0	0	0	6	0	0	5	1	0	0	0	6	0	0	0	0

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

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

Table 5-8 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Water intake and urinalysis (Week 2 of recovery period)

Sex	Dose mg/kg	No.		Water intake mL/24h	Urine volume mL/24h	Osmolality mOsm/kg
Male	0	6	Mean	38	11.4	2087
			S.D.	7	5.0	369
	750	6	Mean	40	9.6	2058
			S.D.	7	4.3	432
Female	0	6	Mean	28	6.5	2384
			S.D.	8	2.9	595
	750	6	Mean	27	5.4	2294
			S.D.	5	1.7	428

No significant difference between treated group and control group.

Table 6-1 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Hematology (After administration period)

Sex	Dose mg/kg	No.		RBC X10⁴/μL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Reticul. %	PLT X10⁴/μL	PT s	APTT s	FIB mg/dL
Male	0	6	Mean	822	16.3	44.7	54.5	19.8	36.4	1.9	117.6	15.8	21.9	318
			S.D.	29	0.5	1.2	2.4	0.8	0.4	0.3	11.6	2.9	5.2	35
	30	6	Mean	828	16.2	44.8	54.1	19.6	36.2	1.8	124.6	16.3	20.9	318
			S.D.	42	0.6	2.2	0.6	0.2	0.5	0.4	12.1	1.6	2.3	28
	150	6	Mean	819	15.8	43.6	53.2	19.3	36.4	1.8	131.7	14.8	21.4	292
			S.D.	38	0.7	2.1	1.0	0.3	0.2	0.2	15.5	1.8	2.1	26
	750	6	Mean	809	16.0	43.3	53.5	19.7	36.9	1.6	129.0	17.5	24.5	297
			S.D.	31	0.4	1.4	0.8	0.4	0.3	0.2	6.7	2.8	2.0	13
Female	0	6	Mean	792	15.6	41.9	52.9	19.7	37.2	1.5	134.4	11.5	15.3	226
			S.D.	33	0.8	2.2	0.8	0.3	0.3	0.4	14.1	0.6	1.5	5
	30	6	Mean	782	15.6	41.7	53.4	20.0	37.4	3.0	131.7	11.7	17.2	227
			S.D.	74	1.0	2.4	2.9	0.7	1.3	3.6	8.4	0.6	1.1	17
	150	6	Mean	798	15.7	41.6	52.1	19.7	37.7	1.3	133.9	11.5	17.9	227
			S.D.	36	0.4	0.9	1.5	0.6	0.3	0.3	13.7	0.6	1.6	20
	750	6	Mean	801	16.2	42.8	53.5	20.2	37.7	1.3	133.6	11.1	17.4	243
			S.D.	52	0.7	1.8	1.4	0.5	0.7	0.4	20.6	0.2	3.1	33

No significant difference in any treated groups from control group.

Table 6-2 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Hematology (After administration period)

Sex	Dose mg/kg	No.		WBC	Differential leukocyte counts (%)					
				$\times 10^2/\mu L$	LYMP	NEUT	EOS	BASO	MONO	LUC
Male	0	6	Mean	115.0	81.9	14.3	1.3	0.4	1.6	0.5
			S.D.	25.7	3.3	3.0	0.5	0.1	0.5	0.2
	30	6	Mean	97.8	76.8	19.3	1.0	0.3	2.0	0.6
			S.D.	28.4	6.9	6.5	0.2	0.1	0.5	0.3
	150	6	Mean	111.5	82.3	14.4	1.0	0.4	1.4	0.6
			S.D.	13.8	3.2	2.9	0.5	0.1	0.3	0.2
	750	6	Mean	150.8	77.4	18.9	0.7	0.5	1.8	0.7
			S.D.	39.1	6.9	6.9	0.3	0.2	0.9	0.4
Female	0	6	Mean	79.3	80.6	15.3	1.4	0.3	1.6	0.8
			S.D.	27.4	7.0	7.3	0.6	0.1	0.2	0.4
	30	6	Mean	68.8	76.5	19.9	1.4	0.3	1.4	0.5
			S.D.	20.5	4.6	4.8	0.4	0.1	0.5	0.2
	150	6	Mean	67.8	77.9	18.5	1.2	0.2	1.6	0.6
			S.D.	16.8	6.3	6.5	0.4	0.1	0.2	0.2
	750	6	Mean	91.1	78.0	17.7	1.3	0.3	2.0	0.7
			S.D.	22.1	6.7	6.5	0.5	0.2	0.7	0.3

LUC : Large unstained cells
No significant difference in any treated groups from control group.

Table 6-3 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Hematology (After administration period)

Sex	Dose mg/kg	No.		Differential leukocyte counts ($\times 10^2/\mu L$)					
				LYMP	NEUT	EOS	BASO	MONO	LUC
Male	0	6	Mean	94.2	16.4	1.5	0.5	1.8	0.6
			S.D.	21.5	4.7	0.6	0.2	0.5	0.3
	30	6	Mean	76.5	17.7	0.9	0.3	1.9	0.6
			S.D.	29.2	3.9	0.1	0.2	0.6	0.2
	150	6	Mean	91.8	16.0	1.1	0.4	1.5	0.7
			S.D.	13.4	3.2	0.6	0.1	0.4	0.3
	750	6	Mean	118.9	26.3**	1.0	0.7	2.7	1.2
			S.D.	40.6	5.1D	0.4	0.4	1.2	0.7
Female	0	6	Mean	64.7	11.3	1.0	0.2	1.3	0.7
			S.D.	25.5	4.0	0.4	0.1	0.5	0.6
	30	6	Mean	53.2	13.2	0.9	0.2	1.0	0.4
			S.D.	17.4	3.3	0.4	0.1	0.5	0.3
	150	6	Mean	52.7	12.6	0.8	0.2	1.1	0.4
			S.D.	13.3	5.5	0.3	0.1	0.3	0.2
	750	6	Mean	71.9	15.4	1.1	0.3	1.8	0.7
			S.D.	21.0	3.6	0.3	0.2	0.6	0.4

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

Table 6-4 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Hematology (After recovery period)

Sex	Dose mg/kg	No.		RBC $\times10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Reticul. %	PLT $\times10^4/\mu L$	PT s	APTT s	FIB mg/dL
Male	0	6	Mean	840	15.8	44.2	52.6	18.8	35.8	1.8	118.9	15.2	20.8	296
			S.D.	31	0.4	1.4	1.6	0.6	0.3	0.1	13.4	2.0	3.9	26
	750	6	Mean	841	15.7	43.6	52.0	18.7	36.0	2.2*	117.3	15.4	19.8	309
			S.D.	43	0.3	1.0	2.0	0.9	0.4	0.4AT	12.9	2.2	2.4	16
Female	0	6	Mean	815	15.6	42.2	51.9	19.2	37.0	1.5	119.0	11.7	16.9	221
			S.D.	36	0.5	1.3	1.4	0.6	0.2	0.3	7.9	0.6	2.1	17
	750	6	Mean	799	15.2	41.0	51.4	19.1	37.1	1.5	117.7	11.9	16.7	215
			S.D.	35	0.6	1.2	1.7	0.6	0.6	0.4	12.8	0.3	2.1	12

* : $p<0.05$ (Significant difference from control group)
AT : Aspin-Welch t-test

Table 6-5 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Hematology (After recovery period)

Sex	Dose mg/kg	No.		WBC	Differential leukocyte counts (%)					
				$\times 10^2/\mu L$	LYMP	NEUT	EOS	BASO	MONO	LUC
Male	0	6	Mean	127.7	80.1	15.8	1.0	0.4	2.0	0.7
			S.D.	28.0	5.7	5.5	0.3	0.1	1.1	0.5
	750	6	Mean	119.9	77.9	18.5	0.9	0.4	1.8	0.4
			S.D.	33.0	6.9	6.5	0.3	0.1	0.7	0.1
Female	0	6	Mean	76.6	74.7	21.4	1.4	0.3	1.6	0.5
			S.D.	19.8	6.6	6.1	0.6	0.1	0.6	0.3
	750	6	Mean	58.1	77.3	19.5	1.0	0.2	1.5	0.4
			S.D.	13.7	5.2	5.4	0.3	0.1	0.3	0.1

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

Table 6-6 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Hematology (After recovery period)

Sex	Dose mg/kg	No.		Differential leukocyte counts ($X10^2/\mu L$)					
				LYMP	NEUT	EOS	BASO	MONO	LUC
Male	0	6	Mean	103.0	19.4	1.2	0.5	2.6	0.9
			S.D.	28.7	6.5	0.3	0.3	1.7	0.8
	750	6	Mean	92.9	22.8	1.1	0.5	2.2	0.5
			S.D.	25.5	11.2	0.3	0.3	0.9	0.2
Female	0	6	Mean	58.0	15.8	1.1	0.2	1.2	0.4
			S.D.	19.6	3.4	0.5	0.1	0.4	0.3
	750	6	Mean	44.8	11.5	0.6	0.1	0.9	0.2
			S.D.	10.3	4.4	0.2	0.1	0.3	0.1

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

Table 7-1 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Blood chemistry (After administration period)

Sex	Dose mg/kg	No.		AST IU/L	ALT IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
Male	0	6	Mean	67	30	62	1	666	53	61	93	0.1	143
			S.D.	12	6	11	1	136	4	14	7	0.1	10
	30	6	Mean	68	28	58	1	751	52	67	93	0.1	140
			S.D.	6	4	9	0	78	4	18	7	0.0	8
	150	6	Mean	67	30	70	1	655	52	47	87	0.1	147
			S.D.	6	6	7	0	133	10	17	14	0.1	12
	750	6	Mean	70	41**	70	1	759	40**	48	79	0.1	122**
			S.D.	6	3D	15	0	95	6D	33	12	0.1	8D
Female	0	6	Mean	63	23	59	1	418	54	17	102	0.1	114
			S.D.	11	4	11	0	113	4	6	11	0.0	20
	30	6	Mean	60	20	69	1	312	62	14	111	0.1	106
			S.D.	6	3	23	0	55	11	5	17	0.1	17
	150	6	Mean	69	23	57	1	437	62	15	109	0.1	103
			S.D.	12	3	8	0	102	9	5	17	0.0	14
	750	6	Mean	68	28	52	1	388	58	34*	112	0.1	101
			S.D.	5	2	12	0	72	9	16D	14	0.1	11

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

Table 7-2 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Blood chemistry (After administration period)

Sex	Dose mg/kg	No.		BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
Male	0	6	Mean	14	0.25	144	4.6	107	9.8	8.1	6.1	2.9	0.88
			S.D.	2	0.02	1	0.3	2	0.2	0.2	0.2	0.1	0.05
	30	6	Mean	12	0.22	143	4.9	106	9.7	8.3	6.0	2.9	0.92
			S.D.	1	0.02	1	0.3	1	0.1	0.3	0.2	0.1	0.03
	150	6	Mean	14	0.24	144	4.8	107	9.8	8.2	5.9	2.9	0.97
			S.D.	2	0.02	1	0.3	1	0.1	0.4	0.3	0.1	0.05
	750	6	Mean	15	0.23	143	4.6	104*	9.7	8.8	5.8	2.9	1.01**
			S.D.	1	0.03	1	0.4	1D	0.1	0.9	0.3	0.1	0.09D
Female	0	6	Mean	18	0.33	142	4.2	108	9.9	7.0	6.2	3.1	1.00
			S.D.	3	0.06	1	0.3	2	0.4	0.7	0.3	0.2	0.07
	30	6	Mean	17	0.29	142	4.8*	110	9.6	6.5	6.3	3.1	0.95
			S.D.	3	0.03	0	0.3D	1	0.3	0.8	0.3	0.2	0.08
	150	6	Mean	15	0.27	142	4.7*	109	9.6	6.5	6.2	3.0	0.92
			S.D.	1	0.02	1	0.4D	1	0.4	1.2	0.5	0.2	0.06
	750	6	Mean	17	0.31	143	4.3	107	9.8	7.3	6.1	3.0	0.96
			S.D.	5	0.06	1	0.2	1	0.2	0.3	0.3	0.2	0.07

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

Table 7-3 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Blood chemistry (After recovery period)

Sex	Dose mg/kg	No.		AST IU/L	ALT IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
Male	0	6	Mean	63	26	50	1	493	59	65	99	0.1	152
			S.D.	6	2	7	1	118	14	29	18	0.0	9
	750	6	Mean	67	30	56	1	551	60	65	103	0.1	143
			S.D.	4	4	7	0	139	8	27	7	0.0	18
Female	0	6	Mean	76	33	62	1	298	70	22	124	0.1	121
			S.D.	9	9	13	0	91	12	17	28	0.0	16
	750	6	Mean	64	23*	61	1	285	65	17	116	0.1	117
			S.D.	10	3AT	12	0	86	8	6	16	0.0	18

* : $p<0.05$ (Significant difference from control group)
AT : Aspin-Welch t-test

Table 7-4 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Blood chemistry (After recovery period)

Sex	Dose mg/kg	No.		BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
Male	0	6	Mean	13	0.27	143	4.8	105	9.4	7.5	6.2	2.9	0.86
			S.D.	3	0.03	1	0.2	1	0.2	0.4	0.2	0.1	0.06
	750	6	Mean	13	0.25	144	4.9	105	9.6	8.0	6.1	2.9	0.92
			S.D.	2	0.03	1	0.2	1	0.1	0.7	0.1	0.0	0.06
Female	0	6	Mean	16	0.32	143	4.3	110	9.5	5.7	6.5	3.1	0.95
			S.D.	2	0.04	1	0.4	1	0.3	0.7	0.4	0.2	0.10
	750	6	Mean	17	0.32	142*	4.7	109	9.4	6.2	6.2	3.0	0.93
			S.D.	1	0.03	1T	0.3	1	0.3	0.6	0.2	0.1	0.04

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

Table 8-1 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Absolute and relative organ weight (After administration period)

Male

	Dose mg/kg		Body weight g	Brain g(g/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R+L) mg(mg/100g BW)
	0	No.	6	6	6	6	6	6	6	6
		Mean	388	2.01	612	1.31	11.57	0.74	2.83	63
		S.D.	13	0.07	178	0.13	1.11	0.06	0.17	8
Absolute	30	No.	6	6	6	6	6	6	6	6
		Mean	379	1.97	489	1.17*	11.72	0.69	2.90	57
		S.D.	15	0.08	80	0.06D	0.55	0.18	0.23	7
	150	No.	6	6	6	6	6	6	6	6
		Mean	367	2.03	517	1.16*	11.60	0.62	2.87	55
		S.D.	21	0.06	123	0.04D	1.16	0.07	0.11	6
	750	No.	6	6	6	6	6	6	6	6
		Mean	333**	2.00	502	1.07**	11.73	0.66	3.03	53
		S.D.	22D	0.08	80	0.09D	1.38	0.06	0.15	3
	0	No.		6	6	6	6	6	6	6
		Mean		0.52	157	0.34	2.98	0.19	0.73	16
		S.D.		0.03	43	0.03	0.24	0.01	0.03	2
Relative	30	No.		6	6	6	6	6	6	6
		Mean		0.52	129	0.31	3.10	0.18	0.77	15
		S.D.		0.01	22	0.02	0.08	0.04	0.05	2
	150	No.		6	6	6	6	6	6	6
		Mean		0.55	140	0.32	3.16	0.17	0.79	15
		S.D.		0.03	30	0.01	0.27	0.02	0.06	2
	750	No.		6	6	6	6	6	6	6
		Mean		0.60**	152	0.32	3.52**	0.20	0.92**	16
		S.D.		0.03D	30	0.02	0.23D	0.02	0.09D	1

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

Table 8-2 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Absolute and relative organ weight (After administration period)

Male

	Dose mg/kg		Testis (R+L) g(g/100g BW)	Epididymis (R+L) mg(mg/100g BW)
	0	No.	6	6
		Mean	3.27	851
		S.D.	0.22	55
Absolute	30	No.	6	6
		Mean	3.27	827
		S.D.	0.14	61
	150	No.	6	6
		Mean	3.16	791
		S.D.	0.17	24
	750	No.	6	6
		Mean	3.09	810
		S.D.	0.25	96
	0	No.	6	6
		Mean	0.84	220
		S.D.	0.05	17
Relative	30	No.	6	6
		Mean	0.87	219
		S.D.	0.05	21
	150	No.	6	6
		Mean	0.86	216
		S.D.	0.05	12
	750	No.	6	6
		Mean	0.93	246
		S.D.	0.10	46

No significant difference in any treated groups from control group.

Table 8-3 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Absolute and relative organ weight (After administration period)

Female

	Dose mg/kg		Body weight g	Brain g(g/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R+L) mg(mg/100g BW)
	0	No.	6	6	6	6	6	6	6	6
		Mean	216	1.79	439	0.72	6.01	0.47	1.52	68
		S.D.	19	0.06	108	0.06	0.62	0.09	0.08	14
Absolute	30	No.	6	6	6	6	6	6	6	6
		Mean	206	1.83	452	0.72	5.67	0.54	1.64	63
		S.D.	13	0.10	68	0.06	0.25	0.18	0.20	9
	150	No.	6	6	6	6	6	6	6	6
		Mean	196	1.80	408	0.69	5.59	0.42	1.54	66
		S.D.	20	0.04	117	0.09	0.86	0.09	0.22	8
	750	No.	6	6	6	6	6	6	6	6
		Mean	200	1.77	345	0.64	6.23	0.39	1.55	57
		S.D.	33	0.06	59	0.10	1.12	0.04	0.25	10
	0	No.		6	6	6	6	6	6	6
		Mean		0.84	205	0.34	2.78	0.22	0.71	31
		S.D.		0.06	55	0.01	0.09	0.03	0.03	5
Relative	30	No.		6	6	6	6	6	6	6
		Mean		0.89	220	0.35	2.76	0.27	0.79	31
		S.D.		0.05	32	0.02	0.15	0.09	0.08	5
	150	No.		6	6	6	6	6	6	6
		Mean		0.93	206	0.35	2.85	0.21	0.79	34
		S.D.		0.09	42	0.02	0.16	0.04	0.06	2
	750	No.		6	6	6	6	6	6	6
		Mean		0.90	175	0.32	3.12**	0.20	0.78	29
		S.D.		0.14	32	0.01	0.20D	0.04	0.06	4

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

Table 8-4 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Absolute and relative organ weight (After administration period)

Female

	Dose mg/kg		Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	0	No.	6	6
		Mean	73.4	438
		S.D.	6.8	121
	30	No.	6	6
		Mean	79.3	409
		S.D.	19.3	92
	150	No.	6	6
		Mean	73.4	402
		S.D.	11.8	91
	750	No.	6	6
		Mean	72.2	394
		S.D.	12.3	107
Relative	0	No.	6	6
		Mean	34.1	206
		S.D.	2.1	68
	30	No.	6	6
		Mean	38.3	199
		S.D.	8.2	47
	150	No.	6	6
		Mean	37.7	210
		S.D.	5.8	65
	750	No.	6	6
		Mean	36.6	202
		S.D.	6.3	62

No significant difference in any treated groups from control group.

Table 8-5 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Absolute and relative organ weight (After recovery period)

Male

	Dose mg/kg		Body weight g	Brain g(g/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R+L) mg(mg/100g BW)
Absolute	0	No.	6	6	6	6	6	6	6	6
		Mean	440	2.11	525	1.36	12.34	0.74	2.95	62
		S.D.	37	0.02	122	0.15	1.32	0.09	0.23	8
	750	No.	6	6	6	6	6	6	6	6
		Mean	411	2.07	466	1.24	11.59	0.71	2.98	62
		S.D.	48	0.09	127	0.09	2.11	0.11	0.38	7
Relative	0	No.		6	6	6	6	6	6	6
		Mean		0.48	121	0.31	2.80	0.17	0.67	14
		S.D.		0.04	32	0.02	0.14	0.03	0.05	1
	750	No.		6	6	6	6	6	6	6
		Mean		0.51	113	0.30	2.80	0.17	0.73	15
		S.D.		0.05	26	0.02	0.19	0.03	0.06	2

No significant difference between treated group and control group.

Table 8-6 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Absolute and relative organ weight (After recovery period)

Male

	Dose mg/kg		Testis (R+L) g(g/100g BW)	Epididymis (R+L) mg(mg/100g BW)
Absolute	0	No.	6	6
		Mean	3.19	1068
		S.D.	0.45	128
	750	No.	6	6
		Mean	3.37	1080
		S.D.	0.18	95
Relative	0	No.	6	6
		Mean	0.73	245
		S.D.	0.14	43
	750	No.	6	6
		Mean	0.83	264
		S.D.	0.09	22

No significant difference between treated group and control group.

Table 8-7 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Absolute and relative organ weight (After recovery period)

Female

	Dose mg/kg		Body weight g	Brain g(g/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R+L) mg(mg/100g BW)
Absolute	0	No.	6	6	6	6	6	6	6	6
		Mean	230	1.84	367	0.73	6.23	0.47	1.71	67
		S.D.	20	0.06	69	0.04	0.55	0.06	0.11	6
	750	No.	6	6	6	6	6	6	6	6
		Mean	224	1.86	369	0.75	6.14	0.47	1.69	72
		S.D.	27	0.06	122	0.07	0.79	0.10	0.19	11
Relative	0	No.		6	6	6	6	6	6	6
		Mean		0.80	159	0.32	2.71	0.20	0.74	29
		S.D.		0.05	25	0.01	0.14	0.02	0.05	5
	750	No.		6	6	6	6	6	6	6
		Mean		0.84	162	0.34	2.74	0.21	0.76	33
		S.D.		0.10	40	0.03	0.19	0.03	0.07	7

No significant difference between treated group and control group.

Table 8-8 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Absolute and relative organ weight (After recovery period)

Female

	Dose mg/kg		Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	0	No.	6	6
		Mean	78.1	452
		S.D.	11.0	132
	750	No.	6	6
		Mean	80.6	505
		S.D.	11.3	143
Relative	0	No.	6	6
		Mean	33.9	198
		S.D.	3.0	63
	750	No.	6	6
		Mean	36.1	224
		S.D.	5.4	53

No significant difference between treated group and control group.

Table 9-1 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Gross pathological findings (After administration period)

Organs / Findings	Sex:	M	M	M	M	F	F	F	F
	Dose(mg/kg):	0	30	150	750	0	30	150	750
	Number:	6	6	6	6	6	6	6	6
Epididymis									
Focus,yellow		0	0	0	1	/	/	/	/
Intestine,cecum									
Dilatation,lumina		0	0	0	5	0	0	1	5
Stomach									
Thickening,wall,forestomach		0	0	0	4	0	0	0	5
Thickening,limiting ridge		0	0	0	2	0	0	0	0

M : Male, F : Female
/ : Not applicable

Table 9-2 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Gross pathological findings (After recovery period)

Organs	Sex:	M	M	F	F
	Dose(mg/kg):	0	750	0	750
Findings	Number:	6	6	6	6
Stomach					
Thickening,wall,forestomach		0	1	0	0
Thickening,limiting ridge		0	0	0	2

M : Male, F : Female

Table 10-1 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Histopathological findings (After administration period)

Organs / Findings	Sex:	M	M	M	M	F	F	F	F
	Dose(mg/kg):	0	30	150	750	0	30	150	750
	Number:	6	6	6	6	6	6	6	6
Adrenal									
Number examined		6	0	0	6	6	0	0	6
Not remarkable		6	0	0	6	6	0	0	6
Bone+Bone marrow,femoral									
Number examined		6	0	0	6	6	0	0	6
Not remarkable		6	0	0	6	6	0	0	6
Bone+Bone marrow,sternal									
Number examined		6	0	0	6	6	0	0	6
Not remarkable		5	0	0	4	4	0	0	3
Degeneration,chondromucinous		1	0	0	2	2	0	0	3
minimal		1	0	0	2	2	0	0	3
Cerebellum									
Number examined		6	0	0	6	6	0	0	6
Not remarkable		6	0	0	6	6	0	0	6
Cerebrum									
Number examined		6	0	0	6	6	0	0	6
Not remarkable		6	0	0	6	6	0	0	6
Epididymis									
Number examined		6	0	0	6	/	/	/	/
Not remarkable		6	0	0	5	/	/	/	/
Granuloma,spermatic		0	0	0	1	/	/	/	/
mild		0	0	0	1	/	/	/	/
Eye									
Number examined		6	0	0	6	6	0	0	6
Not remarkable		6	0	0	6	6	0	0	6
Heart									
Number examined		6	0	0	6	6	0	0	6
Not remarkable		6	0	0	6	5	0	0	6
Cardiomyopathy		0	0	0	0	1	0	0	0
minimal		0	0	0	0	1	0	0	0
Intestine,duodenum									
Number examined		6	0	0	6	6	0	0	6
Not remarkable		6	0	0	6	6	0	0	6
Intestine,jejunum									
Number examined		6	0	0	6	6	0	0	6
Not remarkable		6	0	0	6	6	0	0	6
Intestine,ileum(Peyer's patch)									
Number examined		6	0	0	6	6	0	0	6
Not remarkable		6	0	0	6	6	0	0	6
Intestine,cecum									
Number examined		6	0	0	6	6	0	1	6
Not remarkable		6	0	0	6	6	0	1	6
Intestine,colon									
Number examined		6	0	0	6	6	0	0	6
Not remarkable		6	0	0	6	6	0	0	6
Intestine,rectum									
Number examined		6	0	0	6	6	0	0	6
Not remarkable		6	0	0	6	6	0	0	6

M : Male, F : Female
/ : Not applicable

Table 10-2 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Histopathological findings (After administration period)

Organs / Findings	Sex:	M	M	M	M	F	F	F	F
	Dose(mg/kg):	0	30	150	750	0	30	150	750
	Number:	6	6	6	6	6	6	6	6
Kidney									
Number examined		6	0	0	6	6	0	0	6
Not remarkable		2	0	0	2	5	0	0	2
Regeneration,tubular		4	0	0	4	1	0	0	4
minimal		4	0	0	3	1	0	0	4
mild		0	0	0	1	0	0	0	0
Urinary cast,hyaline		0	0	0	0	0	0	0	1
minimal		0	0	0	0	0	0	0	1
Fibrosis,focal		0	0	0	0	1	0	0	0
mild		0	0	0	0	1	0	0	0
Liver									
Number examined		6	6	6	6	6	6	6	6
Not remarkable		1	1	2	0	1	0	3	1
Vacuolation,hepatocyte,periportal		5	1	1	2	5	4	3	2
minimal		5	1	1	2	4	3	3	2
mild		0	0	0	0	1	1	0	0
Microgranuloma		4	3	1	4	2	4	3	2
minimal		4	3	1	4	2	2	3	2
mild		0	0	0	0	0	2	0	0
Hypertrophy,hepatocytic,central		0	0	3	6	0	0	0	2
minimal		0	0	1	2	0	0	0	2
mild		0	0	2	4	0	0	0	0
Lung(bronchus)									
Number examined		6	0	0	6	6	0	0	6
Not remarkable		4	0	0	5	5	0	0	6
Mineralization,arterial wall		0	0	0	1	0	0	0	0
minimal		0	0	0	1	0	0	0	0
Hemorrhage,focal		0	0	0	0	1	0	0	0
minimal		0	0	0	0	1	0	0	0
Appearance,alveolar macrophage		1	0	0	0	0	0	0	0
minimal		1	0	0	0	0	0	0	0
Pneumonia,focal		1	0	0	0	0	0	0	0
minimal		1	0	0	0	0	0	0	0
Lymph node,mesenteric									
Number examined		6	0	0	6	6	0	0	6
Not remarkable		6	0	0	6	6	0	0	6
Lymph node,submandibular									
Number examined		6	0	0	6	6	0	0	6
Not remarkable		6	0	0	6	6	0	0	6
Ovary									
Number examined		/	/	/	/	6	0	0	6
Not remarkable		/	/	/	/	6	0	0	6
Parathyroid									
Number examined		6	0	0	6	6	0	0	6
Not remarkable		6	0	0	5	6	0	0	6
Cell infiltration,lymphocytic		0	0	0	1	0	0	0	0
minimal		0	0	0	1	0	0	0	0
Pituitary									
Number examined		6	0	0	6	6	0	0	6
Not remarkable		6	0	0	6	6	0	0	6
Prostate									
Number examined		6	0	0	6	/	/	/	/
Not remarkable		2	0	0	4	/	/	/	/
Cell infiltration,interstitial		4	0	0	2	/	/	/	/
minimal		1	0	0	1	/	/	/	/
mild		3	0	0	1	/	/	/	/

M : Male, F : Female
/ : Not applicable

Table 10-3 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Histopathological findings (After administration period)

Organs / Findings	Sex:	M	M	M	M	F	F	F	F
	Dose(mg/kg):	0	30	150	750	0	30	150	750
	Number:	6	6	6	6	6	6	6	6
Sciatic nerve									
Number examined		6	0	0	6	6	0	0	6
Not remarkable		6	0	0	6	6	0	0	6
Skeletal muscle,femoral									
Number examined		6	0	0	6	6	0	0	6
Not remarkable		4	0	0	5	5	0	0	5
Degeneration,muscular		1	0	0	1	1	0	0	1
minimal		1	0	0	1	1	0	0	1
Cell infiltration,interstitial		1	0	0	0	0	0	0	0
minimal		1	0	0	0	0	0	0	0
Spinal cord,thoracic									
Number examined		6	0	0	6	6	0	0	6
Not remarkable		6	0	0	6	6	0	0	6
Spleen									
Number examined		6	0	0	6	6	0	0	6
Not remarkable		2	0	0	3	6	0	0	6
Hematopoiesis,extramedullary		4	0	0	3	0	0	0	0
minimal		4	0	0	3	0	0	0	0
Stomach									
Number examined		6	6	6	6	6	6	6	6
Not remarkable		6	6	1	0	6	6	5	0
Hyperkeratosis,forestomach		0	0	3	6	0	0	1	6
minimal		0	0	3	3	0	0	1	1
mild		0	0	0	3	0	0	0	5
Hyperplasia,squamous,forestomach		0	0	0	5	0	0	0	4
minimal		0	0	0	2	0	0	0	1
mild		0	0	0	3	0	0	0	3
Hyperplasia,squamous,limiting ridge		0	0	5	6	0	0	1	6
minimal		0	0	4	3	0	0	1	2
mild		0	0	1	3	0	0	0	4
Testis									
Number examined		6	0	0	6	/	/	/	/
Not remarkable		6	0	0	6	/	/	/	/
Thyroid									
Number examined		6	0	0	6	6	0	0	6
Not remarkable		5	0	0	4	6	0	0	6
Ectopic thymus		1	0	0	0	0	0	0	0
mild		1	0	0	0	0	0	0	0
Remnant,ultimobranchial body		0	0	0	2	0	0	0	0
minimal		0	0	0	2	0	0	0	0
Thymus									
Number examined		6	0	0	6	6	0	0	6
Not remarkable		6	0	0	6	6	0	0	6
Trachea									
Number examined		6	0	0	6	6	0	0	6
Not remarkable		6	0	0	6	6	0	0	6
Urinary bladder									
Number examined		6	0	0	6	6	0	0	6
Not remarkable		6	0	0	6	6	0	0	6
Uterus									
Number examined		/	/	/	/	6	0	0	6
Not remarkable		/	/	/	/	6	0	0	6

M : Male, F : Female
/ : Not applicable

Table 10-4 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Histopathological findings (After recovery period)

Organs / Findings	Sex:	M	M	F	F
	Dose(mg/kg):	0	750	0	750
	Number:	6	6	6	6
Liver					
Number examined		6	6	6	6
Not remarkable		1	1	1	1
Vacuolation,hepatocyte,periportal		2	1	3	4
minimal		1	1	2	4
mild		1	0	1	0
Microgranuloma		4	4	5	3
minimal		4	4	5	3
Hypertrophy,hepatocytic,central		0	2	0	0
minimal		0	2	0	0
Stomach					
Number examined		6	6	6	6
Not remarkable		6	5	6	2
Hyperkeratosis,forestomach		0	1	0	2
minimal		0	1	0	2
Hyperplasia,squamous,forestomach		0	1	0	2
minimal		0	0	0	2
mild		0	1	0	0
Hyperplasia,squamous,limiting ridge		0	1	0	2
minimal		0	1	0	2

M : Male, F : Female

Appendix 1 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual clinical signs (Administration period)

Dose (mg/kg) : 0

Sex	Animal number	Day of administration													
		1	2	3	4	5	6	7	8	9	10	11	12	13	14
Male	1001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1010	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1011	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1012	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Female	1101	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1102	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1103	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1104	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1106	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1107	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1108	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1109	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1110	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1111	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1112	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- : No abnormality

Appendix 2 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual clinical signs (Administration period)

Dose (mg/kg) : 0

Sex	Animal number	Day of administration													
		15	16	17	18	19	20	21	22	23	24	25	26	27	28
Male	1001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1010	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1011	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1012	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Female	1101	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1102	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1103	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1104	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1106	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1107	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1108	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1109	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1110	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1111	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1112	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- : No abnormality

Appendix 3

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual clinical signs (Administration period)

Dose (mg/kg) : 30

Sex	Animal number	Day of administration													
		1	2	3	4	5	6	7	8	9	10	11	12	13	14
Male	2001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	2002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	2003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	2004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	2005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	2006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Female	2101	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	2102	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	2103	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	2104	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	2105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	2106	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- : No abnormality

Appendix 4

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual clinical signs (Administration period)

Dose (mg/kg) : 30

Sex	Animal number	Day of administration													
		15	16	17	18	19	20	21	22	23	24	25	26	27	28
Male	2001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	2002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	2003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	2004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	2005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	2006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Female	2101	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	2102	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	2103	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	2104	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	2105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	2106	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- : No abnormality

Appendix 5 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual clinical signs (Administration period)

Dose (mg/kg) : 150

Sex	Animal number	Day of administration													
		1	2	3	4	5	6	7	8	9	10	11	12	13	14
Male	3001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Female	3101	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3102	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3103	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3104	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3106	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- : No abnormality

Appendix 6

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual clinical signs (Administration period)

Dose (mg/kg) : 150

Sex	Animal number	Day of administration													
		15	16	17	18	19	20	21	22	23	24	25	26	27	28
Male	3001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Female	3101	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3102	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3103	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3104	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3106	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- : No abnormality

Appendix 7 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual clinical signs (Administration period)

Dose (mg/kg) : 750

Sex	Animal number	Day of administration													
		1	2	3	4	5	6	7	8	9	10	11	12	13	14
Male	4001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4002	-	-	-	-	-	-	-	-	A	-	-	-	-	-
	4003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4006	-	-	-	-	-	A	-	A	-	-	-	-	-	-
	4007	-	-	-	-	A	A	-	-	-	-	-	-	-	-
	4008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4010	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4011	-	-	-	-	-	-	-	A	-	-	-	-	-	-
	4012	-	-	-	-	-	-	-	A	-	-	-	-	-	-
Female	4101	-	-	-	-	-	A	A	A	-	-	-	-	A	-
	4102	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4103	-	-	-	-	A	-	-	-	-	-	-	A	A	-
	4104	-	-	-	-	-	-	-	-	-	-	A	-	A	-
	4105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4106	-	-	-	-	-	-	-	-	-	-	-	A	-	-
	4107	-	-	-	-	-	-	-	A	-	A	A	A	A	-
	4108	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4109	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4110	-	-	-	-	A	-	-	-	-	-	-	-	-	-
	4111	-	-	-	-	-	-	-	A	-	A	-	-	-	-
	4112	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- : No abnormality
A : Salivation

Appendix 8 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual clinical signs (Administration period)

Dose (mg/kg) : 750

Sex	Animal number	Day of administration													
		15	16	17	18	19	20	21	22	23	24	25	26	27	28
Male	4001	-	-	A	A	A	-	-	-	-	-	-	-	-	-
	4002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4004	-	-	-	-	-	-	-	-	-	-	-	-	A	A
	4005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4006	-	-	A	-	-	-	A	A	A	A	-	A	A	A
	4007	-	-	-	-	-	-	-	-	-	A	A	-	-	-
	4008	A	A	-	-	-	-	-	-	-	-	-	-	-	-
	4009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4010	-	-	-	A	-	-	-	-	A	-	A	-	-	-
	4011	A	-	-	-	A	-	-	-	-	-	-	A	A	-
	4012	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Female	4101	-	-	A	-	-	A	-	-	A	-	A	A	A	-
	4102	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4103	-	-	-	-	-	-	-	-	-	A	-	-	A	-
	4104	A	-	A	-	A	-	A	-	A	-	A	A	-	A
	4105	-	-	-	A	-	-	-	-	-	-	-	-	-	-
	4106	-	-	-	-	A	-	-	A	-	A	-	-	A	-
	4107	A	A	-	A	A	A	-	-	-	-	-	-	-	-
	4108	-	-	-	-	-	-	-	-	-	-	-	A	-	A
	4109	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4110	-	A	-	-	A	A	-	A	-	-	-	-	A	-
	4111	-	-	A	-	-	-	-	-	-	-	-	-	-	A
	4112	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- : No abnormality
A : Salivation

Appendix 9

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual clinical signs (Recovery period)

Dose (mg/kg) : 0

Sex	Animal number	Day of recovery													
		1	2	3	4	5	6	7	8	9	10	11	12	13	14
Male	1007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1010	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1011	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1012	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Female	1107	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1108	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1109	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1110	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1111	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1112	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- : No abnormality

Appendix 10

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual clinical signs (Recovery period)

Dose (mg/kg) : 750

Sex	Animal number	Day of recovery													
		1	2	3	4	5	6	7	8	9	10	11	12	13	14
Male	4007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4010	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4011	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4012	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Female	4107	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4108	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4109	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4110	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4111	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4112	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- : No abnormality

Appendix 11 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : home cage observations (Week 1 of administration period)

Dose (mg/kg) : 0

Parameter	Animal number	Male												Female											
		1 0 0 1	1 0 0 2	1 0 0 3	1 0 0 4	1 0 0 5	1 0 0 6	1 0 0 7	1 0 0 8	1 0 0 9	1 0 1 0	1 0 1 1	1 0 1 2	1 1 0 1	1 1 0 2	1 1 0 3	1 1 0 4	1 1 0 5	1 1 0 6	1 1 0 7	1 1 0 8	1 1 0 9	1 1 1 0	1 1 1 1	1 1 1 2
Posture a)		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 12 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : home cage observations (Week 1 of administration period)

Dose (mg/kg) : 30

Parameter	Animal number	Male						Female					
		2 0 0 1	2 0 0 2	2 0 0 3	2 0 0 4	2 0 0 5	2 0 0 6	2 1 0 1	2 1 0 2	2 1 0 3	2 1 0 4	2 1 0 5	2 1 0 6
Posture a)		N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 13 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : home cage observations (Week 1 of administration period)

Dose (mg/kg) : 150

Parameter	Animal number	Male						Female					
		3 0 0 1	3 0 0 2	3 0 0 3	3 0 0 4	3 0 0 5	3 0 0 6	3 1 0 1	3 1 0 2	3 1 0 3	3 1 0 4	3 1 0 5	3 1 0 6
Posture a)		N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 14

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : home cage observations (Week 1 of administration period)

Dose (mg/kg) : 750

Parameter	Animal number	Male												Female											
		4 0 0 1	4 0 0 2	4 0 0 3	4 0 0 4	4 0 0 5	4 0 0 6	4 0 0 7	4 0 0 8	4 0 0 9	4 0 1 0	4 0 1 1	4 0 1 2	4 1 0 1	4 1 0 2	4 1 0 3	4 1 0 4	4 1 0 5	4 1 0 6	4 1 0 7	4 1 0 8	4 1 0 9	4 1 1 0	4 1 1 1	4 1 1 2
Posture a)		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 15 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : home cage observations (Week 2 of administration period)

Dose (mg/kg) : 0

Parameter	Animal number	Male												Female											
		1 0 0 1	1 0 0 2	1 0 0 3	1 0 0 4	1 0 0 5	1 0 0 6	1 0 0 7	1 0 0 8	1 0 0 9	1 0 1 0	1 0 1 1	1 0 1 2	1 1 0 1	1 1 0 2	1 1 0 3	1 1 0 4	1 1 0 5	1 1 0 6	1 1 0 7	1 1 0 8	1 1 0 9	1 1 1 0	1 1 1 1	1 1 1 2
Posture a)		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 16

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : home cage observations (Week 2 of administration period)

Dose (mg/kg) : 30

Parameter	Animal number	Male						Female					
		2 0 0 1	2 0 0 2	2 0 0 3	2 0 0 4	2 0 0 5	2 0 0 6	2 1 0 1	2 1 0 2	2 1 0 3	2 1 0 4	2 1 0 5	2 1 0 6
Posture a)		N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 17 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : home cage observations (Week 2 of administration period)

Dose (mg/kg) : 150

Parameter	Animal number	Male						Female					
		3 0 0 1	3 0 0 2	3 0 0 3	3 0 0 4	3 0 0 5	3 0 0 6	3 1 0 1	3 1 0 2	3 1 0 3	3 1 0 4	3 1 0 5	3 1 0 6
Posture a)		N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 18 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : home cage observations (Week 2 of administration period)

Dose (mg/kg) : 750

Parameter	Animal number	Male												Female											
		4 0 0 1	4 0 0 2	4 0 0 3	4 0 0 4	4 0 0 5	4 0 0 6	4 0 0 7	4 0 0 8	4 0 0 9	4 0 1 0	4 0 1 1	4 0 1 2	4 1 0 1	4 1 0 2	4 1 0 3	4 1 0 4	4 1 0 5	4 1 0 6	4 1 0 7	4 1 0 8	4 1 0 9	4 1 1 0	4 1 1 1	4 1 1 2
Posture a)		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 19 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : home cage observations (Week 3 of administration period)

Dose (mg/kg) : 0

Parameter	Animal number	Male												Female											
		1 0 0 1	1 0 0 2	1 0 0 3	1 0 0 4	1 0 0 5	1 0 0 6	1 0 0 7	1 0 0 8	1 0 0 9	1 0 1 0	1 0 1 1	1 0 1 2	1 1 0 1	1 1 0 2	1 1 0 3	1 1 0 4	1 1 0 5	1 1 0 6	1 1 0 7	1 1 0 8	1 1 0 9	1 1 1 0	1 1 1 1	1 1 1 2
Posture a)		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 20 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : home cage observations (Week 3 of administration period)

Dose (mg/kg) : 30

Parameter	Animal number	Male						Female					
		2 0 0 1	2 0 0 2	2 0 0 3	2 0 0 4	2 0 0 5	2 0 0 6	2 1 0 1	2 1 0 2	2 1 0 3	2 1 0 4	2 1 0 5	2 1 0 6
Posture a)		N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 21 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : home cage observations (Week 3 of administration period)

Dose (mg/kg) : 150

Parameter	Animal number	Male						Female					
		3 0 0 1	3 0 0 2	3 0 0 3	3 0 0 4	3 0 0 5	3 0 0 6	3 1 0 1	3 1 0 2	3 1 0 3	3 1 0 4	3 1 0 5	3 1 0 6
Posture a)		N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 22 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : home cage observations (Week 3 of administration period)

Dose (mg/kg) : 750

Parameter	Animal number	Male												Female											
		4 0 0 1	4 0 0 2	4 0 0 3	4 0 0 4	4 0 0 5	4 0 0 6	4 0 0 7	4 0 0 8	4 0 0 9	4 0 1 0	4 0 1 1	4 0 1 2	4 1 0 1	4 1 0 2	4 1 0 3	4 1 0 4	4 1 0 5	4 1 0 6	4 1 0 7	4 1 0 8	4 1 0 9	4 1 1 0	4 1 1 1	4 1 1 2
Posture a)		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 23 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : home cage observations (Week 4 of administration period)

Dose (mg/kg) : 0

Parameter	Animal number	Male												Female											
		1 0 0 1	1 0 0 2	1 0 0 3	1 0 0 4	1 0 0 5	1 0 0 6	1 0 0 7	1 0 0 8	1 0 0 9	1 0 1 0	1 0 1 1	1 0 1 2	1 1 0 1	1 1 0 2	1 1 0 3	1 1 0 4	1 1 0 5	1 1 0 6	1 1 0 7	1 1 0 8	1 1 0 9	1 1 1 0	1 1 1 1	1 1 1 2
Posture a)		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 24

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : home cage observations (Week 4 of administration period)

Dose (mg/kg) : 30

Parameter	Animal number	Male						Female					
		2 0 0 1	2 0 0 2	2 0 0 3	2 0 0 4	2 0 0 5	2 0 0 6	2 1 0 1	2 1 0 2	2 1 0 3	2 1 0 4	2 1 0 5	2 1 0 6
Posture a)		N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 25 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : home cage observations (Week 4 of administration period)

Dose (mg/kg) : 150

Parameter	Animal number	Male						Female					
		3 0 0 1	3 0 0 2	3 0 0 3	3 0 0 4	3 0 0 5	3 0 0 6	3 1 0 1	3 1 0 2	3 1 0 3	3 1 0 4	3 1 0 5	3 1 0 6
Posture a)		N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 26

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : home cage observations (Week 4 of administration period)

Dose (mg/kg) : 750

Parameter	Animal number	Male												Female											
		4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
		0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1
		0	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0	1	1	1	1
		1	2	3	4	5	6	7	8	9	0	1	2	1	2	3	4	5	6	7	8	9	0	1	2
Posture a)		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 27 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : home cage observations (Week 1 of recovery period)

Dose (mg/kg) : 0

Parameter	Animal number	Male						Female					
		1	1	1	1	1	1	1	1	1	1	1	1
		0	0	0	0	0	0	1	1	1	1	1	1
		0	0	0	1	1	1	0	0	0	1	1	1
		7	8	9	0	1	2	7	8	9	0	1	2
Posture a)		N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 28 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : home cage observations (Week 1 of recovery period)

Dose (mg/kg) : 750

Parameter	Animal number	Male						Female					
		4 0 0 7	4 0 0 8	4 0 0 9	4 0 1 0	4 0 1 1	4 0 1 2	4 1 0 7	4 1 0 8	4 1 0 9	4 1 1 0	4 1 1 1	4 1 1 2
Posture a)		N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 29 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : home cage observations (Week 2 of recovery period)

Dose (mg/kg) : 0

Parameter	Animal number	Male						Female					
		1 0 0 7	1 0 0 8	1 0 0 9	1 0 1 0	1 0 1 1	1 0 1 2	1 1 0 7	1 1 0 8	1 1 0 9	1 1 1 0	1 1 1 1	1 1 1 2
Posture a)		N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 30 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : home cage observations (Week 2 of recovery period)

Dose (mg/kg) : 750

Parameter	Animal number	Male						Female					
		4 0 0 7	4 0 0 8	4 0 0 9	4 0 1 0	4 0 1 1	4 0 1 2	4 1 0 7	4 1 0 8	4 1 0 9	4 1 1 0	4 1 1 1	4 1 1 2
Posture a)		N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 31 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : in-the-hand observations (Week 1 of administration period)

Dose (mg/kg) : 0

Parameter	Animal number	Male												Female											
		1001	1002	1003	1004	1005	1006	1007	1008	1009	1010	1011	1012	1101	1102	1103	1104	1105	1106	1107	1108	1109	1110	1111	1112
Ease of removal from cage 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
Fur condition b)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling m)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 32 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : in-the-hand observations (Week 1 of administration period)

Dose (mg/kg) : 30

Parameter	Animal number	Male						Female					
		20001	20002	20003	20004	20005	20006	21001	21002	21003	21004	21005	21006
Ease of removal from cage a)		0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)		0	0	0	0	0	0	0	0	0	0	0	0
Skin c)		0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)		0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)		0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)		0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)		0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)		0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)		0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)		0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)		0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling m)		0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 33 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : in-the-hand observations (Week 1 of administration period)

Dose (mg/kg) : 150

Parameter	Animal number	Male						Female					
		30001	30002	30003	30004	30005	30006	31101	31102	31103	31104	31105	31106
Ease of removal from cage a)		0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)		0	0	0	0	0	0	0	0	0	0	0	0
Skin c)		0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)		0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)		0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)		0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)		0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)		0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)		0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)		0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)		0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling m)		0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 34

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : in-the-hand observations (Week 1 of administration period)

Dose (mg/kg) : 750

Parameter	Animal number	Male												Female											
		40001	40002	40003	40004	40005	40006	40007	40008	40009	40010	40011	40012	41001	41002	41003	41004	41005	41006	41007	41008	41009	41010	41011	41012
Ease of removal from cage 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
Fur condition b)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling m)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 35 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : in-the-hand observations (Week 2 of administration period)

Dose (mg/kg) : 0

Parameter	Animal number	Male												Female											
		1001	1002	1003	1004	1005	1006	1007	1008	1009	1010	1011	1012	1101	1102	1103	1104	1105	1106	1107	1108	1109	1110	1111	1112
Ease of removal from cage 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
Fur condition b)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling m)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 36

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : in-the-hand observations (Week 2 of administration period)

Dose (mg/kg) : 30

Parameter	Animal number	Male						Female					
		20001	20002	20003	20004	20005	20006	21010	21012	21013	21014	21015	21016
Ease of removal from cage a)		0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)		0	0	0	0	0	0	0	0	0	0	0	0
Skin c)		0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)		0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)		0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)		0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)		0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)		0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)		0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)		0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)		0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling m)		0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 37 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : in-the-hand observations (Week 2 of administration period)

Dose (mg/kg) : 150

Parameter	Animal number	Male						Female					
		30001	30002	30003	30004	30005	30006	31001	31002	31003	31004	31005	31006
Ease of removal from cage a)		0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)		0	0	0	0	0	0	0	0	0	0	0	0
Skin c)		0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)		0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)		0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)		0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)		0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)		0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)		0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)		0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)		0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling m)		0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 38 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : in-the-hand observations (Week 2 of administration period)

Dose (mg/kg) : 750

Parameter	Animal number	Male												Female											
		4001	4002	4003	4004	4005	4006	4007	4008	4009	4010	4011	4012	4101	4102	4103	4104	4105	4106	4107	4108	4109	4110	4111	4112
Ease of removal from cage 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
Fur condition b)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)		0	0	0	0	0	0	1	1	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0
Abnormal respiration l)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling m)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 39 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : in-the-hand observations (Week 3 of administration period)

Dose (mg/kg) : 0

Parameter	Animal number	Male												Female											
		1001	1002	1003	1004	1005	1006	1007	1008	1009	1010	1011	1012	1101	1102	1103	1104	1105	1106	1107	1108	1109	1110	1111	1112
Ease of removal from cage 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
Fur condition b)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling m)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 40 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : in-the-hand observations (Week 3 of administration period)

Dose (mg/kg) : 30

Parameter	Animal number	Male						Female					
		20001	20002	20003	20004	20005	20006	21001	21002	21003	21004	21005	21006
Ease of removal from cage a)		0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)		0	0	0	0	0	0	0	0	0	0	0	0
Skin c)		0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)		0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)		0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)		0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)		0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)		0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)		0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)		0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)		0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling m)		0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 41 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : in-the-hand observations (Week 3 of administration period)

Dose (mg/kg) : 150

Parameter	Animal number	Male						Female					
		30001	30002	30003	30004	30005	30006	31001	31002	31003	31004	31005	31006
Ease of removal from cage a)		0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)		0	0	0	0	0	0	0	0	0	0	0	0
Skin c)		0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)		0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)		0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)		0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)		0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)		0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)		0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)		0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)		0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling m)		0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 42 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : in-the-hand observations (Week 3 of administration period)

Dose (mg/kg) : 750

Parameter	Animal number	Male												Female											
		4001	4002	4003	4004	4005	4006	4007	4008	4009	4010	4011	4012	4101	4102	4103	4104	4105	4106	4107	4108	4109	4110	4111	4112
Ease of removal from cage 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
Fur condition b)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)		1	0	0	0	0	0	1	1	0	0	1	0	0	0	0	1	0	1	1	1	0	0	1	0
Abnormal respiration l)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling m)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 43

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : in-the-hand observations (Week 4 of administration period)

Dose (mg/kg) : 0

Parameter	Animal number	Male												Female											
		1001	1002	1003	1004	1005	1006	1007	1008	1009	1010	1011	1012	1101	1102	1103	1104	1105	1106	1107	1108	1109	1110	1111	1112
Ease of removal from cage 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
Fur condition b)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling m)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 44 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : in-the-hand observations (Week 4 of administration period)

Dose (mg/kg) : 30

Parameter	Animal number	Male						Female					
		20001	20002	20003	20004	20005	20006	21101	21102	21103	21104	21105	21106
Ease of removal from cage a)		0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)		0	0	0	0	0	0	0	0	0	0	0	0
Skin c)		0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)		0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)		0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)		0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)		0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)		0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)		0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)		0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)		0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling m)		0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 45 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : in-the-hand observations (Week 4 of administration period)

Dose (mg/kg) : 150

Parameter	Animal number	Male						Female					
		30001	30002	30003	30004	30005	30006	31012	31023	31034	31045	31056	31067
Ease of removal from cage a)		0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)		0	0	0	0	0	0	0	0	0	0	0	0
Skin c)		0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)		0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)		0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)		0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)		0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)		0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)		0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)		0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)		0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling m)		0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 46 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : in-the-hand observations (Week 4 of administration period)

Dose (mg/kg) : 750

Parameter	Animal number	Male												Female											
		40001	40002	40003	40004	40005	40006	40007	40008	40009	40010	40011	40012	41001	41002	41003	41004	41005	41006	41007	41008	41009	41010	41011	41012
Ease of removal from cage 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
Fur condition b)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)		0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	1	0	0	0	0
Abnormal respiration l)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling m)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 47 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : in-the-hand observations (Week 1 of recovery period)

Dose (mg/kg) : 0

Parameter	Animal number	Male						Female					
		1007	1008	1009	1010	1011	1012	1107	1108	1109	1110	1111	1112
Ease of removal from cage a)		0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)		0	0	0	0	0	0	0	0	0	0	0	0
Skin c)		0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)		0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)		0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)		0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)		0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)		0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)		0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)		0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)		0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling m)		0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 48 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : in-the-hand observations (Week 1 of recovery period)

Dose (mg/kg) : 750

Parameter	Animal number	Male						Female					
		40007	40008	40009	40010	40011	40012	41007	41008	41009	41010	41011	41012
Ease of removal from cage a)		0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)		0	0	0	0	0	0	0	0	0	0	0	0
Skin c)		0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)		0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)		0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)		0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)		0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)		0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)		0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)		0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)		0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling m)		0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 49 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : in-the-hand observations (Week 2 of recovery period)

Dose (mg/kg) : 0

Parameter	Animal number	Male						Female					
		1007	1008	1009	1010	1011	1012	1107	1108	1109	1110	1111	1112
Ease of removal from cage a)		0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)		0	0	0	0	0	0	0	0	0	0	0	0
Skin c)		0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)		0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)		0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)		0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)		0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)		0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)		0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)		0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)		0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling m)		0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 50 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : in-the-hand observations (Week 2 of recovery period)

Dose (mg/kg) : 750

Parameter	Animal number	Male						Female					
		40007	40008	40009	40010	40011	40012	41007	41008	41009	41010	41011	41012
Ease of removal from cage a)		0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)		0	0	0	0	0	0	0	0	0	0	0	0
Skin c)		0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)		0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)		0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)		0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)		0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)		0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)		0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)		0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)		0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling m)		0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 51 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : open field observation (Week 1 of administration period)

Dose (mg/kg) : 0

Parameter	Animal number	Male												Female											
		101	102	103	104	105	106	107	108	109	110	111	112	111	112	113	114	115	116	117	118	119	120	121	122
Arousal 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
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Rearing count		9	9	8	4	9	7	7	7	6	5	8	5	5	3	6	11	8	6	5	2	9	6	7	3
Defecation count		0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)		0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 52 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : open field observation (Week 1 of administration period)

Dose (mg/kg) : 30

Parameter	Animal number	Male						Female					
		20001	20002	20003	20004	20005	20006	21001	21002	21003	21004	21005	21006
Arousal a)		0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)		0	0	0	0	0	0	0	0	0	0	0	0
Gait e)		0	0	0	0	0	0	0	0	0	0	0	0
Posture f)		N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)		0	0	0	0	0	0	0	0	0	0	0	0
Rearing count		5	2	7	4	12	3	2	10	5	5	5	5
Defecation count		1	1	0	0	0	0	0	0	0	0	0	0
Urination h)		0	1	0	0	0	1	0	0	0	0	0	0

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

Appendix 53

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : open field observation (Week 1 of administration period)

Dose (mg/kg) : 150

Parameter	Animal number	Male						Female					
		30001	30002	30003	30004	30005	30006	31001	31002	31003	31004	31005	31006
Arousal a)		0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)		0	0	0	0	0	0	0	0	0	0	0	0
Gait e)		0	0	0	0	0	0	0	0	0	0	0	0
Posture f)		N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)		0	0	0	0	0	0	0	0	0	0	0	0
Rearing count		6	11	5	4	1	8	5	5	6	7	6	6
Defecation count		0	0	0	0	2	0	0	0	0	0	0	0
Urination h)		0	0	0	1	1	0	0	1	0	0	0	0

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

Appendix 54

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : open field observation (Week 1 of administration period)

Dose (mg/kg) : 750

Parameter	Animal number	Male												Female											
		4 0 0 1	4 0 0 2	4 0 0 3	4 0 0 4	4 0 0 5	4 0 0 6	4 0 0 7	4 0 0 8	4 0 0 9	4 0 1 0	4 0 1 1	4 0 1 2	4 1 0 1	4 1 0 2	4 1 0 3	4 1 0 4	4 1 0 5	4 1 0 6	4 1 0 7	4 1 0 8	4 1 0 9	4 1 1 0	4 1 1 1	4 1 1 2
Arousal 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
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Rearing count		4	7	3	0	4	1	8	7	3	2	5	4	5	5	3	7	2	4	9	3	5	2	1	7
Defecation count		0	0	3	0	0	2	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)		0	0	2	2	2	0	0	0	2	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 55 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : open field observation (Week 2 of administration period)

Dose (mg/kg) : 0

Parameter	Animal number	Male												Female											
		1001	1002	1003	1004	1005	1006	1007	1008	1009	1010	1011	1012	1101	1102	1103	1104	1105	1106	1107	1108	1109	1110	1111	1112
Arousal 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
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Rearing count		4	5	6	4	5	2	6	7	2	5	4	1	4	4	3	6	6	4	5	1	11	5	8	5
Defecation count		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 56 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : open field observation (Week 2 of administration period)

Dose (mg/kg) : 30

Parameter	Animal number	Male						Female					
		20001	20002	20003	20004	20005	20006	21001	21002	21003	21004	21005	21006
Arousal a)		0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)		0	0	0	0	0	0	0	0	0	0	0	0
Gait e)		0	0	0	0	0	0	0	0	0	0	0	0
Posture f)		N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)		0	0	0	0	0	0	0	0	0	0	0	0
Rearing count		2	0	2	5	4	2	0	3	6	4	6	4
Defecation count		0	0	0	0	0	0	0	0	0	0	0	0
Urination h)		0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 57 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : open field observation (Week 2 of administration period)

Dose (mg/kg) : 150

Parameter	Animal number	Male						Female					
		30001	30002	30003	30004	30005	30006	31001	31002	31003	31004	31005	31006
Arousal a)		0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)		0	0	0	0	0	0	0	0	0	0	0	0
Gait e)		0	0	0	0	0	0	0	0	0	0	0	0
Posture f)		N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)		0	0	0	0	0	0	0	0	0	0	0	0
Rearing count		0	5	3	5	1	5	6	6	8	5	1	5
Defecation count		0	0	0	0	2	0	0	0	0	0	0	0
Urination h)		0	0	0	0	1	0	0	0	0	0	0	0

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

Appendix 58 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : open field observation (Week 2 of administration period)

Dose (mg/kg) : 750

Parameter	Animal number	Male												Female											
		4 0 0 1	4 0 0 2	4 0 0 3	4 0 0 4	4 0 0 5	4 0 0 6	4 0 0 7	4 0 0 8	4 0 0 9	4 0 1 0	4 0 1 1	4 0 1 2	4 1 0 1	4 1 0 2	4 1 0 3	4 1 0 4	4 1 0 5	4 1 0 6	4 1 0 7	4 1 0 8	4 1 0 9	4 1 1 0	4 1 1 1	4 1 1 2
Arousal 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
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Rearing count		5	6	3	4	2	2	6	2	1	2	3	5	3	4	2	5	2	2	7	0	5	5	3	3
Defecation count		0	0	0	0	0	6	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)		0	0	0	1	0	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 59 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : open field observation (Week 3 of administration period)

Dose (mg/kg) : 0

Parameter	Animal number	Male												Female											
		101	102	103	104	105	106	107	108	109	110	111	112	111	112	113	114	115	116	117	118	119	120	121	122
Arousal 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
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Rearing count		4	8	9	3	8	3	7	8	5	1	6	4	6	10	8	11	7	10	10	3	12	5	8	9
Defecation count		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)		0	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 60 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : open field observation (Week 3 of administration period)

Dose (mg/kg) : 30

Parameter	Animal number	Male						Female					
		20001	20002	20003	20004	20005	20006	21001	21002	21003	21004	21005	21006
Arousal a)		0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)		0	0	0	0	0	0	0	0	0	0	0	0
Gait e)		0	0	0	0	0	0	0	0	0	0	0	0
Posture f)		N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)		0	0	0	0	0	0	0	0	0	0	0	0
Rearing count		5	1	6	6	3	5	10	7	7	7	7	12
Defecation count		0	0	0	0	0	0	0	0	0	0	0	0
Urination h)		0	1	0	0	0	0	0	0	0	0	0	0

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

Appendix 61 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : open field observation (Week 3 of administration period)

Dose (mg/kg) : 150

Parameter	Animal number	Male						Female					
		30001	30002	30003	30004	30005	30006	31001	31002	31003	31004	31005	31006
Arousal a)		0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)		0	0	0	0	0	0	0	0	0	0	0	0
Gait e)		0	0	0	0	0	0	0	0	0	0	0	0
Posture f)		N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)		0	0	0	0	0	0	0	0	0	0	0	0
Rearing count		3	6	4	5	4	5	10	12	10	6	6	11
Defecation count		0	0	0	0	3	0	0	0	0	0	0	0
Urination h)		0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 62

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : open field observation (Week 3 of administration period)

Dose (mg/kg) : 750

Parameter	Animal number	Male												Female											
		4 0 0 1	4 0 0 2	4 0 0 3	4 0 0 4	4 0 0 5	4 0 0 6	4 0 0 7	4 0 0 8	4 0 0 9	4 0 1 0	4 0 1 1	4 0 1 2	4 1 0 1	4 1 0 2	4 1 0 3	4 1 0 4	4 1 0 5	4 1 0 6	4 1 0 7	4 1 0 8	4 1 0 9	4 1 1 0	4 1 1 1	4 1 1 2
Arousal 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
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Rearing count		6	3	3	1	1	4	4	5	2	3	4	8	7	4	4	10	6	3	8	5	5	9	9	9
Defecation count		0	0	0	2	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)		0	0	0	0	0	0	1	0	1	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 63

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : open field observation (Week 4 of administration period)

Dose (mg/kg) : 0

Parameter	Animal number	Male												Female											
		1 0 0 1	1 0 0 2	1 0 0 3	1 0 0 4	1 0 0 5	1 0 0 6	1 0 0 7	1 0 0 8	1 0 0 9	1 0 1 0	1 0 1 1	1 0 1 2	1 1 0 1	1 1 0 2	1 1 0 3	1 1 0 4	1 1 0 5	1 1 0 6	1 1 0 7	1 1 0 8	1 1 0 9	1 1 1 0	1 1 1 1	1 1 1 2
Arousal 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
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Rearing count		2	6	6	4	8	7	8	8	4	3	6	4	4	6	7	17	8	10	8	8	15	7	10	7
Defecation count		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0

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

Appendix 64 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : open field observation (Week 4 of administration period)

Dose (mg/kg) : 30

Parameter	Animal number	Male						Female					
		20001	20002	20003	20004	20005	20006	21001	21002	21003	21004	21005	21006
Arousal a)		0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)		0	0	0	0	0	0	0	0	0	0	0	0
Gait e)		0	0	0	0	0	0	0	0	0	0	0	0
Posture f)		N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)		0	0	0	0	0	0	0	0	0	0	0	0
Rearing count		7	0	4	3	8	6	9	6	10	7	9	11
Defecation count		0	0	0	0	0	0	0	0	0	0	0	0
Urination h)		0	1	0	0	0	0	0	0	0	0	0	0

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

Appendix 65

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : open field observation (Week 4 of administration period)

Dose (mg/kg) : 150

Parameter	Animal number	Male						Female					
		30001	30002	30003	30004	30005	30006	31001	31002	31003	31004	31005	31006
Arousal a)		0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)		0	0	0	0	0	0	0	0	0	0	0	0
Gait e)		0	0	0	0	0	0	0	0	0	0	0	0
Posture f)		N	N	N	F	N	N	N	N	N	N	N	N
Grooming g)		0	0	0	0	0	0	0	0	0	0	0	0
Rearing count		6	6	5	5	7	5	11	11	8	9	5	13
Defecation count		0	0	0	0	0	0	0	0	0	0	0	0
Urination h)		0	0	0	1	0	0	0	0	0	0	0	0

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

Appendix 66

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : open field observation (Week 4 of administration period)

Dose (mg/kg) : 750

Parameter	Animal number	Male												Female											
		4 0 0 1	4 0 0 2	4 0 0 3	4 0 0 4	4 0 0 5	4 0 0 6	4 0 0 7	4 0 0 8	4 0 0 9	4 0 1 0	4 0 1 1	4 0 1 2	4 1 0 1	4 1 0 2	4 1 0 3	4 1 0 4	4 1 0 5	4 1 0 6	4 1 0 7	4 1 0 8	4 1 0 9	4 1 1 0	4 1 1 1	4 1 1 2
Arousal 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
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Rearing count		5	2	4	1	5	6	5	5	1	3	4	6	7	6	5	5	8	6	8	1	4	10	10	7
Defecation count		0	0	0	0	0	0	0	0	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)		0	0	0	0	0	0	0	1	2	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0

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

Appendix 67 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : open field observation (Week 1 of recovery period)

Dose (mg/kg) : 0

Parameter	Animal number	Male						Female					
		1007	1008	1009	1010	1011	1012	1013	1014	1015	1016	1017	1018
Arousal a)		0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)		0	0	0	0	0	0	0	0	0	0	0	0
Gait e)		0	0	0	0	0	0	0	0	0	0	0	0
Posture f)		N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)		0	0	0	0	0	0	0	0	0	0	0	0
Rearing count		8	6	6	4	8	4	7	7	13	7	8	7
Defecation count		0	0	0	0	0	0	0	0	0	0	0	0
Urination h)		0	0	0	0	0	1	0	0	0	0	0	0

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

Appendix 68 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : open field observation (Week 1 of recovery period)

Dose (mg/kg) : 750

Parameter	Animal number	Male						Female					
		4 0 0 7	4 0 0 8	4 0 0 9	4 0 1 0	4 0 1 1	4 0 1 2	4 1 0 7	4 1 0 8	4 1 0 9	4 1 1 0	4 1 1 1	4 1 1 2
Arousal a)		0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)		0	0	0	0	0	0	0	0	0	0	0	0
Gait e)		0	0	0	0	0	0	0	0	0	0	0	0
Posture f)		N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)		0	0	0	0	0	0	0	0	0	0	0	0
Rearing count		7	7	1	4	7	9	12	9	8	8	11	8
Defecation count		0	0	2	0	1	0	0	0	0	0	0	0
Urination h)		0	0	1	1	0	0	0	0	0	0	0	0

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

Appendix 69

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : open field observation (Week 2 of recovery period)

Dose (mg/kg) : 0

Parameter	Animal number	Male						Female					
		1007	1008	1009	1010	1011	1012	1007	1008	1009	1010	1011	1012
Arousal a)		0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)		0	0	0	0	0	0	0	0	0	0	0	0
Gait e)		0	0	0	0	0	0	0	0	0	0	0	0
Posture f)		N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)		0	0	0	0	0	0	0	0	0	0	0	0
Rearing count		7	6	6	4	7	4	9	5	11	7	13	8
Defecation count		0	0	0	0	0	0	0	0	0	0	0	0
Urination h)		0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 70 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual detailed clinical signs : open field observation (Week 2 of recovery period)

Dose (mg/kg) : 750

Parameter	Animal number	Male						Female					
		4 0 0 7	4 0 0 8	4 0 0 9	4 0 1 0	4 0 1 1	4 0 1 2	4 1 0 7	4 1 0 8	4 1 0 9	4 1 1 0	4 1 1 1	4 1 1 2
Arousal a)		0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)		0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)		0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)		0	0	0	0	0	0	0	0	0	0	0	0
Gait e)		0	0	0	0	0	0	0	0	0	0	0	0
Posture f)		N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)		0	0	0	0	0	0	0	0	0	0	0	0
Rearing count		7	5	0	4	7	7	10	8	9	7	11	6
Defecation count		0	0	0	0	0	0	0	0	0	0	0	0
Urination h)		0	2	0	0	0	0	0	0	0	0	0	0

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

Appendix 71 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual manipulative test (Week 4 of administration period)

Dose (mg/kg) : 0

Parameter	Animal number	Male												Female											
		1001	1002	1003	1004	1005	1006	1007	1008	1009	1010	1011	1012	1101	1102	1103	1104	1105	1106	1107	1108	1109	1110	1111	1112
Auditory response 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
Approach response b)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Touch response c)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Tail pinch response d)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Pupillary reflex e)		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
Aerial righting reflex (Total score)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Landing foot splay (mm)		81	65	96	98	73	59	59	71	71	58	55	61	86	40	54	72	41	68	39	47	40	55	96	58

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

Appendix 72 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual manipulative test (Week 4 of administration period)

Dose (mg/kg) : 30

Parameter	Animal number	Male						Female					
		2 0 0 1	2 0 0 2	2 0 0 3	2 0 0 4	2 0 0 5	2 0 0 6	2 1 0 1	2 1 0 2	2 1 0 3	2 1 0 4	2 1 0 5	2 1 0 6
Auditory response a)		0	0	0	0	0	0	0	0	0	0	0	0
Approach response b)		0	0	0	0	0	0	0	0	0	0	0	0
Touch response c)		0	0	0	0	0	0	0	0	0	0	0	0
Tail pinch response d)		0	0	0	0	0	0	0	0	0	0	0	0
Pupillary reflex e)		P	P	P	P	P	P	P	P	P	P	P	P
Aerial righting reflex (Total score)		0	0	0	0	0	0	0	0	0	0	0	0
Landing foot splay (mm)		58	80	61	54	56	63	59	60	55	62	54	56

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

Appendix 73 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual manipulative test (Week 4 of administration period)

Dose (mg/kg) : 150

Parameter	Animal number	Male						Female					
		3 0 0 1	3 0 0 2	3 0 0 3	3 0 0 4	3 0 0 5	3 0 0 6	3 1 0 1	3 1 0 2	3 1 0 3	3 1 0 4	3 1 0 5	3 1 0 6
Auditory response a)		0	0	0	0	0	0	0	0	0	0	0	0
Approach response b)		0	0	0	0	0	0	0	0	0	0	0	0
Touch response c)		0	0	0	0	0	0	0	0	0	0	0	0
Tail pinch response d)		0	0	0	0	0	0	0	0	0	0	0	0
Pupillary reflex e)		P	P	P	P	P	P	P	P	P	P	P	P
Aerial righting reflex (Total score)		0	0	0	0	0	0	0	0	0	0	0	0
Landing foot splay (mm)		59	53	60	71	71	67	56	48	26	58	46	55

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

Appendix 74 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual manipulative test (Week 4 of administration period)

Dose (mg/kg) : 750

Parameter	Animal number	Male												Female											
		4 0 0 1	4 0 0 2	4 0 0 3	4 0 0 4	4 0 0 5	4 0 0 6	4 0 0 7	4 0 0 8	4 0 0 9	4 0 1 0	4 0 1 1	4 0 1 2	4 1 0 1	4 1 0 2	4 1 0 3	4 1 0 4	4 1 0 5	4 1 0 6	4 1 0 7	4 1 0 8	4 1 0 9	4 1 1 0	4 1 1 1	4 1 1 2
Auditory response 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
Approach response b)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Touch response c)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Tail pinch response d)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Pupillary reflex e)		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
Aerial righting reflex (Total score)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Landing foot splay (mm)		59	63	38	53	55	75	77	64	63	83	67	48	66	49	50	49	37	55	37	32	32	51	47	57

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

Appendix 75 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual manipulative test (Week 2 of recovery period)

Dose (mg/kg) : 0

Parameter	Animal number	Male						Female					
		1 0 0 7	1 0 0 8	1 0 0 9	1 0 1 0	1 0 1 1	1 0 1 2	1 1 0 7	1 1 0 8	1 1 0 9	1 1 1 0	1 1 1 1	1 1 1 2
Auditory response a)		0	0	0	0	0	0	0	0	0	0	0	0
Approach response b)		0	0	0	0	0	0	0	0	0	0	0	0
Touch response c)		0	0	0	0	0	0	0	0	0	0	0	0
Tail pinch response d)		0	0	0	0	0	0	0	0	0	0	0	0
Pupillary reflex e)		P	P	P	P	P	P	P	P	P	P	P	P
Aerial righting reflex (Total score)		0	0	0	0	0	0	0	0	0	0	0	0
Landing foot splay (mm)		79	64	102	71	100	90	59	52	60	67	102	68

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

Appendix 76 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual manipulative test (Week 2 of recovery period)

Dose (mg/kg) : 750

Parameter	Animal number	Male						Female					
		4 0 0 7	4 0 0 8	4 0 0 9	4 0 1 0	4 0 1 1	4 0 1 2	4 1 0 7	4 1 0 8	4 1 0 9	4 1 1 0	4 1 1 1	4 1 1 2
Auditory response a)		0	0	0	0	0	0	0	0	0	0	0	0
Approach response b)		0	0	0	0	0	0	0	0	0	0	0	0
Touch response c)		0	0	0	0	0	0	0	0	0	0	0	0
Tail pinch response d)		0	0	0	0	0	0	0	0	0	0	0	0
Pupillary reflex e)		P	P	P	P	P	P	P	P	P	P	P	P
Aerial righting reflex (Total score)		0	0	0	0	0	0	0	0	0	0	0	0
Landing foot splay (mm)		91	87	112	102	106	84	35	66	73	67	69	82

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

Appendix 77 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual grip strength (Week 4 of administration period)

Dose (mg/kg) : 0

Sex	Animal number	Fore limb g	Hind limb g
Male	1001	986	391
	1002	1071	545
	1003	972	327
	1004	1043	640
	1005	1005	520
	1006	1009	511
	1007	1367	333
	1008	970	448
	1009	1081	472
	1010	739	620
	1011	539	439
	1012	928	429
	Mean	976	473
	S.D.	197	100
Female	1101	910	158
	1102	842	303
	1103	815	331
	1104	1006	376
	1105	744	434
	1106	929	442
	1107	786	420
	1108	563	148
	1109	522	312
	1110	778	352
	1111	696	308
	1112	839	304
	Mean	786	324
	S.D.	142	95

Appendix 78 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual grip strength (Week 4 of administration period)

Dose (mg/kg) : 30

Sex	Animal number	Fore limb g	Hind limb g
Male	2001	1000	446
	2002	793	369
	2003	668	333
	2004	831	595
	2005	577	432
	2006	716	398
	Mean	764	429
	S.D.	147	91
Female	2101	976	272
	2102	833	261
	2103	921	377
	2104	826	326
	2105	615	341
	2106	733	245
	Mean	817	304
	S.D.	130	52

Appendix 79 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual grip strength (Week 4 of administration period)

Dose (mg/kg) : 150

Sex	Animal number	Fore limb g	Hind limb g
Male	3001	896	557
	3002	592	360
	3003	1010	544
	3004	908	375
	3005	1044	677
	3006	942	439
	Mean	899	492
	S.D.	161	123
Female	3101	853	330
	3102	769	228
	3103	764	445
	3104	796	354
	3105	683	313
	3106	735	307
	Mean	767	330
	S.D.	57	71

Appendix 80 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual grip strength (Week 4 of administration period)

Dose (mg/kg) : 750

Sex	Animal number	Fore limb g	Hind limb g
Male	4001	762	418
	4002	909	372
	4003	611	648
	4004	971	479
	4005	886	450
	4006	981	353
	4007	988	448
	4008	1124	308
	4009	1479	376
	4010	1264	324
	4011	872	460
	4012	712	463
	Mean	963	425
	S.D.	239	91
Female	4101	938	493
	4102	1067	393
	4103	849	211
	4104	846	309
	4105	926	284
	4106	592	301
	4107	832	393
	4108	1018	541
	4109	554	370
	4110	816	320
	4111	842	311
	4112	686	399
	Mean	831	360
	S.D.	156	92

D : Dead

Appendix 81 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual grip strength (Week 2 of recovery period)

Dose (mg/kg) : 0

Sex	Animal number	Fore limb g	Hind limb g
Male	1007	1353	442
	1008	1134	690
	1009	1859	783
	1010	1059	733
	1011	1322	510
	1012	1185	570
	Mean	1319	621
	S.D.	287	135
Female	1107	649	435
	1108	577	263
	1109	768	383
	1110	817	460
	1111	688	569
	1112	1107	409
	Mean	768	420
	S.D.	187	100

Appendix 82 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual grip strength (Week 2 of recovery period)

Dose (mg/kg) : 750

Sex	Animal number	Fore limb g	Hind limb g
Male	4007	1249	465
	4008	1333	358
	4009	1582	619
	4010	1471	544
	4011	1315	603
	4012	965	477
	Mean	1319	511
	S.D.	211	98
Female	4107	995	342
	4108	970	412
	4109	783	307
	4110	943	299
	4111	1183	508
	4112	918	443
	Mean	965	385
	S.D.	130	83

D : Dead

Appendix 83 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual motor activity (Week 4 of administration period)

Dose (mg/kg) : 0

Sex	Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
Male	1001	442	390	434	347	347	303	2263
	1002	378	353	283	287	240	213	1754
	1003	397	351	348	368	322	241	2027
	1004	385	392	285	317	161	83	1623
	1005	412	365	314	232	219	263	1805
	1006	411	330	334	411	268	201	1955
	1007	411	322	296	353	328	76	1786
	1008	413	376	340	354	303	349	2135
	1009	415	389	300	275	352	351	2082
	1010	285	285	245	254	203	146	1418
	1011	434	301	173	184	440	120	1652
	1012	325	287	164	86	18	34	914
	Mean	392	345	293	289	267	198	1785
	S.D.	45	40	74	91	110	108	365
Female	1101	293	321	244	267	198	217	1540
	1102	414	343	316	212	298	192	1775
	1103	499	359	359	294	320	317	2148
	1104	365	271	345	409	209	97	1696
	1105	389	279	333	200	324	230	1755
	1106	407	165	295	136	23	213	1239
	1107	373	367	299	233	289	123	1684
	1108	435	283	129	283	160	0	1290
	1109	376	322	234	68	177	195	1372
	1110	286	287	307	173	111	266	1430
	1111	366	317	422	294	343	284	2026
	1112	405	286	145	1	1	159	997
	Mean	384	300	286	214	204	191	1579
	S.D.	58	53	85	110	116	87	333

Unit : Count

Appendix 84 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual motor activity (Week 4 of administration period)

Dose (mg/kg) : 30

Sex	Animal number	Interval (minutes)						
		0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
Male	2001	321	278	225	113	275	166	1378
	2002	334	313	296	276	207	356	1782
	2003	403	368	370	260	305	267	1973
	2004	313	302	261	281	185	271	1613
	2005	380	272	268	336	366	273	1895
	2006	418	319	273	63	34	15	1122
	Mean	362	309	282	222	229	225	1627
	S.D.	45	35	49	108	116	119	326
Female	2101	348	232	179	304	142	136	1341
	2102	370	285	252	168	107	27	1209
	2103	410	302	235	83	303	232	1565
	2104	370	294	148	233	63	27	1135
	2105	369	346	95	183	325	115	1433
	2106	430	291	21	8	305	74	1129
	Mean	383	292	155	163	208	102	1302
	S.D.	31	37	87	105	116	78	176

Unit : Count

Appendix 85 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual motor activity (Week 4 of administration period)

Dose (mg/kg) : 150

Sex	Animal number	Interval (minutes)						
		0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
Male	3001	345	236	188	310	216	95	1390
	3002	427	314	363	116	224	363	1807
	3003	312	258	287	242	256	108	1463
	3004	372	293	338	191	293	183	1670
	3005	377	290	272	272	126	219	1556
	3006	302	258	291	325	316	2	1494
	Mean	356	275	290	243	239	162	1563
	S.D.	46	29	61	79	67	124	152
Female	3101	354	237	219	181	262	193	1446
	3102	280	252	223	71	237	266	1329
	3103	374	371	233	202	6	71	1257
	3104	347	357	364	373	265	410	2116
	3105	422	319	313	292	262	261	1869
	3106	313	264	167	88	29	160	1021
	Mean	348	300	253	201	177	227	1506
	S.D.	49	57	72	117	124	115	409

Unit : Count

Appendix 86 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual motor activity (Week 4 of administration period)

Dose (mg/kg) : 750

Sex	Animal number	Interval (minutes)						
		0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
Male	4001	329	257	170	179	248	164	1347
	4002	325	335	221	289	145	102	1417
	4003	328	214	184	178	395	125	1424
	4004	395	345	254	290	69	270	1623
	4005	268	109	300	241	193	85	1196
	4006	335	163	125	241	201	244	1309
	4007	376	320	122	241	191	40	1290
	4008	371	420	326	339	223	39	1718
	4009	374	381	346	362	301	327	2091
	4010	333	314	353	319	213	58	1590
	4011	382	391	353	300	279	378	2083
	4012	374	326	285	232	299	98	1614
	Mean	349	298	253	268	230	161	1559
	S.D.	36	94	87	59	84	116	292
Female	4101	283	320	261	264	267	257	1652
	4102	326	249	277	258	303	86	1499
	4103	294	275	317	127	293	231	1537
	4104	242	286	243	197	202	193	1363
	4105	359	260	299	127	259	217	1521
	4106	431	131	269	236	178	254	1499
	4107	233	285	193	262	133	209	1315
	4108	214	204	167	199	325	207	1316
	4109	138	238	187	151	235	206	1155
	4110	400	345	258	259	93	143	1498
	4111	361	333	235	321	204	249	1703
	4112	379	347	287	165	11	57	1246
	Mean	305	273	249	214	209	192	1442
	S.D.	87	63	47	62	93	65	164

Unit : Count

Appendix 87 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual motor activity (Week 2 of recovery period)

Dose (mg/kg) : 0

Sex	Animal number	Interval (minutes)						
		0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
Male	1007	343	334	246	196	233	81	1433
	1008	447	421	362	382	239	248	2099
	1009	416	323	396	289	376	375	2175
	1010	382	347	282	216	264	253	1744
	1011	407	312	286	229	291	383	1908
	1012	382	310	318	179	9	11	1209
	Mean	396	341	315	249	235	225	1761
	S.D.	36	41	56	75	122	152	379
Female	1107	352	355	236	234	343	333	1853
	1108	369	308	280	87	268	264	1576
	1109	351	287	186	229	289	8	1350
	1110	322	334	305	290	287	195	1733
	1111	290	205	196	230	220	189	1330
	1112	427	388	269	192	320	411	2007
	Mean	352	313	245	210	288	233	1642
	S.D.	46	64	48	68	43	139	273

Unit : Count

Appendix 88 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual motor activity (Week 2 of recovery period)

Dose (mg/kg) : 750

Sex	Animal number	Interval (minutes)						
		0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
Male	4007	390	384	250	189	67	26	1306
	4008	367	363	189	90	9	23	1041
	4009	462	389	284	279	191	35	1640
	4010	420	406	321	270	176	88	1681
	4011	422	340	342	347	296	270	2017
	4012	367	305	245	271	211	170	1569
	Mean	405	365	272	241	158	102	1542
	S.D.	37	37	56	89	104	100	335
Female	4107	385	292	242	206	241	303	1669
	4108	360	295	207	316	288	281	1747
	4109	378	255	164	73	269	194	1333
	4110	410	345	357	391	180	19	1702
	4111	310	242	256	203	206	160	1377
	4112	379	248	309	120	181	122	1359
	Mean	370	280	256	218	228	180	1531
	S.D.	34	39	69	119	46	105	194

Unit : Count

Appendix 89 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual body weight (Administration period)

Dose (mg/kg) : 0

Sex	Animal number	Day of administration 1	4	7	10	14	17	21	24	28	Gain 1-28
Male	1001	218	249	276	308	341	367	391	406	428	210
	1002	210	239	270	300	334	356	382	399	421	211
	1003	220	248	279	301	326	348	375	392	416	196
	1004	214	241	278	302	338	366	397	414	438	224
	1005	205	230	262	287	318	342	367	385	405	200
	1006	205	236	268	293	327	348	374	383	405	200
	1007	200	230	252	274	302	319	342	352	375	175
	1008	202	230	258	284	316	338	364	386	407	205
	1009	213	243	279	309	348	371	403	416	450	237
	1010	214	238	264	293	328	356	383	411	431	217
	1011	200	225	249	274	296	320	331	352	368	168
	1012	215	235	262	288	322	345	375	385	401	186
	Mean	210	237	266	293	325	348	374	390	412	202
	S.D.	7	7	10	12	15	17	21	21	24	20
Female	1101	167	179	188	197	211	222	235	236	245	78
	1102	147	156	159	161	171	186	197	210	213	66
	1103	156	163	175	186	203	213	229	227	238	82
	1104	145	151	153	164	176	185	195	206	214	69
	1105	156	170	175	195	209	225	246	247	257	101
	1106	149	155	160	164	175	184	193	204	214	65
	1107	147	152	156	167	176	190	197	201	204	57
	1108	153	160	167	169	176	186	192	200	205	52
	1109	159	164	177	185	199	210	220	224	230	71
	1110	149	163	176	190	204	223	230	238	250	101
	1111	160	171	179	187	200	207	214	224	226	66
	1112	151	156	171	187	199	210	225	227	236	85
	Mean	153	162	170	179	192	203	214	220	228	74
	S.D.	7	8	11	13	15	16	19	16	18	16

Unit : g

Appendix 90 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual body weight (Administration period)

Dose (mg/kg) : 30

Sex	Animal number	Day of administration									Gain
		1	4	7	10	14	17	21	24	28	1-28
Male	2001	205	227	255	281	317	345	374	388	414	209
	2002	207	233	262	290	327	354	381	399	426	219
	2003	215	237	270	298	333	359	388	395	423	208
	2004	211	243	270	296	320	340	364	383	402	191
	2005	206	237	264	288	319	341	362	374	393	187
	2006	201	224	254	280	312	340	361	371	397	196
	Mean	208	234	263	289	321	347	372	385	409	202
	S.D.	5	7	7	7	8	8	11	11	14	12
Female	2101	144	160	169	175	184	196	207	215	218	74
	2102	167	179	189	198	212	218	224	236	244	77
	2103	145	153	169	178	187	189	201	203	208	63
	2104	149	157	163	173	185	185	195	206	211	62
	2105	150	156	165	166	176	192	203	207	216	66
	2106	154	162	164	177	192	192	209	215	219	65
	Mean	152	161	170	178	189	195	207	214	219	68
	S.D.	8	9	10	11	12	12	10	12	13	6

Unit : g

Appendix 91 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual body weight (Administration period)

Dose (mg/kg) : 150

Sex	Animal number	Day of administration 1	4	7	10	14	17	21	24	28	Gain 1-28
Male	3001	211	238	270	299	331	360	388	408	432	221
	3002	205	229	251	280	305	326	348	362	383	178
	3003	203	225	256	277	305	327	349	367	380	177
	3004	211	238	267	296	325	344	373	398	406	195
	3005	217	239	269	291	319	339	369	382	402	185
	3006	208	238	260	277	299	312	339	357	380	172
	Mean	209	235	262	287	314	335	361	379	397	188
	S.D.	5	6	8	10	13	17	19	21	21	18
Female	3101	157	169	173	176	186	191	204	207	210	53
	3102	154	156	163	161	165	166	175	177	189	35
	3103	148	152	151	166	169	173	180	181	190	42
	3104	164	168	183	192	203	208	216	215	227	63
	3105	148	158	171	186	200	211	219	225	235	87
	3106	141	144	150	152	155	165	173	180	190	49
	Mean	152	158	165	172	180	186	195	198	207	55
	S.D.	8	10	13	15	20	21	21	21	20	18

Unit : g

Appendix 92 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual body weight (Administration period)

Dose (mg/kg) : 750

Sex	Animal number	Day of administration									Gain 1-28
		1	4	7	10	14	17	21	24	28	
Male	4001	217	229	250	275	306	333	355	369	391	174
	4002	212	231	257	277	305	318	326	336	349	137
	4003	203	227	254	282	307	332	345	359	367	164
	4004	214	235	254	274	298	317	329	345	362	148
	4005	201	217	239	267	283	297	307	320	328	127
	4006	204	222	244	271	299	322	343	359	375	171
	4007	218	242	271	306	335	352	369	384	402	184
	4008	212	236	264	284	291	312	316	329	337	125
	4009	219	230	273	301	332	359	384	400	418	199
	4010	209	231	255	279	302	313	328	341	352	143
	4011	203	217	246	280	302	330	359	379	398	195
	4012	210	225	246	268	287	303	314	322	340	130
	Mean	210	229	254	280	304	324	340	354	368	158
	S.D.	6	7	11	12	16	18	24	26	29	27
Female	4101	162	171	188	196	217	229	240	253	258	96
	4102	151	157	171	182	192	196	210	215	227	76
	4103	140	141	140	145	151	154	159	159	159	19
	4104	153	161	163	168	182	193	198	205	217	64
	4105	161	172	187	196	210	218	228	233	231	70
	4106	144	148	154	165	177	185	200	205	195	51
	4107	142	148	151	167	176	182	189	193	197	55
	4108	159	174	183	193	209	216	227	236	242	83
	4109	141	152	158	167	177	186	191	202	206	65
	4110	145	136	150	164	177	185	191	197	207	62
	4111	154	164	176	194	205	217	231	237	243	89
	4112	157	167	172	177	189	185	200	212	217	60
	Mean	151	158	166	176	189	196	205	212	217	66
	S.D.	8	13	16	16	19	21	23	25	27	20

Unit : g

Appendix 93 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual body weight (Recovery period)

Dose (mg/kg) : 0

Sex	Animal number	Day of recovery 1	3	7	10	14	Gain 1-14
Male	1007	380	389	399	403	428	48
	1008	416	417	430	445	464	48
	1009	453	467	482	504	526	73
	1010	435	455	479	499	514	79
	1011	380	384	408	416	425	45
	1012	403	419	442	462	473	70
	Mean	411	422	440	455	472	61
	S.D.	29	34	35	42	42	15
Female	1107	215	211	223	229	236	21
	1108	207	209	213	216	215	8
	1109	232	236	244	241	252	20
	1110	254	259	268	268	275	21
	1111	229	236	241	252	256	27
	1112	235	236	242	244	245	10
	Mean	229	231	239	242	247	18
	S.D.	16	19	19	18	20	7

Unit : g

Appendix 94 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual body weight (Recovery period)

Dose (mg/kg) : 750

Sex	Animal number	Day of recovery 1	3	7	10	14	Gain 1-14
Male	4007	408	413	430	445	465	57
	4008	343	345	367	378	398	55
	4009	421	436	464	484	518	97
	4010	354	359	375	391	407	53
	4011	401	411	438	463	477	76
	4012	344	349	365	383	401	57
	Mean	379	386	407	424	444	66
	S.D.	35	39	43	46	50	17
Female	4107	195	199	205	205	209	14
	4108	243	250	259	262	270	27
	4109	208	212	212	212	216	8
	4110	207	205	209	219	222	15
	4111	248	251	261	267	284	36
	4112	220	223	233	233	232	12
	Mean	220	223	230	233	239	19
	S.D.	21	23	25	26	31	11

Unit : g

Appendix 95 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual food consumption (Administration period)

Dose (mg/kg) : 0

Sex	Animal number	Day of administration								
		1	4	7	10	14	17	21	24	28
Male	1001	23	25	28	27	29	29	28	26	28
	1002	26	25	28	27	29	27	29	26	27
	1003	26	27	30	29	28	28	28	27	28
	1004	23	24	28	26	29	30	31	28	31
	1005	24	24	28	27	28	29	29	26	28
	1006	24	25	27	27	28	29	27	25	27
	1007	22	25	25	27	26	26	26	24	26
	1008	23	24	26	26	27	27	28	27	28
	1009	22	24	27	28	29	28	30	27	30
	1010	22	22	24	24	27	29	28	29	29
	1011	22	26	25	26	26	27	26	25	26
	1012	24	25	26	26	28	28	31	28	29
	Mean	23	25	27	27	28	28	28	27	28
	S.D.	1	1	2	1	1	1	2	1	2
Female	1101	20	18	19	18	19	18	19	17	18
	1102	18	16	15	14	15	17	16	16	15
	1103	19	17	19	18	19	18	20	18	19
	1104	17	15	15	17	16	16	16	16	17
	1105	18	18	18	19	19	20	21	19	19
	1106	15	16	14	15	16	16	16	15	16
	1107	17	16	17	18	17	17	17	16	16
	1108	17	16	17	16	16	17	16	15	16
	1109	16	17	19	17	19	17	19	18	19
	1110	17	18	19	18	19	20	19	18	19
	1111	18	18	17	16	17	17	18	18	18
	1112	17	15	17	16	19	20	20	18	19
	Mean	17	17	17	17	18	18	18	17	18
	S.D.	1	1	2	1	2	1	2	1	2

Unit : g/rat/day

Appendix 96 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual food consumption (Administration period)

Dose (mg/kg) : 30

Sex	Animal number	Day of administration								
		1	4	7	10	14	17	21	24	28
Male	2001	21	23	25	25	28	28	29	26	28
	2002	23	23	25	26	28	30	30	29	31
	2003	26	25	28	29	31	30	30	27	28
	2004	22	26	28	28	28	26	29	27	28
	2005	22	25	27	27	28	27	26	24	25
	2006	22	22	26	26	28	30	30	26	29
	Mean	23	24	27	27	29	29	29	27	28
	S.D.	2	2	1	1	1	2	2	2	2
Female	2101	16	16	16	15	16	17	17	16	16
	2102	19	19	19	18	18	18	18	17	18
	2103	15	16	18	17	17	16	17	15	17
	2104	16	17	17	17	20	18	19	19	17
	2105	15	15	16	14	15	17	16	14	16
	2106	17	16	17	17	18	17	19	16	17
	Mean	16	17	17	16	17	17	18	16	17
	S.D.	2	1	1	2	2	1	1	2	1

Unit : g/rat/day

Appendix 97

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual food consumption (Administration period)

Dose (mg/kg) : 150

Sex	Animal number	Day of administration								
		1	4	7	10	14	17	21	24	28
Male	3001	23	23	25	26	26	27	28	27	29
	3002	23	24	26	27	28	27	28	26	28
	3003	24	22	26	24	26	26	27	25	25
	3004	24	24	28	27	29	29	31	29	28
	3005	24	23	27	27	27	27	28	26	26
	3006	21	24	25	24	25	22	25	25	26
	Mean	23	23	26	26	27	26	28	26	27
	S.D.	1	1	1	1	1	2	2	2	2
Female	3101	16	19	17	16	18	18	19	16	18
	3102	17	15	16	14	14	14	15	14	15
	3103	18	16	16	18	16	16	16	15	17
	3104	18	16	21	17	18	17	17	16	19
	3105	17	16	19	17	19	19	19	17	18
	3106	13	13	14	12	13	14	14	12	15
	Mean	17	16	17	16	16	16	17	15	17
	S.D.	2	2	2	2	2	2	2	2	2

Unit : g/rat/day

Appendix 98 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual food consumption (Administration period)

Dose (mg/kg) : 750

Sex	Animal number	Day of administration								
		1	4	7	10	14	17	21	24	28
Male	4001	23	20	24	26	27	28	29	28	29
	4002	23	20	24	26	26	24	24	25	23
	4003	22	20	25	27	28	33	32	31	35
	4004	25	23	27	27	29	29	28	27	30
	4005	22	19	26	27	27	25	24	22	24
	4006	20	19	22	25	27	27	26	27	27
	4007	25	25	29	31	32	29	29	29	30
	4008	23	24	27	28	20	25	23	23	24
	4009	24	18	28	27	30	29	30	26	28
	4010	26	23	29	28	28	26	28	28	27
	4011	24	17	25	26	26	27	28	30	27
	4012	25	20	25	27	27	26	25	24	25
	Mean	24	21	26	27	27	27	27	27	27
	S.D.	2	2	2	2	3	2	3	3	3
Female	4101	18	17	20	22	21	23	24	21	22
	4102	16	14	18	17	18	16	18	15	19
	4103	16	12	13	14	10	15	15	14	13
	4104	17	15	17	17	17	19	18	16	20
	4105	17	16	19	19	20	19	19	18	19
	4106	14	14	15	16	17	15	18	17	14
	4107	15	14	17	18	17	16	18	15	16
	4108	18	16	19	18	20	18	19	18	18
	4109	15	14	16	17	17	16	19	17	18
	4110	14	5	18	17	17	16	16	16	18
	4111	18	15	17	19	21	21	22	20	19
	4112	20	17	18	17	17	16	18	17	19
	Mean	17	14	17	18	18	18	19	17	18
	S.D.	2	3	2	2	3	3	2	2	3

Unit : g/rat/day

Appendix 99 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual food consumption (Recovery period)

Dose (mg/kg) : 0

Sex	Animal number	Day of recovery 3	7	10	14
Male	1007	25	26	24	26
	1008	26	28	25	27
	1009	30	31	30	29
	1010	30	29	28	29
	1011	27	28	23	27
	1012	31	32	32	30
	Mean	28	29	27	28
	S.D.	2	2	4	2
Female	1107	16	20	19	19
	1108	15	15	14	15
	1109	19	19	17	18
	1110	19	20	17	19
	1111	19	18	18	19
	1112	17	18	17	18
	Mean	18	18	17	18
	S.D.	2	2	2	2

Unit : g/rat/day

Appendix 100 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual food consumption (Recovery period)

Dose (mg/kg) : 750

Sex	Animal number	Day of recovery 3	7	10	14
Male	4007	30	30	30	31
	4008	23	26	24	25
	4009	31	34	31	35
	4010	28	29	27	29
	4011	32	31	32	29
	4012	26	27	24	27
	Mean	28	30	28	29
	S.D.	3	3	4	3
Female	4107	15	17	16	17
	4108	23	22	18	21
	4109	22	20	17	18
	4110	18	18	17	18
	4111	23	23	20	24
	4112	18	20	17	19
	Mean	20	20	18	20
	S.D.	3	2	1	3

Unit : g/rat/day

Appendix 101 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual urinalysis (Week 4 of administration period)

Dose (mg/kg) : 0

Sex	Animal number	pH	1) Pro-tein	2) Ketone body	3) Glu-cose	4) Occult blood	5) Bili-rubin	6) Urobi-linogen	7) Color
Male	1001	8.5	+	+-	-	-	-	+-	Y
	1002	9.0	+	+	-	-	-	+-	Y
	1003	8.0	+-	+	-	-	-	+-	Y
	1004	8.5	+-	-	-	-	-	+-	Y
	1005	9.0	+-	-	-	-	-	+-	Y
	1006	8.5	+-	-	-	-	-	+-	Y
	1007	9.0	+	-	-	++	-	+-	Y
	1008	8.5	+-	-	-	-	-	+-	Y
	1009	9.0	+	+-	-	-	-	+-	Y
	1010	8.5	+-	+-	-	-	-	+-	Y
	1011	8.5	-	-	-	-	-	+-	Y
	1012	8.5	+	+	-	-	-	+	Y
Female	1101	8.5	-	-	-	-	-	+-	Y
	1102	9.0	-	-	-	-	-	+-	Y
	1103	9.0	-	-	-	-	-	+-	Y
	1104	8.0	-	-	-	-	-	+-	Y
	1105	7.0	+-	-	-	-	-	+-	Y
	1106	8.5	+	+	-	-	-	+	Y
	1107	7.0	-	-	-	-	-	+-	Y
	1108	8.5	-	-	-	-	-	+-	Y
	1109	9.0	-	-	-	-	-	+-	Y
	1110	8.5	-	-	-	-	-	+-	Y
	1111	8.5	-	-	-	-	-	+-	Y
	1112	8.5	-	-	-	-	-	+-	Y

1) - : <10 mg/dL +- : 10 - 25 mg/dL + : 26 - 85 mg/dL ++ : 86 - 250 mg/dL +++ : 251 - 600 mg/dL ++++ : >600 mg/dL
2) - : <5 mg/dL +- : 5 - 7.5 mg/dL + : 7.6 - 30 mg/dL ++ : 31 - 70 mg/dL +++ : 71 - 125 mg/dL ++++ : >125 mg/dL
3) - : <30 mg/dL +- : 30 - 60 mg/dL + : 61 - 125 mg/dL ++ : 126 - 250 mg/dL +++ : 251 - 750 mg/dL ++++ : >750 mg/dL
4) - : <0.03 mg/dL +- : 0.03 - 0.05 mg/dL + : 0.06 - 0.15 mg/dL ++ : 0.16 - 0.75 mg/dL +++ : >0.75 mg/dL
5) - : <0.5 mg/dL + : 0.5 - 1.5 mg/dL ++ : 1.6 - 5.0 mg/dL +++ : 5.1 - 10.0 mg/dL ++++ : >10.0 mg/dL
6) +- : <2.0 mg/dL + : 2.0 - 3.5 mg/dL ++ : 3.6 - 7.0 mg/dL +++ : 7.1 - 12.0 mg/dL ++++ : >12.0 mg/dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 102 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual urinalysis (Week 4 of administration period)

Dose (mg/kg) : 0

Sex	Animal number	URINE SEDIMENT						
							CRYSTALLIZATION	
		RBC	WBC	SEC	SREC	Cast	PS	CO
Male	1001	-	-	+-	-	-	+-	-
	1002	-	-	+-	-	-	-	-
	1003	-	-	+-	-	-	-	-
	1004	-	-	+	-	-	-	-
	1005	-	-	+-	-	-	-	-
	1006	-	-	+-	-	-	-	-
	1007	-	-	+-	-	-	-	-
	1008	-	-	+-	-	-	-	-
	1009	-	-	+-	-	-	-	-
	1010	-	-	+-	-	-	-	-
	1011	-	-	+-	-	-	-	-
	1012	-	-	+-	-	-	-	-
Female	1101	-	-	+-	-	-	-	-
	1102	-	-	+-	-	-	-	-
	1103	-	-	+-	-	-	-	-
	1104	-	-	+-	-	-	-	-
	1105	-	-	+-	-	-	+-	-
	1106	-	-	+-	-	-	-	+-
	1107	-	-	+-	-	-	+-	-
	1108	-	+-	+-	-	-	+-	-
	1109	-	-	+-	-	-	-	-
	1110	-	-	+-	-	-	-	-
	1111	-	-	+-	-	-	-	-
	1112	-	-	+-	-	-	-	-

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

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

Appendix 103 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual water intake and urinalysis (Week 4 of administration period)

Dose (mg/kg) : 0

Sex	Animal number	Water intake mL/24h	Urine volume mL/24h	Osmolality mOsm/kg
Male	1001	33	9.3	2138
	1002	24	8.2	2290
	1003	58	10.0	2234
	1004	47	15.0	1640
	1005	35	8.9	2456
	1006	29	6.9	1938
	1007	28	7.1	2196
	1008	42	14.8	1538
	1009	29	10.8	2096
	1010	44	22.0	1260
	1011	33	9.5	2334
	1012	37	7.3	2110
	Mean	37	10.8	2019
	S.D.	10	4.4	360
Female	1101	31	7.2	2398
	1102	32	5.0	2764
	1103	51	5.9	1728
	1104	31	3.1	2472
	1105	30	6.9	2012
	1106	26	3.8	1862
	1107	30	4.8	2124
	1108	26	8.2	1780
	1109	21	3.0	2688
	1110	33	10.0	1750
	1111	41	8.4	1742
	1112	36	9.5	1654
	Mean	32	6.3	2081
	S.D.	8	2.4	401

Appendix 104 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual urinalysis (Week 4 of administration period)

Dose (mg/kg) : 30

Sex	Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
Male	2001	8.5	+-	-	-	-	-	+-	Y
	2002	8.5	+-	-	-	-	-	+-	Y
	2003	8.5	-	-	-	-	-	+-	Y
	2004	8.5	+	+	-	-	-	+	Y
	2005	8.5	+	+	-	-	-	+-	Y
	2006	8.5	-	-	-	-	-	+-	Y
Female	2101	8.5	-	-	-	-	-	+-	Y
	2102	9.0	+-	+-	-	-	-	+-	Y
	2103	7.5	-	+-	-	+-	-	+-	Y
	2104	8.5	-	-	-	-	-	+-	Y
	2105	8.5	-	-	-	-	-	+-	Y
	2106	9.0	+-	+-	-	-	-	+-	Y

1) - : <10 mg/dL +- : 10 - 25 mg/dL + : 26 - 85 mg/dL ++ : 86 - 250 mg/dL +++ : 251 - 600 mg/dL ++++ : >600 mg/dL
2) - : <5 mg/dL +- : 5 - 7.5 mg/dL + : 7.6 - 30 mg/dL ++ : 31 - 70 mg/dL +++ : 71 - 125 mg/dL ++++ : >125 mg/dL
3) - : <30 mg/dL +- : 30 - 60 mg/dL + : 61 - 125 mg/dL ++ : 126 - 250 mg/dL +++ : 251 - 750 mg/dL ++++ : >750 mg/dL
4) - : <0.03 mg/dL +- : 0.03 - 0.05 mg/dL + : 0.06 - 0.15 mg/dL ++ : 0.16 - 0.75 mg/dL +++ : >0.75 mg/dL
5) - : <0.5 mg/dL + : 0.5 - 1.5 mg/dL ++ : 1.6 - 5.0 mg/dL +++ : 5.1 - 10.0 mg/dL ++++ : >10.0 mg/dL
6) +- : <2.0 mg/dL + : 2.0 - 3.5 mg/dL ++ : 3.6 - 7.0 mg/dL +++ : 7.1 - 12.0 mg/dL ++++ : >12.0 mg/dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 105 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual urinalysis (Week 4 of administration period)

Dose (mg/kg) : 30

Sex	Animal number	URINE SEDIMENT						
							CRYSTALLIZATION	
		RBC	WBC	SEC	SREC	Cast	PS	CO
Male	2001	-	+-	+-	-	-	-	-
	2002	-	-	+-	-	-	-	-
	2003	-	-	+-	-	-	-	-
	2004	-	-	+-	-	-	-	-
	2005	-	-	+-	-	-	-	-
	2006	-	-	+-	-	-	-	-
Female	2101	-	-	+-	-	-	-	-
	2102	-	+-	+-	-	-	-	-
	2103	-	-	+-	-	-	-	-
	2104	-	-	+-	-	-	-	-
	2105	-	-	+-	-	-	-	-
	2106	-	-	+-	-	-	+-	-

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

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

Appendix 106 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual water intake and urinalysis (Week 4 of administration period)

Dose (mg/kg) : 30

Sex	Animal number	Water intake mL/24h	Urine volume mL/24h	Osmolality mOsm/kg
Male	2001	29	14.4	1884
	2002	45	16.5	1424
	2003	45	12.5	1906
	2004	25	7.5	2480
	2005	32	8.0	2270
	2006	35	13.5	2064
	Mean	35	12.1	2005
	S.D.	8	3.6	364
Female	2101	46	11.5	1590
	2102	34	5.9	2786
	2103	20	4.0	3078
	2104	25	6.6	2072
	2105	24	5.6	2100
	2106	25	5.1	2330
	Mean	29	6.5	2326
	S.D.	10	2.6	536

Appendix 107 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual urinalysis (Week 4 of administration period)

Dose (mg/kg) : 150

Sex	Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
Male	3001	8.5	+-	+-	-	-	-	+-	Y
	3002	9.0	+	+-	-	-	-	+-	Y
	3003	9.0	+	+-	-	-	-	+-	Y
	3004	7.5	+-	-	-	-	-	+-	Y
	3005	8.5	+	+-	-	-	-	+-	Y
	3006	8.5	+-	+	-	-	-	+-	Y
Female	3101	6.5	+-	+-	-	-	-	+-	Y
	3102	8.0	-	-	-	-	-	+-	Y
	3103	6.5	-	-	-	-	-	+-	Y
	3104	9.0	+-	+-	-	-	-	+-	Y
	3105	7.0	-	-	-	-	-	+-	Y
	3106	8.0	+-	+-	-	-	-	+	Y

1) - : <10 mg/dL +- : 10 - 25 mg/dL + : 26 - 85 mg/dL ++ : 86 - 250 mg/dL +++ : 251 - 600 mg/dL ++++ : >600 mg/dL
2) - : <5 mg/dL +- : 5 - 7.5 mg/dL + : 7.6 - 30 mg/dL ++ : 31 - 70 mg/dL +++ : 71 - 125 mg/dL ++++ : >125 mg/dL
3) - : <30 mg/dL +- : 30 - 60 mg/dL + : 61 - 125 mg/dL ++ : 126 - 250 mg/dL +++ : 251 - 750 mg/dL ++++ : >750 mg/dL
4) - : <0.03 mg/dL +- : 0.03 - 0.05 mg/dL + : 0.06 - 0.15 mg/dL ++ : 0.16 - 0.75 mg/dL +++ : >0.75 mg/dL
5) - : <0.5 mg/dL + : 0.5 - 1.5 mg/dL ++ : 1.6 - 5.0 mg/dL +++ : 5.1 - 10.0 mg/dL ++++ : >10.0 mg/dL
6) +- : <2.0 mg/dL + : 2.0 - 3.5 mg/dL ++ : 3.6 - 7.0 mg/dL +++ : 7.1 - 12.0 mg/dL ++++ : >12.0 mg/dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 108 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual urinalysis (Week 4 of administration period)

Dose (mg/kg) : 150

Sex	Animal number	URINE SEDIMENT						
							CRYSTALLIZATION	
		RBC	WBC	SEC	SREC	Cast	PS	CO
Male	3001	-	-	+-	-	-	-	-
	3002	-	-	+-	-	-	-	-
	3003	-	-	+-	-	-	-	-
	3004	-	-	+	-	-	-	-
	3005	-	-	+-	-	-	-	-
	3006	-	-	+-	-	-	-	-
Female	3101	-	-	+-	-	-	-	-
	3102	-	-	+-	-	-	+-	-
	3103	-	-	+-	-	-	-	-
	3104	-	-	+-	-	-	-	-
	3105	-	-	+-	-	-	-	-
	3106	-	-	+-	-	-	-	-

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

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

Appendix 109

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual water intake and urinalysis (Week 4 of administration period)

Dose (mg/kg) : 150

Sex	Animal number	Water intake mL/24h	Urine volume mL/24h	Osmolality mOsm/kg
Male	3001	42	15.8	1318
	3002	36	9.4	2100
	3003	35	10.9	1882
	3004	60	17.8	1400
	3005	37	13.3	1968
	3006	36	11.4	1584
	Mean	41	13.1	1709
	S.D.	10	3.2	321
Female	3101	43	2.7	2258
	3102	39	8.6	1708
	3103	28	1.5	3222
	3104	20	2.5	2038
	3105	31	8.2	1768
	3106	25	3.6	2270
	Mean	31	4.5	2211
	S.D.	9	3.1	549

Appendix 110

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual urinalysis (Week 4 of administration period)

Dose (mg/kg) : 750

Sex	Animal number	pH	1) Pro-tein	2) Ketone body	3) Glu-cose	4) Occult blood	5) Bili-rubin	6) Urobi-linogen	7) Color
Male	4001	8.5	-	-	-	-	-	+-	Y
	4002	8.5	-	-	-	-	-	+-	Y
	4003	8.0	+	+-	-	-	-	+-	Y
	4004	8.0	+-	-	-	-	-	+-	Y
	4005	8.0	-	-	-	-	-	+-	Y
	4006	8.5	+-	-	-	-	-	+-	Y
	4007	7.0	+-	-	-	-	-	+-	Y
	4008	7.5	-	-	-	-	-	+-	Y
	4009	8.5	+-	-	-	-	-	+-	Y
	4010	8.0	+-	-	-	-	-	+-	Y
	4011	8.5	-	-	-	-	-	+-	Y
	4012	6.5	-	-	-	-	-	+-	Y
Female	4101	6.5	-	-	-	-	-	+-	Y
	4102	7.5	-	-	-	-	-	+-	Y
	4103	7.5	-	-	-	-	-	+-	Y
	4104	7.5	-	-	-	-	-	+-	Y
	4105	8.5	-	-	-	-	-	+-	Y
	4106	7.0	-	-	-	-	-	+-	Y
	4107	7.5	-	-	-	-	-	+-	Y
	4108	7.0	-	-	-	-	-	+-	Y
	4109	7.5	-	-	-	-	-	+-	Y
	4110	8.0	-	-	-	-	-	+-	Y
	4111	8.0	-	-	-	-	-	+-	Y
	4112	7.0	-	-	-	-	-	+-	Y

1) - : <10 mg/dL +- : 10 - 25 mg/dL + : 26 - 85 mg/dL ++ : 86 - 250 mg/dL +++ : 251 - 600 mg/dL ++++ : >600 mg/dL
2) - : <5 mg/dL +- : 5 - 7.5 mg/dL + : 7.6 - 30 mg/dL ++ : 31 - 70 mg/dL +++ : 71 - 125 mg/dL ++++ : >125 mg/dL
3) - : <30 mg/dL +- : 30 - 60 mg/dL + : 61 - 125 mg/dL ++ : 126 - 250 mg/dL +++ : 251 - 750 mg/dL ++++ : >750 mg/dL
4) - : <0.03 mg/dL +- : 0.03 - 0.05 mg/dL + : 0.06 - 0.15 mg/dL ++ : 0.16 - 0.75 mg/dL +++ : >0.75 mg/dL
5) - : <0.5 mg/dL + : 0.5 - 1.5 mg/dL ++ : 1.6 - 5.0 mg/dL +++ : 5.1 - 10.0 mg/dL ++++ : >10.0 mg/dL
6) +- : <2.0 mg/dL + : 2.0 - 3.5 mg/dL ++ : 3.6 - 7.0 mg/dL +++ : 7.1 - 12.0 mg/dL ++++ : >12.0 mg/dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 111 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual urinalysis (Week 4 of administration period)

Dose (mg/kg) : 750

Sex	Animal number	URINE SEDIMENT						
							CRYSTALLIZATION	
		RBC	WBC	SEC	SREC	Cast	PS	CO
Male	4001	-	-	+-	-	-	-	-
	4002	-	-	+-	-	-	-	-
	4003	-	-	+-	-	-	+-	-
	4004	-	-	+-	-	-	-	-
	4005	-	-	+-	-	-	-	-
	4006	-	-	+-	-	-	+-	-
	4007	-	-	+-	-	-	-	-
	4008	-	-	+-	-	-	+-	-
	4009	-	-	+-	-	-	-	-
	4010	-	-	+-	-	-	-	-
	4011	-	-	+-	+-	-	-	-
	4012	-	-	+-	-	-	-	-
Female	4101	-	-	+-	-	-	-	-
	4102	-	-	+-	-	-	-	-
	4103	-	-	+-	-	-	+-	-
	4104	-	-	+-	-	-	+-	-
	4105	-	-	+-	-	-	-	-
	4106	-	-	+-	-	-	-	-
	4107	-	-	+-	-	-	+-	-
	4108	-	-	+-	-	-	+-	-
	4109	-	-	+-	-	-	+-	-
	4110	-	-	+-	-	-	+-	-
	4111	-	-	+-	-	-	-	-
	4112	-	-	+-	-	-	-	-

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

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

Appendix 112 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual water intake and urinalysis (Week 4 of administration period)

Dose (mg/kg) : 750

Sex	Animal number	Water intake mL/24h	Urine volume mL/24h	Osmolality mOsm/kg
Male	4001	59	24.5	1108
	4002	42	17.6	1056
	4003	48	10.5	1366
	4004	50	20.9	1134
	4005	72	14.2	1344
	4006	47	15.8	1564
	4007	61	17.3	1414
	4008	57	11.5	886
	4009	70	25.1	938
	4010	40	8.9	1648
	4011	72	27.1	1004
	4012	60	25.2	1258
	Mean	57	18.2	1227
	S.D.	11	6.3	245
Female	4101	57	20.7	1224
	4102	31	12.3	1200
	4103	27	11.1	1202
	4104	39	8.0	948
	4105	38	9.3	1198
	4106	51	22.7	884
	4107	44	10.8	980
	4108	49	23.5	868
	4109	35	10.8	1588
	4110	29	5.4	1662
	4111	47	7.8	1380
	4112	43	10.0	1548
	Mean	41	12.7	1224
	S.D.	9	6.1	275

Appendix 113 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual urinalysis (Week 2 of recovery period)

Dose (mg/kg) : 0

Sex	Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
Male	1007	8.5	+	+-	-	-	-	+-	Y
	1008	9.0	+	-	-	-	-	+-	Y
	1009	9.0	+	+-	-	-	-	+-	Y
	1010	8.5	+-	-	-	-	-	+-	Y
	1011	8.5	+	-	-	-	-	+-	Y
	1012	8.5	+	+	-	-	-	+-	Y
Female	1107	9.0	-	-	-	-	-	+-	Y
	1108	7.5	-	-	-	-	-	+-	Y
	1109	7.5	+-	+-	-	-	-	+-	Y
	1110	8.5	-	-	-	-	-	+-	Y
	1111	9.0	+-	-	-	-	-	+-	Y
	1112	8.5	+-	-	-	-	-	+-	Y

1) - : <10 mg/dL +- : 10 - 25 mg/dL + : 26 - 85 mg/dL ++ : 86 - 250 mg/dL +++ : 251 - 600 mg/dL ++++ : >600 mg/dL
2) - : <5 mg/dL +- : 5 - 7.5 mg/dL + : 7.6 - 30 mg/dL ++ : 31 - 70 mg/dL +++ : 71 - 125 mg/dL ++++ : >125 mg/dL
3) - : <30 mg/dL +- : 30 - 60 mg/dL + : 61 - 125 mg/dL ++ : 126 - 250 mg/dL +++ : 251 - 750 mg/dL ++++ : >750 mg/dL
4) - : <0.03 mg/dL +- : 0.03 - 0.05 mg/dL + : 0.06 - 0.15 mg/dL ++ : 0.16 - 0.75 mg/dL +++ : >0.75 mg/dL
5) - : <0.5 mg/dL + : 0.5 - 1.5 mg/dL ++ : 1.6 - 5.0 mg/dL +++ : 5.1 - 10.0 mg/dL ++++ : >10.0 mg/dL
6) +- : <2.0 mg/dL + : 2.0 - 3.5 mg/dL ++ : 3.6 - 7.0 mg/dL +++ : 7.1 - 12.0 mg/dL ++++ : >12.0 mg/dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 114 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual urinalysis (Week 2 of recovery period)

Dose (mg/kg) : 0

Sex	Animal number	URINE SEDIMENT						
							CRYSTALLIZATION	
		RBC	WBC	SEC	SREC	Cast	PS	CO
Male	1007	-	-	+-	-	-	-	-
	1008	-	-	+-	-	-	-	-
	1009	-	-	+-	-	-	-	-
	1010	-	-	+-	-	-	-	-
	1011	-	-	+-	-	-	-	-
	1012	-	-	+-	-	-	+-	-
Female	1107	-	-	+-	-	-	-	-
	1108	-	-	+-	-	-	-	-
	1109	-	-	+-	-	-	-	-
	1110	-	-	+-	-	-	-	-
	1111	-	-	+	-	-	-	-
	1112	-	-	+-	-	-	-	-

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

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

Appendix 115 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual water intake and urinalysis (Week 2 of recovery period)

Dose (mg/kg) : 0

Sex	Animal number	Water intake mL/24h	Urine volume mL/24h	Osmolality mOsm/kg
Male	1007	31	5.9	2338
	1008	38	12.0	1808
	1009	31	9.3	2398
	1010	43	20.8	1504
	1011	48	9.6	2408
	1012	35	11.0	2066
	Mean	38	11.4	2087
	S.D.	7	5.0	369
Female	1107	27	6.7	1732
	1108	20	3.9	2562
	1109	21	2.7	3358
	1110	26	9.8	2524
	1111	31	9.5	1800
	1112	41	6.2	2328
	Mean	28	6.5	2384
	S.D.	8	2.9	595

Appendix 116

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual urinalysis (Week 2 of recovery period)

Dose (mg/kg) : 750

Sex	Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
Male	4007	8.0	+	+	-	-	-	+-	Y
	4008	8.5	+	+-	-	-	-	+-	Y
	4009	8.5	+	+-	-	-	-	+-	Y
	4010	8.5	+	+	-	-	-	+	Y
	4011	8.5	+-	+-	-	-	-	+-	Y
	4012	8.5	+	+	-	-	-	+-	Y
Female	4107	8.5	+-	-	-	-	-	+-	Y
	4108	8.5	+-	+-	-	-	-	+-	Y
	4109	8.5	+-	-	-	-	-	+-	Y
	4110	9.0	+	+-	-	-	-	+-	Y
	4111	8.5	-	-	-	-	-	+-	Y
	4112	8.5	+-	+-	-	-	-	+-	Y

1) - : <10 mg/dL +- : 10 - 25 mg/dL + : 26 - 85 mg/dL ++ : 86 - 250 mg/dL +++ : 251 - 600 mg/dL ++++ : >600 mg/dL
2) - : <5 mg/dL +- : 5 - 7.5 mg/dL + : 7.6 - 30 mg/dL ++ : 31 - 70 mg/dL +++ : 71 - 125 mg/dL ++++ : >125 mg/dL
3) - : <30 mg/dL +- : 30 - 60 mg/dL + : 61 - 125 mg/dL ++ : 126 - 250 mg/dL +++ : 251 - 750 mg/dL ++++ : >750 mg/dL
4) - : <0.03 mg/dL +- : 0.03 - 0.05 mg/dL + : 0.06 - 0.15 mg/dL ++ : 0.16 - 0.75 mg/dL +++ : >0.75 mg/dL
5) - : <0.5 mg/dL + : 0.5 - 1.5 mg/dL ++ : 1.6 - 5.0 mg/dL +++ : 5.1 - 10.0 mg/dL ++++ : >10.0 mg/dL
6) +- : <2.0 mg/dL + : 2.0 - 3.5 mg/dL ++ : 3.6 - 7.0 mg/dL +++ : 7.1 - 12.0 mg/dL ++++ : >12.0 mg/dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 117

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual urinalysis (Week 2 of recovery period)

Dose (mg/kg) : 750

Sex	Animal number	URINE SEDIMENT						
							CRYSTALLIZATION	
		RBC	WBC	SEC	SREC	Cast	PS	CO
Male	4007	-	-	+-	-	-	-	-
	4008	-	-	+-	-	-	+-	-
	4009	-	-	+-	-	-	-	-
	4010	-	-	+-	-	-	-	-
	4011	-	-	+-	-	-	+-	-
	4012	-	-	+-	-	-	-	-
Female	4107	-	-	+-	-	-	-	-
	4108	-	-	+-	-	-	-	-
	4109	-	-	+-	-	-	-	-
	4110	-	-	+-	-	-	-	-
	4111	-	-	+-	-	-	+-	-
	4112	-	-	+-	-	-	-	-

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

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

Appendix 118 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual water intake and urinalysis (Week 2 of recovery period)

Dose (mg/kg) : 750

Sex	Animal number	Water intake mL/24h	Urine volume mL/24h	Osmolality mOsm/kg
Male	4007	41	9.2	2324
	4008	32	6.9	2462
	4009	46	9.6	1758
	4010	34	6.0	2428
	4011	50	18.0	1372
	4012	37	7.7	2004
	Mean	40	9.6	2058
	S.D.	7	4.3	432
Female	4107	21	4.7	2044
	4108	29	7.5	1934
	4109	23	4.2	2250
	4110	24	4.6	2762
	4111	34	7.6	1894
	4112	29	3.8	2880
	Mean	27	5.4	2294
	S.D.	5	1.7	428

Appendix 119 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual hematology (After administration period)

Dose (mg/kg) : 0

Sex	Animal number	RBC $\times 10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Reticul. %	PLT $\times 10^4/\mu L$	PT s	APTT s	FIB mg/dL
Male	1001	792	15.4	42.7	53.9	19.5	36.1	1.7	117.4	11.1	13.0	316
	1002	853	16.4	44.5	52.2	19.2	36.9	1.8	109.1	14.7	24.4	310
	1003	788	16.4	45.5	57.8	20.8	36.0	2.4	101.8	15.4	19.9	363
	1004	846	16.1	44.3	52.3	19.1	36.5	2.0	121.4	16.6	23.6	330
	1005	844	16.4	45.3	53.7	19.4	36.2	1.5	135.8	17.6	22.0	257
	1006	806	16.9	46.0	57.1	20.9	36.7	1.8	120.1	19.6	28.3	330
	Mean	822	16.3	44.7	54.5	19.8	36.4	1.9	117.6	15.8	21.9	318
	S.D.	29	0.5	1.2	2.4	0.8	0.4	0.3	11.6	2.9	5.2	35
Female	1101	819	16.2	43.3	52.9	19.8	37.5	0.9	137.9	10.8	14.0	220
	1102	762	14.7	39.7	52.1	19.3	37.0	1.8	127.1	11.9	16.4	222
	1103	781	15.4	40.9	52.4	19.6	37.5	1.3	121.7	11.8	16.7	231
	1104	792	15.4	41.3	52.1	19.5	37.3	1.2	151.5	11.1	14.7	231
	1105	757	14.9	40.5	53.5	19.7	36.9	1.4	118.7	11.2	13.2	228
	1106	843	16.9	45.6	54.1	20.1	37.1	2.1	149.6	12.4	16.7	226
	Mean	792	15.6	41.9	52.9	19.7	37.2	1.5	134.4	11.5	15.3	226
	S.D.	33	0.8	2.2	0.8	0.3	0.3	0.4	14.1	0.6	1.5	5

Appendix 120 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual hematology (After administration period)

Dose (mg/kg) : 0

Sex	Animal number	WBC	Differential leukocyte counts (%)					
		$\times 10^2/\mu L$	LYMP	NEUT	EOS	BASO	MONO	LUC
Male	1001	133.8	85.3	11.5	1.1	0.3	1.5	0.3
	1002	93.9	86.0	10.9	0.7	0.5	1.3	0.5
	1003	127.7	80.3	15.2	1.9	0.4	1.8	0.5
	1004	99.1	82.0	13.6	1.1	0.4	2.4	0.5
	1005	149.8	80.5	15.9	1.2	0.5	1.2	0.8
	1006	85.5	77.4	18.9	1.8	0.2	1.3	0.6
	Mean	115.0	81.9	14.3	1.3	0.4	1.6	0.5
	S.D.	25.7	3.3	3.0	0.5	0.1	0.5	0.2
Female	1101	92.0	86.6	10.0	0.7	0.3	1.5	0.9
	1102	57.5	67.2	29.4	1.2	0.2	1.3	0.7
	1103	61.7	83.0	12.1	2.6	0.3	1.6	0.4
	1104	52.0	82.0	13.8	1.3	0.2	1.8	0.8
	1105	123.7	84.9	10.4	1.2	0.3	1.7	1.5
	1106	89.0	80.0	16.1	1.1	0.4	1.7	0.7
	Mean	79.3	80.6	15.3	1.4	0.3	1.6	0.8
	S.D.	27.4	7.0	7.3	0.6	0.1	0.2	0.4

LUC : Large unstained cells

Appendix 121 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual hematology (After administration period)

Dose (mg/kg) : 0

Sex	Animal number	Differential leukocyte counts ($X10^2/\mu L$)					
		LYMP	NEUT	EOS	BASO	MONO	LUC
Male	1001	114.1	15.3	1.5	0.4	2.0	0.4
	1002	80.7	10.3	0.7	0.5	1.2	0.4
	1003	102.5	19.4	2.4	0.5	2.3	0.6
	1004	81.2	13.5	1.1	0.4	2.4	0.5
	1005	120.6	23.9	1.8	0.7	1.8	1.1
	1006	66.1	16.1	1.5	0.2	1.1	0.5
	Mean	94.2	16.4	1.5	0.5	1.8	0.6
	S.D.	21.5	4.7	0.6	0.2	0.5	0.3
Female	1101	79.7	9.2	0.6	0.3	1.4	0.8
	1102	38.6	16.9	0.7	0.1	0.8	0.4
	1103	51.2	7.4	1.6	0.2	1.0	0.2
	1104	42.6	7.2	0.7	0.1	1.0	0.4
	1105	105.0	12.9	1.5	0.4	2.1	1.9
	1106	71.2	14.3	1.0	0.3	1.5	0.7
	Mean	64.7	11.3	1.0	0.2	1.3	0.7
	S.D.	25.5	4.0	0.4	0.1	0.5	0.6

LUC : Large unstained cells

Appendix 122 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual hematology (After administration period)

Dose (mg/kg) : 30

Sex	Animal number	RBC $\times 10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Reticul. %	PLT $\times 10^4/\mu L$	PT s	APTT s	FIB mg/dL
Male	2001	822	16.0	44.1	53.6	19.5	36.3	1.6	142.8	17.3	17.8	290
	2002	798	15.8	44.0	55.1	19.8	36.0	2.5	127.4	16.3	21.3	355
	2003	766	15.3	41.4	54.0	19.9	36.9	1.9	119.9	13.5	21.1	346
	2004	856	16.8	46.3	54.0	19.6	36.2	1.6	116.3	15.7	19.0	287
	2005	843	16.4	44.9	53.3	19.4	36.5	1.5	132.1	18.2	24.3	316
	2006	884	17.0	48.0	54.3	19.3	35.5	1.8	109.1	16.6	22.1	313
	Mean	828	16.2	44.8	54.1	19.6	36.2	1.8	124.6	16.3	20.9	318
	S.D.	42	0.6	2.2	0.6	0.2	0.5	0.4	12.1	1.6	2.3	28
Female	2101	684	14.0	39.8	58.2	20.5	35.2	10.2	137.6	12.0	15.8	228
	2102	799	16.1	43.8	54.8	20.2	36.8	1.4	122.9	11.6	16.9	229
	2103	793	15.9	41.0	51.7	20.0	38.8	1.4	119.4	11.9	19.0	204
	2104	831	16.2	42.3	50.9	19.5	38.3	1.2	135.2	11.8	17.4	254
	2105	707	14.6	38.3	54.2	20.7	38.2	2.0	140.0	10.7	17.2	213
	2106	879	16.6	44.7	50.8	18.9	37.2	1.5	135.2	12.4	16.7	233
	Mean	782	15.6	41.7	53.4	20.0	37.4	3.0	131.7	11.7	17.2	227
	S.D.	74	1.0	2.4	2.9	0.7	1.3	3.6	8.4	0.6	1.1	17

Appendix 123 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual hematology (After administration period)

Dose (mg/kg) : 30

Sex	Animal number	WBC	Differential leukocyte counts (%)					
		$\times 10^2/\mu L$	LYMP	NEUT	EOS	BASO	MONO	LUC
Male	2001	147.1	86.7	10.4	0.6	0.4	1.5	0.4
	2002	112.6	83.9	12.0	0.9	0.4	2.4	0.4
	2003	67.0	75.8	20.8	1.2	0.2	1.6	0.4
	2004	93.0	72.5	24.2	1.0	0.3	1.6	0.4
	2005	84.1	72.3	22.8	1.0	0.2	2.7	1.1
	2006	82.9	69.8	25.8	1.3	0.2	2.1	0.8
	Mean	97.8	76.8	19.3	1.0	0.3	2.0	0.6
	S.D.	28.4	6.9	6.5	0.2	0.1	0.5	0.3
Female	2101	93.4	80.0	16.9	0.9	0.3	1.0	0.9
	2102	78.4	74.8	20.8	1.4	0.3	2.2	0.4
	2103	68.7	83.2	13.2	1.1	0.3	1.7	0.5
	2104	44.1	74.5	21.7	1.5	0.1	1.6	0.5
	2105	44.8	69.9	27.4	1.2	0.3	1.0	0.3
	2106	83.4	76.8	19.2	2.0	0.3	1.1	0.6
	Mean	68.8	76.5	19.9	1.4	0.3	1.4	0.5
	S.D.	20.5	4.6	4.8	0.4	0.1	0.5	0.2

LUC : Large unstained cells

Appendix 124 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual hematology (After administration period)

Dose (mg/kg) : 30

Sex	Animal number	Differential leukocyte counts ($X10^2/\mu L$)					
		LYMP	NEUT	EOS	BASO	MONO	LUC
Male	2001	127.6	15.3	0.9	0.5	2.3	0.6
	2002	94.5	13.6	1.0	0.4	2.7	0.4
	2003	50.8	13.9	0.8	0.1	1.0	0.3
	2004	67.5	22.5	1.0	0.3	1.5	0.4
	2005	60.8	19.2	0.8	0.2	2.3	0.9
	2006	57.8	21.4	1.1	0.1	1.8	0.7
	Mean	76.5	17.7	0.9	0.3	1.9	0.6
	S.D.	29.2	3.9	0.1	0.2	0.6	0.2
Female	2101	74.7	15.8	0.9	0.3	1.0	0.9
	2102	58.7	16.3	1.1	0.3	1.8	0.3
	2103	57.2	9.1	0.7	0.2	1.2	0.3
	2104	32.9	9.6	0.7	0.1	0.7	0.2
	2105	31.3	12.3	0.5	0.1	0.5	0.1
	2106	64.1	16.0	1.6	0.2	0.9	0.5
	Mean	53.2	13.2	0.9	0.2	1.0	0.4
	S.D.	17.4	3.3	0.4	0.1	0.5	0.3

LUC : Large unstained cells

Appendix 125 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual hematology (After administration period)

Dose (mg/kg) : 150

Sex	Animal number	RBC $\times 10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Reticul. %	PLT $\times 10^4/\mu L$	PT s	APTT s	FIB mg/dL
Male	3001	801	15.8	43.7	54.5	19.7	36.2	2.1	146.7	16.2	22.4	325
	3002	815	15.8	43.4	53.2	19.4	36.5	1.7	117.5	12.7	17.8	260
	3003	762	14.8	40.3	52.9	19.5	36.8	1.9	144.5	12.3	20.5	315
	3004	842	15.7	43.4	51.5	18.7	36.2	1.5	146.4	15.3	22.9	287
	3005	818	15.8	43.7	53.4	19.4	36.3	2.0	116.9	16.7	21.1	268
	3006	876	16.9	46.8	53.5	19.3	36.2	1.7	118.3	15.5	23.5	298
	Mean	819	15.8	43.6	53.2	19.3	36.4	1.8	131.7	14.8	21.4	292
	S.D.	38	0.7	2.1	1.0	0.3	0.2	0.2	15.5	1.8	2.1	26
Female	3101	780	15.5	41.3	53.0	19.9	37.5	1.1	145.8	11.5	18.1	220
	3102	798	15.3	40.7	51.0	19.2	37.6	1.7	118.4	12.2	18.5	208
	3103	785	15.9	41.9	53.4	20.3	38.0	1.1	120.6	11.1	19.0	220
	3104	796	15.9	41.8	52.6	20.0	38.1	1.4	126.9	11.2	16.6	260
	3105	763	15.2	40.5	53.1	20.0	37.7	1.0	150.7	10.6	15.4	244
	3106	867	16.2	43.1	49.7	18.7	37.5	1.3	141.2	12.1	19.5	212
	Mean	798	15.7	41.6	52.1	19.7	37.7	1.3	133.9	11.5	17.9	227
	S.D.	36	0.4	0.9	1.5	0.6	0.3	0.3	13.7	0.6	1.6	20

Appendix 126 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual hematology (After administration period)

Dose (mg/kg) : 150

Sex	Animal number	WBC	Differential leukocyte counts (%)					
		$\times 10^2/\mu L$	LYMP	NEUT	EOS	BASO	MONO	LUC
Male	3001	134.5	86.2	11.8	0.1	0.4	0.9	0.6
	3002	93.7	81.1	16.2	0.5	0.3	1.3	0.5
	3003	104.1	85.7	10.4	1.4	0.4	1.6	0.5
	3004	113.5	82.8	13.9	1.3	0.4	1.1	0.5
	3005	116.3	78.3	17.9	1.1	0.3	1.8	0.5
	3006	106.6	79.6	16.2	1.3	0.5	1.4	1.0
	Mean	111.5	82.3	14.4	1.0	0.4	1.4	0.6
	S.D.	13.8	3.2	2.9	0.5	0.1	0.3	0.2
Female	3101	57.4	79.9	16.6	1.7	0.2	1.3	0.3
	3102	60.2	73.8	22.4	0.9	0.3	1.8	0.8
	3103	67.6	71.4	25.3	0.8	0.2	1.5	0.8
	3104	100.8	76.6	19.5	1.3	0.2	1.6	0.8
	3105	65.3	89.3	6.6	1.4	0.3	1.9	0.4
	3106	55.3	76.2	20.6	0.9	0.2	1.4	0.6
	Mean	67.8	77.9	18.5	1.2	0.2	1.6	0.6
	S.D.	16.8	6.3	6.5	0.4	0.1	0.2	0.2

LUC : Large unstained cells

Appendix 127 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual hematology (After administration period)

Dose (mg/kg) : 150

Sex	Animal number	Differential leukocyte counts ($\times 10^2/\mu L$)					
		LYMP	NEUT	EOS	BASO	MONO	LUC
Male	3001	115.9	15.8	0.2	0.5	1.2	0.9
	3002	76.0	15.2	0.5	0.3	1.2	0.5
	3003	89.2	10.8	1.5	0.4	1.6	0.5
	3004	94.0	15.8	1.5	0.4	1.2	0.5
	3005	91.1	20.8	1.3	0.4	2.1	0.6
	3006	84.8	17.3	1.4	0.5	1.5	1.1
	Mean	91.8	16.0	1.1	0.4	1.5	0.7
	S.D.	13.4	3.2	0.6	0.1	0.4	0.3
Female	3101	45.9	9.5	1.0	0.1	0.8	0.2
	3102	44.5	13.5	0.5	0.2	1.1	0.5
	3103	48.3	17.1	0.5	0.2	1.0	0.5
	3104	77.2	19.6	1.3	0.3	1.7	0.8
	3105	58.4	4.3	0.9	0.2	1.2	0.3
	3106	42.1	11.4	0.5	0.1	0.8	0.3
	Mean	52.7	12.6	0.8	0.2	1.1	0.4
	S.D.	13.3	5.5	0.3	0.1	0.3	0.2

LUC : Large unstained cells

Appendix 128 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual hematology (After administration period)

Dose (mg/kg) : 750

Sex	Animal number	RBC $\times 10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Reticul. %	PLT $\times 10^4/\mu L$	PT s	APTT s	FIB mg/dL
Male	4001	853	16.3	44.4	52.0	19.1	36.8	1.5	134.9	13.0	20.6	308
	4002	789	15.5	42.2	53.5	19.6	36.7	1.8	129.2	15.4	26.1	311
	4003	802	16.1	43.3	54.0	20.1	37.2	1.3	123.4	19.1	24.2	285
	4004	780	15.7	42.2	54.0	20.1	37.3	1.6	132.9	19.5	25.4	301
	4005	842	16.6	45.5	54.0	19.8	36.6	2.0	118.5	20.4	25.2	296
	4006	788	15.6	42.3	53.6	19.7	36.8	1.5	134.8	17.3	25.3	278
	Mean	809	16.0	43.3	53.5	19.7	36.9	1.6	129.0	17.5	24.5	297
	S.D.	31	0.4	1.4	0.8	0.4	0.3	0.2	6.7	2.8	2.0	13
Female	4101	739	15.4	41.0	55.5	20.8	37.5	1.2	133.4	11.1	21.4	226
	4102	847	16.6	44.9	53.0	19.5	36.9	1.0	140.7	11.4	14.1	227
	4103	827	16.3	43.6	52.7	19.7	37.4	1.6	117.1	10.8	17.5	232
	4104	736	15.3	40.1	54.5	20.7	38.1	1.8	126.1	10.9	13.3	210
	4105	807	16.3	43.4	53.8	20.2	37.6	1.0	113.9	11.3	19.6	259
	4106	850	17.0	43.8	51.5	20.0	38.8	0.9	170.5	11.2	18.4	302
	Mean	801	16.2	42.8	53.5	20.2	37.7	1.3	133.6	11.1	17.4	243
	S.D.	52	0.7	1.8	1.4	0.5	0.7	0.4	20.6	0.2	3.1	33

Appendix 129

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual hematology (After administration period)

Dose (mg/kg) : 750

Sex	Animal number	WBC	Differential leukocyte counts (%)					
		X10²/μL	LYMP	NEUT	EOS	BASO	MONO	LUC
Male	4001	164.6	78.9	15.5	0.8	0.5	2.9	1.3
	4002	191.4	82.2	14.4	0.6	0.5	1.6	0.7
	4003	126.2	75.2	21.5	1.2	0.4	1.1	0.6
	4004	99.4	69.8	25.7	0.9	0.3	3.0	0.3
	4005	127.4	70.7	26.7	0.4	0.3	1.4	0.4
	4006	195.6	87.7	9.3	0.4	0.7	1.0	0.9
	Mean	150.8	77.4	18.9	0.7	0.5	1.8	0.7
	S.D.	39.1	6.9	6.9	0.3	0.2	0.9	0.4
Female	4101	74.2	82.4	13.0	2.0	0.2	2.0	0.4
	4102	115.3	84.3	11.7	1.3	0.6	1.0	1.1
	4103	101.8	82.0	14.2	0.7	0.3	2.2	0.6
	4104	102.2	77.2	19.4	0.9	0.3	1.4	0.8
	4105	55.2	66.1	29.3	1.6	0.2	2.5	0.3
	4106	98.1	75.8	18.7	1.2	0.4	2.9	1.0
	Mean	91.1	78.0	17.7	1.3	0.3	2.0	0.7
	S.D.	22.1	6.7	6.5	0.5	0.2	0.7	0.3

LUC : Large unstained cells

Appendix 130 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual hematology (After administration period)

Dose (mg/kg) : 750

Sex	Animal number	Differential leukocyte counts ($\times 10^2/\mu L$)					
		LYMP	NEUT	EOS	BASO	MONO	LUC
Male	4001	129.9	25.6	1.3	0.8	4.8	2.2
	4002	157.3	27.5	1.2	1.0	3.0	1.3
	4003	94.9	27.2	1.5	0.5	1.4	0.7
	4004	69.4	25.5	0.9	0.3	3.0	0.3
	4005	90.1	34.0	0.6	0.4	1.8	0.6
	4006	171.6	18.2	0.7	1.4	1.9	1.8
	Mean	118.9	26.3	1.0	0.7	2.7	1.2
	S.D.	40.6	5.1	0.4	0.4	1.2	0.7
Female	4101	61.2	9.7	1.5	0.1	1.5	0.3
	4102	97.2	13.5	1.5	0.7	1.2	1.3
	4103	83.5	14.5	0.7	0.3	2.2	0.6
	4104	78.9	19.8	0.9	0.3	1.4	0.8
	4105	36.4	16.2	0.9	0.1	1.4	0.1
	4106	74.4	18.4	1.2	0.4	2.8	0.9
	Mean	71.9	15.4	1.1	0.3	1.8	0.7
	S.D.	21.0	3.6	0.3	0.2	0.6	0.4

LUC : Large unstained cells

Appendix 131 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual hematology (After recovery period)

Dose (mg/kg) : 0

Sex	Animal number	RBC $\times 10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Reticul. %	PLT $\times 10^4/\mu L$	PT s	APTT s	FIB mg/dL
Male	1007	883	15.9	44.8	50.7	18.0	35.5	1.7	136.1	14.2	17.4	312
	1008	833	16.1	44.8	53.8	19.3	35.9	1.7	115.8	18.1	26.8	296
	1009	822	15.5	43.1	52.4	18.9	36.0	1.9	131.5	13.0	16.4	288
	1010	865	15.7	44.0	50.8	18.1	35.7	1.9	103.6	16.6	21.8	336
	1011	797	15.3	42.4	53.2	19.2	36.1	1.7	121.4	13.6	19.2	259
	1012	842	16.3	46.2	54.8	19.3	35.3	1.8	105.2	15.9	23.3	286
	Mean	840	15.8	44.2	52.6	18.8	35.8	1.8	118.9	15.2	20.8	296
	S.D.	31	0.4	1.4	1.6	0.6	0.3	0.1	13.4	2.0	3.9	26
Female	1107	803	15.2	41.1	51.3	19.0	37.0	1.9	118.8	11.0	16.6	218
	1108	827	15.7	42.3	51.1	19.0	37.2	1.1	121.3	12.6	20.6	224
	1109	772	14.8	40.3	52.3	19.2	36.7	1.5	116.9	11.3	14.9	206
	1110	796	15.9	42.7	53.7	20.0	37.3	1.6	115.6	11.5	16.1	200
	1111	877	16.2	43.9	50.0	18.4	36.8	1.5	108.8	11.6	15.1	226
	1112	812	16.0	43.0	53.0	19.7	37.1	1.2	132.7	12.2	17.8	249
	Mean	815	15.6	42.2	51.9	19.2	37.0	1.5	119.0	11.7	16.9	221
	S.D.	36	0.5	1.3	1.4	0.6	0.2	0.3	7.9	0.6	2.1	17

Appendix 132 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual hematology (After recovery period)

Dose (mg/kg) : 0

Sex	Animal number	WBC	Differential leukocyte counts (%)					
		$\times 10^2/\mu L$	LYMP	NEUT	EOS	BASO	MONO	LUC
Male	1007	108.3	80.7	16.2	1.1	0.4	1.5	0.2
	1008	139.6	78.2	14.5	1.1	0.4	4.1	1.6
	1009	100.4	81.1	15.5	1.4	0.2	1.5	0.3
	1010	136.7	73.8	22.0	0.6	0.4	2.4	0.7
	1011	174.0	90.3	6.4	0.9	0.6	1.2	0.6
	1012	107.0	76.6	20.4	1.0	0.3	1.2	0.5
	Mean	127.7	80.1	15.8	1.0	0.4	2.0	0.7
	S.D.	28.0	5.7	5.5	0.3	0.1	1.1	0.5
Female	1107	66.1	71.3	25.7	1.1	0.2	1.3	0.4
	1108	70.6	66.8	28.8	1.3	0.3	2.0	0.7
	1109	116.6	83.4	12.8	1.1	0.3	1.3	1.0
	1110	64.4	78.5	17.5	1.6	0.2	1.9	0.3
	1111	71.1	69.1	25.5	2.6	0.2	2.3	0.3
	1112	71.0	79.3	18.3	0.9	0.3	0.8	0.5
	Mean	76.6	74.7	21.4	1.4	0.3	1.6	0.5
	S.D.	19.8	6.6	6.1	0.6	0.1	0.6	0.3

LUC : Large unstained cells

Appendix 133 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual hematology (After recovery period)

Dose (mg/kg) : 0

Sex	Animal number	Differential leukocyte counts ($X10^2/\mu L$)					
		LYMP	NEUT	EOS	BASO	MONO	LUC
Male	1007	87.4	17.5	1.1	0.4	1.6	0.3
	1008	109.1	20.3	1.6	0.6	5.7	2.3
	1009	81.4	15.5	1.4	0.2	1.5	0.3
	1010	100.9	30.1	0.8	0.5	3.3	1.0
	1011	157.1	11.0	1.5	1.1	2.2	1.1
	1012	81.9	21.9	1.0	0.3	1.3	0.6
	Mean	103.0	19.4	1.2	0.5	2.6	0.9
	S.D.	28.7	6.5	0.3	0.3	1.7	0.8
Female	1107	47.2	17.0	0.7	0.1	0.9	0.3
	1108	47.2	20.4	0.9	0.2	1.4	0.5
	1109	97.3	14.9	1.3	0.4	1.5	1.1
	1110	50.6	11.3	1.0	0.2	1.2	0.2
	1111	49.1	18.1	1.9	0.2	1.6	0.2
	1112	56.3	13.0	0.6	0.2	0.6	0.3
	Mean	58.0	15.8	1.1	0.2	1.2	0.4
	S.D.	19.6	3.4	0.5	0.1	0.4	0.3

LUC : Large unstained cells

Appendix 134 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual hematology (After recovery period)

Dose (mg/kg) : 750

Sex	Animal number	RBC $\times 10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Reticul. %	PLT $\times 10^4/\mu L$	PT s	APTT s	FIB mg/dL
Male	4007	782	15.5	42.8	54.8	19.9	36.3	2.8	100.2	14.8	19.0	311
	4008	854	16.1	44.9	52.6	18.8	35.8	2.0	133.1	18.1	21.1	337
	4009	840	15.3	42.4	50.5	18.2	36.0	2.2	105.2	16.4	23.4	307
	4010	905	15.9	44.6	49.3	17.6	35.6	2.0	117.3	16.1	19.6	306
	4011	807	15.7	43.1	53.4	19.5	36.6	1.8	118.8	11.4	16.3	287
	4012	857	15.6	43.7	51.1	18.2	35.7	2.4	129.3	15.3	19.2	308
	Mean	841	15.7	43.6	52.0	18.7	36.0	2.2	117.3	15.4	19.8	309
	S.D.	43	0.3	1.0	2.0	0.9	0.4	0.4	12.9	2.2	2.4	16
Female	4107	799	15.3	40.6	50.8	19.1	37.7	1.7	111.8	12.0	17.1	195
	4108	750	15.2	41.0	54.7	20.2	37.0	1.5	130.7	11.5	13.6	205
	4109	831	15.7	41.6	50.0	18.9	37.9	1.2	132.2	12.0	16.7	227
	4110	785	14.4	39.7	50.6	18.4	36.3	2.1	100.3	11.5	17.5	220
	4111	781	14.7	40.1	51.3	18.9	36.8	1.6	108.7	12.1	15.6	223
	4112	846	15.9	43.1	50.9	18.8	36.9	1.0	122.7	12.1	19.8	219
	Mean	799	15.2	41.0	51.4	19.1	37.1	1.5	117.7	11.9	16.7	215
	S.D.	35	0.6	1.2	1.7	0.6	0.6	0.4	12.8	0.3	2.1	12

Appendix 135 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual hematology (After recovery period)

Dose (mg/kg) : 750

Sex	Animal number	WBC	Differential leukocyte counts (%)					
		X10²/μL	LYMP	NEUT	EOS	BASO	MONO	LUC
Male	4007	157.4	84.6	12.5	0.5	0.6	1.4	0.4
	4008	121.5	70.7	24.1	1.3	0.3	3.0	0.5
	4009	113.1	74.5	21.6	1.1	0.3	2.1	0.4
	4010	87.3	78.1	18.5	1.0	0.2	1.7	0.4
	4011	81.9	87.7	9.2	1.0	0.4	1.3	0.4
	4012	158.3	72.0	25.2	0.6	0.5	1.3	0.5
	Mean	119.9	77.9	18.5	0.9	0.4	1.8	0.4
	S.D.	33.0	6.9	6.5	0.3	0.1	0.7	0.1
Female	4107	42.7	75.6	21.0	1.1	0.1	1.9	0.3
	4108	83.3	76.8	19.8	0.9	0.4	1.7	0.5
	4109	51.6	85.4	11.1	1.4	0.2	1.5	0.4
	4110	59.8	70.0	27.3	1.1	0.2	1.1	0.3
	4111	53.0	80.7	16.3	0.6	0.3	1.5	0.6
	4112	58.2	75.5	21.6	0.9	0.2	1.4	0.3
	Mean	58.1	77.3	19.5	1.0	0.2	1.5	0.4
	S.D.	13.7	5.2	5.4	0.3	0.1	0.3	0.1

LUC : Large unstained cells

Appendix 136 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual hematology (After recovery period)

Dose (mg/kg) : 750

Sex	Animal number	Differential leukocyte counts ($X10^2/\mu L$)					
		LYMP	NEUT	EOS	BASO	MONO	LUC
Male	4007	133.2	19.6	0.8	0.9	2.3	0.6
	4008	85.9	29.3	1.6	0.4	3.7	0.6
	4009	84.3	24.4	1.2	0.3	2.4	0.5
	4010	68.2	16.2	0.9	0.2	1.5	0.4
	4011	71.8	7.5	0.9	0.3	1.1	0.3
	4012	114.0	39.9	0.9	0.7	2.0	0.8
	Mean	92.9	22.8	1.1	0.5	2.2	0.5
	S.D.	25.5	11.2	0.3	0.3	0.9	0.2
Female	4107	32.3	9.0	0.5	0.0	0.8	0.1
	4108	63.9	16.5	0.7	0.3	1.4	0.4
	4109	44.0	5.7	0.7	0.1	0.8	0.2
	4110	41.9	16.3	0.7	0.1	0.7	0.2
	4111	42.8	8.6	0.3	0.2	0.8	0.3
	4112	44.0	12.6	0.6	0.1	0.8	0.2
	Mean	44.8	11.5	0.6	0.1	0.9	0.2
	S.D.	10.3	4.4	0.2	0.1	0.3	0.1

LUC : Large unstained cells

Appendix 137 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual blood chemistry (After administration period)

Dose (mg/kg) : 0

Sex	Animal number	AST IU/L	ALT IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
Male	1001	54	23	42	1	927	58	58	99	0.1	159
	1002	57	24	69	0	611	50	61	81	0.1	140
	1003	66	32	64	1	604	49	66	96	0.1	152
	1004	67	31	75	1	629	54	85	100	0.1	136
	1005	87	38	57	1	539	50	46	88	0.0	137
	1006	73	34	64	0	685	55	50	91	0.0	136
	Mean	67	30	62	1	666	53	61	93	0.1	143
	S.D.	12	6	11	1	136	4	14	7	0.1	10
Female	1101	46	18	55	1	193	57	27	119	0.1	130
	1102	63	20	62	1	467	56	15	102	0.1	130
	1103	78	27	66	1	505	46	15	84	0.1	89
	1104	71	27	60	2	440	58	10	103	0.1	94
	1105	60	25	40	1	442	54	17	99	0.1	106
	1106	60	23	73	1	459	54	19	104	0.1	135
	Mean	63	23	59	1	418	54	17	102	0.1	114
	S.D.	11	4	11	0	113	4	6	11	0.0	20

Appendix 138 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual blood chemistry (After administration period)

Dose (mg/kg) : 0

Sex	Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
Male	1001	13	0.23	142	4.6	105	9.7	8.2	5.9	2.8	0.90
	1002	12	0.23	144	4.6	104	9.8	7.9	6.1	2.8	0.85
	1003	14	0.25	144	4.2	107	9.8	8.4	6.3	2.9	0.85
	1004	16	0.23	143	5.0	106	10.0	8.3	6.2	2.8	0.82
	1005	14	0.26	145	4.7	107	9.6	8.2	5.9	2.9	0.97
	1006	16	0.27	145	4.7	110	10.0	7.8	6.1	2.9	0.91
	Mean	14	0.25	144	4.6	107	9.8	8.1	6.1	2.9	0.88
	S.D.	2	0.02	1	0.3	2	0.2	0.2	0.2	0.1	0.05
Female	1101	16	0.29	143	3.8	106	10.5	6.8	6.8	3.5	1.06
	1102	16	0.33	142	4.0	110	9.3	5.7	6.0	2.9	0.94
	1103	23	0.44	141	4.3	107	9.9	7.3	5.9	2.8	0.90
	1104	19	0.32	142	4.4	110	9.8	6.7	6.2	3.1	1.00
	1105	16	0.29	141	4.5	106	9.8	7.4	6.1	3.0	0.97
	1106	18	0.29	143	4.4	110	10.0	7.8	6.1	3.2	1.10
	Mean	18	0.33	142	4.2	108	9.9	7.0	6.2	3.1	1.00
	S.D.	3	0.06	1	0.3	2	0.4	0.7	0.3	0.2	0.07

Appendix 139 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual blood chemistry (After administration period)

Dose (mg/kg) : 30

Sex	Animal number	AST IU/L	ALT IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
Male	2001	76	34	72	1	700	55	71	92	0.1	144
	2002	62	26	52	1	710	57	45	103	0.1	138
	2003	73	24	63	1	860	49	58	85	0.1	139
	2004	65	28	48	1	658	48	60	87	0.1	133
	2005	62	25	57	1	751	49	98	95	0.0	131
	2006	68	29	54	1	827	51	67	96	0.1	154
	Mean	68	28	58	1	751	52	67	93	0.1	140
	S.D.	6	4	9	0	78	4	18	7	0.0	8
Female	2101	58	21	74	0	272	59	10	108	0.2	134
	2102	56	17	93	1	363	63	20	109	0.1	100
	2103	66	24	96	1	275	44	6	84	0.1	103
	2104	60	20	49	1	352	71	16	121	0.0	118
	2105	50	18	43	1	240	76	17	136	0.1	87
	2106	67	18	56	1	367	59	14	106	0.1	94
	Mean	60	20	69	1	312	62	14	111	0.1	106
	S.D.	6	3	23	0	55	11	5	17	0.1	17

Appendix 140 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual blood chemistry (After administration period)

Dose (mg/kg) : 30

Sex	Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
Male	2001	13	0.25	142	5.1	106	9.7	8.5	5.9	2.8	0.90
	2002	14	0.24	144	4.9	104	9.8	8.7	6.2	2.9	0.88
	2003	11	0.20	143	4.7	105	9.7	7.9	6.1	2.9	0.91
	2004	13	0.22	143	4.9	106	9.9	7.9	5.8	2.8	0.93
	2005	11	0.23	142	5.3	107	9.7	8.5	6.1	2.9	0.91
	2006	12	0.19	145	4.5	107	9.6	8.5	5.7	2.8	0.97
	Mean	12	0.22	143	4.9	106	9.7	8.3	6.0	2.9	0.92
	S.D.	1	0.02	1	0.3	1	0.1	0.3	0.2	0.1	0.03
Female	2101	15	0.30	142	4.8	110	9.9	5.9	6.6	3.4	1.06
	2102	14	0.27	142	4.6	110	9.5	5.6	6.4	2.9	0.83
	2103	18	0.28	141	4.8	109	9.5	7.2	6.0	3.0	1.00
	2104	14	0.25	142	4.6	109	9.1	6.1	6.2	2.9	0.88
	2105	17	0.30	142	5.2	110	9.6	6.8	6.5	3.2	0.97
	2106	21	0.34	142	4.5	111	9.7	7.5	6.0	2.9	0.94
	Mean	17	0.29	142	4.8	110	9.6	6.5	6.3	3.1	0.95
	S.D.	3	0.03	0	0.3	1	0.3	0.8	0.3	0.2	0.08

Appendix 141 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual blood chemistry (After administration period)

Dose (mg/kg) : 150

Sex	Animal number	AST IU/L	ALT IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
Male	3001	63	25	73	1	706	58	52	93	0.1	153
	3002	74	29	72	1	716	59	72	101	0.1	140
	3003	61	34	65	1	456	61	50	101	0.1	150
	3004	74	39	81	1	700	37	29	66	0.0	140
	3005	63	24	61	0	817	43	27	76	0.0	166
	3006	66	29	68	1	534	53	50	83	0.0	131
	Mean	67	30	70	1	655	52	47	87	0.1	147
	S.D.	6	6	7	0	133	10	17	14	0.1	12
Female	3101	57	18	57	1	426	72	18	131	0.1	121
	3102	69	21	58	1	480	46	11	82	0.1	98
	3103	80	25	60	1	400	61	9	103	0.1	82
	3104	86	27	71	1	266	71	24	121	0.0	110
	3105	55	22	48	1	571	62	13	104	0.1	96
	3106	66	23	49	1	479	59	14	112	0.1	113
	Mean	69	23	57	1	437	62	15	109	0.1	103
	S.D.	12	3	8	0	102	9	5	17	0.0	14

Appendix 142 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual blood chemistry (After administration period)

Dose (mg/kg) : 150

Sex	Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
Male	3001	12	0.24	145	5.2	106	9.8	8.4	6.3	3.0	0.91
	3002	12	0.22	145	4.6	108	9.6	7.5	5.5	2.8	1.04
	3003	15	0.23	143	4.9	106	9.8	8.6	6.1	3.0	0.97
	3004	15	0.23	145	5.1	107	9.8	7.8	6.0	2.9	0.94
	3005	14	0.27	143	4.5	107	9.8	8.3	5.8	2.8	0.93
	3006	17	0.27	143	4.6	106	9.8	8.3	5.8	2.9	1.00
	Mean	14	0.24	144	4.8	107	9.8	8.2	5.9	2.9	0.97
	S.D.	2	0.02	1	0.3	1	0.1	0.4	0.3	0.1	0.05
Female	3101	15	0.31	142	4.0	110	10.0	4.9	6.8	3.1	0.84
	3102	14	0.24	142	4.8	110	9.3	5.4	5.8	2.9	1.00
	3103	18	0.28	140	5.0	108	9.1	7.6	5.8	2.8	0.93
	3104	15	0.25	141	4.8	110	9.4	6.5	5.8	2.7	0.87
	3105	15	0.27	142	4.9	108	10.0	7.1	6.7	3.2	0.91
	3106	15	0.27	143	4.7	110	9.5	7.7	6.2	3.0	0.94
	Mean	15	0.27	142	4.7	109	9.6	6.5	6.2	3.0	0.92
	S.D.	1	0.02	1	0.4	1	0.4	1.2	0.5	0.2	0.06

Appendix 143 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual blood chemistry (After administration period)

Dose (mg/kg) : 750

Sex	Animal number	AST IU/L	ALT IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
Male	4001	61	44	90	1	661	49	115	101	0.0	129
	4002	67	36	90	1	694	40	29	80	0.1	112
	4003	75	43	62	1	778	44	31	76	0.0	123
	4004	77	41	63	1	906	39	44	80	0.1	113
	4005	74	42	61	1	826	32	30	67	0.1	127
	4006	65	40	56	0	688	35	39	71	0.1	130
	Mean	70	41	70	1	759	40	48	79	0.1	122
	S.D.	6	3	15	0	95	6	33	12	0.1	8
Female	4101	64	28	77	2	275	64	18	108	0.0	106
	4102	71	26	46	1	486	71	49	136	0.0	115
	4103	74	28	49	1	423	56	24	100	0.1	94
	4104	68	25	44	1	341	59	28	121	0.1	97
	4105	61	27	46	1	406	49	26	107	0.1	109
	4106	67	32	49	1	395	47	57	99	0.0	84
	Mean	68	28	52	1	388	58	34	112	0.1	101
	S.D.	5	2	12	0	72	9	16	14	0.1	11

Appendix 144 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual blood chemistry (After administration period)

Dose (mg/kg) : 750

Sex	Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
Male	4001	14	0.24	141	4.9	102	9.9	8.8	5.9	2.9	0.97
	4002	14	0.21	143	5.1	104	9.8	8.7	6.2	2.9	0.88
	4003	16	0.24	142	4.4	104	9.7	7.9	5.6	2.9	1.07
	4004	15	0.18	143	4.9	105	9.5	8.3	5.3	2.8	1.12
	4005	14	0.22	144	4.2	105	9.7	10.4	5.8	3.0	1.07
	4006	15	0.26	143	4.3	104	9.8	8.5	6.0	2.9	0.94
	Mean	15	0.23	143	4.6	104	9.7	8.8	5.8	2.9	1.01
	S.D.	1	0.03	1	0.4	1	0.1	0.9	0.3	0.1	0.09
Female	4101	14	0.30	142	4.0	106	9.7	7.0	6.1	3.0	0.97
	4102	17	0.32	143	4.3	109	9.4	7.5	5.9	2.9	0.97
	4103	14	0.29	143	4.4	106	9.7	7.7	5.7	2.6	0.84
	4104	15	0.30	142	4.5	108	9.8	7.1	6.1	3.1	1.03
	4105	14	0.25	142	4.2	107	9.9	6.9	6.6	3.2	0.94
	4106	27	0.42	144	4.1	107	10.1	7.4	6.2	3.1	1.00
	Mean	17	0.31	143	4.3	107	9.8	7.3	6.1	3.0	0.96
	S.D.	5	0.06	1	0.2	1	0.2	0.3	0.3	0.2	0.07

Appendix 145 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual blood chemistry (After recovery period)

Dose (mg/kg) : 0

Sex	Animal number	AST IU/L	ALT IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
Male	1007	65	27	57	0	587	64	30	101	0.1	164
	1008	62	27	45	1	333	53	42	82	0.1	149
	1009	54	23	57	1	488	61	107	110	0.1	163
	1010	73	24	50	2	652	50	54	90	0.1	145
	1011	59	28	41	1	396	44	71	83	0.1	144
	1012	63	29	47	1	500	84	85	129	0.1	147
	Mean	63	26	50	1	493	59	65	99	0.1	152
	S.D.	6	2	7	1	118	14	29	18	0.0	9
Female	1107	65	26	52	1	409	82	14	138	0.1	140
	1108	92	48	60	1	341	70	12	119	0.1	112
	1109	74	40	83	1	166	86	52	173	0.1	137
	1110	70	25	58	1	209	64	8	102	0.1	102
	1111	76	33	47	2	320	58	34	115	0.1	109
	1112	76	28	71	1	340	59	13	96	0.1	126
	Mean	76	33	62	1	298	70	22	124	0.1	121
	S.D.	9	9	13	0	91	12	17	28	0.0	16

Appendix 146 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual blood chemistry (After recovery period)

Dose (mg/kg) : 0

Sex	Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
Male	1007	12	0.22	142	5.1	105	9.3	7.4	6.2	2.9	0.88
	1008	13	0.25	142	4.7	104	9.4	7.8	6.3	2.8	0.80
	1009	10	0.27	143	4.8	103	9.6	7.7	6.4	2.8	0.78
	1010	12	0.31	145	4.7	106	9.4	7.3	6.2	2.9	0.88
	1011	18	0.29	143	4.8	107	9.1	7.7	5.7	2.7	0.90
	1012	13	0.29	143	4.6	105	9.6	6.8	6.2	3.0	0.94
	Mean	13	0.27	143	4.8	105	9.4	7.5	6.2	2.9	0.86
	S.D.	3	0.03	1	0.2	1	0.2	0.4	0.2	0.1	0.06
Female	1107	14	0.31	143	4.1	108	9.2	4.5	6.4	3.3	1.06
	1108	14	0.31	142	4.7	110	9.1	5.8	6.1	2.9	0.91
	1109	17	0.26	142	4.5	109	10.0	5.4	7.2	3.5	0.95
	1110	16	0.33	144	4.6	110	9.3	6.4	6.3	3.0	0.91
	1111	17	0.35	144	3.7	110	9.7	6.4	6.2	3.2	1.07
	1112	19	0.36	142	4.4	111	9.4	5.9	6.5	2.9	0.81
	Mean	16	0.32	143	4.3	110	9.5	5.7	6.5	3.1	0.95
	S.D.	2	0.04	1	0.4	1	0.3	0.7	0.4	0.2	0.10

Appendix 147 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual blood chemistry (After recovery period)

Dose (mg/kg) : 750

Sex	Animal number	AST IU/L	ALT IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
Male	4007	68	33	58	1	393	54	44	96	0.1	167
	4008	70	32	62	1	443	64	24	97	0.1	141
	4009	65	32	48	1	700	66	95	114	0.1	149
	4010	68	24	47	1	726	50	70	99	0.1	141
	4011	60	26	60	0	471	69	72	109	0.1	112
	4012	73	34	61	1	574	55	86	103	0.1	147
	Mean	67	30	56	1	551	60	65	103	0.1	143
	S.D.	4	4	7	0	139	8	27	7	0.0	18
Female	4107	68	23	58	1	329	51	8	93	0.1	103
	4108	50	22	54	1	176	61	23	113	0.1	132
	4109	61	21	69	1	352	68	17	115	0.1	98
	4110	71	23	42	1	395	69	23	134	0.1	142
	4111	58	21	74	1	219	76	20	134	0.1	123
	4112	77	30	71	1	236	65	11	108	0.1	105
	Mean	64	23	61	1	285	65	17	116	0.1	117
	S.D.	10	3	12	0	86	8	6	16	0.0	18

Appendix 148 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual blood chemistry (After recovery period)

Dose (mg/kg) : 750

Sex	Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
Male	4007	12	0.21	143	4.5	103	9.6	8.4	6.1	2.9	0.91
	4008	11	0.24	144	5.2	105	9.6	7.1	6.1	2.9	0.91
	4009	10	0.25	144	5.0	106	9.6	8.4	5.9	2.9	0.97
	4010	14	0.25	144	5.1	104	9.6	8.9	6.2	2.8	0.82
	4011	14	0.26	145	4.9	106	9.6	7.5	6.1	2.9	0.91
	4012	15	0.29	144	4.8	105	9.4	7.9	5.9	2.9	0.97
	Mean	13	0.25	144	4.9	105	9.6	8.0	6.1	2.9	0.92
	S.D.	2	0.03	1	0.2	1	0.1	0.7	0.1	0.0	0.06
Female	4107	16	0.33	142	4.5	107	9.3	5.6	6.1	3.0	0.97
	4108	17	0.34	142	4.8	111	9.7	5.8	6.4	3.0	0.88
	4109	17	0.28	141	4.8	109	9.4	6.9	6.0	2.9	0.94
	4110	16	0.31	140	4.3	108	9.1	5.9	6.3	3.0	0.91
	4111	16	0.29	142	5.0	110	9.6	5.9	6.5	3.2	0.97
	4112	17	0.34	142	4.5	109	9.1	6.9	6.1	2.9	0.91
	Mean	17	0.32	142	4.7	109	9.4	6.2	6.2	3.0	0.93
	S.D.	1	0.03	1	0.3	1	0.3	0.6	0.2	0.1	0.04

Appendix 149 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (After administration period)

Sex : Male

Dose (mg/kg) : 0

	Animal number	Body weight g	Brain g(g/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	1001	402	1.97	764	1.27	11.19	0.85	1.41	1.42	2.83
	1002	396	2.02	595	1.29	11.71	0.66	1.37	1.46	2.83
	1003	383	2.01	599	1.54	12.40	0.73	1.45	1.40	2.85
	1004	400	1.98	788	1.30	13.21	0.73	1.58	1.54	3.12
	1005	369	2.13	632	1.27	10.19	0.73	1.32	1.32	2.64
	1006	380	1.92	291	1.16	10.73	0.73	1.31	1.38	2.69
	Mean	388	2.01	612	1.31	11.57	0.74	1.41	1.42	2.83
	S.D.	13	0.07	178	0.13	1.11	0.06	0.10	0.07	0.17
Relative	1001		0.49	190	0.32	2.78	0.21	0.35	0.35	0.70
	1002		0.51	150	0.33	2.96	0.17	0.35	0.37	0.71
	1003		0.52	156	0.40	3.24	0.19	0.38	0.37	0.74
	1004		0.50	197	0.33	3.30	0.18	0.40	0.39	0.78
	1005		0.58	171	0.34	2.76	0.20	0.36	0.36	0.72
	1006		0.51	77	0.31	2.82	0.19	0.34	0.36	0.71
	Mean		0.52	157	0.34	2.98	0.19	0.36	0.37	0.73
	S.D.		0.03	43	0.03	0.24	0.01	0.02	0.01	0.03

Appendix 150

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (After administration period)

Sex : Male

Dose (mg/kg) : 0

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)
Absolute	1001	29	38	67	1.84	1.79	3.63	438	433	871
	1002	31	37	68	1.51	1.47	2.98	400	375	775
	1003	33	35	68	1.63	1.64	3.27	400	390	790
	1004	29	32	61	1.68	1.71	3.39	461	431	892
	1005	31	32	63	1.62	1.58	3.20	444	432	876
	1006	22	26	48	1.54	1.61	3.15	441	462	903
	Mean	29	33	63	1.64	1.63	3.27	431	421	851
	S.D.	4	4	8	0.12	0.11	0.22	25	32	55
Relative	1001	7	9	17	0.46	0.45	0.90	109	108	217
	1002	8	9	17	0.38	0.37	0.75	101	95	196
	1003	9	9	18	0.43	0.43	0.85	104	102	206
	1004	7	8	15	0.42	0.43	0.85	115	108	223
	1005	8	9	17	0.44	0.43	0.87	120	117	237
	1006	6	7	13	0.41	0.42	0.83	116	122	238
	Mean	8	9	16	0.42	0.42	0.84	111	109	220
	S.D.	1	1	2	0.03	0.03	0.05	7	10	17

Appendix 151 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (After administration period)

Sex : Male

Dose (mg/kg) : 30

	Animal number	Body weight g	Brain g(g/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	2001	382	2.02	476	1.25	11.26	0.60	1.37	1.37	2.74
	2002	394	2.01	532	1.14	12.47	0.83	1.39	1.49	2.88
	2003	396	2.10	468	1.18	12.35	0.96	1.65	1.68	3.33
	2004	371	1.91	354	1.24	11.65	0.69	1.49	1.44	2.93
	2005	371	1.89	595	1.11	11.39	0.51	1.28	1.41	2.69
	2006	358	1.90	506	1.10	11.22	0.52	1.41	1.44	2.85
	Mean	379	1.97	489	1.17	11.72	0.69	1.43	1.47	2.90
	S.D.	15	0.08	80	0.06	0.55	0.18	0.13	0.11	0.23
Relative	2001		0.53	125	0.33	2.95	0.16	0.36	0.36	0.72
	2002		0.51	135	0.29	3.16	0.21	0.35	0.38	0.73
	2003		0.53	118	0.30	3.12	0.24	0.42	0.42	0.84
	2004		0.51	95	0.33	3.14	0.19	0.40	0.39	0.79
	2005		0.51	160	0.30	3.07	0.14	0.35	0.38	0.73
	2006		0.53	141	0.31	3.13	0.15	0.39	0.40	0.80
	Mean		0.52	129	0.31	3.10	0.18	0.38	0.39	0.77
	S.D.		0.01	22	0.02	0.08	0.04	0.03	0.02	0.05

Appendix 152

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (After administration period)

Sex : Male

Dose (mg/kg) : 30

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)
Absolute	2001	21	24	45	1.65	1.63	3.28	439	428	867
	2002	27	25	52	1.72	1.68	3.40	376	362	738
	2003	33	31	64	1.58	1.61	3.19	449	410	859
	2004	30	33	63	1.53	1.52	3.05	400	410	810
	2005	28	33	61	1.70	1.75	3.45	388	396	784
	2006	26	29	55	1.59	1.67	3.26	447	455	902
	Mean	28	29	57	1.63	1.64	3.27	417	410	827
	S.D.	4	4	7	0.07	0.08	0.14	32	31	61
Relative	2001	5	6	12	0.43	0.43	0.86	115	112	227
	2002	7	6	13	0.44	0.43	0.86	95	92	187
	2003	8	8	16	0.40	0.41	0.81	113	104	217
	2004	8	9	17	0.41	0.41	0.82	108	111	218
	2005	8	9	16	0.46	0.47	0.93	105	107	211
	2006	7	8	15	0.44	0.47	0.91	125	127	252
	Mean	7	8	15	0.43	0.44	0.87	110	109	219
	S.D.	1	1	2	0.02	0.03	0.05	10	11	21

Appendix 153 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (After administration period)

Sex : Male

Dose (mg/kg) : 150

	Animal number	Body weight g	Brain g(g/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	3001	399	2.13	691	1.16	12.94	0.70	1.37	1.40	2.77
	3002	350	1.95	402	1.17	10.88	0.58	1.54	1.42	2.96
	3003	351	2.05	367	1.12	12.74	0.61	1.49	1.49	2.98
	3004	381	1.98	485	1.21	12.00	0.72	1.43	1.42	2.85
	3005	377	2.02	550	1.18	11.09	0.54	1.48	1.48	2.96
	3006	346	2.05	604	1.10	9.97	0.58	1.29	1.43	2.72
	Mean	367	2.03	517	1.16	11.60	0.62	1.43	1.44	2.87
	S.D.	21	0.06	123	0.04	1.16	0.07	0.09	0.04	0.11
Relative	3001		0.53	173	0.29	3.24	0.18	0.34	0.35	0.69
	3002		0.56	115	0.33	3.11	0.17	0.44	0.41	0.85
	3003		0.58	105	0.32	3.63	0.17	0.42	0.42	0.85
	3004		0.52	127	0.32	3.15	0.19	0.38	0.37	0.75
	3005		0.54	146	0.31	2.94	0.14	0.39	0.39	0.79
	3006		0.59	175	0.32	2.88	0.17	0.37	0.41	0.79
	Mean		0.55	140	0.32	3.16	0.17	0.39	0.39	0.79
	S.D.		0.03	30	0.01	0.27	0.02	0.04	0.03	0.06

Appendix 154 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (After administration period)

Sex : Male

Dose (mg/kg) : 150

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)
Absolute	3001	22	25	47	1.66	1.65	3.31	412	399	811
	3002	27	31	58	1.65	1.61	3.26	380	371	751
	3003	30	31	61	1.54	1.49	3.03	404	395	799
	3004	30	31	61	1.52	1.53	3.05	400	373	773
	3005	22	25	47	1.70	1.65	3.35	409	400	809
	3006	25	30	55	1.48	1.48	2.96	421	382	803
	Mean	26	29	55	1.59	1.57	3.16	404	387	791
	S.D.	4	3	6	0.09	0.08	0.17	14	13	24
Relative	3001	6	6	12	0.42	0.41	0.83	103	100	203
	3002	8	9	17	0.47	0.46	0.93	109	106	215
	3003	9	9	17	0.44	0.42	0.86	115	113	228
	3004	8	8	16	0.40	0.40	0.80	105	98	203
	3005	6	7	12	0.45	0.44	0.89	108	106	215
	3006	7	9	16	0.43	0.43	0.86	122	110	232
	Mean	7	8	15	0.44	0.43	0.86	110	106	216
	S.D.	1	1	2	0.02	0.02	0.05	7	6	12

Appendix 155 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (After administration period)

Sex : Male

Dose (mg/kg) : 750

	Animal number	Body weight g	Brain g(g/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	4001	362	2.04	530	1.11	14.07	0.68	1.54	1.53	3.07
	4002	322	1.99	455	1.00	10.23	0.63	1.51	1.49	3.00
	4003	342	1.97	509	1.19	11.93	0.66	1.46	1.49	2.95
	4004	329	2.10	374	1.12	11.79	0.56	1.62	1.67	3.29
	4005	298	1.88	610	0.94	10.41	0.72	1.49	1.57	3.06
	4006	345	2.04	535	1.04	11.93	0.68	1.43	1.40	2.83
	Mean	333	2.00	502	1.07	11.73	0.66	1.51	1.53	3.03
	S.D.	22	0.08	80	0.09	1.38	0.06	0.07	0.09	0.15
Relative	4001		0.56	146	0.31	3.89	0.19	0.43	0.42	0.85
	4002		0.62	141	0.31	3.18	0.20	0.47	0.46	0.93
	4003		0.58	149	0.35	3.49	0.19	0.43	0.44	0.86
	4004		0.64	114	0.34	3.58	0.17	0.49	0.51	1.00
	4005		0.63	205	0.32	3.49	0.24	0.50	0.53	1.03
	4006		0.59	155	0.30	3.46	0.20	0.41	0.41	0.82
	Mean		0.60	152	0.32	3.52	0.20	0.46	0.46	0.92
	S.D.		0.03	30	0.02	0.23	0.02	0.04	0.05	0.09

Appendix 156

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (After administration period)

Sex : Male

Dose (mg/kg) : 750

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)
Absolute	4001	26	27	53	1.66	1.68	3.34	399	372	771
	4002	24	26	50	1.60	1.60	3.20	410	426	836
	4003	26	29	55	1.58	1.62	3.20	418	374	792
	4004	25	27	52	1.33	1.34	2.67	390	399	789
	4005	24	27	51	1.64	1.56	3.20	443	539	982
	4006	30	29	59	1.46	1.44	2.90	339	353	692
	Mean	26	28	53	1.55	1.54	3.09	400	411	810
	S.D.	2	1	3	0.13	0.13	0.25	35	68	96
Relative	4001	7	7	15	0.46	0.46	0.92	110	103	213
	4002	7	8	16	0.50	0.50	0.99	127	132	260
	4003	8	8	16	0.46	0.47	0.94	122	109	232
	4004	8	8	16	0.40	0.41	0.81	119	121	240
	4005	8	9	17	0.55	0.52	1.07	149	181	330
	4006	9	8	17	0.42	0.42	0.84	98	102	201
	Mean	8	8	16	0.47	0.46	0.93	121	125	246
	S.D.	1	1	1	0.05	0.04	0.10	17	30	46

Appendix 157 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (After administration period)

Sex : Female

Dose (mg/kg) : 0

	Animal number	Body weight g	Brain g(g/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	1101	224	1.79	584	0.75	6.64	0.55	0.80	0.78	1.58
	1102	200	1.82	451	0.68	5.48	0.43	0.70	0.71	1.41
	1103	227	1.84	292	0.74	6.18	0.47	0.71	0.81	1.52
	1104	202	1.71	352	0.67	5.47	0.36	0.74	0.75	1.49
	1105	244	1.86	426	0.82	6.81	0.61	0.82	0.82	1.64
	1106	197	1.74	526	0.67	5.46	0.40	0.74	0.72	1.46
	Mean	216	1.79	439	0.72	6.01	0.47	0.75	0.77	1.52
	S.D.	19	0.06	108	0.06	0.62	0.09	0.05	0.05	0.08
Relative	1101		0.80	261	0.33	2.96	0.25	0.36	0.35	0.71
	1102		0.91	226	0.34	2.74	0.22	0.35	0.36	0.71
	1103		0.81	129	0.33	2.72	0.21	0.31	0.36	0.67
	1104		0.85	174	0.33	2.71	0.18	0.37	0.37	0.74
	1105		0.76	175	0.34	2.79	0.25	0.34	0.34	0.67
	1106		0.88	267	0.34	2.77	0.20	0.38	0.37	0.74
	Mean		0.84	205	0.34	2.78	0.22	0.35	0.36	0.71
	S.D.		0.06	55	0.01	0.09	0.03	0.02	0.01	0.03

Appendix 158 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (After administration period)

Sex : Female

Dose (mg/kg) : 0

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	1101	34	35	69	34.2	37.7	71.9	384
	1102	32	30	62	36.6	33.9	70.5	660
	1103	46	48	94	36.8	34.0	70.8	332
	1104	26	29	55	36.0	38.0	74.0	340
	1105	30	36	66	47.0	39.3	86.3	446
	1106	29	32	61	28.7	37.9	66.6	464
	Mean	33	35	68	36.6	36.8	73.4	438
	S.D.	7	7	14	5.9	2.3	6.8	121
Relative	1101	15	16	31	15.3	16.8	32.1	171
	1102	16	15	31	18.3	17.0	35.3	330
	1103	20	21	41	16.2	15.0	31.2	146
	1104	13	14	27	17.8	18.8	36.6	168
	1105	12	15	27	19.3	16.1	35.4	183
	1106	15	16	31	14.6	19.2	33.8	236
	Mean	15	16	31	16.9	17.2	34.1	206
	S.D.	3	2	5	1.8	1.6	2.1	68

Appendix 159 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (After administration period)

Sex : Female

Dose (mg/kg) : 30

	Animal number	Body weight g	Brain g(g/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	2101	201	1.66	508	0.77	5.35	0.91	0.63	0.63	1.26
	2102	232	1.94	513	0.80	5.96	0.50	0.91	0.96	1.87
	2103	199	1.90	515	0.71	5.49	0.52	0.91	0.80	1.71
	2104	198	1.78	420	0.70	5.97	0.41	0.82	0.85	1.67
	2105	204	1.78	361	0.64	5.70	0.47	0.84	0.81	1.65
	2106	204	1.89	397	0.71	5.56	0.45	0.80	0.85	1.65
	Mean	206	1.83	452	0.72	5.67	0.54	0.82	0.82	1.64
	S.D.	13	0.10	68	0.06	0.25	0.18	0.10	0.11	0.20
Relative	2101		0.83	253	0.38	2.66	0.45	0.31	0.31	0.63
	2102		0.84	221	0.34	2.57	0.22	0.39	0.41	0.81
	2103		0.95	259	0.36	2.76	0.26	0.46	0.40	0.86
	2104		0.90	212	0.35	3.02	0.21	0.41	0.43	0.84
	2105		0.87	177	0.31	2.79	0.23	0.41	0.40	0.81
	2106		0.93	195	0.35	2.73	0.22	0.39	0.42	0.81
	Mean		0.89	220	0.35	2.76	0.27	0.40	0.40	0.79
	S.D.		0.05	32	0.02	0.15	0.09	0.05	0.04	0.08

Appendix 160

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (After administration period)

Sex : Female

Dose (mg/kg) : 30

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	2101	23	27	50	26.9	26.7	53.6	381
	2102	28	31	59	61.5	41.6	103.1	370
	2103	32	31	63	42.7	51.2	93.9	340
	2104	32	30	62	33.9	29.9	63.8	422
	2105	37	40	77	33.1	38.4	71.5	588
	2106	33	36	69	41.6	48.3	89.9	355
	Mean	31	33	63	40.0	39.4	79.3	409
	S.D.	5	5	9	12.1	9.8	19.3	92
Relative	2101	11	13	25	13.4	13.3	26.7	190
	2102	12	13	25	26.5	17.9	44.4	159
	2103	16	16	32	21.5	25.7	47.2	171
	2104	16	15	31	17.1	15.1	32.2	213
	2105	18	20	38	16.2	18.8	35.0	288
	2106	16	18	34	20.4	23.7	44.1	174
	Mean	15	16	31	19.2	19.1	38.3	199
	S.D.	3	3	5	4.6	4.8	8.2	47

Appendix 161 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (After administration period)

Sex : Female

Dose (mg/kg) : 150

	Animal number	Body weight g	Brain g(g/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	3101	200	1.75	372	0.70	5.80	0.30	0.71	0.70	1.41
	3102	176	1.75	370	0.57	4.60	0.44	0.63	0.63	1.26
	3103	184	1.85	264	0.65	5.09	0.37	0.80	0.76	1.56
	3104	213	1.81	550	0.84	6.10	0.51	0.89	0.94	1.83
	3105	223	1.80	551	0.73	6.94	0.52	0.86	0.91	1.77
	3106	177	1.82	339	0.62	4.99	0.37	0.72	0.68	1.40
	Mean	196	1.80	408	0.69	5.59	0.42	0.77	0.77	1.54
	S.D.	20	0.04	117	0.09	0.86	0.09	0.10	0.13	0.22
Relative	3101		0.88	186	0.35	2.90	0.15	0.36	0.35	0.71
	3102		0.99	210	0.32	2.61	0.25	0.36	0.36	0.72
	3103		1.01	143	0.35	2.77	0.20	0.43	0.41	0.85
	3104		0.85	258	0.39	2.86	0.24	0.42	0.44	0.86
	3105		0.81	247	0.33	3.11	0.23	0.39	0.41	0.79
	3106		1.03	192	0.35	2.82	0.21	0.41	0.38	0.79
	Mean		0.93	206	0.35	2.85	0.21	0.40	0.39	0.79
	S.D.		0.09	42	0.02	0.16	0.04	0.03	0.03	0.06

Appendix 162 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (After administration period)

Sex : Female

Dose (mg/kg) : 150

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	3101	31	33	64	25.7	34.1	59.8	374
	3102	26	31	57	37.8	33.5	71.3	512
	3103	34	33	67	37.5	42.5	80.0	309
	3104	33	35	68	29.6	36.6	66.2	331
	3105	37	43	80	42.5	50.8	93.3	365
	3106	31	30	61	35.2	34.5	69.7	518
	Mean	32	34	66	34.7	38.7	73.4	402
	S.D.	4	5	8	6.1	6.8	11.8	91
Relative	3101	16	17	32	12.9	17.1	29.9	187
	3102	15	18	32	21.5	19.0	40.5	291
	3103	18	18	36	20.4	23.1	43.5	168
	3104	15	16	32	13.9	17.2	31.1	155
	3105	17	19	36	19.1	22.8	41.8	164
	3106	18	17	34	19.9	19.5	39.4	293
	Mean	17	18	34	18.0	19.8	37.7	210
	S.D.	1	1	2	3.6	2.6	5.8	65

Appendix 163

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (After administration period)

Sex : Female

Dose (mg/kg) : 750

	Animal number	Body weight g	Brain g(g/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	4101	245	1.82	358	0.79	8.15	0.41	0.92	1.00	1.92
	4102	206	1.74	331	0.64	5.90	0.39	0.73	0.72	1.45
	4103	150	1.66	301	0.52	4.86	0.39	0.66	0.61	1.27
	4104	197	1.79	445	0.62	5.72	0.45	0.73	0.68	1.41
	4105	220	1.76	363	0.71	6.79	0.37	0.88	0.91	1.79
	4106	182	1.83	274	0.58	5.95	0.32	0.75	0.72	1.47
	Mean	200	1.77	345	0.64	6.23	0.39	0.78	0.77	1.55
	S.D.	33	0.06	59	0.10	1.12	0.04	0.10	0.15	0.25
Relative	4101		0.74	146	0.32	3.33	0.17	0.38	0.41	0.78
	4102		0.84	161	0.31	2.86	0.19	0.35	0.35	0.70
	4103		1.11	201	0.35	3.24	0.26	0.44	0.41	0.85
	4104		0.91	226	0.31	2.90	0.23	0.37	0.35	0.72
	4105		0.80	165	0.32	3.09	0.17	0.40	0.41	0.81
	4106		1.01	151	0.32	3.27	0.18	0.41	0.40	0.81
	Mean		0.90	175	0.32	3.12	0.20	0.39	0.39	0.78
	S.D.		0.14	32	0.01	0.20	0.04	0.03	0.03	0.06

Appendix 164 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (After administration period)

Sex : Female

Dose (mg/kg) : 750

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	4101	36	38	74	47.2	49.5	96.7	389
	4102	22	23	45	34.6	34.3	68.9	404
	4103	25	25	50	40.6	29.6	70.2	365
	4104	26	28	54	30.3	33.2	63.5	594
	4105	29	30	59	30.0	34.4	64.4	287
	4106	30	28	58	33.2	36.1	69.3	326
	Mean	28	29	57	36.0	36.2	72.2	394
	S.D.	5	5	10	6.7	6.9	12.3	107
Relative	4101	15	16	30	19.3	20.2	39.5	159
	4102	11	11	22	16.8	16.7	33.4	196
	4103	17	17	33	27.1	19.7	46.8	243
	4104	13	14	27	15.4	16.9	32.2	302
	4105	13	14	27	13.6	15.6	29.3	130
	4106	16	15	32	18.2	19.8	38.1	179
	Mean	14	15	29	18.4	18.2	36.6	202
	S.D.	2	2	4	4.7	2.0	6.3	62

Appendix 165 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (After recovery period)

Sex : Male

Dose (mg/kg) : 0

	Animal number	Body weight g	Brain g(g/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	1007	399	2.13	421	1.20	11.38	0.67	1.38	1.48	2.86
	1008	434	2.14	710	1.22	11.99	0.83	1.63	1.62	3.25
	1009	491	2.11	406	1.38	14.82	0.59	1.43	1.57	3.00
	1010	477	2.09	520	1.62	12.32	0.80	1.51	1.55	3.06
	1011	405	2.11	630	1.31	11.13	0.75	1.30	1.27	2.57
	1012	436	2.09	463	1.40	12.37	0.78	1.49	1.49	2.98
	Mean	440	2.11	525	1.36	12.34	0.74	1.46	1.50	2.95
	S.D.	37	0.02	122	0.15	1.32	0.09	0.11	0.12	0.23
Relative	1007		0.53	106	0.30	2.85	0.17	0.35	0.37	0.72
	1008		0.49	164	0.28	2.76	0.19	0.38	0.37	0.75
	1009		0.43	83	0.28	3.02	0.12	0.29	0.32	0.61
	1010		0.44	109	0.34	2.58	0.17	0.32	0.32	0.64
	1011		0.52	156	0.32	2.75	0.19	0.32	0.31	0.63
	1012		0.48	106	0.32	2.84	0.18	0.34	0.34	0.68
	Mean		0.48	121	0.31	2.80	0.17	0.33	0.34	0.67
	S.D.		0.04	32	0.02	0.14	0.03	0.03	0.03	0.05

Appendix 166

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (After recovery period)

Sex : Male

Dose (mg/kg) : 0

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)
Absolute	1007	29	32	61	1.66	1.62	3.28	556	563	1119
	1008	31	35	66	1.73	1.78	3.51	623	582	1205
	1009	37	39	76	1.61	1.57	3.18	548	506	1054
	1010	31	29	60	1.19	1.13	2.32	441	386	827
	1011	26	30	56	1.61	1.66	3.27	548	556	1104
	1012	25	27	52	1.78	1.79	3.57	564	535	1099
	Mean	30	32	62	1.60	1.59	3.19	547	521	1068
	S.D.	4	4	8	0.21	0.24	0.45	59	71	128
Relative	1007	7	8	15	0.42	0.41	0.82	139	141	280
	1008	7	8	15	0.40	0.41	0.81	144	134	278
	1009	8	8	15	0.33	0.32	0.65	112	103	215
	1010	6	6	13	0.25	0.24	0.49	92	81	173
	1011	6	7	14	0.40	0.41	0.81	135	137	273
	1012	6	6	12	0.41	0.41	0.82	129	123	252
	Mean	7	7	14	0.37	0.37	0.73	125	120	245
	S.D.	1	1	1	0.07	0.07	0.14	20	23	43

Appendix 167

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (After recovery period)

Sex : Male

Dose (mg/kg) : 750

	Animal number	Body weight g	Brain g(g/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	4007	433	2.01	682	1.38	12.98	0.88	1.74	1.87	3.61
	4008	362	1.96	359	1.15	9.61	0.64	1.26	1.41	2.67
	4009	476	2.16	415	1.26	14.59	0.66	1.51	1.57	3.08
	4010	378	2.12	347	1.22	10.04	0.55	1.38	1.45	2.83
	4011	449	2.18	539	1.28	12.68	0.77	1.52	1.58	3.10
	4012	369	2.00	456	1.16	9.66	0.73	1.25	1.32	2.57
	Mean	411	2.07	466	1.24	11.59	0.71	1.44	1.53	2.98
	S.D.	48	0.09	127	0.09	2.11	0.11	0.19	0.19	0.38
Relative	4007		0.46	158	0.32	3.00	0.20	0.40	0.43	0.83
	4008		0.54	99	0.32	2.65	0.18	0.35	0.39	0.74
	4009		0.45	87	0.26	3.07	0.14	0.32	0.33	0.65
	4010		0.56	92	0.32	2.66	0.15	0.37	0.38	0.75
	4011		0.49	120	0.29	2.82	0.17	0.34	0.35	0.69
	4012		0.54	124	0.31	2.62	0.20	0.34	0.36	0.70
	Mean		0.51	113	0.30	2.80	0.17	0.35	0.37	0.73
	S.D.		0.05	26	0.02	0.19	0.03	0.03	0.04	0.06

Appendix 168

A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (After recovery period)

Sex : Male

Dose (mg/kg) : 750

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)
Absolute	4007	31	35	66	1.73	1.73	3.46	583	585	1168
	4008	28	26	54	1.66	1.71	3.37	547	552	1099
	4009	29	30	59	1.79	1.80	3.59	605	561	1166
	4010	29	32	61	1.54	1.52	3.06	493	506	999
	4011	34	39	73	1.64	1.63	3.27	578	534	1112
	4012	28	30	58	1.75	1.69	3.44	451	482	933
	Mean	30	32	62	1.69	1.68	3.37	543	537	1080
	S.D.	2	5	7	0.09	0.10	0.18	59	38	95
Relative	4007	7	8	15	0.40	0.40	0.80	135	135	270
	4008	8	7	15	0.46	0.47	0.93	151	152	304
	4009	6	6	12	0.38	0.38	0.75	127	118	245
	4010	8	8	16	0.41	0.40	0.81	130	134	264
	4011	8	9	16	0.37	0.36	0.73	129	119	248
	4012	8	8	16	0.47	0.46	0.93	122	131	253
	Mean	8	8	15	0.42	0.41	0.83	132	132	264
	S.D.	1	1	2	0.04	0.04	0.09	10	12	22

Appendix 169 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (After recovery period)

Sex : Female

Dose (mg/kg) : 0

	Animal number	Body weight g	Brain g(g/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	1107	216	1.82	337	0.73	6.25	0.42	0.84	0.82	1.66
	1108	203	1.75	272	0.68	5.17	0.42	0.81	0.80	1.61
	1109	238	1.89	361	0.73	6.65	0.45	0.93	0.92	1.85
	1110	261	1.88	414	0.81	6.65	0.54	0.89	0.94	1.83
	1111	235	1.80	345	0.71	6.36	0.54	0.83	0.77	1.60
	1112	228	1.88	474	0.73	6.27	0.42	0.84	0.84	1.68
	Mean	230	1.84	367	0.73	6.23	0.47	0.86	0.85	1.71
	S.D.	20	0.06	69	0.04	0.55	0.06	0.04	0.07	0.11
Relative	1107		0.84	156	0.34	2.89	0.19	0.39	0.38	0.77
	1108		0.86	134	0.33	2.55	0.21	0.40	0.39	0.79
	1109		0.79	152	0.31	2.79	0.19	0.39	0.39	0.78
	1110		0.72	159	0.31	2.55	0.21	0.34	0.36	0.70
	1111		0.77	147	0.30	2.71	0.23	0.35	0.33	0.68
	1112		0.82	208	0.32	2.75	0.18	0.37	0.37	0.74
	Mean		0.80	159	0.32	2.71	0.20	0.37	0.37	0.74
	S.D.		0.05	25	0.01	0.14	0.02	0.02	0.02	0.05

Appendix 170 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (After recovery period)

Sex : Female

Dose (mg/kg) : 0

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	1107	35	37	72	42.8	38.3	81.1	662
	1108	38	36	74	29.9	31.8	61.7	403
	1109	31	29	60	40.2	34.6	74.8	366
	1110	30	31	61	47.4	45.5	92.9	439
	1111	31	33	64	45.0	40.7	85.7	546
	1112	35	38	73	37.8	34.4	72.2	298
	Mean	33	34	67	40.5	37.6	78.1	452
	S.D.	3	4	6	6.2	5.0	11.0	132
Relative	1107	16	17	33	19.8	17.7	37.5	306
	1108	19	18	36	14.7	15.7	30.4	199
	1109	13	12	25	16.9	14.5	31.4	154
	1110	11	12	23	18.2	17.4	35.6	168
	1111	13	14	27	19.1	17.3	36.5	232
	1112	15	17	32	16.6	15.1	31.7	131
	Mean	15	15	29	17.6	16.3	33.9	198
	S.D.	3	3	5	1.9	1.4	3.0	63

Appendix 171 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (After recovery period)

Sex : Female

Dose (mg/kg) : 750

	Animal number	Body weight g	Brain g(g/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	4107	199	1.86	333	0.63	5.06	0.37	0.72	0.70	1.42
	4108	252	1.75	505	0.79	6.72	0.50	0.80	0.84	1.64
	4109	202	1.85	364	0.75	5.82	0.48	0.78	0.79	1.57
	4110	208	1.85	256	0.73	6.26	0.39	0.89	0.83	1.72
	4111	261	1.94	523	0.80	7.28	0.65	0.96	1.02	1.98
	4112	224	1.89	234	0.82	5.67	0.44	0.89	0.92	1.81
	Mean	224	1.86	369	0.75	6.14	0.47	0.84	0.85	1.69
	S.D.	27	0.06	122	0.07	0.79	0.10	0.09	0.11	0.19
Relative	4107		0.93	167	0.32	2.54	0.19	0.36	0.35	0.71
	4108		0.69	200	0.31	2.67	0.20	0.32	0.33	0.65
	4109		0.92	180	0.37	2.88	0.24	0.39	0.39	0.78
	4110		0.89	123	0.35	3.01	0.19	0.43	0.40	0.83
	4111		0.74	200	0.31	2.79	0.25	0.37	0.39	0.76
	4112		0.84	104	0.37	2.53	0.20	0.40	0.41	0.81
	Mean		0.84	162	0.34	2.74	0.21	0.38	0.38	0.76
	S.D.		0.10	40	0.03	0.19	0.03	0.04	0.03	0.07

Appendix 172 A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (After recovery period)

Sex : Female

Dose (mg/kg) : 750

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	4107	27	27	54	29.8	29.6	59.4	381
	4108	35	37	72	41.8	41.0	82.8	450
	4109	39	39	78	39.8	44.5	84.3	441
	4110	43	45	88	39.8	41.9	81.7	611
	4111	32	34	66	36.0	45.9	81.9	745
	4112	38	37	75	48.8	44.6	93.4	400
	Mean	36	37	72	39.3	41.3	80.6	505
	S.D.	6	6	11	6.3	6.0	11.3	143
Relative	4107	14	14	27	15.0	14.9	29.8	191
	4108	14	15	29	16.6	16.3	32.9	179
	4109	19	19	39	19.7	22.0	41.7	218
	4110	21	22	42	19.1	20.1	39.3	294
	4111	12	13	25	13.8	17.6	31.4	285
	4112	17	17	33	21.8	19.9	41.7	179
	Mean	16	17	33	17.7	18.5	36.1	224
	S.D.	3	3	7	3.0	2.7	5.4	53

Appendix 173(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 1001 Male 0 mg/kg Day 29 End of administration period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Vacuolation,hepatocyte,periportal: minimal Microgranuloma: minimal
Prostate	Cell infiltration,interstitial: minimal
Spleen	Hematopoiesis,extramedullary: minimal, erythroid

Following tissues : Not remarkable

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

Appendix 174(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 1002 Male 0 mg/kg Day 29 End of administration period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal
Liver	Vacuolation,hepatocyte,periportal: minimal Microgranuloma: minimal
Skeletal muscle,femoral	Cell infiltration,interstitial: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Bone+Bone marrow,sternal, Cerebellum
Cerebrum, Epididymis, Eye, Heart, Intestine,duodenum, Intestine,jejunum
Intestine,ileum(Peyer's patch), Intestine,cecum, Intestine,colon
Intestine,rectum, Lymph node,mesenteric, Lymph node,submandibular
Lung(bronchus), Parathyroid, Pituitary, Prostate, Sciatic nerve, Spleen, Stomach
Spinal cord,thoracic, Testis, Thymus, Trachea, Thyroid, Urinary bladder

Appendix 175(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 1003 Male 0 mg/kg Day 29 End of administration period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal
Liver	Vacuolation,hepatocyte,periportal: minimal Microgranuloma: minimal
Skeletal muscle,femoral	Degeneration,muscular: minimal
Thyroid	Ectopic thymus: mild

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Bone+Bone marrow,sternal, Cerebellum
Cerebrum, Epididymis, Eye, Heart, Intestine,duodenum, Intestine,jejunum
Intestine,ileum(Peyer's patch), Intestine,cecum, Intestine,colon
Intestine,rectum, Lymph node,mesenteric, Lymph node,submandibular
Lung(bronchus), Parathyroid, Pituitary, Prostate, Sciatic nerve, Spleen, Stomach
Spinal cord,thoracic, Testis, Thymus, Trachea, Urinary bladder

Appendix 176(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 1004 Male 0 mg/kg Day 29 End of administration period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal
Liver	Vacuolation,hepatocyte,periportal: minimal
Prostate	Cell infiltration,interstitial: mild
Spleen	Hematopoiesis,extramedullary: minimal, erythroid

Following tissues : Not remarkable

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

Appendix 177(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 1005 Male 0 mg/kg Day 29 End of administration period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Bone+Bone marrow,sternal	Degeneration,chondromucinous: minimal
Lung(bronchus)	Appearance,alveolar macrophage: minimal
Prostate	Cell infiltration,interstitial: mild
Spleen	Hematopoiesis,extramedullary: minimal, erythroid

Following tissues : Not remarkable

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

Appendix 178(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 1006 Male 0 mg/kg Day 29 End of administration period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal
Liver	Vacuolation,hepatocyte,periportal: minimal Microgranuloma: minimal
Lung(bronchus)	Pneumonia,focal: minimal
Prostate	Cell infiltration,interstitial: mild
Spleen	Hematopoiesis,extramedullary: minimal, erythroid

Following tissues : Not remarkable

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

Appendix 179(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 2001 Male 30 mg/kg Day 29 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Liver, Stomach

Appendix 180(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 2002 Male 30 mg/kg Day 29 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Liver, Stomach

Appendix 181(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 2003 Male 30 mg/kg Day 29 End of administration period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Vacuolation,hepatocyte,periportal: minimal

Following tissues : Not remarkable

Stomach

Appendix 182(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 2004 Male 30 mg/kg Day 29 End of administration period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Stomach

Appendix 183(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 2005 Male 30 mg/kg Day 29 End of administration period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Stomach

Appendix 184(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 2006 Male 30 mg/kg Day 29 End of administration period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Stomach

Appendix 185(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 3001 Male 150 mg/kg Day 29 End of administration period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Hypertrophy,hepatocytic,central: mild
Stomach	Hyperkeratosis,forestomach: minimal, limiting ridge Hyperplasia,squamous,limiting ridge: minimal

Appendix 186(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 3002 Male 150 mg/kg Day 29 End of administration period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,central: mild

Following tissues : Not remarkable

Stomach

Appendix 187(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 3003 Male 150 mg/kg Day 29 End of administration period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Stomach	Hyperkeratosis,forestomach: minimal, limiting ridge Hyperplasia,squamous,limiting ridge: minimal

Following tissues : Not remarkable

Liver

Appendix 188(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 3004 Male 150 mg/kg Day 29 End of administration period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Stomach	Hyperplasia,squamous,limiting ridge: minimal

Following tissues : Not remarkable

Liver

Appendix 189(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 3005 Male 150 mg/kg Day 29 End of administration period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Hypertrophy,hepatocytic,central: minimal
Stomach	Hyperplasia,squamous,limiting ridge: mild

Appendix 190(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 3006 Male 150 mg/kg Day 29 End of administration period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Vacuolation,hepatocyte,periportal: minimal
Stomach	Hyperkeratosis,forestomach: minimal Hyperplasia,squamous,limiting ridge: minimal

Appendix 191(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 4001 Male 750 mg/kg Day 29 End of administration period

Gross pathology:

Intestine,cecum	Dilatation,lumina: mild
Stomach	Thickening,wall,forestomach: mild
Other tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal
Liver	Vacuolation,hepatocyte,periportal: minimal Microgranuloma: minimal Hypertrophy,hepatocytic,central: mild
Spleen	Hematopoiesis,extramedullary: minimal, erythroid
Stomach	Hyperkeratosis,forestomach: mild Hyperplasia,squamous,forestomach: mild Hyperplasia,squamous,limiting ridge: minimal

Following tissues : Not remarkable

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

Appendix 192(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 4002 Male 750 mg/kg Day 29 End of administration period

Gross pathology:

Intestine,cecum	Dilatation,lumina: mild
Stomach	Thickening,wall,forestomach: mild
Other tissues	Not remarkable

Histopathology:

Bone+Bone marrow,sternal	Degeneration,chondromucinous: minimal
Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,central: mild
Parathyroid	Cell infiltration,lymphocytic: minimal, interstitial
Prostate	Cell infiltration,interstitial: minimal
Stomach	Hyperkeratosis,forestomach: minimal Hyperplasia,squamous,forestomach: minimal Hyperplasia,squamous,limiting ridge: minimal

Following tissues : Not remarkable

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

Appendix 193(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 4003 Male 750 mg/kg Day 29 End of administration period

Gross pathology:

Intestine,cecum	Dilatation,lumina: mild
Stomach	Thickening,wall,forestomach: mild
Other tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,central: mild
Stomach	Hyperkeratosis,forestomach: mild Hyperplasia,squamous,forestomach: mild Hyperplasia,squamous,limiting ridge: mild
Skeletal muscle,femoral	Degeneration,muscular: minimal
Thyroid	Remnant,ultimobranchial body: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Bone+Bone marrow,sternal, Cerebellum
Cerebrum, Epididymis, Eye, Heart, Intestine,duodenum, Intestine,jejunum
Intestine,ileum(Peyer's patch), Intestine,cecum, Intestine,colon
Intestine,rectum, Lymph node,mesenteric, Lymph node,submandibular
Lung(bronchus), Parathyroid, Pituitary, Prostate, Sciatic nerve, Spleen
Spinal cord,thoracic, Testis, Thymus, Trachea, Urinary bladder

Appendix 194(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 4004 Male 750 mg/kg Day 29 End of administration period

Gross pathology:

Intestine,cecum	Dilatation,lumina: mild
Stomach	Thickening,limiting ridge: mild
Other tissues	Not remarkable

Histopathology:

Bone+Bone marrow,sternal	Degeneration,chondromucinous: minimal
Liver	Hypertrophy,hepatocytic,central: minimal
Spleen	Hematopoiesis,extramedullary: minimal, erythroid
Stomach	Hyperkeratosis,forestomach: minimal Hyperplasia,squamous,limiting ridge: mild

Following tissues : Not remarkable

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

Appendix 195(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 4005 Male 750 mg/kg Day 29 End of administration period

Gross pathology:

Epididymis	Focus,yellow: 1 present, left caudal, 3x5mm
Intestine,cecum	Dilatation,lumina: mild
Stomach	Thickening,limiting ridge: mild
Other tissues	Not remarkable

Histopathology:

Epididymis	Granuloma,spermatic: mild, cauda
Kidney	Regeneration,tubular: mild
Liver	Hypertrophy,hepatocytic,central: mild
Lung(bronchus)	Mineralization,arterial wall: minimal
Spleen	Hematopoiesis,extramedullary: minimal, erythroid
Stomach	Hyperkeratosis,forestomach: minimal Hyperplasia,squamous,forestomach: minimal Hyperplasia,squamous,limiting ridge: mild
Thyroid	Remnant,ultimobranchial body: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Bone+Bone marrow,sternal, Cerebellum
Cerebrum, Eye, Heart, Intestine,duodenum, Intestine,jejunum
Intestine,ileum(Peyer's patch), Intestine,cecum, Intestine,colon
Intestine,rectum, Lymph node,mesenteric, Lymph node,submandibular, Parathyroid
Pituitary, Prostate, Sciatic nerve, Skeletal muscle,femoral
Spinal cord,thoracic, Testis, Thymus, Trachea, Urinary bladder

Appendix 196(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 4006 Male 750 mg/kg Day 29 End of administration period

Gross pathology:

Stomach	Thickening,wall,forestomach: mild
Other tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal
Liver	Vacuolation,hepatocyte,periportal: minimal Microgranuloma: minimal Hypertrophy,hepatocytic,central: minimal
Prostate	Cell infiltration,interstitial: mild
Stomach	Hyperkeratosis,forestomach: mild Hyperplasia,squamous,forestomach: mild Hyperplasia,squamous,limiting ridge: minimal

Following tissues : Not remarkable

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

Appendix 197(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 1101 Female 0 mg/kg Day 29 End of administration period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Bone+Bone marrow,sternal	Degeneration,chondromucinous: minimal
Liver	Vacuolation,hepatocyte,periportal: minimal Microgranuloma: minimal

Following tissues : Not remarkable

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

Appendix 198(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 1102 Female 0 mg/kg Day 29 End of administration period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Vacuolation,hepatocyte,periportal: minimal

Following tissues : Not remarkable

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

Appendix 199(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 1103 Female 0 mg/kg Day 29 End of administration period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Vacuolation,hepatocyte,periportal: minimal
Lung(bronchus)	Hemorrhage,focal: minimal

Following tissues : Not remarkable

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

Appendix 200(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 1104 Female 0 mg/kg Day 29 End of administration period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Bone+Bone marrow,sternal	Degeneration,chondromucinous: minimal
Kidney	Regeneration,tubular: minimal Fibrosis,focal: mild
Liver	Vacuolation,hepatocyte,periportal: minimal

Following tissues : Not remarkable

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

Appendix 201(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 1105 Female 0 mg/kg Day 29 End of administration period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Vacuolation,hepatocyte,periportal: mild Microgranuloma: minimal
Skeletal muscle,femoral	Degeneration,muscular: minimal

Following tissues : Not remarkable

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

Appendix 202(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 1106 Female 0 mg/kg Day 29 End of administration period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Heart	Cardiomyopathy: minimal

Following tissues : Not remarkable

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

Appendix 203(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 2101 Female 30 mg/kg Day 29 End of administration period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Stomach

Appendix 204(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 2102 Female 30 mg/kg Day 29 End of administration period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Vacuolation,hepatocyte,periportal: minimal

Following tissues : Not remarkable

Stomach

Appendix 205(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 2103 Female 30 mg/kg Day 29 End of administration period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Vacuolation,hepatocyte,periportal: minimal Microgranuloma: mild

Following tissues : Not remarkable

Stomach

Appendix 206(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 2104 Female 30 mg/kg Day 29 End of administration period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Vacuolation,hepatocyte,periportal: minimal

Following tissues : Not remarkable

Stomach

Appendix 207(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 2105 Female 30 mg/kg Day 29 End of administration period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: mild

Following tissues : Not remarkable

Stomach

Appendix 208(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 2106 Female 30 mg/kg Day 29 End of administration period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Vacuolation,hepatocyte,periportal: mild Microgranuloma: minimal

Following tissues : Not remarkable

Stomach

Appendix 209(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 3101 Female 150 mg/kg Day 29 End of administration period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Vacuolation,hepatocyte,periportal: minimal Microgranuloma: minimal
Stomach	Hyperkeratosis,forestomach: minimal, limiting ridge Hyperplasia,squamous,limiting ridge: minimal

Appendix 210(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 3102 Female 150 mg/kg Day 29 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Liver, Stomach

Appendix 211(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 3103 Female 150 mg/kg Day 29 End of administration period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Vacuolation,hepatocyte,periportal: minimal Microgranuloma: minimal

Following tissues : Not remarkable

Stomach

Appendix 212(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 3104 Female 150 mg/kg Day 29 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Liver, Stomach

Appendix 213(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 3105 Female 150 mg/kg Day 29 End of administration period

Gross pathology:

Intestine,cecum	Dilatation,lumina: mild
Other tissues	Not remarkable

Histopathology:

Liver	Vacuolation,hepatocyte,periportal: minimal Microgranuloma: minimal

Following tissues : Not remarkable

Intestine,cecum, Stomach

Appendix 214(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 3106 Female 150 mg/kg Day 29 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Liver, Stomach

Appendix 215(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 4101 Female 750 mg/kg Day 29 End of administration period

Gross pathology:

Intestine,cecum	Dilatation,lumina: mild
Stomach	Thickening,wall,forestomach: moderate
Other tissues	Not remarkable

Histopathology:

Bone+Bone marrow,sternal	Degeneration,chondromucinous: minimal
Kidney	Regeneration,tubular: minimal
Liver	Vacuolation,hepatocyte,periportal: minimal
Stomach	Hyperkeratosis,forestomach: mild Hyperplasia,squamous,forestomach: mild Hyperplasia,squamous,limiting ridge: mild

Following tissues : Not remarkable

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

Appendix 216(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 4102 Female 750 mg/kg Day 29 End of administration period

Gross pathology:

Intestine,cecum	Dilatation,lumina: mild
Stomach	Thickening,wall,forestomach: mild
Other tissues	Not remarkable

Histopathology:

Liver	Vacuolation,hepatocyte,periportal: minimal
Stomach	Hyperkeratosis,forestomach: mild Hyperplasia,squamous,forestomach: minimal Hyperplasia,squamous,limiting ridge: mild

Following tissues : Not remarkable

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

Appendix 217(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 4103 Female 750 mg/kg Day 29 End of administration period

Gross pathology:

Intestine,cecum	Dilatation,lumina: mild
Other tissues	Not remarkable

Histopathology:

Bone+Bone marrow,sternal	Degeneration,chondromucinous: minimal
Kidney	Regeneration,tubular: minimal
Stomach	Hyperkeratosis,forestomach: mild Hyperplasia,squamous,forestomach: mild Hyperplasia,squamous,limiting ridge: mild

Following tissues : Not remarkable

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

Appendix 218(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 4104 Female 750 mg/kg Day 29 End of administration period

Gross pathology:

Intestine,cecum	Dilatation,lumina: mild
Stomach	Thickening,wall,forestomach: mild
Other tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal Urinary cast,hyaline: minimal
Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,central: minimal
Stomach	Hyperkeratosis,forestomach: minimal Hyperplasia,squamous,limiting ridge: minimal
Skeletal muscle,femoral	Degeneration,muscular: minimal

Following tissues : Not remarkable

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

Appendix 219(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 4105 Female 750 mg/kg Day 29 End of administration period

Gross pathology:

Intestine,cecum	Dilatation,lumina: mild
Stomach	Thickening,wall,forestomach: mild
Other tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal
Liver	Hypertrophy,hepatocytic,central: minimal
Stomach	Hyperkeratosis,forestomach: mild Hyperplasia,squamous,forestomach: mild Hyperplasia,squamous,limiting ridge: mild

Following tissues : Not remarkable

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

Appendix 220(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 4106 Female 750 mg/kg Day 29 End of administration period

Gross pathology:

Stomach	Thickening,wall,forestomach: mild
Other tissues	Not remarkable

Histopathology:

Bone+Bone marrow,sternal	Degeneration,chondromucinous: minimal
Liver	Microgranuloma: minimal
Stomach	Hyperkeratosis,forestomach: mild Hyperplasia,squamous,limiting ridge: minimal

Following tissues : Not remarkable

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

Appendix 221(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 1007 Male 0 mg/kg Day 43 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Stomach

Appendix 222(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 1008 Male 0 mg/kg Day 43 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Stomach

Appendix 223(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 1009 Male 0 mg/kg Day 43 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Vacuolation,hepatocyte,periportal: mild Microgranuloma: minimal

Following tissues : Not remarkable

Stomach

Appendix 224(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 1010 Male 0 mg/kg Day 43 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Stomach

Appendix 225(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 1011 Male 0 mg/kg Day 43 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Liver, Stomach

Appendix 226(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 1012 Male 0 mg/kg Day 43 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Vacuolation,hepatocyte,periportal: minimal

Following tissues : Not remarkable

Stomach

Appendix 227(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 4007 Male 750 mg/kg Day 43 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Stomach

Appendix 228(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 4008 Male 750 mg/kg Day 43 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,central: minimal

Following tissues : Not remarkable

Stomach

Appendix 229(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 4009 Male 750 mg/kg Day 43 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Liver, Stomach

Appendix 230(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 4010 Male 750 mg/kg Day 43 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Stomach

Appendix 231(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 4011 Male 750 mg/kg Day 43 End of recovery period

Gross pathology:

Stomach	Thickening,wall,forestomach: mild
Other tissues	Not remarkable

Histopathology:

Liver	Vacuolation,hepatocyte,periportal: minimal
Stomach	Hyperkeratosis,forestomach: minimal Hyperplasia,squamous,forestomach: mild Hyperplasia,squamous,limiting ridge: minimal

Appendix 232(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 4012 Male 750 mg/kg Day 43 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,central: minimal

Following tissues : Not remarkable

Stomach

Appendix 233(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 1107 Female 0 mg/kg Day 43 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Stomach

Appendix 234(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 1108 Female 0 mg/kg Day 43 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Vacuolation,hepatocyte,periportal: minimal Microgranuloma: minimal

Following tissues : Not remarkable

Stomach

Appendix 235(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 1109 Female 0 mg/kg Day 43 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Liver, Stomach

Appendix 236(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 1110 Female 0 mg/kg Day 43 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Vacuolation,hepatocyte,periportal: mild Microgranuloma: minimal

Following tissues : Not remarkable

Stomach

Appendix 237(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 1111 Female 0 mg/kg Day 43 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Vacuolation,hepatocyte,periportal: minimal Microgranuloma: minimal

Following tissues : Not remarkable

Stomach

Appendix 238(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 1112 Female 0 mg/kg Day 43 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Stomach

Appendix 239(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 4107 Female 750 mg/kg Day 43 End of recovery period

Gross pathology:

Stomach	Thickening,limiting ridge: mild
Other tissues	Not remarkable

Histopathology:

Liver	Vacuolation,hepatocyte,periportal: minimal
Stomach	Hyperkeratosis,forestomach: minimal, limiting ridge Hyperplasia,squamous,limiting ridge: minimal

Appendix 240(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 4108 Female 750 mg/kg Day 43 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Stomach

Appendix 241(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 4109 Female 750 mg/kg Day 43 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Vacuolation,hepatocyte,periportal: minimal Microgranuloma: minimal
Stomach	Hyperplasia,squamous,limiting ridge: minimal

Appendix 242(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 4110 Female 750 mg/kg Day 43 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Stomach	Hyperplasia,squamous,forestomach: minimal

Following tissues : Not remarkable

Liver

Appendix 243(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 4111 Female 750 mg/kg Day 43 End of recovery period

Gross pathology:

Stomach	Thickening,limiting ridge: mild
Other tissues	Not remarkable

Histopathology:

Liver	Vacuolation,hepatocyte,periportal: minimal Microgranuloma: minimal
Stomach	Hyperkeratosis,forestomach: minimal, limiting ridge Hyperplasia,squamous,forestomach: minimal

Appendix 244(1/1) A 28-day oral toxicity study of 4-Hydroxydiphenylmethane in rats with a recovery period of 2 week

Individual gross and histopathological findings

Animal No. 4112 Female 750 mg/kg Day 43 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Vacuolation,hepatocyte,periportal: minimal

Following tissues : Not remarkable

Stomach

B-6355

信頼性保証書（1/3）

試験番号　：　B-6355

試験表題　：　4-ヒドロキシジフェニルメタンのラットを用いた
2週間回復性観察を含む28日間反復経口投与毒性試験

本試験は以下に示す基準を遵守して実施されたことを保証致します。

- 「新規化学物質等に係る試験を実施する試験施設に関する基準について」
（平成15年11月21日：薬食発第1121003号、平成15・11・17製局第3号、
環保企発第031121004号、平成17年4月1日最終改正）

なお、調査は下記の通り実施致しました。

2009年8月7日
株式会社ボゾリサーチセンター
信頼性保証部門責任者　[redacted]

試験における調査

調査項目	調査担当者	調査日	試験責任者及び運営管理者への報告日
試験計画書	[redacted]	2008年　7月　3日	2008年　7月　3日
作業予定表・コンピュータプロトコール		2008年　7月　10日	2008年　7月　11日
調製・被験物質の保存		2008年　7月　11日	2008年　7月　14日
被験液の濃度・均一性確認		2008年　7月　11日	2008年　7月　14日
群分け		2008年　7月　12日	2008年　7月　14日
体重・摂餌量測定・投与・一般状態の観察		2008年　7月　15日	2008年　7月　16日

B-6355

信頼性保証書（2/3）

調　査　項　目	調査担当者	調　査　日	試験責任者及び運営管理者への報告日
詳細な一般状態の観察	[redacted]	2008年　7月　17日	2008年　7月　18日
尿検査（尿量・色調・定性）		2008年　8月　6日	2008年　8月　7日
摂水量測定		2008年　8月　7日	2008年　8月　7日
試験計画書変更書（1）		2008年　8月　7日	2008年　8月　8日
機能検査・握力及び自発運動量測定		2008年　8月　8日	2008年　8月　11日
採血・剖検		2008年　8月　12日	2008年　8月　13日
病理組織学検査（切り出し）		2008年　8月　29日	2008年　8月　30日
試験計画書変更書（2）		2008年　9月　3日	2008年　9月　3日
中間報告書		2008年　10月　1日	2008年　10月　2日
試験計画書変更書（3）		2008年　10月　14日	2008年　10月　15日
試験計画書変更書（4）		2008年　11月　27日	2008年　12月　1日
生データ（入荷～臨床検査、器官重量測定）		2008年　12月　11日	
		2008年　12月　12日	
		2008年　12月　15日	2008年　12月　16日
最終報告書草案・図・表・付表		2008年　12月　11日	
		2008年　12月　12日	
		2008年　12月　13日	
		2008年　12月　15日	2008年　12月　16日
改善確認		2008年　12月　17日	2008年　12月　19日
生データ（被験物質関係、被験液の濃度・均一性確認、剖検・病理、飼育関係）		2009年　1月　23日	
		2009年　1月　26日	
		2009年　2月　2日	
		2009年　2月　3日	2009年　2月　4日
改善確認		2009年　2月　9日	2009年　2月　10日
最終報告書		2009年　8月　7日	2009年　8月　7日

B-6355

信頼性保証書（3/3）

プロセス調査

調　査　項　目	調査担当者	調　査　日	部門責任者及び運営管理者への報告日
動物入荷	[redacted]	2008年　6月　2日	2008年　6月　3日
検疫・馴化、飼育管理		2008年　6月　2日	2008年　6月　3日
		2008年　6月　6日	2008年　6月　9日
		2008年　6月　9日	2008年　6月　10日
尿検査（沈査・浸透圧）		2008年　9月　3日	2008年　9月　4日
		2008年　9月　4日	2008年　9月　5日
血液学検査・血液化学検査		2008年　9月　4日	2008年　9月　5日
病理組織学検査		2008年　9月　9日	2008年　9月　12日
（包埋・薄切・染色）		2008年　9月　9日	2008年　9月　12日
		2008年　9月　9日	2008年　9月　12日