



最 終 報 告 書

グルタル酸ジメチルのラットを用いた
経口投与による反復投与毒性・生殖発生毒性併合試験

試験番号：R-1134

試験期間：2013年9月20日-2014年3月27日

試験施設

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R-1134

1. GLP 陳述書

試験番号 : R-1134

試験表題 : グルタル酸ジメチルのラットを用いた経口投与による
反復投与毒性・生殖発生毒性併合試験

本試験は以下に示す基準を遵守して実施したものであります。

 2014 年 3 月 27 日 

試験責任者

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2. 目次

1.	GLP陳述書	2
2.	目次	3
3.	試験実施概要	8
3.1	試験番号	8
3.2	試験表題	8
3.3	試験目的	8
3.4	試験委託者	8
3.5	試験受託者	8
3.6	試験実施施設	8
3.7	被験物質	8
3.8	試験日程	9
3.9	試験責任者	9
3.10	試験担当者	9
3.11	試験成績の信頼性に影響を及ぼしたと思われる環境要因	9
3.12	予見することができなかった試験の信頼性に影響を及ぼす疑いの ある事態及び試験計画書に従わなかったこと	9
3.13	資料保存	10
3.14	試験責任者の記名・なつ印	11
4.	要約	12
4.1	反復投与毒性	12
4.2	生殖発生毒性	12
5.	緒言	13
5.1	GLP	13
5.2	毒性試験ガイドライン	13
5.3	動物の福祉	13
6.	試験材料及び方法	14
6.1	被験物質及び媒体	14
6.1.1	被験物質	14
6.1.2	媒体	15
6.2	投与液の調製及び保存方法	15
6.2.1	対照群投与液の採取	15
6.2.2	被験液の調製	15
6.2.3	投与液の保存	16
6.2.4	被験液の安定性	16
6.2.5	被験液の濃度確認	16
6.3	試験動物種及び系統の選択理由	17

6.4	試験動物.....	18
6.5	飼育条件.....	18
6.6	動物の識別.....	19
6.7	投与経路、投与期間及び投与回数並びに回復期間と それらの 選択理由.....	19
6.8	投与方法.....	19
6.9	投与量及び群構成.....	19
6.10	投与量の設定根拠.....	20
6.11	観察及び検査の方法.....	20
6.11.1	一般状態の観察.....	21
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.....	21
6.11.3	体重測定.....	22
6.11.4	摂餌量測定.....	22
6.11.5	膣垢検査.....	22
6.11.6	交配方法.....	22
6.11.7	分娩及び哺育観察.....	23
6.11.8	尿検査（摂水量測定を含む）.....	24
6.11.9	血液学検査.....	25
6.11.10	血液化学検査.....	26
6.11.11	血中ホルモン測定.....	26
6.11.12	病理学検査.....	27
6.12	統計解析.....	28
6.12.1	パラメータの算出.....	28
6.12.2	検定.....	28
7.	試験結果.....	30
7.1	一般状態（Table 1-1~1-7、Appendix 1-1~1-22）.....	30
7.2	詳細な一般状態の観察、機能検査、握力測定及び自発運動量の測定 （Fig. 1~5、Table 2-1~2-84、Appendix 2-1~2-258）.....	30
7.2.1	ホームケージ内観察（Table 2-1~2-23、Appendix 2-1~2-72）.....	30
7.2.2	手に持つての観察（Table 2-24~2-46、Appendix 2-73~2-144）.....	30
7.2.3	オープンフィールド内観察（Table 2-47~2-69、 Appendix 2-145~2-216）.....	30
7.2.4	機能検査（Table 2-70~2-74、Appendix 2-217~2-230）.....	30
7.2.5	握力（Table 2-75~2-79、Appendix 2-231~2-244）.....	31
7.2.6	自発運動量（Fig. 1~5、Table 2-80~2-84、 Appendix 2-245~2-258）.....	31
7.3	体重（Fig. 6~8、Table 3-1~3-7、Appendix 3-1~3-22）.....	31
7.4	摂餌量（Fig. 9~11、Table 4-1~4-7、Appendix 4-1~4-22）.....	31

7.5	尿検査（摂水量測定を含む）（Table 5-1~5-16、Appendix 5-1~5-30）	32
7.6	血液学検査（Table 6-1~6-10、Appendix 6-1~6-28）	32
7.7	血液化学検査（Table 7-1~7-10、Appendix 7-1~7-28）	33
7.8	器官重量（Table 8-1~8-10、Appendix 8-1~8-48）	33
7.9	剖検所見（Table 9-1~9-7、Appendix 9-1~9-116）	34
7.10	病理組織学検査（Table 10-1~10-19、Appendix 9-1~9-116）	34
7.11	性周期（Table 11、Appendix 10-1~10-4）	35
7.12	交配成績（Table 12、Appendix 11-1~11-4）	35
7.13	分娩成績（Table 13、Appendix 12-1~12-4）並びに分娩及び哺育状態 （Table 1-3 及び 1-4、Appendix 1-9~1-16）	35
7.14	出生児の生存率（Table 14、Appendix 13-1~13-4）	35
7.15	出生児の性比（Table 15、Appendix 14-1~14-4）	36
7.16	出生児の体重（Table 16、Appendix 15-1~15-4）	36
7.17	死亡児の肉眼観察所見（Table 17、Appendix 16-1~16-4）	36
7.18	出生児の生後4日肉眼観察所見（Table 18、Appendix 17-1~17-4）	36
8.	考察	37
8.1	反復投与毒性	37
8.2	生殖発生毒性	37
9.	文献	39

添付資料

Attached Data 1	試験成績書（被験物質の特性）	40
Attached Data 2	試験成績書（被験物質の安定性）	41
Attached Data 3	試験成績書（被験液中グルタル酸ジメチルの安定性）	43
Attached Data 4	被験液中の被験物質濃度分析結果（初回投与）	44
Attached Data 5	被験液中の被験物質濃度分析結果（投与6週）	45
Attached Data 6	グルタル酸ジメチルのラットを用いた14日間反復 経口投与毒性試験（投与量設定試験）における所見	46



Fig. 1~5	自発運動量	47
Fig. 6~8	体重	52
Fig. 9~11	摂餌量	55

表

Table 1-1~1-7	一般状態.....	58
Table 2-1~2-23	ホームケージ内観察.....	65
Table 2-24~2-46	手に持っでの観察.....	88
Table 2-47~2-69	オープンフィールド内観察.....	111
Table 2-70~2-74	機能検査.....	134
Table 2-75~2-79	握力.....	139
Table 2-80~2-84	自発運動量.....	144
Table 3-1~3-7	体重.....	149
Table 4-1~4-7	摂餌量.....	156
Table 5-1~5-16	尿検査（含、摂水量）.....	163
Table 6-1~6-10	血液学検査.....	179
Table 7-1~7-10	血液化学検査.....	189
Table 8-1~8-10	器官重量.....	199
Table 9-1~9-7	剖検所見.....	209
Table 10-1~10-19	病理組織学検査.....	216
Table 11	性周期.....	235
Table 12	交配成績.....	236
Table 13	分娩成績.....	237
Table 14	出生児の生存率.....	238
Table 15	出生児の性比.....	239
Table 16	出生児の体重.....	240
Table 17	死亡児の肉眼観察所見.....	241
Table 18	出生児の生後4日肉眼観察所見.....	242

個体別表

Appendix 1-1~1-22	一般状態.....	243
Appendix 2-1~2-72	ホームケージ内観察.....	265
Appendix 2-73~2-144	手に持っでの観察.....	337
Appendix 2-145~2-216	オープンフィールド内観察.....	409
Appendix 2-217~2-230	機能検査.....	481
Appendix 2-231~2-244	握力.....	485
Appendix 2-245~2-258	自発運動量.....	509
Appendix 3-1~3-22	体重.....	523
Appendix 4-1~4-22	摂餌量.....	545
Appendix 5-1~5-30	尿検査（含、摂水量）.....	567
Appendix 6-1~6-28	血液学検査.....	597
Appendix 7-1~7-28	血液化学検査.....	625

R-1134

Appendix 8-1~8-48	器官重量.....	653
Appendix 9-1~9-116	剖検所見及び病理組織学検査.....	701
Appendix 10-1~10-4	性周期.....	817
Appendix 11-1~11-4	交配成績.....	821
Appendix 12-1~12-4	分娩成績.....	825
Appendix 13-1~13-4	出生児の生存率.....	829
Appendix 14-1~14-4	出生児の性比.....	833
Appendix 15-1~15-4	出生児の体重.....	837
Appendix 16-1~16-4	死亡児の肉眼観察所見.....	841
Appendix 17-1~17-4	出生児の生後4日肉眼観察所見.....	845
信頼性保証書.....		849

R-1134

3. 試験実施概要

3.1 試験番号

R-1134

3.2 試験表題

グルタル酸ジメチルのラットを用いた経口投与による反復投与毒性・生殖発生毒性併合試験

(Combined repeated dose toxicity study with the reproduction / developmental toxicity screening test of dimethyl glutarate by oral administration in rats)

3.3 試験目的

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

3.4 試験委託者

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

3.5 試験受託者

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

3.6 試験実施施設

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

3.7 被験物質

製造者	:	東京化成工業株式会社
名称	:	グルタル酸ジメチル
CAS 番号	:	1119-40-0
官報公示整理番号	:	(2)-857、(2)-925 (化審法)
入手日	:	2013年6月20日

3.8 試験日程

試験開始日	:	2013年 9月 20日
被験物質出庫日	:	2013年 10月 9日
動物入荷日	:	2013年 9月 25日
実験開始日（投与開始日）	:	2013年 10月 15日
交配開始日	:	2013年 10月 29日
分娩開始日	:	2013年 11月 20日
母動物剖検開始日	:	2013年 11月 25日
投与終了剖検日	:	2013年 11月 26日（雄及び非交配群）
回復開始日	:	2013年 11月 26日
回復終了剖検日	:	2013年 12月 10日
動物試験終了日	:	2013年 12月 10日
実験終了日（病理組織学検査終了日）	:	2014年 1月 28日
試験終了日	:	2014年 3月 27日

3.9 試験責任者

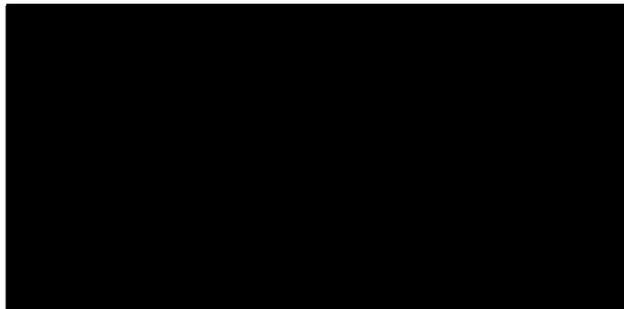
株式会社ボゾリサーチセンター 御殿場研究所 研究部



3.10 試験担当者

試験主担当者 :
被験物質保存責任者 :

臨床検査責任者 :
化学分析責任者 :
病理検査責任者 :
統計解析責任者 :



3.11 試験成績の信頼性に影響を及ぼしたと思われる環境要因

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

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

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

3.13 資料保存

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

R-1134

3.14 試験責任者の記名・なつ印



2014年3月27日



4. 要約

グルタル酸ジメチルをコーン油で溶解し、100、300 及び 1000 mg/kg の投与量で Sprague-Dawley 系 SPF ラット（交配群として雌雄各 12 匹/群、雌には非交配群として対照群及び 1000 mg/kg 投与群に各 10 匹を追加）の雄には交配前 14 日間に加え交配期間を通して剖検前日まで（42 日間）、雌には交配前 14 日間に加え交配期間及び妊娠期間を通して授乳 4 日まで（41~55 日間）、非交配群雌には 42 日間強制経口投与し、反復投与毒性及び生殖発生毒性を検討した。更に、0 及び 1000 mg/kg 投与群の一部の動物（交配群雄 5 匹と非交配群雌 5 匹）については、雄及び非交配群雌ともに 42 日間投与した後 14 日間の回復期間を設け、毒性変化の可逆性を検討した。なお、対照群には媒体であるコーン油を投与した。

4.1 反復投与毒性

1000 mg/kg 投与群の交配群雌で妊娠 23 日に 1 例が死亡し、雄及び雌（非交配群）で尿 pH に低値傾向、胃に境界縁の扁平上皮過形成が認められた以外には、いずれの検査にも被験物質投与の影響は認められなかった。

なお、尿 pH の低値傾向は回復期間終了週検査では認められず、胃の変化は回復終了時に雄では消失し、雌（非交配群）では頻度が軽減したことから、いずれも回復性がみられた。

4.2 生殖発生毒性

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

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

5. 緒言

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

なお、本試験は以下の基準を遵守し、ガイドライン等に準拠して、株式会社ボゾリサーチセンターで実施した。また、本試験は試験実施施設の動物実験委員会の承認（承認番号：G130271）を受けて実施した。

5.1 GLP

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

5.2 毒性試験ガイドライン

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

5.3 動物の福祉

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

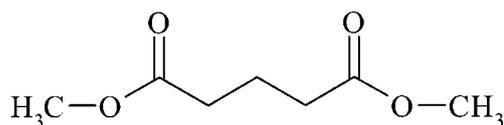
6. 試験材料及び方法

6.1 被験物質及び媒体

6.1.1 被験物質

グルタル酸ジメチルは理科研株式会社から以下の情報とともに購入した。また、試験開始前に赤外吸収スペクトルの測定により特性が確認されている（試験番号：A-2584、Attached Data 1）。

製造者	:	東京化成工業株式会社
名称	:	グルタル酸ジメチル
英語名称	:	Dimethyl Glutarate
別名	:	Glutaric acid dimethyl ester
CAS 番号	:	1119-40-0
官報公示整理番号	:	(2)-857、(2)-925（化審法）
構造式又は示性式	:	



分子式	:	C ₇ H ₁₂ O ₄
分子量	:	160.17
常温における性状	:	無色透明液体*
沸点/沸騰範囲	:	214°C*
引火点	:	110°C*
蒸気圧	:	0.25kPa/25°C*
溶解性	:	易溶；アルコール、エーテル 微溶；水（20.2 g/L、25°C）*
オクタノール/水分配係数	:	0.62*
ロット番号	:	AVBRN
純度	:	99.5%
不純物	:	不明
比重（20/20）	:	1.0896
屈折率（n ₂₀ /D）	:	1.4245
保存条件	:	密栓、冷暗所
保存方法	:	気密容器に入れ冷蔵庫内（許容値：1~10°C、実測値：3~8°C）に保存した。
保存場所	:	御殿場研究所被験物質保存室、第2研究棟4階被験物質調製室及び生化学部標準物質保存場所

- 取扱い上の注意 : 作業場の換気を十分に行い、マスク、保護眼鏡、保護手袋等の適切な保護具を着用し、直接の接触を防ぐ。取り扱い後は、手、顔等を良く洗い、うがいをする。
- 安定性 : 投与期間終了後に株式会社ボゾリサーチセンター御殿場研究所において、残余被験物質の赤外吸収スペクトルを確認した結果、実験実施前に確認した参照スペクトルとほぼ同様であり安定性に問題はなかった (Attached Data 2)。
- 被験物質残余の処理 : 被験物質 5 g を保存試料として御殿場研究所の資料保存施設に保存した。動物試験及び分析終了後の残量は全て焼却処分した。

* : 製造元の東京化成工業株式会社発行の製品安全データシートに基づく

6.1.2 媒体

- 名称 : コーン油
- 規格 : 生化学用
- 製造者 : 和光純薬工業株式会社
- ロット番号 (有効期限) : PDQ0071 (2018年8月7日、2018年10月8日)、PDM2984 (2018年11月17日)
- 保存方法 : 室温
- 保存場所 : 御殿場研究所第2研究棟4階被験物質調製室

なお、媒体については、本試験に先立って実施した被験液中濃度測定法バリデーション及び安定性試験 (試験番号 : A-2584) [1]において、コーン油中での被験物質の安定性に良好な結果が得られていることから、コーン油を選択した。

6.2 投与液の調製及び保存方法

6.2.1 対照群投与液の採取

対照群投与液として、被験液調製当日の被験物質を取り扱う前に必要量のコーン油を1日使用分ずつ、貼付したラベルを確認しながら褐色ガラス瓶に分注した。

6.2.2 被験液の調製

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

R-1134

オル等に吸着させて焼却処分した。

6.2.3 投与液の保存

対照群投与液及び被験液は褐色ガラス瓶に入れ、冷所（冷蔵庫内、許容値：1~10°C、実測値：3~6°C）に保存し、安定性の確認された範囲内で投与に使用した。

6.2.4 被験液の安定性

本被験物質の 1.00 及び 200 mg/mL濃度の被験液（媒体：コーン油）は、褐色ガラス瓶に入れ冷所（冷蔵庫内、許容値：1~10°C）で 8 日間保存後、更に室温下（許容値：1~30°C）で 24 時間保存（冷所 8 日間+室温 24 時間）したときに安定であることが試験施設で確認されている（試験番号：A-2584、Attached Data 3） [1]。

6.2.5 被験液の濃度確認

初回投与及び投与 6 週の投与に使用する各濃度の被験液（各 10 mL採取）について、株式会社ボゾリサーチセンター御殿場研究所でGCにより濃度確認を実施した。なお、初回投与に使用する被験液については、投与開始前に確認を行った。その結果、各濃度液における表示値に対する被験物質の割合は 99.5~102.0%であり（Attached Data 4、5）、いずれも許容範囲内（濃度：表示値に対する割合；100.0±10.0%）であったことから、被験液の調製に問題はなかったと考えられた。なお、GCを用いた被験液中濃度測定法バリデーションは株式会社ボゾリサーチセンター御殿場研究所（試験番号：A-2584） [1]で実施された。分析法の概略を以下に示した。

[標準物質]

被験物質から一部分配したものをを用いた。

名称	:	グルタル酸ジメチル
ロット番号	:	AVBRN
保存条件	:	密栓、冷暗所
保存方法	:	気密容器に入れ冷蔵庫内（許容値：1~10°C、実測値：3~8°C）に保存した。
保存場所	:	御殿場研究所 被験物質保存室及び生化学部標準物質保存場所

[測定実測試料の調製]

各測定試料を転倒混和した後、任意の場所から n=3 で採取し、以下の表に示すように、測定実測試料を用時調製した。

R-1134

測定試料濃度 (mg/mL)	1次希釈		2次希釈		希釈率
	採取量 (mL)	定容量 (mL)	1次希釈液 採取量 (mL)	定容量 (mL)	
20	1	50	2.5	20	400
60	1	100	2.5	30	1200
200	1	100	2.5	100	4000

溶媒：アセトン

[GC システム]

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

[GC 測定条件]

カラム	:	DB-5 (0.53 mm I.D.×25 m、膜厚 5 μm、 Agilent Technologies Inc.)
キャリアガス	:	He
流量モード	:	コンスタントフローモード
流量	:	5.0 mL/min
注入口	:	スプリット注入口
スプリット比	:	5:1
注入口温度	:	180°C
検出器	:	Flame ionization detector (FID)
検出器温度	:	250°C
H ₂ 流量	:	45 mL/min
Air 流量	:	450 mL/min
メイクアップガス (N ₂) 流量	:	40 mL/min
オープン温度	:	150°C (Hold 0分) →210°C (10°C/min、Hold 2分)
注入量	:	1 μL

6.3 試験動物種及び系統の選択理由

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

6.4 試験動物

Sprague-Dawley 系 SPF ラット [CrI:CD(SD)、日本チャールス・リバー株式会社、厚木飼育センター] の雄 62 匹及び雌 83 匹をそれぞれ 8 週齢で入手^{注)}し、入荷日を馴化 1 日と起算して、3 日間の検疫期間を含む 20 日間の馴化飼育を行った。その間、一般状態の観察 (1 回/日)、体重測定 (馴化 1、3、6、13 及び 20 日の 5 回)、詳細な一般状態の観察 (群分け 3 日前の馴化 17 日に 1 回) を実施した。更に、雄について馴化終了日に陰嚢内の精巢の触診及び陰茎亀頭の観察を実施し、雌については膣垢を検疫期間終了後群分け日まで採取して性周期 (検疫期間終了後 14 日間) を調べた。その結果、性周期の異常が 6 例 (耳標番号: 79、84、99、128、141、144) にみられ、外傷 (陰茎部) が雄 1 例 (耳標番号: 12) にみられた。それらの異常例を除き、検疫・馴化期間中の一般状態、詳細な一般状態、体重推移、精巢の触診結果及び性周期に異常がなく、性成熟に達した陰茎亀頭であり、健康と思われる雄 61 匹中 48 匹及び雌 77 匹中 68 匹を選択し、10 週齢で投与に使用した。投与開始時 (10 週齢) の体重の変動範囲は雄で 406~441 g (平均体重: 423 g)、雌は 228~283 g (平均体重: 250 g) であり、雌雄それぞれ平均体重の $\pm 20\%$ 以内であった。

なお、動物は検疫・馴化期間中の体重増加量 (入荷日~群分け時) により選別後、群分け当日 (投与開始の前日) の体重に基づいて、非交配群も含め各群の平均体重ができるだけ均等となるよう各群に割付けた。個体の割付けはコンピュータを用いたブロック配置法及び無作為抽出法の組み合わせ (ブロック配置法に必要な群を構成し、試験群及び群内の個体番号を無作為に割当てた) により行った。供試個体の選択条件を満たして余剰となった雌は交配予備動物として継続飼育したが、使用しなかったため、交配予備動物は全て交配終了後に試験から除外した。その他の雌雄残余動物は群分け当日に試験から除外した。なお、試験から除外された動物は、有効利用を目的として動物管理責任者に移管した (移管日: 2013 年 10 月 14 日及び 11 月 12 日)。

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

6.5 飼育条件

動物は、温度 $23\pm 3^{\circ}\text{C}$ (実測値: $22\sim 25^{\circ}\text{C}$)、相対湿度 $50\pm 20\%$ (実測値: $40\sim 59\%$)、換気回数 10~15 回/h、照明 12 時間/日 (07:00~19:00) の動物飼育室 (飼育室番号: 903 号室) でブラケット式金属製網ケージ (W254×D350×H170 mm: リードエンジニアリング株式会社) に交配中を除いて個別に収容した。なお、妊娠 17 日から授乳 4 日までは、床敷 (ホワイトフレーク: 日本チャールス・リバー株式会社、ロット番号: 2013-3) を入れたプラスチック製エコケージ (W340×D400×H185 mm: 日本クリア株式会社) に 1 腹単位で収容した。

飼料は NMF 固形 (放射線滅菌、オリエンタル酵母工業株式会社、ロット番号: 130718、130822) をステンレス製給餌器により自由に摂取させた。

飲料水は御殿場市営水道水を自動給水装置 (ブラケット式金属製網ケージでの飼育

時)又は給水瓶(プラスチック製エコンケージでの飼育時)により自由に摂取させた。

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

6.6 動物の識別

動物は番号(雄:1~62、雌:63~145)が刻印された耳標を入荷時に装着し、個体識別を行った。群分け後は、1000の位は群(対照群、低、中及び高用量の順)、100の位は性別(0番を雄、1番を雌)、10と1の位は個体番号を示す4桁の動物番号を設定した。各飼育ケージに投与量(群)ごとに色分けしたケージラベルをつけ、試験番号、投与経路、投与量、性別、動物番号、耳標番号、剖検予定日(雄及び非交配群の雌)、交尾成立日(交配群の雌雄)及び分娩日(交配群の雌)を明記した。

6.7 投与経路、投与期間及び投与回数並びに回復期間とそれらの選択理由

投与経路は毒性試験法ガイドラインに準じ、経口投与を選択した。投与期間は、投与日数として、交配群雌雄ともに交配前14日、更に、雄については交配開始後28日(計42日)、雌については交配期間及び妊娠期間を通して授乳4日まで(計41~55日)とした。非交配群の雌については42日とした。また、不妊であった動物(動物番号1111、2110、3105及び3109)については41~43日であった。回復動物については、42日の投与期間が終了した後、被験物質投与に起因した変化の可逆性、持続性並びに遅発性毒性等について観察するため、14日間の回復期間を設けた。投与回数は反復投与試験で一般的に行われている1日1回とした。

6.8 投与方法

投与方法は、げっ歯類の経口投与に際して一般的な強制経口投与とした。投与容量は5 mL/kg体重とし、胃ゾンデを用いて投与液を08:01~11:35の間に投与した。ただし、投与時に分娩中であった動物は分娩終了を待って、13:40~14:33の間に投与した。対照群には媒体のみを同様に投与した。個体ごとの投与液量(表示単位:0.1 mL)は、直近の体重を基準に算出した。

6.9 投与量及び群構成

投与量は100、300及び1000 mg/kgの3用量とし、試験群はこれらの用量群に媒体を投与する対照群を加え4群構成とした。1群当たりの動物数は交配を行う交配群として各群で雌雄各12匹、交配しない非交配群として対照群及び高用量群で雌各10匹

とした。なお、対照群及び高用量群における雄の群内番号 8 番以降、非交配群雌の群内番号 18 番以降の各 5 匹は、最終投与終了日以降、回復動物とした。群構成を表 1-1、及び 1-2. に示した。

表 1-1. 群構成表 (雄)

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

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

表 1-2. 群構成表 (雌)

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

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

6.10 投与量の設定根拠

本試験の投与量は、先に実施した「グルタル酸ジメチルのラットを用いた 14 日間反復経口投与毒性試験（投与量設定試験）、株式会社ボゾリサーチセンター、試験番号：N-R041、投与量：100、300 及び 1000 mg/kg/day」[2]の結果（Attached Data 6）を参考に設定した。投与量設定試験では、1000 mg/kg 投与群においても死亡例はみられず、一般状態、体重、摂餌量、血液学検査及び剖検所見に被験物質投与の影響が疑われる変化はみられなかった。しかし、300 mg/kg 以上の投与群の雄で腎臓重量に高値及び尿素窒素に低値が、1000 mg/kg 投与群の雌で総たん白質に低値が認められた。したがって、本試験では毒性試験法ガイドラインに示されている限度試験の最高投与量である 1000 mg/kg を高用量とし、以下公比約 3 で除して 300 及び 100 mg/kg をそれぞれ中及び低用量に設定した。

6.11 観察及び検査の方法

試験日の起算は、投与開始日を投与 1 日、投与 1 日から 7 日を投与 1 週、回復開始日（投与 42 日の翌日）を回復 1 日、回復 1 日から 7 日を回復 1 週、交尾成立日を妊娠 0 日、分娩終了日（出産日）を授乳 0 日、出生日を生後 0 日とし、以下に示す項目について、それぞれ記載の時期に観察及び検査を実施した。また、死亡動物は、発見後体重を測定し、速やかに病理学検査に供した。

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、投与直後及び投与1~3時間後）、回復期間中は毎日2回（午前・午後）、剖検日は1回（午前）、それぞれ生死、身体の外観、姿勢、行動及び排泄物（尿、糞）などの一般状態における異常の有無を観察した。なお、投与2週以降の動物のハンドリングを伴った定期的な観察は、詳細な一般状態の観察と兼ねて行った。

6.11.2 詳細な一般状態の観察、機能検査、握力及び自発運動量の測定

詳細な一般状態の観察は全個体について行った。雄及び非交配群は投与期間中及び回復期間中毎週1回、交配群雌は交配前投与期間中毎週1回、交配期間中、妊娠期間中及び授乳期間中は指定された日（交尾動物は妊娠1、7、14及び20日、未交尾動物は交配開始後6及び13日、分娩動物は授乳4日）にそれぞれ行った。

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

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

注：交配群雌の検査対象動物を以下に示した。

試験群	動物番号
対照群	1102、1103、1104、1108、1112
低用量群	2102、2103、2104、2105、2112
中用量群	3101、3102、3103、3104、3108
高用量群	4101、4105、4106、4110、4111

1) 詳細な一般状態の観察

ケージ内観察は姿勢、痙攣、異常行動を、手に持つての観察はケージからの取り出し易さ、被毛・皮膚の状態、眼・鼻の分泌物、眼球突出、眼瞼閉鎖状態、可視粘膜、自律神経機能（流涙、流涎、立毛、瞳孔径、異常呼吸）、ハンドリングに対する反応、ハンドリング時の発声を、オープンフィールド内観察は覚醒状態、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）を調べた。

2) 機能検査

検査は聴覚反応、接近反応、接触反応、痛覚反応、瞳孔反射、空中正向反射、着地開脚幅とした。

3) 握力測定

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

4) 自発運動量の測定

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

6.11.3 体重測定

全個体について、交配群の雄及び非交配群の雌は投与 1、8、15、22、29、36、42 日及び剖検日に、回復動物は更に回復 1、8、14 日及び剖検日に、交配群の雌は投与 1、8、15 及び 22 日、妊娠 0、7、14 及び 20 日、授乳 0 及び 4 日並びに剖検日に体重を測定した。なお、午後の分娩観察時に分娩の終了が確認された個体の授乳 0 日の体重測定（13:24~17:01 の間）を除き、体重測定は測定日の 07:38~10:44 の間（投与期間中は投与前）に行った。剖検日には、前日から約 16 時間絶食させた後、相対器官重量算出に備えて体重を 07:33~08:59 の間に測定した。また、死亡動物及び妊娠 25 日未分娩動物については、搬出前に体重を測定したが統計解析からは除外した。

6.11.4 摂餌量測定

全個体について、交配群の雄及び非交配群の雌は投与 2、8、15、30、36 及び 42 日に、回復動物は更に回復 2、8 及び 14 日に、交配群の雌は投与 2、8 及び 15 日、妊娠 1、7、14 及び 20 日並びに授乳 2 及び 4 日に残餌量を測定し、前日の給餌量との差から 1 匹当たりの 1 日摂餌量を算出した。給餌量及び残餌量の測定は測定日の 07:38~11:07 の間（投与期間中は投与前）に行った。

6.11.5 膣垢検査

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

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

6.11.6 交配方法

交配前投与期間終了後、交配群の同じ投与群内の雌雄を 1:1 で終夜同居させ、翌朝、膣栓形成あるいは膣垢中に精子を確認したものを交尾成立とみなした。交配開始日を

0日と起算して交尾までに要した日数を求めた。同一雌雄による同居期間は最長14日間であった。

6.11.7 分娩及び哺育観察

1) 母動物の観察

交尾成立雌動物は、妊娠21日から妊娠25日の午前まで1日2回（午前・午後、妊娠25日は午前に1回）、分娩の有無並びにその終了を確認するとともに分娩状態（胎盤の処理及び出産児の状態）を観察した。交尾成立から分娩終了までを妊娠期間とし、妊娠期間を0.5日単位で求めた。ただし、1日単位で集計した。なお、分娩終了の確認は17:00までとした。

分娩が終了した母動物は授乳4日まで出生児を哺育させ、児集め、営巣及び授乳を指標として哺育状態を観察し、授乳5日に病理学検査に供した。なお、妊娠25日の午前までに分娩が終了しなかった対照群、100及び300 mg/kg投与群の各1、1及び2例（動物番号1111、2110、3105及び3109）は、イソフルラン麻酔下で採血後、腹大動脈切断により放血致死させ、病理学検査に供した。妊娠の有無を確認した結果、着床が認められなかったため不妊とみなした。

2) 出生児の観察

生後0日に出生児数及び死産児数を数え、合わせて出産児数とした。出産児は口腔内を含む外表異常^(注)の有無を肉眼的に観察して性別を確認した。出生児は体重を個別に測定した後、母動物に哺育させた。死産児はブアン液で固定して保存した。

生後4日まで毎日1回、死亡児の有無を確認した。死亡児は肉眼による異常の有無を観察した後、ブアン液で固定して保存した。生後4日に全生存児の性別を確認し、個別に体重を測定した。口腔内を含む外表異常の有無を肉眼的に観察した後、イソフルラン深麻酔下でブアン液に浸漬し、固定して保存した。

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

6.11.8 尿検査（摂水量測定を含む）

投与期間終了週（投与 6 週、投与 37~38 日）及び回復期間終了週（回復 2 週、回復 9~10 日）に検査を実施した。投与期間中は検査当日の投与後に各群の 5 匹（雄の群内番号 8~12 番、非交配群の群内番号 18~22 番）について、回復期間中は回復動物の全個体について、それぞれ採尿器をセットしたケージに収容し、絶食・自由摂水下で 4 時間尿を、次いで自由摂食・自由摂水下でその後の 20 時間尿を採取した。検査項目を表 2. に示した。採取した最初の 4 時間尿について pH 以下沈渣までの検査と尿量を、その後得られた 20 時間尿について浸透圧、電解質（ナトリウム、カリウム及び塩素）及び尿量の測定を行った。尿量は 4 時間の尿量と 20 時間の尿量を合計して 1 日量を算出した。電解質は 20 時間尿について濃度を測定し、測定濃度と 24 時間の尿量から 1 日当たりの排泄量を算出した。摂水量は、採尿器をセットしたケージに収容した状態で前日からの 1 日の摂取量を、給水瓶を用いて測定した。

表 2.尿検査の項目、測定法及び使用機器など

検査項目	測定方法
pH	マルティステイクス試験紙 [シーメンスヘルスケア・タ [®] イアグ [®] ノスティクス株式会社] ^{a)}
たん白質	マルティステイクス試験紙 [シーメンスヘルスケア・タ [®] イアグ [®] ノスティクス株式会社] ^{a)}
ケトン体	マルティステイクス試験紙 [シーメンスヘルスケア・タ [®] イアグ [®] ノスティクス株式会社] ^{a)}
グルコース	マルティステイクス試験紙 [シーメンスヘルスケア・タ [®] イアグ [®] ノスティクス株式会社] ^{a)}
潜血	マルティステイクス試験紙 [シーメンスヘルスケア・タ [®] イアグ [®] ノスティクス株式会社] ^{a)}
ビリルビン	マルティステイクス試験紙 [シーメンスヘルスケア・タ [®] イアグ [®] ノスティクス株式会社] ^{a)}
ウロビリノーゲン	マルティステイクス試験紙 [シーメンスヘルスケア・タ [®] イアグ [®] ノスティクス株式会社] ^{a)}
色調	肉眼観察
沈渣	鏡検法
尿量（4 時間量）	目盛付スピッツ管を用いた容量測定（単位：mL）
浸透圧	氷点降下法 ^{b)} （単位：mOsm/kg）
ナトリウム	イオン選択電極法 ^{c)} （単位：mmol/24h）
カリウム	イオン選択電極法 ^{c)} （単位：mmol/24h）
塩素	イオン選択電極法 ^{c)} （単位：mmol/24h）
尿量（20 時間量）	メスシリンダーを用いた容量測定（単位：mL）
摂水量（24 時間量）	重量測定
使用測定機器	
a)：尿自動分析装置 クリニテック 500 (Siemens Healthcare Diagnostics Inc., Illinois, USA)	
b)：自動浸透圧測定装置 オートアンドスタット OM-6030 (アークレイ株式会社)	
c)：臨床化学自動分析装置 TBA-120FR 形 (東芝メディカルシステムズ株式会社)	

6.11.9 血液学検査

全例について、剖検前日（最終投与日あるいは回復 14 日）から一夜（16~18 時間）絶食させた。そのうちの各群雌雄各 5 匹（動物番号が若い順、ただし、交配群雌は分娩順の 5 匹^注）について、イソフルラン麻酔下に開腹し、腹大動脈から EDTA-2K 加採血瓶（SB-41：シスメックス株式会社）に血液を採取した。得られた血液について、次の表 3.-1)に記載した項目及び方法により検査した。なお、採血した全例について、May-Grünwald-Giemsa 染色法による血液塗抹標本を作製した。また、3.8%クエン酸ナトリウム溶液加試験管（血液 9 容に対し 1 容の割合）に採取した血液を遠心分離（3,000 rpm、1,600×g、10 分間）し、得られた血漿について表 3.-2)に記載の項目及び方法により検査した。妊娠 25 日未分娩動物についても採血し同様に検査したが、その成績は統計解析から除外した。

注：交配群雌の検査対象動物を以下に示した。

試験群	動物番号
対照群	1102、1103、1104、1108、1112
低用量群	2102、2103、2104、2105、2112
中用量群	3101、3102、3103、3104、3108
高用量群	4101、4105、4106、4110、4111

表 3.血液学検査の項目、測定法及び使用機器など

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

6.11.10 血液化学検査

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

表 4.血液化学検査の項目、測定法及び使用機器など

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

6.11.11 血中ホルモン測定

他の観察及び検査結果から下垂体-甲状腺系への影響が認められなかったため 6.11.10 で得られた血清について血中ホルモン（T₃、T₄ 及び TSH）測定は実施しなかった。

6.11.12 病理学検査

1) 剖検及び器官重量測定

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

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

2) 病理組織学検査

全ての個体について、以下に示す全検査対象器官/組織をリン酸緩衝 10 vol%ホルマリン液で固定し、保存した。固定時に肺にはリン酸緩衝 10 vol%ホルマリン液を注入した。ただし、眼球、視神経はリン酸緩衝液で調製した 3 vol%グルタルアルデヒド・2.5 vol%ホルマリン液で固定後、精巣及び精巣上体はブアン液で固定した後、リン酸緩衝 10 vol%ホルマリン液に置換し保存した。次いで、投与終了時及び回復終了時の計画剖検時に採血を実施した各群雌雄各 5 匹（動物番号が若い順、ただし、交配群雌は分娩順の 5 匹）並びに死亡動物、妊娠 25 日未分娩動物及びその交配相手雄についてパラフィン包埋した後、切片とし（下線を施した器官・組織は固定・保存のみとした）、ヘマトキシリン・エオジン（H・E）染色標本作製した。

鏡検は、まず投与終了時剖検群における対照群及び高用量群の採血を行った動物、並びに死亡動物、不妊であった妊娠 25 日未分娩動物及びその交配相手雄の全検査対象器官/組織について行った。両側性の器官については両側を摘出し、坐骨神経、眼球、甲状腺、上皮小体、副腎、顎下腺、腎臓、乳腺（鼠径部）、大腿骨（骨髄を含む）及び大腿部骨格筋は片側、精巣、卵巣、精巣上体及び精嚢（凝固腺含む）は両側並びに子宮は両角部を鏡検した。なお、舌下腺、視神経及び皮膚（鼠径部）は H・E 染色標本作製までとし、病理組織学検査は実施しなかった。その結果、雌雄の胃については、被験物質投与による影響が疑われたため、低、中用量群及び回復動物についても鏡検を行った。

大脳、小脳（橋を含む）、坐骨神経、脊髄（胸部）、眼球、視神経、ハーダー腺、下垂体、甲状腺、上皮小体、副腎、胸腺、脾臓、顎下リンパ節、腸間膜リンパ節、

心臓、胸大動脈、気管、肺（気管支を含む）、舌、喉頭、食道、胃、十二指腸、空腸、回腸（パイエル板を含む）、盲腸、結腸、直腸、顎下腺、舌下腺、肝臓、膵臓、腎臓、膀胱、精巣、卵巣、精巣上体、子宮、陰、前立腺、精嚢（凝固腺を含む）、皮膚（鼠径部）、乳腺（鼠径部）、胸骨（骨髄を含む）、大腿骨（骨髄を含む）、大腿部骨格筋、個体識別部（耳標を装着した耳介）

6.12 統計解析

6.12.1 パラメータの算出

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

性周期異常率(%) = (性周期異常を示した個体数/観察雌個体数) × 100

交尾率(%) = (交尾動物数/同居動物数) × 100

授精率(%) = (雌を妊娠させた雄の数/交尾した雄の数) × 100

受胎率(%) = (妊娠した雌の数/交尾した雌の数) × 100

出産率(%) = (出生児出産雌数/妊娠雌数) × 100

妊娠期間(日) = 妊娠0日から分娩した日までの日数

着床率(%) = (着床痕数/黄体数) × 100

分娩率(%) = (出産児数/着床痕数) × 100

死産児率(%) = (死産児数/出産児数) × 100

外表異常率(%) = (外表異常児数/出産児数) × 100

出生率(%) = (出生児数/出産児数) × 100

生後4日生存率(%) = (生後4日の生存児数/出生児数) × 100

生後0日（死産児含む）の性比 = 雄出産児数/出産児数

生後0日（出生児）の性比 = 雄出生児数/出生児数

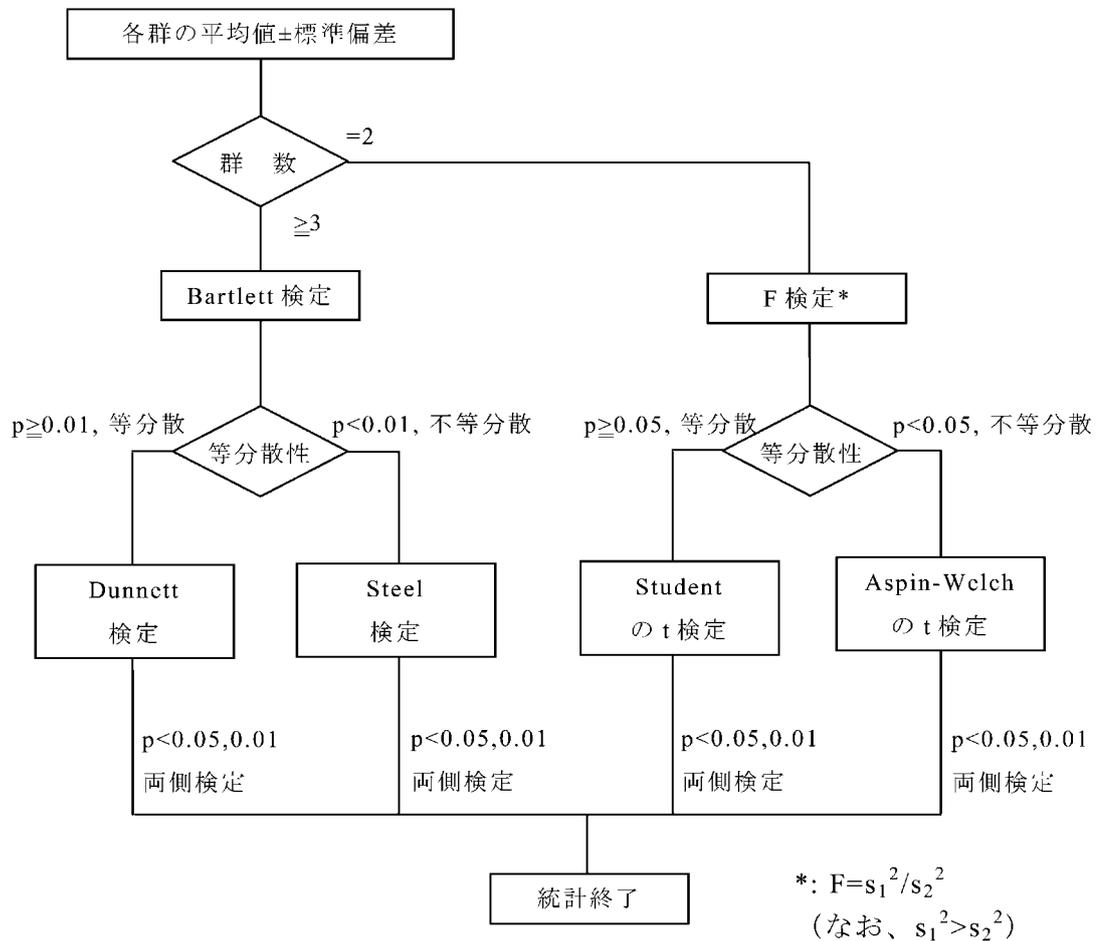
生後4日の性比 = 生後4日の雄生存児数/生後4日の生存児数

6.12.2 検定

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

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

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



着床率、分娩率、出生率、死産児率、外表異常率及び生後4日生存率については、群ごとに平均値及び標準偏差を求め、Wilcoxonの順位和検定(有意水準0.05及び0.01、両側)を行った[6]。

性周期異常率、交尾率、授精率、受胎率及び出産率並びに聴覚反応、接近反応、接触反応、痛覚反応、瞳孔反射及び空中正向反射の各反応・反射率は、各群の性周期異常を示した個体数、交尾動物数、雌を妊娠させた雄動物数、妊娠雌動物数、出生児・出産雌動物数、正常反射のみられた動物数より算出し、期待度数が5以下のセルがみられたためFisherの直接確率計算法により検定(有意水準0.05及び0.01、両側)を行った[7]。

7. 試験結果

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

1000 mg/kg 投与群の交配群雌 1 例 (動物番号 4104) が妊娠 22 日に自発運動の減少を呈し、妊娠 23 日に死亡した。その他にはいずれの投与群においても死亡動物はみられず、いずれの動物にも投与期間及び回復期間を通じて哺育状態を含め異常はみられなかった。

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

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

いずれの動物にも投与期間及び回復期間とも異常はみられなかった。

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

いずれの動物にも投与期間及び回復期間とも被験物質投与に関連すると考えられる異常はみられなかった。

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

いずれの動物にも投与期間及び回復期間とも被験物質投与に関連すると考えられる異常はみられなかった。

なお、1000 mg/kg 投与群の交配群雌で投与 1 週の立ち上がり回数に対照群と比べ有意な低値が認められたが、非交配群雌の同時点に異常はないことから偶発性と判断した。同群では、妊娠 14 及び 20 日の立ち上がり回数に対照群と比べ有意な低値が認められたが、その他の詳細な一般状態に異常はみられず、いずれも個体値は試験施設の背景データ (妊娠 14 日: 6 ± 4 、妊娠 20 日: 5 ± 4 、Mean \pm 2S.D.、N=149、2009/04-2014/03) の範囲内であることから生理的変動範囲内の偶発的な有意差と判断した。1000 mg/kg 投与群の非交配群雌で投与 3 週の立ち上がり回数に対照群と比べ有意な高値が認められたが、一過性の変化であり前後の観察時点及びその他の詳細な一般状態に異常はないことから偶発性と判断した。排糞の個数には対照群と各被験物質投与群との間に有意差は認められなかった。

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

1) 投与期間終了週検査

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

2) 回復期間終了週検査

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

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

1) 投与期間終了週測定

1000 mg/kg 投与群の非交配群雌で前肢の握力に対照群と比べ有意な高値が認められたが、前肢のみの変化であり、その他の詳細な一般状態に異常はみられず、個体値は試験施設の背景データ (1072±382、Mean±2S.D.、N=65、2009/04-2014/03) の範囲内であることから生理的変動範囲内の偶発的な有意差と判断した。その他には対照群と各被験物質投与群との間に有意差は認められなかった。

2) 回復期間終了週測定

対照群と 1000 mg/kg 投与群との間に有意差は認められなかった。

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

1) 投与期間終了週測定

いずれの投与群にも被験物質投与に関連すると考えられる変化はみられなかった。

なお、300 mg/kg 投与群の交配群雌で 10-20 分間の運動量に対照群と比べ有意な高値が認められたが、用量と関連しない偶発的な有意差と判断した。

2) 回復期間終了週測定

対照群と 1000 mg/kg 投与群との間に有意差は認められなかった。

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

1) 投与期間

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

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

2) 回復期間

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

雌では 1000 mg/kg 投与群の回復 8 日の体重に対照群と比べ有意な高値が認められたが、一過性であり、回復期間中の増加量に変化はないことから、偶発性と判断した。

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

1) 投与期間

雄では 300 及び 1000 mg/kg 投与群で投与 42 日の摂餌量に対照群と比べ有意な高値

が認められたが、対照群の低値に起因した相対的な高値であることから、偶発性と判断した。その他の時点ではいずれの被験物質投与群も対照群と同様な摂餌量を示し、有意差は認められなかった。

交配群雌では 100 mg/kg 投与群で授乳 4 日の摂餌量に対照群と比べ有意な低値が認められたが、用量と関連しないことから偶発的な有意差と判断した。その他には交配前、妊娠及び授乳の各期間中、各被験物質投与群ともに対照群と同様な摂餌量を示し、有意差は認められなかった。

非交配群雌では投与期間を通じ対照群と同様な摂餌量を示し、対照群と 1000 mg/kg 投与群との間に有意差は認められなかった。

2) 回復期間

対照群と 1000 mg/kg 投与群との間に有意差は認められなかった。

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

1) 投与期間終了週検査

定性項目については、1000 mg/kg 投与群の雄及び非交配群雌で尿 pH の低値傾向が認められた。

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

2) 回復期間終了週検査

定性項目については、いずれの動物にも異常はみられなかった。

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

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

1) 投与期間終了時検査

雄では 100 mg/kg 投与群で対照群と比べ赤血球数の有意な高値が認められたが、用量と関連しないことから偶発的な有意差と判断した。

交配群雌では 100 mg/kg 投与群で対照群と比べ白血球分画におけるリンパ球比率に有意な低値、好中球比率に有意な高値が認められたが、いずれも用量と関連しないことから偶発的な有意差と判断した。

非交配群雌では 1000 mg/kg 投与群で対照群と比べ平均赤血球容積に有意な低値（対照群と比べ-2%）が認められたが、軽微な変化であり他の赤血球系パラメータに変動はないことから偶発性と判断した。また、好中球数に有意な低値が認められたが、分画比率に異常はないことから、偶発的な有意差と判断した。

2) 回復期間終了時検査

1000 mg/kg 投与群の雄では対照群と比べ活性化部分トロンボプラスチン時間に有意な延長、大型非染色球数に有意な高値が認められたが、投与期間終了時検査には異常はなく、他の血液凝固系パラメータに異常はないこと、あるいは白血球に占める割

合の少ない分画における絶対数のみの変動であること、白血球数等の関連項目に異常はないことから、いずれも偶発的な有意差と判断した。

1000 mg/kg 投与群の雌では対照群と比べ網赤血球率に有意な低値、リンパ球比率に有意な高値が認められたが、投与期間終了時検査には異常はなく、他の赤血球系パラメータあるいは白血球数等の関連項目に異常はみられないことから、偶発的な有意差と判断した。また、好中球数に有意な低値が認められたが、分画比率に異常はないことから、偶発的な有意差と判断した。

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

1) 投与期間終了時検査

雄では 300 mg/kg 投与群でグルコースに対照群と比べ有意な高値が認められたが、用量と関連しないことから偶発的な有意差と判断した。

交配群雌では 100 及び 1000 mg/kg 投与群で ALT に対照群と比べ有意な低値が認められたが、通常毒性とする高値ではなく低値であり明確な用量との相関性はないことから、生理的変動範囲内の偶発的な有意差と判断した。また、1000 mg/kg 投与群で尿素窒素に対照群と比べ有意な低値が認められたが、通常毒性とする高値ではなく低値であり、毒性学的意義はないと判断した。

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

2) 回復期間終了時検査

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

1000 mg/kg 投与群の雌で対照群と比べナトリウム及び塩素に有意な低値が認められたが、軽微な変化 (対照群と比べ-2~-1%) であり投与期間終了時検査には異常がないことから生理的変動範囲内の偶発的な有意差と判断した。

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

1) 投与期間終了時検査

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

2) 回復期間終了時検査

1000 mg/kg 投与群の雄で心臓、脾臓及び精巣上体の絶対重量に対照群と比べ有意な高値が認められたが、絶対重量のみの軽微な変化であり投与終了時検査には異常はないことから偶発的な有意差と判断した。

1000 mg/kg 投与群の雌で腎臓の絶対及び相対重量に対照群と比べ有意な高値が認められたが、非交配群雌の投与終了時検査における対照群と同等の値であり、いずれも個体値は試験施設の背景データ (絶対重量: 1.90 ± 0.32 、相対重量: 0.68 ± 0.12 、 $\text{Mean} \pm 2\text{S.D.}$ 、 $N=65$ 、2009/04-2014/03) のほぼ範囲内であることから、生理的変動範囲内の偶発的な有意差と判断した。

7.9 剖検所見 (Table 9-1~9-7、Appendix 9-1~9-116)

1) 投与期間終了時検査

いずれの動物にも被験物質投与に起因すると考えられる変化はみられなかった。

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

妊娠 23 日に死亡した 1000 mg/kg 投与群の交配群雌 1 例 (動物番号 4104) で前胃に暗赤色巣がみられた。

妊娠 25 日未分娩 (不妊) であった対照群、100 及び 300 mg/kg 投与群の各 1、1 及び 2 例 (動物番号 1111、2110、3105 及び 3109) では肉眼的異常はみられなかった。

2) 回復期間終了時検査

対照群の雌 1/5 例で腺胃に暗赤色巣がみられたが、偶発性変化と考えられた。その他にはいずれの動物にも肉眼的異常はみられなかった。

7.10 病理組織学検査 (Table 10-1~10-19、Appendix 9-1~9-116)

1) 投与期間終了時検査

被験物質投与の影響と考えられる変化が、雄及び非交配群雌の胃にみられた。総括を表 5-1.及び 5-2.に示した。なお、交配群雌については、被験物質投与の影響が疑われたため、低、中用量群についても検索を行ったが、授乳 5 日の母動物の生理的範囲内の組織像であると判断されたことから被験物質投与の影響を否定した。

胃 : 1000 mg/kg 投与群の雄及び非交配群雌に境界縁の扁平上皮過形成がみられた。

表 5-1.病理組織学検査所見 (雄) の総括 (胃)

器官/組織 所見	投与量(mg/kg): 検査例数:	性別: 雄			
		群: 交配群			
		0	100	300	1000
胃		5	6	6	5
境界縁の扁平上皮過形成		0	0	0	1
軽微		0	0	0	1

表 5-2.病理組織学検査所見 (交配及び非交配群雌) の総括 (胃)

器官/組織 所見	投与量(mg/kg): 検査例数:	性別: 雌				雌	
		群: 交配群				非交配群	
		0	100	300	1000	0	1000
胃		6(5/1)*	6(5/1)*	7(5/2)*	6(5/1)**	5	5
境界縁の扁平上皮過形成		0(0/0)	0(0/0)	0(0/0)	0(0/0)	0	3
軽微		0(0/0)	0(0/0)	0(0/0)	0(0/0)	0	3

()* 内は(授乳 4 日母動物/25 日未分娩動物)

()** 内は(授乳 4 日母動物/死亡動物)

妊娠 23 日に死亡した 1000 mg/kg 投与群の交配群雌 1 例（動物番号 4104）では、大腿骨の骨髄細胞数の減少、腸間膜リンパ節、顎下リンパ節、脾臓及び胸腺の萎縮、副腎の皮質細胞の肥大がみられた。

妊娠 25 日未分娩（不妊）であった対照群、100 及び 300 mg/kg 投与群の各 1、1 及び 2 例並びにその交配相手雄では、いくつかの器官/組織に組織学的変化がみられたが、不妊を示唆する変化はみられなかった。

その他、各被験物質投与群に種々の変化がみられたが、その発現状況から偶発性変化と判断した。

2) 回復期間終了時検査

1000 mg/kg 群の雌の胃で軽微な境界縁の扁平上皮過形成が 1/5 例にみられた。

7.11 性周期 (Table 11、Appendix 10-1~10-4)

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

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

対照群の 1 組を除き、交配 4 日までに全例の交尾が成立し、交尾までに要した日数、交尾率、授精率及び受胎率には対照群と各被験物質投与群との間に有意差は認められなかった。なお、妊娠 25 日未分娩（不妊）動物が、対照群、100 及び 300 mg/kg 投与群の各 1、1 及び 2 例にみられたが、用量との関連性はなく、偶発性にも発現しうることから、被験物質投与による影響は否定した。

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

出産率、妊娠期間、黄体数、着床痕数、分娩率、死産児率及び外表異常率には対照群と各被験物質投与群との間に有意差は認められなかった。なお、対照群と比べ 300 mg/kg 投与群で着床率に有意な高値、100 mg/kg 投与群で出生児数に有意な低値が認められたが、用量と関連しないことからいずれも偶発的な有意差と判断した。

妊娠動物の分娩状態では妊娠 23 日に死亡した 1000 mg/kg 投与群の 1 例（動物番号 4104）を除き全例が妊娠 21 から 23 日に分娩し、胎盤及び羊膜の処理は正常に行われ、哺育状態ではいずれの母動物にも児集め、営巣及び授乳行動に異常はみられなかった。

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

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

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

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

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

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

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

いずれの死亡児にも肉眼的異常はみられなかった。

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

いずれの出生児にも肉眼的異常はみられなかった。

8. 考察

グルタル酸ジメチルの 0（対照群：コーン油）、100、300 及び 1000 mg/kg を Sprague-Dawley 系 SPF ラットの雄には交配前 14 日間に加え交配期間を通して剖検前日まで（42 日間）、雌には交配前 14 日間に加え交配期間及び妊娠期間を通して授乳 4 日まで（41~55 日間）、非交配群雌には 42 日間強制経口投与し、反復投与毒性及び生殖発生毒性を検討した。更に、0 及び 1000 mg/kg 群の一部の動物については、雌雄ともに 42 日間投与した後、14 日間の回復期間を設け、毒性変化の可逆性を検討した。

8.1 反復投与毒性

いずれの投与群においても、一般状態、詳細な一般状態、機能検査、握力、自発運動量、体重、摂餌量、尿検査の定量項目（摂水量を含む）、血液学検査、血液化学検査、剖検及び器官重量には被験物質投与の影響は認められなかった。

1000 mg/kg 投与群の雄及び非交配群雌で尿 pH に低値傾向が認められたが、腎臓及び尿路系の病理組織に異常はみられないことから、毒性学的意義はないと判断した。

交配群雌の 1000 mg/kg 投与群で妊娠 23 日に 1 例が死亡した。死亡前の一般状態に自発運動の減少がみられたが、死亡までの体重及び摂餌量に異常はみられなかった。病理学検査では肉眼的に前胃の暗赤色巣がみられ、組織学的には前胃の潰瘍、リンパ・造血器系組織の萎縮（大腿骨の骨髓細胞数の減少、腸間膜リンパ節、顎下リンパ節、脾臓及び胸腺の萎縮）、副腎の皮質細胞の肥大がみられたが、死因は不明であった。死亡動物は 1 例のみの発現で、同様の変化は、他の投与終了時剖検群の雄、雌（交配群及び非交配群）にはみられないことから、被験物質投与と関連しない動物の状態悪化及びストレスに伴った変化である可能性が推察されたが、偶発的な死亡とは断定できない。

病理組織学検査では、胃に境界縁の扁平上皮過形成が 1000 mg/kg 投与群の雄及び雌（非交配群）でみられ、被験物質投与の影響と考えられた。これらの変化は、回復終了時に雄では消失し、雌（非交配群）では頻度が軽減したことから病変の回復性がみられた。

8.2 生殖発生毒性

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

出生児では、生後 0 日の外表観察、生後 0 及び 4 日の雌雄体重並びに性比、死亡児の肉眼観察所見、生後 4 日の生存率及び肉眼観察所見に被験物質投与による影響は認

R-1134

められないことから、1000 mg/kg 投与群においても児の子宮内発生、発育及び分化並びに生存性などへの影響はないと判断した。

これらの結果から、本試験条件下でグルタル酸ジメチルを反復経口投与することにより、1000 mg/kg 投与群の交配群雌で妊娠 23 日に 1 例が死亡し、雄及び雌（非交配群）で尿 pH に低値傾向、胃に境界縁の扁平上皮過形成が認められたが、その他に被験物質に起因すると考えられる変化はみられなかった。したがって、本被験物質の反復投与毒性に対する無影響量及び無毒性量は雌雄ともに 300 mg/kg と判断した。また、雌雄親動物と児動物における生殖発生毒性に対する無影響量及び無毒性量はいずれも 1000 mg/kg と判断した。

9. 文献

- [1] ██████████: グルタル酸ジメチルの IR を用いた特性試験及び安定性試験並びに GC を用いた被験液 (媒体: コーン油) 中濃度測定法バリデーション及び安定性試験 (株式会社ボゾリサーチセンター 御殿場研究所、試験番号: A-2584、2013 年)

- [2] ██████████: グルタル酸ジメチルのラットを用いた 14 日間反復経口投与毒性試験 (投与量設定試験) (株式会社ボゾリサーチセンター、試験番号: N-R041、2013 年)

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

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

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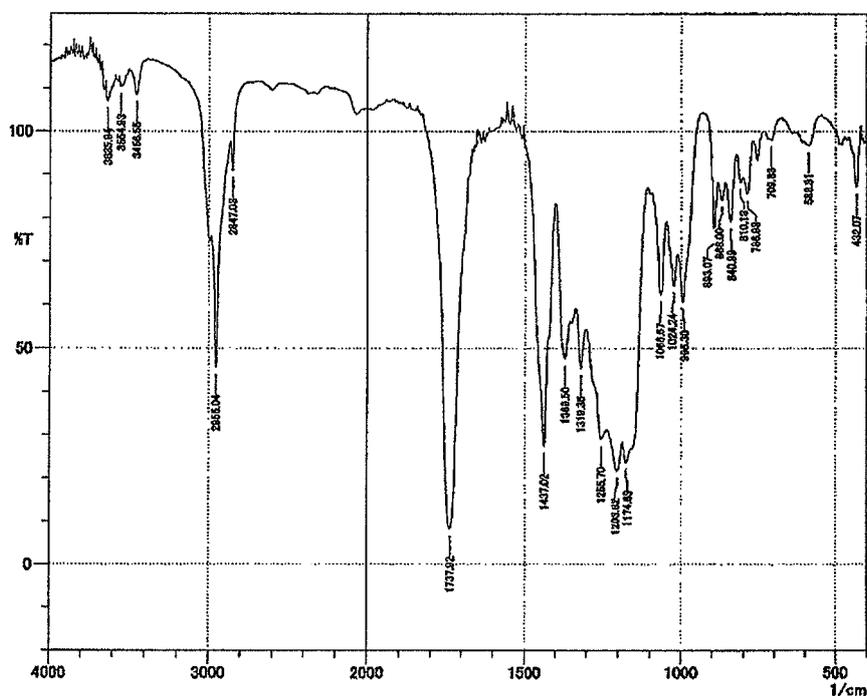
- [6] Siegel S, Castellan NJ. Jr. Nonparametric statistics for the behavioral sciences. 2nd ed. New York: McGraw-Hill; 1988.

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試験番号：A-2584

試験成績書
(グルタル酸ジメチルの特性)

ステージ : 初期値
測定日 : 2013年9月3日
被験物質 : グルタル酸ジメチル
(ロット番号：AVBRN)
測定項目 : 赤外吸収スペクトル (液膜法)
結果 : 特性のスペクトルを以下に示す。



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

[Redacted Signature]

2013 年 10 月 1 日

試験責任者
株式会社ボゾリサーチセンター 御殿場研究所

試験成績書
(被験物質の安定性)

ステージ : 投与期間終了後

測定日 : 2013年12月11日
2013年9月3日 (特性のスペクトル¹⁾)

被験物質 : グルタル酸ジメチル
(ロット番号：AVBRN)

測定項目 : 赤外吸収スペクトル (液膜法)

判定基準 : 安定性のスペクトルを特性のスペクトル¹⁾と比較する
とき、同様な赤外吸収スペクトルである。
1) : グルタル酸ジメチルの IR を用いた特性試
験及び安定性試験並びに GC を用いた被験液 (媒体：
コーン油) 中濃度測定法バリデーション及び安定性試験
(株式会社ボゾリサーチセンター 御殿場研究所、試験
番号：A-2584)

結果 : 安定性のスペクトルを特性のスペクトルと比較したと
き、同様な赤外吸収スペクトルが得られた。なお、赤
外吸収スペクトルは次のページに示す。

判定 : 適

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

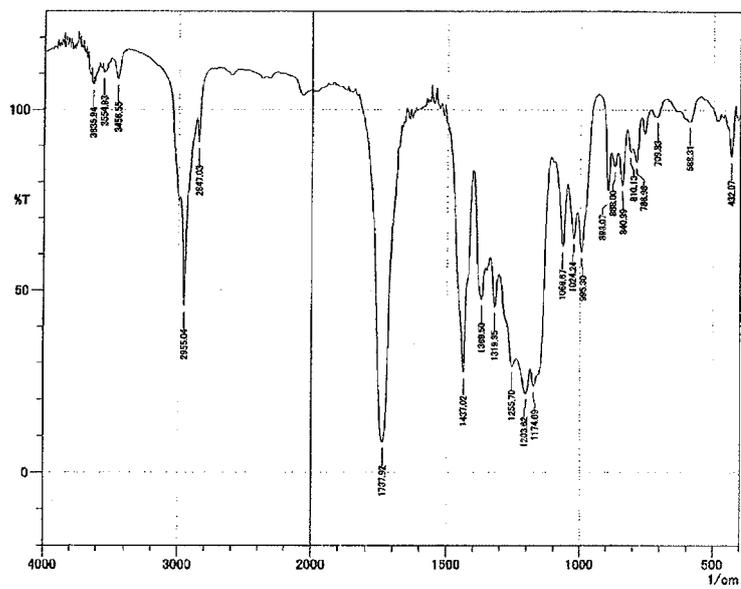
2013 年 12 月 25 日

化学分析責任者
株式会社ボゾリサーチセンター 御殿場研究所

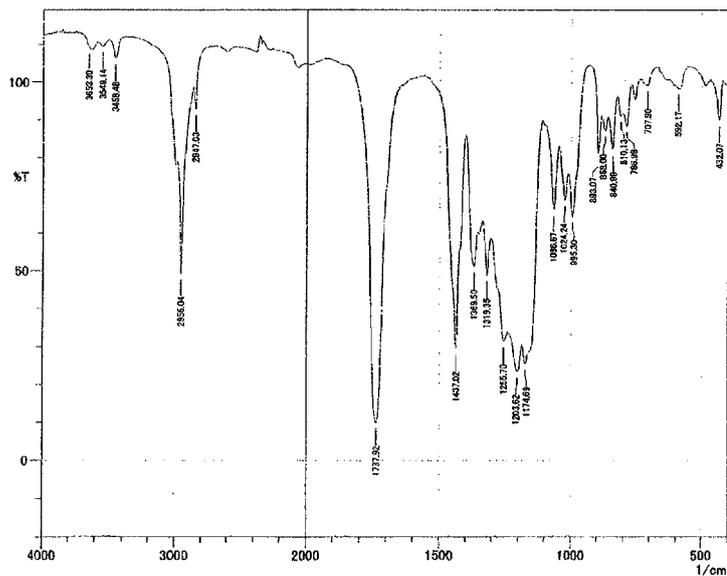
試験成績書
(被験物質の安定性)

結果 : 赤外吸収スペクトル

(特性のスペクトル)



(安定性のスペクトル)



試験番号 : A-2584

試験成績書
(被験液中グルタル酸ジメチルの安定性)

被験物質 : グルタル酸ジメチル
(ロット番号 : AVBRN)

形態 (媒体) : 溶液 (コーン油)

保存条件 : 褐色ガラス瓶にて、冷所 (冷蔵庫内、許容値 : 1~10°C)
又は室温保存

保存期間 : 冷所で 8 日間保存した後、室温で 24 時間保存

評価基準
安定性 : 残存率 {調製直後の測定濃度の平均値 (100) に対する保存後の測定濃度の平均値の割合} が 100.0±10.0% 以内。

結果 :

調製濃度 (mg/mL)	測定濃度 (mg/mL)		
	調製直後	冷所で 8 日間保存した後、 室温で 24 時間保存後	
1.00	1.04	1.02	
	1.05	1.03	
	1.06	1.01	
	平均値	1.05	1.02
	残存率 (%)	100	97.1
200	212	210	
	213	209	
	215	207	
	平均値	213	209
	残存率 (%)	100	98.1

判定 : 適

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

 2013 年 10 月 1 日
試験責任者
株式会社ボゾリサーチセンター 御殿場研究所

分析結果

試験番号 : R-1134
項目 : 濃度
ステージ : 初回投与
分析日 : 2013年10月10日

測定試料
被験物質 : グルタル酸ジメチル
(ロット番号: AVBRN)
形態 : 溶液
媒体 : コーン油
調製日 : 2013年10月10日

測定対象物質 : グルタル酸ジメチル

評価基準
濃度 : 表示値に対する割合 ; 100.0±10.0%

結果 :

表示値 (mg/mL)	測定濃度 (mg/mL)	平均値	表示値に対する割合 (%)
20	20.2	20.0	100.0
	19.9		
	20.0		
60	60.1	59.7	99.5
	59.8		
	59.2		
200	201	202	101.0
	202		
	203		

判定 : 適

分析結果

試験番号 : R-1134
項目 : 濃度
ステージ : 投与 6 週
分析日 : 2013 年 11 月 15 日

測定試料

被験物質 : グルタル酸ジメチル
(ロット番号 : AVBRN)
形態 : 溶液
媒体 : コーン油
調製日 : 2013 年 11 月 15 日

測定対象物質 : グルタル酸ジメチル

評価基準

濃度 : 表示値に対する割合 ; 100.0±10.0%

結果 :

表示値 (mg/mL)	測定濃度 (mg/mL)	平均値	表示値に対する割合 (%)
20	20.4	20.3	101.5
	20.1		
	20.4		
60	60.9	60.5	100.8
	59.1		
	61.6		
200	205	204	102.0
	204		
	203		

判定 : 適

グルタル酸ジメチルのラットを用いた
14日間反復経口投与毒性試験（投与量設定試験）における所見

試験番号：N-R041

被験物質	媒体 ^{a)}	グルタル酸ジメチル			
投与量(mg/kg)	0	100	300	1000	
投与容量 (mL/kg)	5	5	5	5	
使用動物数 (♂/♀)	5/5	5/5	5/5	5/5	
死亡動物数 (♂/♀)	0/0	0/0	0/0	0/0	
死亡発現時期	—	—	—	—	
一般状態	生存	—	—	—	
	死亡	—	—	—	
体重	—	—	—	—	
体重増加量	—	—	—	—	
摂餌量	—	—	—	—	
血液学検査	—	—	—	—	
血液化学検査	—	—	尿素窒素：↓(♂)	尿素窒素：↓(♂) 総たん白質：↓(♀)	
器官重量	絶対	—	腎臓：↑(♂)	—	
	相対	—	腎臓：↑↑(♂)	腎臓：↑(♂)	
剖検	生存	—	—	—	
	死亡	—	—	—	

a)：コーン油

—：著変なし

/：データなし又は判別不明あるいは検定不能

↑又は↓；p<0.05，↑↑又は↓↓；p<0.01，(対照群との間に有意差あり)

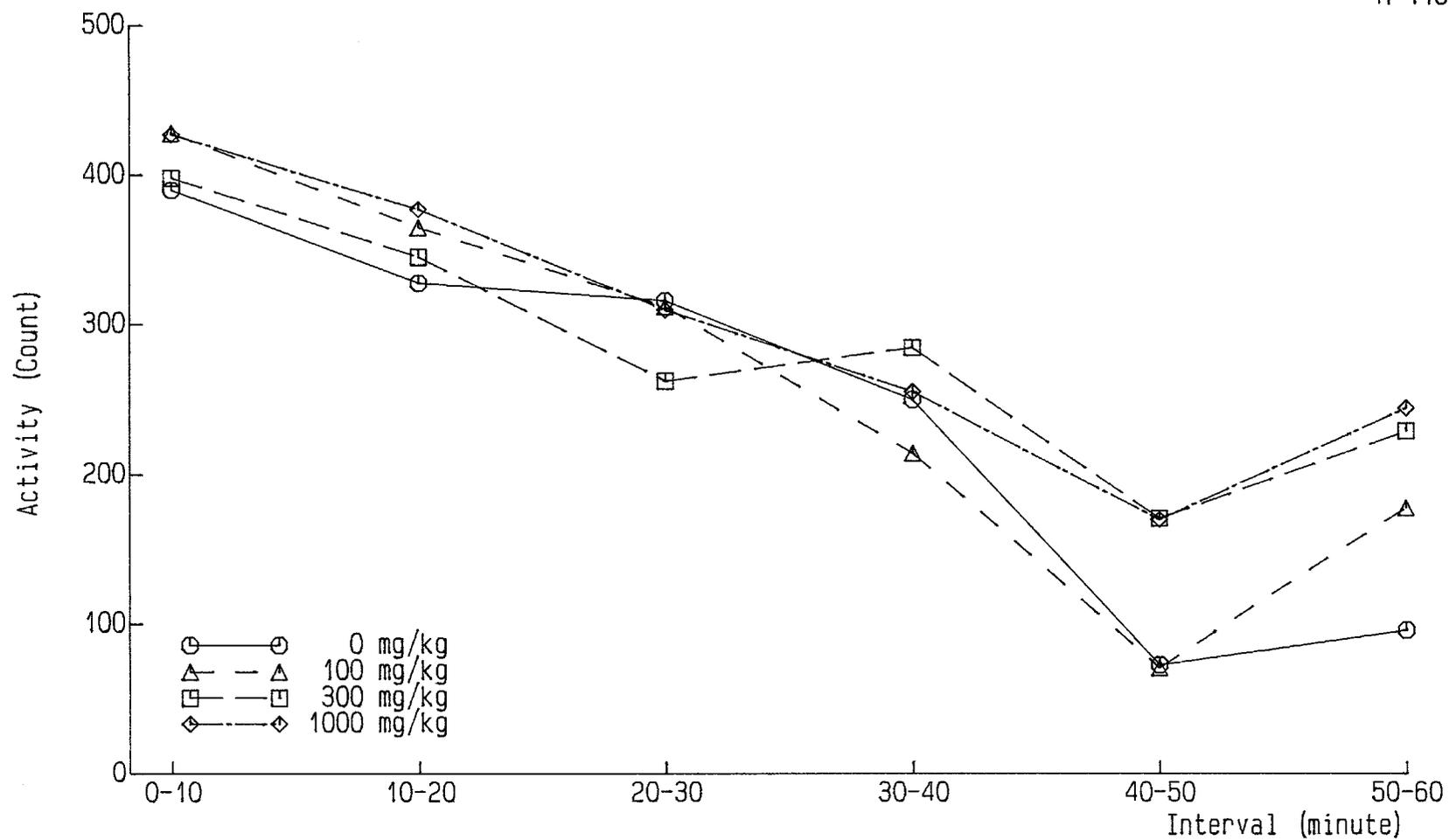


Fig.1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Motor activity of male rats (Week 6 of administration)

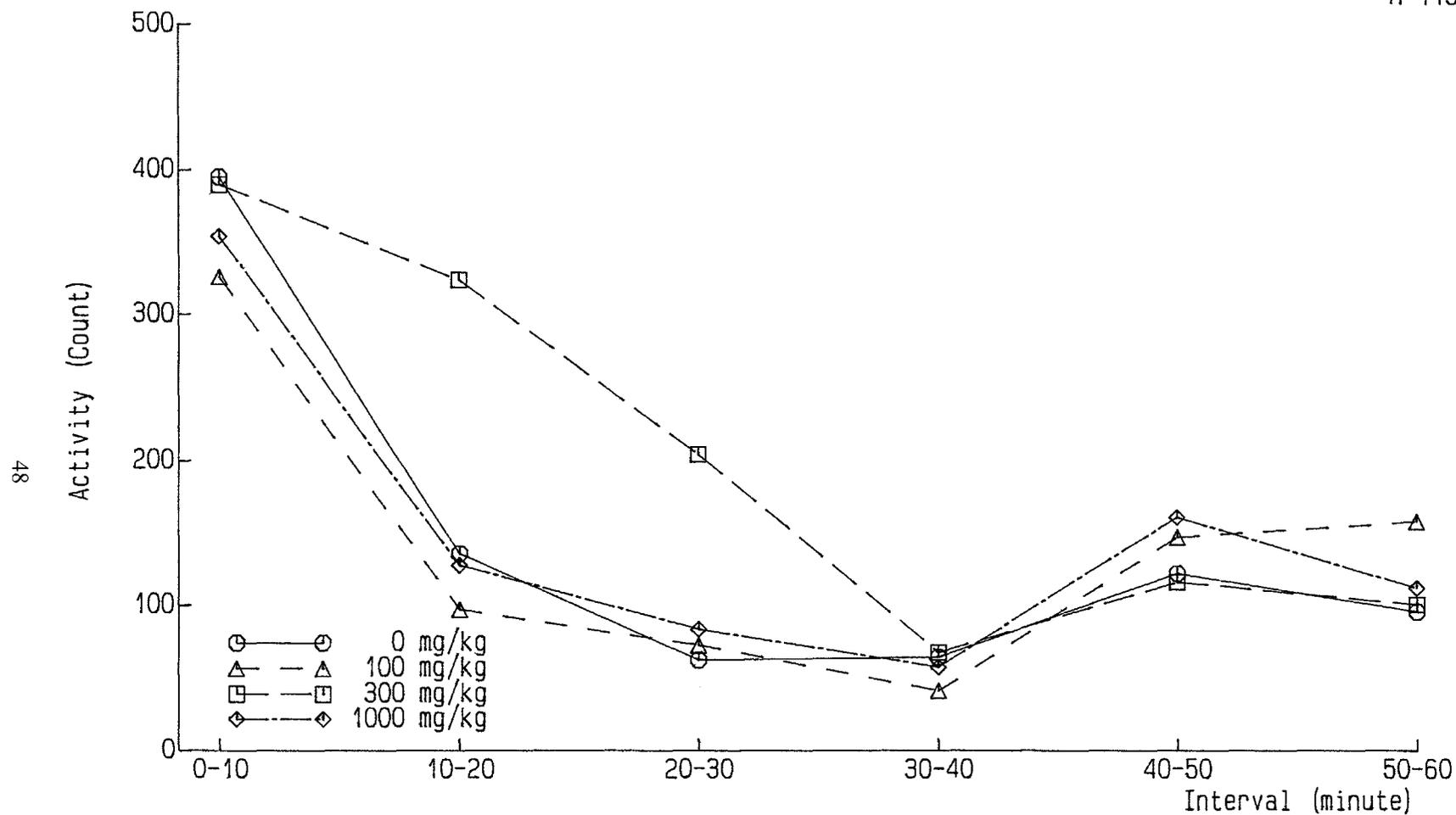


Fig.2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Motor activity of female rats (Main group, Lactation day 4)

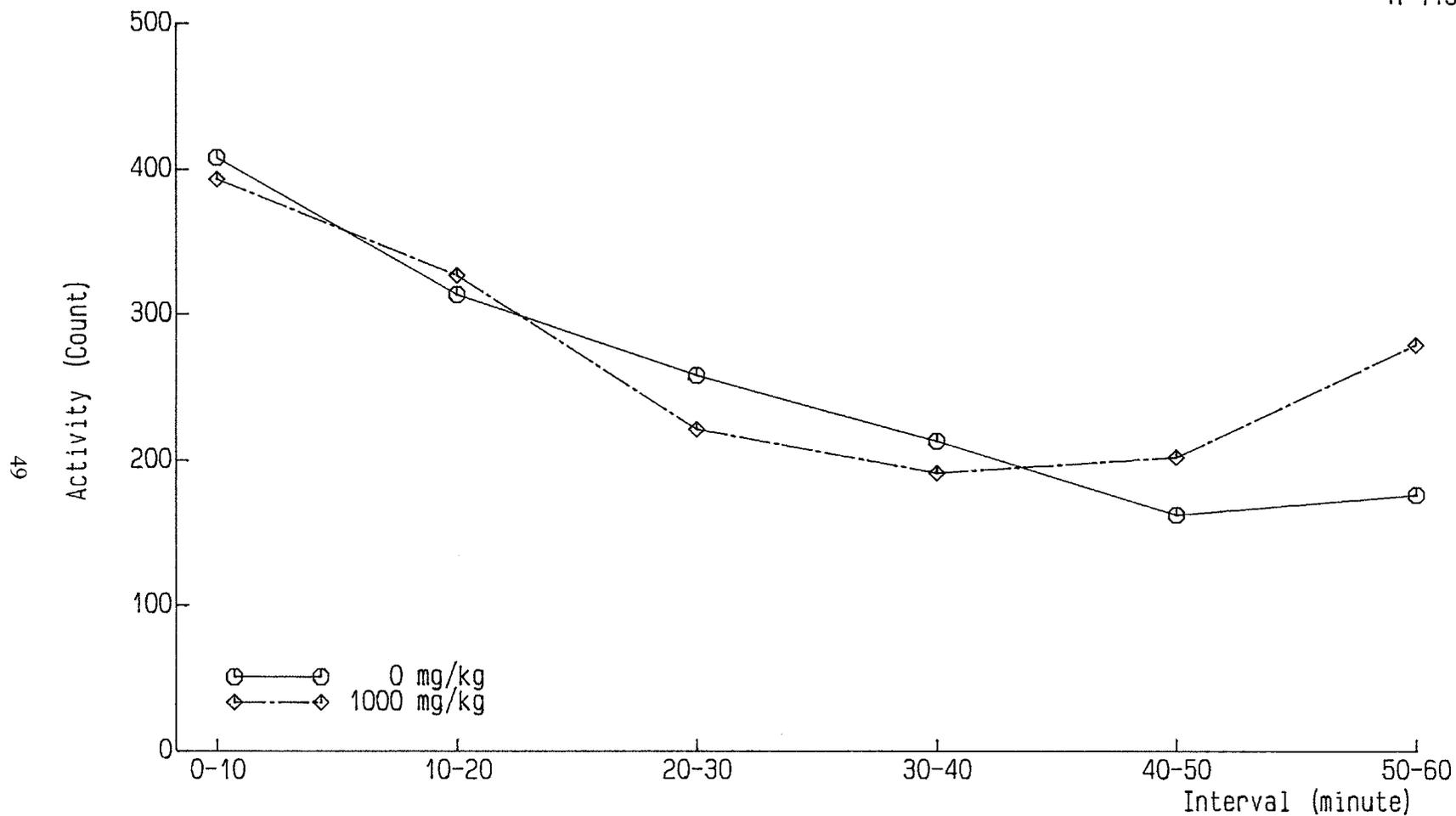


Fig.3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Motor activity of female rats (Satellite group, Week 6 of administration)

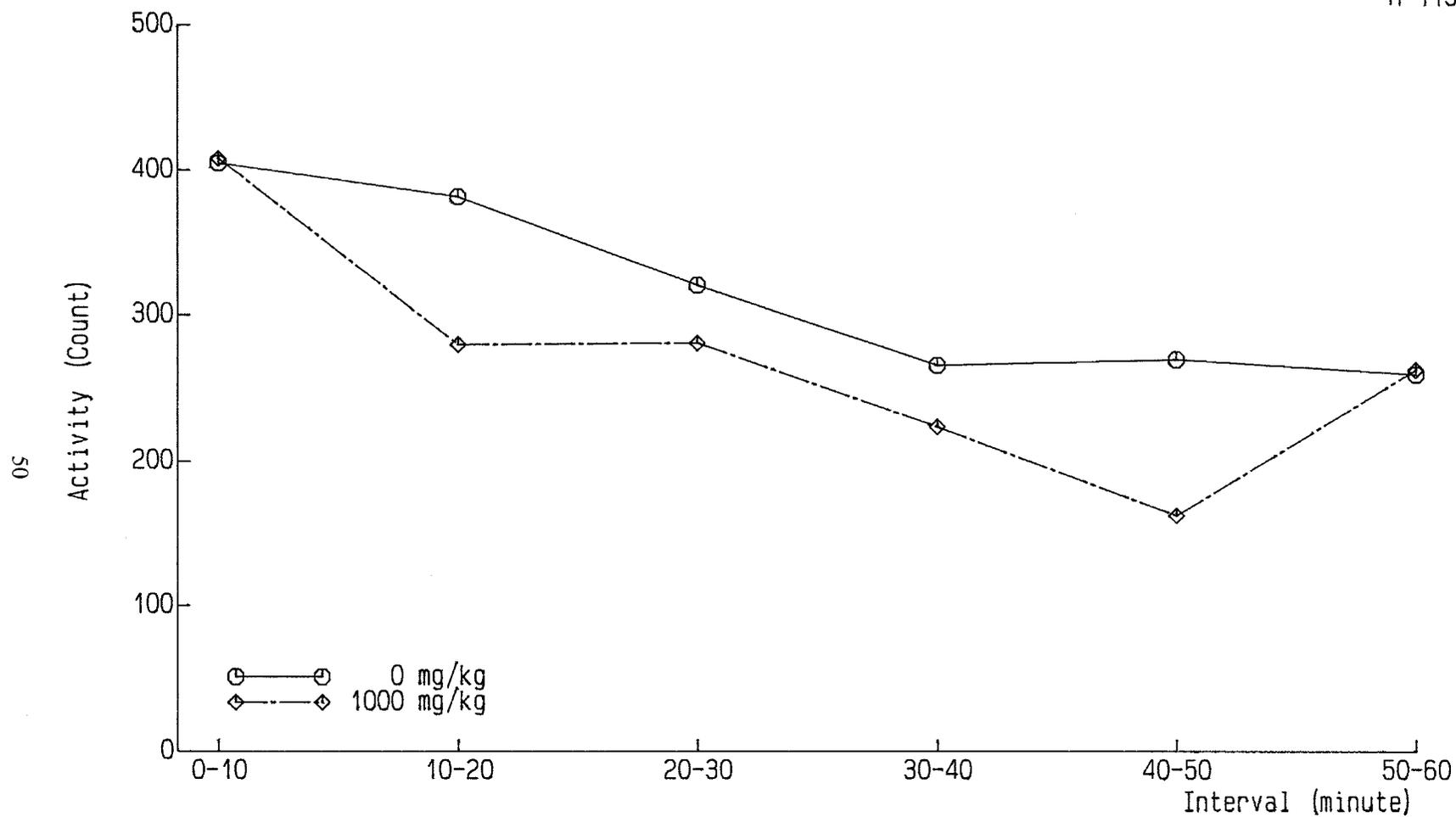


Fig.4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Motor activity of male rats (Week 2 of recovery)

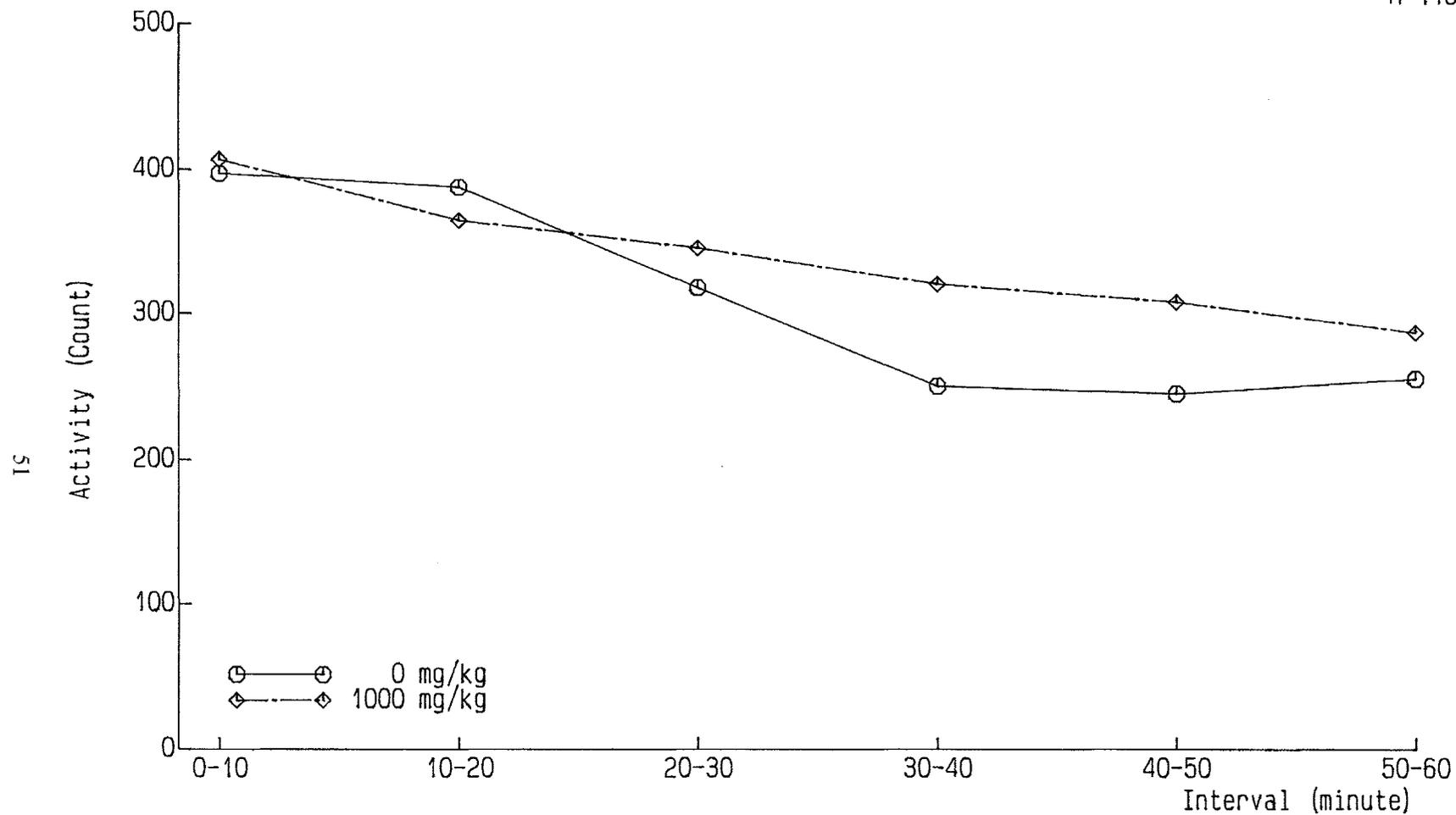


Fig.5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Motor activity of female rats (Week 2 of recovery)

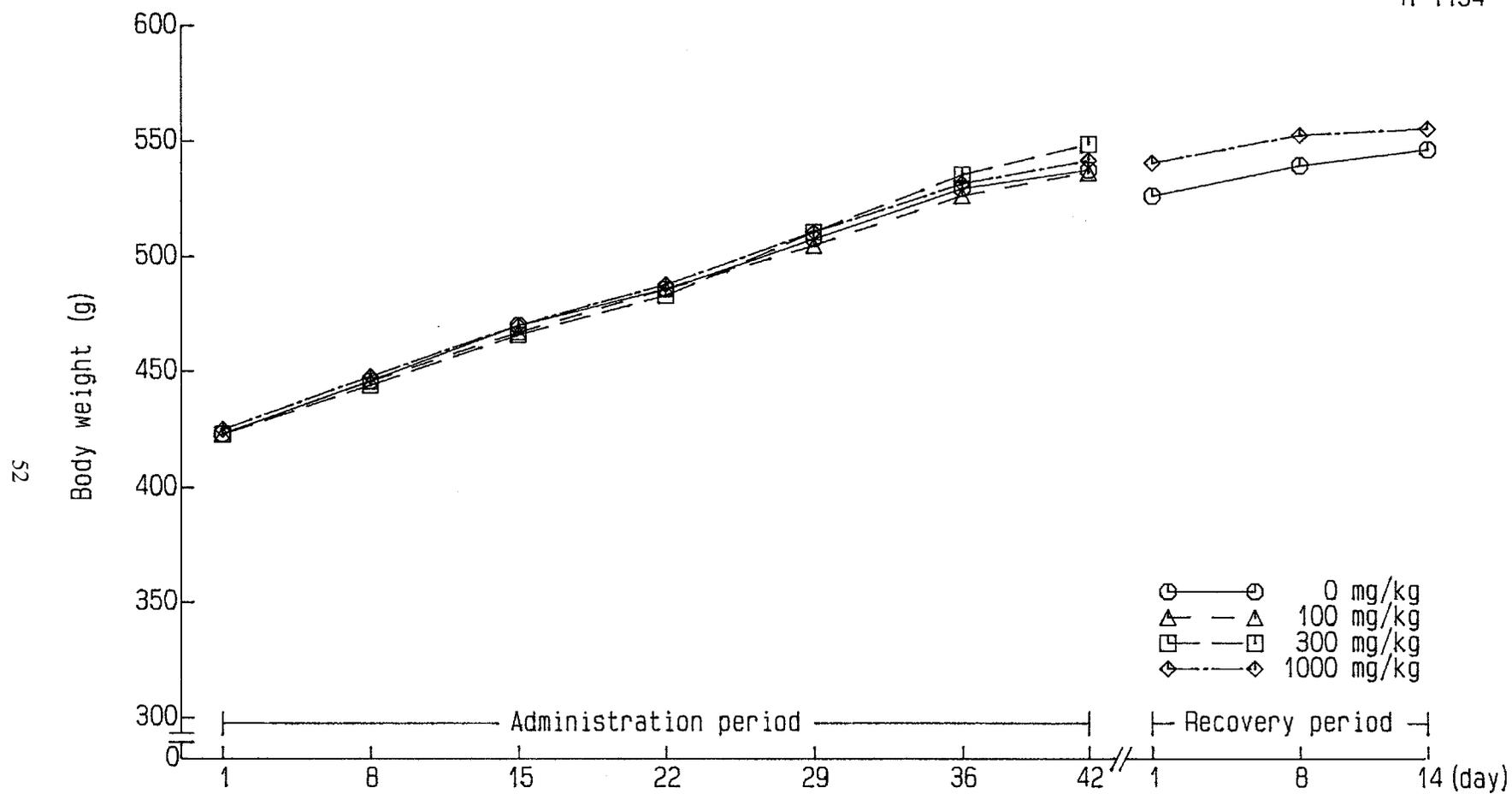


Fig.6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats

Body weight of male rats

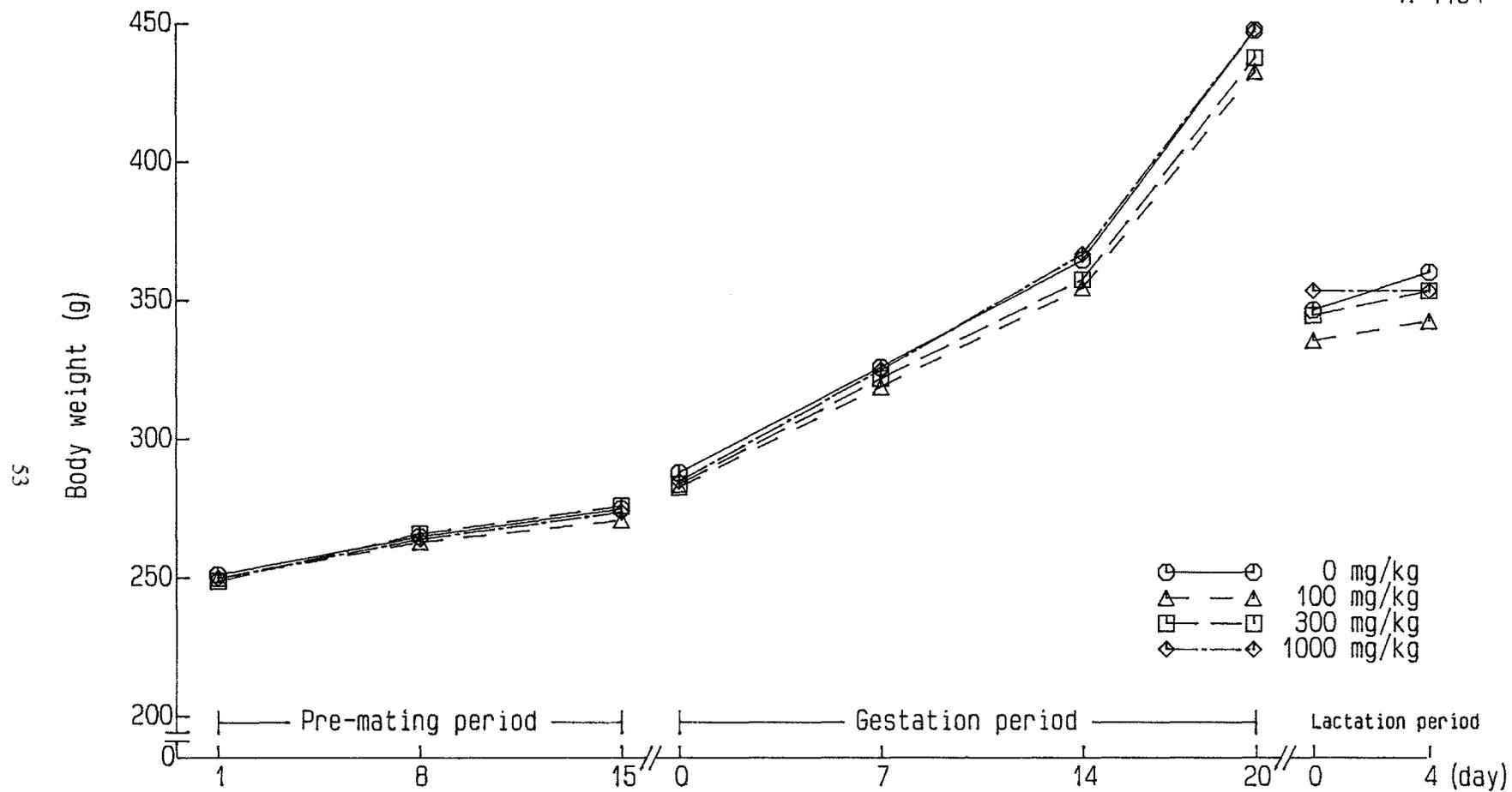


Fig.7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats

Body weight of female rats (Main group)

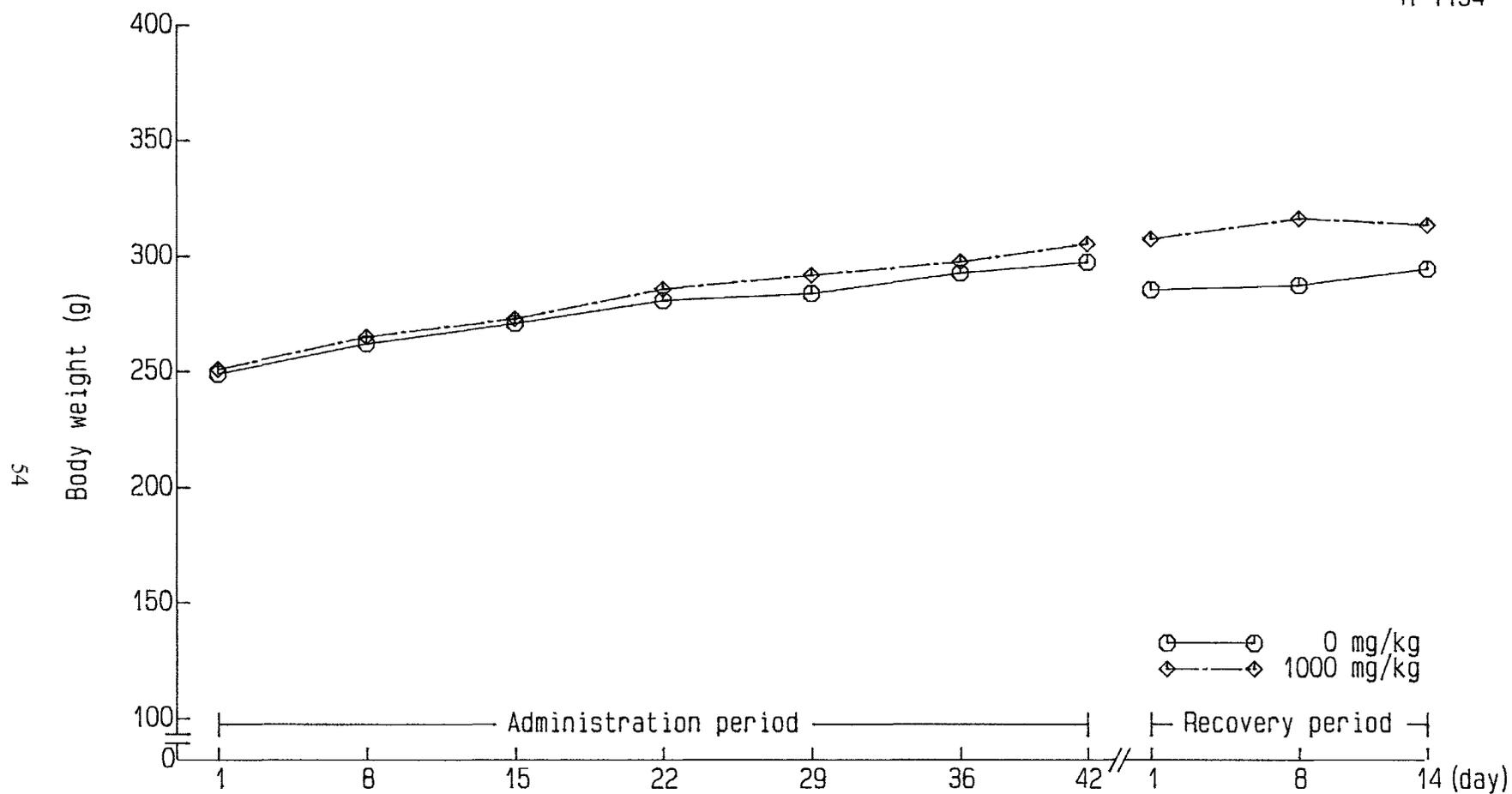


Fig.8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats

Body weight of female rats (Satellite group)

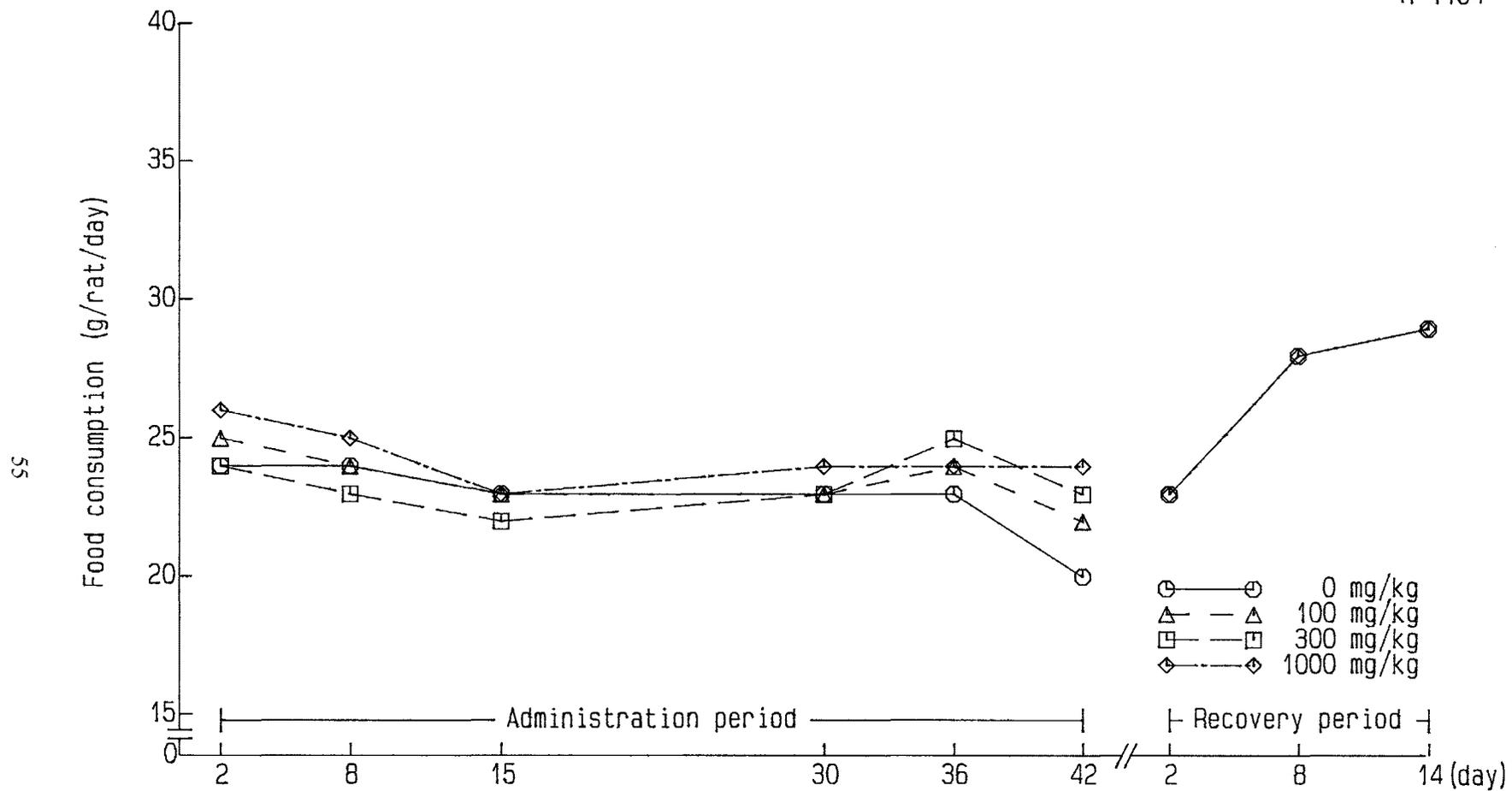


Fig.9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats

Food consumption of male rats

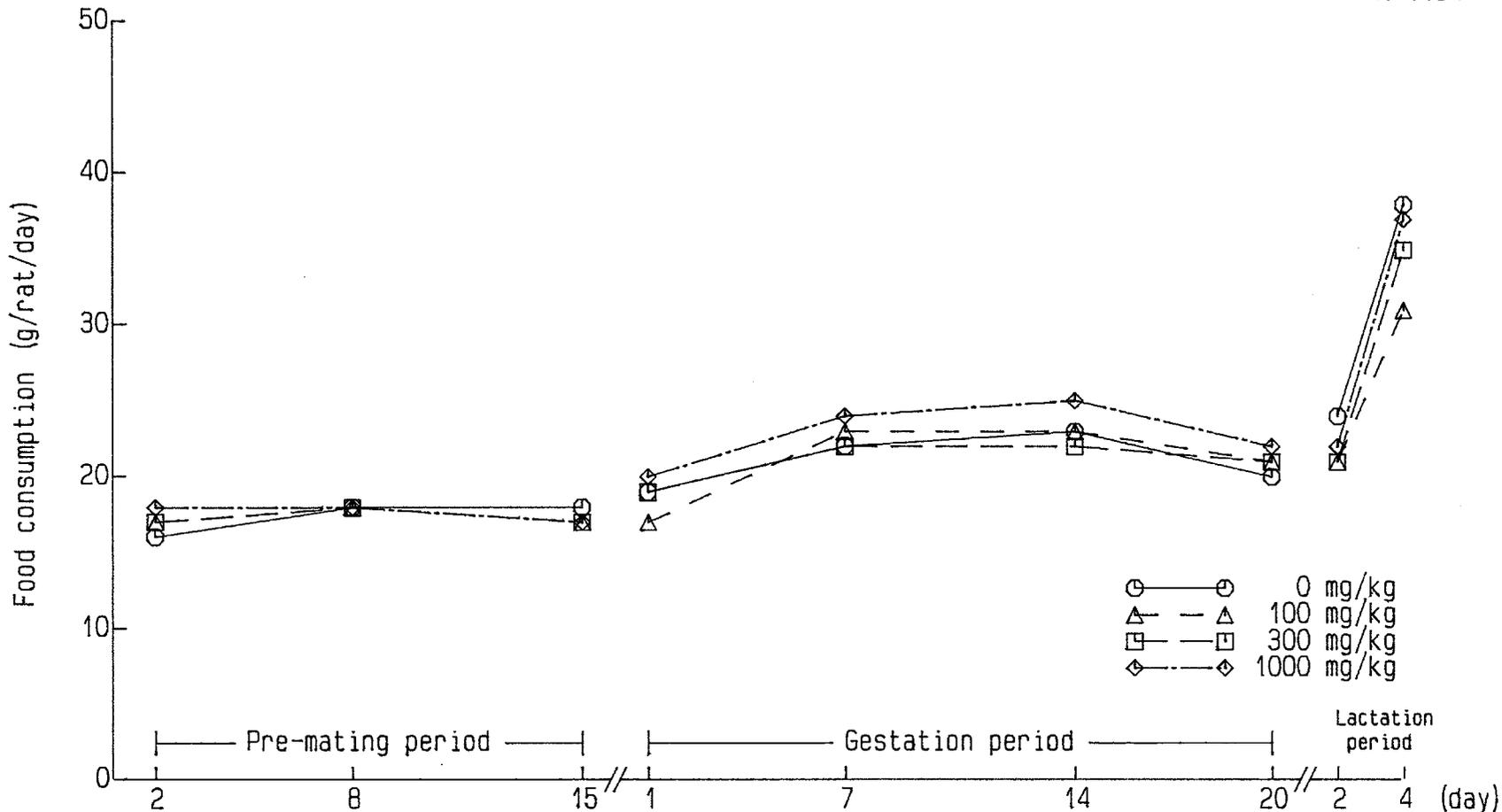


Fig.10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Food consumption of female rats (Main group)

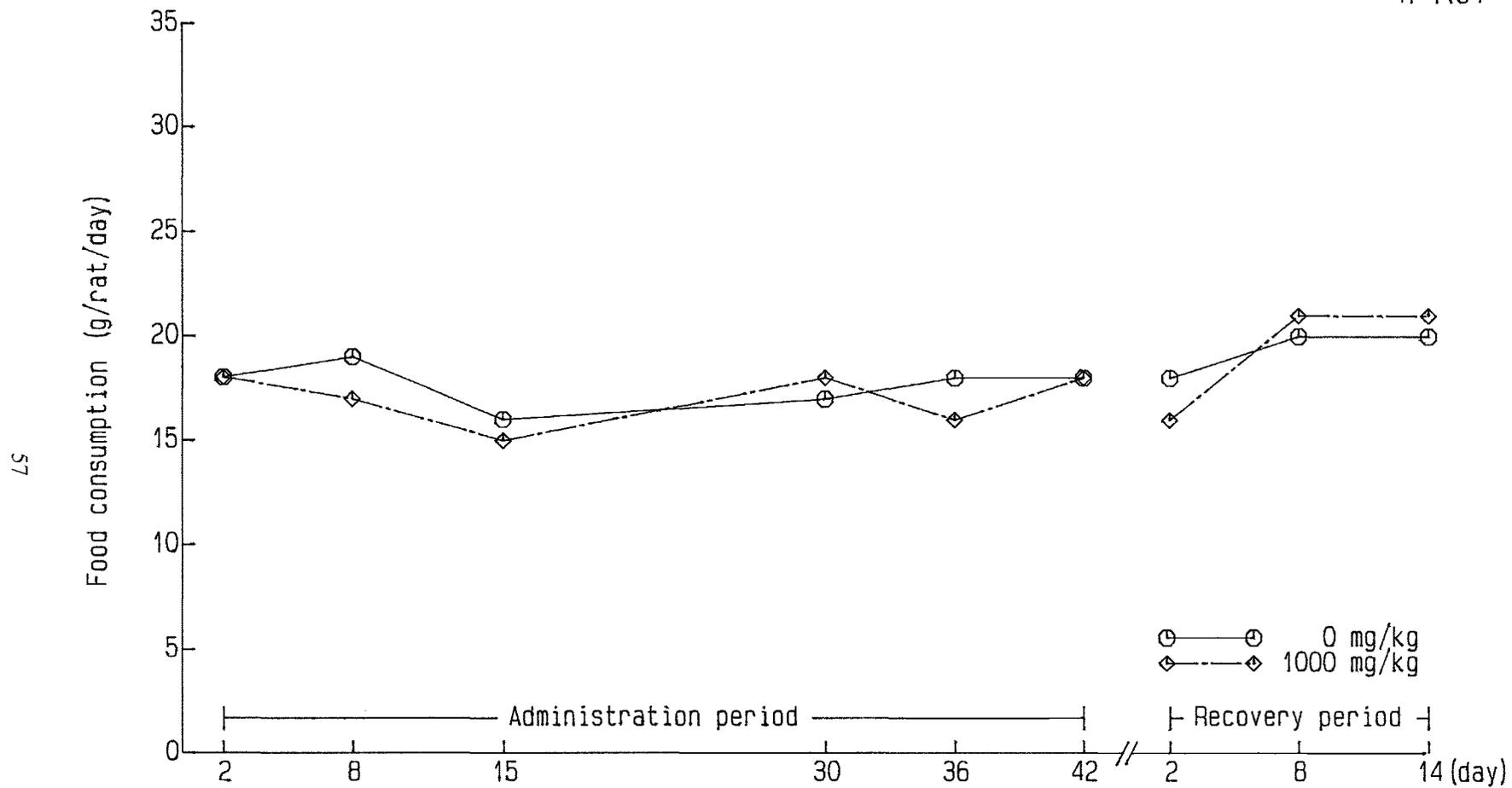


Fig.11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats

Food consumption of female rats (Satellite group)

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

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

a): Day of necropsy

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

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

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

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

a): Gestation day

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

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

a): Lactation day
b): Day of necropsy

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

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

a): Day of necropsy

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

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

a): Day of necropsy

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

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

a): Day of necropsy

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	11	11	10	12
Posture					
Normal		11	11	10	12
Convulsion					
None		11	11	10	12
Abnormal behavior					
None		11	11	10	12

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

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	11	11	10	12
Posture					
Normal		11	11	10	12
Convulsion					
None		11	11	10	12
Abnormal behavior					
None		11	11	10	12

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

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	11	11	10	12
Posture					
Normal		11	11	10	12
Convulsion					
None		11	11	10	12
Abnormal behavior					
None		11	11	10	12

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

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	11	11	10	12
Posture					
Normal		11	11	10	12
Convulsion					
None		11	11	10	12
Abnormal behavior					
None		11	11	10	12

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

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	11	11	10	11
Posture					
Normal		11	11	10	11
Convulsion					
None		11	11	10	11
Abnormal behavior					
None		11	11	10	11

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		5± 2	4± 2	3± 2	3± 2
Defecation count (Mean±S.D.)		0± 1	0± 0	0± 0	0± 1
Urination					
None		11	9	10	8
Small amount		1	3	2	4

No significant difference in any treated groups from control group.

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

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

No significant difference in any treated groups from control group.

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

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
No/minimal location		0	0	0	1
Normal		12	12	12	11
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		5± 2	3± 2	4± 1	4± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 1	0± 0
Urination					
None		9	10	11	11
Small amount		3	2	1	1

No significant difference in any treated groups from control group.

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

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

No significant difference in any treated groups from control group.

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

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

No significant difference in any treated groups from control group.

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

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

No significant difference in any treated groups from control group.

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

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

*: p<0.05 (Significant difference from control group)

D: Dunnett's test

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

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		8± 3	7± 2	7± 2	7± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	12	12	11
Small amount		0	0	0	1

No significant difference in any treated groups from control group.

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

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	11	11	10	12
Arousal					
Normal		11	11	10	12
Convulsion					
None		11	11	10	12
Abnormal behavior					
None		11	11	10	12
Stereotypy					
None		11	11	10	12
Gait					
Normal		11	11	10	12
Posture					
Normal		11	11	10	12
Grooming					
None		11	11	10	12
Rearing (Mean+S.D.)		8+ 2	7+ 1	7+ 2	6+ 2
Defecation count (Mean+S.D.)		0+ 0	0+ 0	0+ 0	0+ 0
Urination					
None		11	11	10	12

No significant difference in any treated groups from control group.

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

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	11	11	10	12
Arousal					
Normal		11	11	10	12
Convulsion					
None		11	11	10	12
Abnormal behavior					
None		11	11	10	12
Stereotypy					
None		11	11	10	12
Gait					
Normal		11	11	10	12
Posture					
Normal		11	11	10	12
Grooming					
None		11	11	10	12
Rearing (Mean+S.D.)		7+ 2	7+ 2	6+ 3	6+ 2
Defecation count (Mean+S.D.)		0+ 0	0+ 0	0+ 0	0+ 0
Urination					
None		11	10	10	11
Small amount		0	1	0	1

No significant difference in any treated groups from control group.

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

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

*: p<0.05 (Significant difference from control group)

D: Dunnett's test

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

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	11	11	10	12
Arousal					
Normal		11	11	10	12
Convulsion					
None		11	11	10	12
Abnormal behavior					
None		11	11	10	12
Stereotypy					
None		11	11	10	12
Gait					
Normal		11	11	10	12
Posture					
Normal		11	11	10	12
Grooming					
None		11	11	10	12
Rearing (Mean+S.D.)		6+ 2	5+ 1	5+ 1	4+ 1*D
Defecation count (Mean+S.D.)		0+ 0	0+ 0	0+ 0	0+ 0
Urination					
None		11	10	9	12
Small amount		0	1	1	0

*: p<0.05 (Significant difference from control group)

D: Dunnett's test

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

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	11	11	10	11
Arousal					
Normal		11	11	10	11
Convulsion					
None		11	11	10	11
Abnormal behavior					
None		11	11	10	11
Stereotypy					
None		11	11	10	11
Gait					
Normal		11	11	10	11
Posture					
Normal		11	11	10	11
Grooming					
None		11	11	10	11
Rearing (Mean+S.D.)		6+ 1	6+ 2	6+ 1	5+ 2
Defecation count (Mean+S.D.)		0+ 0	0+ 0	0+ 0	0+ 0
Urination					
None		11	11	9	11
Small amount		0	0	1	0

No significant difference in any treated groups from control group.

Table 2-60

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Satellite group, Week 1 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	-----	-----
Arousal			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10
Stereotypy			
None		10	10
Gait			
Normal		10	10
Posture			
Normal		10	10
Grooming			
None		10	10
Rearing (Mean±S.D.)		6± 2	6± 3
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	10

No significant difference between treated group and control group.

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

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

No significant difference between treated group and control group.

Table 2-62

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Satellite group, Week 3 of administration)

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

*: p<0.05 (Significant difference from control group)

T: Student's t-test

Table 2-63

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Satellite group, Week 4 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	----- 10	----- 10
Arousal			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10
Stereotypy			
None		10	10
Gait			
Normal		10	10
Posture			
Normal		10	10
Grooming			
None		10	10
Rearing (Mean±S.D.)		8± 3	9± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	9
Small amount		0	1

No significant difference between treated group and control group.

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

Parameter	Dose (mg/kg)	0	1000
	No. of animals	----- 10	----- 10
Arousal			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10
Stereotypy			
None		10	10
Gait			
Normal		10	10
Posture			
Normal		10	10
Grooming			
None		10	10
Rearing (Mean±S.D.)		9± 4	9± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	9
Small amount		0	1

No significant difference between treated group and control group.

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

Parameter	Dose (mg/kg)	0	1000
	No. of animals	-----	-----
Arousal			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10
Stereotypy			
None		10	10
Gait			
Normal		10	10
Posture			
Normal		10	10
Grooming			
None		10	10
Rearing (Mean±S.D.)		8± 2	7± 3
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		9	10
Small amount		1	0

No significant difference between treated group and control group.

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

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

No significant difference between treated group and control group.

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

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

No significant difference between treated group and control group.

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

Parameter	Dose (mg/kg)	0	1000
	No. of animals	----- 5	----- 5
Arousal			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5
Stereotypy			
None		5	5
Gait			
Normal		5	5
Posture			
Normal		5	5
Grooming			
None		5	5
Rearing (Mean+S.D.)		9+ 4	7+ 1
Defecation count (Mean+S.D.)		0+ 0	0+ 0
Urination			
None		5	5

No significant difference between treated group and control group.

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

Parameter	Dose (mg/kg)	0	1000
	No. of animals	----- 5	----- 5
Arousal			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5
Stereotypy			
None		5	5
Gait			
Normal		5	5
Posture			
Normal		5	5
Grooming			
None		5	5
Rearing (Mean+S.D.)		9+ 4	7+ 1
Defecation count (Mean+S.D.)		0+ 0	0+ 0
Urination			
None		5	5

No significant difference between treated group and control group.

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

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	5	5	5	5
Auditory response					
Normal		5	5	5	5
Approach response					
Normal		5	5	5	5
Touch response					
Normal		5	5	5	5
Tail pinch response					
Normal		5	5	5	5
Pupillary reflex					
Pass, both		5	5	5	5
Aerial righting reflex					
(Total score: Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Landing foot splay (mm: Mean±S.D.)		69±19	63±16	71±19	80±11

No significant difference in any treated groups from control group.

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

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	5	5	5	5
Auditory response					
Normal		5	5	5	5
Approach response					
Normal		5	5	5	5
Touch response					
Normal		5	5	5	5
Tail pinch response					
Normal		5	5	5	5
Pupillary reflex					
Pass, both		5	5	5	5
Aerial righting reflex					
(Total score: Mean+S.D.)		0+ 0	0+ 0	0+ 0	0+ 0
Landing foot splay (mm: Mean+S.D.)		49+20	44+13	59+21	43+16

No significant difference in any treated groups from control group.

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

Parameter	Dose (mg/kg)	0	1000
	No. of animals	----- 5	----- 5
Auditory response			
Normal		5	5
Approach response			
Normal		5	5
Touch response			
Normal		5	5
Tail pinch response			
Normal		5	5
Pupillary reflex			
Pass, both		5	5
Aerial righting reflex			
(Total score: Mean±S.D.)		0± 0	0± 0
Landing foot splay (mm: Mean±S.D.)		53±27	70±18

No significant difference between treated group and control group.

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

Parameter	Dose (mg/kg)	0	1000
	No. of animals	-----	-----
Auditory response			
Normal		5	5
Approach response			
Normal		5	5
Touch response			
Normal		5	5
Tail pinch response			
Normal		5	5
Pupillary reflex			
Pass, both		5	5
Aerial righting reflex			
(Total score: Mean+S.D.)		0+ 0	0+ 0
Landing foot splay (mm: Mean+S.D.)		66+31	90+25

No significant difference between treated group and control group.

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

Parameter	Dose (mg/kg)	0	1000
	No. of animals	-----	-----
Auditory response			
Normal		5	5
Approach response			
Normal		5	5
Touch response			
Normal		5	5
Tail pinch response			
Normal		5	5
Pupillary reflex			
Pass, both		5	5
Aerial righting reflex			
(Total score: Mean+S.D.)		0+ 0	0+ 0
Landing foot splay (mm: Mean+S.D.)		56+21	66+ 9

No significant difference between treated group and control group.

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

Dose mg/kg		Fore limb g	Hind limb g
0	No.	5	5
	Mean	1417	1014
	S.D.	280	124
100	No.	5	5
	Mean	1709	1083
	S.D.	232	245
300	No.	5	5
	Mean	1643	1111
	S.D.	299	54
1000	No.	5	5
	Mean	1564	1114
	S.D.	322	220

No.: No. of animals

No significant difference in any treated groups from control group.

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

Dose mg/kg		Fore limb g	Hind limb g
0	No.	5	5
	Mean	1339	856
	S.D.	181	205
100	No.	5	5
	Mean	1478	802
	S.D.	174	58
300	No.	5	5
	Mean	1355	815
	S.D.	155	136
1000	No.	5	5
	Mean	1451	958
	S.D.	95	81

No.: No. of animals

No significant difference in any treated groups from control group.

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

Dose mg/kg		Fore limb g	Hind limb g
0	No.	5	5
	Mean	1020	670
	S.D.	87	115
1000	No.	5	5
	Mean	1179*	742
	S.D.	71T	68

No.: No. of animals

*: p<0.05 (Significant difference from control group)

T: Student's t-test

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

Dose mg/kg		Fore limb g	Hind limb g
0	No.	5	5
	Mean	1638	1042
	S.D.	321	53
1000	No.	5	5
	Mean	1797	1103
	S.D.	216	127

No.: No. of animals

No significant difference between treated group and control group.

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

Dose mg/kg		Fore limb g	Hind limb g
0	No.	5	5
	Mean	1229	794
	S.D.	219	57
1000	No.	5	5
	Mean	1319	873
	S.D.	283	72

No.: No. of animals

No significant difference between treated group and control group.

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

Dose mg/kg	Interval (minutes)							Total(0-60)
	0-10	10-20	20-30	30-40	40-50	50-60		
0	No.	5	5	5	5	5	5	5
	Mean	390	328	316	251	73	96	1454
	S.D.	83	130	153	131	67	155	564
100	No.	5	5	5	5	5	5	5
	Mean	428	365	312	215	71	178	1568
	S.D.	27	38	74	171	94	148	435
300	No.	5	5	5	5	5	5	5
	Mean	398	345	263	285	171	230	1693
	S.D.	65	75	121	139	157	161	560
1000	No.	5	5	5	5	5	5	5
	Mean	427	377	310	256	170	245	1785
	S.D.	37	27	101	152	163	153	485

Unit: Count

No.: No. of animals

No significant difference in any treated groups from control group.

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

Dose mg/kg		Interval (minutes)						
		0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
0	No.	5	5	5	5	5	5	5
	Mean	395	136	63	65	122	96	877
	S.D.	64	111	125	46	89	129	412
100	No.	5	5	5	5	5	5	5
	Mean	326	97	73	42	147	158	842
	S.D.	73	33	80	37	130	150	310
300	No.	5	5	5	5	5	5	5
	Mean	390	324*	205	68	116	101	1204
	S.D.	119	50D	76	77	143	118	185
1000	No.	5	5	5	5	5	5	5
	Mean	354	128	84	58	161	112	896
	S.D.	119	144	95	74	131	138	495

Unit: Count

No.: No. of animals

*: p<0.05 (Significant difference from control group)

D: Dunnett's test

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

Dose mg/kg	Interval (minutes)							Total(0-60)
	0-10	10-20	20-30	30-40	40-50	50-60		
0	No.	5	5	5	5	5	5	5
	Mean	408	314	259	214	163	177	1535
	S.D.	42	28	145	145	145	150	168
1000	No.	5	5	5	5	5	5	5
	Mean	393	327	222	192	203	280	1617
	S.D.	32	48	162	175	137	98	483

Unit: Count

No.: No. of animals

No significant difference between treated group and control group.

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

Dose mg/kg		Interval (minutes)						
		0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
0	No.	5	5	5	5	5	5	5
	Mean	405	382	321	266	270	260	1904
	S.D.	66	66	66	77	61	89	359
1000	No.	5	5	5	5	5	5	5
	Mean	408	280	281	224	163	263	1618
	S.D.	23	107	97	169	135	168	551

Unit: Count

No.: No. of animals

No significant difference between treated group and control group.

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

Dose mg/kg	Interval (minutes)							Total(0-60)
	0-10	10-20	20-30	30-40	40-50	50-60		
0	No.	5	5	5	5	5	5	5
	Mean	397	388	318	251	246	256	1856
	S.D.	49	60	67	138	86	60	275
1000	No.	5	5	5	5	5	5	5
	Mean	407	365	346	321	309	288	2035
	S.D.	44	28	51	26	33	48	138

Unit: Count

No.: No. of animals

No significant difference between treated group and control group.

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

Dose mg/kg		Day of administration							Gain 1-42
		1	8	15	22	29	36	42	
0	No.	12	12	12	12	12	12	12	12
	Mean	423	446	470	486	508	530	538	115
	S.D.	10	14	14	15	18	20	20	17
100	No.	12	12	12	12	12	12	12	12
	Mean	423	446	467	486	505	527	537	114
	S.D.	11	14	18	17	20	22	22	13
300	No.	12	12	12	12	12	12	12	12
	Mean	423	444	466	483	511	536	549	126
	S.D.	9	13	14	16	20	21	22	20
1000	No.	12	12	12	12	12	12	12	12
	Mean	425	448	470	488	511	532	542	117
	S.D.	9	12	15	18	21	24	26	24

Unit: g

No.: No. of animals

No significant difference in any treated groups from control group.

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

Dose mg/kg		Day of administration			Gain 1-15
		1	8	15	
0	No.	12	12	12	12
	Mean	251	265	275	24
	S.D.	18	20	21	10
100	No.	12	12	12	12
	Mean	250	263	271	21
	S.D.	18	17	22	9
300	No.	12	12	12	12
	Mean	249	266	276	26
	S.D.	15	14	13	8
1000	No.	12	12	12	12
	Mean	250	264	274	24
	S.D.	13	17	19	10

Unit: g

No.: No. of animals

No significant difference in any treated groups from control group.

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

Dose mg/kg		Administration				Gain 0-20
		0	7	14	20a)	
0	No.	11	11	11	11	11
	Mean	288	326	365	448	161
	S.D.	25	26	29	34	17
100	No.	11	11	11	11	11
	Mean	283	319	355	433	149
	S.D.	22	24	28	27	14
300	No.	10	10	10	10	10
	Mean	284	322	358	438	154
	S.D.	15	17	20	20	11
1000	No.	12	12	12	12	12
	Mean	285	325	367	448	163
	S.D.	18	22	28	40	32

Unit: g

No.: No. of dams

a): Gestation day

No significant difference in any treated groups from control group.

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

Dose mg/kg		Administration		Gain 0-4
		0	4a)	
0	No.	11	11	11
	Mean	347	361	15
	S.D.	41	28	19
100	No.	11	11	11
	Mean	336	343	7
	S.D.	34	28	14
300	No.	10	10	10
	Mean	345	354	9
	S.D.	19	18	8
1000	No.	11	11	11
	Mean	354	354	1
	S.D.	31	30	36

Unit: g

No.: No. of dams

a): Lactation day

No significant difference in any treated groups from control group.

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

Dose mg/kg		Day of administration							Gain 1-42
		1	8	15	22	29	36	42	
0	No.	10	10	10	10	10	10	10	10
	Mean	249	262	271	281	284	293	298	48
	S.D.	16	18	20	21	22	25	25	12
1000	No.	10	10	10	10	10	10	10	10
	Mean	251	265	273	286	292	298	306	55
	S.D.	15	18	18	21	22	20	23	12

Unit: g

No.: No. of animals

No significant difference between treated group and control group.

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

Dose mg/kg		Day of recovery			Gain 1-14
		1	8	14	
0	No.	5	5	5	5
	Mean	527	540	547	20
	S.D.	28	26	29	5
1000	No.	5	5	5	5
	Mean	541	553	556	14
	S.D.	38	37	42	9

Unit: g

No.: No. of animals

No significant difference between treated group and control group.

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

Dose mg/kg		Day of recovery			Gain 1-14
		1	8	14	
0	No.	5	5	5	5
	Mean	286	288	295	9
	S.D.	19	17	23	5
1000	No.	5	5	5	5
	Mean	308	317*	314	6
	S.D.	21	21T	18	5

Unit: g

No.: No. of animals

*: $p < 0.05$ (Significant difference from control group)

T: Student's t-test

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

Dose mg/kg		Day of administration					
		2	8	15	30	36	42
0	No.	12	12	12	12	12	12
	Mean	24	24	23	23	23	20
	S.D.	2	1	2	2	2	3
100	No.	12	12	12	12	12	12
	Mean	25	24	23	23	24	22
	S.D.	2	3	2	2	2	2
300	No.	12	12	12	12	12	12
	Mean	24	23	22	23	25	23*
	S.D.	3	3	2	2	2	2D
1000	No.	12	12	12	12	12	12
	Mean	26	25	23	24	24	24**
	S.D.	3	3	3	3	3	3D

Unit: g/rat/day

No.: No. of animals

*: p<0.05; **: p<0.01 (Significant difference from control group)

D: Dunnett's test

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

Dose mg/kg		Day of administration		
		2	8	15
0	No.	12	12	12
	Mean	16	18	18
	S.D.	3	4	3
100	No.	12	12	12
	Mean	17	18	17
	S.D.	3	2	3
300	No.	12	12	12
	Mean	17	18	17
	S.D.	2	1	2
1000	No.	12	12	12
	Mean	18	18	17
	S.D.	3	4	3

Unit: g/rat/Gay

No.: No. of animals

No significant difference in any treated groups from control group.

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

Dose mg/kg		Administration			
		1	7	14	20a)
0	No.	11	11	11	11
	Mean	19	22	23	20
	S.D.	4	2	2	4
100	No.	11	11	11	11
	Mean	17	23	23	21
	S.D.	3	2	3	2
300	No.	10	10	10	10
	Mean	19	22	22	21
	S.D.	2	3	2	2
1000	No.	12	12	12	12
	Mean	20	24	25	22
	S.D.	3	3	4	4

Unit: g/rat/day

No.: No. of dams

a): Gestation day

No significant difference in any treated groups from control group.

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

Dose mg/kg		Administration	
		2	4a)
0	No.	11	11
	Mean	24	38
	S.D.	5	5
100	No.	11	11
	Mean	21	31*
	S.D.	6	6ST
300	No.	10	10
	Mean	21	35
	S.D.	5	3
1000	No.	11	11
	Mean	22	37
	S.D.	16	20

Unit: g/rat/day

No.: No. of dams

a): Lactation day

*: p<0.05 (Significant difference from control group)

ST: Steel's test

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

Dose mg/kg		Day of administration					
		2	8	15	30	36	42
0	No.	10	10	10	10	10	10
	Mean	18	19	16	17	18	18
	S.D.	3	3	4	3	3	2
1000	No.	10	10	10	10	10	10
	Mean	18	17	15	18	16	18
	S.D.	2	3	3	3	2	2

Unit: g/rat/day

No.: No. of animals

No significant difference between treated group and control group.

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

Dose mg/kg		Day of recovery		
		2	8	14
0	No.	5	5	5
	Mean	23	28	29
	S.D.	1	2	1
1000	No.	5	5	5
	Mean	23	28	29
	S.D.	4	3	6

Unit: g/rat/day

No.: No. of animals

No significant difference between treated group and control group.

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

Dose mg/kg		Day of recovery		
		2	8	14
0	No.	5	5	5
	Mean	18	20	20
	S.D.	3	3	4
1000	No.	5	5	5
	Mean	16	21	21
	S.D.	3	5	2

Unit: g/rat/day

No.: No. of animals

No significant difference between treated group and control group.

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

Dose mg/kg	No.	pH										Protein 1)					Ketone body 2)					Glucose 3)				
		5.0	5.5	6.0	6.5	7.0	7.5	8.0	8.5	>=9.0	-	+-	+	++	+++	-	+-	+	++	+++	-	+	++	+++	++++	
0	5	0	0	0	0	1	0	1	2	1	0	1	2	2	0	0	1	2	2	0	5	0	0	0	0	
100	5	0	0	0	0	1	0	0	3	1	0	0	1	4	0	0	0	2	3	0	4	1	0	0	0	
300	5	0	0	0	1	0	0	0	2	2	0	0	3	2	0	0	1	4	0	0	5	0	0	0	0	
1000	5	0	1	4	0	0	0	0	0	0	0	0	5	0	0	4	1	0	0	0	5	0	0	0	0	
1)		- : 0 mg/dL		+- : 15 mg/dL		+ : 30 mg/dL		++ : 100 mg/dL		+++ : >=300 mg/dL																
2)		- : 0 mg/dL		+- : 5 mg/dL		+ : 15 mg/dL		++ : 40 mg/dL		+++ : 80 mg/dL																
3)		- : 0 mg/dL		+ : 100 mg/dL		++ : 250 mg/dL		+++ : 500 mg/dL		++++ : >=1000 mg/dL																

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

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

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

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

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

SEC : Squamous Epithelial Cell - : Negative
 SREC : Small Round Epithelial Cell +- : Slight
 PS : Phosphate Salts + : Mild
 CO : Calcium Oxalate ++ : Moderate
 +++ : Severe

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

Dose mg/kg	No.		Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
0	5	Mean	38	12.1	1725	0.89	2.79	1.22
		S.D.	8	9.5	593	0.37	0.98	0.53
100	5	Mean	34	10.2	2084	1.01	3.33	1.38
		S.D.	4	4.9	402	0.39	0.92	0.45
300	5	Mean	36	11.9	1944	1.18	3.57	1.49
		S.D.	5	3.4	198	0.30	0.79	0.35
1000	5	Mean	46	15.7	2057	0.93	4.08	2.01
		S.D.	12	8.8	522	0.47	1.17	0.61

No significant difference in any treated groups from control group.

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

Dose mg/kg	No.	pH									Protein 1)					Ketone body 2)					Glucose 3)				
		5.0	5.5	6.0	6.5	7.0	7.5	8.0	8.5	>=9.0	-	+-	+	++	+++	-	+-	+	++	+++	-	+	++	+++	++++
0	5	0	0	0	1	2	1	0	0	1	4	1	0	0	0	5	0	0	0	0	5	0	0	0	0
1000	5	0	1	4	0	0	0	0	0	0	2	3	0	0	0	5	0	0	0	0	5	0	0	0	0
1)		- : 0 mg/dL			+- : 15 mg/dL			+ : 30 mg/dL			++ : 100 mg/dL			+++ : >=300 mg/dL											
2)		- : 0 mg/dL			+- : 5 mg/dL			+ : 15 mg/dL			++ : 40 mg/dL			+++ : 80 mg/dL											
3)		- : 0 mg/dL			+ : 100 mg/dL			++ : 250 mg/dL			+++ : 500 mg/dL			++++ : >=1000 mg/dL											

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

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

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

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

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

SEC : Squamous Epithelial Cell - : Negative
 SREC : Small Round Epithelial Cell +- : Slight
 PS : Phosphate Salts + : Mild
 CO : Calcium Oxalate ++ : Moderate
 +++ : Severe

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

Dose mg/kg	No.		Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
0	5	Mean	32	9.5	1584	0.73	2.33	1.02
		S.D.	3	3.7	237	0.21	0.84	0.24
1000	5	Mean	38	12.3	1678	0.61	2.73	1.38
		S.D.	8	4.0	588	0.24	0.59	0.32

No significant difference between treated group and control group.

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

Dose mg/kg	No.	pH										Protein 1)					Ketone body 2)					Glucose 3)				
		5.0	5.5	6.0	6.5	7.0	7.5	8.0	8.5	>=9.0	-	+-	+	++	+++	-	+-	+	++	+++	-	+	++	+++	++++	
0	5	0	0	0	0	0	1	0	3	1	2	1	2	0	0	2	1	2	0	0	5	0	0	0	0	
1000	5	0	0	0	0	0	0	0	4	1	1	0	4	0	0	1	0	4	0	0	5	0	0	0	0	
1)		- : 0 mg/dL		+- : 15 mg/dL			+ : 30 mg/dL					++ : 100 mg/dL					+++ : >=300 mg/dL									
2)		- : 0 mg/dL		+- : 5 mg/dL			+ : 15 mg/dL					++ : 40 mg/dL					+++ : 80 mg/dL									
3)		- : 0 mg/dL		+ : 100 mg/dL			++ : 250 mg/dL					+++ : 500 mg/dL					++++ : >=1000 mg/dL									

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

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

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

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

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

SEC : Squamous Epithelial Cell - : Negative
 SREC : Small Round Epithelial Cell +- : Slight
 PS : Phosphate Salts + : Mild
 CO : Calcium Oxalate ++ : Moderate
 +++ : Severe

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

Dose mg/kg	No.		Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
0	5	Mean	49	19.9	1904	1.74	6.01	2.36
		S.D.	10	5.3	292	0.23	0.97	0.21
1000	5	Mean	50	19.0	1858	1.48	4.99	2.02
		S.D.	20	13.1	458	0.75	1.32	0.70

No significant difference between treated group and control group.

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

Dose mg/kg	No.	pH									Protein 1)				Ketone body 2)				Glucose 3)						
		5.0	5.5	6.0	6.5	7.0	7.5	8.0	8.5	>=9.0	-	+-	+	++	+++	-	+-	+	++	+++	-	+	++	+++	++++
0	5	0	0	0	0	3	0	0	2	0	4	0	1	0	0	4	1	0	0	0	5	0	0	0	0
1000	5	0	0	0	1	1	1	0	2	0	4	0	1	0	0	4	1	0	0	0	5	0	0	0	0
1)		- : 0 mg/dL			+- : 15 mg/dL			+ : 30 mg/dL			++ : 100 mg/dL			+++ : >=300 mg/dL											
2)		- : 0 mg/dL			+- : 5 mg/dL			+ : 15 mg/dL			++ : 40 mg/dL			+++ : 80 mg/dL											
3)		- : 0 mg/dL			+ : 100 mg/dL			++ : 250 mg/dL			+++ : 500 mg/dL			++++ : >=1000 mg/dL											

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

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

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

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

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

SEC : Squamous Epithelial Cell - : Negative
 SREC : Small Round Epithelial Cell +- : Slight
 PS : Phosphate Salts + : Mild
 CO : Calcium Oxalate ++ : Moderate
 +++ : Severe

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

Dose mg/kg	No.		Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
0	5	Mean	41	15.4	1698	1.22	3.74	1.62
		S.D.	13	10.0	371	0.48	1.18	0.69
1000	5	Mean	39	10.9	1950	1.05	2.91	1.25
		S.D.	9	5.2	491	0.37	0.97	0.41

No significant difference between treated group and control group.

Table 6-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Hematology of male rats (End of administration)

Dose mg/kg	No.		RBC	HGB	HCT	MCV	MCH	MCHC	Retic	PLT	PT	APTT	FIB
			10E4/ μ L	g/dL	%	fL	pg	g/dL	%	10E4/ μ L	s	s	mg/dL
0	5	Mean	857	15.7	44.9	52.4	18.3	34.9	2.0	97.3	13.1	18.0	233
		S.D.	30	0.6	1.7	0.9	0.3	0.5	0.3	8.7	1.3	0.8	26
100	5	Mean	901*	15.6	44.9	49.9	17.3	34.7	1.8	104.0	13.7	17.7	249
		S.D.	33D	0.3	0.9	1.2	0.5	0.2	0.2	9.1	1.9	2.1	3
300	5	Mean	890	15.7	45.0	50.6	17.6	34.8	1.9	112.7	12.6	17.4	239
		S.D.	13	0.2	0.4	0.9	0.4	0.3	0.3	14.2	0.7	1.5	11
1000	5	Mean	885	15.5	44.5	50.3	17.5	34.8	2.1	114.4	12.7	17.0	238
		S.D.	24	1.0	2.1	2.9	1.3	0.8	0.3	16.2	0.7	1.9	29

*: $p < 0.05$ (Significant difference from control group)

D: Dunnett's test

Table 6-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Hematology of male rats (End of administration)

Dose mg/kg	No.		WBC 10E2/ μ L	Differential leukocyte ratio (%)						Differential leukocyte counts (10E2/ μ L)					
				Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	5	Mean	74.2	69.9	25.8	1.8	0.3	2.0	0.2	51.7	19.2	1.4	0.2	1.5	0.2
		S.D.	10.5	3.0	3.5	0.2	0.1	0.7	0.2	6.8	4.3	0.1	0.1	0.6	0.1
100	5	Mean	71.7	70.8	24.8	1.5	0.4	2.0	0.5	50.6	18.0	1.2	0.2	1.4	0.3
		S.D.	14.6	5.1	5.2	0.4	0.1	0.7	0.2	10.2	5.5	0.5	0.1	0.5	0.2
300	5	Mean	84.4	72.8	23.0	1.4	0.3	2.2	0.4	61.5	19.3	1.1	0.3	1.8	0.3
		S.D.	7.8	5.7	5.0	0.3	0.1	0.6	0.1	7.9	4.0	0.3	0.1	0.5	0.1
1000	5	Mean	72.7	73.2	21.3	2.0	0.3	2.6	0.6	53.4	15.3	1.4	0.2	1.8	0.4
		S.D.	12.7	4.5	4.6	0.6	0.1	0.5	0.4	10.8	4.0	0.3	0.1	0.3	0.3

LUC: Large unstained cells

No significant difference in any treated groups from control group.

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

Dose mg/kg	No.		RBC	HGB	HCT	MCV	MCH	MCHC	Retic	PLT	PT	APTT	FIB
			10E4/ μ L	g/dL	%	fL	pg	g/dL	%	10E4/ μ L	s	s	mg/dL
0	5	Mean	706	13.3	39.2	55.6	18.9	34.0	7.6	134.2	11.9	13.9	317
		S.D.	44	0.7	1.6	1.3	0.6	0.9	2.6	20.5	1.2	1.7	84
100	5	Mean	700	13.4	39.0	55.7	19.1	34.3	6.8	131.0	12.3	13.8	243
		S.D.	11	0.3	0.6	1.3	0.3	0.5	1.6	14.3	0.7	1.9	32
300	5	Mean	686	13.0	38.1	55.6	19.0	34.1	7.7	137.0	12.2	15.0	284
		S.D.	55	0.8	2.5	2.0	0.7	0.4	2.4	15.3	0.9	2.5	46
1000	5	Mean	743	14.0	40.6	54.6	18.9	34.6	6.5	130.4	11.9	14.1	311
		S.D.	38	0.7	2.2	1.9	0.7	0.4	1.2	20.5	0.6	1.2	53

No significant difference in any treated groups from control group.

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

Dose mg/kg	No.		WBC 10E2/ μ L	Differential leukocyte ratio (%)						Differential leukocyte counts (10E2/ μ L)					
				Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	5	Mean	110.2	60.3	36.1	0.8	0.2	2.0	0.5	66.5	39.8	0.8	0.3	2.3	0.5
		S.D.	22.1	4.1	3.7	0.4	0.1	0.9	0.1	14.5	9.0	0.3	0.1	1.1	0.1
100	5	Mean	118.2	49.7*	47.1**	0.6	0.2	2.1	0.3	59.9	54.5	0.7	0.3	2.5	0.4
		S.D.	36.9	6.6D	6.4D	0.3	0.1	0.5	0.1	23.6	14.4	0.2	0.2	1.2	0.2
300	5	Mean	107.7	52.3	43.8	0.9	0.2	2.4	0.3	55.5	47.9	1.0	0.2	2.7	0.3
		S.D.	22.2	5.0	4.7	0.3	0.1	0.6	0.2	7.6	14.3	0.5	0.1	0.9	0.2
1000	5	Mean	108.9	54.2	41.5	0.7	0.3	2.7	0.6	59.0	45.2	0.7	0.3	2.9	0.7
		S.D.	6.7	5.3	4.0	0.3	0.1	0.8	0.3	6.9	5.2	0.3	0.1	0.9	0.3

LUC: Large unstained cells

*: $p < 0.05$; **: $p < 0.01$ (Significant difference from control group)

D: Dunnett's test

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

Dose mg/kg	No.		RBC	HGB	HCT	MCV	MCH	MCHC	Retic	PLT	PT	APTT	FIB
			10E4/ μ L	g/dL	%	fL	pg	g/dL	%	10E4/ μ L	s	s	mg/dL
0	5	Mean	781	14.8	41.7	53.4	18.9	35.5	2.4	111.9	12.1	15.2	184
		S.D.	33	0.7	2.2	0.8	0.3	0.6	0.3	8.8	0.4	1.5	14
1000	5	Mean	817	15.1	42.6	52.2*	18.5	35.5	2.2	107.6	11.7	14.0	203
		S.D.	24	0.3	1.2	0.7T	0.3	0.3	0.2	10.4	0.6	1.6	15

*: $p < 0.05$ (Significant difference from control group)

T: Student's t-test

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

Dose mg/kg	No.		WBC 10E2/ μ L	Differential leukocyte ratio (%)					Differential leukocyte counts (10E2/ μ L)						
				Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	5	Mean	53.7	69.8	25.9	1.8	0.3	2.0	0.2	38.1	13.2	0.9	0.2	1.1	0.1
		S.D.	12.9	7.2	7.3	0.4	0.1	0.5	0.1	12.3	2.4	0.2	0.1	0.4	0.1
1000	5	Mean	55.0	78.9	17.3	1.3	0.3	2.0	0.4	44.0	8.8*	0.7	0.2	1.1	0.2
		S.D.	14.2	6.9	7.2	0.4	0.1	0.6	0.2	14.4	1.7T	0.2	0.1	0.3	0.2

LUC: Large unstained cells

*: $p < 0.05$ (Significant difference from control group)

T: Student's t-test

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

Dose mg/kg	No.		RBC	HGB	HCT	MCV	MCH	MCHC	Retic	PLT	PT	APTT	FIB
			10E4/ μ L	g/dL	%	fL	pg	g/dL	%	10E4/ μ L	s	s	mg/dL
0	5	Mean	926	16.1	46.4	50.1	17.4	34.8	1.8	117.1	15.6	19.1	261
		S.D.	38	0.7	2.5	1.6	0.4	0.4	0.5	5.1	2.3	1.5	38
1000	5	Mean	915	16.0	45.9	50.2	17.4	34.8	1.9	109.1	15.8	23.1*	268
		S.D.	28	0.7	1.8	1.6	0.7	0.4	0.5	15.2	1.9	2.3T	25

*: $p < 0.05$ (Significant difference from control group)

T: Student's t-test

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

Dose mg/kg	No.		WBC 10E2/ μ L	Differential leukocyte ratio (%)					Differential leukocyte counts (10E2/ μ L)						
				Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	5	Mean	74.1	77.4	17.4	2.0	0.4	2.4	0.4	57.4	12.9	1.4	0.3	1.8	0.3
		S.D.	12.1	6.5	5.5	0.7	0.1	0.9	0.2	11.6	4.8	0.5	0.1	0.7	0.1
1000	5	Mean	90.7	75.8	19.6	1.6	0.3	2.2	0.6	68.4	18.1	1.5	0.3	2.0	0.5*
		S.D.	16.2	2.9	2.7	0.6	0.1	0.4	0.2	10.6	5.2	0.7	0.0	0.4	0.1T

LUC: Large unstained cells

*: $p < 0.05$ (Significant difference from control group)

T: Student's t-test

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

Dose mg/kg	No.		RBC	HGB	HCT	MCV	MCH	MCHC	Retic	PLT	PT	APTT	FIB
			10E4/ μ L	g/dL	%	fL	pg	g/dL	%	10E4/ μ L	s	s	mg/dL
0	5	Mean	830	15.7	43.1	51.9	18.9	36.4	2.4	137.4	12.5	15.6	201
		S.D.	24	0.3	0.8	1.1	0.6	0.8	0.5	46.8	0.8	1.6	21
1000	5	Mean	857	15.8	44.2	51.5	18.5	35.8	1.8*	121.7	12.8	15.3	181
		S.D.	15	0.2	1.1	1.0	0.2	0.7	0.2T	12.5	0.6	2.8	14

*: $p < 0.05$ (Significant difference from control group)

T: Student's t-test

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

Dose mg/kg	No.		WBC 10E2/ μ L	Differential leukocyte ratio (%)					Differential leukocyte counts (10E2/ μ L)						
				Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	5	Mean	53.2	69.3	25.5	2.4	0.3	2.2	0.3	37.0	13.4	1.3	0.2	1.2	0.2
		S.D.	7.9	8.1	8.9	0.9	0.1	0.8	0.3	8.2	4.3	0.6	0.1	0.5	0.1
1000	5	Mean	54.7	79.6*	15.7	1.7	0.3	2.2	0.5	43.7	8.4*	1.0	0.1	1.2	0.3
		S.D.	8.6	5.1T	4.5	0.4	0.1	0.7	0.2	8.4	2.1T	0.2	0.1	0.4	0.1

LUC: Large unstained cells

*: $p < 0.05$ (Significant difference from control group)

T: Student's t-test

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

Dose mg/kg	No.		AST	ALT	LDH	γ -GTP	ALP	TBA	T-CHO	TG	PL	T-BIL	GLU
			IU/L	IU/L	IU/L	IU/L	IU/L	umol/L	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL
0	5	Mean	62	26	52	1	357	10.1	51	27	76	0.0	134
		S.D.	9	5	19	0	19	3.7	18	5	16	0.1	15
100	5	Mean	69	30	51	1	360	20.9	50	24	75	0.1	135
		S.D.	15	7	17	0	96	31.3	9	7	9	0.0	6
300	5	Mean	59	28	46	1	482	9.5	49	41	81	0.1	154*
		S.D.	13	5	18	0	107	4.4	9	9	15	0.0	4D
1000	5	Mean	64	26	45	1	374	9.0	47	26	74	0.0	134
		S.D.	11	2	9	0	56	5.9	4	12	10	0.1	10

*: $p < 0.05$ (Significant difference from control group)

D: Dunnett's test

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

Dose mg/kg	No.		BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
0	5	Mean	12	0.23	144	4.6	108	9.7	6.0	5.6	3.2	1.35
		S.D.	1	0.04	2	0.3	1	0.2	0.4	0.1	0.1	0.07
100	5	Mean	12	0.24	144	4.6	108	9.4	6.4	5.6	3.2	1.30
		S.D.	2	0.01	1	0.2	1	0.3	0.3	0.1	0.1	0.09
300	5	Mean	12	0.24	142	4.9	107	9.7	6.3	5.7	3.2	1.30
		S.D.	1	0.04	1	0.4	2	0.3	0.6	0.1	0.1	0.09
1000	5	Mean	14	0.27	144	4.9	108	9.7	6.3	5.6	3.3	1.46
		S.D.	1	0.05	1	0.2	1	0.3	0.6	0.2	0.1	0.05

No significant difference in any treated groups from control group.

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

Dose mg/kg	No.		AST	ALT	LDH	γ -GTP	ALP	TBA	T-CHO	TG	PL	T-BIL	GLU
			IU/L	IU/L	IU/L	IU/L	IU/L	umol/L	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL
0	5	Mean	93	62	46	1	229	27.8	68	63	128	0.1	118
		S.D.	29	18	17	0	27	7.9	13	20	19	0.0	16
100	5	Mean	67	43*	35	1	251	31.3	53	42	101	0.1	135
		S.D.	8	5D	6	0	85	32.1	8	9	12	0.0	12
300	5	Mean	73	47	33	1	290	20.1	57	42	104	0.1	126
		S.D.	8	7	5	0	159	6.4	20	13	32	0.1	12
1000	5	Mean	75	44*	40	0	241	21.9	65	72	116	0.1	118
		S.D.	13	4D	5	1	47	11.2	17	20	18	0.1	15

*: $p < 0.05$ (Significant difference from control group)

D: Dunnett's test

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

Dose mg/kg	No.		BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
0	5	Mean	16	0.23	141	4.1	106	10.3	7.0	6.0	3.7	1.58
		S.D.	2	0.02	2	0.4	2	0.3	0.7	0.2	0.2	0.11
100	5	Mean	13	0.23	140	4.5	106	10.1	6.5	5.9	3.5	1.47
		S.D.	2	0.04	2	0.4	2	0.1	0.7	0.2	0.1	0.09
300	5	Mean	13	0.23	141	4.3	106	10.1	6.9	6.0	3.5	1.43
		S.D.	1	0.02	1	0.3	1	0.2	0.5	0.2	0.1	0.06
1000	5	Mean	12*	0.22	141	4.0	105	10.3	7.0	6.0	3.5	1.39
		S.D.	2D	0.05	2	0.3	2	0.3	1.9	0.2	0.1	0.19

*: $p < 0.05$ (Significant difference from control group)

D: Dunnett's test

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

Dose mg/kg	No.		AST	ALT	LDH	γ -GTP	ALP	TBA	T-CHO	TG	PL	T-BIL	GLU
			IU/L	IU/L	IU/L	IU/L	IU/L	umol/L	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL
0	5	Mean	61	29	41	1	174	15.3	57	19	111	0.1	130
		S.D.	11	8	5	0	44	8.5	16	5	33	0.0	16
1000	5	Mean	60	28	46	1	235	16.8	70	20	126	0.1	125
		S.D.	12	14	8	1	109	9.8	15	9	20	0.0	14

No significant difference between treated group and control group.

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

Dose mg/kg	No.		BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
0	5	Mean	16	0.30	142	4.3	108	9.7	4.2	6.3	3.9	1.61
		S.D.	2	0.03	2	0.1	2	0.2	0.8	0.3	0.2	0.19
1000	5	Mean	15	0.29	142	4.2	107	9.9	4.2	6.4	3.9	1.56
		S.D.	1	0.02	1	0.2	1	0.3	0.2	0.4	0.3	0.15

No significant difference between treated group and control group.

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

Dose mg/kg	No.		AST	ALT	LDH	γ -GTP	ALP	TBA	T-CHO	TG	PL	T-BIL	GLU
			IU/L	IU/L	IU/L	IU/L	IU/L	umol/L	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL
0	5	Mean	69	34	48	1	303	19.2	53	28	82	0.1	135
		S.D.	10	7	14	0	63	22.2	4	10	9	0.1	8
1000	5	Mean	74	36	51	1	314	23.7	52	26	78	0.1	127
		S.D.	18	9	22	0	69	17.3	12	6	11	0.0	8

No significant difference between treated group and control group.

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

Dose mg/kg	No.		BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
0	5	Mean	18	0.25	142	4.6	107	9.5	6.0	5.7	3.2	1.30
		S.D.	2	0.02	2	0.2	2	0.2	0.2	0.3	0.1	0.18
1000	5	Mean	16	0.26	144	4.4	107	9.5	5.5	6.1	3.4	1.24
		S.D.	2	0.04	1	0.1	1	0.2	0.5	0.2	0.1	0.13

No significant difference between treated group and control group.

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

Dose mg/kg	No.		AST	ALT	LDH	γ -GTP	ALP	TBA	T-CHO	TG	PL	T-BIL	GLU
			IU/L	IU/L	IU/L	IU/L	IU/L	umol/L	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL
0	5	Mean	73	41	37	1	162	14.1	64	15	115	0.1	123
		S.D.	23	27	5	1	39	12.8	10	5	15	0.0	17
1000	5	Mean	81	37	52	1	155	26.9	65	18	116	0.1	123
		S.D.	44	22	29	0	42	24.3	8	2	13	0.0	12

No significant difference between treated group and control group.

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

Dose mg/kg	No.		BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
0	5	Mean	19	0.30	143	4.4	110	9.8	4.8	6.4	3.8	1.45
		S.D.	3	0.03	0	0.3	1	0.2	0.9	0.3	0.2	0.08
1000	5	Mean	19	0.29	142*	4.2	108*	10.0	4.5	6.4	3.9	1.51
		S.D.	3	0.02	1T	0.2	1T	0.2	0.3	0.3	0.2	0.03

*: p<0.05 (Significant difference from control group)

T: Student's t-test

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

Dose mg/kg	Body weight g	No.	Brain	Pituitary	Thyroid (R+L)	Thymus	Heart	Liver	
			g(g/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	g(g/100g BW)	g(g/100g BW)	
Absolute	0	No.	7	7	7	7	7	7	
		Mean	525	2.14	13.6	23.3	316	1.53	13.22
		S.D.	8	0.05	1.3	4.0	71	0.09	0.87
	100	No.	12	12	12	12	12	12	12
		Mean	515	2.12	14.1	21.4	286	1.51	13.19
		S.D.	21	0.08	1.9	2.6	61	0.09	0.88
	300	No.	12	12	12	12	12	12	12
		Mean	525	2.15	12.4	22.4	276	1.53	14.25
		S.D.	22	0.09	1.8	3.9	55	0.12	1.38
	1000	No.	7	7	7	7	7	7	7
		Mean	516	2.16	13.4	23.6	264	1.45	13.38
		S.D.	14	0.08	1.3	6.8	79	0.08	1.33
Relative	0	No.		7	7	7	7	7	
		Mean		0.41	2.6	4.5	60	0.29	2.52
		S.D.		0.01	0.2	0.8	14	0.02	0.19
	100	No.		12	12	12	12	12	12
		Mean		0.41	2.7	4.2	55	0.29	2.56
		S.D.		0.02	0.4	0.5	10	0.02	0.13
	300	No.		12	12	12	12	12	12
		Mean		0.41	2.4	4.3	53	0.29	2.71
		S.D.		0.02	0.3	0.8	11	0.03	0.19
	1000	No.		7	7	7	7	7	7
		Mean		0.42	2.6	4.6	51	0.28	2.59
		S.D.		0.02	0.3	1.3	15	0.01	0.25

No significant difference in any treated groups from control group.

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

Dose mg/kg		Spleen	Kidney (R+L)	Adrenal (R+L)	Testis (R+L)	Epididymis (R+L)	Seminal vesicle	Prostate	
		g(g/100g BW)	g(g/100g BW)	mg(mg/100g BW)	g(g/100g BW)	mg(mg/100g BW)	g(g/100g BW)	g(g/100g BW)	
Absolute	0	No.	7	7	7	7	7	7	
		Mean	0.80	3.56	63	3.27	1305	1.92	1.39
		S.D.	0.16	0.16	8	0.24	115	0.23	0.24
	100	No.	12	12	12	12	12	12	12
		Mean	0.70	3.51	63	3.34	1297	1.81	1.38
		S.D.	0.08	0.31	12	0.32	159	0.29	0.24
	300	No.	12	12	12	12	12	12	12
		Mean	0.76	3.46	61	3.33	1368	1.84	1.35
		S.D.	0.09	0.17	7	0.24	101	0.24	0.21
	1000	No.	7	7	7	7	7	7	7
		Mean	0.75	3.46	61	3.14	1341	1.86	1.38
		S.D.	0.08	0.34	7	0.13	127	0.32	0.24
Relative	0	No.	7	7	7	7	7	7	
		Mean	0.15	0.68	12	0.62	249	0.37	0.26
		S.D.	0.03	0.03	2	0.05	23	0.05	0.05
	100	No.	12	12	12	12	12	12	12
		Mean	0.14	0.68	12	0.65	252	0.35	0.27
		S.D.	0.02	0.06	3	0.08	35	0.07	0.05
	300	No.	12	12	12	12	12	12	12
		Mean	0.15	0.66	12	0.64	261	0.35	0.26
		S.D.	0.02	0.04	2	0.05	18	0.05	0.04
	1000	No.	7	7	7	7	7	7	7
		Mean	0.15	0.67	12	0.61	260	0.36	0.27
		S.D.	0.02	0.07	2	0.04	24	0.06	0.05

No significant difference in any treated groups from control group.

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

Dose mg/kg	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)	Liver g(g/100g BW)												
								No.	Mean	S.D.	No.	Mean	S.D.	No.	Mean	S.D.	No.	Mean	S.D.
Absolute	0	No.	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	
		Mean	332	2.00	18.4	16.0	211	1.07	11.07										
		S.D.	26	0.06	3.2	2.3	66	0.12	1.17										
	100	No.	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
		Mean	321	2.03	17.6	15.4	243	1.03	10.49										
		S.D.	27	0.08	2.9	2.2	128	0.07	0.76										
	300	No.	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
		Mean	328	2.01	19.3	15.7	224	1.04	10.44										
		S.D.	18	0.07	1.4	2.0	45	0.06	0.76										
	1000	No.	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
		Mean	328	1.96	17.2	15.5	191	1.05	10.74										
		S.D.	25	0.08	1.6	2.3	84	0.09	1.06										
Relative	0	No.	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	
		Mean	0.60	5.5	4.8	63	0.32	3.33											
		S.D.	0.05	0.8	0.6	18	0.02	0.25											
	100	No.	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
		Mean	0.63	5.5	4.8	73	0.32	3.27											
		S.D.	0.04	0.6	0.7	32	0.02	0.15											
	300	No.	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
		Mean	0.62	5.9	4.8	68	0.32	3.18											
		S.D.	0.04	0.5	0.7	12	0.02	0.17											
	1000	No.	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
		Mean	0.60	5.2	4.8	57	0.32	3.27											
		S.D.	0.05	0.5	1.0	24	0.03	0.19											

No significant difference in any treated groups from control group.

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

Dose mg/kg		Spleen	Kidney (R+L)	Adrenal (R+L)	Ovary (R+L)	Uterus	
		g(g/100g BW)	g(g/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	
Absolute	0	No.	11	11	11	11	
		Mean	0.66	2.27	75	110.4	744
		S.D.	0.10	0.13	12	12.3	201
	100	No.	11	11	11	11	11
		Mean	0.68	2.23	79	105.9	732
		S.D.	0.09	0.12	12	12.5	151
	300	No.	10	10	10	10	10
		Mean	0.73	2.24	77	103.0	715
		S.D.	0.15	0.09	9	10.0	130
	1000	No.	11	11	11	11	11
		Mean	0.71	2.45	82	107.9	780
		S.D.	0.12	0.26	12	11.4	110
Relative	0	No.	11	11	11	11	
		Mean	0.20	0.69	23	33.4	222
		S.D.	0.03	0.05	5	4.1	48
	100	No.	11	11	11	11	11
		Mean	0.21	0.70	25	33.1	230
		S.D.	0.03	0.06	5	3.6	54
	300	No.	10	10	10	10	10
		Mean	0.22	0.68	24	31.4	218
		S.D.	0.04	0.04	3	3.3	38
	1000	No.	11	11	11	11	11
		Mean	0.22	0.75	25	33.0	240
		S.D.	0.04	0.13	4	3.1	44

No significant difference in any treated groups from control group.

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

Dose mg/kg	Body weight g	No.	Brain	Pituitary	Thyroid (R+L)	Thymus	Heart	Liver	
			g(g/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	g(g/100g BW)	g(g/100g BW)	
Absolute	0	No.	5	5	5	5	5	5	
		Mean	295	2.02	17.9	15.5	291	0.94	7.71
		S.D.	28	0.07	2.4	2.8	48	0.07	0.46
	1000	No.	5	5	5	5	5	5	
		Mean	290	1.96	17.1	16.7	312	0.91	7.97
		S.D.	28	0.07	2.6	2.2	60	0.05	0.57
Relative	0	No.	5	5	5	5	5	5	
		Mean	0.69	6.1	5.3	99	0.32	2.63	
		S.D.	0.08	0.8	1.2	12	0.03	0.20	
	1000	No.	5	5	5	5	5	5	
		Mean	0.68	5.9	5.8	107	0.31	2.75	
		S.D.	0.06	1.0	0.7	14	0.02	0.14	

No significant difference between treated group and control group.

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

Dose			Spleen	Kidney	Adrenal	Ovary	Uterus
mg/kg			g(g/100g BW)	(R+L) g(g/100g BW)	(R+L) mg(mg/100g BW)	(R+L) mg(mg/100g BW)	mg(mg/100g BW)
Absolute	0	No.	5	5	5	5	5
		Mean	0.48	2.03	74	92.9	608
		S.D.	0.03	0.12	11	17.4	126
	1000	No.	5	5	5	5	5
		Mean	0.51	1.96	73	92.6	632
		S.D.	0.06	0.11	7	13.5	99
Relative	0	No.	5	5	5	5	5
		Mean	0.17	0.70	25	31.4	210
		S.D.	0.02	0.07	3	4.0	60
	1000	No.	5	5	5	5	5
		Mean	0.18	0.68	25	31.9	220
		S.D.	0.01	0.06	1	3.8	47

No significant difference between treated group and control group.

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

Dose mg/kg	Body weight g	No.	Brain	Pituitary	Thyroid (R+L)	Thymus	Heart	Liver	
			g(g/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	g(g/100g BW)	g(g/100g BW)	
Absolute	0	No.	5	5	5	5	5	5	
		Mean	512	2.19	13.9	25.1	274	1.35	12.80
		S.D.	28	0.09	2.5	4.4	54	0.04	1.12
	1000	No.	5	5	5	5	5	5	
		Mean	523	2.20	13.2	23.5	294	1.44*	12.92
		S.D.	40	0.09	1.6	6.1	66	0.07T	1.70
Relative	0	No.	5	5	5	5	5	5	
		Mean	0.43	2.7	4.9	54	0.26	2.49	
		S.D.	0.02	0.4	0.7	9	0.02	0.12	
	1000	No.	5	5	5	5	5	5	
		Mean	0.42	2.5	4.5	56	0.28	2.46	
		S.D.	0.04	0.2	1.0	11	0.02	0.18	

*: p<0.05 (Significant difference from control group)

T: Student's t-test

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

Dose mg/kg		Spleen g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Testis (R+L) g(g/100g BW)	Epididymis (R+L) mg(mg/100g BW)	Seminal vesicle g(g/100g BW)	Prostate g(g/100g BW)						
									No.	Mean	S.D.	No.	Mean	S.D.
Absolute	0	No.	5	5	5	5	5	5						
		Mean	0.69	3.43	57	3.26	1291	1.90						
		S.D.	0.03	0.18	5	0.16	94	0.28						
	1000	No.	5	5	5	5	5	5						
		Mean	0.79*	3.61	59	3.31	1411*	1.89						
		S.D.	0.07T	0.30	6	0.22	49T	0.18						
Relative	0	No.	5	5	5	5	5	5						
		Mean	0.14	0.67	11	0.64	252	0.37						
		S.D.	0.01	0.04	1	0.04	23	0.06						
	1000	No.	5	5	5	5	5	5						
		Mean	0.15	0.69	11	0.63	272	0.36						
		S.D.	0.01	0.06	2	0.04	29	0.03						

*: p<0.05 (Significant difference from control group)

T: Student's t-test

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

Dose mg/kg	Body weight g	No.	Brain	Pituitary	Thyroid (R+L)	Thymus	Heart	Liver	
			g(g/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)	g(g/100g BW)	g(g/100g BW)	
Absolute	0	No.	5	5	5	5	5	5	
		Mean	275	1.96	16.5	15.7	266	0.87	6.46
		S.D.	18	0.06	2.7	2.7	67	0.07	0.52
	1000	No.	5	5	5	5	5	5	
		Mean	296	2.00	16.5	16.8	293	0.93	7.14
		S.D.	18	0.09	1.4	2.4	64	0.05	0.74
Relative	0	No.	5	5	5	5	5	5	
		Mean	0.71	6.0	5.7	98	0.32	2.35	
		S.D.	0.05	0.9	0.9	30	0.03	0.09	
	1000	No.	5	5	5	5	5	5	
		Mean	0.68	5.6	5.7	99	0.31	2.40	
		S.D.	0.03	0.5	0.8	21	0.02	0.14	

No significant difference between treated group and control group.

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

Dose mg/kg		Spleen g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)								
							No.	Mean	S.D.	No.	Mean	S.D.	No.	Mean
Absolute	0	No.	5	5	5	5	5							
		Mean	0.50	1.76	65	90.1	552							
		S.D.	0.08	0.10	9	18.4	134							
	1000	No.	5	5	5	5	5							
		Mean	0.59	2.06**	73	96.3	488							
		S.D.	0.13	0.14T	9	19.0	47							
Relative	0	No.	5	5	5	5	5							
		Mean	0.18	0.64	24	33.0	200							
		S.D.	0.02	0.03	2	7.4	42							
	1000	No.	5	5	5	5	5							
		Mean	0.20	0.70*	25	32.5	165							
		S.D.	0.03	0.03T	3	6.0	9							

*: $p < 0.05$; **: $p < 0.01$ (Significant difference from control group)

T: Student's t-test

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

Organs	Sex:	M	M	M	M
	Dose (mg/kg) :	0	100	300	1000
Findings	Number:	7	12	12	7
Epididymis					
Focus, white, unilateral		0	0	1	0
Stomach					
Focus, dark red, glandular stomach		0	0	1	0

M : Male

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

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

F : Female

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

Organs	Sex:	F	F	F	F
	Dose (mg/kg) :	0	100	300	1000
Findings	Number:	11	11	10	11
Kidney					
Discoloration, pale, bilateral		0	0	0	1
Lung (bronchus)					
Focus, dark red		0	0	2	0
Stomach					
Focus, dark red, glandular stomach		0	1	2	1
Thymus					
Small		0	0	0	1

F : Female

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

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

M : Male

Table 9-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Gross pathological findings (End of recovery period)

Organs	Sex:	F	F
	Dose (mg/kg) :	0	1000
Findings	Number:	5	5
Stomach			
Focus, dark red, glandular stomach		1	0

F : Female

Table 9-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Gross pathological findings (Undelivered)

Organs	Sex:	F	F	F
	Dose (mg/kg):	0	100	300
Findings	Number:	1	1	2
All tissues				
Not remarkable		1	1	2

F : Female

Table 9-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Gross pathological findings (Found dead)

Organs	Sex:	F
Findings	Dose (mg/kg):	1000
	Number:	1
Stomach		
Focus, dark red, forstomach		1

F : Female

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

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

M : Male

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

Organs	Sex:	M	M	M	M
	Dose (mg/kg) :	0	100	300	1000
Findings	Number:	7	12	12	7
Liver					
Number examined		5	1	2	5
Not remarkable		5	1	2	5
Lung (bronchus)					
Number examined		5	1	2	5
Not remarkable		5	1	1	5
Hemorrhage		0	0	1	0
minimal		0	0	1	0
Lymph node, mesenteric					
Number examined		5	1	2	5
Not remarkable		5	1	2	5
Lymph node, submandibular					
Number examined		5	1	2	5
Not remarkable		5	1	2	5
Mammary gland, inguinal					
Number examined		5	1	2	5
Not remarkable		5	1	2	5
Pancreas					
Number examined		5	1	2	5
Not remarkable		5	1	2	5
Parathyroid					
Number examined		5	1	2	5
Not remarkable		5	1	2	5
Pituitary					
Number examined		5	1	2	5
Not remarkable		5	1	2	5
Prostate					
Number examined		5	1	2	5
Not remarkable		1	1	1	3
Cell infiltration		4	0	1	2
minimal		4	0	1	2
Salivary gland, submandibular					
Number examined		5	1	2	5
Not remarkable		5	1	2	5
Sciatic nerve					
Number examined		5	1	2	5
Not remarkable		5	1	2	5
Seminal vesicle (coagulating gland)					
Number examined		5	1	2	5
Not remarkable		5	1	2	5
Skeletal muscle, femoral					
Number examined		5	1	2	5
Not remarkable		5	1	2	5
Spinal cord, thoracic					
Number examined		5	1	2	5
Not remarkable		5	1	2	5
Spleen					
Number examined		5	1	2	5
Not remarkable		3	0	0	4

M : Male

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

Organs	Sex:	M	M	M	M
	Dose (mg/kg) :	0	100	300	1000
Findings	Number:	7	12	12	7
Spleen (continued)					
Hematopoiesis, extramedullary		2	1	2	1
minimal		2	1	2	1
Stomach					
Number examined		5	6	6	5
Not remarkable		5	6	6	4
Hyperplasia, squamous, limiting ridge		0	0	0	1
minimal		0	0	0	1
Testis					
Number examined		5	1	2	5
Not remarkable		5	1	2	5
Thymus					
Number examined		5	1	2	5
Not remarkable		5	1	2	5
Thyroid					
Number examined		5	1	2	5
Not remarkable		5	1	2	5
Trachea					
Number examined		5	1	2	5
Not remarkable		5	1	2	5
Urinary bladder					
Number examined		5	1	2	5
Not remarkable		5	1	2	5

M : Male

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

Organs	Sex:	F	F
Findings	Dose (mg/kg):	0	1000
	Number:	5	5
Adrenal			
Number examined		5	5
Not remarkable		5	5
Bone+Bone marrow, femoral			
Number examined		5	5
Not remarkable		5	5
Cerebrum			
Number examined		5	5
Not remarkable		5	5
Cerebellum(pons)			
Number examined		5	5
Not remarkable		5	5
Eye			
Number examined		5	5
Not remarkable		5	4
Dysplasia, retinal		0	1
minimal		0	1
Heart			
Number examined		5	5
Not remarkable		5	5
Intestine, duodenum			
Number examined		5	5
Not remarkable		5	5
Intestine, jejunum			
Number examined		5	5
Not remarkable		5	5
Intestine, ileum(Peyer's patch)			
Number examined		5	5
Not remarkable		5	5
Intestine, cecum			
Number examined		5	5
Not remarkable		5	5
Intestine, colon			
Number examined		5	5
Not remarkable		5	5
Intestine, rectum			
Number examined		5	5
Not remarkable		5	5
Kidney			
Number examined		5	5
Not remarkable		5	3
Regeneration, tubular		0	1
minimal		0	1
Fibrosis		0	1
minimal		0	1
Liver			
Number examined		5	5
Not remarkable		5	5

F : Female

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

Organs	Sex:	F	F
Findings	Dose (mg/kg):	0	1000
	Number:	5	5
Lung (bronchus)			
Number examined		5	5
Not remarkable		4	4
Hemorrhage		0	1
minimal		0	1
Cell infiltration		1	0
minimal		1	0
Lymph node, mesenteric			
Number examined		5	5
Not remarkable		5	5
Lymph node, submandibular			
Number examined		5	5
Not remarkable		5	5
Mammary gland, inguinal			
Number examined		5	5
Not remarkable		5	5
Ovary			
Number examined		5	5
Not remarkable		5	4
Atrophy		0	1
minimal		0	1
Pancreas			
Number examined		5	5
Not remarkable		5	5
Parathyroid			
Number examined		5	5
Not remarkable		5	5
Pituitary			
Number examined		5	5
Not remarkable		5	5
Salivary gland, submandibular			
Number examined		5	5
Not remarkable		5	5
Sciatic nerve			
Number examined		5	5
Not remarkable		5	5
Skeletal muscle, femoral			
Number examined		5	5
Not remarkable		5	5
Spinal cord, thoracic			
Number examined		5	5
Not remarkable		5	5
Spleen			
Number examined		5	5
Not remarkable		3	4
Hematopoiesis, extramedullary		2	1
minimal		2	1
Stomach			
Number examined		5	5
Not remarkable		5	2

F : Female

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

Organs	Sex:	F	F
Findings	Dose (mg/kg):	0	1000
	Number:	5	5
Stomach (continued)			
Hyperplasia, squamous, limiting ridge		0	3
minimal		0	3
Thymus			
Number examined		5	5
Not remarkable		5	5
Thyroid			
Number examined		5	5
Not remarkable		5	5
Trachea			
Number examined		5	5
Not remarkable		5	5
Urinary bladder			
Number examined		5	5
Not remarkable		5	5
Uterus			
Number examined		5	5
Not remarkable		5	5
Vagina			
Number examined		5	5
Not remarkable		5	5

F : Female

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

Organs	Sex:	F	F	F	F
Findings	Dose (mg/kg):	0	100	300	1000
	Number:	11	11	10	11
Adrenal					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Bone+Bone marrow, femoral					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Cerebrum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Cerebellum(pons)					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Eye					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Heart					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine, duodenum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine, jejunum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine, ileum(Peyer's patch)					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine, cecum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine, colon					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine, rectum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Kidney					
Number examined		5	0	0	5
Not remarkable		3	0	0	2
Regeneration, tubular		1	0	0	3
minimal		1	0	0	3
Cell infiltration		1	0	0	0
minimal		1	0	0	0
Liver					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Lung (bronchus)					
Number examined		5	0	0	5
Not remarkable		5	0	0	5

F : Female

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

Organs	Sex:	F	F	F	F
	Dose (mg/kg) :	0	100	300	1000
Findings	Number:	11	11	10	11
Lymph node, mesenteric					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Lymph node, submandibular					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Mammary gland, inguinal					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Ovary					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Pancreas					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Parathyroid					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Pituitary					
Number examined		5	0	0	5
Not remarkable		5	0	0	4
Cyst, pars intermedia		0	0	0	1
minimal		0	0	0	1
Salivary gland, submandibular					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Sciatic nerve					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Skeletal muscle, femoral					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Spinal cord, thoracic					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Spleen					
Number examined		5	0	0	5
Hematopoiesis, extramedullary		5	0	0	5
minimal		1	0	0	1
mild		4	0	0	4
Stomach					
Number examined		5	5	5	5
Not remarkable		5	5	4	4
Erosion/ulcer, glandular stomach		0	0	1	1
minimal		0	0	1	1
Thymus					
Number examined		5	0	0	5
Not remarkable		5	0	0	5

F : Female

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

Organs	Sex:	F	F	F	F
Findings	Dose (mg/kg):	0	100	300	1000
	Number:	11	11	10	11
Thyroid					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Trachea					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Urinary bladder					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Uterus					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Vagina					
Number examined		5	0	0	5
Not remarkable		5	0	0	5

F : Female

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

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

M : Male

Table 10-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Histopathological findings (End of recovery period)

Organs	Sex:	M	M
Findings	Dose (mg/kg):	0	1000
	Number:	5	5
Lung (bronchus)			
Number examined		1	0
Not remarkable		1	0
Lymph node, mesenteric			
Number examined		1	0
Not remarkable		1	0
Lymph node, submandibular			
Number examined		1	0
Not remarkable		1	0
Mammary gland, inguinal			
Number examined		1	0
Not remarkable		1	0
Pancreas			
Number examined		1	0
Not remarkable		1	0
Parathyroid			
Number examined		1	0
Not remarkable		1	0
Pituitary			
Number examined		1	0
Not remarkable		1	0
Prostate			
Number examined		1	0
Cell infiltration		1	0
minimal		1	0
Salivary gland, submandibular			
Number examined		1	0
Not remarkable		1	0
Sciatic nerve			
Number examined		1	0
Not remarkable		1	0
Seminal vesicle (coagulating gland)			
Number examined		1	0
Not remarkable		1	0
Skeletal muscle, femoral			
Number examined		1	0
Not remarkable		1	0
Spinal cord, thoracic			
Number examined		1	0
Not remarkable		1	0
Spleen			
Number examined		1	0
Not remarkable		1	0
Stomach			
Number examined		5	5
Not remarkable		5	5

M : Male

Table 10-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Histopathological findings (End of recovery period)

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

M : Male

Table 10-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Histopathological findings (End of recovery period)

Organs	Sex:	F	F
Findings	Dose (mg/kg):	0	1000
	Number:	5	5
Stomach			
Number examined		5	5
Not remarkable		4	4
Erosion/ulcer, glandular stomach		1	0
minimal		1	0
Hyperplasia, squamous, limiting ridge		0	1
minimal		0	1

F : Female

Table 10-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Histopathological findings (Undelivered)

Organs	Sex:	F	F	F
Findings	Dose (mg/kg):	0	100	300
	Number:	1	1	2
Adrenal				
Number examined		1	1	2
Not remarkable		1	1	2
Bone+Bone marrow, femoral				
Number examined		1	1	2
Not remarkable		1	1	2
Cerebrum				
Number examined		1	1	2
Not remarkable		1	1	2
Cerebellum(pons)				
Number examined		1	1	2
Not remarkable		1	1	2
Eye				
Number examined		1	1	2
Not remarkable		1	1	2
Heart				
Number examined		1	1	2
Not remarkable		0	0	2
Cell infiltration		1	1	0
minimal		1	1	0
Intestine, duodenum				
Number examined		1	1	2
Not remarkable		1	1	2
Intestine, jejunum				
Number examined		1	1	2
Not remarkable		1	1	2
Intestine, ileum(Peyer's patch)				
Number examined		1	1	2
Not remarkable		1	1	2
Intestine, cecum				
Number examined		1	1	2
Not remarkable		1	1	2
Intestine, colon				
Number examined		1	1	2
Not remarkable		1	1	2
Intestine, rectum				
Number examined		1	1	2
Not remarkable		1	1	2
Kidney				
Number examined		1	1	2
Not remarkable		1	1	2
Liver				
Number examined		1	1	2
Not remarkable		1	1	2
Lung (bronchus)				
Number examined		1	1	2
Not remarkable		1	1	2

F : Female

Table 10-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Histopathological findings (Undelivered)

Organs	Sex:	F	F	F
	Dose (mg/kg) :	0	100	300
Findings	Number:	1	1	2
Lymph node, mesenteric				
Number examined		1	1	2
Not remarkable		1	1	2
Lymph node, submandibular				
Number examined		1	1	2
Not remarkable		1	1	2
Mammary gland, inguinal				
Number examined		1	1	2
Not remarkable		1	0	2
Hyperplasia, lobular, acinar		0	1	0
minimal		0	1	0
Ovary				
Number examined		1	1	2
Not remarkable		1	0	2
Increased, eosinophilic large corpus luteum		0	1	0
minimal		0	1	0
Pancreas				
Number examined		1	1	2
Not remarkable		1	1	2
Parathyroid				
Number examined		1	1	2
Not remarkable		1	1	2
Pituitary				
Number examined		1	1	2
Not remarkable		1	1	2
Salivary gland, submandibular				
Number examined		1	1	2
Not remarkable		1	1	2
Sciatic nerve				
Number examined		1	1	2
Not remarkable		1	1	2
Skeletal muscle, femoral				
Number examined		1	1	2
Not remarkable		1	1	2
Spinal cord, thoracic				
Number examined		1	1	2
Not remarkable		1	1	2
Spleen				
Number examined		1	1	2
Not remarkable		1	1	2
Stomach				
Number examined		1	1	2
Not remarkable		1	1	2
Thymus				
Number examined		1	1	2
Not remarkable		1	1	1
Atrophy		0	0	1
minimal		0	0	1

F : Female

Table 10-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Histopathological findings (Undelivered)

Organs	Sex:	F	F	F
Findings	Dose (mg/kg):	0	100	300
	Number:	1	1	2
Thyroid				
Number examined		1	1	2
Not remarkable		1	1	2
Trachea				
Number examined		1	1	2
Not remarkable		1	1	2
Urinary bladder				
Number examined		1	1	2
Not remarkable		1	1	2
Uterus				
Number examined		1	1	2
Not remarkable		1	1	2
Vagina				
Number examined		1	1	2
Not remarkable		1	0	2
Mucification		0	1	0
minimal		0	1	0

F : Female

Table 10-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Histopathological findings (Found dead)

Organs	Sex:	F
Findings	Dose (mg/kg): Number:	1000 1
Adrenal		
Number examined		1
Hypertrophy, cortical cell minimal		1 1
Bone+Bone marrow, femoral		
Number examined		1
Hypocellularity, bone marrow minimal		1 1
Cerebrum		
Number examined		1
Not remarkable		1
Cerebellum (pons)		
Number examined		1
Not remarkable		1
Eye		
Number examined		1
Not remarkable		1
Heart		
Number examined		1
Not remarkable		1
Intestine, duodenum		
Number examined		1
Not remarkable		1
Intestine, jejunum		
Number examined		1
Not remarkable		1
Intestine, ileum (Peyer's patch)		
Number examined		1
Not remarkable		1
Intestine, cecum		
Sample autolysed		1
Intestine, colon		
Number examined		1
Not remarkable		1
Intestine, rectum		
Number examined		1
Not remarkable		1
Kidney		
Number examined		1
Vacuolation, tubular cell mild		1 1
Liver		
Number examined		1
Not remarkable		1
Lung (bronchus)		
Number examined		1
Not remarkable		1

F : Female

Table 10-18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Histopathological findings (Found dead)

Organs	Sex:	F
Findings	Dose (mg/kg): Number:	1000 1
Lymph node, mesenteric		
Number examined		1
Atrophy		1
moderate		1
Lymph node, submandibular		
Number examined		1
Atrophy		1
mild		1
Mammary gland, inguinal		
Number examined		1
Not remarkable		1
Ovary		
Number examined		1
Not remarkable		1
Pancreas		
Number examined		1
Not remarkable		1
Parathyroid		
Number examined		1
Not remarkable		1
Pituitary		
Number examined		1
Not remarkable		1
Salivary gland, submandibular		
Number examined		1
Not remarkable		1
Sciatic nerve		
Number examined		1
Not remarkable		1
Skeletal muscle, femoral		
Number examined		1
Not remarkable		1
Spinal cord, thoracic		
Number examined		1
Not remarkable		1
Spleen		
Number examined		1
Atrophy, lymphoid		1
moderate		1
Stomach		
Number examined		1
Ulcer, forestomach		1
minimal		1
Thymus		
Number examined		1
Atrophy		1
severe		1

F : Female

Table 10-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Histopathological findings (Found dead)

Organs	Sex:	F
Findings	Dose (mg/kg): Number:	1000 1
Thyroid		
Number examined		1
Not remarkable		1
Trachea		
Number examined		1
Not remarkable		1
Urinary bladder		
Number examined		1
Not remarkable		1
Uterus		
Number examined		1
Not remarkable		1
Vagina		
Number examined		1
Not remarkable		1

F : Female

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

Dose mg/kg	No. of animals	Count of estrus					Mean+S.D.	Mean duration of cycles Mean+S.D.	Index of animals with abnormal estrous cycle (%) ^{a)}
		0	1	2	3	4			
0	12	0	0	0	3	9	3.8+0.5	4.1+0.3	0/12 (0.0)
100	12	0	0	0	3	9	3.8+0.5	4.2+0.3	0/12 (0.0)
300	12	0	0	0	3	9	3.8+0.5	4.2+0.3	0/12 (0.0)
1000	12	0	0	0	3	9	3.8+0.5	4.2+0.2	0/12 (0.0)

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

Table 12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Mating and fertility of animals

Dose mg/kg	Male				Female			
	No. of males	Days until copulation Mean+S.D.	Copulation index (%) a)	Insemination index (%) b)	No. of females	Days until copulation Mean+S.D.	Copulation index (%) a)	Fertility index (%) c)
0	12	3.4+3.5	12/12(100.0)	11/12(91.7)	12	3.4+3.5	12/12(100.0)	11/12(91.7)
100	12	2.7+1.1	12/12(100.0)	11/12(91.7)	12	2.7+1.1	12/12(100.0)	11/12(91.7)
300	12	2.5+0.7	12/12(100.0)	10/12(83.3)	12	2.5+0.7	12/12(100.0)	10/12(83.3)
1000	12	2.4+1.2	12/12(100.0)	12/12(100.0)	12	2.4+1.2	12/12(100.0)	12/12(100.0)

a): (No. of copulated animals / No. of mated animals)×100

b): (No. of males which impregnated females / No. of copulated males)×100

c): (No. of pregnant females / No. of copulated females)×100

No significant difference in any treated groups from control group.

Table 13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Delivery data on dams

Dose mg/kg		No. of pregnant females	No. of females with liveborns	Gestation index % a)	Gestation length in days	No. of corpora lutea	No. of implantation sites	Implantation index % b)	Delivery index % c)	No. of stillborns (%)d)	No. of liveborns	External abnormalities(%)f)
0	Total	11	11	100.0		194	180			2	165	0
	Mean				22.0	17.6	16.4	93.0	93.2	(1.2)	15.0	(0.0)
	S.D.				0.4	1.4	1.6	8.4	6.7	(2.7)	1.2	(0.0)
100	Total	11	11	100.0		174	161			5	146	0
	Mean				21.8	15.8	14.6	92.5	93.7	(2.7)	13.3*	(0.0)
	S.D.				0.4	2.2	2.4	8.2	4.9	(6.8)	2.0ST	(0.0)
300	Total	10	10	100.0		163	163			3	142	0
	Mean				21.8	16.3	16.3	100.0**	89.9	(2.0)	14.2	(0.0)
	S.D.				0.4	2.2	2.2	0.0J	12.3	(3.2)	1.7	(0.0)
1000	Total	11	11	100.0		177	165			3	149	0
	Mean				21.9	16.1	15.0	90.9	92.9	(1.7)	13.5	(0.0)
	S.D.				0.3	2.4	4.2	20.6	7.0	(2.9)	3.6	(0.0)

a): (No. of females which delivered liveborns / No. of pregnant females)×100

b): (No. of implantation sites / No. of corpora lutea)×100

c): (No. of delivered pups / No. of implantation sites)×100

d): (No. of stillborns / No. of delivered pups)×100

e): No. of delivered pups with external abnormalities

f): (No. of delivered pups with external abnormalities / No. of delivered pups)×100

*: p<0.05; **: p<0.01 (Significant difference from control group)

ST: Steel's test

J: Wilcoxon's rank sum test

Table 14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Viability index of pups

Dose mg/kg		No. of dams	No. of live- borns	No. of delivered pups	Live birth index % a)	No. of dams	No. of live pups		Viability index on postnatal day 4 % b)
							----- Day 0	Day 4	
0	Total	11	165	167		11	165	161	
	Mean		15.0	15.2	98.8		15.0	14.6	97.5
	S.D.		1.2	1.1	2.7		1.2	1.4	4.5
100	Total	11	146	151		11	146	136	
	Mean		13.3	13.7	97.3		13.3	12.4	93.0
	S.D.		2.0	2.4	6.8		2.0	3.3	19.4
300	Total	10	142	145		10	142	138	
	Mean		14.2	14.5	98.0		14.2	13.8	97.2
	S.D.		1.7	1.8	3.2		1.7	1.8	4.7
1000	Total	11	149	152		11	149	148	
	Mean		13.5	13.8	98.3		13.5	13.5	99.4
	S.D.		3.6	3.8	2.9		3.6	3.6	2.0

a): (No. of liveborns / No. of delivered pups)×100

b): (No. of live pups on postnatal day 4 / No. of liveborns)×100

No significant difference in any treated groups from control group.

Table 15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Sex ratio of pups

Dose mg/kg	No. of dams		Liveborns		Stillborns		Sex ratio of delivered pups	Sex ratio of liveborns	No. of dams	Postnatal day 4		Sex ratio of live pups on day 4
			No. of males	No. of females	No. of males	No. of females	a)	b)		No. of males	No. of females	c)
0	11	Total	81	84	1	1				79	82	
		Mean	7.4	7.6	0.1	0.1	0.49	0.49	11	7.2	7.5	0.49
		S.D.	2.3	1.6	0.3	0.3	0.12	0.12		2.3	1.8	0.13
100	11	Total	86	60	2	3				82	54	
		Mean	7.8	5.5	0.2	0.3	0.58	0.59	11	7.5	4.9	0.63
		S.D.	1.5	1.0	0.4	0.9	0.06	0.06		1.7	2.0	0.14
300	10	Total	81	61	1	2				80	58	
		Mean	8.1	6.1	0.1	0.2	0.57	0.57	10	8.0	5.8	0.58
		S.D.	2.6	2.5	0.3	0.4	0.15	0.16		2.6	2.8	0.18
1000	11	Total	71	78	2	1				71	77	
		Mean	6.5	7.1	0.2	0.1	0.46	0.46	11	6.5	7.0	0.47
		S.D.	2.7	2.3	0.4	0.3	0.13	0.12		2.7	2.3	0.12

a): No. of delivered males / No. of delivered pups

b): No. of liveborn males / No. of liveborns

c): No. of live males on day 4 / No. of live pups on day 4

No significant difference in any treated groups from control group.

Table 16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Body weight of pups

Dose mg/kg		Male			Female		
		0	4a)	Gain	0	4a)	Gain
0	No.	11	11	11	11	11	11
	Mean	6.6	10.1	3.5	6.2	9.6	3.4
	S.D.	0.3	0.6	0.6	0.4	0.7	0.5
100	No.	11	11	11	11	10	10
	Mean	6.7	10.0	3.3	6.2	9.7	3.5
	S.D.	0.5	1.7	1.4	0.4	1.1	0.9
300	No.	10	10	10	10	10	10
	Mean	6.5	10.0	3.5	6.2	9.6	3.4
	S.D.	0.4	1.0	0.7	0.4	1.1	0.8
1000	No.	11	11	11	11	11	11
	Mean	6.9	9.8	2.9	6.4	9.3	2.9
	S.D.	0.7	1.3	1.1	0.7	1.2	0.9

Unit: g

No.: No. of dams

a): Postnatal day

No significant difference in any treated groups from control group.

Table 17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Externally for gross abnormalities in dead pups

	Dose (mg/kg)	0	100	300	1000
Male					
No. of pups examined		1	5	0	0
No. of pups with abnormal findings		0	0	0	0
Female					
No. of pups examined		2	5	2	1
No. of pups with abnormal findings		0	0	0	0

Table 18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Externally for gross abnormalities in pups on postnatal day 4

	Dose (mg/kg)	0	100	300	1000
Male					
No. of pups examined		79	82	80	71
No. of pups with abnormal findings		0	0	0	0
Female					
No. of pups examined		82	54	58	77
No. of pups with abnormal findings		0	0	0	0

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

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

a): Day of necropsy
 -: No abnormal findings

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

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

a): Day of necropsy
 -: No abnormal findings

Appendix 1-3

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Individual clinical signs in male rats (Administration period)
Dose (mg/kg): 300

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

a): Day of necropsy
-: No abnormal findings

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

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

a): Day of necropsy
 -: No abnormal findings

Appendix 1-5

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Individual clinical signs in female rats during the pre-mating period (Main group)
Dose (mg/kg): 0

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

-: No abnormal findings

Appendix 1-6

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Individual clinical signs in female rats during the pre-mating period (Main group)
Dose (mg/kg): 100

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

-: No abnormal findings

Appendix 1-7

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Individual clinical signs in female rats during the pre-mating period (Main group)
Dose (mg/kg): 300

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

-: No abnormal findings

Appendix 1-8

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Individual clinical signs in female rats during the pre-mating period (Main group)
Dose (mg/kg): 1000

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

-: No abnormal findings

Appendix 1-9

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual clinical signs in dams during the gestation period (Main group)
 Dose (mg/kg): 0

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

a): Gestation day

-: No abnormal findings

d: Delivery

/d: Found delivery after the observation of general conditions.

Appendix 1-10

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual clinical signs in dams during the gestation period (Main group)
 Dose (mg/kg): 100

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

a): Gestation day

-: No abnormal findings

d: Delivery

/d: Found delivery after the observation of general conditions.

Appendix 1-11

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual clinical signs in dams during the gestation period (Main group)
 Dose (mg/kg): 300

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

a): Gestation day

-: No abnormal findings

d: Delivery

/d: Found delivery after the observation of general conditions.

Appendix 1-12

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual clinical signs in dams during the gestation period (Main group)
 Dose (mg/kg): 1000

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

a): Gestation day

-: No abnormal findings

A: Decrease in spontaneous movement

+: Dead

d: Delivery

/d: Found delivery after the observation of general conditions.

Appendix 1-13

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of
 dimethyl glutarate by oral administration in rats
 Individual clinical signs in dams during the lactation period (Main group)
 Dose (mg/kg): 0

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

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

Appendix 1-14

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual clinical signs in dams during the lactation period (Main group)
 Dose (mg/kg): 100

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

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

Appendix 1-15

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual clinical signs in dams during the lactation period (Main group)
 Dose (mg/kg): 300

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

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

Appendix 1-16

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual clinical signs in dams during the lactation period (Main group)
 Dose (mg/kg): 1000

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

a): Lactation day
 b): Day of necropsy
 c): Died on day 23 of gestation
 -: No abnormal findings

Appendix 1-17

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual clinical signs in female rats (Satellite group, Administration period)
 Dose (mg/kg): 0

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

a): Day of necropsy
 -: No abnormal findings

Appendix 1-18

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual clinical signs in female rats (Satellite group, Administration period)
 Dose (mg/kg): 1000

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

a): Day of necropsy
 -: No abnormal findings

Appendix 1-19

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of
 dimethyl glutarate by oral administration in rats
 Individual clinical signs in male rats (Recovery period)
 Dose (mg/kg): 0

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

a): Day of necropsy

-: No abnormal findings

Appendix 1-20

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Individual clinical signs in male rats (Recovery period)
Dose (mg/kg): 1000

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

a): Day of necropsy

-: No abnormal findings

Appendix 1-21

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Individual clinical signs in female rats (Recovery period)
Dose (mg/kg): 0

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

a): Day of necropsy
-: No abnormal findings

Appendix 1-22

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of
 dimethyl glutarate by oral administration in rats
 Individual clinical signs in female rats (Recovery period)
 Dose (mg/kg): 1000

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

a): Day of necropsy

-: No abnormal findings

Appendix 2-1

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: home cage observation
 (Week 1 of administration)
 Dose (mg/kg): 0

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-2

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: home cage observation
 (Week 1 of administration)
 Dose (mg/kg): 100

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-3

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: home cage observation
 (Week 1 of administration)
 Dose (mg/kg): 300

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-4

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: home cage observation
 (Week 1 of administration)
 Dose (mg/kg): 1000

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-5

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: home cage observation
 (Week 2 of administration)
 Dose (mg/kg): 0

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-6

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: home cage observation
 (Week 2 of administration)
 Dose (mg/kg): 100

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-7

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: home cage observation
 (Week 2 of administration)
 Dose (mg/kg): 300

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-8

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: home cage observation
 (Week 2 of administration)
 Dose (mg/kg): 1000

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-9

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: home cage observation
 (Week 3 of administration)
 Dose (mg/kg): 0

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-10

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: home cage observation
 (Week 3 of administration)
 Dose (mg/kg): 100

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-11

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: home cage observation
 (Week 3 of administration)
 Dose (mg/kg): 300

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-12

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: home cage observation
 (Week 3 of administration)
 Dose (mg/kg): 1000

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-13

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: home cage observation
 (Week 4 of administration)
 Dose (mg/kg): 0

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-14

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: home cage observation
 (Week 4 of administration)
 Dose (mg/kg): 100

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-15

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: home cage observation
 (Week 4 of administration)
 Dose (mg/kg): 300

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-16

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: home cage observation
 (Week 4 of administration)
 Dose (mg/kg): 1000

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-17

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: home cage observation
 (Week 5 of administration)
 Dose (mg/kg): 0

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-18

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: home cage observation
 (Week 5 of administration)
 Dose (mg/kg): 100

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-19

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: home cage observation
 (Week 5 of administration)
 Dose (mg/kg): 300

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-20

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: home cage observation
 (Week 5 of administration)
 Dose (mg/kg): 1000

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-21

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: home cage observation
 (Week 6 of administration)
 Dose (mg/kg): 0

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-22

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: home cage observation
 (Week 6 of administration)
 Dose (mg/kg): 100

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-23

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: home cage observation
 (Week 6 of administration)
 Dose (mg/kg): 300

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-24

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: home cage observation
 (Week 6 of administration)
 Dose (mg/kg): 1000

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-25

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Main group, Week 1 of administration)
 Dose (mg/kg): 0

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-26

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Main group, Week 1 of administration)
 Dose (mg/kg): 100

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-27

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Main group, Week 1 of administration)
 Dose (mg/kg): 300

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-28

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Main group, Week 1 of administration)
 Dose (mg/kg): 1000

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-29

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Main group, Week 2 of administration)
 Dose (mg/kg): 0

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-30

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Main group, Week 2 of administration)
 Dose (mg/kg): 100

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-31

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Main group, Week 2 of administration)
 Dose (mg/kg): 300

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-32

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Main group, Week 2 of administration)
 Dose (mg/kg): 1000

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-33

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Main group, Gestation day 1)
 Dose (mg/kg): 0

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

NP: Non-pregnant

Appendix 2-34

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Main group, Gestation day 1)
 Dose (mg/kg): 100

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

NP: Non-pregnant

Appendix 2-35

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Main group, Gestation day 1)
 Dose (mg/kg): 300

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

NP: Non-pregnant

Appendix 2-36

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Main group, Gestation day 1)
 Dose (mg/kg): 1000

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-37

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Main group, Gestation day 7)
 Dose (mg/kg): 0

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

NP: Non-pregnant

Appendix 2-38

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Main group, Gestation day 7)
 Dose (mg/kg): 100

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

NP: Non-pregnant

Appendix 2-39

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Main group, Gestation day 7)
 Dose (mg/kg): 300

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

NP: Non-pregnant

Appendix 2-40

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Main group, Gestation day 7)
 Dose (mg/kg): 1000

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-41

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Main group, Gestation day 14)
 Dose (mg/kg): 0

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

NP: Non-pregnant

Appendix 2-42

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Main group, Gestation day 14)
 Dose (mg/kg): 100

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

NP: Non-pregnant

Appendix 2-43

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Main group, Gestation day 14)
 Dose (mg/kg): 300

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

NP: Non-pregnant

Appendix 2-44

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Main group, Gestation day 14)
 Dose (mg/kg): 1000

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-45

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Main group, Gestation day 20)
 Dose (mg/kg): 0

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

NP: Non-pregnant

Appendix 2-46

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Main group, Gestation day 20)
 Dose (mg/kg): 100

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

NP: Non-pregnant

Appendix 2-47

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Main group, Gestation day 20)
 Dose (mg/kg): 300

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

NP: Non-pregnant

Appendix 2-48

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Main group, Gestation day 20)
 Dose (mg/kg): 1000

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-49

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Main group, Lactation day 4)
 Dose (mg/kg): 0

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

NP: Non-pregnant

Appendix 2-50

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Main group, Lactation day 4)
 Dose (mg/kg): 100

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

NP: Non-pregnant

Appendix 2-51

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Main group, Lactation day 4)
 Dose (mg/kg): 300

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

NP: Non-pregnant

Appendix 2-52

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Main group, Lactation day 4)
 Dose (mg/kg): 1000

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

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

D: Dead

Appendix 2-53

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Satellite group, Week 1 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-54

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Satellite group, Week 1 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-55

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Satellite group, Week 2 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-56

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Satellite group, Week 2 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-57

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Satellite group, Week 3 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-58

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Satellite group, Week 3 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-59

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Satellite group, Week 4 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-60

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Satellite group, Week 4 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-61

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Satellite group, Week 5 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-62

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Satellite group, Week 5 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-63

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Satellite group, Week 6 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-64

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Satellite group, Week 6 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-65

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: home cage observation
 (Week 1 of recovery)
 Dose (mg/kg): 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-66

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: home cage observation
 (Week 1 of recovery)
 Dose (mg/kg): 1000

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-67

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: home cage observation
 (Week 2 of recovery)
 Dose (mg/kg): 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-68

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 2 of recovery)
Dose (mg/kg): 1000

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-69

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Week 1 of recovery)
 Dose (mg/kg): 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-70

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Week 1 of recovery)
 Dose (mg/kg): 1000

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-71

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Week 2 of recovery)
 Dose (mg/kg): 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-72

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: home cage observation
 (Week 2 of recovery)
 Dose (mg/kg): 1000

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched

b) 0: None, 1: Minor, 2: Moderate, 3: Severe

c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-73

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: in-the-hand observation
 (Week 1 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-74

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: in-the-hand observation
 (Week 1 of administration)
 Dose (mg/kg): 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	1	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-75

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: in-the-hand observation
 (Week 1 of administration)
 Dose (mg/kg): 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	1
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-76

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: in-the-hand observation
 (Week 1 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-77

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: in-the-hand observation
 (Week 2 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	1	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-78

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: in-the-hand observation
 (Week 2 of administration)
 Dose (mg/kg): 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-79

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: in-the-hand observation
 (Week 2 of administration)
 Dose (mg/kg): 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-80

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: in-the-hand observation
 (Week 2 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-81

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: in-the-hand observation
 (Week 3 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-82

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: in-the-hand observation
 (Week 3 of administration)
 Dose (mg/kg): 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	1	0	0	0	0	0	0	1	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-83

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: in-the-hand observation
 (Week 3 of administration)
 Dose (mg/kg): 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	1	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-84

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: in-the-hand observation
 (Week 3 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	1	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	1	0

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

Appendix 2-85

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: in-the-hand observation
 (Week 4 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-86

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: in-the-hand observation
 (Week 4 of administration)
 Dose (mg/kg): 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-87

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: in-the-hand observation
 (Week 4 of administration)
 Dose (mg/kg): 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-88

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: in-the-hand observation
 (Week 4 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-89

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: in-the-hand observation
 (Week 5 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-90

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: in-the-hand observation
 (Week 5 of administration)
 Dose (mg/kg): 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-91

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: in-the-hand observation
 (Week 5 of administration)
 Dose (mg/kg): 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-92

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: in-the-hand observation
 (Week 5 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-93

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: in-the-hand observation
 (Week 6 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-94

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: in-the-hand observation
 (Week 6 of administration)
 Dose (mg/kg): 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-95

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: in-the-hand observation
 (Week 6 of administration)
 Dose (mg/kg): 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-96

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: in-the-hand observation
 (Week 6 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-97

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Main group, Week 1 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-98

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Main group, Week 1 of administration)
 Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-99

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Main group, Week 1 of administration)
 Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-100

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Main group, Week 1 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-101 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Main group, Week 2 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-102 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Main group, Week 2 of administration)
 Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	1	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-103

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Main group, Week 2 of administration)
 Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-104 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Main group, Week 2 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-105 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Main group, Gestation day 1)
 Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
												NP
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	1	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-106 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Main group, Gestation day 1)
 Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
	NP											
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-107 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Main group, Gestation day 1)
 Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
					NP					NP		
Ease of removal from cage a)	0	0	0	0		0	0	0		0	0	0
Fur condition b)	0	0	0	0		0	0	0		0	0	0
Skin c)	0	0	0	0		0	0	0		0	0	0
Secretions-Eye, Nose d)	0	0	0	0		0	0	0		0	0	0
Exophthalmos e)	0	0	0	0		0	0	0		0	0	0
Palpebral closure f)	0	0	0	0		0	0	0		0	0	0
Mucosal membranes g)	0	0	0	0		0	0	0		0	0	0
Lacrimation h)	0	0	0	0		0	0	0		0	0	0
Piloerection i)	0	0	0	0		0	0	0		0	0	0
Pupil size j)	0	0	0	0		0	0	0		0	0	0
Salivation k)	0	0	0	0		0	0	0		0	0	0
Abnormal respiration l)	0	0	0	0		0	0	0		0	0	0
Vocalization m)	0	0	0	0		0	0	0		0	0	0
Reactivity to handling n)	0	0	0	0		0	0	0		0	0	0

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

Appendix 2-108

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Main group, Gestation day 1)
 Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-109

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Main group, Gestation day 7)
 Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
												NP
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

NP: Non-pregnant

Appendix 2-110

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Main group, Gestation day 7)
 Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
	NP											
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

NP: Non-pregnant

Appendix 2-111 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Main group, Gestation day 7)
 Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
					NP				NP			
Ease of removal from cage a)	0	0	0	0		0	0	0		0	0	0
Fur condition b)	0	0	0	0		0	0	0		0	0	0
Skin c)	0	0	0	0		0	0	0		0	0	0
Secretions-Eye, Nose d)	0	0	0	0		0	0	0		0	0	0
Exophthalmos e)	0	0	0	0		0	0	0		0	0	0
Palpebral closure f)	0	0	0	0		0	0	0		0	0	0
Mucosal membranes g)	0	0	0	0		0	0	0		0	0	0
Lacrimation h)	0	0	0	0		0	0	0		0	0	0
Piloerection i)	0	0	0	0		0	0	0		0	0	0
Pupil size j)	0	0	0	0		0	0	0		0	0	0
Salivation k)	0	0	0	0		0	0	0		0	0	0
Abnormal respiration l)	0	0	0	0		0	0	0		0	0	0
Vocalization m)	0	0	0	0		0	0	0		0	0	0
Reactivity to handling n)	0	0	0	0		0	0	0		0	0	0

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

Appendix 2-112 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Main group, Gestation day 7)
 Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-113 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Main group, Gestation day 14)
 Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
												NP
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-114 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Main group, Gestation day 14)
 Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
	NP											
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-115 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 14)
Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
					NP					NP		
Ease of removal from cage a)	0	0	0	0		0	0	0		0	0	0
Fur condition b)	0	0	0	0		0	0	0		0	0	0
Skin c)	0	0	0	0		0	0	0		0	0	0
Secretions-Eye, Nose d)	0	0	0	0		0	0	0		0	0	0
Exophthalmos e)	0	0	0	0		0	0	0		0	0	0
Palpebral closure f)	0	0	0	0		0	0	0		0	0	0
Mucosal membranes g)	0	0	0	0		0	0	0		0	0	0
Lacrimation h)	0	0	0	0		0	0	0		0	0	0
Piloerection i)	0	0	0	0		0	0	0		0	0	0
Pupil size j)	0	0	0	0		0	0	0		0	0	0
Salivation k)	0	0	0	0		0	0	0		0	0	0
Abnormal respiration l)	0	0	0	0		0	0	0		0	0	0
Vocalization m)	0	0	0	0		0	0	0		0	0	0
Reactivity to handling n)	0	0	0	0		0	0	0		0	0	0

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

Appendix 2-116

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Main group, Gestation day 14)
 Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-117

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Main group, Gestation day 20)
 Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
												NP
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

NP: Non-pregnant

Appendix 2-118 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Main group, Gestation day 20)
 Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
												NP
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-119

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Main group, Gestation day 20)
 Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
					NP					NP		
Ease of removal from cage a)	0	0	0	0		0	0	0		0	0	0
Fur condition b)	0	0	0	0		0	0	0		0	0	0
Skin c)	0	0	0	0		0	0	0		0	0	0
Secretions-Eye, Nose d)	0	0	0	0		0	0	0		0	0	0
Exophthalmos e)	0	0	0	0		0	0	0		0	0	0
Palpebral closure f)	0	0	0	0		0	0	0		0	0	0
Mucosal membranes g)	0	0	0	0		0	0	0		0	0	0
Lacrimation h)	0	0	0	0		0	0	0		0	0	0
Piloerection i)	0	0	0	0		0	0	0		0	0	0
Pupil size j)	0	0	0	0		0	0	0		0	0	0
Salivation k)	0	0	0	0		0	0	0		0	0	0
Abnormal respiration l)	0	0	0	0		0	0	0		0	0	0
Vocalization m)	0	0	0	0		0	0	0		0	0	0
Reactivity to handling n)	0	0	0	0		0	0	0		0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult

b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

d) 0: Absent, 1: Present

e) 0: Absent, 1: Present

f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed

g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked

h) 0: Normal, 1: Present

i) 0: Absent, 1: Present

j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis

k) 0: None, 1: Slight, 2: Moderate, 3: Marked

l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked

m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive

n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

NP: Non-pregnant

Appendix 2-120

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Main group, Gestation day 20)
 Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-121 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Main group, Lactation day 4)
 Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
												NP
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-122

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Main group, Lactation day 4)
 Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
	NP											
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-123 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Lactation day 4)
Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
					NP					NP		
Ease of removal from cage a)	0	0	0	0		0	0	0		0	0	0
Fur condition b)	0	0	0	0		0	0	0		0	0	0
Skin c)	0	0	0	0		0	0	0		0	0	0
Secretions-Eye, Nose d)	0	0	0	0		0	0	0		0	0	0
Exophthalmos e)	0	0	0	0		0	0	0		0	0	0
Palpebral closure f)	0	0	0	0		0	0	0		0	0	0
Mucosal membranes g)	0	0	0	0		0	0	0		0	0	0
Lacrimation h)	0	0	0	0		0	0	0		0	0	0
Piloerection i)	0	0	0	0		0	0	0		0	0	0
Pupil size j)	0	0	0	0		0	0	0		0	0	0
Salivation k)	0	0	0	0		0	0	0		0	0	0
Abnormal respiration l)	0	0	0	0		0	0	0		0	0	0
Vocalization m)	0	0	0	0		0	0	0		0	0	0
Reactivity to handling n)	0	0	0	0		0	0	0		0	0	0

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

Appendix 2-124 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Main group, Lactation day 4)
 Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
	D											
Ease of removal from cage a)	0	0	0		0	0	0	0	0	0	0	0
Fur condition b)	0	0	0		0	0	0	0	0	0	0	0
Skin c)	0	0	0		0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0		0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0		0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0		0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0		0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0		0	0	0	0	0	0	0	0
Piloerection i)	0	0	0		0	0	0	0	0	0	0	0
Pupil size j)	0	0	0		0	0	0	0	0	0	0	0
Salivation k)	0	0	0		0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0		0	0	0	0	0	0	0	0
Vocalization m)	0	0	0		0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0		0	0	0	0	0	0	0	0

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

Appendix 2-125 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Satellite group, Week 1 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-126

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Satellite group, Week 1 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-127 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Satellite group, Week 2 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-128

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Satellite group, Week 2 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-129

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Satellite group, Week 3 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-130

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Satellite group, Week 3 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-131 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Satellite group, Week 4 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-132

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Satellite group, Week 4 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-133

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Satellite group, Week 5 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-134 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Satellite group, Week 5 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-135

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Satellite group, Week 6 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-136

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Satellite group, Week 6 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-137 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: in-the-hand observation
 (Week 1 of recovery)
 Dose (mg/kg): 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

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

Appendix 2-138

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: in-the-hand observation
 (Week 1 of recovery)
 Dose (mg/kg): 1000

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

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

Appendix 2-139

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: in-the-hand observation
 (Week 2 of recovery)
 Dose (mg/kg): 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

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

Appendix 2-140

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: in-the-hand observation
 (Week 2 of recovery)
 Dose (mg/kg): 1000

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

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

Appendix 2-141 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Week 1 of recovery)
 Dose (mg/kg): 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

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

Appendix 2-142

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Week 1 of recovery)
 Dose (mg/kg): 1000

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

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

Appendix 2-143 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Week 2 of recovery)
 Dose (mg/kg): 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

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

Appendix 2-144

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: in-the-hand observation
 (Week 2 of recovery)
 Dose (mg/kg): 1000

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

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

Appendix 2-145

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: open field observation
 (Week 1 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	5	5	4	3	5	5	4	6	2	4	10
Defecation count	0	0	0	0	0	0	2	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 2-146

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: open field observation
 (Week 1 of administration)
 Dose (mg/kg): 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	6	1	6	2	5	3	4	3	3	1	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	1	0	0	0	1	0	0	1	0

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

Appendix 2-147

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: open field observation
 (Week 1 of administration)
 Dose (mg/kg): 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	3	4	2	0	4	4	8	5	1	2	3	5
Defecation count	0	0	0	0	0	0	0	0	0	0	1	0
Urination h)	0	0	0	0	1	0	0	0	0	0	1	0

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

Appendix 2-148

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: open field observation
 (Week 1 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	1	1	6	5	4	3	2	2	4	4	2
Defecation count	0	0	0	0	0	0	0	1	0	0	4	0
Urination h)	0	0	0	0	0	0	0	1	1	0	1	1

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

Appendix 2-149

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: open field observation
 (Week 2 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	4	7	2	10	4	4	3	3	4	7	7
Defecation count	0	0	0	0	2	2	2	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 2-150

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: open field observation
 (Week 2 of administration)
 Dose (mg/kg): 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	4	6	4	1	3	4	8	2	6	0	4
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	1	0	0	0	0

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

Appendix 2-151

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: open field observation
 (Week 2 of administration)
 Dose (mg/kg): 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	U	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	3	6	9	0	4	5	5	3	2	2	2	3
Defecation count	0	0	0	0	0	0	0	0	0	0	3	2
Urination h)	0	1	1	0	0	0	0	0	0	1	0	0

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

Appendix 2-152

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: open field observation
 (Week 2 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	4	4	4	4	4	3	5	1	4	1	7
Defecation count	0	0	0	1	0	0	0	0	0	0	2	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-153

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: open field observation
 (Week 3 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	7	7	3	5	4	2	4	3	2	8	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	1	0	0	0	0	0	0	0	0	0	1	1

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

Appendix 2-154

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: open field observation
 (Week 3 of administration)
 Dose (mg/kg): 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	1	2	5	3	1	4	4	7	3	2	4	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	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 2-155

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: open field observation
 (Week 3 of administration)
 Dose (mg/kg): 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	4	4	2	5	5	5	3	4	4	1	6
Defecation count	0	0	0	0	0	0	0	0	0	1	0	2
Urination h)	0	0	0	0	0	0	0	0	0	1	0	0

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

Appendix 2-156

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: open field observation
 (Week 3 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	U
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	4	3	4	4	7	3	2	3	5	0	3
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	1	0

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

Appendix 2-157

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: open field observation
 (Week 4 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	6	5	6	5	5	3	5	5	6	5	7
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-158

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: open field observation
 (Week 4 of administration)
 Dose (mg/kg): 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	3	4	4	3	5	4	7	4	4	7	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	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 2-159

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: open field observation
 (Week 4 of administration)
 Dose (mg/kg): 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	8	3	7	4	4	5	5	4	4	4	3	4
Defecation count	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	0

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

Appendix 2-160

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: open field observation
 (Week 4 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	7	7	7	9	3	3	5	5	4	0	3
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-161

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: open field observation
 (Week 5 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	3	6	4	4	4	5	4	5	4	6	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	1

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

Appendix 2-162

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: open field observation
 (Week 5 of administration)
 Dose (mg/kg): 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	4	6	6	4	4	5	6	3	5	5	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	1	0	1	0	0

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

Appendix 2-163

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: open field observation
 (Week 5 of administration)
 Dose (mg/kg): 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	4	5	4	6	6	5	5	5	2	4	3
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	1	0	0	1	0	0	0	0	0	0	0

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

Appendix 2-164

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: open field observation
 (Week 5 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	U
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	6	5	8	7	2	3	5	4	2	1	6
Defecation count	0	0	0	0	0	0	0	0	0	0	4	0
Urination h)	0	0	0	0	0	0	0	0	0	0	1	0

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

Appendix 2-165

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: open field observation
 (Week 6 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	4	3	5	6	4	7	3	5	4	7	8
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	1	0	1	0	1	0	0	0	1	0	1	1

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

Appendix 2-166

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: open field observation
 (Week 6 of administration)
 Dose (mg/kg): 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	2	4	7	2	6	2	3	6	6	6	7	4
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	1	0	1	0	0	0	0

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

Appendix 2-167

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: open field observation
 (Week 6 of administration)
 Dose (mg/kg): 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	2	5	3	5	6	4	3	6	3	4	6
Defecation count	0	0	0	0	0	0	0	0	0	1	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-168

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: open field observation
 (Week 6 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	5	1	5	6	5	5	5	3	5	2	2
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	1	0

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

Appendix 2-169

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Main group, Week 1 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	8	6	6	11	7	7	9	6	5	10	3	7
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-170

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Main group, Week 1 of administration)
 Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	9	8	5	6	8	8	3	6	8	7	3	8
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-171

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Main group, Week 1 of administration)
 Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	8	8	4	6	11	6	6	9	7	7	9	7
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-172

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Main group, Week 1 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	4	7	6	2	4	4	8	6	7	2	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	1	0	0	0

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

Appendix 2-173

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Main group, Week 2 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	8	8	7	11	13	6	8	10	4	6	4	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-174

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Main group, Week 2 of administration)
 Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	9	8	5	10	6	10	5	6	7	6	8	8
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-175

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Main group, Week 2 of administration)
 Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	9	8	6	4	8	8	10	7	6	6	9	7
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-176

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Main group, Week 2 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	9	8	7	4	5	4	10	7	10	5	9
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	1	0	0	0	0	0	0

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

Appendix 2-177

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Main group, Gestation day 1)
 Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
												NP
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	8	9	5	7	12	8	8	9	4	9		5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-178

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Main group, Gestation day 1)
 Dose (mg/kg): 100

Parameter	Animal number (2101-2112)												
	1	2	3	4	5	6	7	8	9	10	11	12	
													NP
Arousal a)	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
Abnormal behavior c)	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
Gait e)	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
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	7	6	7	9	9	6	6	7		10	7	
Defecation count	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

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

Appendix 2-179

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Main group, Gestation day 1)
 Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
					NP					NP		
Arousal a)	0	0	0	0		0	0	0		0	0	0
Convulsion b)	0	0	0	0		0	0	0		0	0	0
Abnormal behavior c)	0	0	0	0		0	0	0		0	0	0
Stereotypy d)	0	0	0	0		0	0	0		0	0	0
Gait e)	0	0	0	0		0	0	0		0	0	0
Posture f)	N	N	N	N		N	N	N		N	N	N
Grooming g)	0	0	0	0		0	0	0		0	0	0
Rearing	8	10	4	6		7	7	8		7	6	5
Defecation count	0	0	0	0		0	0	0		0	0	0
Urination h)	0	0	0	0		0	0	0		0	0	0

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

Appendix 2-180

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Main group, Gestation day 1)
 Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	4	8	5	3	7	5	7	7	9	4	7
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-181

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Main group, Gestation day 7)
 Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
												NP
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	6	4	8	10	9	7	8	3	10		7
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-182

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Main group, Gestation day 7)
 Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
	NP											
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	9	7	8	9	5	6	5	2	5	10	6	
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	1	0	0	0	0	0	0	0	0	0

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

Appendix 2-183

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Main group, Gestation day 7)
 Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
					NP					NP		
Arousal a)	0	0	0	0		0	0	0		0	0	0
Convulsion b)	0	0	0	0		0	0	0		0	0	0
Abnormal behavior c)	0	0	0	0		0	0	0		0	0	0
Stereotypy d)	0	0	0	0		0	0	0		0	0	0
Gait e)	0	0	0	0		0	0	0		0	0	0
Posture f)	N	N	N	N		N	N	N		N	N	N
Grooming g)	0	0	0	0		0	0	0		0	0	0
Rearing	10	5	3	4		5	3	12		9	5	6
Defecation count	0	0	0	0		0	0	0		0	0	0
Urination h)	0	0	0	0		0	0	0		0	0	0

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

Appendix 2-184

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Main group, Gestation day 7)
 Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	4	9	7	3	7	3	7	4	8	5	5
Defecation count	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	0

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

Appendix 2-185

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Main group, Gestation day 14)
 Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
												NP
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	7	4	7	9	8	8	4	4	6		5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-186

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Main group, Gestation day 14)
 Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
												NP
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	5	8	7	5	5	3	3	7	7	6	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-187

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Main group, Gestation day 14)
 Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
					NP					NP		
Arousal a)	0	0	0	0		0	0	0		0	0	0
Convulsion b)	0	0	0	0		0	0	0		0	0	0
Abnormal behavior c)	0	0	0	0		0	0	0		0	0	0
Stereotypy d)	0	0	0	0		0	0	0		0	0	0
Gait e)	0	0	0	0		0	0	0		0	0	0
Posture f)	N	N	N	N		N	N	N		N	N	N
Grooming g)	0	0	0	0		0	0	0		0	0	0
Rearing	7	6	5	4		4	4	6		4	7	6
Defecation count	0	0	0	0		0	0	0		0	0	0
Urination h)	0	0	0	0		0	0	0		0	0	0

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

Appendix 2-188

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Main group, Gestation day 14)
 Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	2	6	6	2	2	2	8	5	4	6	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	1	0	0	0	0	0	0

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

Appendix 2-189

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Main group, Gestation day 20)
 Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
												NP
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	6	4	6	10	5	4	6	3	9		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
 NP: Non-pregnant

Appendix 2-190

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Main group, Gestation day 20)
 Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
	NP											
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	6	5	5	5	7	4	4	5		7	4
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	1	0	0	0	0	0

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

Appendix 2-191

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Main group, Gestation day 20)
 Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
					NP				NP			
Arousal a)	0	0	0	0		0	0	0		0	0	0
Convulsion b)	0	0	0	0		0	0	0		0	0	0
Abnormal behavior c)	0	0	0	0		0	0	0		0	0	0
Stereotypy d)	0	0	0	0		0	0	0		0	0	0
Gait e)	0	0	0	0		0	0	0		0	0	0
Posture f)	N	N	N	N		N	N	N		N	N	N
Grooming g)	0	0	0	0		0	0	0		0	0	0
Rearing	6	6	5	4		6	5	4		5	6	6
Defecation count	0	0	0	0		0	0	0		0	0	0
Urination h)	0	0	0	0		0	0	0		0	1	0

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

Appendix 2-192

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Main group, Gestation day 20)
 Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	3	4	6	5	2	5	4	5	5	4	3	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-193

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Main group, Lactation day 4)
 Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
												NP
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	6	5	5	8	6	6	7	6	6	6	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-194

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Main group, Lactation day 4)
 Dose (mg/kg): 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
	NP											
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	5	4	7	7	10	6	4	7	9	4	4
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-195

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Main group, Lactation day 4)
 Dose (mg/kg): 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
					NP				NP			
Arousal a)	0	0	0	0		0	0	0		0	0	0
Convulsion b)	0	0	0	0		0	0	0		0	0	0
Abnormal behavior c)	0	0	0	0		0	0	0		0	0	0
Stereotypy d)	0	0	0	0		0	0	0		0	0	0
Gait e)	0	0	0	0		0	0	0		0	0	0
Posture f)	N	N	N	N		N	N	N		N	N	N
Grooming g)	0	0	0	0		0	0	0		0	0	0
Rearing	6	5	4	6		6	7	7		6	5	7
Defecation count	0	0	0	0		0	0	0		0	0	0
Urination h)	0	0	0	0		0	0	0		0	1	0

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

Appendix 2-196

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Main group, Lactation day 4)
 Dose (mg/kg): 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
	D											
Arousal a)	0	0	0		0	0	0	0	0	0	0	0
Convulsion b)	0	0	0		0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0		0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0		0	0	0	0	0	0	0	0
Gait e)	0	0	0		0	0	0	0	0	0	0	0
Posture f)	N	N	N		N	N	N	N	N	N	N	N
Grooming g)	0	0	0		0	0	0	0	0	0	0	0
Rearing	5	2	10		5	6	5	8	2	4	6	4
Defecation count	0	0	0		0	0	0	0	0	0	0	0
Urination h)	0	0	0		0	0	0	0	0	0	0	0

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

Appendix 2-197

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Satellite group, Week 1 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	4	9	6	6	9	7	4	6	5	4
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-198

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Satellite group, Week 1 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	7	8	4	7	6	12	5	5	3	4
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-199

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Satellite group, Week 2 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	4	5	9	10	8	10	3	10	9	6
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-200

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Satellite group, Week 2 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	10	13	8	9	9	6	5	7	8	4
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-201

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Satellite group, Week 3 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	4	7	7	10	9	9	7	7	4	5
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-202

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Satellite group, Week 3 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	9	13	9	6	11	10	7	10	11	5
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-203

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Satellite group, Week 4 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	6	12	9	9	6	10	4	13	8	3
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-204

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Satellite group, Week 4 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	8	14	8	5	8	11	8	8	7	8
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	1	0	0	0

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

Appendix 2-205

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Satellite group, Week 5 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	4	12	9	9	11	13	3	10	15	3
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-206

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Satellite group, Week 5 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	8	12	7	6	11	10	11	8	9	6
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	1	0	0	0	0	0	0	0	0

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

Appendix 2-207

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Satellite group, Week 6 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	6	10	7	9	8	8	4	9	9	5
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	1	0

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

Appendix 2-208

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Satellite group, Week 6 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	2	10	5	4	7	11	10	8	8	7
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

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

Appendix 2-209

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: open field observation
 (Week 1 of recovery)
 Dose (mg/kg): 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	6	4	4	9	8
Defecation count	0	0	0	0	0
Urination h)	0	0	0	0	1

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

Appendix 2-210

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: open field observation
 (Week 1 of recovery)
 Dose (mg/kg): 1000

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	6	3	3	2	3
Defecation count	0	0	0	0	0
Urination h)	0	0	0	1	0

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

Appendix 2-211

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: open field observation
 (Week 2 of recovery)
 Dose (mg/kg): 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	4	2	3	5	6
Defecation count	0	0	0	0	0
Urination h)	0	0	0	0	1

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

Appendix 2-212

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in male rats: open field observation
 (Week 2 of recovery)
 Dose (mg/kg): 1000

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	2	3	3	0	2
Defecation count	0	0	0	1	0
Urination h)	0	0	1	0	0

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

Appendix 2-213

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Week 1 of recovery)
 Dose (mg/kg): 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	7	6	13	12	5
Defecation count	0	0	0	0	0
Urination h)	0	0	0	0	0

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

Appendix 2-214

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Week 1 of recovery)
 Dose (mg/kg): 1000

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	7	8	7	6	6
Defecation count	0	0	0	0	0
Urination h)	0	0	0	0	0

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

Appendix 2-215

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Week 2 of recovery)
 Dose (mg/kg): 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	9	6	10	14	4
Defecation count	0	0	0	0	0
Urination h)	0	0	0	0	0

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

Appendix 2-216

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual detailed clinical signs in female rats: open field observation
 (Week 2 of recovery)
 Dose (mg/kg): 1000

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	7	9	7	5	6
Defecation count	0	0	0	0	0
Urination h)	0	0	0	0	0

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

Appendix 2-217

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual manipulative test of male rats (Week 6 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	53	69	54	69	100

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

Appendix 2-218

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual manipulative test of male rats (Week 6 of administration)
 Dose (mg/kg): 100

Parameter	Animal number (2008-2012)				
	8	9	10	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	42	52	83	71	66

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

Appendix 2-219

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual manipulative test of male rats (Week 6 of administration)
 Dose (mg/kg): 300

Parameter	Animal number (3008-3012)				
	8	9	10	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	102	52	67	72	60

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

Appendix 2-220

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual manipulative test of male rats (Week 6 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	62	88	83	79	87

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

Appendix 2-221

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual manipulative test of female rats (Main group, Lactation day 4)
 Dose (mg/kg): 0

Parameter	Animal number (1102-1112)				
	2	3	4	8	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	77	27	60	45	38

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

Appendix 2-222

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual manipulative test of female rats (Main group, Lactation day 4)
 Dose (mg/kg): 100

Parameter	Animal number (2102-2112)				
	2	3	4	5	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	27	40	60	53	40

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

Appendix 2-223

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual manipulative test of female rats (Main group, Lactation day 4)
 Dose (mg/kg): 300

Parameter	Animal number (3101-3108)				
	1	2	3	4	8
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	47	80	40	85	44

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

Appendix 2-224

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual manipulative test of female rats (Main group, Lactation day 4)
 Dose (mg/kg): 1000

Parameter	Animal number (4101-4111)				
	1	5	6	10	11
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	42	35	68	25	45

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

Appendix 2-225

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual manipulative test of female rats (Satellite group, Week 6 of administration)
 Dose (mg/kg): 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	37	56	39	98	33

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

Appendix 2-226

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual manipulative test of female rats (Satellite group, Week 6 of administration)
 Dose (mg/kg): 1000

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	45	76	59	78	91

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

Appendix 2-227

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual manipulative test of male rats (Week 2 of recovery)
 Dose (mg/kg): 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	36	45	52	96	103

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

Appendix 2-228

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual manipulative test of male rats (Week 2 of recovery)
 Dose (mg/kg): 1000

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	63	88	117	68	114

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

Appendix 2-229

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual manipulative test of female rats (Week 2 of recovery)
 Dose (mg/kg): 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	28	58	47	86	59

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

Appendix 2-230

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
 Individual manipulative test of female rats (Week 2 of recovery)
 Dose (mg/kg): 1000

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	62	68	66	54	78

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

Appendix 2-231

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Individual grip strength of male rats (Week 6 of administration)
Dose (mg/kg): 0

Animal number	Fore limb g	Hind limb g
1008	1347	922
1009	1043	870
1010	1728	1183
1011	1307	1023
1012	1662	1072
Mean	1417	1014
S.D.	280	124

Appendix 2-232

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Individual grip strength of male rats (Week 6 of administration)
Dose (mg/kg): 100

Animal number	Fore limb g	Hind limb g
2008	1321	868
2009	1811	1059
2010	1685	827
2011	1808	1284
2012	1920	1377
Mean	1709	1083
S.D.	232	245

Appendix 2-233

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Individual grip strength of male rats (Week 6 of administration)
Dose (mg/kg): 300

Animal number	Fore limb g	Hind limb g
3008	1970	1146
3009	1545	1134
3010	1388	1127
3011	1361	1016
3012	1952	1134
Mean	1643	1111
S.D.	299	54

Appendix 2-234

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Individual grip strength of male rats (Week 6 of administration)
Dose (mg/kg): 1000

Animal number	Fore limb g	Hind limb g
4008	1443	931
4009	1472	1121
4010	1162	945
4011	1725	1095
4012	2017	1476
Mean	1564	1114
S.D.	322	220

Appendix 2-235

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Individual grip strength of female rats (Main group, Lactation day 4)
Dose (mg/kg): 0

Animal number	Fore limb g	Hind limb g
1102	1310	659
1103	1130	720
1104	1206	775
1108	1514	967
1112	1535	1158
Mean	1339	856
S.D.	181	205

Appendix 2-236

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of dimethyl glutarate by oral administration in rats
Individual grip strength of female rats (Main group, Lactation day 4)
Dose (mg/kg): 100

Animal number	Fore limb g	Hind limb g
2102	1633	883
2103	1427	814
2104	1581	721
2105	1552	788
2112	1197	804
Mean	1478	802
S.D.	174	58