最終報告書

指定添加物の安全性に関する試験
(2-メチルブチリックアシドに関する 90 日間
反復投与毒性試験)

試験番号：[redacted]

[redacted]

[redacted]

[redacted]

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試験情報

試験表題　：指定添加物の安全性に関する試験（2-メチルブチリックアシドに関する90日間反復投与毒性試験）

試験番号　：[redacted]

試験目的　：2-メチルブチリックアシドを90日間強制経口投与し、反復投与による毒性を明らかにすることを目的とした。

適用GLP　：「医薬品の安全性に関する非臨床試験の実施の基準に関する省令」（平成9年3月26日厚生省令第21号、一部改正、平成20年6月13日厚生労働省令第114号）に従って実施した。

ガイドライン　：「食品添加物の指定及び使用基準改正に関する指針」平成8年3月22日公示（厚生省生活衛生局通知）に従って実施した。

動物愛護　：「動物の愛護及び管理に関する法律」（平成24年9月法律第79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25年9月環境省告示第84号）、「厚生労働省の所管する実施機関における動物実験等の実施に関する基本指針」（厚生労働省大臣官房厚生科学課長通知平成18年6月科発第0601005号）及び「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）に基づいた[redacted]に従って実施した。

試験委託者　：国立医薬品食品衛生研究所
[redacted]

試験実施施設　：[redacted]

試験開始日　：[redacted]

試験日程

動物入荷日	：	[redacted]
群分け実施日	：	
実験開始日	：	
被験物質投与開始日	：	
被験物質投与終了日	：	
剖検日	：	
中間報告書提出日	：	
実験終了日	：	
（病理組織学的検査終了日）		

試験終了日　：[redacted]

報告書の作成

試験表題　：指定添加物の安全性に関する試験(2-メチルブチリックアシドに関する 90 日間反復投与毒性試験)

試験番号　：[redacted]

試験責任者　：[redacted]

試験責任者及び試験従事者

試験責任者 ：[redacted]

試験主担当者 ：

動物飼育管理 ：

動物入荷･群分け ：

被験物質投与液の調製・投与 ：

投与液中の被験物質の安定性・濃度分析 ：

一般状態観察 ：[redacted]

体重・摂餌量・摂水量測定 ：

眼科学的検査 ：

尿検査 ：

血液学的検査 ：

血液生化学的検査 ：

肉眼的病理学検査（器官重量測定を含む）

：[redacted]

病理組織標本作製（切り出しを含む）

：[redacted]

病理組織学的検査　：

病理組織学的検査責任者　：

集計処理　：

被験物質管理責任者　：

注）アンダーラインは部門責任者を示す。

1　要約

本試験において、被験物質の2-メチルブチリックアシドを0 （対照）、80、250及び800 mg/kgの用量で、Crl:CD(SD)系ラットの雌雄各群10匹に90日間強制経口投与し、反復投与による毒性影響を検討した。

摂餌量、摂水量、眼科学的検査、尿検査、血液学的検査及び肉眼的病理学検査において、被験物質投与の影響は認められなかった。

一般状態では、雌雄の800 mg/kg/day群及び雄の250 mg/kg/day群で投与後に流涎がみられたが、投与後のみにみられた変化であった。

体重では、雌の800 mg/kg/day群で、第6週以降に体重の低値傾向がみられたことから、被験物質投与の影響であった可能性が考えられた。

血液生化学的検査では、雄の800及び250 mg/kg/day群で総蛋白の有意な低値がみられた。雌の800 mg/kg/day群では尿素窒素及びマグネシウムの有意な高値がみられ、腎臓の相対重量の有意な高値がみられたが、生体への影響としては弱いものであったと判断した。

病理組織学的検査では、雌雄の800 mg/kg/day群の胃で境界縁の軽度の過形成が全例にみられ、雄の250 mg/kg/day群でも1例にみられ、被験物質の影響と考えられた。

雌の800 mg/kg/day群では、第70日及び第75日に各1例が死亡したことから被験物質の影響が考えられたが、死因の詳細は明確とならなかった。

以上の結果から、雌雄の800 mg/kg/day群の胃で、境界縁の過形成が全例にみられたこと、血液生化学的検査において雄の800及び250 mg/kg/day群で総蛋白の有意な低値がみられたことから、無毒性量（NOAEL）は、雄で80 mg/kg/day、雌で250 mg/kg/dayであると判断された。

2　緒言

2-メチルブチリックアシドの一般毒性学的性質を検討し、あわせて無毒性量(NOAEL)を明らかにする目的で、0、80、250及び800 mg/kgを雌雄のCrl:CD(SD)系ラットに90日間強制経口投与する反復投与毒性試験を実施した。

3　試験材料及び方法

3.1　被験物質

名称	：2-メチルブチリックアシド
供給源	：日本香料工業会
ロット番号	：[redacted]
成分含量	：99.9%
外観及び性状	：無色～微黄色の透明な液体
試験責任者入手年月日	：[redacted]
保管条件	：冷暗所
保管場所	：[redacted]（許容範囲2～10℃）

使用期限　：[redacted]
保管温度　：被験物質管理責任者管理：実測値 6~8℃
[redacted]
試験責任者管理：実測値 6~8℃
[redacted]

3.2　媒体

名称　：トウモロコシ油
製造元　：ナカライテスク株式会社
ロット番号　：[redacted]
保管条件　：室温
保管場所　：[redacted]

3.3　供試動物

動物種	：ラット
系統	：Crl:CD(SD)（SPF 動物）
性	：雌雄
入荷時週齢	：4 週齢
実験開始時週齢	：5 週齢
被験物質投与開始時週齢	：6 週齢
購入（使用）匹数	：雌雄各 46 匹（雌雄各 40 匹）
供給源	：日本チャールス・リバー株式会社
所在地	：〒529-1633　滋賀県蒲生郡日野町下駒月 735 番地
検疫・馴化期間	：6 日間（雄）、7 日間（雌）
検疫･馴化期間中の検査	：体重測定（入手翌日及び群分け体重） 一般状態の観察（1 日 2 回）
群分け後の余剰動物の処置	：雌雄各 2 匹を微生物学的なモニタリング用として同一飼育室で飼育し、残りの雌雄各 4 匹は試験系から除外した。
モニタリング動物の検査結果	：飼育期間中を通して体重、一般状態のいずれも異常は認められなかった。また、計画屠殺時における剖検でも異常は認められなかった。

3.4　試験系選択理由

「食品添加物の指定及び使用基準改正に関する指針」に基づいてげっ歯類の 1 つとしてラットを選択した。本系統は、微生物学的に統御され、遺伝的に安定であることから決定した。

3.5 動物管理

3.5.1 飼育条件

飼育室	：[redacted]（検疫・馴化期間も同様に[redacted]で飼育）
温度	：実測値；21.4～23.8 ℃（設定温度；22±3 ℃）
相対湿度	：実測値；52～68 %（設定範囲；55±15 %）
照明時間	：12 時間／日(7:00~19:00)
換気回数	：10 回以上／時間
飼育	：2 匹／ケージ （検疫・馴化期間中も 2 匹／ケージ）
ケージ（床敷）交換頻度	：2～3 回／週
ケージ蓋交換頻度	：1 回／月
給水瓶交換頻度	：2～3 回／週

3.5.2 収容ケージ及び床敷

ケージ	：プラスチック製ケージ（W257×D426×H200 mm）
ケージ蓋	：ステンレス製
消毒方法	：プラスチック製ケージは常圧蒸気殺菌 ケージ蓋は高圧蒸気滅菌
床敷	：ソフトチップ（有限会社　原商店）
消毒方法	：高圧蒸気滅菌
床敷中の環境汚染物質	：中部科学資材株式会社（有限会社　原商店の代理店）より分析値を入手し、当研究所で定める最大許容濃度以下であり、試験への影響がないことを確認した（9 添付資料 9.1）。

3.5.3 飼料及び給餌方法

飼料	：オリエンタル酵母工業株式会社製固型飼料 MF ロット番号[redacted]
給餌方法	：ケージ蓋に取り付けられている給餌器に入れて、自由摂取
給餌器の消毒方法	：高圧蒸気滅菌
飼料中の汚染物質	：オリエンタル酵母工業株式会社よりロットごとに分析値を入手し、当研究所における最大許容濃度以下であり、試験への影響がないことを確認した（9 添付資料 9.2）。

3.5.4 飲料水及び給水方法

飲料水	：[redacted]
給水方法	：透明な給水瓶を用いて自由摂取

給水瓶の消毒方法　：給水瓶は常圧蒸気殺菌、給水栓はピューラックス（株式会社オーヤラックス）にて消毒

飲料水中の汚染物質　：下記の分析機関に分析を依頼し、当研究所における水質基準に適合していることを定期的（年2回）に確認し、試験への影響がないことを確認した（9 添付資料 9.3）。

[redacted]

3.5.5　個体識別法

検疫・馴化期間中　：ケージラベルに試験番号、仮ケージ番号、仮動物番号及び動物管理責任者名を明記した。動物の個体識別は、上記内容及び油性インク法により行った。

群分け後　：ケージラベルに試験番号、性別、群番号、ケージ番号、被験物質名及び投与濃度（投与濃度ごとに異なった色を用いて識別）、動物番号、実験開始日、被験物質投与開始日、剖検日、試験責任者名を明記した。動物の個体識別は、上記内容とイヤータグ法（株式会社サイテック、ら・ピアス）及び油性インク法（尾部に補助的に群内番号を付した）で行った。

3.6　投与期間及び投与方法

実験を開始する前日に群分けを行った後、1週間無処置で飼育し、被験物質の投与を6週齢より開始した。被験物質の投与は、毎日1回（週7日）、投与期間は92日とした。被験物質投与液はディスポーザブルシリンジ及びプラスチック製ディスポーザブル経口ゾンデを用いて10 mL/kgの容量で強制経口投与した。対照群には同様の方法で媒体を投与した。投与用量は直近の体重に基づいて個体別に算出した。

3.7　被験物質投与量の設定理由

本試験における被験物質の投与量は、「指定添加物の安全性に関する試験（2-メチルブチリックアシドに関する90日間反復投与毒性試験のための用量設定試験）」（試験番号：[redacted]）に基づき最高用量を800 mg/kg/dayとし、以下公比約3で除した250 mg/kg/day及び80 mg/kg/dayに設定した。

3.8　投与経路・投与方法の選択理由

投与経路は、ヒトが被験物質に暴露される可能性の最も大きい経路である経口投与とした。被験物質のUV吸収が無く、混餌投与法では飼料中被験物質濃度の分析が困難であり、さらに被験物質が香料であるため、対照群への暴露が懸念されることから、強制経口投与法を選択した。

3.9　被験物質投与液の調製方法

被験物質の必要量を電子天秤LA4200S型(ザルトリウス株式会社)を用いてビーカーに秤量し、媒体であるトウモロコシ油を少量加えて混和した。その後媒体で共洗いをしながらメスシリンダーに移しメスアップした。調製した投与液は日数分に小分けし、調製後は検体調製室内冷蔵庫（実測値：2～7 ℃）で使用時まで保存した。被験物質投与液は4～7日間に1回調製した。

3.10　投与液中における被験物質の安定性及び濃度確認試験

3.10.1　安定性試験

投与開始前に8 mg/mL（低濃度）及び80 mg/mL（高濃度）濃度投与液を各10 mL作製後3点に小分けし、保存開始前[redacted]、冷蔵保存5日＋室温24時間後[redacted]及び冷蔵保存10日＋室温24時間後[redacted]の計3点について投与液中濃度を分析した。投与液は[redacted]（実測値：6～7℃）及び[redacted]（実測値：18.0～22.0℃）で保存した。分析は「3.15 被験物質投与液の分析方法」に従って実施し、安定性は保存開始前の分析値の±10%で評価した。

3.10.2　濃度確認試験

初回[redacted]及び最終調製時[redacted]の各濃度投与液（0 mg/mLを含む）について調製容器より約5 mLを採取し、投与液中被験物質濃度を分析した。投与液中被験物質濃度は設定濃度の±10%で評価した。

3.11　群構成及び使用動物数

雌雄ラット各46匹よりそれぞれ40匹の動物をコンピューターによる体重を基にした乱塊法により選び、次表の如く8群（10匹／群）に群分けした。群分けは実験開始日の前日に行い、群分け時の体重が各群間で統計学的に有意差のないことをBartlett法による等分散検定（5%水準）及びTukey検定（両側5%水準）で確認した。実験開始時におけるラットの体重範囲は雄で137～155 g、雌で125～143 gであり、雌雄ともに平均体重の± 20 %以内であった。

性別	群	被験物質	投与量 (mg/kg/day)	匹数	動物番号
雄	1	2-メチルブチリックアシド	0	10	1437001~010
	2	2-メチルブチリックアシド	80	10	1437011~020
	3	2-メチルブチリックアシド	250	10	1437021~030
	4	2-メチルブチリックアシド	800	10	1437031~040
雌	5	2-メチルブチリックアシド	0	10	1437041~050
	6	2-メチルブチリックアシド	80	10	1437051~060
	7	2-メチルブチリックアシド	250	10	1437061~070
	8	2-メチルブチリックアシド	800	10	1437071~080

3.12 観察及び測定項目

3.12.1 一般状態

実験開始日から被験物質投与前日は午前中、被験物質投与開始日から[redacted]（雄：投与 71 日、雌：投与 70 日）までは被験物質の投与後に、すべての動物について一般状態、中毒症状、生死などについて観察し、個体別に記録した。また午後の観察時には動物の生死の確認を行った。[redacted]（雄：投与 72 日、雌：投与 71 日）から投与終了日までは被験物質の投与後及び午後に、すべての動物について一般状態、中毒症状、生死などについて観察し、個体別に記録した。

3.12.2 体重

実験開始時及びその後、毎週 1 回、全動物について電子天秤 LA4200 型（ザルトリウス株式会社）を用いて個体別に体重を測定した。また、計画屠殺時に各動物の 1 晩絶食後の体重（剖検日体重）を測定した。

3.12.3 摂餌量

実験開始後、毎週 1 回、2 日間の摂取量を電子天秤 LA4200 型（ザルトリウス株式会社）を用いてケージ単位で測定し、1 匹当りの 1 日平均摂取量を算出した。

3.12.4 摂水量

実験開始後、毎週 1 回、2 日間の摂取量を電子天秤 LA4200 型（ザルトリウス株式会社）を用いてケージ単位で測定し、1 匹当りの 1 日平均摂取量を算出した。

3.12.5 眼科学的検査

投与第 13 週に、対照群及び各用量群の雌雄各 6 匹（動物番号順）について前眼房、中間透光体、眼底あるいはその他の部位をハロゲン双眼倒像検眼鏡 IO-α 型（株式会社ナイツ）を用いて散瞳条件下で検査を行った。散瞳剤としてミドリン P（参天製薬株式会社）を使用した。

3.12.6　尿検査

投与第13週に、対照群及び各用量群の雌雄各6匹(動物番号順)について採尿ラック(日本チャールス・リバー株式会社）を用いて4時間（09:00～13:00）の蓄尿を行い、項目1)から13)の尿検査を実施した。なお、採尿中の給餌・給水は行わなかった。項目14)の尿pHは、別に強制排尿にて得た新鮮尿についてpHメーターを用いて実施した。

測定項目及び測定法は次の通りであった。

項目	測定法及び測定機器
1) 尿量	重量測定法　電子天秤LA4200型（ザルトリウス株式会社）
2) 色調	肉眼的観察法
3) 潜血	マルティスティックス（ｼｰﾒﾝｽﾍﾙｽｹｱ･ﾀﾞｲｱｸﾞﾉｽﾃｨｸｽ株式会社）
4) ケトン体	マルティスティックス（ｼｰﾒﾝｽﾍﾙｽｹｱ･ﾀﾞｲｱｸﾞﾉｽﾃｨｸｽ株式会社）
5) 尿糖	マルティスティックス（ｼｰﾒﾝｽﾍﾙｽｹｱ･ﾀﾞｲｱｸﾞﾉｽﾃｨｸｽ株式会社）
6) 蛋白	マルティスティックス（ｼｰﾒﾝｽﾍﾙｽｹｱ･ﾀﾞｲｱｸﾞﾉｽﾃｨｸｽ株式会社）
7) ウロビリノーゲン	マルティスティックス（ｼｰﾒﾝｽﾍﾙｽｹｱ･ﾀﾞｲｱｸﾞﾉｽﾃｨｸｽ株式会社）
8) ビリルビン	マルティスティックス（ｼｰﾒﾝｽﾍﾙｽｹｱ･ﾀﾞｲｱｸﾞﾉｽﾃｨｸｽ株式会社）
9) 沈渣	Sternheimer & Malbin染色後鏡検
10) 比重	アタゴ血清蛋白屈折計N（株式会社アタゴ）
11) ナトリウム(NA)	イオン選択電極法（日立7070形自動分析装置　株式会社日立製作所）
12) カリウム(K)	イオン選択電極法（日立7070形自動分析装置　株式会社日立製作所）
13) 塩素(CL)	イオン選択電極法（日立7070形自動分析装置　株式会社日立製作所）
14) 尿pH	pHメーターF-51型（株式会社堀場製作所）

3.12.7　血液学的検査

被験物質投与期間終了時の全生存動物について下記の検査を実施した。検査試料（血液）の採取は、採取前日の夕方（16:00 頃）から絶食させた動物を、当日に実験小動物用簡易吸入麻酔装置 NARCOBIT-E（KN1070、株式会社夏目製作所）を用い、イソフルラン（マイラン製薬株式会社、ロット番号[redacted]）麻酔下で開腹し、剥離後の腹部大動脈から行った。動物の採血（屠殺）順は、雌雄毎に最初の群の最も若い動物番号を第 1 番目とし、以後、次群の最も若い動物番号へと順次進め、最終群到達後は最初の群に戻る方法とした。

採取した血液の一部を抗凝固剤入りの試験管に移し、下表項目 1)~10)は多項目自動血球分析装置 XT-2000i（シスメックス株式会社）を、項目 11), 12)は全自動血液凝固測定装置 CA-530（シスメックス株式会社）を用いて測定した。抗凝固剤として項目 1)~10)には EDTA-2K を、項目 11), 12)にはクエン酸ナトリウムを用いた。なお、多項目自動血球分析装置 XT-2000i で型別白血球数及び網状赤血球数が測定できなかった動物はみられなかったことから、血液塗抹標本は作製しなかった。

	項目	測定法
1)	赤血球数(RBC)	シースフローDC 検出法
2)	血色素量(HGB)	SLS ヘモグロビン法
3)	ヘマトクリット値(HCT)	シースフローDC 検出法
4)	平均赤血球容積(MCV)	シースフローDC 検出法及び計算法
5)	平均赤血球血色素量(MCH)	シースフローDC 検出法及び計算法
6)	平均赤血球血色素濃度(MCHC)	シースフローDC 検出法及び計算法
7)	血小板数(PLT)	シースフローDC 検出法
8)	白血球数(WBC)	フローサイトメトリー法
9)	型別白血球数(DIFFERENTIAL LEUKOCYTE COUNTS)	
	リンパ球数(LYMPH)	フローサイトメトリー法
	好中球数(NEUT)	フローサイトメトリー法
	単球数(MONO)	フローサイトメトリー法
	好酸球数(EO)	フローサイトメトリー法
	好塩基球数(BASO)	フローサイトメトリー法
10)	網状赤血球数(RET)	フローサイトメトリー法
11)	ﾌﾟﾛﾄﾛﾝﾋﾞﾝ時間(PT)	凝固時間法：光散乱検出方式
12)	活性化部分ﾄﾛﾝﾎﾞﾌﾟﾗｽﾁﾝ時間(APTT)	凝固時間法：光散乱検出方式

3.12.8　血液生化学的検査

検査は、全生存動物について、前項で採取した血液の残りを遠心分離して得た血清を用いて実施した。測定項目及び測定法は以下の通りであった。

測定機器は、日立 7070 形自動分析装置を用いた。

	項目	測定法
1)	ｱｽﾊﾟﾗｷﾞﾝ酸ｱﾐﾉﾄﾗﾝｽﾌｪﾗｰｾﾞ(AST)	ﾘﾝｺﾞ酸脱水素酵素共役・UV 法（JSCC 標準化対応法）
2)	ｱﾗﾆﾝｱﾐﾉﾄﾗﾝｽﾌｪﾗｰｾﾞ(ALT)	乳酸脱水素酵素共役・UV 法（JSCC 標準化対応法）
3)	ｱﾙｶﾘﾌｫｽﾌｧﾀｰｾﾞ(ALP)	酵素活性測定法（JSCC 標準化対応法）
4)	γ-ｸﾞﾙﾀﾐﾙﾄﾗﾝｽﾍﾟﾌﾟﾁﾀﾞｰｾﾞ(γ-GTP)	酵素活性測定法（JSCC 標準化対応法）
5)	総ﾋﾞﾘﾙﾋﾞﾝ(T-BIL)	ﾊﾞﾅｼﾞﾝ酸酸化法
6)	尿素窒素(BUN)	酵素法（ｳﾚｱｰｾﾞ・GLDH 法）
7)	ｸﾚｱﾁﾆﾝ(CRE)	酵素法
8)	ﾌﾞﾄﾞｳ糖(GLU)	ﾍｷｿｷﾅｰｾﾞ法
9)	総ｺﾚｽﾃﾛｰﾙ(T-CHO)	酵素法
10)	ﾘﾝ脂質(PL)	酵素法
11)	ﾄﾘｸﾞﾘｾﾘﾄﾞ(TG)	酵素法（遊離ｸﾞﾘｾﾛｰﾙ消去法）
12)	総蛋白(TP)	ﾋﾞｳﾚｯﾄ法
13)	ｱﾙﾌﾞﾐﾝ(ALB)	BCG 法
14)	A/G 比(A/G)	算出法
15)	無機ﾘﾝ(IP)	ﾌｨｽｹ・ｻﾊﾞﾛｰ法
16)	ｶﾙｼｳﾑ(CA)	OCPC 法
17)	ﾏｸﾞﾈｼｳﾑ(MG)	ｷｼﾘｼﾞﾙﾌﾞﾙｰ法
18)	ﾅﾄﾘｳﾑ(NA)	ｲｵﾝ選択電極法
19)	ｶﾘｳﾑ(K)	ｲｵﾝ選択電極法
20)	塩素(CL)	ｲｵﾝ選択電極法

3.12.9　病理学的検査

投与期間終了時に、前記 3.12.7 項において採血し、放血致死させた動物について、下記の病理学的検査を行った。

3.12.9.1　肉眼的病理学検査

全生存動物について、全身の諸器官・組織の肉眼的病理学検査を実施し、下記の器官･組織を摘出し、10%緩衝ホルマリン液（ただし、精巣は Glutaraldehyde Formalin Acetic acid(GFA)液にて前固定後、眼球は Glutaraldehyde-Formaldehyde(G-F)混合固定液にて前固定後）にて保存した。

心臓、脾臓、リンパ節（頸部、腸間膜）、胸腺、下垂体、甲状腺（上皮小体を含む）、副腎、鼻腔（鼻甲介）、気管、肺（気管支を含む）、舌、唾液腺（顎下腺、舌下腺）、食道、胃、小腸（十二指腸、空腸、回腸）、大腸（盲腸、結腸、直腸）、肝臓、膵臓、腎臓、膀胱、精巣、

精巣上体、前立腺、精嚢、卵巣（卵管を含む）、子宮、乳腺、膣、脳（大脳、小脳）、
脊髄（胸部）、坐骨神経、大動脈、眼球、ハーダー氏腺、皮膚、骨及び骨髄（胸骨、大腿骨）、
骨格筋、ジンバル腺、その他肉眼病変部

3.12.9.2 器官重量

全生存動物の下記の器官について電子天秤 CP323S 型（ザルトリウス株式会社）を用いて重量を測定し、剖検日体重を用いて器官重量体重比（相対重量）を算出した。

脳、下垂体*、心臓、肺（気管支を含む）、肝臓、脾臓、腎臓、副腎、精巣、
前立腺*、精嚢*、卵巣（卵管を含む）、子宮、唾液腺、胸腺、甲状腺（上皮小体を含む）*
* ：固定後測定した。

3.12.9.3 病理組織学的検査

対照群及び最高用量投与群（第 1,4,5 及び 8 群）並びに死亡動物のすべてについては、採取した器官・組織（3.12.9.1 項参照）について常法に従い、パラフィン包埋、薄切、ヘマトキシリン・エオジン染色標本を作製し、鏡検した。その他の群については、肉眼病変部及び最高用量投与群で被験物質投与に起因すると考えられる病理組織学的変化を認めた胃について検査した。

3.13 死亡動物の処置

投与期間中に死亡した動物は速かに剖検した。採取した器官、組織（3.12.9.1 項参照）は 10%緩衝ホルマリン液にて固定し保存したが、器官重量の測定は行わなかった。

3.14 統計処理

対照群と各用量群（第 1 群と第 2～4 群, 第 5 群と第 6～8 群）との間の統計学的な有意差検定を行い、危険率 5% (P<0.05)又は 1%(P<0.01)のレベルで判定した。統計学的解析は、対照群と各用量群の体重、摂餌量、摂水量、尿検査（尿試験紙検査及び尿沈渣を除く）、血液学的検査、血液生化学的検査及び器官重量の平均値の差について、5%有意水準で Bartlett 法による等分散検定を行い、等分散の場合は、パラメトリックの Dunnett 法による両側検定を、不等分散の場合は、ノンパラメトリックの Steel 法による両側検定を行った。また、尿検査（尿試験紙検査及び尿沈渣）、肉眼的病理学検査及び病理組織学的検査における発生頻度の差の検定については、Fisher の直接確率検定（片側）を、程度のある病変については Wilcoxon 検定（両側）を行った。なお、一般状態及び所見がみられなかった眼科学的検査においては統計処理を行わなかった。

3.15 被験物質投与液の分析方法

3.15.1 標準物質

3.1 項の被験物質を標準品として使用した。

3.15.2　分析用試薬及び機器

3.15.2.1　試薬

アセトニトリル	：	HPLC 用、和光純薬工業株式会社 ロット番号：[redacted]
エタノール	：	HPLC 用、和光純薬工業株式会社 ロット番号：[redacted]
りん酸二水素カリウム	：	試薬特級、和光純薬工業株式会社、分子量 136.09 ロット番号：[redacted]
純水	：	Elix 純水システムを用いて製造した水

3.15.2.2　使用機器

名称	型式	製造業者
電子天秤	CPA225D	SARTORIUS K.K.
HPLC	LC-VP シリーズ	株式会社島津製作所
UV 検出器	SPD-20A	
データ処理装置	LC solution	
超音波洗浄器	ASU-3	アズワン株式会社
スターラー	HS-3E	井内盛栄堂
Elix 純水装置システム	Elix UV3	日本ミリポア株式会社

3.15.3　溶液の調製

3.15.3.1　10 mmol/L りん酸二水素カリウム溶液

りん酸二水素カリウム 2.04012 又は 1.36000 g を純水に溶かし、全量を 1500 又は 1000 mL とした。

3.15.3.2　移動相［10 mmol/L りん酸二水素カリウム溶液／アセトニトリル（70：30）］

10 mmol/L りん酸二水素カリウム溶液及びアセトニトリルを 70：30（v/v）の割合で混合し、超音波洗浄器で脱気を行ったものを移動相とした。

3.15.3.3　希釈液

純水及びアセトニトリルを 75：25（v/v）の割合で混合した液を希釈液とした。

3.15.4　分析用試料の調製

3.15.4.1　標準原液

標準物質 0.02000 g を精密に量り、アセトニトリルを用いて正確に 20 mL として 2-メチルブチリックアシド標準原液（SS）を調製した（1 mg/mL）。

3.15.4.2 検量線用標準溶液

次表に示すように希釈液を用いて正確に希釈し、検量線用標準溶液（S1～S6）を調製した。

検量線用標準溶液 No.	採取液	採取量 (mL)	全量 (mL)	2-メチルブチリックアシド濃度 (μg/mL)
S6	SS	3	20	150
S5	SS	2	20	100
S4	SS	1	20	50
S3	S5	5	20	25
S2	S5	2	20	10
S1	S2	4	20	2

3.15.4.3 QC 用試料

次表に示すように希釈液を用いて正確に希釈し、QC 用試料溶液（QC1 及び QC2）を調製した。

QC 用試料 No.	採取液	採取量 (mL)	全量 (mL)	2-メチルブチリックアシド濃度 (μg/mL)
QC2	SS	2	20	100
QC1	QC2	2	20	10

3.15.4.4 試料前処理法

投与液試料を次表に従い 1000 倍希釈した後、孔径 0.45 μm のフィルター（メルクミリポア マイレックス-LH、ロット番号：[redacted] でろ過し、測定用試料とした。なお、1 次希釈液にはエタノールを、2 次希釈液には希釈液を用いた。

投与液試料 (mg/mL)	1 次希釈		2 次希釈		2-メチルブチリックアシド濃度 (μg/mL)
	採取量 (mL)	全量 (mL)	1 次希釈液採取量 (mL)	全量 (mL)	
0	1	100	1	10	0
8	1	100	1	10	8
25	1	100	1	10	25
80	1	100	1	10	80

3.15.5　HPLC 条件

カラム	：Develosil ODS-UG-5 （4.6 mm I.D.×150 mm、5 μm、野村化学株式会社） ロット番号：[redacted]
移動相	：10 mmol/L りん酸二水素カリウム溶液／アセトニトリル （70：30、v/v）
測定波長	：210 nm
カラム温度	：30℃（測定開始時温度）
サンプルクーラー	：10℃（測定開始時温度）
流量	：1.0 mL/min
試料注入量	：10 μL
分析時間	：10 分

3.15.6　システム再現性

システムの適正な稼動を確認するため、標準溶液（S4）を測定試料の測定前に 3 回注入し、再現性を確認した。判定基準は、2-メチルブチリックアシドのピーク面積値の相対標準偏差（RSD）が、5.0 %以下とした。

RSD（%）＝（標準偏差 / 平均値）×100

3.15.7　分析項目及び判定基準

3.15.7.1　濃度の算出

検量線用標準溶液（S1~S6、各 n=1）を分析法に従って測定し、得られたピーク面積値を用いて、最小二乗法による一次回帰直線式から検量線（Y = aX + b、Y：ピーク面積比、X：濃度、重み付け：なし）を作成した。検量線の判定基準は、相関係数 r が 0.995 以上、逆回帰値の真度（相対誤差：RE）が±10%以内とした。希釈して測定した試料は、希釈試料の測定値に希釈倍数を乗じた値を試料の測定値とした。

RE（%）＝［(測定濃度－設定濃度）/ 設定濃度］×100

3.15.7.2　測定試料実測時の測定系の精度管理方法

試料を測定するときは、検量線用標準溶液（S1~S6、各 n=1）、QC 用試料（2 濃度：10 及び 100 μg/mL、各 n=1）、測定試料、QC 用試料（2 濃度：10 及び 100 μg/mL、各 n=1）の順に測定し、測定法の信頼性を確認した。QC 用試料は、RE が±10%以内であるとき適合とした。

3.15.8　データ処理方法

データ処理装置でクロマトグラム、ピーク面積値、濃度、検量線（重み付け：なし）の相関係数（r）、検量線の傾き及び y 切片を算出した。

平均値、濃度、相対誤差（RE）、標準偏差（SD）及び相対標準偏差（RSD）は表計算ソフト Excel（Microsoft Excel）を使用した。

3.15.8.1 数値の取り扱い

数値は（n＋1）桁目を四捨五入してn桁（次表の算出桁数）で表示した。

算出項目	単位	算出桁数
ピーク面積値	μAU·sec	整数
濃度	μg/mL	有効数字4桁
	mg/mL	有効数字4桁
平均値	個別値の単位にあわせた。	個別値と同じ桁数
RE	%	小数点以下1桁
SD	－	平均値の桁にあわせた。
RSD	%	小数点以下1桁
相関係数	－	有効数字3桁

3.15.8.2 再測定

再測定は行わなかった。

3.16 資料の保管

本試験で発生した試験計画書及び変更書（原本）、最終報告書（原本）、動物、被験物質、飼育環境に関する記録、試験成績、投与液の分析及びQAUの査察に関する記録、標本類、その他本試験に係る記録文書、並びに被験物質保存サンプルは最終報告書提出後10年間、[redacted]がGLP適合施設にて保管する。なお、保管場所については、当初5年間は[redacted]にて保管し、その後外部の資料保管施設を利用する場合は、試験委託者と協議の上、保管場所を決定する。保管期間の満了後の措置については、試験委託者と試験受託者との協議の上、決定する。

3.17 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

1. [redacted]の11時17分頃に、第3群の動物番号1437023の動物が、投与後に死亡した。肉眼的病理学検査で肺の右後葉の変色がみられたことから、投与液の誤嚥の可能性が考えられたため、肉眼的病理学検査及び病理組織学的検査については評価から除外した。死亡動物は中用量群の10例中の1例であり、試験の評価には影響しないと判断した。
2. 雄の対照群の1例（動物番号：1437006）の上皮小体が病理組織標本中に存在せず、病理組織学的検査ができなかった。しかしながら、10例中の1例であり、他の動物では上皮小体に異常を認めなかったことから毒性評価は可能であると判断した。

4　試験結果

4.1　生存率及び一般状態

各群の生存動物数を TABLE 1 に、一般状態を TABLE 2 に要約した。また個体別の一般状態を APPENDIX A に示した。

第 35 日に雄の 250 mg/kg/day 群の 1 例（動物番号 1437023）が死亡し、剖検時の生存率は 90%であった。第 70 日及び第 75 日に雌の 800 mg/kg/day 群の各 1 例（動物番号 1437071 及び 1437078）が死亡し、剖検時の生存率は 80%であった。その他の群では、死亡あるいは切迫屠殺動物はみられず、剖検時の生存率はいずれも 100%であった。

一般状態において、第 69 日に雌の 800 mg/kg/day 群の 1 例で深大呼吸がみられ、翌日に死亡した。雄で第 72 日、雌で第 71 日以降、投与後の観察時に雄の 800 mg/kg/day 群で 2～8 例、雄の 250 mg/kg/day 群で 0～2 例、雌の 800 mg/kg/day 群で 0～4 例に、それぞれ流涎が観察された。流涎は、午後の観察時にはすべて消失しており、投与後のみにみられた変化であった。その他の群では異常所見は観察されなかった。

4.2　体重

各群の平均体重を FIGURE 1 に図示し、平均体重及び標準偏差を TABLE 3 に示した。また個体別の値を APPENDIX B に示した。

雌の 800 mg/kg/day 群で、第 6 週以降に体重の低値傾向がみられた。その他の群においては、投与期間中、対照群と比較して統計学的に有意な差はみられなかった。

4.3　摂餌量

各群の平均摂餌量及び標準偏差を TABLE 4 に、また個体別の摂餌量を APPENDIX C に示した。

雌の 250 mg/kg/day 群で、第 13 週に対照群と比較して摂餌量の有意な低値がみられたが、用量との関連が認められないことから偶発的な変動と判断した。その他の群においては、投与期間中、対照群と比較して統計学的に有意な差はみられなかった。

4.4　摂水量

各群の平均摂水量及び標準偏差を TABLE 5 に、また個体別の摂水量を APPENDIX D に示した。

投与期間中、雌雄の被験物質投与各群において、対照群と比較して統計学的に有意な差はみられなかった。

4.5　眼科学的検査

各群の眼科学的検査結果を TABLE 6 に、また個体別の結果を APPENDIX E に示した。

雌雄の対照群及び被験物質投与各群に異常所見は観察されなかった。

4.6　尿検査

各群の尿検査結果を TABLE 7 に、また個体別の結果を APPENDIX F に示した。

雄の 80 mg/kg/day 群で、対照群と比較して比重及びカリウム(K)の有意な高値がみられたが、用量との関連が認められないことから偶発的な変動と判断した。

その他の群では、対照群と比較して統計学的に有意な差はみられなかった。

4.7　血液学的検査

各群の血液学的検査結果を TABLE 8 に、また個体別の結果を APPENDIX G に示した。

単球数(MONO)及び好酸球数(EO)の有意な高値が、雌の 80 mg/kg/day 群でみられたが、用量との関連が認められないことから偶発的な変動と判断した。プロトロンビン時間(PT)の有意な延長が、雌の 800 mg/kg/day 群でみられた。その他の検査項目においては、対照群と被験物質投与各群との間に統計学的に有意な差は認められなかった。

4.8　血液生化学的検査

各群の血液生化学的検査結果を TABLE 9 に、また個体別の結果を APPENDIX H に示した。

アラニンアミノトランスフェラーゼ(ALT)の有意な低値が、雌の 800 及び 250 mg/kg/day 群でみられたが、ALT は逸脱酵素であるため、低値は毒性学的意義の乏しい変化と判断した。尿素窒素(BUN)及びマグネシウム(MG)の有意な高値が、雌の 800 mg/kg/day 群でみられた。総蛋白(TP)の有意な低値が、雄の 800 及び 250 mg/kg/day 群でみられた。その他の検査項目においては、対照群と被験物質投与各群との間に統計学的に有意な差は認められなかった。

4.9　病理学的検査

4.9.1　肉眼的病理学検査

各群の肉眼的病理学所見を TABLE 10 に、また個体別の所見を APPENDIX I に示した。

第 70 日に死亡した雌の 800 mg/kg/day 群の 1 例では、脾臓の小型化及び消化管（胃～盲腸）のガス貯留が観察され、第 75 日に死亡した 1 例では、胃の拡張が観察された。

生存動物で観察された所見は以下の通りである。雄の 800 mg/kg/day 群では、肝臓の小型化及び変色域（1 個）と精巣及び精巣上体の小型化（左右）が 1/10 例にみられた。250 mg/kg/day 群では、腹腔内脂肪の結節（1 個）が 1/9 例にみられた。対照群では、脾臓の嚢胞（1 個）が 1/10 例にみられた。雌の 800 mg/kg/day 群では、子宮角の拡張（左右）が 1/8 例にみられた。250 mg/kg/day 群では、胸腺の変色（赤色）、下垂体の変色斑（1 個）及び肝臓の横隔膜結節が各 1/10 例にみられた。対照群では、肝臓の変色域（1 個）が 1/10 例にみられ、卵巣の嚢胞（片側）が 2/10 例にみられた。雌雄の 80 mg/kg/day 群では、異常所見はみられなかった。被験物質投与群でみられた所見は、いずれも対照群と比較して発現率に統計学的差異は認められなかった。

4.9.2　器官重量及び器官重量体重比

各群の器官重量（絶対重量）及び器官重量体重比（相対重量）の平均値及び標準偏差をそれぞれ TABLE 11, 12 に、また個体別の値を APPENDIX J, K に示した。

下垂体の相対重量の有意な高値が、雌の 250 mg/kg/day 群でみられたが、用量との関連が認められないことから偶発的な変動と判断した。腎臓の相対重量の有意な高値が雌の 800 mg/kg/day 群でみられた。その他の器官においては、対照群と被験物質投与各群との間に統計学的に有意な差は認められなかった。

4.9.3　病理組織学的検査

各群の病理組織学的所見を TABLE 13 に要約し、また個体別の所見を APPENDIX L に示した。

雌雄の 800 mg/kg/day 群の胃で、境界縁の軽度の過形成が全例（雄 10/10 例、雌 10/10 例）にみられ、対照群と比較して統計学的に有意に高い出現率を示した。このため、雌雄の 250 及び 80 mg/kg/day 群についても胃の病理組織学的検査を実施したところ、同所見は雄の 250 mg/kg/day 群で 1/9 例にみられた。甲状腺の鰓後体遺残が、雌の対照群で 4/10 例にみられ、800 mg/kg/day 群では 0/10 例であったことから、有意に低い出現率を示したが、先天性の変化であり、被験物質の影響ではないと判断した。そのため、250 及び 80 mg/kg/day 群の検査は実施しなかった。その他、雌雄の 800 mg/kg/day 群において、心臓の心筋症、下垂体のラトケ嚢遺残、前立腺のリンパ球浸潤、肝臓の脂肪変性及び単核細胞浸潤などの所見が観察されたが、いずれも対照群と比較して統計学的差異は認められなかった。

第 70 日に死亡した雌の 800 mg/kg/day 群の 1 例で観察された脾臓の小型化は、重篤な萎縮であった。消化管（胃～盲腸）のガス貯留に対応する所見は観察されなかった。その他、脾臓の中等度の色素沈着、鼻腔の軽度の炎症、前胃の中等度の糜爛及び過形成、胃の境界縁の軽度の過形成が観察された。第 75 日に死亡した 1 例では、胃の境界縁の軽度の過形成が観察されたが、胃の拡張に対応する所見は観察されなかった。

なお、肉眼的病理学検査において、雄の 800 mg/kg/day 群の 1 例に観察された肝臓の小型化及び変色域（1 個）は、中等度の梗塞であった。同じ個体にみられた精巣及び精巣上体の小型化（左右）は、それぞれ顕著な精細管の萎縮、中等度の精巣上体管の萎縮及び顕著な精子減少であった。250 mg/kg/day 群の 1 例に観察された腹腔内脂肪の結節（1 個）は、軽度の壊死であった。対照群の 1 例に観察された脾臓の嚢胞（1 個）は、軽度の被膜の嚢胞であった。雌の 800 mg/kg/day 群の 1 例に観察された子宮角の拡張（左右）は、中等度の内腔の拡張であった。250 mg/kg/day 群の各 1 例にみられた胸腺の変色（赤色）及び下垂体の変色斑（1 個）は、それぞれ軽微な出血及び嚢胞であった。同群の 1 例に観察された肝臓の横隔膜結節は、病理組織学的にも横隔膜結節であることが確認された。対照群の 1 例に観察された肝臓の変色域（1 個）は、軽度の Tension lipidosis であり、2 例にみられた卵巣の嚢胞（片側）は、いずれも軽度の包性嚢胞であった。

4.10　投与液中における被験物質の安定性及び濃度確認試験結果

4.10.1　投与液中における被験物質の安定性試験結果

投与液中における被験物質の安定性試験結果を TABLE 14 に示した。

8 mg/mL 投与液の冷蔵保存 5 日＋室温 24 時間後及び冷蔵保存 10 日＋室温 24 時間後の分析値は、保存開始前の分析値に対してそれぞれ 100.9 %及び 99.5 %、80 mg/mL 投与液の分析値は、保存開始時の分析値に対してそれぞれ 100.0 %及び 100.4 %で、いずれも許容範囲内（保存開始前の分析値の±10%以内）であり、冷蔵保存 10 日＋室温 24 時間安定であることが示された。

4.10.2　投与液中における被験物質の濃度確認試験結果

投与液中における被験物質の濃度確認試験結果を TABLE 15 に示した。

初回及び最終回調製時の濃度確認試験では、8、25 及び 80 mg/mL の分析値は、それぞれ設定値の 100.1 %及び 100.3 %、102.4 %及び 102.7 %、並びに 103.6 %及び 101.7 %であり、いずれも許容範囲内（設定値の± 10 %以内）であり、適正に調製されていることを確認した。

4.10.3　投与液分析時の精度管理結果

システム再現性、検量線及び QC サンプルの分析結果をそれぞれ TABLE 16, 17, 18 に示した。

検量線の相関係数、RE（%）及び RSD（%）のすべての結果が判定基準内であり、測定法の信頼性が確認された。

5　考察及び結論

本試験において、被験物質の 2-メチルブチリックアシドを 0（対照）、80、250 及び 800 mg/kg/day の用量で、Crl:CD(SD)系ラットの雌雄各群 10 匹に 90 日間強制経口投与し、反復投与による毒性影響を検討した。

摂餌量、摂水量、眼科学的検査、尿検査及び肉眼的病理学検査においては、被験物質投与の影響は認められなかった。

一般状態では、雌雄の 800 mg/kg/day 群及び雄の 250 mg/kg/day 群で投与後に流涎がみられ、投与直後の一過性変化であることから、被験物質の刺激性による変化であると考えられた。

体重では、雌の 800 mg/kg/day 群で、第 6 週以降に体重の低値傾向がみられたことから、被験物質投与の影響であった可能性が考えられた。

血液学的検査では、プロトロンビン時間の有意な延長が雌の 800 mg/kg/day 群でみられたが、軽微な変動であり、用量との明らかな関連もみられていない。さらに活性化部分トロンボプラスチン時間及び血小板数に変化がみられていないことから、毒性学的意義の乏しい変化と判断した。

血液生化学的検査では、総蛋白の有意な低値が雄の 800 及び 250 mg/kg/day 群でみられたが、体重の低値、尿検査における蛋白の変動、あるいは病理組織学的に肝障害を示唆する変化などがみられていないことから、生体への影響としては弱いものであったと判断した。

また、雌の 800 mg/kg/day 群では、血液生化学的検査において、尿素窒素及びマグネシウムの有意な高値がみられ、腎臓の相対重量の有意な高値もみられた。しかしながら、病理組織学的検査において腎障害を示唆する変化がみられなかったことから、生体への影響としては弱いものであったと判断した。

病理組織学的検査において、雌雄の 800 mg/kg/day 群の胃で境界縁の軽度の過形成が全例にみられ、雄の 250 mg/kg/day 群でも 1 例にみられた。実験動物では、化学物質の経口投与時に、さまざまな刺激に対する反応性の変化として前胃の過形成が認められ、境界縁において好発することが報告されている[1]。2-メチルブチリックアシドは腐食性物質に分類されており（製品安全データシート）、さらにラットを用いた急性経口毒性試験[2]において、消化管の運動過剰及び下痢が報告されていることから、本試験でみられた変化は、前胃粘膜への持続的な刺激もしくは直接的な傷害による影響が考えられた。

第 70 日及び第 75 日に雌の 800 mg/kg/day 群の各 1 例が死亡し、消化管（胃～盲腸）のガス貯留あるいは胃の拡張が観察された。第 70 日に死亡した個体では、一般状態で深大呼吸がみられていたことから、これらの死亡は、拡張した消化管による呼吸器の圧迫が直接的な原因と考えられた。被験物質を 2 週間強制経口投与した用量設定試験[3]においても、雌の 800 mg/kg/day 群の 1 例に、肉眼的病理学検査で食道～盲腸のガス貯留が観察された。ラットでみられる消化管のガス貯留の原因の一つとして、鼻孔の閉鎖により空気が嚥下されて腸管内に過剰な空気が貯留することが実験的に認められており[4]、第 70 日に死亡した個体において、鼻腔の炎症がみられた。しかしながら、炎症は軽度であり、その他にもガス貯留の原因となる明らかな変化はみられなかった。これらのことから、雌の 800 mg/kg/day 群でみられた死亡動物の発生には被験物質投与の影響が考えられたものの、死因の詳細は明確とならなかった。

以上、Crl:CD(SD)系ラットの雌雄に 2-メチルブチリックアシドを 0 （対照）、80、250 及び 800 mg/kg/day の用量で 90 日間強制経口投与した結果、雌雄の 800 mg/kg/day 群の胃で、境界縁の過形成がみられたこと、血液生化学的検査において雄の 800 及び 250 mg/kg/day 群で総蛋白の有意な低値がみられたことから、無毒性量（NOAEL）は、雄で 80 mg/kg/day、雌で 250 mg/kg/day であると判断された。

6　文献

1) 日本毒性病理学会（2000 年）毒性病理組織学

2) Butanoic acid, 2-methyl- RTECS - Registry of Toxic Effects of Chemical Substances RightAnswer.com, Inc., 2014　http://www.rightanswerknowledge.com/assm.asp?RTEK7897000

3) [redacted]（2014 年）「指定添加物の安全性に関する試験（2-メチルブチリックアシドに関する 90 日間反復投与毒性試験のための用量設定試験）（試験番号[redacted]」[redacted] 最終報告書

4) Katsuyuki, N. and Gen O. Aerophagia induced by the nasal obstruction on experimental animals. Exp. Anim., 26 (2), 149-159, 1977

7　図及び総括表

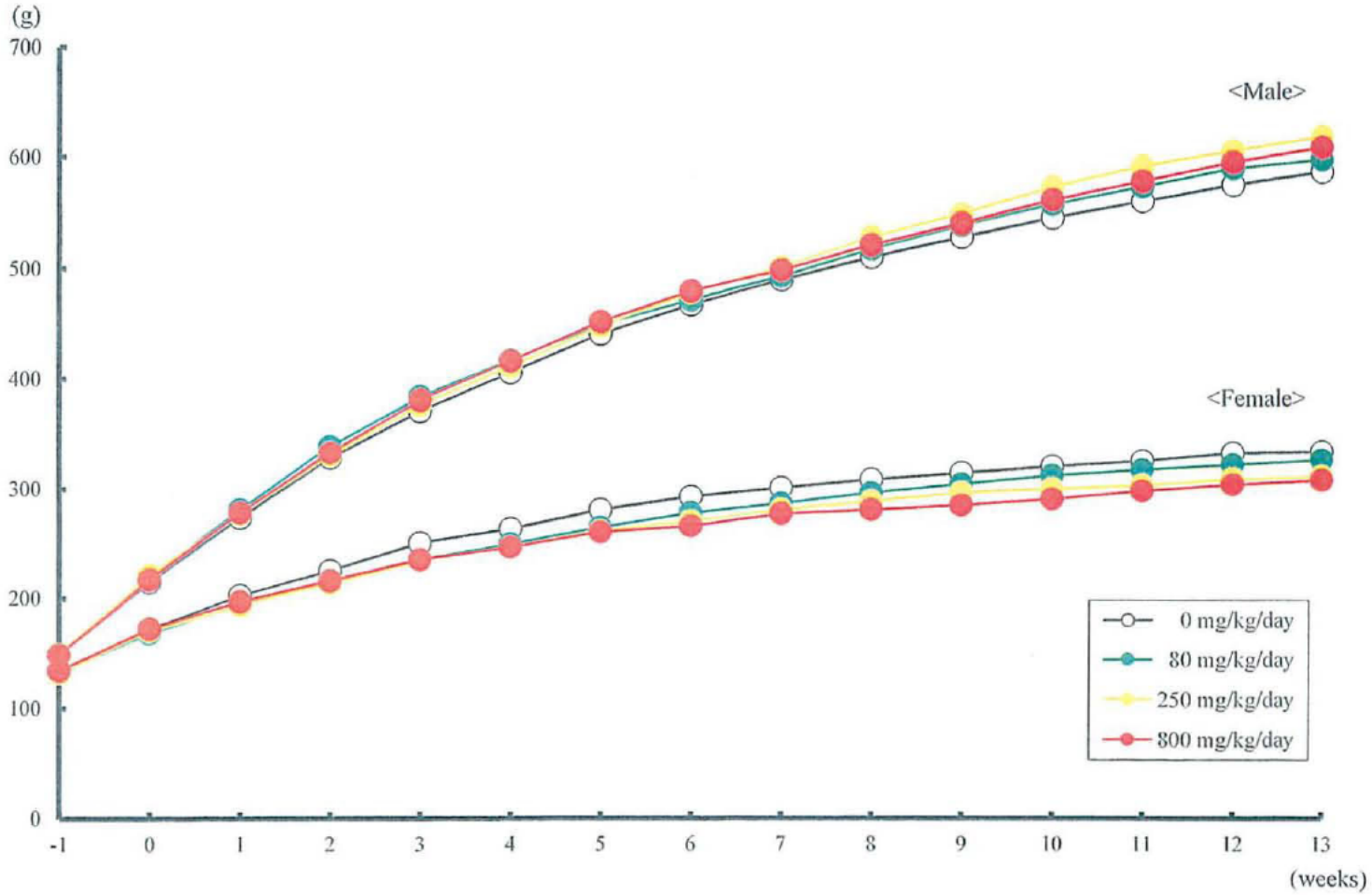

FIGURE 1
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
BODY WEIGHT CURVES
STUDY NO. [redacted]

TABLE 1
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
SURVIVAL DATA (NO. OF SURVIVALS)
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	NO. OF ANIMALS	WEEKS															TOTAL NO. OF SURVIVALS(%)
				-1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
MALE	1	0	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10(100)
	2	80	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10(100)
	3	250	10	10	10	10	10	10	9	9	9	9	9	9	9	9	9	9	9(90)
	4	800	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10(100)
FEMALE	5	0	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10(100)
	6	80	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10(100)
	7	250	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10(100)
	8	800	10	10	10	10	10	10	10	10	10	10	10	9	8	8	8	8	8(80)

TABLE 2
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
GENERAL CONDITION DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	SIGNS AND SYMPTOMS	DAYS																						
				-7	-6	-5	-4	-3	-2	-1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
MALE	1	0	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	2	80	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	3	250	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	4	800	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
FEMALE	5	0	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	6	80	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	7	250	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	8	800	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10

TABLE 2
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
GENERAL CONDITION DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	SIGNS AND SYMPTOMS	DAYS																						
				18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41
MALE	1	0	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	2	80	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	3	250	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	9	9	9	9	9	9	9
			Found dead	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
	4	800	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
FEMALE	5	0	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	6	80	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	7	250	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	8	800	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10

TABLE 2
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
GENERAL CONDITION DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	SIGNS AND SYMPTOMS	DAYS																						
				42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65
MALE	1	0	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	2	80	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	3	250	Normal	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9
	4	800	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
FEMALE	5	0	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	6	80	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	7	250	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	8	800	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10

TABLE 2
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
GENERAL CONDITION DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	SIGNS AND SYMPTOMS	DAYS						
				66	67	68	69	70	71	
									AM	PM
MALE	1	0	Normal	10	10	10	10	10	10	-
	2	80	Normal	10	10	10	10	10	10	-
	3	250	Normal	9	9	9	9	9	9	-
	4	800	Normal	10	10	10	10	10	10	-
FEMALE	5	0	Normal	10	10	10	10	10	10	10
	6	80	Normal	10	10	10	10	10	10	10
	7	250	Normal	10	10	10	10	10	10	10
	8	800	Normal	10	10	10	9	9	7	9
			Breathing/Deep respiration	0	0	0	1	0	0	0
			Mouth/Salivation	0	0	0	0	0	2	0
			Found dead	0	0	0	0	1	0	0

AM : Animals were observed for general condition after the treatment.

TABLE 2
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
GENERAL CONDITION DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	SIGNS AND SYMPTOMS	DAYS																					
				72		73		74		75		76		77		78		79		80		81		82	
				AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
MALE	1	0	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	2	80	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	3	250	Normal	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	7	9	9	9	9	9
			Mouth/Salivation	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0
	4	800	Normal	4	10	5	10	5	10	8	10	5	10	8	10	6	10	5	10	5	10	6	10	7	10
			Mouth/Salivation	6	0	5	0	5	0	2	0	5	0	2	0	4	0	5	0	5	0	4	0	3	0
FEMALE	5	0	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	6	80	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	7	250	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	8	800	Normal	8	9	5	9	8	9	8	8	7	8	7	8	7	8	7	8	7	8	7	8	7	8
			Mouth/Salivation	1	0	4	0	1	0	1	0	1	0	1	0	1	0	1	0	1	0	1	0	1	0
			Found dead	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0

AM : Animals were observed for general condition after the treatment.

TABLE 2

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

GENERAL CONDITION DATA

STUDY N[redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	SIGNS AND SYMPTOMS	DAYS																						
				83		84		85		86		87		88		89		90		91		92		93				
				AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM		
MALE	1	0	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10		
	2	80	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10		
	3	250	Normal	8	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	8	9	9	9	9		
			Mouth/Salivation	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0		
	4	800	Normal	5	10	8	10	2	10	6	10	7	10	8	10	6	10	7	10	7	10	5	10	10		
			Mouth/Salivation	5	0	2	0	8	0	4	0	3	0	2	0	4	0	3	0	3	0	5	0	0		
FEMALE	5	0	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10		
	6	80	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10		
	7	250	Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10		
	8	800	Normal	7	8	8	8	7	8	7	8	8	8	8	8	5	8	7	8	8	8	8	8	8		
			Mouth/Salivation	1	0	0	0	1	0	1	0	0	0	0	0	3	0	1	0	0	0	0	0	0		

AM : Animals were observed for general condition after the treatment.

TABLE 3
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
BODY WEIGHT DATA (G, MEAN ± S.D.)
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	WEEKS -1	0	1	2	3
MALE	1	0	148.0 ± 3.9	214.6 ± 6.7	273.3 ± 12.6	328.2 ± 19.5	370.8 ± 26.1
	2	80	148.8 ± 4.0	218.3 ± 11.1	280.3 ± 17.9	338.4 ± 30.7	383.1 ± 44.0
	3	250	148.2 ± 5.5	219.7 ± 10.6	277.2 ± 15.2	330.4 ± 22.9	376.4 ± 31.0
	4	800	147.7 ± 4.8	216.4 ± 9.4	277.8 ± 12.5	332.8 ± 11.8	380.7 ± 11.8
FEMALE	5	0	133.0 ± 4.7	172.1 ± 8.0	202.4 ± 12.4	224.6 ± 18.4	249.8 ± 19.9
	6	80	132.1 ± 4.5	167.8 ± 10.9	193.4 ± 16.0	214.8 ± 24.1	234.2 ± 27.6
	7	250	132.1 ± 4.0	169.6 ± 4.6	192.6 ± 7.5	213.5 ± 12.5	233.7 ± 15.2
	8	800	133.7 ± 4.7	171.8 ± 8.8	196.3 ± 9.7	215.2 ± 13.7	234.2 ± 16.7

TABLE 3
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
BODY WEIGHT DATA (G, MEAN ± S.D.)
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	WEEKS 4	5	6	7	8
MALE	1	0	405.2 ± 30.2	440.3 ± 36.7	466.7 ± 38.7	489.0 ± 38.6	509.8 ± 41.6
	2	80	416.4 ± 52.9	448.5 ± 58.7	470.7 ± 63.9	492.0 ± 65.7	516.8 ± 69.3
	3	250	410.7 ± 36.5	447.4 ± 44.6	477.7 ± 50.3	500.4 ± 52.6	528.0 ± 56.7
	4	800	415.8 ± 15.6	451.3 ± 19.8	478.7 ± 24.8	497.4 ± 26.4	520.2 ± 27.8
FEMALE	5	0	262.9 ± 24.1	280.2 ± 29.1	292.2 ± 30.6	300.5 ± 32.9	308.0 ± 32.7
	6	80	248.5 ± 27.9	263.8 ± 30.0	277.2 ± 31.8	285.7 ± 32.5	295.5 ± 34.8
	7	250	246.0 ± 15.5	260.9 ± 15.2	269.7 ± 18.8	280.0 ± 18.3	287.9 ± 20.5
	8	800	245.4 ± 19.4	259.5 ± 21.1	265.0 ± 22.9	276.0 ± 24.0	279.8 ± 23.2

TABLE 3
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
BODY WEIGHT DATA (G, MEAN ± S.D.)
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	WEEKS 9	10	11	12	13
MALE	1	0	527.7 ± 43.0	544.9 ± 43.7	560.0 ± 43.3	574.8 ± 46.5	586.4 ± 46.5
	2	80	538.1 ± 76.0	557.0 ± 79.5	572.8 ± 83.0	589.2 ± 85.1	597.2 ± 94.0
	3	250	548.4 ± 60.3	572.1 ± 62.5	591.1 ± 64.0	605.0 ± 64.6	617.8 ± 66.6
	4	800	539.7 ± 32.9	560.7 ± 35.8	577.7 ± 42.3	594.8 ± 42.7	608.3 ± 44.7
FEMALE	5	0	314.2 ± 33.8	320.2 ± 33.8	325.2 ± 35.0	332.4 ± 35.9	333.7 ± 36.5
	6	80	303.7 ± 35.9	311.5 ± 38.9	316.9 ± 39.5	321.4 ± 40.4	326.0 ± 39.1
	7	250	296.0 ± 20.6	299.4 ± 21.4	302.9 ± 22.4	308.6 ± 23.5	310.8 ± 25.3
	8	800	284.0 ± 26.7	289.9 ± 27.4	297.4 ± 29.1	303.4 ± 31.3	307.5 ± 29.5

TABLE 4

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

FOOD CONSUMPTION DATA (G/ANIMAL/DAY, MEAN ± S.D.)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	WEEKS -1	1	2	3	4
MALE	1	0	21.98 ± 1.34	19.98 ± 1.03	18.22 ± 1.63	17.18 ± 1.61	16.78 ± 1.63
	2	80	22.12 ± 1.20	20.28 ± 2.09	19.60 ± 2.49	18.22 ± 3.07	16.98 ± 3.00
	3	250	22.44 ± 0.50	20.30 ± 1.06	18.98 ± 1.47	17.32 ± 0.82	16.52 ± 1.12
	4	800	21.48 ± 1.51	20.02 ± 0.87	18.82 ± 1.45	17.42 ± 1.74	16.12 ± 1.68
FEMALE	5	0	16.16 ± 0.87	13.18 ± 1.27	12.60 ± 1.75	12.08 ± 1.45	11.72 ± 2.46
	6	80	15.76 ± 1.61	12.26 ± 1.32	12.90 ± 2.22	11.72 ± 2.18	11.74 ± 1.20
	7	250	16.26 ± 1.12	11.32 ± 1.42	12.12 ± 1.51	11.62 ± 1.90	10.88 ± 1.08
	8	800	16.82 ± 1.35	12.42 ± 0.43	12.48 ± 1.58	11.58 ± 1.53	11.42 ± 1.20

TABLE 4

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

FOOD CONSUMPTION DATA (G/ANIMAL/DAY, MEAN ± S.D.)

STUDY N[redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	WEEKS 5	6	7	8	9
MALE	1	0	16.82 ± 1.87	15.12 ± 2.17	14.62 ± 1.46	14.08 ± 1.56	13.02 ± 1.18
	2	80	16.42 ± 2.36	14.58 ± 2.20	14.62 ± 2.15	14.34 ± 1.93	13.92 ± 2.33
	3	250	17.65 ± 1.18 a	15.58 ± 1.36	14.58 ± 2.01	14.32 ± 1.53	14.06 ± 1.61
	4	800	16.08 ± 1.75	14.04 ± 1.55	13.68 ± 1.04	13.84 ± 1.27	12.74 ± 1.25
FEMALE	5	0	11.62 ± 1.43	10.86 ± 1.65	10.16 ± 1.53	9.38 ± 0.60	9.28 ± 0.64
	6	80	11.24 ± 1.39	11.26 ± 2.19	9.72 ± 1.26	9.68 ± 1.67	8.82 ± 0.98
	7	250	10.36 ± 1.82	9.42 ± 1.05	9.34 ± 1.44	8.92 ± 1.58	8.46 ± 1.29
	8	800	11.22 ± 1.05	9.62 ± 1.85	10.22 ± 1.18	9.08 ± 1.00	8.32 ± 1.68

a : One cage data was omitted from the statistical analysis.

TABLE 4

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

FOOD CONSUMPTION DATA (G/ANIMAL/DAY, MEAN ± S.D.)

STUDY [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	WEEKS 10	11	12	13
MALE	1	0	12.54 ± 2.00	11.82 ± 1.71	12.02 ± 1.13	11.14 ± 1.42
	2	80	13.04 ± 2.30	12.68 ± 1.75	12.02 ± 2.11	11.48 ± 2.41
	3	250	13.50 ± 1.90	12.52 ± 1.10	11.46 ± 1.44	10.82 ± 1.45
	4	800	13.22 ± 1.55	12.32 ± 1.50	11.68 ± 1.67	11.10 ± 1.67
FEMALE	5	0	9.18 ± 1.15	8.66 ± 1.21	9.22 ± 1.25	7.72 ± 0.89
	6	80	9.68 ± 1.70	9.38 ± 1.01	8.42 ± 1.26	6.92 ± 0.99
	7	250	7.68 ± 0.73	8.28 ± 1.00	7.88 ± 1.85	5.58 ± 0.89 *
	8	800	8.65 ± 2.34 a	8.96 ± 1.67	8.96 ± 1.35	7.16 ± 1.47

a : One cage data was omitted from the statistical analysis.

* : Significantly different from control group at $P<0.05$.

TABLE 5
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
WATER CONSUMPTION DATA (G/ANIMAL/DAY, MEAN ± S.D.)
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	WEEKS -1	1	2	3	4
MALE	1	0	31.18 ± 2.35	32.82 ± 3.19	32.76 ± 5.01	31.76 ± 2.80	33.16 ± 4.20
	2	80	30.48 ± 4.58	31.74 ± 4.33	33.18 ± 5.45	33.78 ± 7.35	34.92 ± 9.87
	3	250	30.58 ± 2.41	30.88 ± 2.54	31.58 ± 3.70	31.48 ± 4.05	31.28 ± 3.14
	4	800	29.88 ± 2.05	30.18 ± 2.37	30.28 ± 3.89	30.40 ± 4.14	29.80 ± 4.69
FEMALE	5	0	23.98 ± 3.25	22.42 ± 1.64	22.42 ± 3.38	23.62 ± 5.67	23.44 ± 4.74
	6	80	23.76 ± 2.44	21.22 ± 2.88	22.54 ± 2.77	21.92 ± 2.87	22.60 ± 2.71
	7	250	23.82 ± 2.64	19.70 ± 2.07	20.78 ± 2.98	20.86 ± 2.55	21.18 ± 2.12
	8	800	24.16 ± 1.34	21.50 ± 3.33	22.08 ± 3.72	23.58 ± 4.24	24.26 ± 6.00

TABLE 5
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
WATER CONSUMPTION DATA (G/ANIMAL/DAY, MEAN ± S.D.)
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	WEEKS 5	6	7	8	9
MALE	1	0	31.14 ± 2.72	30.86 ± 3.53	31.92 ± 3.52	29.98 ± 4.44	29.08 ± 3.32
	2	80	33.86 ± 9.70	32.32 ± 6.35	33.28 ± 8.99	32.38 ± 8.17	33.12 ± 8.58
	3	250	31.35 ± 3.94 a	30.84 ± 4.87	30.02 ± 3.98	29.62 ± 2.60	27.92 ± 2.16
	4	800	27.98 ± 2.92	28.78 ± 3.95	30.28 ± 4.47	29.98 ± 4.64	28.78 ± 5.81
FEMALE	5	0	23.58 ± 2.81	24.82 ± 5.57	23.36 ± 4.98	22.64 ± 3.21	22.50 ± 2.09
	6	80	21.44 ± 2.39	23.24 ± 2.52	20.92 ± 3.09	21.82 ± 2.51	20.46 ± 1.79
	7	250	19.76 ± 2.36	19.70 ± 2.68	20.36 ± 3.45	19.86 ± 2.87	18.44 ± 2.14
	8	800	25.14 ± 4.74	23.98 ± 7.08	24.56 ± 4.01	23.60 ± 2.77	20.58 ± 3.82

a : One cage data was omitted from the statistical analysis.

TABLE 5
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
WATER CONSUMPTION DATA (G/ANIMAL/DAY, MEAN ± S.D.)
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	WEEKS 10	11	12	13
MALE	1	0	35.38 ± 9.07	27.40 ± 3.70	28.74 ± 3.10	27.54 ± 2.72
	2	80	32.06 ± 8.65	30.38 ± 6.89	30.32 ± 7.99	27.68 ± 7.39
	3	250	28.56 ± 2.96	28.82 ± 3.03	27.26 ± 3.12	24.38 ± 2.07
	4	800	28.72 ± 5.28	28.44 ± 5.21	27.76 ± 4.77	27.22 ± 6.12
FEMALE	5	0	23.42 ± 5.69	24.44 ± 6.76	23.88 ± 3.49	20.36 ± 3.27
	6	80	20.98 ± 3.16	21.00 ± 2.31	20.38 ± 1.93	18.14 ± 2.29
	7	250	18.02 ± 2.10	19.34 ± 2.48	19.78 ± 3.05	16.62 ± 2.95
	8	800	20.68 ± 3.75 a	21.28 ± 4.88	21.72 ± 3.67	20.40 ± 4.99

a : One cage data was omitted from the statistical analysis.

TABLE 6
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
OPHTHALMOSCOPIC FINDING DATA
STUDY NO. [redacted]

STRUCTURE[a]	SEX ----------	MALE				FEMALE			
AND	GROUP NO. ----------	1	2	3	4	5	6	7	8
FINDINGS	LEVEL (mg/kg/day) ---	0	80	250	800	0	80	250	800
	No. of examined	6	6	6	6	6	6	6	6
Normal		6	6	6	6	6	6	6	6

a : Anterior chamber, Optic media, Ocular fundus and others were examined.

TABLE 7
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
URINALYSIS DATA
STUDY NO. [redacted]

SEX	GROUP	LEVEL	NO. OF	GLUCOSE					BILIRUBIN				KETONE BODIES					OCCULT BLOOD				
	NO.	(mg/kg/day)	EXAMINED	-	±	1+	2+	3+	-	1+	2+	3+	-	±	1+	2+	3+	-	±	1+	2+	3+
MALE	1	0	6	6	0	0	0	0	6	0	0	0	0	3	3	0	0	6	0	0	0	0
	2	80	6	6	0	0	0	0	6	0	0	0	0	1	3	1	1	6	0	0	0	0
	3	250	6	6	0	0	0	0	6	0	0	0	0	3	2	1	0	6	0	0	0	0
	4	800	6	6	0	0	0	0	6	0	0	0	1	1	4	0	0	6	0	0	0	0
FEMALE	5	0	6	6	0	0	0	0	6	0	0	0	6	0	0	0	0	6	0	0	0	0
	6	80	6	6	0	0	0	0	6	0	0	0	6	0	0	0	0	6	0	0	0	0
	7	250	6	6	0	0	0	0	6	0	0	0	6	0	0	0	0	6	0	0	0	0
	8	800	6	6	0	0	0	0	6	0	0	0	6	0	0	0	0	6	0	0	0	0

TABLE 7
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
URINALYSIS DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	NO. OF EXAMINED	PROTEIN					UROBILINOGEN					pH	SPECIFIC GRAVITY
				-	±	1+	2+	3+	0.1	1	2	4	8		
MALE	1	0	6	2	1	2	1	0	6	0	0	0	0	6.927 ± 0.669	1.0380 ± 0.0219
	2	80	6	1	0	2	3	0	6	0	0	0	0	6.825 ± 0.605	1.0717 ± 0.0211 *
	3	250	6	0	2	3	1	0	6	0	0	0	0	6.898 ± 0.739	1.0328 ± 0.0081
	4	800	6	0	2	3	1	0	6	0	0	0	0	6.907 ± 0.954	1.0398 ± 0.0225
FEMALE	5	0	6	2	3	1	0	0	6	0	0	0	0	6.852 ± 0.781	1.0322 ± 0.0237
	6	80	6	0	5	1	0	0	6	0	0	0	0	7.338 ± 0.771	1.0395 ± 0.0281
	7	250	6	2	3	1	0	0	6	0	0	0	0	7.122 ± 0.947	1.0375 ± 0.0157
	8	800	6	1	2	3	0	0	6	0	0	0	0	7.442 ± 0.674	1.0333 ± 0.0164

* : Significantly different from control group at <0.05.

TABLE 7
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
URINALYSIS DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	NO. OF EXAMINED	APPEARANCE					MICROSCOPIC EXAMINATION														
									EPITHELIAL CELLS					CRYSTALS					CASTS				
				N	Y	B	R	C	-	±	1+	2+	3+	-	±	1+	2+	3+	-	±	1+	2+	3+
MALE	1	0	6	6	0	0	0	0	6	0	0	0	0	2	0	1	1	2	6	0	0	0	0
	2	80	6	6	0	0	0	0	6	0	0	0	0	4	0	1	0	1	6	0	0	0	0
	3	250	6	6	0	0	0	0	6	0	0	0	0	3	0	0	1	2	6	0	0	0	0
	4	800	6	6	0	0	0	0	6	0	0	0	0	2	0	2	1	1	6	0	0	0	0
FEMALE	5	0	6	6	0	0	0	0	6	0	0	0	0	5	0	0	0	1	6	0	0	0	0
	6	80	6	6	0	0	0	0	6	0	0	0	0	4	0	0	0	2	6	0	0	0	0
	7	250	6	6	0	0	0	0	6	0	0	0	0	5	0	0	0	1	6	0	0	0	0
	8	800	6	6	0	0	0	0	6	0	0	0	0	6	0	0	0	0	6	0	0	0	0

N : Normal(Pale yellow), Y : Yellow, B : Brown, R : Red, C : Cloudy

TABLE 7
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
URINALYSIS DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	NO. OF EXAMINED	MICROSCOPIC EXAMINATION										URINE VOLUME (IN GRAMS)
				RBC					WBC					
				-	±	1+	2+	3+	-	±	1+	2+	3+	
MALE	1	0	6	6	0	0	0	0	6	0	0	0	0	1.52 ± 0.88
	2	80	6	6	0	0	0	0	6	0	0	0	0	0.70 ± 0.64
	3	250	6	6	0	0	0	0	6	0	0	0	0	1.88 ± 0.88
	4	800	6	6	0	0	0	0	6	0	0	0	0	1.12 ± 0.65
FEMALE	5	0	6	6	0	0	0	0	6	0	0	0	0	0.77 ± 0.45
	6	80	6	6	0	0	0	0	6	0	0	0	0	0.82 ± 0.63
	7	250	6	6	0	0	0	0	6	0	0	0	0	0.58 ± 0.48
	8	800	6	6	0	0	0	0	6	0	0	0	0	1.05 ± 0.81

TABLE 7
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
URINALYSIS DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	NO. OF EXAMINED	NA (mEq/L)	K (mEq/L)	CL (mEq/L)
MALE	1	0	6	51.82 ± 43.55	116.775 ± 66.656	54.82 ± 33.41
	2	80	6	53.60 ± 10.95	280.623 ± 113.215 **	38.32 ± 23.60
	3	250	6	77.85 ± 45.26	126.740 ± 48.456	49.18 ± 17.30
	4	800	6	84.25 ± 58.53	135.005 ± 69.117	56.95 ± 19.37
FEMALE	5	0	6	66.15 ± 26.08	110.015 ± 69.230	56.06 ± 63.11 (n=5)a
	6	80	6	70.65 ± 43.67	113.010 ± 85.262	46.40 ± 72.03
	7	250	6	59.05 ± 44.09	111.120 ± 30.123	20.37 ± 9.09
	8	800	6	85.50 ± 45.27 (n=5)a	116.600 ± 65.600	29.08 ± 23.36

a : One sample omitted from the analysis since value was under the measuring limit.
** : Significantly different from control group at <0.01.

TABLE 8
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
HEMATOLOGY DATA (MEAN ± S.D.)
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	NO. OF EXAMINED	RBC ($x10^4/\mu L$)	HGB (g/dL)	HCT (%)	MCV (fL)
MALE	1	0	10	832.6 ± 32.2	15.00 ± 0.47	40.45 ± 1.17	48.62 ± 1.30
	2	80	10	828.4 ± 36.4	14.95 ± 0.39	40.53 ± 1.16	48.98 ± 1.64
	3	250	9	824.4 ± 51.3	14.67 ± 0.84	39.91 ± 2.16	48.46 ± 2.12
	4	800	10	843.0 ± 38.8	15.29 ± 0.61	41.82 ± 2.12	49.65 ± 2.72
FEMALE	5	0	10	744.1 ± 31.3	14.07 ± 0.37	38.17 ± 0.68	51.36 ± 1.90
	6	80	10	741.5 ± 30.0	14.16 ± 0.37	38.27 ± 1.01	51.66 ± 1.56
	7	250	10	744.5 ± 29.1	14.36 ± 0.49	38.84 ± 1.12	52.20 ± 1.66
	8	800	8	760.5 ± 35.8	14.43 ± 0.50	39.05 ± 1.05	51.41 ± 1.65

TABLE 8
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
HEMATOLOGY DATA (MEAN ± S.D.)
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	NO. OF EXAMINED	MCH (pg)	MCHC (g/dL)	PLT ($x10^4/\mu L$)	RETICULOCYTE ($x10^4/\mu L$)
MALE	1	0	10	18.01 ± 0.33	37.09 ± 0.52	109.88 ± 11.39	23.066 ± 2.925
	2	80	10	18.05 ± 0.49	36.90 ± 0.56	107.30 ± 10.55	25.358 ± 2.807
	3	250	9	17.79 ± 0.56	36.73 ± 0.59	107.02 ± 14.48	24.220 ± 2.925
	4	800	10	18.15 ± 0.74	36.60 ± 0.71	107.06 ± 7.05	24.937 ± 3.128
FEMALE	5	0	10	18.92 ± 0.68	36.86 ± 0.68	104.86 ± 18.30	20.424 ± 2.433
	6	80	10	19.12 ± 0.58	37.01 ± 0.21	109.87 ± 8.84	20.871 ± 4.495
	7	250	10	19.30 ± 0.59	36.97 ± 0.49	104.93 ± 8.66	18.473 ± 4.758
	8	800	8	18.98 ± 0.53	36.94 ± 0.46	112.09 ± 12.12	18.871 ± 4.065

TABLE 8
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
HEMATOLOGY DATA (MEAN ± S.D.)
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	NO. OF EXAMINED	WBC ($x10^2/\mu L$)	DIFFERENTIAL LEUCOCYTE COUNT($x10^2/\mu L$)		
					LYMPH	NEUT	MONO
MALE	1	0	10	70.58 ± 19.64	53.42 ± 14.94	14.28 ± 5.09	2.29 ± 0.96
	2	80	10	83.81 ± 24.53	65.98 ± 20.24	14.74 ± 4.66	2.38 ± 1.15
	3	250	9	71.03 ± 19.65	54.88 ± 15.81	13.33 ± 4.48	2.14 ± 0.67
	4	800	10	81.93 ± 27.66	60.79 ± 20.78	17.82 ± 8.70	2.54 ± 1.02
FEMALE	5	0	10	31.00 ± 7.21	24.32 ± 5.91	5.59 ± 2.63	0.68 ± 0.29
	6	80	10	44.43 ± 17.42	35.12 ± 15.54	7.50 ± 2.58	1.18 ± 0.39 *
	7	250	10	35.44 ± 11.20	28.45 ± 8.97	5.88 ± 3.02	0.74 ± 0.46
	8	800	8	36.43 ± 14.92	29.85 ± 14.19	5.09 ± 1.44	0.90 ± 0.55

* : Significantly different from control group at $P<0.05$.

TABLE 8

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

HEMATOLOGY DATA (MEAN ± S.D.)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	NO. OF EXAMINED	DIFFERENTIAL LEUCOCYTE COUNT($x10^2/\mu L$) EO	DIFFERENTIAL LEUCOCYTE COUNT($x10^2/\mu L$) BASO	PT (sec)	APTT (sec)
MALE	1	0	10	0.59 ± 0.43	0.00 ± 0.00	12.05 ± 1.54	15.64 ± 2.29
	2	80	10	0.71 ± 0.28	0.00 ± 0.00	11.60 ± 0.83	16.21 ± 1.95
	3	250	9	0.68 ± 0.29	0.00 ± 0.00	11.91 ± 0.87	15.52 ± 2.34
	4	800	10	0.78 ± 0.35	0.00 ± 0.00	12.42 ± 0.81	16.26 ± 2.17
FEMALE	5	0	10	0.41 ± 0.10	0.00 ± 0.00	9.42 ± 0.12	11.99 ± 1.18
	6	80	10	0.63 ± 0.23 *	0.00 ± 0.00	9.54 ± 0.38	12.64 ± 1.69
	7	250	10	0.37 ± 0.15	0.00 ± 0.00	9.51 ± 0.25	11.85 ± 1.35
	8	800	8	0.59 ± 0.39	0.00 ± 0.00	9.69 ± 0.22 *	12.99 ± 1.58

* : Significantly different from control group at $P<0.05$.

TABLE 9
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
CLINICAL CHEMISTRY DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	NO. OF EXAMINED	AST (U/L)	ALT (U/L)	ALP (U/L)	γ-GTP (U/L)	T-BIL (mg/dL)
MALE	1	0	10	129.6 ± 95.2	48.1 ± 43.9	452.8 ± 91.7	0.37 ± 0.13	0.053 ± 0.012
	2	80	10	89.0 ± 15.8	32.3 ± 4.1	504.1 ± 171.2	0.36 ± 0.10	0.045 ± 0.008
	3	250	9	109.4 ± 27.6	42.3 ± 12.3	481.7 ± 145.3	0.42 ± 0.12	0.051 ± 0.009
	4	800	10	89.8 ± 22.6	35.1 ± 7.1	431.8 ± 121.3	0.36 ± 0.12	0.056 ± 0.008
FEMALE	5	0	10	91.2 ± 15.0	32.7 ± 4.6	190.7 ± 40.5	0.43 ± 0.08	0.059 ± 0.007
	6	80	10	93.6 ± 13.5	29.2 ± 5.8	197.4 ± 72.4	0.41 ± 0.11	0.052 ± 0.014
	7	250	10	86.7 ± 15.2	24.8 ± 4.4 **	223.8 ± 94.3	0.49 ± 0.12	0.057 ± 0.009
	8	800	8	80.4 ± 10.3	26.1 ± 7.5 *	207.1 ± 46.8	0.36 ± 0.09	0.054 ± 0.012

*, ** : Significantly different from control group at $P<0.05$, 0.01, respectively.

TABLE 9
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
CLINICAL CHEMISTRY DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	NO. OF EXAMINED	BUN (mg/dL)	CRE (mg/dL)	GLU (mg/dL)	T-CHO (mg/dL)	PL (mg/dL)
MALE	1	0	10	9.47 ± 2.83	0.424 ± 0.070	126.5 ± 13.6	51.5 ± 9.5	96.0 ± 15.4
	2	80	10	9.46 ± 1.39	0.388 ± 0.045	130.0 ± 16.3	54.9 ± 7.9	99.8 ± 10.0
	3	250	9	8.49 ± 0.96	0.410 ± 0.015	125.4 ± 9.2	51.6 ± 6.4	94.1 ± 9.4
	4	800	10	8.20 ± 1.45	0.383 ± 0.034	129.7 ± 12.0	50.3 ± 6.1	92.9 ± 7.6
FEMALE	5	0	10	9.56 ± 2.06	0.439 ± 0.049	128.3 ± 18.9	60.1 ± 4.4	120.1 ± 9.6
	6	80	10	10.94 ± 1.19	0.452 ± 0.051	131.3 ± 12.9	63.5 ± 9.8	129.0 ± 21.7
	7	250	10	9.82 ± 1.37	0.459 ± 0.058	124.4 ± 12.2	55.0 ± 5.2	112.5 ± 7.8
	8	800	8	12.34 ± 2.11 **	0.421 ± 0.039	125.0 ± 11.0	58.3 ± 11.8	119.3 ± 16.5

** : Significantly different from control group at $P<0.01$.

TABLE 9
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
CLINICAL CHEMISTRY DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	NO. OF EXAMINED	TG (mg/dL)	TP (g/dL)	ALB (g/dL)	A/G	IP (mg/dL)
MALE	1	0	10	62.3 ± 23.2	5.78 ± 0.20	2.80 ± 0.05	0.944 ± 0.059	5.81 ± 0.65
	2	80	10	71.7 ± 26.9	5.81 ± 0.17	2.76 ± 0.11	0.909 ± 0.093	6.04 ± 0.63
	3	250	9	61.1 ± 15.4	5.57 ± 0.17 *	2.73 ± 0.09	0.969 ± 0.068	6.06 ± 0.36
	4	800	10	74.6 ± 23.8	5.55 ± 0.14 *	2.77 ± 0.13	1.003 ± 0.102	6.20 ± 0.45
FEMALE	5	0	10	43.8 ± 21.4	6.23 ± 0.41	3.27 ± 0.17	1.109 ± 0.079	4.73 ± 0.93
	6	80	10	40.0 ± 14.7	6.38 ± 0.32	3.36 ± 0.24	1.113 ± 0.079	4.88 ± 0.72
	7	250	10	29.2 ± 15.4	6.38 ± 0.13	3.37 ± 0.07	1.121 ± 0.056	4.88 ± 0.78
	8	800	8	27.1 ± 10.7	6.15 ± 0.34	3.28 ± 0.23	1.144 ± 0.095	5.14 ± 0.54

* : Significantly different from control group at $P<0.05$.

TABLE 9
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
CLINICAL CHEMISTRY DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	NO. OF EXAMINED	CA (mg/dL)	MG (mg/dL)	NA (mEq/L)	K (mEq/L)	CL (mEq/L)
MALE	1	0	10	9.82 ± 0.24	2.11 ± 0.17	147.56 ± 1.14	4.698 ± 0.238	111.38 ± 4.07
	2	80	10	9.90 ± 0.30	2.13 ± 0.14	147.44 ± 1.03	4.814 ± 0.125	111.05 ± 3.25
	3	250	9	9.68 ± 0.27	2.12 ± 0.13	147.71 ± 1.12	4.781 ± 0.161	111.21 ± 2.87
	4	800	10	9.83 ± 0.25	2.12 ± 0.15	147.31 ± 1.18	4.744 ± 0.274	111.69 ± 3.31
FEMALE	5	0	10	10.20 ± 0.29	2.19 ± 0.10	144.87 ± 1.32	4.100 ± 0.162	110.73 ± 5.71
	6	80	10	10.14 ± 0.24	2.24 ± 0.13	144.24 ± 1.36	4.221 ± 0.284	109.89 ± 5.23
	7	250	10	10.18 ± 0.19	2.27 ± 0.15	144.86 ± 1.09	4.066 ± 0.186	110.51 ± 5.10
	8	800	8	10.08 ± 0.28	2.34 ± 0.11 *	145.16 ± 0.97	4.191 ± 0.249	111.59 ± 5.17

* : Significantly different from control group at $P<0.05$.

TABLE 10
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
GROSS PATHOLOGY DATA
STUDY NO. [redacted]

ORGAN AND FINDINGS	SEX / GROUP NO. / LEVEL (mg/kg/day)	MALE 1	MALE 2	MALE 3	MALE 4	FEMALE 5	FEMALE 6	FEMALE 7	FEMALE 8	
		0	80	250	800	0	80	250	800	
	No. of animals examined	10	10	9b	10	10	10	10	10	[2]a
	Not remarkable	9	10	8	9	7	10	7	7	
Spleen										
	Small	0	0	0	0	0	0	0	1	[1]a
	Cyst/Single	1	0	0	0	0	0	0	0	
Thymus										
	Discolored/Red	0	0	0	0	0	0	1	0	
Pituitary										
	Discolored spot/Single	0	0	0	0	0	0	1	0	
Stomach										
	Dilatation	0	0	0	0	0	0	0	1	[1]a
Stomach~Cecum										
	Contained gas	0	0	0	0	0	0	0	1	[1]a
Liver										
	Small	0	0	0	1	0	0	0	0	
	Diaphragmatic nodule	0	0	0	0	0	0	1	0	
	Discolored area/Single	0	0	0	1	1	0	0	0	
Testis										
	Small/Bilateral	0	0	0	1	-	-	-	-	
Epididymis										
	Small/Bilateral	0	0	0	1	-	-	-	-	
Ovary										
	Cyst/Unilateral	-	-	-	-	2	0	0	0	
Uterus										
	Dilatation/Horn/Bilateral	-	-	-	-	0	0	0	1	
Abdominal fat										
	Nodule/Single	0	0	1	0	0	0	0	0	

a : Brackets are number of dead animal.
b : Data of one animal (Animal No. 1437023) was excluded from this table.

TABLE 11
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
ORGAN WEIGHT DATA (G, MEAN ± S.D.)
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	NO. OF EXAMINED	Body[a] weight	Brain	Pituitary	Thyroids	Lungs
MALE	1	0	10	571.5 ± 44.9	2.2315 ± 0.1447	0.0120 ± 0.0015	0.0218 ± 0.0040	1.4775 ± 0.1352
	2	80	10	584.2 ± 90.4	2.1968 ± 0.1082	0.0121 ± 0.0014	0.0228 ± 0.0034	1.5081 ± 0.1653
	3	250	9	603.1 ± 67.4	2.1771 ± 0.0836	0.0123 ± 0.0018	0.0226 ± 0.0049	1.4514 ± 0.1405
	4	800	10	592.9 ± 45.8	2.1775 ± 0.0762	0.0122 ± 0.0010	0.0232 ± 0.0044	1.4151 ± 0.0903
FEMALE	5	0	10	326.1 ± 34.8	2.0250 ± 0.0704	0.0155 ± 0.0016	0.0186 ± 0.0047	1.1050 ± 0.0677
	6	80	10	316.6 ± 38.1	2.0176 ± 0.0735	0.0164 ± 0.0033	0.0179 ± 0.0055	1.0618 ± 0.0830
	7	250	10	301.3 ± 23.8	2.0513 ± 0.0743	0.0166 ± 0.0022	0.0185 ± 0.0031	1.0819 ± 0.0810
	8	800	8	295.5 ± 29.3	1.9780 ± 0.0797	0.0163 ± 0.0023	0.0168 ± 0.0024	1.0664 ± 0.0677

a : The value presented were obtained after the animals were fasted overnight.

TABLE 11
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
ORGAN WEIGHT DATA (G, MEAN ± S.D.)
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	NO. OF EXAMINED	Heart	Thymus	Liver	Kidneys
MALE	1	0	10	1.5857 ± 0.1594	0.2677 ± 0.0696	14.0292 ± 1.6220	2.9899 ± 0.2737
	2	80	10	1.6487 ± 0.2131	0.2833 ± 0.0503	15.0118 ± 3.3082	3.1939 ± 0.4237
	3	250	9	1.6091 ± 0.1702	0.2561 ± 0.0567	14.3571 ± 1.8323	3.0033 ± 0.3170
	4	800	10	1.5518 ± 0.1447	0.2542 ± 0.0710	14.2241 ± 1.7148	3.0223 ± 0.2620
FEMALE	5	0	10	1.0074 ± 0.0747	0.2562 ± 0.0473	8.0462 ± 0.9950	1.7637 ± 0.1750
	6	80	10	0.9637 ± 0.1145	0.2305 ± 0.0281	7.8125 ± 1.1673	1.7853 ± 0.2379
	7	250	10	0.9144 ± 0.0537	0.2357 ± 0.0476	7.3592 ± 0.6569	1.7087 ± 0.1693
	8	800	8	0.9340 ± 0.1027	0.2743 ± 0.0661	7.1743 ± 0.8938	1.7904 ± 0.1832

TABLE 11
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
ORGAN WEIGHT DATA (G, MEAN ± S.D.)
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	NO. OF EXAMINED	Spleen	Adrenals	Salivary glands	Testes
MALE	1	0	10	0.6541 ± 0.1138	0.0510 ± 0.0069	0.6990 ± 0.1234	3.5013 ± 0.2072
	2	80	10	0.6792 ± 0.1345	0.0533 ± 0.0102	0.7613 ± 0.1211	3.4529 ± 0.3495
	3	250	9	0.6276 ± 0.0966	0.0527 ± 0.0073	0.7073 ± 0.0766	3.4384 ± 0.2228
	4	800	10	0.6612 ± 0.1124	0.0529 ± 0.0109	0.6647 ± 0.0881	3.1294 ± 0.9311
FEMALE	5	0	10	0.5016 ± 0.1017	0.0610 ± 0.0095	0.4592 ± 0.0535	-
	6	80	10	0.4875 ± 0.1016	0.0607 ± 0.0106	0.4404 ± 0.0491	-
	7	250	10	0.4624 ± 0.0631	0.0589 ± 0.0109	0.4196 ± 0.0377	-
	8	800	8	0.4555 ± 0.0702	0.0595 ± 0.0101	0.4380 ± 0.0541	-

TABLE 11
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
ORGAN WEIGHT DATA (G, MEAN ± S.D.)
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	NO. OF EXAMINED	Seminal vesicles	Prostate	Ovaries	Uterus
MALE	1	0	10	1.2889 ± 0.1315	1.6613 ± 0.3073	-	-
	2	80	10	1.2986 ± 0.1781	1.7692 ± 0.2965	-	-
	3	250	9	1.2548 ± 0.1447	1.7747 ± 0.2681	-	-
	4	800	10	1.2058 ± 0.2239	1.7576 ± 0.3042	-	-
FEMALE	5	0	10	-	-	0.1229 ± 0.0272	0.6572 ± 0.1912
	6	80	10	-	-	0.0970 ± 0.0246	0.6190 ± 0.1822
	7	250	10	-	-	0.1113 ± 0.0093	0.5640 ± 0.1970
	8	800	8	-	-	0.1084 ± 0.0152	0.6013 ± 0.1556

TABLE 12
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
ORGAN TO BODY WEIGHT RATIO DATA (G/100G BW, MEAN ± S.D.)
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	NO. OF EXAMINED	Brain	Pituitary	Thyroids	Lungs
MALE	1	0	10	0.3925 ± 0.0381	0.0020 ± 0.0000	0.0038 ± 0.0008	0.2587 ± 0.0162
	2	80	10	0.3840 ± 0.0609	0.0020 ± 0.0000	0.0039 ± 0.0009	0.2607 ± 0.0230
	3	250	9	0.3642 ± 0.0343	0.0020 ± 0.0000	0.0037 ± 0.0007	0.2428 ± 0.0296
	4	800	10	0.3695 ± 0.0338	0.0021 ± 0.0003	0.0038 ± 0.0008	0.2395 ± 0.0164
FEMALE	5	0	10	0.6285 ± 0.0803	0.0048 ± 0.0004	0.0057 ± 0.0014	0.3417 ± 0.0362
	6	80	10	0.6447 ± 0.0713	0.0052 ± 0.0008	0.0058 ± 0.0015	0.3378 ± 0.0263
	7	250	10	0.6847 ± 0.0591	0.0056 ± 0.0007 *	0.0062 ± 0.0011	0.3595 ± 0.0158
	8	800	8	0.6743 ± 0.0602	0.0055 ± 0.0008	0.0056 ± 0.0007	0.3624 ± 0.0223

* : Significantly different from control group at $P<0.05$.

TABLE 12
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
ORGAN TO BODY WEIGHT RATIO DATA (G/100G BW, MEAN ± S.D.)
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	NO. OF EXAMINED	Heart	Thymus	Liver	Kidneys
MALE	1	0	10	0.2775 ± 0.0191	0.0471 ± 0.0121	2.4497 ± 0.1222	0.5256 ± 0.0561
	2	80	10	0.2849 ± 0.0328	0.0487 ± 0.0060	2.5464 ± 0.1895	0.5502 ± 0.0480
	3	250	9	0.2674 ± 0.0162	0.0431 ± 0.0124	2.3779 ± 0.0931	0.4991 ± 0.0301
	4	800	10	0.2626 ± 0.0259	0.0429 ± 0.0112	2.3993 ± 0.2200	0.5105 ± 0.0359
FEMALE	5	0	10	0.3105 ± 0.0255	0.0792 ± 0.0167	2.4674 ± 0.1534	0.5417 ± 0.0215
	6	80	10	0.3050 ± 0.0202	0.0739 ± 0.0137	2.4670 ± 0.2098	0.5662 ± 0.0598
	7	250	10	0.3043 ± 0.0176	0.0787 ± 0.0176	2.4427 ± 0.1087	0.5670 ± 0.0338
	8	800	8	0.3165 ± 0.0227	0.0935 ± 0.0230	2.4259 ± 0.1692	0.6078 ± 0.0528 *

* : Significantly different from control group at P<0.05.

TABLE 12
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
ORGAN TO BODY WEIGHT RATIO DATA (G/100G BW, MEAN ± S.D.)
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	NO. OF EXAMINED	Spleen	Adrenals	Salivary glands	Testes
MALE	1	0	10	0.1141 ± 0.0137	0.0089 ± 0.0011	0.1229 ± 0.0225	0.6152 ± 0.0483
	2	80	10	0.1157 ± 0.0105	0.0094 ± 0.0022	0.1316 ± 0.0195	0.6051 ± 0.1149
	3	250	9	0.1041 ± 0.0101	0.0089 ± 0.0016	0.1182 ± 0.0141	0.5749 ± 0.0571
	4	800	10	0.1115 ± 0.0157	0.0090 ± 0.0021	0.1125 ± 0.0145	0.5321 ± 0.1684
FEMALE	5	0	10	0.1544 ± 0.0305	0.0188 ± 0.0031	0.1414 ± 0.0160	-
	6	80	10	0.1536 ± 0.0221	0.0194 ± 0.0028	0.1397 ± 0.0127	-
	7	250	10	0.1535 ± 0.0181	0.0195 ± 0.0037	0.1398 ± 0.0144	-
	8	800	8	0.1548 ± 0.0219	0.0204 ± 0.0033	0.1486 ± 0.0137	-

TABLE 12
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
ORGAN TO BODY WEIGHT RATIO DATA (G/100G BW, MEAN ± S.D.)
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	NO. OF EXAMINED	Seminal vesicles	Prostate	Ovaries	Uterus
MALE	1	0	10	0.2273 ± 0.0334	0.2941 ± 0.0707	-	-
	2	80	10	0.2250 ± 0.0310	0.3086 ± 0.0622	-	-
	3	250	9	0.2098 ± 0.0293	0.2979 ± 0.0565	-	-
	4	800	10	0.2049 ± 0.0416	0.2985 ± 0.0572	-	-
FEMALE	5	0	10	-	-	0.0377 ± 0.0062	0.2016 ± 0.0573
	6	80	10	-	-	0.0307 ± 0.0073	0.1974 ± 0.0618
	7	250	10	-	-	0.0369 ± 0.0019	0.1855 ± 0.0572
	8	800	8	-	-	0.0370 ± 0.0060	0.2035 ± 0.0516

TABLE 13
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
SUMMARY OF HISTOPATHOLOGICAL FINDINGS - ALL ANIMALS
STUDY NO. [redacted]

ORGAN AND FINDINGS	SEX / GROUP NO. / LEVEL(mg/kg/day)	MALE 1	2	3	4	
	No. of animals/group	10	10	9b	10	
Heart						
	Normal	5			8	
	Cardiomyopathy/(1)a	0			1	
	Cardiomyopathy/(2)a	5			1	
Aorta						
	Normal	10			10	
Mandibular lymph node						
	Normal	10			10	
Mesenteric lymph node						
	Normal	10			10	
Spleen						
	Normal	9			10	
	Cyst, capsular/(2)a	1			0	
Bone marrow						
	Normal	10			10	
Thymus						
	Normal	10			10	
Pituitary						
	Normal	8			7	
	Persistence of Rathke's pouch	2			3	
Thyroid						
	Normal	10			10	
Parathyroid						
	Normal	9			10	
	Not examined	1			0	
Adrenal						
	Normal	10			10	
Nasal cavity						
	Normal	10			10	
Trachea						
	Normal	10			10	
Lung/bronchial						
	Normal	10			10	
Tongue						
	Normal	10			10	
Salivary gland						
	Normal	10			10	
Esophagus						
	Normal	10			10	
Stomach						
	Normal	10	10	8	0	
	Cyst, forestomach/(2)a	0	0	1	0	
	Hyperplasia, limiting ridge/(2)a	0	0	1	10	**

a : Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe
b : Data of one animal (Animal No. 1437023) was excluded from this table.
** : Significantly different from control group at $P<0.01$.

TABLE 13
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
SUMMARY OF HISTOPATHOLOGICAL FINDINGS - ALL ANIMALS
STUDY NO [redacted]

ORGAN AND FINDINGS	SEX / GROUP NO. / LEVEL(mg/kg/day)	MALE 1	2	3	4
		0	80	250	800
	No. of animals/group	10	10	9b	10
Duodenum					
	Normal	10			10
Jejunum					
	Normal	10			10
Ileum					
	Normal	10			10
Cecum					
	Normal	10			10
Colon					
	Normal	10			10
Rectum					
	Normal	10			10
Pancreas					
	Normal	9			10
	Cellular infiltration, lymphocyte/(1)a	1			0
Liver					
	Normal	8			7
	Infarction/(3)a	0			1
	Infiltration, mononuclear/(1)a	1			0
	Necrosis, multifocal/(2)a	1			0
	Tension lipidosis/(2)a	0			2
Kidney					
	Normal	10			10
Urinary bladder					
	Normal	10			10
Testis					
	Normal	10			9
	Atrophy, tubular/(4)a	0			1
Prostate					
	Normal	3			6
	Infiltrate, inflammatory cell, lymphocytic/(1)a	0			1
	Infiltrate, inflammatory cell, lymphocytic/(2)a	4			3
	Infiltrate, inflammatory cell, lymphocytic/(3)a	2			0
	Inflammation/(2)a	1			0
Epididymis					
	Normal	10			9
	Atrophy, ductal/(3)a	0			1
	Reduced sperm, luminal/(4)a	0			1
Seminal vesicle					
	Normal	10			10
Mammary gland					
	Normal	10			10
Femur					
	Normal	10			10
Sternum					
	Normal	10			10

a : Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe
b : Data of one animal (Animal No. 1437023) was excluded from this table.

TABLE 13
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
SUMMARY OF HISTOPATHOLOGICAL FINDINGS - ALL ANIMALS
STUDY N[redacted]

ORGAN AND FINDINGS	SEX / GROUP NO. / LEVEL(mg/kg/day)	MALE 1	2	3	4
		0	80	250	800
	No. of animals/group	10	10	9b	10
Musculature					
Normal		10			10
Skin/subcutis					
Normal		10			10
Zymbal's gland					
Normal		10			10
Eye					
Normal		10			10
Harderian gland					
Normal		10			10
Brain					
Normal		10			10
Spinal cord					
Normal		10			10
Sciatic nerve					
Normal		10			10
Abdominal fat				[1]c	
Necrosis/(2)a				1	

a : Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe
b : Data of one animal (Animal No. 1437023) was excluded from this table.
c : Numbers in square bracket are for animals examined microscopically.

TABLE 13
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
SUMMARY OF HISTOPATHOLOGICAL FINDINGS - ALL ANIMALS
STUDY NO. [redacted]

ORGAN AND FINDINGS	SEX / GROUP NO. / LEVEL(mg/kg/day)	FEMALE 5	6	7	8	
		0	80	250	800	
	No. of animals/group	10	10	10	10	
Heart						
	Normal	10			10	
Aorta						
	Normal	10			10	
Mandibular lymph node						
	Normal	10			10	
Mesenteric lymph node						
	Normal	10			10	
Spleen						
	Normal	10			9	
	Atrophy/(5)a	0			1	
	Pigmentation/(3)a	0			1	
Bone marrow						
	Normal	10			10	
Thymus				[1]b		
	Normal	10		0	10	
	Hemorrhage/(1)a	0		1	0	
Pituitary				[1]b		
	Normal	9		0	9	
	Cyst	0		1	0	
	Persistence of Rathke's pouch	1		0	1	
Thyroid						
	Normal	6			10	
	Ultimobranchial rest	4			0	*
Parathyroid						
	Normal	10			10	
Adrenal						
	Normal	10			10	
Nasal cavity						
	Normal	10			9	
	Inflammation/(2)a	0			1	
Trachea						
	Normal	10			10	
Lung/bronchial						
	Normal	10			10	
Tongue						
	Normal	10			10	
Salivary gland						
	Normal	10			10	
Esophagus						
	Normal	10			10	

a : Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe
b : Numbers in square bracket are for animals examined microscopically.
* : Significantly different from control group at $P<0.05$.

TABLE 13
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
SUMMARY OF HISTOPATHOLOGICAL FINDINGS - ALL ANIMALS
STUDY NO. [redacted]

ORGAN AND FINDINGS	SEX / GROUP NO. / LEVEL(mg/kg/day)	FEMALE 5	6	7	8	
		0	80	250	800	
	No. of animals/group	10	10	10	10	
Stomach						
	Normal	10	10	10	0	
	Erosion, forestomach/(3)a	0	0	0	1	
	Hyperplasia, forestomach/(3)a	0	0	0	1	
	Hyperplasia, limiting ridge/(2)a	0	0	0	10	**
Duodenum						
	Normal	10			10	
Jejunum						
	Normal	10			10	
Ileum						
	Normal	10			10	
Cecum						
	Normal	10			10	
Colon						
	Normal	10			10	
Rectum						
	Normal	10			10	
Pancreas						
	Normal	10			10	
Liver				[1]b		
	Normal	2		0	7	
	Hepatodiaphragmatic nodule	0		1	0	
	Fatty change/(1)a	2		0	1	
	Fatty change/(2)a	2		0	2	
	Fatty change/(3)a	2		0	0	
	Infiltration, mononuclear/(1)a	3		0	0	
	Infiltration, mononuclear/(2)a	3		0	2	
	Tension lipidosis/(2)a	2		0	0	
Kidney						
	Normal	10			10	
Urinary bladder						
	Normal	10			10	
Mammary gland						
	Normal	10			10	
Ovary						
	Normal	8			10	
	Cyst, bursal/(2)a	2			0	
Oviduct						
	Normal	10			10	
Uterus						
	Normal	7			7	
	Dilatation, lumen/(2)a	2			2	
	Dilatation, lumen/(3)a	1			1	
Vagina						
	Normal	10			10	

a : Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe
b : Numbers in square bracket are for animals examined microscopically.
** : Significantly different from control group at P<0.01.

TABLE 13
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
SUMMARY OF HISTOPATHOLOGICAL FINDINGS - ALL ANIMALS
STUDY NO. [redacted]

ORGAN AND FINDINGS	SEX / GROUP NO. / LEVEL(mg/kg/day)	FEMALE 5	6	7	8
		0	80	250	800
	No. of animals/group	10	10	10	10
Femur					
	Normal	10			10
Sternum					
	Normal	10			10
Musculature					
	Normal	10			10
Skin/subcutis					
	Normal	10			10
Zymbal's gland					
	Normal	10			10
Eye					
	Normal	10			10
Harderian gland					
	Normal	9			10
	Cellular infiltration, lymphocyte/(1)a	1			0
Brain					
	Normal	10			10
Spinal cord					
	Normal	10			10
Sciatic nerve					
	Normal	10			10

a : Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

TABLE 14
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
RESULTS FOR STABILITY
STUDY NO. [redacted]

INTENDED CONCENTRATION (mg/mL)	STORAGE PERIOD (DATE OF ANALYSIS)	FOUND CONCENTRATION (mg/mL)	STABILITY[a] (%)
8	Immediately after preparation [redacted]	7.719	-
	5 days in a refrigerator following 24 hours at room temperature [redacted]	7.791	100.9
	10 days in a refrigerator following 24 hours at room temperature [redacted]	7.684	99.5
80	Immediately after preparation [redacted]	80.19	-
	5 days in a refrigerator following 24 hours at room temperature [redacted]	80.22	100.0
	10 days in a refrigerator following 24 hours at room temperature [redacted]	80.54	100.4

a : Stability (%) = after storage / immediately after preparation × 100

TABLE 15
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
RESULTS FOR CONTENT ANALYSES
STUDY NO. [redacted]

DATE OF ANALYSIS	INTENDED CONCENTRATION (mg/mL)	FOUND CONCENTRATION (mg/mL)	RATIO[a] (%)
December 1, 2014	0	-[b]	-
(Sample prepared firstly)	8	8.005	100.1
	25	25.59	102.4
	80	82.87	103.6
March 3, 2015	0	-[b]	-
(Sample prepared finally)	8	8.026	100.3
	25	25.67	102.7
	80	81.39	101.7

a : Ratio (%) = found concentration (mg/mL) / intended concentration (mg/mL)×100
b : Below the lower limit of quantification.

TABLE 16
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
DATA OF SYSTEM REPRODUCIBILITY
STUDY NO. [redacted]

DATE OF ANALYSIS	INJECTION TIME	PEAK AREA (μAU·sec)
November 20, 2014	1	24959
	2	25010
	3	24950
	MEAN	24973
	SD	32
	RSD (%)	0.1
November 26, 2014	1	25065
	2	24974
	3	24927
	MEAN	24989
	SD	70
	RSD (%)	0.3
December 1, 2014	1	24450
	2	24434
	3	24426
	MEAN	24437
	SD	12
	RSD (%)	0.0
March 3, 2015	1	24565
	2	24416
	3	24432
	MEAN	24471
	SD	82
	RSD (%)	0.3

SD : standard deviation
RSD : relative standard deviation

TABLE 17
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
DATA OF CALIBRATION CURVE
STUDY NO. [redacted]

DATE OF ANALYSIS	CONCENTRATION IN CALIBRATION SAMPLE (μg/mL)	BACK CALCULATED CONCENTRATION (μg/mL)	RE (%)	PEAK AREA (μAU·sec)	SLOPE	Y INTERCEPT	CORRELATION COEFFICIENT (r)
November 20, 2014	2	2.002	0.1	1046	493.424	58.6014	1.00
	10	9.991	-0.1	4989			
	25	25.02	0.1	12404			
	50	49.98	0.0	24721			
	100	100.0	0.0	49405			
	150	150.0	0.0	74071			
November 26, 2014	2	1.977	-1.2	1004	496.088	23.7333	1.00
	10	9.839	-1.6	4905			
	25	24.96	-0.2	12408			
	50	50.21	0.4	24930			
	100	100.2	0.2	49731			
	150	149.8	-0.1	74346			
December 1, 2014	2	1.958	-2.1	1002	483.286	55.3881	1.00
	10	9.975	-0.3	4876			
	25	24.99	0.0	12133			
	50	49.95	-0.1	24197			
	100	100.3	0.3	48536			
	150	149.8	-0.1	72457			
March 3, 2015	2	2.010	0.5	989	489.135	6.22027	1.00
	10	10.00	0.0	4899			
	25	24.98	-0.1	12227			
	50	50.03	0.1	24477			
	100	99.95	-0.1	48894			
	150	150.0	0.0	73391			

RE : relative error
Weighting factor : none

TABLE 18
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
DATA OF QC SAMPLE
STUDY NO. [redacted]

DATE OF ANALYSIS	CONCENTRATION IN QC SAMPLE (μg/mL)	BACK CALCULATED CONCENTRATION (μg/mL)	RE (%)
November 20, 2014	10	9.942	-0.6
		9.957	-0.4
	100	99.84	-0.2
		99.89	-0.1
November 26, 2014	10	10.09	0.9
		10.02	0.2
	100	100.4	0.4
		100.4	0.4
December 1, 2014	10	10.04	0.4
		10.02	0.2
	100	100.0	0.0
		100.0	0.0
March 3, 2015	10	9.882	-1.2
		9.853	-1.5
	100	100.0	0.0
		100.0	0.0

RE : relative error

APPENDIX A

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GENERAL CONDITION DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																							
				-7	-6	-5	-4	-3	-2	-1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
MALE	1	0	1437001	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437002	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437003	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437004	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437005	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437006	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437007	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437008	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437009	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437010	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal

APPENDIX A
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL GENERAL CONDITION DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																								
				20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45
MALE	1	0	1437001	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437002	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437003	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437004	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437005	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437006	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437007	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437008	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437009	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437010	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal

APPENDIX A

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GENERAL CONDITION DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																								
				46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71
MALE	1	0	1437001	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437002	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437003	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437004	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437005	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437006	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437007	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437008	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437009	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437010	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal

APPENDIX A

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GENERAL CONDITION DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																							
				72		73		74		75		76		77		78		79		80		81		82		83		84	
				AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
MALE	1	0	1437001	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437002	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437003	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437004	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437005	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437006	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437007	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437008	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437009	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437010	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal

AM : Animals were observed for general condition after the treatment.

APPENDIX A

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GENERAL CONDITION DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																	
				85		86		87		88		89		90		91		92		93	
				AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	
MALE	1	0	1437001	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			1437002	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			1437003	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			1437004	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			1437005	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			1437006	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			1437007	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			1437008	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			1437009	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			1437010	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	

N : Normal

AM : Animals were observed for general condition after the treatment.

APPENDIX A

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GENERAL CONDITION DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																							
				-7	-6	-5	-4	-3	-2	-1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
MALE	2	80	1437011	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437012	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437013	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437014	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437015	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437016	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437017	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437018	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437019	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437020	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal

APPENDIX A
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL GENERAL CONDITION DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																								
				20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45
MALE	2	80	1437011	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437012	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437013	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437014	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437015	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437016	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437017	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437018	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437019	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437020	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal

APPENDIX A

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GENERAL CONDITION DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																								
				46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71
MALE	2	80	1437011	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437012	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437013	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437014	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437015	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437016	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437017	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437018	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437019	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437020	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal

APPENDIX A

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GENERAL CONDITION DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																							
				72		73		74		75		76		77		78		79		80		81		82		83		84	
				AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
MALE	2	80	1437011	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437012	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437013	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437014	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437015	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437016	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437017	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437018	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437019	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437020	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal

AM : Animals were observed for general condition after the treatment.

APPENDIX A

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GENERAL CONDITION DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																	
				85		86		87		88		89		90		91		92		93	
				AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	
MALE	2	80	1437011	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			1437012	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			1437013	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			1437014	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			1437015	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			1437016	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			1437017	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			1437018	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			1437019	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			1437020	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	

N : Normal

AM : Animals were observed for general condition after the treatment.

APPENDIX A

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GENERAL CONDITION DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																							
				-7	-6	-5	-4	-3	-2	-1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
MALE	3	250	1437021	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437022	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437023	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437024	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437025	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437026	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437027	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437028	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437029	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437030	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal

APPENDIX A

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GENERAL CONDITION DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																								
				20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45
MALE	3	250	1437021	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437022	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437023	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	FD										
			1437024	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437025	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437026	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437027	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437028	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437029	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437030	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal, FD : Found dead

APPENDIX A

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GENERAL CONDITION DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																								
				46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71
MALE	3	250	1437021	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437022	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437023a																									
			1437024	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437025	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437026	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437027	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437028	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437029	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437030	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal

a : Found dead on day 35.

APPENDIX A

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GENERAL CONDITION DATA

STUDY NO [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																							
				72		73		74		75		76		77		78		79		80		81		82		83		84	
				AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
MALE	3	250	1437021	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	S	N	N	N	N	N	N	N
			1437022	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	S	N	N	N	N	N	S	N	N	N
			1437023a																								
			1437024	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437025	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437026	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437027	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437028	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437029	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437030	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal, S : Mouth/Salivation

AM : Animals were observed for general condition after the treatment.

a : Found dead on day 35.

APPENDIX A

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GENERAL CONDITION DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																			
				85		86		87		88		89		90		91		92		93	
				AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	
MALE	3	250	1437021	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			1437022	N	N	N	N	N	N	N	N	N	N	N	N	S	N	N	N	N	
			1437023a																		
			1437024	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			1437025	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			1437026	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			1437027	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			1437028	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			1437029	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			1437030	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	

N : Normal, S : Mouth/Salivation

AM : Animals were observed for general condition after the treatment.

a : Found dead on day 35.

APPENDIX A

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GENERAL CONDITION DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																							
				-7	-6	-5	-4	-3	-2	-1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
MALE	4	800	1437031	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437032	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437033	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437034	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437035	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437036	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437037	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437038	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437039	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437040	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal

APPENDIX A
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL GENERAL CONDITION DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																								
				20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45
MALE	4	800	1437031	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437032	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437033	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437034	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437035	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437036	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437037	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437038	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437039	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437040	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal

APPENDIX A

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GENERAL CONDITION DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																								
				46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71
MALE	4	800	1437031	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437032	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437033	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437034	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437035	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437036	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437037	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437038	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437039	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437040	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal

APPENDIX A

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GENERAL CONDITION DATA

STUDY NO [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																							
				72		73		74		75		76		77		78		79		80		81		82		83		84	
				AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
MALE	4	800	1437031	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437032	S	N	S	N	S	N	N	N	S	N	S	N	S	N	N	N	N	N	N	N	N	N	N	N
			1437033	S	N	S	N	S	N	N	N	N	N	N	N	S	N	S	N	S	N	N	N	N	N	N	N
			1437034	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437035	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437036	S	N	N	N	S	N	N	N	S	N	N	N	N	N	N	N	N	N	S	N	N	N	S	N	N	N
			1437037	N	N	N	N	N	N	N	N	N	N	N	N	N	N	S	N	S	N	S	N	S	N	S	N	N	N
			1437038	S	N	S	N	S	N	N	N	S	N	S	N	S	N	S	N	S	N	S	N	S	N	S	N	S	N
			1437039	S	N	S	N	N	N	S	N	S	N	N	N	N	N	S	N	S	N	N	N	N	N	S	N	N	N
			1437040	S	N	S	N	S	N	S	N	S	N	N	N	S	N	S	N	S	N	S	N	S	N	S	N	S	N

N : Normal, S : Mouth/Salivation

AM : Animals were observed for general condition after the treatment.

APPENDIX A

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GENERAL CONDITION DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																	
				85		86		87		88		89		90		91		92		93	
				AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	
MALE	4	800	1437031	N	N	N	N	N	N	N	N	S	N	N	N	N	N	N	N	N	
			1437032	S	N	N	N	N	N	N	N	S	N	N	N	N	N	S	N	N	
			1437033	S	N	S	N	S	N	N	N	N	N	N	N	N	N	S	N	N	
			1437034	S	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			1437035	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			1437036	S	N	S	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			1437037	S	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			1437038	S	N	S	N	S	N	S	N	S	N	S	N	S	N	S	N	N	
			1437039	S	N	S	N	N	N	N	N	N	N	S	N	S	N	S	N	N	
			1437040	S	N	N	N	S	N	S	N	S	N	S	N	S	N	S	N	N	

N : Normal, S : Mouth/Salivation

AM : Animals were observed for general condition after the treatment.

APPENDIX A
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL GENERAL CONDITION DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																							
				-7	-6	-5	-4	-3	-2	-1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
FEMALE	5	0	1437041	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437042	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437043	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437044	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437045	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437046	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437047	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437048	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437049	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437050	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal

APPENDIX A

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GENERAL CONDITION DATA

STUDY NO [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																								
				20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45
FEMALE	5	0	1437041	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437042	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437043	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437044	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437045	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437046	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437047	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437048	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437049	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437050	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal

APPENDIX A
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL GENERAL CONDITION DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																							
				46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70
FEMALE	5	0	1437041	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437042	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437043	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437044	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437045	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437046	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437047	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437048	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437049	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437050	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal

APPENDIX A

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GENERAL CONDITION DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																							
				71		72		73		74		75		76		77		78		79		80		81		82		83	
				AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
FEMALE	5	0	1437041	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437042	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437043	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437044	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437045	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437046	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437047	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437048	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437049	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437050	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal

AM : Animals were observed for general condition after the treatment.

APPENDIX A

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GENERAL CONDITION DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																	
				84		85		86		87		88		89		90		91		92		93
				AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM
FEMALE	5	0	1437041	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437042	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437043	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437044	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437045	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437046	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437047	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437048	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437049	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437050	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal

AM : Animals were observed for general condition after the treatment.

APPENDIX A

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GENERAL CONDITION DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																								
				-7	-6	-5	-4	-3	-2	-1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
FEMALE	6	80	1437051	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437052	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437053	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437054	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437055	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437056	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437057	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437058	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437059	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437060	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal

APPENDIX A
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL GENERAL CONDITION DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																								
				20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45
FEMALE	6	80	1437051	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437052	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437053	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437054	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437055	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437056	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437057	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437058	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437059	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437060	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal

APPENDIX A
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL GENERAL CONDITION DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																							
				46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70
FEMALE	6	80	1437051	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437052	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437053	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437054	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437055	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437056	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437057	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437058	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437059	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437060	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal

APPENDIX A

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GENERAL CONDITION DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																									
				71		72		73		74		75		76		77		78		79		80		81		82		83	
				AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
FEMALE	6	80	1437051	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437052	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437053	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437054	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437055	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437056	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437057	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437058	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437059	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437060	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal

AM : Animals were observed for general condition after the treatment.

APPENDIX A

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GENERAL CONDITION DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																	
				84		85		86		87		88		89		90		91		92		93
				AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM
FEMALE	6	80	1437051	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437052	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437053	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437054	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437055	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437056	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437057	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437058	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437059	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437060	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal

AM : Animals were observed for general condition after the treatment.

APPENDIX A

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GENERAL CONDITION DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																							
				-7	-6	-5	-4	-3	-2	-1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
FEMALE	7	250	1437061	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437062	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437063	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437064	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437065	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437066	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437067	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437068	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437069	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437070	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal

APPENDIX A
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL GENERAL CONDITION DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																								
				20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45
FEMALE	7	250	1437061	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437062	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437063	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437064	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437065	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437066	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437067	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437068	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437069	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437070	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal

APPENDIX A

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GENERAL CONDITION DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																							
				46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70
FEMALE	7	250	1437061	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437062	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437063	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437064	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437065	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437066	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437067	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437068	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437069	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437070	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal

APPENDIX A

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GENERAL CONDITION DATA

STUDY NO [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																							
				71		72		73		74		75		76		77		78		79		80		81		82		83	
				AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
FEMALE	7	250	1437061	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437062	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437063	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437064	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437065	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437066	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437067	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437068	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437069	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437070	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal

AM : Animals were observed for general condition after the treatment.

APPENDIX A

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GENERAL CONDITION DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																	
				84		85		86		87		88		89		90		91		92		93
				AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM
FEMALE	7	250	1437061	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437062	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437063	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437064	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437065	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437066	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437067	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437068	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437069	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437070	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal

AM : Animals were observed for general condition after the treatment.

APPENDIX A
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL GENERAL CONDITION DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																							
				-7	-6	-5	-4	-3	-2	-1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
FEMALE	8	800	1437071	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437072	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437073	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437074	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437075	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437076	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437077	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437078	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437079	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437080	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal

APPENDIX A
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL GENERAL CONDITION DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																								
				20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45
FEMALE	8	800	1437071	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437072	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437073	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437074	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437075	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437076	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437077	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437078	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437079	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437080	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal

APPENDIX A

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GENERAL CONDITION DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																						
				46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70
FEMALE	8	800	1437071	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	B	FD
			1437072	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437073	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437074	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437075	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437076	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437077	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437078	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437079	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437080	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal, B : Breathing/Deep respiration, FD : Found dead

APPENDIX A

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GENERAL CONDITION DATA

STUDY NO [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																									
				71		72		73		74		75		76		77		78		79		80		81		82		83	
				AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
FEMALE	8	800	1437071b																										
			1437072	S	N	N	N	S	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437073	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437074	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437075	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437076	S	N	S	N	S	N	N	N	N	N	S	N	S	N	S	N	S	N	S	N	S	N	S	N	S	N
			1437077	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437078	N	N	N	N	S	N	S	N	S	FD																
			1437079	N	N	N	N	S	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437080	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal, S : Mouth/Salivation

AM : Animals were observed for general condition after the treatment.

b : Found dead on day 70.

APPENDIX A

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GENERAL CONDITION DATA

STUDY NO [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	DAYS																	
				84		85		86		87		88		89		90		91		92		93
				AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM
FEMALE	8	800	1437071b																			
			1437072	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437073	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437074	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437075	N	N	N	N	N	N	N	N	N	N	S	N	N	N	N	N	N	N	N
			1437076	N	N	N	N	S	N	N	N	N	N	S	N	S	N	N	N	N	N	N
			1437077	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			1437078c																			
			1437079	N	N	S	N	N	N	N	N	N	N	S	N	N	N	N	N	N	N	N
			1437080	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : Normal, S : Mouth/Salivation

AM : Animals were observed for general condition after the treatment.

b : Found dead on day 70.

c : Found dead on day 75.

APPENDIX B

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL BODY WEIGHT DATA (G)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	WEEKS														
				-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13
MALE	1	0	1437001	145	202	250	292	323	351	375	390	417	425	443	453	469	478	490
			1437002	151	223	287	347	390	430	462	489	516	541	569	585	603	622	644
			1437003	150	215	266	315	352	384	414	443	462	490	506	531	544	556	572
			1437004	144	210	262	317	353	385	412	439	454	474	489	506	527	539	552
			1437005	152	225	293	352	402	443	482	517	539	557	578	592	608	626	636
			1437006	154	214	269	310	353	386	424	458	494	516	537	560	574	583	596
			1437007	147	220	279	330	366	398	426	457	476	499	513	533	542	559	568
			1437008	144	211	281	342	396	429	473	492	505	523	532	550	573	581	588
			1437009	143	213	276	347	400	442	491	516	540	566	582	598	608	632	637
			1437010	150	213	270	330	373	404	444	466	487	507	528	541	552	572	581
			N	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
			MEAN	148.0	214.6	273.3	328.2	370.8	405.2	440.3	466.7	489.0	509.8	527.7	544.9	560.0	574.8	586.4
			S.D.	3.9	6.7	12.6	19.5	26.1	30.2	36.7	38.7	38.6	41.6	43.0	43.7	43.3	46.5	46.5

APPENDIX B

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL BODY WEIGHT DATA (G)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	WEEKS														
				-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13
MALE	2	80	1437011	142	213	278	339	397	439	473	501	530	557	583	605	629	640	655
			1437012	143	205	277	353	422	460	493	502	527	557	586	601	604	616	639
			1437013	151	213	275	332	363	385	419	437	465	479	497	531	537	564	552
			1437014	150	213	274	335	374	407	440	454	471	509	517	537	555	580	589
			1437015	147	218	274	325	363	387	412	427	445	459	471	493	503	513	516
			1437016	146	201	240	262	278	292	309	327	343	362	376	383	396	409	407
			1437017	153	232	298	362	416	458	505	547	568	597	629	656	684	712	731
			1437018	152	228	302	375	432	472	503	537	557	581	613	640	656	671	698
			1437019	152	229	298	352	399	436	467	494	514	540	568	578	601	617	620
			1437020	152	231	287	349	387	428	464	481	500	527	541	546	563	570	565
			N	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
			MEAN	148.8	218.3	280.3	338.4	383.1	416.4	448.5	470.7	492.0	516.8	538.1	557.0	572.8	589.2	597.2
			S.D.	4.0	11.1	17.9	30.7	44.0	52.9	58.7	63.9	65.7	69.3	76.0	79.5	83.0	85.1	94.0

APPENDIX B
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL BODY WEIGHT DATA (G)
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	WEEKS														
				-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13
MALE	3	250	1437021	138	205	272	340	402	445	492	515	543	565	590	607	630	634	643
			1437022	144	224	288	347	401	439	483	523	544	559	577	597	623	642	659
			1437023	147	227	286	343	393	431	DEAD	-	-	-	-	-	-	-	-
			1437024	146	206	250	287	317	341	376	405	423	442	463	479	501	510	526
			1437025	151	231	290	341	388	417	453	467	498	536	536	567	581	600	616
			1437026	145	220	271	319	356	382	423	452	474	496	509	535	541	560	573
			1437027	154	226	284	339	384	421	462	500	533	573	605	630	660	675	697
			1437028	155	221	287	348	400	437	481	528	547	591	616	652	662	684	702
			1437029	155	232	291	347	393	434	478	512	529	553	584	603	624	627	623
			1437030	147	205	253	293	330	360	379	397	413	437	456	479	498	513	521
			N	10	10	10	10	10	10	9	9	9	9	9	9	9	9	9
			MEAN	148.2	219.7	277.2	330.4	376.4	410.7	447.4	477.7	500.4	528.0	548.4	572.1	591.1	605.0	617.8
			S.D.	5.5	10.6	15.2	22.9	31.0	36.5	44.6	50.3	52.6	56.7	60.3	62.5	64.0	64.6	66.6

APPENDIX B
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL BODY WEIGHT DATA (G)
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	WEEKS -1	0	1	2	3	4	5	6	7	8	9	10	11	12	13
MALE	4	800	1437031	144	213	278	335	391	435	473	507	527	558	584	610	647	665	675
			1437032	149	219	284	338	379	405	435	460	471	500	513	530	537	554	568
			1437033	152	230	294	353	401	433	467	494	512	535	561	580	598	611	626
			1437034	137	193	248	310	369	412	451	481	500	526	541	561	574	595	613
			1437035	150	218	277	328	376	411	446	477	503	529	543	565	589	615	635
			1437036	154	221	288	335	371	394	419	435	454	473	482	499	503	523	528
			1437037	151	219	286	343	386	423	457	480	496	511	530	545	559	570	577
			1437038	146	220	274	330	375	412	445	480	495	520	544	572	588	601	614
			1437039	147	217	276	335	394	437	485	519	542	560	588	613	628	646	662
			1437040	147	214	273	321	365	396	435	454	474	490	511	532	554	568	585
			N	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
			MEAN	147.7	216.4	277.8	332.8	380.7	415.8	451.3	478.7	497.4	520.2	539.7	560.7	577.7	594.8	608.3
			S.D.	4.8	9.4	12.5	11.8	11.8	15.6	19.8	24.8	26.4	27.8	32.9	35.8	42.3	42.7	44.7

APPENDIX B

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL BODY WEIGHT DATA (G)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	WEEKS														
				-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13
FEMALE	5	0	1437041	133	178	203	232	249	266	286	294	300	307	313	315	325	328	329
			1437042	134	170	205	225	251	262	281	292	302	304	319	320	321	327	336
			1437043	128	158	185	197	221	231	253	268	277	284	289	294	300	303	305
			1437044	133	168	188	203	223	235	240	252	260	266	270	280	288	296	294
			1437045	134	171	200	213	236	237	250	250	249	262	266	273	268	279	279
			1437046	132	173	204	236	258	274	287	300	309	321	324	340	341	346	346
			1437047	143	183	217	240	275	285	317	325	333	352	358	365	365	378	388
			1437048	125	165	189	208	243	251	259	278	289	294	297	300	309	314	314
			1437049	135	171	211	240	262	288	307	327	339	337	348	349	364	374	371
			1437050	133	184	222	252	280	300	322	336	347	353	358	366	371	379	375
			N	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
			MEAN	133.0	172.1	202.4	224.6	249.8	262.9	280.2	292.2	300.5	308.0	314.2	320.2	325.2	332.4	333.7
			S.D.	4.7	8.0	12.4	18.4	19.9	24.1	29.1	30.6	32.9	32.7	33.8	33.8	35.0	35.9	36.5

APPENDIX B

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL BODY WEIGHT DATA (G)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	WEEKS														
				-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13
FEMALE	6	80	1437051	128	164	182	208	212	226	238	257	269	273	274	281	289	292	294
			1437052	129	157	190	204	232	246	267	286	293	312	315	325	332	333	347
			1437053	139	176	207	230	235	259	276	286	290	301	311	317	325	331	335
			1437054	127	156	167	177	195	204	211	224	230	235	242	248	255	252	252
			1437055	130	165	195	219	247	265	275	299	303	323	339	343	349	357	363
			1437056	132	173	201	217	230	247	264	264	269	275	286	289	287	296	304
			1437057	133	168	212	241	271	288	309	325	340	350	360	381	386	393	384
			1437058	129	153	169	175	194	209	227	234	247	257	267	274	277	289	298
			1437059	134	180	206	237	259	265	288	298	305	309	318	320	324	323	330
			1437060	140	186	205	240	267	276	283	299	311	320	325	337	345	348	353
			N	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
			MEAN	132.1	167.8	193.4	214.8	234.2	248.5	263.8	277.2	285.7	295.5	303.7	311.5	316.9	321.4	326.0
			S.D.	4.5	10.9	16.0	24.1	27.6	27.9	30.0	31.8	32.5	34.8	35.9	38.9	39.5	40.4	39.1

APPENDIX B
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL BODY WEIGHT DATA (G)
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	WEEKS -1	0	1	2	3	4	5	6	7	8	9	10	11	12	13
FEMALE	7	250	1437061	135	163	184	193	211	223	238	242	249	264	271	277	273	278	287
			1437062	127	163	185	203	213	230	242	255	261	274	276	278	285	297	293
			1437063	131	172	188	202	234	247	262	263	281	292	306	299	312	314	310
			1437064	129	169	200	223	244	262	278	293	303	311	322	329	330	348	354
			1437065	133	169	184	205	223	225	245	246	264	253	265	268	271	277	272
			1437066	133	176	204	228	253	257	270	285	293	299	308	307	310	311	320
			1437067	129	168	190	211	224	240	253	260	270	275	282	286	287	289	291
			1437068	138	172	194	219	242	256	270	279	291	300	308	318	319	321	325
			1437069	128	168	196	230	252	264	277	291	302	315	319	325	332	336	339
			1437070	138	176	201	221	241	256	274	283	286	296	303	307	310	315	317
			N	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
			MEAN	132.1	169.6	192.6	213.5	233.7	246.0	260.9	269.7	280.0	287.9	296.0	299.4	302.9	308.6	310.8
			S.D.	4.0	4.6	7.5	12.5	15.2	15.5	15.2	18.8	18.3	20.5	20.6	21.4	22.4	23.5	25.3

APPENDIX B

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL BODY WEIGHT DATA (G)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	WEEKS														
				-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13
FEMALE	8	800	1437071	134	166	187	206	219	226	246	255	264	262	245	DEAD	-	-	-
			1437072	126	168	200	222	239	259	271	279	284	296	303	310	307	317	322
			1437073	133	160	179	191	213	219	231	228	238	248	249	248	259	259	264
			1437074	139	173	201	215	247	261	281	283	296	301	306	307	320	335	331
			1437075	136	167	189	216	221	227	245	258	264	263	277	277	277	278	291
			1437076	130	173	203	228	258	271	280	297	303	309	312	326	335	338	338
			1437077	128	167	194	207	218	230	239	246	254	261	265	265	266	274	278
			1437078	134	186	206	219	240	247	261	256	272	275	287	284	DEAD	-	-
			1437079	141	188	211	241	258	271	294	297	317	314	323	322	328	333	342
			1437080	136	170	193	207	229	243	247	251	268	269	273	270	287	293	294
			N	10	10	10	10	10	10	10	10	10	10	10	9	8	8	8
			MEAN	133.7	171.8	196.3	215.2	234.2	245.4	259.5	265.0	276.0	279.8	284.0	289.9	297.4	303.4	307.5
			S.D.	4.7	8.8	9.7	13.7	16.7	19.4	21.1	22.9	24.0	23.2	26.7	27.4	29.1	31.3	29.5

APPENDIX C
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL FOOD CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: -1

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	F.C. (g/animal/day)
MALE	1	0	C-001	325	241	84	2	2	21.0
			C-002	326	244	82	2	2	20.5
			C-003	311	216	95	2	2	23.8
			C-004	337	246	91	2	2	22.8
			C-005	295	208	87	2	2	21.8
								MEAN	21.98
								S.D.	1.34
	2	80	C-006	291	205	86	2	2	21.5
			C-007	317	231	86	2	2	21.5
			C-008	305	222	83	2	2	20.8
			C-009	300	207	93	2	2	23.3
			C-010	335	241	94	2	2	23.5
								MEAN	22.12
								S.D.	1.20
	3	250	C-011	319	231	88	2	2	22.0
			C-012	327	238	89	2	2	22.3
			C-013	333	240	93	2	2	23.3
			C-014	329	240	89	2	2	22.3
			C-015	316	227	89	2	2	22.3
								MEAN	22.44
								S.D.	0.50
	4	800	C-016	315	225	90	2	2	22.5
			C-017	324	242	82	2	2	20.5
			C-018	306	229	77	2	2	19.3
			C-019	328	237	91	2	2	22.8
			C-020	304	215	89	2	2	22.3
								MEAN	21.48
								S.D.	1.51

APPENDIX C
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL FOOD CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: -1

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	F.C. (g/animal/day)
FEMALE	5	0	C-021	356	288	68	2	2	17.0
			C-022	373	313	60	2	2	15.0
			C-023	379	317	62	2	2	15.5
			C-024	397	331	66	2	2	16.5
			C-025	374	307	67	2	2	16.8
								MEAN	16.16
								S.D.	0.87
	6	80	C-026	387	330	57	2	2	14.3
			C-027	389	327	62	2	2	15.5
			C-028	404	342	62	2	2	15.5
			C-029	385	325	60	2	2	15.0
			C-030	373	299	74	2	2	18.5
								MEAN	15.76
								S.D.	1.61
	7	250	C-031	399	341	58	2	2	14.5
			C-032	384	320	64	2	2	16.0
			C-033	408	338	70	2	2	17.5
			C-034	384	318	66	2	2	16.5
			C-035	397	330	67	2	2	16.8
								MEAN	16.26
								S.D.	1.12
	8	800	C-036	407	347	60	2	2	15.0
			C-037	398	333	65	2	2	16.3
			C-038	405	339	66	2	2	16.5
			C-039	410	337	73	2	2	18.3
			C-040	404	332	72	2	2	18.0
								MEAN	16.82
								S.D.	1.35

APPENDIX C
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL FOOD CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 1

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	F.C. (g/animal/day)
MALE	1	0	C-001	411	332	79	2	2	19.8
			C-002	420	347	73	2	2	18.3
			C-003	386	302	84	2	2	21.0
			C-004	355	273	82	2	2	20.5
			C-005	359	278	81	2	2	20.3
								MEAN	19.98
								S.D.	1.03
	2	80	C-006	412	330	82	2	2	20.5
			C-007	402	323	79	2	2	19.8
			C-008	402	334	68	2	2	17.0
			C-009	362	275	87	2	2	21.8
			C-010	377	288	89	2	2	22.3
								MEAN	20.28
								S.D.	2.09
	3	250	C-011	368	281	87	2	2	21.8
			C-012	374	297	77	2	2	19.3
			C-013	391	314	77	2	2	19.3
			C-014	403	322	81	2	2	20.3
			C-015	407	324	83	2	2	20.8
								MEAN	20.30
								S.D.	1.06
	4	800	C-016	400	319	81	2	2	20.3
			C-017	405	327	78	2	2	19.5
			C-018	396	320	76	2	2	19.0
			C-019	403	323	80	2	2	20.0
			C-020	393	308	85	2	2	21.3
								MEAN	20.02
								S.D.	0.87

APPENDIX C
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL FOOD CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 1

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	F.C. (g/animal/day)
FEMALE	5	0	C-021	379	324	55	2	2	13.8
			C-022	419	372	47	2	2	11.8
			C-023	392	344	48	2	2	12.0
			C-024	409	355	54	2	2	13.5
			C-025	396	337	59	2	2	14.8
								MEAN	13.18
								S.D.	1.27
	6	80	C-026	398	350	48	2	2	12.0
			C-027	394	352	42	2	2	10.5
			C-028	412	360	52	2	2	13.0
			C-029	424	377	47	2	2	11.8
			C-030	417	361	56	2	2	14.0
								MEAN	12.26
								S.D.	1.32
	7	250	C-031	425	383	42	2	2	10.5
			C-032	418	379	39	2	2	9.8
			C-033	411	367	44	2	2	11.0
			C-034	406	359	47	2	2	11.8
			C-035	384	330	54	2	2	13.5
								MEAN	11.32
								S.D.	1.42
	8	800	C-036	390	338	52	2	2	13.0
			C-037	398	351	47	2	2	11.8
			C-038	383	333	50	2	2	12.5
			C-039	406	356	50	2	2	12.5
			C-040	413	364	49	2	2	12.3
								MEAN	12.42
								S.D.	0.43

APPENDIX C
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL FOOD CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 2

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	F.C. (g/animal/day)
MALE	1	0	C-001	403	336	67	2	2	16.8
			C-002	421	356	65	2	2	16.3
			C-003	355	281	74	2	2	18.5
			C-004	400	320	80	2	2	20.0
			C-005	395	317	78	2	2	19.5
								MEAN	18.22
								S.D.	1.63
	2	80	C-006	413	332	81	2	2	20.3
			C-007	372	291	81	2	2	20.3
			C-008	416	355	61	2	2	15.3
			C-009	422	335	87	2	2	21.8
			C-010	398	317	81	2	2	20.3
								MEAN	19.60
								S.D.	2.49
	3	250	C-011	438	355	83	2	2	20.8
			C-012	394	324	70	2	2	17.5
			C-013	393	321	72	2	2	18.0
			C-014	393	312	81	2	2	20.3
			C-015	396	323	73	2	2	18.3
								MEAN	18.98
								S.D.	1.47
	4	800	C-016	386	309	77	2	2	19.3
			C-017	386	308	78	2	2	19.5
			C-018	384	319	65	2	2	16.3
			C-019	428	352	76	2	2	19.0
			C-020	416	336	80	2	2	20.0
								MEAN	18.82
								S.D.	1.45

APPENDIX C
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL FOOD CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 2

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	F.C. (g/animal/day)
FEMALE	5	0	C-021	409	359	50	2	2	12.5
			C-022	419	377	42	2	2	10.5
			C-023	419	373	46	2	2	11.5
			C-024	404	350	54	2	2	13.5
			C-025	440	380	60	2	2	15.0
								MEAN	12.60
								S.D.	1.75
	6	80	C-026	407	358	49	2	2	12.3
			C-027	441	394	47	2	2	11.8
			C-028	415	366	49	2	2	12.3
			C-029	428	383	45	2	2	11.3
			C-030	425	358	67	2	2	16.8
								MEAN	12.90
								S.D.	2.22
	7	250	C-031	411	371	40	2	2	10.0
			C-032	440	394	46	2	2	11.5
			C-033	437	389	48	2	2	12.0
			C-034	406	353	53	2	2	13.3
			C-035	414	359	55	2	2	13.8
								MEAN	12.12
								S.D.	1.51
	8	800	C-036	401	349	52	2	2	13.0
			C-037	424	381	43	2	2	10.8
			C-038	414	358	56	2	2	14.0
			C-039	420	377	43	2	2	10.8
			C-040	413	358	55	2	2	13.8
								MEAN	12.48
								S.D.	1.58

APPENDIX C
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL FOOD CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 3

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	F.C. (g/animal/day)
MALE	1	0	C-001	428	364	64	2	2	16.0
			C-002	376	316	60	2	2	15.0
			C-003	376	303	73	2	2	18.3
			C-004	406	331	75	2	2	18.8
			C-005	388	317	71	2	2	17.8
								MEAN	17.18
								S.D.	1.61
	2	80	C-006	427	341	86	2	2	21.5
			C-007	420	356	64	2	2	16.0
			C-008	416	359	57	2	2	14.3
			C-009	413	330	83	2	2	20.8
			C-010	423	349	74	2	2	18.5
								MEAN	18.22
								S.D.	3.07
	3	250	C-011	397	323	74	2	2	18.5
			C-012	394	328	66	2	2	16.5
			C-013	399	332	67	2	2	16.8
			C-014	414	343	71	2	2	17.8
			C-015	391	323	68	2	2	17.0
								MEAN	17.32
								S.D.	0.82
	4	800	C-016	417	347	70	2	2	17.5
			C-017	394	321	73	2	2	18.3
			C-018	395	336	59	2	2	14.8
			C-019	418	350	68	2	2	17.0
			C-020	426	348	78	2	2	19.5
								MEAN	17.42
								S.D.	1.74

APPENDIX C
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL FOOD CONSUMPTION DATA
STUDY NO[redacted]
WEEK: 3

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	F.C. (g/animal/day)
FEMALE	5	0	C-021	437	390	47	2	2	11.8
			C-022	461	420	41	2	2	10.3
			C-023	458	413	45	2	2	11.3
			C-024	423	367	56	2	2	14.0
			C-025	451	399	52	2	2	13.0
								MEAN	12.08
								S.D.	1.45
	6	80	C-026	470	423	47	2	2	11.8
			C-027	470	434	36	2	2	9.0
			C-028	468	426	42	2	2	10.5
			C-029	456	406	50	2	2	12.5
			C-030	460	401	59	2	2	14.8
								MEAN	11.72
								S.D.	2.18
	7	250	C-031	462	426	36	2	2	9.0
			C-032	444	393	51	2	2	12.8
			C-033	441	386	55	2	2	13.8
			C-034	493	451	42	2	2	10.5
			C-035	483	435	48	2	2	12.0
								MEAN	11.62
								S.D.	1.90
	8	800	C-036	440	396	44	2	2	11.0
			C-037	459	409	50	2	2	12.5
			C-038	485	444	41	2	2	10.3
			C-039	468	427	41	2	2	10.3
			C-040	440	385	55	2	2	13.8
								MEAN	11.58
								S.D.	1.53

APPENDIX C
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL FOOD CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 4

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	F.C. (g/animal/day)
MALE	1	0	C-001	416	351	65	2	2	16.3
			C-002	425	367	58	2	2	14.5
			C-003	404	335	69	2	2	17.3
			C-004	420	344	76	2	2	19.0
			C-005	413	346	67	2	2	16.8
								MEAN	16.78
								S.D.	1.63
	2	80	C-006	373	293	80	2	2	20.0
			C-007	420	356	64	2	2	16.0
			C-008	388	339	49	2	2	12.3
			C-009	377	302	75	2	2	18.8
			C-010	367	296	71	2	2	17.8
								MEAN	16.98
								S.D.	3.00
	3	250	C-011	402	330	72	2	2	18.0
			C-012	390	329	61	2	2	15.3
			C-013	416	354	62	2	2	15.5
			C-014	390	323	67	2	2	16.8
			C-015	400	332	68	2	2	17.0
								MEAN	16.52
								S.D.	1.12
	4	800	C-016	425	361	64	2	2	16.0
			C-017	402	339	63	2	2	15.8
			C-018	396	341	55	2	2	13.8
			C-019	391	325	66	2	2	16.5
			C-020	385	311	74	2	2	18.5
								MEAN	16.12
								S.D.	1.68

APPENDIX C
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL FOOD CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 4

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	F.C. (g/animal/day)
FEMALE	5	0	C-021	446	393	53	2	2	13.3
			C-022	424	378	46	2	2	11.5
			C-023	419	387	32	2	2	8.0
			C-024	429	384	45	2	2	11.3
			C-025	422	364	58	2	2	14.5
								MEAN	11.72
								S.D.	2.46
	6	80	C-026	421	368	53	2	2	13.3
			C-027	426	385	41	2	2	10.3
			C-028	429	381	48	2	2	12.0
			C-029	441	398	43	2	2	10.8
			C-030	443	394	49	2	2	12.3
								MEAN	11.74
								S.D.	1.20
	7	250	C-031	416	375	41	2	2	10.3
			C-032	429	380	49	2	2	12.3
			C-033	435	397	38	2	2	9.5
			C-034	462	419	43	2	2	10.8
			C-035	415	369	46	2	2	11.5
								MEAN	10.88
								S.D.	1.08
	8	800	C-036	412	363	49	2	2	12.3
			C-037	436	387	49	2	2	12.3
			C-038	406	362	44	2	2	11.0
			C-039	469	431	38	2	2	9.5
			C-040	421	373	48	2	2	12.0
								MEAN	11.42
								S.D.	1.20

APPENDIX C
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL FOOD CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 5

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	F.C. (g/animal/day)
MALE	1	0	C-001	396	333	63	2	2	15.8
			C-002	406	350	56	2	2	14.0
			C-003	377	305	72	2	2	18.0
			C-004	377	305	72	2	2	18.0
			C-005	438	365	73	2	2	18.3
								MEAN	16.82
								S.D.	1.87
	2	80	C-006	402	327	75	2	2	18.8
			C-007	386	320	66	2	2	16.5
			C-008	388	338	50	2	2	12.5
			C-009	414	344	70	2	2	17.5
			C-010	411	344	67	2	2	16.8
								MEAN	16.42
								S.D.	2.36
	3	250	C-011	372	302	70	2	2	17.5
			C-012	NEa	-	-	-	-	-
			C-013	400	334	66	2	2	16.5
			C-014	370	293	77	2	2	19.3
			C-015	371	302	69	2	2	17.3
								MEAN	17.65
								S.D.	1.18
	4	800	C-016	366	305	61	2	2	15.3
			C-017	386	322	64	2	2	16.0
			C-018	394	339	55	2	2	13.8
			C-019	414	347	67	2	2	16.8
			C-020	411	337	74	2	2	18.5
								MEAN	16.08
								S.D.	1.75

a : Data were omitted from the evaluation, since one animal died during the measuring period.

APPENDIX C
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL FOOD CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 5

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	F.C. (g/animal/day)
FEMALE	5	0	C-021	404	358	46	2	2	11.5
			C-022	431	391	40	2	2	10.0
			C-023	417	374	43	2	2	10.8
			C-024	403	355	48	2	2	12.0
			C-025	383	328	55	2	2	13.8
								MEAN	11.62
								S.D.	1.43
	6	80	C-026	388	343	45	2	2	11.3
			C-027	427	391	36	2	2	9.0
			C-028	413	368	45	2	2	11.3
			C-029	363	316	47	2	2	11.8
			C-030	383	332	51	2	2	12.8
								MEAN	11.24
								S.D.	1.39
	7	250	C-031	398	364	34	2	2	8.5
			C-032	393	357	36	2	2	9.0
			C-033	379	327	52	2	2	13.0
			C-034	408	368	40	2	2	10.0
			C-035	397	352	45	2	2	11.3
								MEAN	10.36
								S.D.	1.82
	8	800	C-036	423	375	48	2	2	12.0
			C-037	422	383	39	2	2	9.8
			C-038	416	370	46	2	2	11.5
			C-039	413	371	42	2	2	10.5
			C-040	383	334	49	2	2	12.3
								MEAN	11.22
								S.D.	1.05

APPENDIX C
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL FOOD CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 6

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	F.C. (g/animal/day)
MALE	1	0	C-001	378	325	53	2	2	13.3
			C-002	476	424	52	2	2	13.0
			C-003	458	390	68	2	2	17.0
			C-004	447	376	71	2	2	17.8
			C-005	422	364	58	2	2	14.5
								MEAN	15.12
								S.D.	2.17
	2	80	C-006	387	325	62	2	2	15.5
			C-007	419	363	56	2	2	14.0
			C-008	420	375	45	2	2	11.3
			C-009	417	348	69	2	2	17.3
			C-010	483	424	59	2	2	14.8
								MEAN	14.58
								S.D.	2.20
	3	250	C-011	433	372	61	2	2	15.3
			C-012	428	400	28	1	2	14.0
			C-013	473	408	65	2	2	16.3
			C-014	444	374	70	2	2	17.5
			C-015	394	335	59	2	2	14.8
								MEAN	15.58
								S.D.	1.36
	4	800	C-016	415	360	55	2	2	13.8
			C-017	422	367	55	2	2	13.8
			C-018	451	404	47	2	2	11.8
			C-019	459	400	59	2	2	14.8
			C-020	482	418	64	2	2	16.0
								MEAN	14.04
								S.D.	1.55

APPENDIX C
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL FOOD CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 6

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	F.C. (g/animal/day)
FEMALE	5	0	C-021	392	350	42	2	2	10.5
			C-022	408	366	42	2	2	10.5
			C-023	379	345	34	2	2	8.5
			C-024	426	378	48	2	2	12.0
			C-025	400	349	51	2	2	12.8
								MEAN	10.86
								S.D.	1.65
	6	80	C-026	395	344	51	2	2	12.8
			C-027	411	377	34	2	2	8.5
			C-028	385	345	40	2	2	10.0
			C-029	390	346	44	2	2	11.0
			C-030	383	327	56	2	2	14.0
								MEAN	11.26
								S.D.	2.19
	7	250	C-031	410	379	31	2	2	7.8
			C-032	402	362	40	2	2	10.0
			C-033	380	344	36	2	2	9.0
			C-034	389	347	42	2	2	10.5
			C-035	373	334	39	2	2	9.8
								MEAN	9.42
								S.D.	1.05
	8	800	C-036	394	351	43	2	2	10.8
			C-037	392	358	34	2	2	8.5
			C-038	420	372	48	2	2	12.0
			C-039	392	363	29	2	2	7.3
			C-040	401	363	38	2	2	9.5
								MEAN	9.62
								S.D.	1.85

APPENDIX C
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL FOOD CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 7

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	F.C. (g/animal/day)
MALE	1	0	C-001	406	353	53	2	2	13.3
			C-002	409	357	52	2	2	13.0
			C-003	394	328	66	2	2	16.5
			C-004	402	342	60	2	2	15.0
			C-005	376	315	61	2	2	15.3
								MEAN	14.62
								S.D.	1.46
	2	80	C-006	372	304	68	2	2	17.0
			C-007	422	368	54	2	2	13.5
			C-008	408	362	46	2	2	11.5
			C-009	414	351	63	2	2	15.8
			C-010	395	334	61	2	2	15.3
								MEAN	14.62
								S.D.	2.15
	3	250	C-011	411	350	61	2	2	15.3
			C-012	410	386	24	1	2	12.0
			C-013	418	355	63	2	2	15.8
			C-014	392	325	67	2	2	16.8
			C-015	395	343	52	2	2	13.0
								MEAN	14.58
								S.D.	2.01
	4	800	C-016	424	372	52	2	2	13.0
			C-017	391	332	59	2	2	14.8
			C-018	386	337	49	2	2	12.3
			C-019	423	365	58	2	2	14.5
			C-020	403	348	55	2	2	13.8
								MEAN	13.68
								S.D.	1.04

APPENDIX C
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL FOOD CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 7

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	F.C. (g/animal/day)
FEMALE	5	0	C-021	413	377	36	2	2	9.0
			C-022	398	359	39	2	2	9.8
			C-023	429	395	34	2	2	8.5
			C-024	404	358	46	2	2	11.5
			C-025	407	359	48	2	2	12.0
								MEAN	10.16
								S.D.	1.53
	6	80	C-026	413	372	41	2	2	10.3
			C-027	412	380	32	2	2	8.0
			C-028	376	336	40	2	2	10.0
			C-029	379	343	36	2	2	9.0
			C-030	409	364	45	2	2	11.3
								MEAN	9.72
								S.D.	1.26
	7	250	C-031	419	390	29	2	2	7.3
			C-032	427	382	45	2	2	11.3
			C-033	397	358	39	2	2	9.8
			C-034	400	363	37	2	2	9.3
			C-035	390	354	36	2	2	9.0
								MEAN	9.34
								S.D.	1.44
	8	800	C-036	381	340	41	2	2	10.3
			C-037	375	333	42	2	2	10.5
			C-038	413	376	37	2	2	9.3
			C-039	405	369	36	2	2	9.0
			C-040	408	360	48	2	2	12.0
								MEAN	10.22
								S.D.	1.18

APPENDIX C
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL FOOD CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 8

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	F.C. (g/animal/day)
MALE	1	0	C-001	421	371	50	2	2	12.5
			C-002	417	368	49	2	2	12.3
			C-003	389	330	59	2	2	14.8
			C-004	406	345	61	2	2	15.3
			C-005	406	344	62	2	2	15.5
								MEAN	14.08
								S.D.	1.56
	2	80	C-006	392	327	65	2	2	16.3
			C-007	391	336	55	2	2	13.8
			C-008	403	358	45	2	2	11.3
			C-009	427	368	59	2	2	14.8
			C-010	408	346	62	2	2	15.5
								MEAN	14.34
								S.D.	1.93
	3	250	C-011	412	359	53	2	2	13.3
			C-012	401	376	25	1	2	12.5
			C-013	426	367	59	2	2	14.8
			C-014	392	326	66	2	2	16.5
			C-015	393	335	58	2	2	14.5
								MEAN	14.32
								S.D.	1.53
	4	800	C-016	401	346	55	2	2	13.8
			C-017	390	331	59	2	2	14.8
			C-018	407	360	47	2	2	11.8
			C-019	433	378	55	2	2	13.8
			C-020	415	355	60	2	2	15.0
								MEAN	13.84
								S.D.	1.27

APPENDIX C
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL FOOD CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 8

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	F.C. (g/animal/day)
FEMALE	5	0	C-021	399	362	37	2	2	9.3
			C-022	398	363	35	2	2	8.8
			C-023	395	355	40	2	2	10.0
			C-024	410	370	40	2	2	10.0
			C-025	415	380	35	2	2	8.8
								MEAN	9.38
								S.D.	0.60
	6	80	C-026	400	361	39	2	2	9.8
			C-027	400	373	27	2	2	6.8
			C-028	407	366	41	2	2	10.3
			C-029	435	391	44	2	2	11.0
			C-030	401	359	42	2	2	10.5
								MEAN	9.68
								S.D.	1.67
	7	250	C-031	389	347	42	2	2	10.5
			C-032	417	375	42	2	2	10.5
			C-033	399	368	31	2	2	7.8
			C-034	407	379	28	2	2	7.0
			C-035	408	373	35	2	2	8.8
								MEAN	8.92
								S.D.	1.58
	8	800	C-036	379	338	41	2	2	10.3
			C-037	383	344	39	2	2	9.8
			C-038	418	384	34	2	2	8.5
			C-039	399	368	31	2	2	7.8
			C-040	403	367	36	2	2	9.0
								MEAN	9.08
								S.D.	1.00

APPENDIX C
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL FOOD CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 9

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	F.C. (g/animal/day)
MALE	1	0	C-001	428	373	55	2	2	13.8
			C-002	428	384	44	2	2	11.0
			C-003	385	333	52	2	2	13.0
			C-004	390	335	55	2	2	13.8
			C-005	414	360	54	2	2	13.5
								MEAN	13.02
								S.D.	1.18
	2	80	C-006	412	347	65	2	2	16.3
			C-007	438	386	52	2	2	13.0
			C-008	425	383	42	2	2	10.5
			C-009	446	383	63	2	2	15.8
			C-010	390	334	56	2	2	14.0
								MEAN	13.92
								S.D.	2.33
	3	250	C-011	434	388	46	2	2	11.5
			C-012	396	365	31	1	2	15.5
			C-013	422	368	54	2	2	13.5
			C-014	420	361	59	2	2	14.8
			C-015	419	359	60	2	2	15.0
								MEAN	14.06
								S.D.	1.61
	4	800	C-016	404	355	49	2	2	12.3
			C-017	420	365	55	2	2	13.8
			C-018	394	351	43	2	2	10.8
			C-019	408	356	52	2	2	13.0
			C-020	398	343	55	2	2	13.8
								MEAN	12.74
								S.D.	1.25

APPENDIX C
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL FOOD CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 9

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	F.C. (g/animal/day)
FEMALE	5	0	C-021	426	388	38	2	2	9.5
			C-022	408	375	33	2	2	8.3
			C-023	386	350	36	2	2	9.0
			C-024	381	342	39	2	2	9.8
			C-025	381	342	39	2	2	9.8
								MEAN	9.28
								S.D.	0.64
	6	80	C-026	380	347	33	2	2	8.3
			C-027	374	344	30	2	2	7.5
			C-028	399	361	38	2	2	9.5
			C-029	374	339	35	2	2	8.8
			C-030	395	355	40	2	2	10.0
								MEAN	8.82
								S.D.	0.98
	7	250	C-031	386	356	30	2	2	7.5
			C-032	386	346	40	2	2	10.0
			C-033	391	355	36	2	2	9.0
			C-034	399	372	27	2	2	6.8
			C-035	369	333	36	2	2	9.0
								MEAN	8.46
								S.D.	1.29
	8	800	C-036	373	345	28	2	2	7.0
			C-037	388	360	28	2	2	7.0
			C-038	411	368	43	2	2	10.8
			C-039	343	313	30	2	2	7.5
			C-040	388	351	37	2	2	9.3
								MEAN	8.32
								S.D.	1.68

APPENDIX C
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL FOOD CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 10

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	F.C. (g/animal/day)
MALE	1	0	C-001	447	398	49	2	2	12.3
			C-002	437	396	41	2	2	10.3
			C-003	410	361	49	2	2	12.3
			C-004	382	319	63	2	2	15.8
			C-005	401	353	48	2	2	12.0
								MEAN	12.54
								S.D.	2.00
	2	80	C-006	399	334	65	2	2	16.3
			C-007	391	340	51	2	2	12.8
			C-008	433	394	39	2	2	9.8
			C-009	427	374	53	2	2	13.3
			C-010	390	338	52	2	2	13.0
								MEAN	13.04
								S.D.	2.30
	3	250	C-011	418	370	48	2	2	12.0
			C-012	417	394	23	1	2	11.5
			C-013	425	373	52	2	2	13.0
			C-014	395	333	62	2	2	15.5
			C-015	387	325	62	2	2	15.5
								MEAN	13.50
								S.D.	1.90
	4	800	C-016	410	362	48	2	2	12.0
			C-017	393	336	57	2	2	14.3
			C-018	412	367	45	2	2	11.3
			C-019	418	364	54	2	2	13.5
			C-020	410	350	60	2	2	15.0
								MEAN	13.22
								S.D.	1.55

APPENDIX C
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL FOOD CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 10

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	F.C. (g/animal/day)
FEMALE	5	0	C-021	401	368	33	2	2	8.3
			C-022	414	371	43	2	2	10.8
			C-023	395	362	33	2	2	8.3
			C-024	387	347	40	2	2	10.0
			C-025	396	362	34	2	2	8.5
								MEAN	9.18
								S.D.	1.15
	6	80	C-026	384	350	34	2	2	8.5
			C-027	414	381	33	2	2	8.3
			C-028	398	363	35	2	2	8.8
			C-029	392	350	42	2	2	10.5
			C-030	360	311	49	2	2	12.3
								MEAN	9.68
								S.D.	1.70
	7	250	C-031	383	356	27	2	2	6.8
			C-032	393	363	30	2	2	7.5
			C-033	396	366	30	2	2	7.5
			C-034	397	362	35	2	2	8.8
			C-035	393	362	31	2	2	7.8
								MEAN	7.68
								S.D.	0.73
	8	800	C-036	NEa	-	-	-	-	-
			C-037	421	385	36	2	2	9.0
			C-038	384	338	46	2	2	11.5
			C-039	385	362	23	2	2	5.8
			C-040	376	343	33	2	2	8.3
								MEAN	8.65
								S.D.	2.34

a : Data were omitted from the evaluation, since one animal died during the measuring period.

APPENDIX C
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL FOOD CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 11

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	F.C. (g/animal/day)
MALE	1	0	C-001	428	382	46	2	2	11.5
			C-002	427	385	42	2	2	10.5
			C-003	407	362	45	2	2	11.3
			C-004	429	370	59	2	2	14.8
			C-005	397	353	44	2	2	11.0
								MEAN	11.82
								S.D.	1.71
	2	80	C-006	421	362	59	2	2	14.8
			C-007	416	364	52	2	2	13.0
			C-008	419	379	40	2	2	10.0
			C-009	419	366	53	2	2	13.3
			C-010	399	350	49	2	2	12.3
								MEAN	12.68
								S.D.	1.75
	3	250	C-011	404	355	49	2	2	12.3
			C-012	434	412	22	1	2	11.0
			C-013	388	336	52	2	2	13.0
			C-014	417	368	49	2	2	12.3
			C-015	395	339	56	2	2	14.0
								MEAN	12.52
								S.D.	1.10
	4	800	C-016	399	353	46	2	2	11.5
			C-017	419	366	53	2	2	13.3
			C-018	419	377	42	2	2	10.5
			C-019	443	395	48	2	2	12.0
			C-020	392	335	57	2	2	14.3
								MEAN	12.32
								S.D.	1.50

APPENDIX C
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL FOOD CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 11

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	F.C. (g/animal/day)
FEMALE	5	0	C-021	395	366	29	2	2	7.3
			C-022	413	375	38	2	2	9.5
			C-023	410	380	30	2	2	7.5
			C-024	413	373	40	2	2	10.0
			C-025	421	385	36	2	2	9.0
								MEAN	8.66
								S.D.	1.21
	6	80	C-026	412	372	40	2	2	10.0
			C-027	434	403	31	2	2	7.8
			C-028	408	372	36	2	2	9.0
			C-029	386	347	39	2	2	9.8
			C-030	389	348	41	2	2	10.3
								MEAN	9.38
								S.D.	1.01
	7	250	C-031	383	352	31	2	2	7.8
			C-032	440	400	40	2	2	10.0
			C-033	416	383	33	2	2	8.3
			C-034	421	390	31	2	2	7.8
			C-035	402	372	30	2	2	7.5
								MEAN	8.28
								S.D.	1.00
	8	800	C-036	401	384	17	1	2	8.5
			C-037	396	352	44	2	2	11.0
			C-038	398	362	36	2	2	9.0
			C-039	387	374	13	1	2	6.5
			C-040	365	326	39	2	2	9.8
								MEAN	8.96
								S.D.	1.67

APPENDIX C
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL FOOD CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 12

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	F.C. (g/animal/day)
MALE	1	0	C-001	421	378	43	2	2	10.8
			C-002	456	412	44	2	2	11.0
			C-003	421	373	48	2	2	12.0
			C-004	422	369	53	2	2	13.3
			C-005	436	384	52	2	2	13.0
								MEAN	12.02
								S.D.	1.13
	2	80	C-006	428	372	56	2	2	14.0
			C-007	434	390	44	2	2	11.0
			C-008	426	389	37	2	2	9.3
			C-009	432	375	57	2	2	14.3
			C-010	410	364	46	2	2	11.5
								MEAN	12.02
								S.D.	2.11
	3	250	C-011	412	366	46	2	2	11.5
			C-012	431	409	22	1	2	11.0
			C-013	409	362	47	2	2	11.8
			C-014	410	356	54	2	2	13.5
			C-015	398	360	38	2	2	9.5
								MEAN	11.46
								S.D.	1.44
	4	800	C-016	424	382	42	2	2	10.5
			C-017	437	390	47	2	2	11.8
			C-018	416	376	40	2	2	10.0
			C-019	415	368	47	2	2	11.8
			C-020	407	350	57	2	2	14.3
								MEAN	11.68
								S.D.	1.67

APPENDIX C
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL FOOD CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 12

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	F.C. (g/animal/day)
FEMALE	5	0	C-021	412	377	35	2	2	8.8
			C-022	405	373	32	2	2	8.0
			C-023	393	360	33	2	2	8.3
			C-024	401	361	40	2	2	10.0
			C-025	400	356	44	2	2	11.0
								MEAN	9.22
								S.D.	1.25
	6	80	C-026	387	359	28	2	2	7.0
			C-027	397	368	29	2	2	7.3
			C-028	440	401	39	2	2	9.8
			C-029	391	357	34	2	2	8.5
			C-030	395	357	38	2	2	9.5
								MEAN	8.42
								S.D.	1.26
	7	250	C-031	426	395	31	2	2	7.8
			C-032	403	360	43	2	2	10.8
			C-033	404	372	32	2	2	8.0
			C-034	393	370	23	2	2	5.8
			C-035	396	368	28	2	2	7.0
								MEAN	7.88
								S.D.	1.85
	8	800	C-036	408	386	22	1	2	11.0
			C-037	397	360	37	2	2	9.3
			C-038	431	401	30	2	2	7.5
			C-039	406	388	18	1	2	9.0
			C-040	382	350	32	2	2	8.0
								MEAN	8.96
								S.D.	1.35

APPENDIX C
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL FOOD CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 13

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	F.C. (g/animal/day)
MALE	1	0	C-001	406	369	37	2	2	9.3
			C-002	391	350	41	2	2	10.3
			C-003	326	279	47	2	2	11.8
			C-004	325	273	52	2	2	13.0
			C-005	326	281	45	2	2	11.3
								MEAN	11.14
								S.D.	1.42
	2	80	C-006	367	318	49	2	2	12.3
			C-007	365	314	51	2	2	12.8
			C-008	366	335	31	2	2	7.8
			C-009	340	284	56	2	2	14.0
			C-010	338	296	42	2	2	10.5
								MEAN	11.48
								S.D.	2.41
	3	250	C-011	364	324	40	2	2	10.0
			C-012	410	392	18	1	2	9.0
			C-013	362	319	43	2	2	10.8
			C-014	318	272	46	2	2	11.5
			C-015	319	268	51	2	2	12.8
								MEAN	10.82
								S.D.	1.45
	4	800	C-016	368	324	44	2	2	11.0
			C-017	337	285	52	2	2	13.0
			C-018	362	328	34	2	2	8.5
			C-019	365	321	44	2	2	11.0
			C-020	339	291	48	2	2	12.0
								MEAN	11.10
								S.D.	1.67

APPENDIX C
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL FOOD CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 13

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	F.C. (g/animal/day)
FEMALE	5	0	C-021	428	397	31	2	2	7.8
			C-022	389	363	26	2	2	6.5
			C-023	413	382	31	2	2	7.8
			C-024	407	371	36	2	2	9.0
			C-025	383	353	30	2	2	7.5
								MEAN	7.72
								S.D.	0.89
	6	80	C-026	376	354	22	2	2	5.5
			C-027	341	314	27	2	2	6.8
			C-028	357	329	28	2	2	7.0
			C-029	378	350	28	2	2	7.0
			C-030	371	338	33	2	2	8.3
								MEAN	6.92
								S.D.	0.99
	7	250	C-031	358	341	17	2	2	4.3
			C-032	329	305	24	2	2	6.0
			C-033	347	327	20	2	2	5.0
			C-034	316	291	25	2	2	6.3
			C-035	326	301	25	2	2	6.3
								MEAN	5.58
								S.D.	0.89
	8	800	C-036	389	373	16	1	2	8.0
			C-037	340	315	25	2	2	6.3
			C-038	356	322	34	2	2	8.5
			C-039	354	344	10	1	2	5.0
			C-040	341	309	32	2	2	8.0
								MEAN	7.16
								S.D.	1.47

APPENDIX D
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL WATER CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: -1

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	W.C. (g/animal/day)
MALE	1	0	C-001	546	427	119	2	2	29.8
			C-002	548	433	115	2	2	28.8
			C-003	556	424	132	2	2	33.0
			C-004	557	420	137	2	2	34.3
			C-005	552	432	120	2	2	30.0
								MEAN	31.18
								S.D.	2.35
	2	80	C-006	553	444	109	2	2	27.3
			C-007	568	458	110	2	2	27.5
			C-008	574	465	109	2	2	27.3
			C-009	546	415	131	2	2	32.8
			C-010	553	403	150	2	2	37.5
								MEAN	30.48
								S.D.	4.58
	3	250	C-011	553	428	125	2	2	31.3
			C-012	555	431	124	2	2	31.0
			C-013	549	413	136	2	2	34.0
			C-014	553	438	115	2	2	28.8
			C-015	551	440	111	2	2	27.8
								MEAN	30.58
								S.D.	2.41
	4	800	C-016	555	438	117	2	2	29.3
			C-017	562	447	115	2	2	28.8
			C-018	562	450	112	2	2	28.0
			C-019	559	426	133	2	2	33.3
			C-020	558	438	120	2	2	30.0
								MEAN	29.88
								S.D.	2.05

APPENDIX D
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL WATER CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: -1

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	W.C. (g/animal/day)
FEMALE	5	0	C-021	554	457	97	2	2	24.3
			C-022	560	471	89	2	2	22.3
			C-023	574	485	89	2	2	22.3
			C-024	572	454	118	2	2	29.5
			C-025	572	486	86	2	2	21.5
								MEAN	23.98
								S.D.	3.25
	6	80	C-026	560	464	96	2	2	24.0
			C-027	560	468	92	2	2	23.0
			C-028	574	492	82	2	2	20.5
			C-029	561	465	96	2	2	24.0
			C-030	570	461	109	2	2	27.3
								MEAN	23.76
								S.D.	2.44
	7	250	C-031	558	476	82	2	2	20.5
			C-032	563	468	95	2	2	23.8
			C-033	573	466	107	2	2	26.8
			C-034	576	472	104	2	2	26.0
			C-035	578	490	88	2	2	22.0
								MEAN	23.82
								S.D.	2.64
	8	800	C-036	556	456	100	2	2	25.0
			C-037	578	482	96	2	2	24.0
			C-038	569	481	88	2	2	22.0
			C-039	566	469	97	2	2	24.3
			C-040	559	457	102	2	2	25.5
								MEAN	24.16
								S.D.	1.34

APPENDIX D
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL WATER CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 1

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	W.C. (g/animal/day)
MALE	1	0	C-001	546	414	132	2	2	33.0
			C-002	562	450	112	2	2	28.0
			C-003	550	421	129	2	2	32.3
			C-004	535	388	147	2	2	36.8
			C-005	555	419	136	2	2	34.0
								MEAN	32.82
								S.D.	3.19
	2	80	C-006	560	429	131	2	2	32.8
			C-007	566	451	115	2	2	28.8
			C-008	543	438	105	2	2	26.3
			C-009	555	422	133	2	2	33.3
			C-010	567	417	150	2	2	37.5
								MEAN	31.74
								S.D.	4.33
	3	250	C-011	566	433	133	2	2	33.3
			C-012	547	414	133	2	2	33.3
			C-013	556	431	125	2	2	31.3
			C-014	570	456	114	2	2	28.5
			C-015	569	457	112	2	2	28.0
								MEAN	30.88
								S.D.	2.54
	4	800	C-016	549	426	123	2	2	30.8
			C-017	563	453	110	2	2	27.5
			C-018	571	458	113	2	2	28.3
			C-019	557	423	134	2	2	33.5
			C-020	526	403	123	2	2	30.8
								MEAN	30.18
								S.D.	2.37

APPENDIX D
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL WATER CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 1

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	W.C. (g/animal/day)
FEMALE	5	0	C-021	532	436	96	2	2	24.0
			C-022	539	456	83	2	2	20.8
			C-023	536	454	82	2	2	20.5
			C-024	533	440	93	2	2	23.3
			C-025	525	431	94	2	2	23.5
								MEAN	22.42
								S.D.	1.64
	6	80	C-026	543	443	100	2	2	25.0
			C-027	544	476	68	2	2	17.0
			C-028	544	457	87	2	2	21.8
			C-029	532	445	87	2	2	21.8
			C-030	549	467	82	2	2	20.5
								MEAN	21.22
								S.D.	2.88
	7	250	C-031	544	471	73	2	2	18.3
			C-032	538	465	73	2	2	18.3
			C-033	530	453	77	2	2	19.3
			C-034	548	455	93	2	2	23.3
			C-035	540	463	77	2	2	19.3
								MEAN	19.70
								S.D.	2.07
	8	800	C-036	542	435	107	2	2	26.8
			C-037	526	443	83	2	2	20.8
			C-038	539	462	77	2	2	19.3
			C-039	540	451	89	2	2	22.3
			C-040	514	441	73	2	2	18.3
								MEAN	21.50
								S.D.	3.33

APPENDIX D
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL WATER CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 2

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	W.C. (g/animal/day)
MALE	1	0	C-001	564	438	126	2	2	31.5
			C-002	571	465	106	2	2	26.5
			C-003	561	437	124	2	2	31.0
			C-004	557	397	160	2	2	40.0
			C-005	552	413	139	2	2	34.8
								MEAN	32.76
								S.D.	5.01
	2	80	C-006	576	437	139	2	2	34.8
			C-007	565	437	128	2	2	32.0
			C-008	550	453	97	2	2	24.3
			C-009	552	401	151	2	2	37.8
			C-010	562	414	148	2	2	37.0
								MEAN	33.18
								S.D.	5.45
	3	250	C-011	554	423	131	2	2	32.8
			C-012	543	403	140	2	2	35.0
			C-013	561	424	137	2	2	34.3
			C-014	567	448	119	2	2	29.8
			C-015	564	460	104	2	2	26.0
								MEAN	31.58
								S.D.	3.70
	4	800	C-016	555	438	117	2	2	29.3
			C-017	557	439	118	2	2	29.5
			C-018	573	468	105	2	2	26.3
			C-019	568	421	147	2	2	36.8
			C-020	553	435	118	2	2	29.5
								MEAN	30.28
								S.D.	3.89

APPENDIX D
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL WATER CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 2

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	W.C. (g/animal/day)
FEMALE	5	0	C-021	562	485	77	2	2	19.3
			C-022	567	489	78	2	2	19.5
			C-023	561	476	85	2	2	21.3
			C-024	561	455	106	2	2	26.5
			C-025	561	459	102	2	2	25.5
								MEAN	22.42
								S.D.	3.38
	6	80	C-026	548	453	95	2	2	23.8
			C-027	570	487	83	2	2	20.8
			C-028	558	473	85	2	2	21.3
			C-029	553	473	80	2	2	20.0
			C-030	556	449	107	2	2	26.8
								MEAN	22.54
								S.D.	2.77
	7	250	C-031	556	477	79	2	2	19.8
			C-032	551	478	73	2	2	18.3
			C-033	556	472	84	2	2	21.0
			C-034	570	467	103	2	2	25.8
			C-035	567	491	76	2	2	19.0
								MEAN	20.78
								S.D.	2.98
	8	800	C-036	558	449	109	2	2	27.3
			C-037	551	479	72	2	2	18.0
			C-038	555	462	93	2	2	23.3
			C-039	563	487	76	2	2	19.0
			C-040	560	469	91	2	2	22.8
								MEAN	22.08
								S.D.	3.72

APPENDIX D
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL WATER CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 3

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	W.C. (g/animal/day)
MALE	1	0	C-001	552	430	122	2	2	30.5
			C-002	552	442	110	2	2	27.5
			C-003	549	418	131	2	2	32.8
			C-004	549	411	138	2	2	34.5
			C-005	545	411	134	2	2	33.5
								MEAN	31.76
								S.D.	2.80
	2	80	C-006	545	378	167	2	2	41.8
			C-007	546	428	118	2	2	29.5
			C-008	547	453	94	2	2	23.5
			C-009	549	408	141	2	2	35.3
			C-010	550	395	155	2	2	38.8
								MEAN	33.78
								S.D.	7.35
	3	250	C-011	543	399	144	2	2	36.0
			C-012	546	418	128	2	2	32.0
			C-013	537	402	135	2	2	33.8
			C-014	547	426	121	2	2	30.3
			C-015	546	445	101	2	2	25.3
								MEAN	31.48
								S.D.	4.05
	4	800	C-016	557	433	124	2	2	31.0
			C-017	551	435	116	2	2	29.0
			C-018	542	442	100	2	2	25.0
			C-019	545	399	146	2	2	36.5
			C-020	541	419	122	2	2	30.5
								MEAN	30.40
								S.D.	4.14

APPENDIX D
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL WATER CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 3

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	W.C. (g/animal/day)
FEMALE	5	0	C-021	527	448	79	2	2	19.8
			C-022	532	452	80	2	2	20.0
			C-023	547	451	96	2	2	24.0
			C-024	543	410	133	2	2	33.3
			C-025	532	448	84	2	2	21.0
								MEAN	23.62
								S.D.	5.67
	6	80	C-026	540	453	87	2	2	21.8
			C-027	536	463	73	2	2	18.3
			C-028	530	448	82	2	2	20.5
			C-029	532	440	92	2	2	23.0
			C-030	533	429	104	2	2	26.0
								MEAN	21.92
								S.D.	2.87
	7	250	C-031	533	465	68	2	2	17.0
			C-032	529	440	89	2	2	22.3
			C-033	536	446	90	2	2	22.5
			C-034	538	446	92	2	2	23.0
			C-035	535	457	78	2	2	19.5
								MEAN	20.86
								S.D.	2.55
	8	800	C-036	523	401	122	2	2	30.5
			C-037	544	449	95	2	2	23.8
			C-038	545	468	77	2	2	19.3
			C-039	541	456	85	2	2	21.3
			C-040	533	441	92	2	2	23.0
								MEAN	23.58
								S.D.	4.24

APPENDIX D
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL WATER CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 4

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	W.C. (g/animal/day)
MALE	1	0	C-001	555	427	128	2	2	32.0
			C-002	546	438	108	2	2	27.0
			C-003	545	406	139	2	2	34.8
			C-004	555	401	154	2	2	38.5
			C-005	553	419	134	2	2	33.5
								MEAN	33.16
								S.D.	4.20
	2	80	C-006	550	358	192	2	2	48.0
			C-007	562	448	114	2	2	28.5
			C-008	567	478	89	2	2	22.3
			C-009	560	411	149	2	2	37.3
			C-010	562	408	154	2	2	38.5
								MEAN	34.92
								S.D.	9.87
	3	250	C-011	558	428	130	2	2	32.5
			C-012	560	432	128	2	2	32.0
			C-013	564	425	139	2	2	34.8
			C-014	560	437	123	2	2	30.8
			C-015	563	458	105	2	2	26.3
								MEAN	31.28
								S.D.	3.14
	4	800	C-016	559	442	117	2	2	29.3
			C-017	565	456	109	2	2	27.3
			C-018	562	465	97	2	2	24.3
			C-019	558	411	147	2	2	36.8
			C-020	560	435	125	2	2	31.3
								MEAN	29.80
								S.D.	4.69

APPENDIX D
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL WATER CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 4

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	W.C. (g/animal/day)
FEMALE	5	0	C-021	553	472	81	2	2	20.3
			C-022	558	456	102	2	2	25.5
			C-023	550	483	67	2	2	16.8
			C-024	565	452	113	2	2	28.3
			C-025	551	446	105	2	2	26.3
								MEAN	23.44
								S.D.	4.74
	6	80	C-026	549	442	107	2	2	26.8
			C-027	532	447	85	2	2	21.3
			C-028	549	454	95	2	2	23.8
			C-029	543	460	83	2	2	20.8
			C-030	542	461	81	2	2	20.3
								MEAN	22.60
								S.D.	2.71
	7	250	C-031	547	467	80	2	2	20.0
			C-032	556	461	95	2	2	23.8
			C-033	560	479	81	2	2	20.3
			C-034	537	445	92	2	2	23.0
			C-035	556	481	75	2	2	18.8
								MEAN	21.18
								S.D.	2.12
	8	800	C-036	557	419	138	2	2	34.5
			C-037	561	467	94	2	2	23.5
			C-038	548	468	80	2	2	20.0
			C-039	565	486	79	2	2	19.8
			C-040	553	459	94	2	2	23.5
								MEAN	24.26
								S.D.	6.00

APPENDIX D
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL WATER CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 5

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	W.C. (g/animal/day)
MALE	1	0	C-001	551	424	127	2	2	31.8
			C-002	562	455	107	2	2	26.8
			C-003	559	437	122	2	2	30.5
			C-004	548	417	131	2	2	32.8
			C-005	556	421	135	2	2	33.8
								MEAN	31.14
								S.D.	2.72
	2	80	C-006	544	356	188	2	2	47.0
			C-007	552	437	115	2	2	28.8
			C-008	552	468	84	2	2	21.0
			C-009	555	413	142	2	2	35.5
			C-010	564	416	148	2	2	37.0
								MEAN	33.86
								S.D.	9.70
	3	250	C-011	538	405	133	2	2	33.3
			C-012	NEa	-	-	-	-	-
			C-013	554	415	139	2	2	34.8
			C-014	550	424	126	2	2	31.5
			C-015	552	449	103	2	2	25.8
								MEAN	31.35
								S.D.	3.94
	4	800	C-016	556	448	108	2	2	27.0
			C-017	557	446	111	2	2	27.8
			C-018	548	453	95	2	2	23.8
			C-019	553	427	126	2	2	31.5
			C-020	543	424	119	2	2	29.8
								MEAN	27.98
								S.D.	2.92

a : Data were omitted from the evaluation, since one animal died during the measuring period.

APPENDIX D
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL WATER CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 5

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	W.C. (g/animal/day)
FEMALE	5	0	C-021	546	454	92	2	2	23.0
			C-022	552	462	90	2	2	22.5
			C-023	543	460	83	2	2	20.8
			C-024	550	437	113	2	2	28.3
			C-025	550	457	93	2	2	23.3
								MEAN	23.58
								S.D.	2.81
	6	80	C-026	560	475	85	2	2	21.3
			C-027	576	505	71	2	2	17.8
			C-028	557	470	87	2	2	21.8
			C-029	571	473	98	2	2	24.5
			C-030	561	474	87	2	2	21.8
								MEAN	21.44
								S.D.	2.39
	7	250	C-031	571	498	73	2	2	18.3
			C-032	573	503	70	2	2	17.5
			C-033	574	488	86	2	2	21.5
			C-034	564	472	92	2	2	23.0
			C-035	566	492	74	2	2	18.5
								MEAN	19.76
								S.D.	2.36
	8	800	C-036	562	430	132	2	2	33.0
			C-037	555	468	87	2	2	21.8
			C-038	558	463	95	2	2	23.8
			C-039	558	473	85	2	2	21.3
			C-040	552	449	103	2	2	25.8
								MEAN	25.14
								S.D.	4.74

APPENDIX D
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL WATER CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 6

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	W.C. (g/animal/day)
MALE	1	0	C-001	511	389	122	2	2	30.5
			C-002	484	383	101	2	2	25.3
			C-003	525	397	128	2	2	32.0
			C-004	533	393	140	2	2	35.0
			C-005	522	396	126	2	2	31.5
								MEAN	30.86
								S.D.	3.53
	2	80	C-006	515	361	154	2	2	38.5
			C-007	515	405	110	2	2	27.5
			C-008	515	420	95	2	2	23.8
			C-009	554	407	147	2	2	36.8
			C-010	514	374	140	2	2	35.0
								MEAN	32.32
								S.D.	6.35
	3	250	C-011	543	398	145	2	2	36.3
			C-012	503	452	51	1	2	25.5
			C-013	518	379	139	2	2	34.8
			C-014	538	413	125	2	2	31.3
			C-015	526	421	105	2	2	26.3
								MEAN	30.84
								S.D.	4.87
	4	800	C-016	525	406	119	2	2	29.8
			C-017	504	397	107	2	2	26.8
			C-018	515	420	95	2	2	23.8
			C-019	533	395	138	2	2	34.5
			C-020	515	399	116	2	2	29.0
								MEAN	28.78
								S.D.	3.95

APPENDIX D
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL WATER CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 6

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	W.C. (g/animal/day)
FEMALE	5	0	C-021	555	469	86	2	2	21.5
			C-022	554	429	125	2	2	31.3
			C-023	559	489	70	2	2	17.5
			C-024	563	447	116	2	2	29.0
			C-025	549	450	99	2	2	24.8
								MEAN	24.82
								S.D.	5.57
	6	80	C-026	557	452	105	2	2	26.3
			C-027	552	461	91	2	2	22.8
			C-028	545	464	81	2	2	20.3
			C-029	556	470	86	2	2	21.5
			C-030	537	436	101	2	2	25.3
								MEAN	23.24
								S.D.	2.52
	7	250	C-031	550	471	79	2	2	19.8
			C-032	536	459	77	2	2	19.3
			C-033	552	475	77	2	2	19.3
			C-034	558	463	95	2	2	23.8
			C-035	549	484	65	2	2	16.3
								MEAN	19.70
								S.D.	2.68
	8	800	C-036	535	392	143	2	2	35.8
			C-037	534	456	78	2	2	19.5
			C-038	552	467	85	2	2	21.3
			C-039	557	484	73	2	2	18.3
			C-040	542	442	100	2	2	25.0
								MEAN	23.98
								S.D.	7.08

APPENDIX D
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL WATER CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 7

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	W.C. (g/animal/day)
MALE	1	0	C-001	547	425	122	2	2	30.5
			C-002	532	423	109	2	2	27.3
			C-003	534	405	129	2	2	32.3
			C-004	536	388	148	2	2	37.0
			C-005	536	406	130	2	2	32.5
								MEAN	31.92
								S.D.	3.52
	2	80	C-006	558	374	184	2	2	46.0
			C-007	547	434	113	2	2	28.3
			C-008	544	456	88	2	2	22.0
			C-009	558	413	145	2	2	36.3
			C-010	547	412	135	2	2	33.8
								MEAN	33.28
								S.D.	8.99
	3	250	C-011	575	446	129	2	2	32.3
			C-012	544	493	51	1	2	25.5
			C-013	557	434	123	2	2	30.8
			C-014	560	420	140	2	2	35.0
			C-015	558	452	106	2	2	26.5
								MEAN	30.02
								S.D.	3.98
	4	800	C-016	572	468	104	2	2	26.0
			C-017	543	420	123	2	2	30.8
			C-018	545	438	107	2	2	26.8
			C-019	573	424	149	2	2	37.3
			C-020	553	431	122	2	2	30.5
								MEAN	30.28
								S.D.	4.47

APPENDIX D
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL WATER CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 7

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	W.C. (g/animal/day)
FEMALE	5	0	C-021	542	468	74	2	2	18.5
			C-022	547	437	110	2	2	27.5
			C-023	548	468	80	2	2	20.0
			C-024	551	432	119	2	2	29.8
			C-025	553	469	84	2	2	21.0
								MEAN	23.36
								S.D.	4.98
	6	80	C-026	562	461	101	2	2	25.3
			C-027	560	480	80	2	2	20.0
			C-028	561	493	68	2	2	17.0
			C-029	565	485	80	2	2	20.0
			C-030	565	476	89	2	2	22.3
								MEAN	20.92
								S.D.	3.09
	7	250	C-031	576	506	70	2	2	17.5
			C-032	572	476	96	2	2	24.0
			C-033	562	476	86	2	2	21.5
			C-034	569	478	91	2	2	22.8
			C-035	573	509	64	2	2	16.0
								MEAN	20.36
								S.D.	3.45
	8	800	C-036	572	450	122	2	2	30.5
			C-037	571	477	94	2	2	23.5
			C-038	562	480	82	2	2	20.5
			C-039	569	482	87	2	2	21.8
			C-040	566	460	106	2	2	26.5
								MEAN	24.56
								S.D.	4.01

APPENDIX D
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL WATER CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 8

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	W.C. (g/animal/day)
MALE	1	0	C-001	560	458	102	2	2	25.5
			C-002	558	457	101	2	2	25.3
			C-003	547	424	123	2	2	30.8
			C-004	550	410	140	2	2	35.0
			C-005	549	416	133	2	2	33.3
								MEAN	29.98
								S.D.	4.44
	2	80	C-006	563	399	164	2	2	41.0
			C-007	563	452	111	2	2	27.8
			C-008	551	468	83	2	2	20.8
			C-009	554	401	153	2	2	38.3
			C-010	553	417	136	2	2	34.0
								MEAN	32.38
								S.D.	8.17
	3	250	C-011	572	455	117	2	2	29.3
			C-012	566	513	53	1	2	26.5
			C-013	551	421	130	2	2	32.5
			C-014	553	425	128	2	2	32.0
			C-015	555	444	111	2	2	27.8
								MEAN	29.62
								S.D.	2.60
	4	800	C-016	573	462	111	2	2	27.8
			C-017	568	457	111	2	2	27.8
			C-018	552	446	106	2	2	26.5
			C-019	554	402	152	2	2	38.0
			C-020	555	436	119	2	2	29.8
								MEAN	29.98
								S.D.	4.64

APPENDIX D
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL WATER CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 8

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	W.C. (g/animal/day)
FEMALE	5	0	C-021	545	462	83	2	2	20.8
			C-022	556	451	105	2	2	26.3
			C-023	546	457	89	2	2	22.3
			C-024	518	417	101	2	2	25.3
			C-025	557	483	74	2	2	18.5
								MEAN	22.64
								S.D.	3.21
	6	80	C-026	547	449	98	2	2	24.5
			C-027	554	481	73	2	2	18.3
			C-028	547	452	95	2	2	23.8
			C-029	559	471	88	2	2	22.0
			C-030	554	472	82	2	2	20.5
								MEAN	21.82
								S.D.	2.51
	7	250	C-031	568	486	82	2	2	20.5
			C-032	551	454	97	2	2	24.3
			C-033	558	482	76	2	2	19.0
			C-034	560	484	76	2	2	19.0
			C-035	557	491	66	2	2	16.5
								MEAN	19.86
								S.D.	2.87
	8	800	C-036	553	446	107	2	2	26.8
			C-037	564	465	99	2	2	24.8
			C-038	537	450	87	2	2	21.8
			C-039	547	468	79	2	2	19.8
			C-040	560	461	99	2	2	24.8
								MEAN	23.60
								S.D.	2.77

APPENDIX D
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL WATER CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 9

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	W.C. (g/animal/day)
MALE	1	0	C-001	554	449	105	2	2	26.3
			C-002	567	466	101	2	2	25.3
			C-003	553	434	119	2	2	29.8
			C-004	569	435	134	2	2	33.5
			C-005	569	447	122	2	2	30.5
								MEAN	29.08
								S.D.	3.32
	2	80	C-006	556	393	163	2	2	40.8
			C-007	568	465	103	2	2	25.8
			C-008	553	465	88	2	2	22.0
			C-009	550	394	156	2	2	39.0
			C-010	560	408	152	2	2	38.0
								MEAN	33.12
								S.D.	8.58
	3	250	C-011	564	460	104	2	2	26.0
			C-012	554	500	54	1	2	27.0
			C-013	553	428	125	2	2	31.3
			C-014	567	452	115	2	2	28.8
			C-015	572	466	106	2	2	26.5
								MEAN	27.92
								S.D.	2.16
	4	800	C-016	551	450	101	2	2	25.3
			C-017	546	434	112	2	2	28.0
			C-018	563	466	97	2	2	24.3
			C-019	561	406	155	2	2	38.8
			C-020	559	449	110	2	2	27.5
								MEAN	28.78
								S.D.	5.81

APPENDIX D
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL WATER CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 9

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	W.C. (g/animal/day)
FEMALE	5	0	C-021	557	463	94	2	2	23.5
			C-022	564	466	98	2	2	24.5
			C-023	558	476	82	2	2	20.5
			C-024	550	454	96	2	2	24.0
			C-025	564	484	80	2	2	20.0
								MEAN	22.50
								S.D.	2.09
	6	80	C-026	571	478	93	2	2	23.3
			C-027	567	493	74	2	2	18.5
			C-028	557	479	78	2	2	19.5
			C-029	561	479	82	2	2	20.5
			C-030	565	483	82	2	2	20.5
								MEAN	20.46
								S.D.	1.79
	7	250	C-031	565	499	66	2	2	16.5
			C-032	555	474	81	2	2	20.3
			C-033	554	473	81	2	2	20.3
			C-034	567	490	77	2	2	19.3
			C-035	574	511	63	2	2	15.8
								MEAN	18.44
								S.D.	2.14
	8	800	C-036	567	498	69	2	2	17.3
			C-037	559	491	68	2	2	17.0
			C-038	565	467	98	2	2	24.5
			C-039	559	482	77	2	2	19.3
			C-040	551	452	99	2	2	24.8
								MEAN	20.58
								S.D.	3.82

APPENDIX D
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL WATER CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 10

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	W.C. (g/animal/day)
MALE	1	0	C-001	552	435	117	2	2	29.3
			C-002	560	358	202	2	2	50.5
			C-003	553	440	113	2	2	28.3
			C-004	545	398	147	2	2	36.8
			C-005	548	420	128	2	2	32.0
								MEAN	35.38
								S.D.	9.07
	2	80	C-006	558	380	178	2	2	44.5
			C-007	554	436	118	2	2	29.5
			C-008	540	457	83	2	2	20.8
			C-009	540	400	140	2	2	35.0
			C-010	555	433	122	2	2	30.5
								MEAN	32.06
								S.D.	8.65
	3	250	C-011	561	457	104	2	2	26.0
			C-012	550	490	60	1	2	30.0
			C-013	551	421	130	2	2	32.5
			C-014	559	443	116	2	2	29.0
			C-015	549	448	101	2	2	25.3
								MEAN	28.56
								S.D.	2.96
	4	800	C-016	544	438	106	2	2	26.5
			C-017	541	419	122	2	2	30.5
			C-018	552	461	91	2	2	22.8
			C-019	561	414	147	2	2	36.8
			C-020	555	447	108	2	2	27.0
								MEAN	28.72
								S.D.	5.28

APPENDIX D
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL WATER CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 10

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	W.C. (g/animal/day)
FEMALE	5	0	C-021	541	456	85	2	2	21.3
			C-022	561	441	120	2	2	30.0
			C-023	569	495	74	2	2	18.5
			C-024	531	415	116	2	2	29.0
			C-025	552	479	73	2	2	18.3
								MEAN	23.42
								S.D.	5.69
	6	80	C-026	556	453	103	2	2	25.8
			C-027	565	492	73	2	2	18.3
			C-028	554	482	72	2	2	18.0
			C-029	529	445	84	2	2	21.0
			C-030	548	461	87	2	2	21.8
								MEAN	20.98
								S.D.	3.16
	7	250	C-031	557	489	68	2	2	17.0
			C-032	550	472	78	2	2	19.5
			C-033	530	457	73	2	2	18.3
			C-034	558	477	81	2	2	20.3
			C-035	576	516	60	2	2	15.0
								MEAN	18.02
								S.D.	2.10
	8	800	C-036	NEa	-	-	-	-	-
			C-037	526	453	73	2	2	18.3
			C-038	549	458	91	2	2	22.8
			C-039	550	483	67	2	2	16.8
			C-040	545	446	99	2	2	24.8
								MEAN	20.68
								S.D.	3.75

a : Data were omitted from the evaluation, since one animal died during the measuring period.

APPENDIX D
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL WATER CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 11

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	W.C. (g/animal/day)
MALE	1	0	C-001	546	447	99	2	2	24.8
			C-002	539	444	95	2	2	23.8
			C-003	534	425	109	2	2	27.3
			C-004	540	407	133	2	2	33.3
			C-005	550	439	111	2	2	27.8
								MEAN	27.40
								S.D.	3.70
	2	80	C-006	557	405	152	2	2	38.0
			C-007	538	426	112	2	2	28.0
			C-008	557	478	79	2	2	19.8
			C-009	566	433	133	2	2	33.3
			C-010	555	424	131	2	2	32.8
								MEAN	30.38
								S.D.	6.89
	3	250	C-011	563	462	101	2	2	25.3
			C-012	542	478	64	1	2	32.0
			C-013	537	409	128	2	2	32.0
			C-014	556	447	109	2	2	27.3
			C-015	561	451	110	2	2	27.5
								MEAN	28.82
								S.D.	3.03
	4	800	C-016	558	457	101	2	2	25.3
			C-017	542	418	124	2	2	31.0
			C-018	546	457	89	2	2	22.3
			C-019	553	410	143	2	2	35.8
			C-020	552	441	111	2	2	27.8
								MEAN	28.44
								S.D.	5.21

APPENDIX D
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL WATER CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 11

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	W.C. (g/animal/day)
FEMALE	5	0	C-021	544	467	77	2	2	19.3
			C-022	548	417	131	2	2	32.8
			C-023	543	464	79	2	2	19.8
			C-024	545	422	123	2	2	30.8
			C-025	545	467	78	2	2	19.5
								MEAN	24.44
								S.D.	6.76
	6	80	C-026	572	473	99	2	2	24.8
			C-027	578	499	79	2	2	19.8
			C-028	572	497	75	2	2	18.8
			C-029	562	481	81	2	2	20.3
			C-030	571	486	85	2	2	21.3
								MEAN	21.00
								S.D.	2.31
	7	250	C-031	567	488	79	2	2	19.8
			C-032	575	487	88	2	2	22.0
			C-033	574	493	81	2	2	20.3
			C-034	569	492	77	2	2	19.3
			C-035	564	503	61	2	2	15.3
								MEAN	19.34
								S.D.	2.48
	8	800	C-036	552	518	34	1	2	17.0
			C-037	555	466	89	2	2	22.3
			C-038	555	478	77	2	2	19.3
			C-039	554	517	37	1	2	18.5
			C-040	554	437	117	2	2	29.3
								MEAN	21.28
								S.D.	4.88

APPENDIX D
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL WATER CONSUMPTION DATA
STUDY NO [redacted]
WEEK: 12

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	W.C. (g/animal/day)
MALE	1	0	C-001	548	441	107	2	2	26.8
			C-002	566	463	103	2	2	25.8
			C-003	548	440	108	2	2	27.0
			C-004	552	427	125	2	2	31.3
			C-005	557	426	131	2	2	32.8
								MEAN	28.74
								S.D.	3.10
	2	80	C-006	560	414	146	2	2	36.5
			C-007	540	433	107	2	2	26.8
			C-008	553	479	74	2	2	18.5
			C-009	555	402	153	2	2	38.3
			C-010	561	435	126	2	2	31.5
								MEAN	30.32
								S.D.	7.99
	3	250	C-011	539	439	100	2	2	25.0
			C-012	543	482	61	1	2	30.5
			C-013	568	447	121	2	2	30.3
			C-014	568	460	108	2	2	27.0
			C-015	548	454	94	2	2	23.5
								MEAN	27.26
								S.D.	3.12
	4	800	C-016	553	447	106	2	2	26.5
			C-017	563	447	116	2	2	29.0
			C-018	561	473	88	2	2	22.0
			C-019	534	394	140	2	2	35.0
			C-020	535	430	105	2	2	26.3
								MEAN	27.76
								S.D.	4.77

APPENDIX D
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL WATER CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 12

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	W.C. (g/animal/day)
FEMALE	5	0	C-021	566	477	89	2	2	22.3
			C-022	575	475	100	2	2	25.0
			C-023	570	485	85	2	2	21.3
			C-024	572	454	118	2	2	29.5
			C-025	572	487	85	2	2	21.3
								MEAN	23.88
								S.D.	3.49
	6	80	C-026	565	470	95	2	2	23.8
			C-027	568	491	77	2	2	19.3
			C-028	563	486	77	2	2	19.3
			C-029	565	487	78	2	2	19.5
			C-030	563	483	80	2	2	20.0
								MEAN	20.38
								S.D.	1.93
	7	250	C-031	556	476	80	2	2	20.0
			C-032	556	463	93	2	2	23.3
			C-033	563	475	88	2	2	22.0
			C-034	542	471	71	2	2	17.8
			C-035	554	491	63	2	2	15.8
								MEAN	19.78
								S.D.	3.05
	8	800	C-036	540	500	40	1	2	20.0
			C-037	543	456	87	2	2	21.8
			C-038	546	471	75	2	2	18.8
			C-039	539	499	40	1	2	20.0
			C-040	541	429	112	2	2	28.0
								MEAN	21.72
								S.D.	3.67

APPENDIX D
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL WATER CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 13

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	W.C. (g/animal/day)
MALE	1	0	C-001	550	452	98	2	2	24.5
			C-002	560	451	109	2	2	27.3
			C-003	552	451	101	2	2	25.3
			C-004	562	441	121	2	2	30.3
			C-005	558	437	121	2	2	30.3
								MEAN	27.54
								S.D.	2.72
	2	80	C-006	552	424	128	2	2	32.0
			C-007	559	452	107	2	2	26.8
			C-008	551	486	65	2	2	16.3
			C-009	559	415	144	2	2	36.0
			C-010	555	446	109	2	2	27.3
								MEAN	27.68
								S.D.	7.39
	3	250	C-011	545	448	97	2	2	24.3
			C-012	556	510	46	1	2	23.0
			C-013	546	435	111	2	2	27.8
			C-014	553	456	97	2	2	24.3
			C-015	547	457	90	2	2	22.5
								MEAN	24.38
								S.D.	2.07
	4	800	C-016	560	465	95	2	2	23.8
			C-017	561	450	111	2	2	27.8
			C-018	548	460	88	2	2	22.0
			C-019	558	408	150	2	2	37.5
			C-020	559	459	100	2	2	25.0
								MEAN	27.22
								S.D.	6.12

APPENDIX D
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL WATER CONSUMPTION DATA
STUDY NO. [redacted]
WEEK: 13

SEX	GROUP NO.	LEVEL (mg/kg/day)	CAGE NO.	INITIAL (g)	FINAL (g)	NET (g)	NO. OF ANIMALS	DAYS	W.C. (g/animal/day)
FEMALE	5	0	C-021	543	464	79	2	2	19.8
			C-022	562	474	88	2	2	22.0
			C-023	555	481	74	2	2	18.5
			C-024	542	442	100	2	2	25.0
			C-025	561	495	66	2	2	16.5
								MEAN	20.36
								S.D.	3.27
	6	80	C-026	542	469	73	2	2	18.3
			C-027	570	501	69	2	2	17.3
			C-028	559	499	60	2	2	15.0
			C-029	545	470	75	2	2	18.8
			C-030	564	479	85	2	2	21.3
								MEAN	18.14
								S.D.	2.29
	7	250	C-031	546	490	56	2	2	14.0
			C-032	557	476	81	2	2	20.3
			C-033	554	494	60	2	2	15.0
			C-034	545	468	77	2	2	19.3
			C-035	558	500	58	2	2	14.5
								MEAN	16.62
								S.D.	2.95
	8	800	C-036	533	495	38	1	2	19.0
			C-037	530	466	64	2	2	16.0
			C-038	541	467	74	2	2	18.5
			C-039	530	491	39	1	2	19.5
			C-040	552	436	116	2	2	29.0
								MEAN	20.40
								S.D.	4.99

APPENDIX E

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL OPHTHALMOSCOPIC FINDING DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	STRUCTURE[a] AND FINDINGS
MALE	1	0	1437001	Normal
			1437002	Normal
			1437003	Normal
			1437004	Normal
			1437005	Normal
			1437006	Normal

a : Anterior chamber, Optic media, Ocular fundus and others were examined.

APPENDIX E

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL OPHTHALMOSCOPIC FINDING DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	STRUCTURE[a] AND FINDINGS
MALE	2	80	1437011	Normal
			1437012	Normal
			1437013	Normal
			1437014	Normal
			1437015	Normal
			1437016	Normal

a : Anterior chamber, Optic media, Ocular fundus and others were examined.

APPENDIX E

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL OPHTHALMOSCOPIC FINDING DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	STRUCTURE[a] AND FINDINGS
MALE	3	250	1437021	Normal
			1437022	Normal
			1437024	Normal
			1437025	Normal
			1437026	Normal
			1437027	Normal

a : Anterior chamber, Optic media, Ocular fundus and others were examined.

APPENDIX E

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL OPHTHALMOSCOPIC FINDING DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	STRUCTURE[a] AND FINDINGS
MALE	4	800	1437031	Normal
			1437032	Normal
			1437033	Normal
			1437034	Normal
			1437035	Normal
			1437036	Normal

a : Anterior chamber, Optic media, Ocular fundus and others were examined.

APPENDIX E

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL OPHTHALMOSCOPIC FINDING DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	STRUCTURE[a] AND FINDINGS
FEMALE	5	0	1437041	Normal
			1437042	Normal
			1437043	Normal
			1437044	Normal
			1437045	Normal
			1437046	Normal

a : Anterior chamber, Optic media, Ocular fundus and others were examined.

APPENDIX E

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL OPHTHALMOSCOPIC FINDING DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	STRUCTURE[a] AND FINDINGS
FEMALE	6	80	1437051	Normal
			1437052	Normal
			1437053	Normal
			1437054	Normal
			1437055	Normal
			1437056	Normal

a : Anterior chamber, Optic media, Ocular fundus and others were examined.

APPENDIX E

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL OPHTHALMOSCOPIC FINDING DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	STRUCTURE[a] AND FINDINGS
FEMALE	7	250	1437061	Normal
			1437062	Normal
			1437063	Normal
			1437064	Normal
			1437065	Normal
			1437066	Normal

a : Anterior chamber, Optic media, Ocular fundus and others were examined.

APPENDIX E
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL OPHTHALMOSCOPIC FINDING DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	STRUCTURE[a] AND FINDINGS
FEMALE	8	800	1437072	Normal
			1437073	Normal
			1437074	Normal
			1437075	Normal
			1437076	Normal
			1437077	Normal

a : Anterior chamber, Optic media, Ocular fundus and others were examined.

APPENDIX F

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL URINALYSIS DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	GLUCOSE	BILIRUBIN	KETONE BODIES	OCCULT BLOOD	PROTEIN	UROBI-LINOGEN	pH	SPECIFIC GRAVITY	APPEARANCE
MALE	1	0	1437001	-	-	1+	-	1+	0.1	6.17	1.066	Pale yellow
			1437002	-	-	±	-	-	0.1	7.42	1.020	Pale yellow
			1437003	-	-	±	-	-	0.1	7.58	1.025	Pale yellow
			1437004	-	-	1+	-	2+	0.1	7.57	1.066	Pale yellow
			1437005	-	-	±	-	±	0.1	6.26	1.022	Pale yellow
			1437006	-	-	1+	-	1+	0.1	6.56	1.029	Pale yellow
			N							6	6	
			MEAN							6.927	1.0380	
			S.D.							0.669	0.0219	

APPENDIX F

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL URINALYSIS DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	GLUCOSE	BILIRUBIN	KETONE BODIES	OCCULT BLOOD	PROTEIN	UROBI-LINOGEN	pH	SPECIFIC GRAVITY	APPEARANCE
MALE	2	80	1437011	-	-	2+	-	-	0.1	7.62	1.069	Pale yellow
			1437012	-	-	±	-	1+	0.1	7.41	1.034	Pale yellow
			1437013	-	-	1+	-	1+	0.1	6.15	1.075	Pale yellow
			1437014	-	-	3+	-	2+	0.1	6.28	1.090	Pale yellow
			1437015	-	-	1+	-	2+	0.1	6.96	1.069	Pale yellow
			1437016	-	-	1+	-	2+	0.1	6.53	1.093	Pale yellow
			N							6	6	
			MEAN							6.825	1.0717	
			S.D.							0.605	0.0211	

APPENDIX F

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL URINALYSIS DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	GLUCOSE	BILIRUBIN	KETONE BODIES	OCCULT BLOOD	PROTEIN	UROBI-LINOGEN	pH	SPECIFIC GRAVITY	APPEARANCE
MALE	3	250	1437021	-	-	±	-	±	0.1	6.03	1.028	Pale yellow
			1437022	-	-	±	-	±	0.1	7.30	1.025	Pale yellow
			1437024	-	-	1+	-	1+	0.1	7.44	1.025	Pale yellow
			1437025	-	-	1+	-	1+	0.1	7.84	1.036	Pale yellow
			1437026	-	-	±	-	1+	0.1	6.15	1.038	Pale yellow
			1437027	-	-	2+	-	2+	0.1	6.63	1.045	Pale yellow
			N							6	6	
			MEAN							6.898	1.0328	
			S.D.							0.739	0.0081	

APPENDIX F

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL URINALYSIS DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	GLUCOSE	BILIRUBIN	KETONE BODIES	OCCULT BLOOD	PROTEIN	UROBI-LINOGEN	pH	SPECIFIC GRAVITY	APPEARANCE
MALE	4	800	1437031	-	-	1+	-	±	0.1	6.48	1.037	Pale yellow
			1437032	-	-	1+	-	1+	0.1	6.22	1.050	Pale yellow
			1437033	-	-	±	-	1+	0.1	8.13	1.020	Pale yellow
			1437034	-	-	1+	-	2+	0.1	8.09	1.050	Pale yellow
			1437035	-	-	-	-	±	0.1	5.97	1.010	Pale yellow
			1437036	-	-	1+	-	1+	0.1	6.55	1.072	Pale yellow
			N							6	6	
			MEAN							6.907	1.0398	
			S.D.							0.954	0.0225	

APPENDIX F

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL URINALYSIS DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	GLUCOSE	BILIRUBIN	KETONE BODIES	OCCULT BLOOD	PROTEIN	UROBI-LINOGEN	pH	SPECIFIC GRAVITY	APPEARANCE
FEMALE	5	0	1437041	-	-	-	-	1+	0.1	5.86	1.078	Pale yellow
			1437042	-	-	-	-	±	0.1	7.50	1.026	Pale yellow
			1437043	-	-	-	-	-	0.1	7.49	1.015	Pale yellow
			1437044	-	-	-	-	±	0.1	6.91	1.031	Pale yellow
			1437045	-a	-a	-a	-a	±a	0.1a	5.91	1.030 a	Pale yellow[a]
			1437046	-	-	-	-	-	0.1	7.44	1.013	Pale yellow
a : Reanalysis was performed.			N							6	6	
			MEAN							6.852	1.0322	
			S.D.							0.781	0.0237	

APPENDIX F

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL URINALYSIS DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	GLUCOSE	BILIRUBIN	KETONE BODIES	OCCULT BLOOD	PROTEIN	UROBI-LINOGEN	pH	SPECIFIC GRAVITY	APPEARANCE
FEMALE	6	80	1437051	-	-	-	-	±	0.1	8.18	1.017	Pale yellow
			1437052	-	-	-	-	±	0.1	7.13	1.030	Pale yellow
			1437053	-	-	-	-	±	0.1	6.29	1.020	Pale yellow
			1437054	-	-	-	-	±	0.1	7.75	1.020	Pale yellow
			1437055	-a	-a	-a	-a	±a	0.1a	6.65	1.081 a	Pale yellow[a]
			1437056	-a	-a	-a	-a	±+a	0.1a	8.03	1.069 a	Pale yellow[a]
a : Reanalysis was performed.			N							6	6	
			MEAN							7.338	1.0395	
			S.D.							0.771	0.0281	

APPENDIX F

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL URINALYSIS DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	GLUCOSE	BILIRUBIN	KETONE BODIES	OCCULT BLOOD	PROTEIN	UROBI-LINOGEN	pH	SPECIFIC GRAVITY	APPEARANCE
FEMALE	7	250	1437061	-	-	-	-	±	0.1	7.61	1.030	Pale yellow
			1437062	-	-	-	-	±	0.1	6.13	1.030	Pale yellow
			1437063	-	-	-	-	-	0.1	6.85	1.026	Pale yellow
			1437064	-a	-a	-a	-a	1+a	0.1a	5.97	1.063 a	Pale yellow[a]
			1437065	-	-	-	-	-	0.1	8.13	1.025	Pale yellow
			1437066	-a	-a	-a	-a	±a	0.1a	8.04	1.051 a	Pale yellow[a]
a : Reanalysis was performed.			N							6	6	
			MEAN							7.122	1.0375	
			S.D.							0.947	0.0157	

APPENDIX F

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL URINALYSIS DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	GLUCOSE	BILIRUBIN	KETONE BODIES	OCCULT BLOOD	PROTEIN	UROBI-LINOGEN	pH	SPECIFIC GRAVITY	APPEARANCE
FEMALE	8	800	1437072	-	-	-	-	-	0.1	6.83	1.009	Pale yellow
			1437073	-	-	-	-	1+	0.1	7.45	1.045	Pale yellow
			1437074	-	-	-	-	1+	0.1	7.93	1.054	Pale yellow
			1437075	-	-	-	-	±	0.1	7.70	1.022	Pale yellow
			1437076	-	-	-	-	±	0.1	6.48	1.030	Pale yellow
			1437077	-	-	-	-	1+	0.1	8.26	1.040	Pale yellow
			N							6	6	
			MEAN							7.442	1.0333	
			S.D.							0.674	0.0164	

APPENDIX F

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL URINALYSIS DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	MICROSCOPIC EXAMINATION					URINE VOLUME (IN GRAMS)	NA (mEq/L)	K (mEq/L)	CL (mEq/L)
				EPITHELIAL CELLS	CRYSTALS	CASTS	RBC	WBC				
MALE	1	0	1437001	-	-	-	-	-	0.5	33.3	138.66	90.0
			1437002	-	3+	-	-	-	2.7	60.9	68.01	43.2
			1437003	-	-	-	-	-	1.8	19.3 a	46.74	49.5
			1437004	-	3+	-	-	-	0.5	131.4	235.95	99.0
			1437005	-	1+	-	-	-	2.1	54.9	104.49	35.4
			1437006	-	2+	-	-	-	1.5	11.1 a	106.80	11.8 a
a : Reanalysis was performed.			N						6	6	6	6
			MEAN						1.52	51.82	116.775	54.82
			S.D.						0.88	43.55	66.656	33.41

APPENDIX F

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL URINALYSIS DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	MICROSCOPIC EXAMINATION					URINE VOLUME (IN GRAMS)	NA (mEq/L)	K (mEq/L)	CL (mEq/L)
				EPITHELIAL CELLS	CRYSTALS	CASTS	RBC	WBC				
MALE	2	80	1437011	-	1+	-	-	-	0.2	60.0	171.99	81.3
			1437012	-	-	-	-	-	1.9	54.0	121.05	37.8
			1437013	-	-	-	-	-	0.8	37.5	416.24 a	30.0
			1437014	-	3+	-	-	-	0.7	69.9	286.68	44.1
			1437015	-	-	-	-	-	0.4	52.2	329.94 a	14.1 a
			1437016	-	-	-	-	-	0.2	48.0	357.84 a	22.6 a
a : Reanalysis was performed.			N						6	6	6	6
			MEAN						0.70	53.60	280.623	38.32
			S.D.						0.64	10.95	113.215	23.60

APPENDIX F

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL URINALYSIS DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	MICROSCOPIC EXAMINATION					URINE VOLUME (IN GRAMS)	NA (mEq/L)	K (mEq/L)	CL (mEq/L)
				EPITHELIAL CELLS	CRYSTALS	CASTS	RBC	WBC				
MALE	3	250	1437021	-	-	-	-	-	1.8	34.5	71.31	15.8 a
			1437022	-	-	-	-	-	3.5	49.2	124.02	56.7
			1437024	-	-	-	-	-	2.1	71.1	95.49	57.3
			1437025	-	2+	-	-	-	1.6	48.9	144.78	53.7
			1437026	-	3+	-	-	-	1.1	152.4	113.37	64.5
			1437027	-	3+	-	-	-	1.2	111.0	211.47	47.1
a : Reanalysis was performed.			N						6	6	6	6
			MEAN						1.88	77.85	126.740	49.18
			S.D.						0.88	45.26	48.456	17.30

APPENDIX F

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL URINALYSIS DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	MICROSCOPIC EXAMINATION					URINE VOLUME (IN GRAMS)	NA (mEq/L)	K (mEq/L)	CL (mEq/L)
				EPITHELIAL CELLS	CRYSTALS	CASTS	RBC	WBC				
MALE	4	800	1437031	-	-	-	-	-	1.6	74.1	129.51	51.0
			1437032	-	1+	-	-	-	0.3	30.0	145.86	47.7
			1437033	-	1+	-	-	-	1.4	84.0	84.18	57.0
			1437034	-	-	-	-	-	0.6	195.9	221.61	88.2
			1437035	-	2+	-	-	-	2.0	44.7	34.41	30.9
			1437036	-	3+	-	-	-	0.8	76.8	194.46	66.9
			N						6	6	6	6
			MEAN						1.12	84.25	135.005	56.95
			S.D.						0.65	58.53	69.117	19.37

APPENDIX F
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL URINALYSIS DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	MICROSCOPIC EXAMINATION					URINE VOLUME (IN GRAMS)	NA (mEq/L)	K (mEq/L)	CL (mEq/L)
				EPITHELIAL CELLS	CRYSTALS	CASTS	RBC	WBC				
FEMALE	5	0	1437041	-	-	-	-	-	0.2	83.1	212.43	32.7
			1437042	-	-	-	-	-	1.1	62.4	68.82	44.4
			1437043	-	-	-	-	-	1.0	55.2	36.66	22.0 a
			1437044	-	-	-	-	-	0.9	56.4	116.10	14.1 a
			1437045	-a	3+a	-a	-a	-a	0.2 a	107.7	169.35	167.1
			1437046	-	-	-	-	-	1.2	32.1	56.73	(9.7) a,b
			N						6	6	6	5
			MEAN						0.77	66.15	110.015	56.06
			S.D.						0.45	26.08	69.230	63.11

a : Reanalysis was performed.
b : Value was under the measuring limit.

APPENDIX F

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL URINALYSIS DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	MICROSCOPIC EXAMINATION					URINE VOLUME (IN GRAMS)	NA (mEq/L)	K (mEq/L)	CL (mEq/L)
				EPITHELIAL CELLS	CRYSTALS	CASTS	RBC	WBC				
FEMALE	6	80	1437051	-	-	-	-	-	1.5	83.1	56.67	21.1 a
			1437052	-	3+	-	-	-	0.8	79.5	70.80	22.6 a
			1437053	-	-	-	-	-	1.6	45.6	55.83	14.6 a
			1437054	-	-	-	-	-	0.7	61.8	51.09	13.7 a
			1437055	-a	-a	-a	-a	-a	0.2 a	11.7 a	204.48	13.2 a
			1437056	-a	3+a	-a	-a	-a	0.1 a	142.2	239.19	193.2
a : Reanalysis was performed.			N						6	6	6	6
			MEAN						0.82	70.65	113.010	46.40
			S.D.						0.63	43.67	85.262	72.03

APPENDIX F

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL URINALYSIS DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	MICROSCOPIC EXAMINATION					URINE VOLUME (IN GRAMS)	NA (mEq/L)	K (mEq/L)	CL (mEq/L)
				EPITHELIAL CELLS	CRYSTALS	CASTS	RBC	WBC				
FEMALE	7	250	1437061	-	-	-	-	-	0.3	48.6	72.90	20.2 a
			1437062	-	-	-	-	-	1.3	38.4	116.55	18.2 a
			1437063	-	-	-	-	-	1.1	37.5	122.46	11.0 a
			1437064	-a	-a	-a	-a	-a	0.3 a	36.0	136.65	17.2 a
			1437065	-	3+	-	-	-	0.2	45.3	75.48	17.8 a
			1437066	-a	-a	-a	-a	-a	0.3 a	148.5	142.68	37.8
a : Reanalysis was performed.			N						6	6	6	6
			MEAN						0.58	59.05	111.120	20.37
			S.D.						0.48	44.09	30.123	9.09

APPENDIX F

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL URINALYSIS DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	MICROSCOPIC EXAMINATION					URINE VOLUME (IN GRAMS)	NA (mEq/L)	K (mEq/L)	CL (mEq/L)
				EPITHELIAL CELLS	CRYSTALS	CASTS	RBC	WBC				
FEMALE	8	800	1437072	-	-	-	-	-	1.1	(8.8) a,b	8.46	11.7 a
			1437073	-	-	-	-	-	0.3	40.5	167.55	15.2 a
			1437074	-	-	-	-	-	0.9	161.1	193.89	72.9
			1437075	-	-	-	-	-	1.2	68.7	86.52	11.7 a
			1437076	-	-	-	-	-	2.5	72.3	109.38	31.2
			1437077	-	-	-	-	-	0.3	84.9	133.80	31.8
			N						6	5	6	6
			MEAN						1.05	85.50	116.600	29.08
			S.D.						0.81	45.27	65.600	23.36

a : Reanalysis was performed.

b : Value was under the measuring limit.

APPENDIX G

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL HEMATOLOGY DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	RBC ($x10^4/\mu L$)	HGB (g/dL)	HCT (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	PLT ($x10^4/\mu L$)	RETICULOCYTE ($x10^4/\mu L$)
MALE	1	0	1437001	858	15.8	42.6	49.7	18.4	37.1	100.6	18.10
			1437002	874	15.3	41.5	47.5	17.5	36.9	111.2	27.62
			1437003	817	14.6	39.4	48.2	17.9	37.1	119.8	24.76
			1437004	850	15.3	41.8	49.2	18.0	36.6	112.8	20.91
			1437005	806	14.7	39.3	48.8	18.2	37.4	92.8	25.95
			1437006	836	15.0	40.1	48.0	17.9	37.4	107.2	24.91
			1437007	806	14.6	40.0	49.6	18.1	36.5	107.1	19.75
			1437008 a	877	15.6	40.8	46.5	17.8	38.2	101.7	23.77
			1437009	824	14.6	39.3	47.7	17.7	37.2	134.3	22.25
			1437010	778	14.5	39.7	51.0	18.6	36.5	111.3	22.64
a : Reanalysis was performed.			N	10	10	10	10	10	10	10	10
			MEAN	832.6	15.00	40.45	48.62	18.01	37.09	109.88	23.066
			S.D.	32.2	0.47	1.17	1.30	0.33	0.52	11.39	2.925

APPENDIX G

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL HEMATOLOGY DATA

STUDY NO [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	WBC ($x10^2/\mu L$)	DIFFERENTIAL LEUCOCYTE COUNT($x10^2/\mu L$)					PT (sec)	APTT (sec)
					LYMPH	NEUT	MONO	EO	BASO		
MALE	1	0	1437001	52.4	39.1	11.2	2.0	0.1	0.0	15.3	17.7
			1437002	70.1	54.4	12.9	2.5	0.3	0.0	11.4	15.3
			1437003	50.2	40.5	7.8	1.3	0.6	0.0	12.1	10.2
			1437004	79.2	65.1	11.6	2.1	0.4	0.0	12.5	17.1
			1437005	72.2	55.1	15.4	1.2	0.5	0.0	10.7	15.3
			1437006	46.6	36.5	8.2	1.4	0.5	0.0	13.8	17.9
			1437007	51.9	33.7	15.9	1.8	0.5	0.0	12.4	17.8
			1437008	91.8 a	71.2 a	15.3 a	3.6 a	1.7 a	0.0 a	11.0	15.1
			1437009	98.0	69.9	23.6	3.9	0.6	0.0	10.8	14.9
			1437010	93.4	68.7	20.9	3.1	0.7	0.0	10.5	15.1
a : Reanalysis was performed.			N	10	10	10	10	10	10	10	10
			MEAN	70.58	53.42	14.28	2.29	0.59	0.00	12.05	15.64
			S.D.	19.64	14.94	5.09	0.96	0.43	0.00	1.54	2.29

APPENDIX G
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HEMATOLOGY DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	RBC ($x10^4/\mu L$)	HGB (g/dL)	HCT (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	PLT ($x10^4/\mu L$)	RETICULOCYTE ($x10^4/\mu L$)
MALE	2	80	1437011	841	15.0	41.2	49.0	17.8	36.4	118.9	24.14
			1437012	843	15.2	41.3	49.0	18.0	36.8	111.8	27.48
			1437013	900	15.7	42.9	47.7	17.4	36.6	108.6	26.37
			1437014	814	14.9	40.7	50.0	18.3	36.6	120.8	24.18
			1437015	811	15.1	40.9	50.4	18.6	36.9	94.8	23.11
			1437016	826	14.6	39.4	47.7	17.7	37.1	88.4	22.22
			1437017	812	14.8	39.1	48.2	18.2	37.9	104.0	29.23
			1437018	787	14.9	40.6	51.6	18.9	36.7	105.0	30.14
			1437019	781	14.2	39.2	50.2	18.2	36.2	117.9	24.29
			1437020	869	15.1	40.0	46.0	17.4	37.8	102.8	22.42
			N	10	10	10	10	10	10	10	10
			MEAN	828.4	14.95	40.53	48.98	18.05	36.90	107.30	25.358
			S.D.	36.4	0.39	1.16	1.64	0.49	0.56	10.55	2.807

APPENDIX G

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL HEMATOLOGY DATA

STUDY NO [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	WBC ($x10^2/\mu L$)	DIFFERENTIAL LEUCOCYTE COUNT($x10^2/\mu L$)					PT (sec)	APTT (sec)
					LYMPH	NEUT	MONO	EO	BASO		
MALE	2	80	1437011	106.7	83.5	19.7	2.5	1.0	0.0	11.4	16.0
			1437012	97.8	73.6	19.9	3.7	0.6	0.0	12.4	16.6
			1437013	100.8	86.6	11.1	2.4	0.7	0.0	12.2	17.6
			1437014	73.1	55.6	15.5	1.5	0.5	0.0	10.9	13.8
			1437015	45.5	33.9	10.0	1.2	0.4	0.0	11.6	15.2
			1437016	50.3	38.0	10.5	1.4	0.4	0.0	10.9	13.8
			1437017	114.7	90.6	18.6	4.6	0.9	0.0	11.1	15.7
			1437018	92.2	68.0	19.8	3.2	1.2	0.0	10.6	16.5
			1437019	96.1	78.5	14.6	2.1	0.9	0.0	11.6	16.3
			1437020	60.9	51.5	7.7	1.2	0.5	0.0	13.3	20.6
			N	10	10	10	10	10	10	10	10
			MEAN	83.81	65.98	14.74	2.38	0.71	0.00	11.60	16.21
			S.D.	24.53	20.24	4.66	1.15	0.28	0.00	0.83	1.95

APPENDIX G

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL HEMATOLOGY DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	RBC ($x10^4/\mu L$)	HGB (g/dL)	HCT (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	PLT ($x10^4/\mu L$)	RETICULOCYTE ($x10^4/\mu L$)
MALE	3	250	1437021	898	15.9	42.5	47.3	17.7	37.4	115.1	28.02
			1437022	849	15.4	41.5	48.9	18.1	37.1	98.0	23.77
			1437023	DEAD	-	-	-	-	-	-	-
			1437024	826	15.2	42.4	51.3	18.4	35.8	85.5	29.16
			1437025	747	14.0	39.1	52.3	18.7	35.8	90.5	25.70
			1437026	857	15.0	40.6	47.4	17.5	36.9	109.9	20.91
			1437027	828	14.2	38.9	47.0	17.1	36.5	119.0	23.35
			1437028	738	13.2	35.9	48.6	17.9	36.8	126.8	23.99
			1437029	846	15.0	40.3	47.6	17.7	37.2	98.2	20.81
			1437030	831	14.1	38.0	45.7	17.0	37.1	120.2	22.27
			N	9	9	9	9	9	9	9	9
			MEAN	824.4	14.67	39.91	48.46	17.79	36.73	107.02	24.220
			S.D.	51.3	0.84	2.16	2.12	0.56	0.59	14.48	2.925

APPENDIX G

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL HEMATOLOGY DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	WBC ($x10^2/\mu L$)	DIFFERENTIAL LEUCOCYTE COUNT($x10^2/\mu L$)					PT (sec)	APTT (sec)
					LYMPH	NEUT	MONO	EO	BASO		
MALE	3	250	1437021	55.2	44.8	8.0	1.9	0.5	0.0	13.8	16.5
			1437022	90.6	68.3	19.0	2.6	0.7	0.0	11.6	11.7
			1437023	-	-	-	-	-	-	-	-
			1437024	61.9	44.4	15.0	2.1	0.4	0.0	11.9	18.0
			1437025	41.4	33.4	6.6	1.0	0.4	0.0	12.2	16.8
			1437026	65.0	53.8	9.2	1.6	0.4	0.0	11.6	17.7
			1437027	63.2	47.8	12.9	1.6	0.9	0.0	12.6	15.6
			1437028	75.4	53.6	18.4	2.8	0.6	0.0	11.0	13.9
			1437029	107.2	87.5	15.7	3.0	1.0	0.0	11.2	12.3
			1437030	79.4	60.3	15.2	2.7	1.2	0.0	11.3	17.2
			N	9	9	9	9	9	9	9	9
			MEAN	71.03	54.88	13.33	2.14	0.68	0.00	11.91	15.52
			S.D.	19.65	15.81	4.48	0.67	0.29	0.00	0.87	2.34

APPENDIX G

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL HEMATOLOGY DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	RBC ($x10^4/\mu L$)	HGB (g/dL)	HCT (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	PLT ($x10^4/\mu L$)	RETICULOCYTE ($x10^4/\mu L$)
MALE	4	800	1437031	834	15.9	44.8	53.7	19.1	35.5	101.0	24.85
			1437032	931	16.2	44.0	47.3	17.4	36.8	113.1	27.84
			1437033	794	15.0	42.4	53.4	18.9	35.4	104.8	27.15
			1437034	850	14.3	38.7	45.5	16.8	37.0	108.3	27.46
			1437035	808	15.3	41.4	51.2	18.9	37.0	108.6	25.05
			1437036	818	14.8	40.0	48.9	18.1	37.0	102.7	24.46
			1437037	860	16.0	44.5	51.7	18.6	36.0	110.9	20.04
			1437038	818	14.8	39.5	48.3	18.1	37.5	97.1	19.80
			1437039 a	857	15.1	41.0	47.8	17.6	36.8	121.6	23.74
			1437040	860	15.5	41.9	48.7	18.0	37.0	102.5	28.98
a : Reanalysis was performed.			N	10	10	10	10	10	10	10	10
			MEAN	843.0	15.29	41.82	49.65	18.15	36.60	107.06	24.937
			S.D.	38.8	0.61	2.12	2.72	0.74	0.71	7.05	3.128

APPENDIX G

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL HEMATOLOGY DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	WBC ($x10^2/\mu L$)	DIFFERENTIAL LEUCOCYTE COUNT($x10^2/\mu L$)					PT (sec)	APTT (sec)
					LYMPH	NEUT	MONO	EO	BASO		
MALE	4	800	1437031	107.3	75.4	26.9	3.6	1.4	0.0	13.1	17.8
			1437032	74.9	53.7	18.3	2.4	0.5	0.0	13.8	17.3
			1437033	100.2	79.9	15.8	3.7	0.8	0.0	11.5	13.3
			1437034	53.1	40.2	10.9	1.3	0.7	0.0	11.6	14.1
			1437035	113.7	94.7	16.1	2.3	0.6	0.0	13.4	18.9
			1437036	62.0	46.6	12.9	1.9	0.6	0.0	12.2	16.0
			1437037	37.8	29.9	6.5	1.0	0.4	0.0	12.1	12.6
			1437038	93.8	71.1	19.4	2.6	0.7	0.0	11.6	17.3
			1437039	115.2 a	72.5 a	37.2 a	4.1 a	1.4 a	0.0 a	12.1	18.0
			1437040	61.3	43.9	14.2	2.5	0.7	0.0	12.8	17.3
a : Reanalysis was performed.			N	10	10	10	10	10	10	10	10
			MEAN	81.93	60.79	17.82	2.54	0.78	0.00	12.42	16.26
			S.D.	27.66	20.78	8.70	1.02	0.35	0.00	0.81	2.17

APPENDIX G
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HEMATOLOGY DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	RBC ($x10^4/\mu L$)	HGB (g/dL)	HCT (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	PLT ($x10^4/\mu L$)	RETICULOCYTE ($x10^4/\mu L$)
FEMALE	5	0	1437041	774	14.6	39.5	51.0	18.9	37.0	119.6	23.22
			1437042	726	13.9	38.1	52.5	19.1	36.5	104.4	20.26
			1437043	764	14.0	38.0	49.7	18.3	36.8	121.4	14.75
			1437044	760	14.6	38.5	50.7	19.2	37.9	87.9	20.29
			1437045	706	14.0	38.6	54.7	19.8	36.3	118.5	20.40
			1437046 a	710	13.3	37.2	52.4	18.7	35.8	61.8	20.80
			1437047	751	14.2	37.5	49.9	18.9	37.9	101.8	18.62
			1437048	698	14.0	37.5	53.7	20.1	37.3	116.5	22.27
			1437049	769	14.1	38.6	50.2	18.3	36.5	104.7	20.69
			1437050	783	14.0	38.2	48.8	17.9	36.6	112.0	22.94
a : Reanalysis was performed.			N	10	10	10	10	10	10	10	10
			MEAN	744.1	14.07	38.17	51.36	18.92	36.86	104.86	20.424
			S.D.	31.3	0.37	0.68	1.90	0.68	0.68	18.30	2.433

APPENDIX G
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HEMATOLOGY DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	WBC ($x10^2/\mu L$)	DIFFERENTIAL LEUCOCYTE COUNT($x10^2/\mu L$)					PT (sec)	APTT (sec)
					LYMPH	NEUT	MONO	EO	BASO		
FEMALE	5	0	1437041	28.2	22.7	4.8	0.3	0.4	0.0	9.4	12.8
			1437042	37.0	27.4	8.3	0.8	0.5	0.0	9.3	14.1
			1437043	25.3	20.0	4.2	0.7	0.4	0.0	9.3	12.6
			1437044	26.3	21.1	4.0	0.6	0.6	0.0	9.6	11.7
			1437045	22.2	19.6	2.0	0.2	0.4	0.0	9.4	12.1
			1437046	24.7 a	19.8 a	3.9 a	0.7 a	0.3 a	0.0 a	9.5	12.1
			1437047	33.8	24.1	8.8	0.6	0.3	0.0	9.5	10.2
			1437048	46.3	38.2	6.5	1.2	0.4	0.0	9.6	12.7
			1437049	32.3	20.9	9.9	1.0	0.5	0.0	9.3	11.3
			1437050	33.9	29.4	3.5	0.7	0.3	0.0	9.3	10.3
a : Reanalysis was performed.			N	10	10	10	10	10	10	10	10
			MEAN	31.00	24.32	5.59	0.68	0.41	0.00	9.42	11.99
			S.D.	7.21	5.91	2.63	0.29	0.10	0.00	0.12	1.18

APPENDIX G
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HEMATOLOGY DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	RBC ($x10^4/\mu L$)	HGB (g/dL)	HCT (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	PLT ($x10^4/\mu L$)	RETICULOCYTE ($x10^4/\mu L$)
FEMALE	6	80	1437051	755	14.5	39.3	52.1	19.2	36.9	105.6	16.69
			1437052 a	798	14.6	39.5	49.5	18.3	37.0	100.0	27.13
			1437053	723	14.0	38.0	52.6	19.4	36.8	107.5	16.63
			1437054	752	14.6	39.7	52.8	19.4	36.8	102.0	23.54
			1437055	730	13.6	36.7	50.3	18.6	37.1	123.4	18.25
			1437056	762	14.6	38.9	51.0	19.2	37.5	115.2	24.00
			1437057	700	14.0	37.6	53.7	20.0	37.2	99.0	14.98
			1437058	702	13.9	37.7	53.7	19.8	36.9	107.1	23.10
			1437059	733	13.9	37.6	51.3	19.0	37.0	119.6	26.68
			1437060	760	13.9	37.7	49.6	18.3	36.9	119.3	17.71
a : Reanalysis was performed.			N	10	10	10	10	10	10	10	10
			MEAN	741.5	14.16	38.27	51.66	19.12	37.01	109.87	20.871
			S.D.	30.0	0.37	1.01	1.56	0.58	0.21	8.84	4.495

APPENDIX G

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL HEMATOLOGY DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	WBC ($x10^2/\mu L$)	DIFFERENTIAL LEUCOCYTE COUNT($x10^2/\mu L$)					PT (sec)	APTT (sec)
					LYMPH	NEUT	MONO	EO	BASO		
FEMALE	6	80	1437051	42.6	30.8	9.7	1.3	0.8	0.0	9.9	14.1
			1437052	85.8 a	71.2 a	11.5 a	1.9 a	1.2 a	0.0 a	10.3	12.4
			1437053	31.5	25.5	4.8	0.8	0.4	0.0	9.3	12.2
			1437054	58.1	49.2	7.2	1.0	0.7	0.0	9.8	15.2
			1437055	46.4	38.8	5.7	1.4	0.5	0.0	9.2	13.8
			1437056	36.4	30.2	5.0	0.7	0.5	0.0	9.3	10.5
			1437057	43.3	29.4	11.8	1.5	0.6	0.0	9.5	12.3
			1437058	24.1	17.0	5.9	0.7	0.5	0.0	9.6	14.3
			1437059	31.0	22.4	6.8	1.2	0.6	0.0	9.5	11.6
			1437060	45.1	36.7	6.6	1.3	0.5	0.0	9.0	10.0
a : Reanalysis was performed.			N	10	10	10	10	10	10	10	10
			MEAN	44.43	35.12	7.50	1.18	0.63	0.00	9.54	12.64
			S.D.	17.42	15.54	2.58	0.39	0.23	0.00	0.38	1.69

APPENDIX G
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HEMATOLOGY DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	RBC ($x10^4/\mu L$)	HGB (g/dL)	HCT (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	PLT ($x10^4/\mu L$)	RETICULOCYTE ($x10^4/\mu L$)
FEMALE	7	250	1437061	733	14.9	39.6	54.0	20.3	37.6	114.6	23.46
			1437062	755	14.3	38.8	51.4	18.9	36.9	111.7	13.59
			1437063	808	14.8	39.6	49.0	18.3	37.4	110.5	11.07
			1437064	709	14.0	38.1	53.7	19.7	36.7	102.8	22.83
			1437065	757	14.6	38.9	51.4	19.3	37.5	105.4	13.55
			1437066	748	15.0	40.6	54.3	20.1	36.9	95.8	18.18
			1437067	757	14.5	39.7	52.4	19.2	36.5	100.7	21.50
			1437068	716	13.6	36.6	51.1	19.0	37.2	100.1	17.69
			1437069	748	14.2	38.4	51.3	19.0	37.0	117.5	17.58
			1437070	714	13.7	38.1	53.4	19.2	36.0	90.2	25.28
			N	10	10	10	10	10	10	10	10
			MEAN	744.5	14.36	38.84	52.20	19.30	36.97	104.93	18.473
			S.D.	29.1	0.49	1.12	1.66	0.59	0.49	8.66	4.758

APPENDIX G

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL HEMATOLOGY DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	WBC ($x10^2/\mu L$)	DIFFERENTIAL LEUCOCYTE COUNT($x10^2/\mu L$)					PT (sec)	APTT (sec)
					LYMPH	NEUT	MONO	EO	BASO		
FEMALE	7	250	1437061	32.8	28.1	3.8	0.5	0.4	0.0	9.7	10.4
			1437062	35.8	27.4	7.0	0.9	0.5	0.0	9.2	12.6
			1437063	24.1	20.3	2.9	0.6	0.3	0.0	9.2	10.2
			1437064	20.4	15.4	4.4	0.4	0.2	0.0	9.9	13.1
			1437065	48.5	42.7	4.6	0.8	0.4	0.0	9.7	13.7
			1437066	39.0	26.9	10.8	1.0	0.3	0.0	9.6	13.7
			1437067	36.6	30.0	6.0	0.3	0.3	0.0	9.3	10.9
			1437068	35.0	30.0	4.1	0.5	0.4	0.0	9.5	10.7
			1437069	57.2	43.1	11.5	1.9	0.7	0.0	9.3	12.0
			1437070	25.0	20.6	3.7	0.5	0.2	0.0	9.7	11.2
			N	10	10	10	10	10	10	10	10
			MEAN	35.44	28.45	5.88	0.74	0.37	0.00	9.51	11.85
			S.D.	11.20	8.97	3.02	0.46	0.15	0.00	0.25	1.35

APPENDIX G

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL HEMATOLOGY DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	RBC ($x10^4/\mu L$)	HGB (g/dL)	HCT (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	PLT ($x10^4/\mu L$)	RETICULOCYTE ($x10^4/\mu L$)
FEMALE	8	800	1437071	DEAD	-	-	-	-	-	-	-
			1437072	793	14.7	39.6	49.9	18.5	37.1	134.4	19.83
			1437073 a	784	14.8	39.9	50.9	18.9	37.1	123.5	17.72
			1437074	764	14.7	39.7	52.0	19.2	37.0	108.3	14.13
			1437075	694	13.7	38.0	54.8	19.7	36.1	97.8	19.85
			1437076	716	13.9	37.3	52.1	19.4	37.3	101.0	15.68
			1437077	783	14.8	40.0	51.1	18.9	37.0	116.4	26.31
			1437078	DEAD	-	-	-	-	-	-	-
			1437079	777	14.9	39.7	51.1	19.2	37.5	107.6	22.22
			1437080	773	13.9	38.2	49.4	18.0	36.4	107.7	15.23
a : Reanalysis was performed.			N	8	8	8	8	8	8	8	8
			MEAN	760.5	14.43	39.05	51.41	18.98	36.94	112.09	18.871
			S.D.	35.8	0.50	1.05	1.65	0.53	0.46	12.12	4.065

APPENDIX G

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL HEMATOLOGY DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	WBC ($x10^2/\mu L$)	DIFFERENTIAL LEUCOCYTE COUNT($x10^2/\mu L$)					PT (sec)	APTT (sec)
					LYMPH	NEUT	MONO	EO	BASO		
FEMALE	8	800	1437071	-	-	-	-	-	-	-	-
			1437072	58.2	53.1	3.8	0.8	0.5	0.0	9.5	13.0
			1437073	39.3 a	29.8 a	6.2 a	2.0 a	1.3 a	0.0 a	9.9	13.6
			1437074	37.3	29.3	6.2	1.2	0.6	0.0	9.4	13.3
			1437075	14.4	9.1	4.6	0.3	0.4	0.0	9.6	13.1
			1437076	19.5	15.1	3.7	0.4	0.3	0.0	9.5	12.0
			1437077	50.6	41.2	7.7	0.7	1.0	0.0	10.0	16.2
			1437078	-	-	-	-	-	-	-	-
			1437079	28.9	23.9	4.3	0.6	0.1	0.0	9.9	11.7
			1437080	43.2	37.3	4.2	1.2	0.5	0.0	9.7	11.0
a : Reanalysis was performed.			N	8	8	8	8	8	8	8	8
			MEAN	36.43	29.85	5.09	0.90	0.59	0.00	9.69	12.99
			S.D.	14.92	14.19	1.44	0.55	0.39	0.00	0.22	1.58

APPENDIX H
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL CLINICAL CHEMISTRY DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	AST (U/L)	ALT (U/L)	ALP (U/L)	γ-GTP (U/L)	T-BIL (mg/dL)	BUN (mg/dL)	CRE (mg/dL)	GLU (mg/dL)	T-CHO (mg/dL)	PL (mg/dL)
MALE	1	0	1437001	81	27	427	0.3	0.04	8.5	0.36	136	45	86
			1437002	129	27	316	0.3	0.05	9.5	0.42	121	36	78
			1437003	93	29	357	0.2	0.04	6.6	0.34	150	40	77
			1437004	78	29	368	0.4	0.05	7.5	0.41	127	60	111
			1437005	110	29	468	0.4	0.05	7.7	0.41	141	52	88
			1437006	92	34	587	0.3	0.04	7.9	0.41	110	51	96
			1437007	129	56	552	0.4	0.06	8.3	0.37	110	57	104
			1437008	78	33	553	0.3	0.07	15.1 a	0.54	132	56	108
			1437009	395 a	170 a	480	0.7	0.06	14.0	0.55 a	112	68	124
			1437010	111	47	420	0.4	0.07	9.6	0.43	126	50	88
a : Reanalysis was performed.			N	10	10	10	10	10	10	10	10	10	10
			MEAN	129.6	48.1	452.8	0.37	0.053	9.47	0.424	126.5	51.5	96.0
			S.D.	95.2	43.9	91.7	0.13	0.012	2.83	0.070	13.6	9.5	15.4

APPENDIX H
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL CLINICAL CHEMISTRY DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	TG (mg/dL)	TP (g/dL)	ALB (g/dL)	A/G	IP (mg/dL)	CA (mg/dL)	MG (mg/dL)	NA (mEq/L)	K (mEq/L)	CL (mEq/L)
MALE	1	0	1437001	63	5.8	2.8	0.93	5.7	9.5	1.8	144.8	4.71	105.6
			1437002	84	6.1	2.8	0.85	5.8	9.9	1.9	147.1	5.04	109.7
			1437003	50	5.8	2.8	0.93	5.4	10.0	1.9	148.6	4.49	115.1
			1437004	89	5.5	2.8	1.04	5.4	9.7	2.2	149.0	4.74	119.1
			1437005	39	5.6	2.8	1.00	4.9	9.4	2.2	148.1	4.59	116.0
			1437006	67	6.0	2.9	0.94	5.7	10.0	2.2	147.4	4.82	111.0
			1437007	44	5.7	2.8	0.97	5.5	9.9	2.2	147.7	4.71	110.2
			1437008	102	5.7	2.7	0.90	5.9	9.9	2.2	148.1	4.28	109.4
			1437009	54	6.0	2.8	0.88	7.1	10.2	2.3	147.5	5.05	108.8
			1437010	31	5.6	2.8	1.00	6.7	9.7	2.2	147.3	4.55	108.9
			N	10	10	10	10	10	10	10	10	10	10
			MEAN	62.3	5.78	2.80	0.944	5.81	9.82	2.11	147.56	4.698	111.38
			S.D.	23.2	0.20	0.05	0.059	0.65	0.24	0.17	1.14	0.238	4.07

APPENDIX H

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL CLINICAL CHEMISTRY DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	AST (U/L)	ALT (U/L)	ALP (U/L)	γ-GTP (U/L)	T-BIL (mg/dL)	BUN (mg/dL)	CRE (mg/dL)	GLU (mg/dL)	T-CHO (mg/dL)	PL (mg/dL)
MALE	2	80	1437011	93	39	758	0.5	0.04	8.5	0.36	134	58	106
			1437012	82	31	763	0.2	0.05	10.1	0.41	144	67	116
			1437013	97	38	446	0.4	0.03	11.7	0.47	120	56	93
			1437014	79	35	603	0.4	0.04	11.3	0.44	147	40	83
			1437015	117	30	494	0.3	0.05	9.3	0.37	120	56	106
			1437016	94	31	563	0.4	0.05	9.3	0.36	119	43	87
			1437017	76	34	337	0.4	0.04	8.7	0.32	126	57	108
			1437018	109	30	418	0.4	0.06	7.9	0.39	99	57	99
			1437019	76	28	231	0.2	0.05	10.3	0.41	138	60	102
			1437020	67	27	428	0.4	0.04	7.5	0.35	153	55	98
			N	10	10	10	10	10	10	10	10	10	10
			MEAN	89.0	32.3	504.1	0.36	0.045	9.46	0.388	130.0	54.9	99.8
			S.D.	15.8	4.1	171.2	0.10	0.008	1.39	0.045	16.3	7.9	10.0

APPENDIX H

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL CLINICAL CHEMISTRY DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	TG (mg/dL)	TP (g/dL)	ALB (g/dL)	A/G	IP (mg/dL)	CA (mg/dL)	MG (mg/dL)	NA (mEq/L)	K (mEq/L)	CL (mEq/L)
MALE	2	80	1437011	72	6.1	2.6	0.74	5.2	9.4	2.0	145.6	4.85	107.1
			1437012	120	5.8	2.8	0.93	5.5	10.0	2.0	146.2	4.85	109.8
			1437013	58	5.6	2.7	0.93	5.8	9.9	2.3	148.1	4.87	115.7
			1437014	77	5.9	2.7	0.84	5.8	10.0	2.2	146.9	4.82	115.9
			1437015	94	5.8	3.0	1.07	5.3	9.9	2.0	148.5	4.79	114.1
			1437016	38	5.6	2.7	0.93	6.1	9.7	2.1	147.8	4.80	112.5
			1437017	98	6.0	2.7	0.82	7.0	10.4	2.0	148.7	4.68	108.1
			1437018	70	5.9	2.8	0.90	6.7	10.0	2.4	148.0	4.60	108.3
			1437019	55	5.6	2.8	1.00	6.7	9.5	2.1	147.9	4.80	109.5
			1437020	35	5.8	2.8	0.93	6.3	10.2	2.2	146.7	5.08	109.5
			N	10	10	10	10	10	10	10	10	10	10
			MEAN	71.7	5.81	2.76	0.909	6.04	9.90	2.13	147.44	4.814	111.05
			S.D.	26.9	0.17	0.11	0.093	0.63	0.30	0.14	1.03	0.125	3.25

APPENDIX H

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL CLINICAL CHEMISTRY DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	AST (U/L)	ALT (U/L)	ALP (U/L)	γ-GTP (U/L)	T-BIL (mg/dL)	BUN (mg/dL)	CRE (mg/dL)	GLU (mg/dL)	T-CHO (mg/dL)	PL (mg/dL)
MALE	3	250	1437021	112	44	584	0.4	0.05	8.1	0.41	114	61	102
			1437022	87	28	325	0.5	0.06	9.6	0.40	129	48	89
			1437023	DEAD	-	-	-	-	-	-	-	-	-
			1437024	97	46	379	0.3	0.06	6.3	0.40	125	54	100
			1437025	170	65	817	0.4	0.05	8.3	0.40	134	51	100
			1437026	120	36	439	0.3	0.06	9.2	0.42	118	41	75
			1437027	79	27	476	0.4 a	0.05	8.5	0.44	136	44	85
			1437028	92	38	394	0.4 a	0.03	9.3	0.42	134	54	99
			1437029	100	56	477	0.4	0.05	8.6	0.39	111	58	103
			1437030	128	41	444	0.7	0.05	8.5	0.41	128	53	94
a : Reanalysis was performed.			N	9	9	9	9	9	9	9	9	9	9
			MEAN	109.4	42.3	481.7	0.42	0.051	8.49	0.410	125.4	51.6	94.1
			S.D.	27.6	12.3	145.3	0.12	0.009	0.96	0.015	9.2	6.4	9.4

APPENDIX H

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL CLINICAL CHEMISTRY DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	TG (mg/dL)	TP (g/dL)	ALB (g/dL)	A/G	IP (mg/dL)	CA (mg/dL)	MG (mg/dL)	NA (mEq/L)	K (mEq/L)	CL (mEq/L)
MALE	3	250	1437021	72	5.7	2.9	1.04	6.1	10.1	1.9	147.4	4.96	109.6
			1437022	73	5.6	2.7	0.93	5.5	10.0	2.0	147.3	4.68	111.7
			1437023	-	-	-	-	-	-	-	-	-	-
			1437024	73	5.6	2.8	1.00	5.7	9.7	2.2	147.3	4.55	116.3
			1437025	60	5.4	2.7	1.00	6.4	9.6	2.1	148.2	4.67	114.0
			1437026	34	5.7	2.8	0.97	5.6	9.5	2.3	149.1	4.66	112.2
			1437027	43	5.6	2.7	0.93	6.3	9.8	2.2	148.5	5.00	110.5
			1437028	81	5.7	2.7	0.90	6.2	9.6	2.2	149.2	4.97	111.6
			1437029	57	5.6	2.6	0.87	6.2	9.6	2.0	146.3	4.75	107.5
			1437030	57	5.2	2.7	1.08	6.5	9.2	2.2	146.1	4.79	107.5
			N	9	9	9	9	9	9	9	9	9	9
			MEAN	61.1	5.57	2.73	0.969	6.06	9.68	2.12	147.71	4.781	111.21
			S.D.	15.4	0.17	0.09	0.068	0.36	0.27	0.13	1.12	0.161	2.87

APPENDIX H
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL CLINICAL CHEMISTRY DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	AST (U/L)	ALT (U/L)	ALP (U/L)	γ-GTP (U/L)	T-BIL (mg/dL)	BUN (mg/dL)	CRE (mg/dL)	GLU (mg/dL)	T-CHO (mg/dL)	PL (mg/dL)
MALE	4	800	1437031	78	48	769	0.2	0.06	5.8	0.38	113	48	100
			1437032	141	43	441	0.3	0.06	8.3	0.41	133	53	99
			1437033	78	31	421	0.4 a	0.05	8.2	0.41	124	52	101
			1437034	102	26	376	0.6	0.06	8.2	0.38	145	48	97
			1437035	94	32	386	0.3	0.07	6.7	0.37	126	41	78
			1437036	88	26	409	0.4	0.05	8.0	0.40	134	46	85
			1437037	62	35	383	0.2	0.05	10.7	0.42	140	63	97
			1437038	105	35	411	0.4	0.06	8.7	0.39	108	53	92
			1437039	69	34	360	0.4	0.04	10.1	0.30	134	54	94
			1437040	81	41	362	0.4	0.06	7.3	0.37	140	45	86
a : Reanalysis was performed.			N	10	10	10	10	10	10	10	10	10	10
			MEAN	89.8	35.1	431.8	0.36	0.056	8.20	0.383	129.7	50.3	92.9
			S.D.	22.6	7.1	121.3	0.12	0.008	1.45	0.034	12.0	6.1	7.6

APPENDIX H
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL CLINICAL CHEMISTRY DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	TG (mg/dL)	TP (g/dL)	ALB (g/dL)	A/G	IP (mg/dL)	CA (mg/dL)	MG (mg/dL)	NA (mEq/L)	K (mEq/L)	CL (mEq/L)
MALE	4	800	1437031	117	5.6	2.8	1.00	5.9	9.9	1.9	146.6	4.56	109.6
			1437032	88	5.4	2.7	1.00	6.0	9.4	2.1	146.1	5.27	113.5
			1437033	92	5.6	2.7	0.93	6.0	9.7	2.4	148.4	4.52	117.4
			1437034	92	5.5	2.8	1.04	5.6	9.6	2.1	146.3	4.89	115.8
			1437035	47	5.6	2.8	1.00	6.9	9.8	2.2	147.7	4.92	112.4
			1437036	51	5.4	2.6	0.93	5.8	9.6	2.1	148.3	4.64	111.9
			1437037	49	5.3	2.9	1.21	6.5	10.0	2.2	149.7	4.38	111.7
			1437038	66	5.7	2.8	0.97	6.7	10.1	2.2	147.1	4.94	109.9
			1437039	87	5.7	2.6	0.84	6.7	10.2	2.1	146.4	4.84	107.5
			1437040	57	5.7	3.0	1.11	5.9	10.0	1.9	146.5	4.48	107.2
			N	10	10	10	10	10	10	10	10	10	10
			MEAN	74.6	5.55	2.77	1.003	6.20	9.83	2.12	147.31	4.744	111.69
			S.D.	23.8	0.14	0.13	0.102	0.45	0.25	0.15	1.18	0.274	3.31

APPENDIX H

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL CLINICAL CHEMISTRY DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	AST (U/L)	ALT (U/L)	ALP (U/L)	γ-GTP (U/L)	T-BIL (mg/dL)	BUN (mg/dL)	CRE (mg/dL)	GLU (mg/dL)	T-CHO (mg/dL)	PL (mg/dL)
FEMALE	5	0	1437041	89	35	201	0.4	0.06	13.9	0.54	110	64	129
			1437042	97	30	247	0.5	0.06	8.3	0.42	117	57	119
			1437043	124 a	38	239	0.4	0.06	7.9	0.45	116	60	133
			1437044	106	31	173	0.6	0.06	8.1	0.41	122	56	112
			1437045	88	33	145	0.4	0.06	9.7	0.42	123	61	113
			1437046	74	32	238	0.3	0.06	9.0	0.43	111	61	129
			1437047	80	42	194	0.5	0.06	8.5	0.39	167	64	115
			1437048	86	31	181	0.4	0.06	12.7	0.39	128	68	132
			1437049	92	28	137	0.4	0.07	8.5	0.43	155	56	110
			1437050	76	27	152	0.4	0.04	9.0	0.51	134	54	109
a : Reanalysis was performed.			N	10	10	10	10	10	10	10	10	10	10
			MEAN	91.2	32.7	190.7	0.43	0.059	9.56	0.439	128.3	60.1	120.1
			S.D.	15.0	4.6	40.5	0.08	0.007	2.06	0.049	18.9	4.4	9.6

APPENDIX H

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL CLINICAL CHEMISTRY DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	TG (mg/dL)	TP (g/dL)	ALB (g/dL)	A/G	IP (mg/dL)	CA (mg/dL)	MG (mg/dL)	NA (mEq/L)	K (mEq/L)	CL (mEq/L)
FEMALE	5	0	1437041	72	6.4	3.4	1.13	4.9	10.2	2.1	142.9	4.19	104.7
			1437042	46	6.2	3.3	1.14	3.8	10.2	2.0	144.2	4.07	109.1
			1437043	85	6.4	3.3	1.06	3.4	10.0	2.3	144.7	3.87	111.5
			1437044	18	6.2	3.2	1.07	3.2	9.8	2.3	144.6	4.05	121.5
			1437045	43	5.5	3.0	1.20	5.5	10.0	2.2	147.9	3.92	119.3
			1437046	49	6.7	3.6	1.16	5.1	10.6	2.2	146.1	4.04	112.6
			1437047	16	6.1	3.1	1.03	5.4	10.4	2.1	144.1	4.36	108.7
			1437048	38	6.9	3.4	0.97	5.7	10.7	2.2	144.8	4.17	104.6
			1437049	35	5.8	3.2	1.23	4.8	9.9	2.3	144.7	4.00	108.2
			1437050	36	6.1	3.2	1.10	5.5	10.2	2.2	144.7	4.33	107.1
			N	10	10	10	10	10	10	10	10	10	10
			MEAN	43.8	6.23	3.27	1.109	4.73	10.20	2.19	144.87	4.100	110.73
			S.D.	21.4	0.41	0.17	0.079	0.93	0.29	0.10	1.32	0.162	5.71

APPENDIX H
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL CLINICAL CHEMISTRY DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	AST (U/L)	ALT (U/L)	ALP (U/L)	γ-GTP (U/L)	T-BIL (mg/dL)	BUN (mg/dL)	CRE (mg/dL)	GLU (mg/dL)	T-CHO (mg/dL)	PL (mg/dL)
FEMALE	6	80	1437051	82	22	115	0.3	0.07	11.2	0.47	124	49	98
			1437052	109	31	345	0.6	0.05	8.4	0.46	150	55	112
			1437053	91 a	39	228	0.3	0.07	11.9	0.41	117	76	162
			1437054	89	22	163	0.4	0.04	11.9	0.49	132	51	103
			1437055	101	27	179	0.4	0.04	11.9	0.55	131	71	142
			1437056	80	30	286	0.3	0.05	10.4	0.41	144	60	129
			1437057	101	26	151	0.5	0.07	11.5	0.48	146	61	113
			1437058	118	38	193	0.5	0.05	11.2	0.39	115	67	149
			1437059	75	30	119	0.5	0.03	9.4	0.39	117	69	134
			1437060	90	27	195	0.3	0.05	11.6	0.47	137	76	148
a : Reanalysis was performed.			N	10	10	10	10	10	10	10	10	10	10
			MEAN	93.6	29.2	197.4	0.41	0.052	10.94	0.452	131.3	63.5	129.0
			S.D.	13.5	5.8	72.4	0.11	0.014	1.19	0.051	12.9	9.8	21.7

APPENDIX H

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL CLINICAL CHEMISTRY DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	TG (mg/dL)	TP (g/dL)	ALB (g/dL)	A/G	IP (mg/dL)	CA (mg/dL)	MG (mg/dL)	NA (mEq/L)	K (mEq/L)	CL (mEq/L)
FEMALE	6	80	1437051	24	6.4	3.4	1.13	4.1	9.9	2.2	141.7	4.22	106.1
			1437052	45	6.1	3.3	1.18	4.2	10.0	2.0	144.7	4.08	108.8
			1437053	63	6.8	3.6	1.12	4.3	10.1	2.2	144.2	4.21	113.6
			1437054	20	5.9	3.1	1.11	4.4	9.9	2.3	144.5	4.11	121.6
			1437055	38	6.2	3.1	1.00	4.7	9.9	2.3	143.0	4.70	114.0
			1437056	43	6.4	3.4	1.13	4.6	10.1	2.2	144.9	3.62	110.9
			1437057	29	6.4	3.2	1.00	5.3	10.2	2.5	142.8	4.39	105.4
			1437058	39	7.0	3.9 a	1.26	5.2	10.6	2.2	146.3	4.34	106.0
			1437059	35	6.4	3.3	1.06	6.3	10.3	2.3	145.2	4.44	105.8
			1437060	64	6.2	3.3	1.14	5.7	10.4	2.2	145.1	4.10	106.7
a : Reanalysis was performed.			N	10	10	10	10	10	10	10	10	10	10
			MEAN	40.0	6.38	3.36	1.113	4.88	10.14	2.24	144.24	4.221	109.89
			S.D.	14.7	0.32	0.24	0.079	0.72	0.24	0.13	1.36	0.284	5.23

APPENDIX H

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL CLINICAL CHEMISTRY DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	AST (U/L)	ALT (U/L)	ALP (U/L)	γ-GTP (U/L)	T-BIL (mg/dL)	BUN (mg/dL)	CRE (mg/dL)	GLU (mg/dL)	T-CHO (mg/dL)	PL (mg/dL)
FEMALE	7	250	1437061	108	35	278	0.5	0.05	10.1	0.50	106	59	122
			1437062	110	27	458 a	0.6	0.07	7.6	0.43	114	62	122
			1437063	84	27	205	0.7	0.06	9.9	0.47	121	61	110
			1437064	87	26	226	0.4 a	0.05	9.3	0.43	122	53	116
			1437065	84	23	264	0.5	0.06	13.0	0.59	114	46	99
			1437066	75	19	152	0.6	0.06	10.4	0.47	147	49	106
			1437067	81	23	150	0.4	0.04	9.2	0.46	120	57	115
			1437068	85	21	184	0.3	0.06	10.1	0.44	132	56	114
			1437069	95	23	152	0.5	0.07	9.5	0.43	133	51	103
			1437070	58	24	169	0.4	0.05	9.1	0.37	135	56	118
a : Reanalysis was performed.			N	10	10	10	10	10	10	10	10	10	10
			MEAN	86.7	24.8	223.8	0.49	0.057	9.82	0.459	124.4	55.0	112.5
			S.D.	15.2	4.4	94.3	0.12	0.009	1.37	0.058	12.2	5.2	7.8

APPENDIX H

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL CLINICAL CHEMISTRY DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	TG (mg/dL)	TP (g/dL)	ALB (g/dL)	A/G	IP (mg/dL)	CA (mg/dL)	MG (mg/dL)	NA (mEq/L)	K (mEq/L)	CL (mEq/L)
FEMALE	7	250	1437061	43	6.2	3.3	1.14	4.3	10.2	2.1	144.8	4.25	108.4
			1437062	19	6.5	3.3	1.03	3.9	10.1	2.2	143.6	4.09	108.4
			1437063	11	6.5	3.4	1.10	4.2	10.4	2.4	145.0	3.86	117.3
			1437064	65	6.2	3.4	1.21	4.2	10.2	2.0	145.4	3.92	120.2
			1437065	21	6.2	3.3	1.14	4.7	10.0	2.3	144.0	4.27	113.8
			1437066	33	6.4	3.4	1.13	5.2	10.3	2.2	145.2	3.82	110.6
			1437067	20	6.4	3.4	1.13	4.9	10.1	2.3	144.2	3.87	107.2
			1437068	22	6.4	3.4	1.13	5.5	9.8	2.4	146.5	4.10	107.1
			1437069	28	6.5	3.3	1.03	6.4	10.3	2.5	143.4	4.31	103.6
			1437070	30	6.5	3.5	1.17	5.5	10.4	2.3	146.5	4.17	108.5
			N	10	10	10	10	10	10	10	10	10	10
			MEAN	29.2	6.38	3.37	1.121	4.88	10.18	2.27	144.86	4.066	110.51
			S.D.	15.4	0.13	0.07	0.056	0.78	0.19	0.15	1.09	0.186	5.10

APPENDIX H

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL CLINICAL CHEMISTRY DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	AST (U/L)	ALT (U/L)	ALP (U/L)	γ-GTP (U/L)	T-BIL (mg/dL)	BUN (mg/dL)	CRE (mg/dL)	GLU (mg/dL)	T-CHO (mg/dL)	PL (mg/dL)
FEMALE	8	800	1437071	DEAD	-	-	-	-	-	-	-	-	-
			1437072	93	39	226	0.3	0.07	10.6	0.41	104	62	136
			1437073	91	22	238	0.4	0.06	14.7	0.48	116	42	97
			1437074	76	25	215	0.4	0.05	12.0	0.37	126	56	114
			1437075	89	15	155	0.5	0.03	12.2	0.42	132	46	101
			1437076	82	25	249	0.4	0.06	15.8	0.47	129	57	119
			1437077	65	22	168	0.2	0.05	10.9	0.44	130	63	121
			1437078	DEAD	-	-	-	-	-	-	-	-	-
			1437079	78	34	140	0.4	0.06	13.0	0.39	140	81	147
			1437080	69	27	266	0.3	0.05	9.5	0.39	123	59	119
			N	8	8	8	8	8	8	8	8	8	8
			MEAN	80.4	26.1	207.1	0.36	0.054	12.34	0.421	125.0	58.3	119.3
			S.D.	10.3	7.5	46.8	0.09	0.012	2.11	0.039	11.0	11.8	16.5

APPENDIX H

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL CLINICAL CHEMISTRY DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	TG (mg/dL)	TP (g/dL)	ALB (g/dL)	A/G	IP (mg/dL)	CA (mg/dL)	MG (mg/dL)	NA (mEq/L)	K (mEq/L)	CL (mEq/L)
FEMALE	8	800	1437071	-	-	-	-	-	-	-	-	-	-
			1437072	33	6.6	3.5	1.13	4.4	10.0	2.4	144.7	4.43	109.3
			1437073	14	6.2	3.2	1.07	5.6	9.7	2.4	145.7	4.42	120.4
			1437074	28	6.6	3.6	1.20	5.1	10.6	2.5	144.5	4.32	117.2
			1437075	20	5.8	3.2	1.23	5.5	9.8	2.4	145.4	4.23	114.4
			1437076	30	5.9	3.1	1.11	4.6	10.0	2.2	143.4	3.93	108.5
			1437077	13	6.2	3.5	1.30	4.6	10.1	2.2	145.8	3.84	109.4
			1437078	-	-	-	-	-	-	-	-	-	-
			1437079	43	6.2	3.1	1.00	5.8	10.3	2.3	145.2	4.42	105.4
			1437080	36	5.7	3.0	1.11	5.5	10.1	2.3	146.6	3.94	108.1
			N	8	8	8	8	8	8	8	8	8	8
			MEAN	27.1	6.15	3.28	1.144	5.14	10.08	2.34	145.16	4.191	111.59
			S.D.	10.7	0.34	0.23	0.095	0.54	0.28	0.11	0.97	0.249	5.17

APPENDIX I

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GROSS PATHOLOGY DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	GROSS PATHOLOGICAL FINDINGS	
MALE	1	0	1437001	Not remarkable	
			1437002	Not remarkable	
			1437003	Not remarkable	
			1437004	Spleen	: Cyst/Single
			1437005	Not remarkable	
			1437006	Not remarkable	
			1437007	Not remarkable	
			1437008	Not remarkable	
			1437009	Not remarkable	
			1437010	Not remarkable	

APPENDIX I

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GROSS PATHOLOGY DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	GROSS PATHOLOGICAL FINDINGS
MALE	2	80	1437011	Not remarkable
			1437012	Not remarkable
			1437013	Not remarkable
			1437014	Not remarkable
			1437015	Not remarkable
			1437016	Not remarkable
			1437017	Not remarkable
			1437018	Not remarkable
			1437019	Not remarkable
			1437020	Not remarkable

APPENDIX I

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GROSS PATHOLOGY DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	GROSS PATHOLOGICAL FINDINGS	
MALE	3	250	1437021	Not remarkable	
			1437022	Not remarkable	
			1437023 a,b	Lung	: Discolored
			1437024	Not remarkable	
			1437025	Not remarkable	
			1437026	Not remarkable	
			1437027	Not remarkable	
			1437028	Abdominal fat	: Nodule/Single
			1437029	Not remarkable	
			1437030	Not remarkable	

a : Died during the study.

b : Data was omitted from the evaluation and not reflected to TABLE 10.

APPENDIX I
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL GROSS PATHOLOGY DATA
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	GROSS PATHOLOGICAL FINDINGS	
MALE	4	800	1437031	Not remarkable	
			1437032	Not remarkable	
			1437033	Not remarkable	
			1437034	Liver	: Small
					: Discolored area/Single
				Testis	: Small/Bilateral
				Epididymis	: Small/Bilateral
			1437035	Not remarkable	
			1437036	Not remarkable	
			1437037	Not remarkable	
			1437038	Not remarkable	
			1437039	Not remarkable	
			1437040	Not remarkable	

APPENDIX I

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GROSS PATHOLOGY DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	GROSS PATHOLOGICAL FINDINGS	
FEMALE	5	0	1437041	Not remarkable	
			1437042	Liver	: Discolored area/Single
			1437043	Not remarkable	
			1437044	Not remarkable	
			1437045	Not remarkable	
			1437046	Ovary	: Cyst/Unilateral
			1437047	Not remarkable	
			1437048	Not remarkable	
			1437049	Not remarkable	
			1437050	Ovary	: Cyst/Unilateral

APPENDIX I

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GROSS PATHOLOGY DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	GROSS PATHOLOGICAL FINDINGS
FEMALE	6	80	1437051	Not remarkable
			1437052	Not remarkable
			1437053	Not remarkable
			1437054	Not remarkable
			1437055	Not remarkable
			1437056	Not remarkable
			1437057	Not remarkable
			1437058	Not remarkable
			1437059	Not remarkable
			1437060	Not remarkable

APPENDIX I

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GROSS PATHOLOGY DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	GROSS PATHOLOGICAL FINDINGS	
FEMALE	7	250	1437061	Not remarkable	
			1437062	Thymus	: Discolored/Red
			1437063	Not remarkable	
			1437064	Liver	: Diaphragmatic nodule
			1437065	Pituitary	: Discolored spot/Single
			1437066	Not remarkable	
			1437067	Not remarkable	
			1437068	Not remarkable	
			1437069	Not remarkable	
			1437070	Not remarkable	

APPENDIX I

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL GROSS PATHOLOGY DATA

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	GROSS PATHOLOGICAL FINDINGS	
FEMALE	8	800	1437071 a	Spleen	: Small
				Stomach~Cecum	: Contained gas
			1437072	Not remarkable	
			1437073	Not remarkable	
			1437074	Not remarkable	
			1437075	Not remarkable	
			1437076	Not remarkable	
			1437077	Uterus	: Dilatation/Horn/Bilateral
			1437078 a	Stomach	: Dilatation
			1437079	Not remarkable	
			1437080	Not remarkable	

a : Died during the study.

APPENDIX J

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL ORGAN WEIGHT DATA (G)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Body[a] weight	Brain	Pituitary	Thyroids	Lungs	Heart	Thymus	Liver	Kidneys
MALE	1	0	1437001	476	2.068	0.011	0.016	1.231	1.379	0.222	11.333	2.756
			1437002	621	2.046	0.014	0.028	1.423	1.648	0.290	16.605	2.521
			1437003	565	2.188	0.011	0.022	1.453	1.554	0.163	13.808	3.010
			1437004	536	2.321	0.011	0.023	1.377	1.396	0.383	12.426	2.967
			1437005	619	2.353	0.014	0.023	1.531	1.835	0.319	15.462	3.336
			1437006	582	2.018	0.011	0.017	1.510	1.612	0.195	13.305	2.668
			1437007	553	2.337	0.012	0.018	1.362	1.382	0.198	12.844	3.025
			1437008	571	2.377	0.010	0.023	1.619	1.654	0.298	14.380	3.135
			1437009	622	2.219	0.012	0.021	1.677	1.626	0.292	15.737	3.123
			1437010	570	2.388	0.014	0.027	1.592	1.771	0.317	14.392	3.358
			N	10	10	10	10	10	10	10	10	10
			MEAN	571.5	2.2315	0.0120	0.0218	1.4775	1.5857	0.2677	14.0292	2.9899
			S.D.	44.9	0.1447	0.0015	0.0040	0.1352	0.1594	0.0696	1.6220	0.2737

a : The value presented was obtained after the animal was fasted overnight.

APPENDIX J

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL ORGAN WEIGHT DATA (G)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Spleen	Adrenals	Salivary glands	Testes	Seminal vesicles	Prostate
MALE	1	0	1437001	0.518	0.049	0.679	3.170	1.458	2.116
			1437002	0.845	0.047	0.581	3.463	1.120	1.300
			1437003	0.619	0.048	0.516	3.674	1.212	1.921
			1437004	0.582	0.041	0.835	3.753	1.240	1.716
			1437005	0.767	0.066	0.814	3.514	1.383	1.923
			1437006	0.551	0.055	0.571	3.773	1.173	1.308
			1437007	0.539	0.049	0.642	3.317	1.236	1.630
			1437008	0.752	0.057	0.733	3.253	1.185	1.658
			1437009	0.744	0.051	0.888	3.611	1.504	1.843
			1437010	0.624	0.047	0.731	3.485	1.378	1.198
			N	10	10	10	10	10	10
			MEAN	0.6541	0.0510	0.6990	3.5013	1.2889	1.6613
			S.D.	0.1138	0.0069	0.1234	0.2072	0.1315	0.3073

APPENDIX J

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL ORGAN WEIGHT DATA (G)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Body[a] weight	Brain	Pituitary	Thyroids	Lungs	Heart	Thymus	Liver	Kidneys
MALE	2	80	1437011	639	2.067	0.013	0.027	1.660	1.692	0.306	17.249	3.385
			1437012	613	2.331	0.010	0.021	1.605	1.970	0.262	15.999	3.117
			1437013	548	2.045	0.011	0.027	1.496	1.800	0.323	12.669	2.976
			1437014	566	2.319	0.013	0.017	1.578	1.693	0.306	14.322	3.143
			1437015	510	2.146	0.011	0.019	1.256	1.350	0.236	11.833	2.716
			1437016	402	2.076	0.010	0.020	1.204	1.230	0.192	9.293	2.354
			1437017	721	2.188	0.014	0.025	1.535	1.634	0.310	20.231	3.515
			1437018	680	2.247	0.013	0.023	1.735	1.736	0.330	19.017	3.647
			1437019	608	2.292	0.013	0.024	1.514	1.654	0.340	15.157	3.407
			1437020	555	2.257	0.013	0.025	1.498	1.728	0.228	14.348	3.679
			N	10	10	10	10	10	10	10	10	10
			MEAN	584.2	2.1968	0.0121	0.0228	1.5081	1.6487	0.2833	15.0118	3.1939
			S.D.	90.4	0.1082	0.0014	0.0034	0.1653	0.2131	0.0503	3.3082	0.4237

a : The value presented was obtained after the animal was fasted overnight.

APPENDIX J

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL ORGAN WEIGHT DATA (G)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Spleen	Adrenals	Salivary glands	Testes	Seminal vesicles	Prostate
MALE	2	80	1437011	0.752	0.055	0.670	3.551	1.127	1.392
			1437012	0.681	0.052	0.871	3.151	1.469	2.127
			1437013	0.692	0.055	0.876	3.340	1.234	1.760
			1437014	0.647	0.063	0.857	3.668	1.412	2.065
			1437015	0.503	0.039	0.601	3.087	1.200	1.448
			1437016	0.408	0.052	0.572	3.287	1.023	1.618
			1437017	0.849	0.041	0.707	2.979	1.164	1.612
			1437018	0.814	0.072	0.906	3.662	1.595	1.887
			1437019	0.703	0.044	0.818	3.671	1.430	2.237
			1437020	0.743	0.060	0.735	4.133	1.332	1.546
			N	10	10	10	10	10	10
			MEAN	0.6792	0.0533	0.7613	3.4529	1.2986	1.7692
			S.D.	0.1345	0.0102	0.1211	0.3495	0.1781	0.2965

APPENDIX J

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL ORGAN WEIGHT DATA (G)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Body[a] weight	Brain	Pituitary	Thyroids	Lungs	Heart	Thymus	Liver	Kidneys
MALE	3	250	1437021	629	2.231	0.012	0.016	1.358	1.683	0.253	15.664	2.959
			1437022	641	2.139	0.011	0.026	1.431	1.647	0.320	15.070	3.219
			1437023	DEAD	-	-	-	-	-	-	-	-
			1437024	510	2.093	0.010	0.028	1.391	1.398	0.201	11.578	2.675
			1437025	599	2.290	0.014	0.020	1.719	1.639	0.228	14.139	3.160
			1437026	551	2.174	0.011	0.019	1.546	1.633	0.321	13.750	2.839
			1437027	684	2.187	0.016	0.029	1.435	1.889	0.261	16.949	3.482
			1437028	691	2.200	0.012	0.027	1.547	1.760	0.176	16.339	3.045
			1437029	612	2.259	0.013	0.019	1.417	1.458	0.215	13.696	3.214
			1437030	511	2.021	0.012	0.019	1.219	1.375	0.330	12.029	2.437
			N	9	9	9	9	9	9	9	9	9
			MEAN	603.1	2.1771	0.0123	0.0226	1.4514	1.6091	0.2561	14.3571	3.0033
			S.D.	67.4	0.0836	0.0018	0.0049	0.1405	0.1702	0.0567	1.8323	0.3170

a : The value presented was obtained after the animal was fasted overnight.

APPENDIX J

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL ORGAN WEIGHT DATA (G)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Spleen	Adrenals	Salivary glands	Testes	Seminal vesicles	Prostate
MALE	3	250	1437021	0.554	0.060	0.583	3.552	0.958	1.338
			1437022	0.632	0.044	0.799	3.798	1.237	1.624
			1437023	-	-	-	-	-	-
			1437024	0.556	0.046	0.637	3.473	1.133	1.593
			1437025	0.609	0.056	0.683	3.575	1.321	2.132
			1437026	0.655	0.065	0.726	3.268	1.174	1.982
			1437027	0.803	0.058	0.822	3.556	1.393	2.119
			1437028	0.743	0.046	0.679	3.466	1.392	1.678
			1437029	0.604	0.050	0.757	3.136	1.345	1.632
			1437030	0.492	0.049	0.680	3.122	1.340	1.874
			N	9	9	9	9	9	9
			MEAN	0.6276	0.0527	0.7073	3.4384	1.2548	1.7747
			S.D.	0.0966	0.0073	0.0766	0.2228	0.1447	0.2681

APPENDIX J

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL ORGAN WEIGHT DATA (G)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Body[a] weight	Brain	Pituitary	Thyroids	Lungs	Heart	Thymus	Liver	Kidneys
MALE	4	800	1437031	666	2.038	0.013	0.018	1.425	1.521	0.226	14.477	3.058
			1437032	557	2.173	0.011	0.024	1.352	1.381	0.310	12.345	2.586
			1437033	617	2.237	0.012	0.020	1.554	1.757	0.255	17.684	3.245
			1437034	600	2.056	0.011	0.031	1.283	1.328	0.230	13.050	2.830
			1437035	615	2.262	0.011	0.018	1.530	1.745	0.225	13.829	3.275
			1437036	513	2.206	0.012	0.023	1.297	1.415	0.205	12.382	2.776
			1437037	567	2.184	0.013	0.023	1.368	1.634	0.304	13.435	2.789
			1437038	591	2.161	0.013	0.024	1.451	1.584	0.173	15.543	3.144
			1437039	646	2.250	0.012	0.021	1.446	1.554	0.414	15.985	3.388
			1437040	557	2.208	0.014	0.030	1.445	1.599	0.200	13.511	3.132
			N	10	10	10	10	10	10	10	10	10
			MEAN	592.9	2.1775	0.0122	0.0232	1.4151	1.5518	0.2542	14.2241	3.0223
			S.D.	45.8	0.0762	0.0010	0.0044	0.0903	0.1447	0.0710	1.7148	0.2620

a : The value presented was obtained after the animal was fasted overnight.

APPENDIX J

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL ORGAN WEIGHT DATA (G)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Spleen	Adrenals	Salivary glands	Testes	Seminal vesicles	Prostate
MALE	4	800	1437031	0.663	0.055	0.551	2.955	0.877	1.504
			1437032	0.629	0.044	0.625	2.900	1.118	2.138
			1437033	0.913	0.055	0.845	3.378	1.631	2.238
			1437034	0.582	0.029	0.631	0.702	0.942	1.449
			1437035	0.674	0.061	0.638	3.606	1.343	1.970
			1437036	0.502	0.060	0.560	3.657	1.149	1.436
			1437037	0.552	0.058	0.713	4.112	1.346	1.843
			1437038	0.686	0.043	0.656	3.240	1.298	1.767
			1437039	0.727	0.063	0.751	3.659	1.048	1.390
			1437040	0.684	0.061	0.677	3.085	1.306	1.841
			N	10	10	10	10	10	10
			MEAN	0.6612	0.0529	0.6647	3.1294	1.2058	1.7576
			S.D.	0.1124	0.0109	0.0881	0.9311	0.2239	0.3042

APPENDIX J

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL ORGAN WEIGHT DATA (G)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Body[a] weight	Brain	Pituitary	Thyroids	Lungs	Heart	Thymus	Liver	Kidneys
FEMALE	5	0	1437041	325	2.038	0.015	0.030	1.022	0.895	0.218	7.645	1.827
			1437042	321	1.992	0.015	0.018	1.042	1.006	0.183	7.612	1.694
			1437043	299	2.051	0.016	0.016	1.034	0.951	0.203	7.718	1.565
			1437044	288	2.083	0.015	0.015	1.077	0.907	0.280	6.438	1.604
			1437045	275	2.103	0.013	0.019	1.167	0.977	0.309	7.157	1.562
			1437046	338	1.935	0.018	0.017	1.084	1.059	0.261	7.780	1.729
			1437047	375	2.125	0.018	0.020	1.215	1.109	0.334	9.507	2.040
			1437048	308	2.038	0.016	0.015	1.114	1.053	0.261	8.311	1.728
			1437049	362	1.917	0.014	0.014	1.100	1.098	0.234	8.712	1.851
			1437050	370	1.968	0.015	0.022	1.195	1.019	0.279	9.582	2.037
			N	10	10	10	10	10	10	10	10	10
			MEAN	326.1	2.0250	0.0155	0.0186	1.1050	1.0074	0.2562	8.0462	1.7637
			S.D.	34.8	0.0704	0.0016	0.0047	0.0677	0.0747	0.0473	0.9950	0.1750

a : The value presented was obtained after the animal was fasted overnight.

APPENDIX J

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL ORGAN WEIGHT DATA (G)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Spleen	Adrenals	Salivary glands	Ovaries	Uterus
FEMALE	5	0	1437041	0.350	0.053	0.482	0.114	0.723
			1437042	0.447	0.049	0.388	0.124	0.692
			1437043	0.408	0.056	0.390	0.111	0.488
			1437044	0.583	0.073	0.464	0.112	0.401
			1437045	0.512	0.056	0.460	0.108	0.878
			1437046	0.386	0.053	0.430	0.110	0.604
			1437047	0.619	0.074	0.472	0.124	1.032
			1437048	0.514	0.065	0.440	0.106	0.467
			1437049	0.546	0.073	0.494	0.122	0.628
			1437050	0.651	0.058	0.572	0.198	0.659
			N	10	10	10	10	10
			MEAN	0.5016	0.0610	0.4592	0.1229	0.6572
			S.D.	0.1017	0.0095	0.0535	0.0272	0.1912

APPENDIX J

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL ORGAN WEIGHT DATA (G)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Body[a] weight	Brain	Pituitary	Thyroids	Lungs	Heart	Thymus	Liver	Kidneys
FEMALE	6	80	1437051	289	2.066	0.013	0.016	1.031	0.894	0.245	6.883	1.515
			1437052	335	2.087	0.014	0.011	1.070	0.991	0.195	6.898	1.565
			1437053	325	2.063	0.020	0.018	1.183	1.063	0.252	8.791	1.942
			1437054	248	1.907	0.015	0.015	0.971	0.784	0.253	5.788	1.548
			1437055	358	2.103	0.017	0.021	1.101	1.036	0.253	8.082	2.059
			1437056	291	2.031	0.014	0.014	0.989	0.768	0.233	7.162	1.591
			1437057	373	1.945	0.024	0.021	1.155	1.100	0.216	9.496	2.121
			1437058	286	1.901	0.016	0.013	0.931	0.954	0.173	7.605	1.790
			1437059	318	2.046	0.015	0.020	1.052	1.002	0.229	8.199	2.048
			1437060	343	2.027	0.016	0.030	1.135	1.045	0.256	9.221	1.674
			N	10	10	10	10	10	10	10	10	10
			MEAN	316.6	2.0176	0.0164	0.0179	1.0618	0.9637	0.2305	7.8125	1.7853
			S.D.	38.1	0.0735	0.0033	0.0055	0.0830	0.1145	0.0281	1.1673	0.2379

a : The value presented was obtained after the animal was fasted overnight.

APPENDIX J
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL ORGAN WEIGHT DATA (G)
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Spleen	Adrenals	Salivary glands	Ovaries	Uterus
FEMALE	6	80	1437051	0.376	0.051	0.394	0.115	0.371
			1437052	0.547	0.062	0.404	0.097	0.534
			1437053	0.551	0.063	0.440	0.092	0.688
			1437054	0.455	0.049	0.404	0.080	0.467
			1437055	0.497	0.053	0.476	0.077	0.770
			1437056	0.404	0.060	0.446	0.094	0.946
			1437057	0.691	0.074	0.501	0.120	0.484
			1437058	0.391	0.052	0.365	0.048	0.614
			1437059	0.398	0.082	0.456	0.130	0.818
			1437060	0.565	0.061	0.518	0.117	0.498
			N	10	10	10	10	10
			MEAN	0.4875	0.0607	0.4404	0.0970	0.6190
			S.D.	0.1016	0.0106	0.0491	0.0246	0.1822

APPENDIX J

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL ORGAN WEIGHT DATA (G)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Body[a] weight	Brain	Pituitary	Thyroids	Lungs	Heart	Thymus	Liver	Kidneys
FEMALE	7	250	1437061	272	1.908	0.014	0.019	0.999	0.812	0.216	6.357	1.459
			1437062	289	2.034	0.017	0.015	0.978	0.864	0.174	6.748	1.582
			1437063	300	2.175	0.021	0.021	1.108	0.960	0.243	7.670	1.752
			1437064	338	1.973	0.016	0.018	1.156	0.976	0.294	7.691	1.925
			1437065	267	2.088	0.016	0.019	1.003	0.929	0.298	6.858	1.643
			1437066	306	2.046	0.018	0.024	1.113	0.919	0.170	7.602	1.667
			1437067	284	2.084	0.013	0.016	1.067	0.858	0.280	6.680	1.495
			1437068	318	2.065	0.016	0.015	1.150	0.954	0.220	8.123	1.761
			1437069	332	2.025	0.017	0.022	1.222	0.960	0.265	8.312	1.869
			1437070	307	2.115	0.018	0.016	1.023	0.912	0.197	7.551	1.934
			N	10	10	10	10	10	10	10	10	10
			MEAN	301.3	2.0513	0.0166	0.0185	1.0819	0.9144	0.2357	7.3592	1.7087
			S.D.	23.8	0.0743	0.0022	0.0031	0.0810	0.0537	0.0476	0.6569	0.1693

a : The value presented was obtained after the animal was fasted overnight.

APPENDIX J

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL ORGAN WEIGHT DATA (G)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Spleen	Adrenals	Salivary glands	Ovaries	Uterus
FEMALE	7	250	1437061	0.391	0.039	0.361	0.104	0.522
			1437062	0.352	0.051	0.374	0.098	0.442
			1437063	0.474	0.068	0.478	0.118	0.722
			1437064	0.468	0.055	0.407	0.127	0.918
			1437065	0.489	0.068	0.408	0.107	0.324
			1437066	0.463	0.078	0.428	0.108	0.606
			1437067	0.405	0.051	0.437	0.103	0.356
			1437068	0.560	0.062	0.436	0.111	0.497
			1437069	0.519	0.059	0.398	0.124	0.443
			1437070	0.503	0.058	0.469	0.113	0.810
			N	10	10	10	10	10
			MEAN	0.4624	0.0589	0.4196	0.1113	0.5640
			S.D.	0.0631	0.0109	0.0377	0.0093	0.1970

APPENDIX J

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL ORGAN WEIGHT DATA (G)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Body[a] weight	Brain	Pituitary	Thyroids	Lungs	Heart	Thymus	Liver	Kidneys
FEMALE	8	800	1437071	DEAD	-	-	-	-	-	-	-	-
			1437072	312	1.999	0.015	0.017	1.111	0.895	0.254	7.440	1.940
			1437073	251	1.964	0.016	0.013	1.025	0.839	0.295	5.562	1.714
			1437074	316	1.994	0.015	0.015	1.095	1.026	0.326	8.319	2.077
			1437075	275	1.921	0.019	0.016	1.023	0.930	0.265	7.307	1.740
			1437076	329	1.996	0.020	0.017	1.096	0.993	0.170	7.656	1.891
			1437077	270	1.994	0.014	0.020	0.953	0.762	0.290	6.134	1.461
			1437078	DEAD	-	-	-	-	-	-	-	-
			1437079	327	2.119	0.017	0.020	1.175	1.081	0.383	7.691	1.755
			1437080	284	1.837	0.014	0.016	1.053	0.946	0.211	7.285	1.745
			N	8	8	8	8	8	8	8	8	8
			MEAN	295.5	1.9780	0.0163	0.0168	1.0664	0.9340	0.2743	7.1743	1.7904
			S.D.	29.3	0.0797	0.0023	0.0024	0.0677	0.1027	0.0661	0.8938	0.1832

a : The value presented was obtained after the animal was fasted overnight.

APPENDIX J

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL ORGAN WEIGHT DATA (G)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Spleen	Adrenals	Salivary glands	Ovaries	Uterus
FEMALE	8	800	1437071	-	-	-	-	-
			1437072	0.442	0.065	0.423	0.110	0.711
			1437073	0.402	0.047	0.419	0.111	0.415
			1437074	0.574	0.063	0.529	0.139	0.452
			1437075	0.432	0.075	0.406	0.117	0.595
			1437076	0.360	0.048	0.430	0.097	0.668
			1437077	0.459	0.056	0.377	0.089	0.805
			1437078	-	-	-	-	-
			1437079	0.541	0.069	0.514	0.100	0.746
			1437080	0.434	0.053	0.406	0.104	0.418
			N	8	8	8	8	8
			MEAN	0.4555	0.0595	0.4380	0.1084	0.6013
			S.D.	0.0702	0.0101	0.0541	0.0152	0.1556

APPENDIX K

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL ORGAN TO BODY WEIGHT RATIO DATA (G/100G BW)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Brain	Pituitary	Thyroids	Lungs	Heart	Thymus	Liver	Kidneys
MALE	1	0	1437001	0.434	0.002	0.003	0.259	0.290	0.047	2.381	0.579
			1437002	0.329	0.002	0.005	0.229	0.265	0.047	2.674	0.406
			1437003	0.387	0.002	0.004	0.257	0.275	0.029	2.444	0.533
			1437004	0.433	0.002	0.004	0.257	0.260	0.071	2.318	0.554
			1437005	0.380	0.002	0.004	0.247	0.296	0.052	2.498	0.539
			1437006	0.347	0.002	0.003	0.259	0.277	0.034	2.286	0.458
			1437007	0.423	0.002	0.003	0.246	0.250	0.036	2.323	0.547
			1437008	0.416	0.002	0.004	0.284	0.290	0.052	2.518	0.549
			1437009	0.357	0.002	0.003	0.270	0.261	0.047	2.530	0.502
			1437010	0.419	0.002	0.005	0.279	0.311	0.056	2.525	0.589
			N	10	10	10	10	10	10	10	10
			MEAN	0.3925	0.0020	0.0038	0.2587	0.2775	0.0471	2.4497	0.5256
			S.D.	0.0381	0.0000	0.0008	0.0162	0.0191	0.0121	0.1222	0.0561

APPENDIX K
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL ORGAN TO BODY WEIGHT RATIO DATA (G/100G BW)
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Spleen	Adrenals	Salivary glands	Testes	Seminal vesicles	Prostate
MALE	1	0	1437001	0.109	0.010	0.143	0.666	0.306	0.445
			1437002	0.136	0.008	0.094	0.558	0.180	0.209
			1437003	0.110	0.008	0.091	0.650	0.215	0.340
			1437004	0.109	0.008	0.156	0.700	0.231	0.320
			1437005	0.124	0.011	0.132	0.568	0.223	0.311
			1437006	0.095	0.009	0.098	0.648	0.202	0.225
			1437007	0.097	0.009	0.116	0.600	0.224	0.295
			1437008	0.132	0.010	0.128	0.570	0.208	0.290
			1437009	0.120	0.008	0.143	0.581	0.242	0.296
			1437010	0.109	0.008	0.128	0.611	0.242	0.210
			N	10	10	10	10	10	10
			MEAN	0.1141	0.0089	0.1229	0.6152	0.2273	0.2941
			S.D.	0.0137	0.0011	0.0225	0.0483	0.0334	0.0707

APPENDIX K

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL ORGAN TO BODY WEIGHT RATIO DATA (G/100G BW)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Brain	Pituitary	Thyroids	Lungs	Heart	Thymus	Liver	Kidneys
MALE	2	80	1437011	0.323	0.002	0.004	0.260	0.265	0.048	2.699	0.530
			1437012	0.380	0.002	0.003	0.262	0.321	0.043	2.610	0.508
			1437013	0.373	0.002	0.005	0.273	0.328	0.059	2.312	0.543
			1437014	0.410	0.002	0.003	0.279	0.299	0.054	2.530	0.555
			1437015	0.421	0.002	0.004	0.246	0.265	0.046	2.320	0.533
			1437016	0.516	0.002	0.005	0.300	0.306	0.048	2.312	0.586
			1437017	0.303	0.002	0.003	0.213	0.227	0.043	2.806	0.488
			1437018	0.330	0.002	0.003	0.255	0.255	0.049	2.797	0.536
			1437019	0.377	0.002	0.004	0.249	0.272	0.056	2.493	0.560
			1437020	0.407	0.002	0.005	0.270	0.311	0.041	2.585	0.663
			N	10	10	10	10	10	10	10	10
			MEAN	0.3840	0.0020	0.0039	0.2607	0.2849	0.0487	2.5464	0.5502
			S.D.	0.0609	0.0000	0.0009	0.0230	0.0328	0.0060	0.1895	0.0480

APPENDIX K

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL ORGAN TO BODY WEIGHT RATIO DATA (G/100G BW)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Spleen	Adrenals	Salivary glands	Testes	Seminal vesicles	Prostate
MALE	2	80	1437011	0.118	0.009	0.105	0.556	0.176	0.218
			1437012	0.111	0.008	0.142	0.514	0.240	0.347
			1437013	0.126	0.010	0.160	0.609	0.225	0.321
			1437014	0.114	0.011	0.151	0.648	0.249	0.365
			1437015	0.099	0.008	0.118	0.605	0.235	0.284
			1437016	0.101	0.013	0.142	0.818	0.254	0.402
			1437017	0.118	0.006	0.098	0.413	0.161	0.224
			1437018	0.120	0.011	0.133	0.539	0.235	0.278
			1437019	0.116	0.007	0.135	0.604	0.235	0.368
			1437020	0.134	0.011	0.132	0.745	0.240	0.279
			N	10	10	10	10	10	10
			MEAN	0.1157	0.0094	0.1316	0.6051	0.2250	0.3086
			S.D.	0.0105	0.0022	0.0195	0.1149	0.0310	0.0622

APPENDIX K
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL ORGAN TO BODY WEIGHT RATIO DATA (G/100G BW)
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Brain	Pituitary	Thyroids	Lungs	Heart	Thymus	Liver	Kidneys
MALE	3	250	1437021	0.355	0.002	0.003	0.216	0.268	0.040	2.490	0.470
			1437022	0.334	0.002	0.004	0.223	0.257	0.050	2.351	0.502
			1437023	-	-	-	-	-	-	-	-
			1437024	0.410	0.002	0.005	0.273	0.274	0.039	2.270	0.525
			1437025	0.382	0.002	0.003	0.287	0.274	0.038	2.360	0.528
			1437026	0.395	0.002	0.003	0.281	0.296	0.058	2.495	0.515
			1437027	0.320	0.002	0.004	0.210	0.276	0.038	2.478	0.509
			1437028	0.318	0.002	0.004	0.224	0.255	0.025	2.365	0.441
			1437029	0.369	0.002	0.003	0.232	0.238	0.035	2.238	0.525
			1437030	0.395	0.002	0.004	0.239	0.269	0.065	2.354	0.477
			N	9	9	9	9	9	9	9	9
			MEAN	0.3642	0.0020	0.0037	0.2428	0.2674	0.0431	2.3779	0.4991
			S.D.	0.0343	0.0000	0.0007	0.0296	0.0162	0.0124	0.0931	0.0301

APPENDIX K
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL ORGAN TO BODY WEIGHT RATIO DATA (G/100G BW)
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Spleen	Adrenals	Salivary glands	Testes	Seminal vesicles	Prostate
MALE	3	250	1437021	0.088	0.010	0.093	0.565	0.152	0.213
			1437022	0.099	0.007	0.125	0.593	0.193	0.253
			1437023	-	-	-	-	-	-
			1437024	0.109	0.009	0.125	0.681	0.222	0.312
			1437025	0.102	0.009	0.114	0.597	0.221	0.356
			1437026	0.119	0.012	0.132	0.593	0.213	0.360
			1437027	0.117	0.008	0.120	0.520	0.204	0.310
			1437028	0.108	0.007	0.098	0.502	0.201	0.243
			1437029	0.099	0.008	0.124	0.512	0.220	0.267
			1437030	0.096	0.010	0.133	0.611	0.262	0.367
			N	9	9	9	9	9	9
			MEAN	0.1041	0.0089	0.1182	0.5749	0.2098	0.2979
			S.D.	0.0101	0.0016	0.0141	0.0571	0.0293	0.0565

APPENDIX K
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL ORGAN TO BODY WEIGHT RATIO DATA (G/100G BW)
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Brain	Pituitary	Thyroids	Lungs	Heart	Thymus	Liver	Kidneys
MALE	4	800	1437031	0.306	0.002	0.003	0.214	0.228	0.034	2.174	0.459
			1437032	0.390	0.002	0.004	0.243	0.248	0.056	2.216	0.464
			1437033	0.363	0.002	0.003	0.252	0.285	0.041	2.866	0.526
			1437034	0.343	0.002	0.005	0.214	0.221	0.038	2.175	0.472
			1437035	0.368	0.002	0.003	0.249	0.284	0.037	2.249	0.533
			1437036	0.430	0.002	0.004	0.253	0.276	0.040	2.414	0.541
			1437037	0.385	0.002	0.004	0.241	0.288	0.054	2.369	0.492
			1437038	0.366	0.002	0.004	0.246	0.268	0.029	2.630	0.532
			1437039	0.348	0.002	0.003	0.224	0.241	0.064	2.474	0.524
			1437040	0.396	0.003	0.005	0.259	0.287	0.036	2.426	0.562
			N	10	10	10	10	10	10	10	10
			MEAN	0.3695	0.0021	0.0038	0.2395	0.2626	0.0429	2.3993	0.5105
			S.D.	0.0338	0.0003	0.0008	0.0164	0.0259	0.0112	0.2200	0.0359

APPENDIX K

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL ORGAN TO BODY WEIGHT RATIO DATA (G/100G BW)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Spleen	Adrenals	Salivary glands	Testes	Seminal vesicles	Prostate
MALE	4	800	1437031	0.100	0.008	0.083	0.444	0.132	0.226
			1437032	0.113	0.008	0.112	0.521	0.201	0.384
			1437033	0.148	0.009	0.137	0.547	0.264	0.363
			1437034	0.097	0.005	0.105	0.117	0.157	0.242
			1437035	0.110	0.010	0.104	0.586	0.218	0.320
			1437036	0.098	0.012	0.109	0.713	0.224	0.280
			1437037	0.097	0.010	0.126	0.725	0.237	0.325
			1437038	0.116	0.007	0.111	0.548	0.220	0.299
			1437039	0.113	0.010	0.116	0.566	0.162	0.215
			1437040	0.123	0.011	0.122	0.554	0.234	0.331
			N	10	10	10	10	10	10
			MEAN	0.1115	0.0090	0.1125	0.5321	0.2049	0.2985
			S.D.	0.0157	0.0021	0.0145	0.1684	0.0416	0.0572

APPENDIX K
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL ORGAN TO BODY WEIGHT RATIO DATA (G/100G BW)
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Brain	Pituitary	Thyroids	Lungs	Heart	Thymus	Liver	Kidneys
FEMALE	5	0	1437041	0.627	0.005	0.009	0.314	0.275	0.067	2.352	0.562
			1437042	0.621	0.005	0.006	0.325	0.313	0.057	2.371	0.528
			1437043	0.686	0.005	0.005	0.346	0.318	0.068	2.581	0.523
			1437044	0.723	0.005	0.005	0.374	0.315	0.097	2.235	0.557
			1437045	0.765	0.005	0.007	0.424	0.355	0.112	2.603	0.568
			1437046	0.572	0.005	0.005	0.321	0.313	0.077	2.302	0.512
			1437047	0.567	0.005	0.005	0.324	0.296	0.089	2.535	0.544
			1437048	0.662	0.005	0.005	0.362	0.342	0.085	2.698	0.561
			1437049	0.530	0.004	0.004	0.304	0.303	0.065	2.407	0.511
			1437050	0.532	0.004	0.006	0.323	0.275	0.075	2.590	0.551
			N	10	10	10	10	10	10	10	10
			MEAN	0.6285	0.0048	0.0057	0.3417	0.3105	0.0792	2.4674	0.5417
			S.D.	0.0803	0.0004	0.0014	0.0362	0.0255	0.0167	0.1534	0.0215

APPENDIX K

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL ORGAN TO BODY WEIGHT RATIO DATA (G/100G BW)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Spleen	Adrenals	Salivary glands	Ovaries	Uterus
FEMALE	5	0	1437041	0.108	0.016	0.148	0.035	0.222
			1437042	0.139	0.015	0.121	0.039	0.216
			1437043	0.136	0.019	0.130	0.037	0.163
			1437044	0.202	0.025	0.161	0.039	0.139
			1437045	0.186	0.020	0.167	0.039	0.319
			1437046	0.114	0.016	0.127	0.033	0.179
			1437047	0.165	0.020	0.126	0.033	0.275
			1437048	0.167	0.021	0.143	0.034	0.152
			1437049	0.151	0.020	0.136	0.034	0.173
			1437050	0.176	0.016	0.155	0.054	0.178
			N	10	10	10	10	10
			MEAN	0.1544	0.0188	0.1414	0.0377	0.2016
			S.D.	0.0305	0.0031	0.0160	0.0062	0.0573

APPENDIX K

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL ORGAN TO BODY WEIGHT RATIO DATA (G/100G BW)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Brain	Pituitary	Thyroids	Lungs	Heart	Thymus	Liver	Kidneys
FEMALE	6	80	1437051	0.715	0.004	0.006	0.357	0.309	0.085	2.382	0.524
			1437052	0.623	0.004	0.003	0.319	0.296	0.058	2.059	0.467
			1437053	0.635	0.006	0.006	0.364	0.327	0.078	2.705	0.598
			1437054	0.769	0.006	0.006	0.392	0.316	0.102	2.334	0.624
			1437055	0.587	0.005	0.006	0.308	0.289	0.071	2.258	0.575
			1437056	0.698	0.005	0.005	0.340	0.264	0.080	2.461	0.547
			1437057	0.521	0.006	0.006	0.310	0.295	0.058	2.546	0.569
			1437058	0.665	0.006	0.005	0.326	0.334	0.060	2.659	0.626
			1437059	0.643	0.005	0.006	0.331	0.315	0.072	2.578	0.644
			1437060	0.591	0.005	0.009	0.331	0.305	0.075	2.688	0.488
			N	10	10	10	10	10	10	10	10
			MEAN	0.6447	0.0052	0.0058	0.3378	0.3050	0.0739	2.4670	0.5662
			S.D.	0.0713	0.0008	0.0015	0.0263	0.0202	0.0137	0.2098	0.0598

APPENDIX K

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL ORGAN TO BODY WEIGHT RATIO DATA (G/100G BW)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Spleen	Adrenals	Salivary glands	Ovaries	Uterus
FEMALE	6	80	1437051	0.130	0.018	0.136	0.040	0.128
			1437052	0.163	0.019	0.121	0.029	0.159
			1437053	0.170	0.019	0.135	0.028	0.212
			1437054	0.183	0.020	0.163	0.032	0.188
			1437055	0.139	0.015	0.133	0.022	0.215
			1437056	0.139	0.021	0.153	0.032	0.325
			1437057	0.185	0.020	0.134	0.032	0.130
			1437058	0.137	0.018	0.128	0.017	0.215
			1437059	0.125	0.026	0.143	0.041	0.257
			1437060	0.165	0.018	0.151	0.034	0.145
			N	10	10	10	10	10
			MEAN	0.1536	0.0194	0.1397	0.0307	0.1974
			S.D.	0.0221	0.0028	0.0127	0.0073	0.0618

APPENDIX K

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL ORGAN TO BODY WEIGHT RATIO DATA (G/100G BW)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Brain	Pituitary	Thyroids	Lungs	Heart	Thymus	Liver	Kidneys
FEMALE	7	250	1437061	0.701	0.005	0.007	0.367	0.299	0.079	2.337	0.536
			1437062	0.704	0.006	0.005	0.338	0.299	0.060	2.335	0.547
			1437063	0.725	0.007	0.007	0.369	0.320	0.081	2.557	0.584
			1437064	0.584	0.005	0.005	0.342	0.289	0.087	2.275	0.570
			1437065	0.782	0.006	0.007	0.376	0.348	0.112	2.569	0.615
			1437066	0.669	0.006	0.008	0.364	0.300	0.056	2.484	0.545
			1437067	0.734	0.005	0.006	0.376	0.302	0.099	2.352	0.526
			1437068	0.649	0.005	0.005	0.362	0.300	0.069	2.554	0.554
			1437069	0.610	0.005	0.007	0.368	0.289	0.080	2.504	0.563
			1437070	0.689	0.006	0.005	0.333	0.297	0.064	2.460	0.630
			N	10	10	10	10	10	10	10	10
			MEAN	0.6847	0.0056	0.0062	0.3595	0.3043	0.0787	2.4427	0.5670
			S.D.	0.0591	0.0007	0.0011	0.0158	0.0176	0.0176	0.1087	0.0338

APPENDIX K

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL ORGAN TO BODY WEIGHT RATIO DATA (G/100G BW)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Spleen	Adrenals	Salivary glands	Ovaries	Uterus
FEMALE	7	250	1437061	0.144	0.014	0.133	0.038	0.192
			1437062	0.122	0.018	0.129	0.034	0.153
			1437063	0.158	0.023	0.159	0.039	0.241
			1437064	0.138	0.016	0.120	0.038	0.272
			1437065	0.183	0.025	0.153	0.040	0.121
			1437066	0.151	0.025	0.140	0.035	0.198
			1437067	0.143	0.018	0.154	0.036	0.125
			1437068	0.176	0.019	0.137	0.035	0.156
			1437069	0.156	0.018	0.120	0.037	0.133
			1437070	0.164	0.019	0.153	0.037	0.264
			N	10	10	10	10	10
			MEAN	0.1535	0.0195	0.1398	0.0369	0.1855
			S.D.	0.0181	0.0037	0.0144	0.0019	0.0572

APPENDIX K

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL ORGAN TO BODY WEIGHT RATIO DATA (G/100G BW)

STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Brain	Pituitary	Thyroids	Lungs	Heart	Thymus	Liver	Kidneys
FEMALE	8	800	1437071	-	-	-	-	-	-	-	-
			1437072	0.641	0.005	0.005	0.356	0.287	0.081	2.385	0.622
			1437073	0.782	0.006	0.005	0.408	0.334	0.118	2.216	0.683
			1437074	0.631	0.005	0.005	0.347	0.325	0.103	2.633	0.657
			1437075	0.699	0.007	0.006	0.372	0.338	0.096	2.657	0.633
			1437076	0.607	0.006	0.005	0.333	0.302	0.052	2.327	0.575
			1437077	0.739	0.005	0.007	0.353	0.282	0.107	2.272	0.541
			1437078	-	-	-	-	-	-	-	-
			1437079	0.648	0.005	0.006	0.359	0.331	0.117	2.352	0.537
			1437080	0.647	0.005	0.006	0.371	0.333	0.074	2.565	0.614
			N	8	8	8	8	8	8	8	8
			MEAN	0.6743	0.0055	0.0056	0.3624	0.3165	0.0935	2.4259	0.6078
			S.D.	0.0602	0.0008	0.0007	0.0223	0.0227	0.0230	0.1692	0.0528

APPENDIX K
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL ORGAN TO BODY WEIGHT RATIO DATA (G/100G BW)
STUDY NO. [redacted]

SEX	GROUP NO.	LEVEL (mg/kg/day)	ANIMAL NO.	Spleen	Adrenals	Salivary glands	Ovaries	Uterus
FEMALE	8	800	1437071	-	-	-	-	-
			1437072	0.142	0.021	0.136	0.035	0.228
			1437073	0.160	0.019	0.167	0.044	0.165
			1437074	0.182	0.020	0.167	0.044	0.143
			1437075	0.157	0.027	0.148	0.043	0.216
			1437076	0.109	0.015	0.131	0.029	0.203
			1437077	0.170	0.021	0.140	0.033	0.298
			1437078	-	-	-	-	-
			1437079	0.165	0.021	0.157	0.031	0.228
			1437080	0.153	0.019	0.143	0.037	0.147
			N	8	8	8	8	8
			MEAN	0.1548	0.0204	0.1486	0.0370	0.2035
			S.D.	0.0219	0.0033	0.0137	0.0060	0.0516

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE GROUP : 1 LEVEL(mg/kg/day) : 0 ANIMAL NO. : 1437001
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Normal
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Normal
Kidney	Normal
Urinary bladder	Normal
Testis	Normal
Prostate	Infiltrate, inflammatory cell, lymphocytic/(2)
Epididymis	Normal
Seminal vesicle	Normal
Mammary gland	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE GROUP : 1 LEVEL(mg/kg/day) : 0 ANIMAL NO. : 1437002
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Cardiomyopathy/(2)
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Normal
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Normal
Kidney	Normal
Urinary bladder	Normal
Testis	Normal
Prostate	Normal
Epididymis	Normal
Seminal vesicle	Normal
Mammary gland	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]
SEX : MALE GROUP : 1 LEVEL(mg/kg/day) : 0 ANIMAL NO. : 1437003
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Normal
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Normal
Kidney	Normal
Urinary bladder	Normal
Testis	Normal
Prostate	Infiltrate, inflammatory cell, lymphocytic/(2)
Epididymis	Normal
Seminal vesicle	Normal
Mammary gland	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE GROUP : 1 LEVEL(mg/kg/day) : 0 ANIMAL NO. : 1437004
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Cyst, capsular/(2)
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Normal
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Cellular infiltration, lymphocyte/(1)
Liver	Normal
Kidney	Normal
Urinary bladder	Normal
Testis	Normal
Prostate	Normal
Epididymis	Normal
Seminal vesicle	Normal
Mammary gland	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE GROUP : 1 LEVEL(mg/kg/day) : 0 ANIMAL NO. : 1437005
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Normal
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Normal
Kidney	Normal
Urinary bladder	Normal
Testis	Normal
Prostate	Infiltrate, inflammatory cell, lymphocytic/(2)
Epididymis	Normal
Seminal vesicle	Normal
Mammary gland	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE GROUP : 1 LEVEL(mg/kg/day) : 0 ANIMAL NO. : 1437006
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Cardiomyopathy/(2)
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Normal
Parathyroid	Not examined
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Normal
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Normal
Kidney	Normal
Urinary bladder	Normal
Testis	Normal
Prostate	Infiltrate, inflammatory cell, lymphocytic/(2)
Epididymis	Normal
Seminal vesicle	Normal
Mammary gland	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE GROUP : 1 LEVEL(mg/kg/day) : 0 ANIMAL NO. : 1437007
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Normal
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Infiltration, mononuclear/(1)
Kidney	Normal
Urinary bladder	Normal
Testis	Normal
Prostate	Infiltrate, inflammatory cell, lymphocytic/(3)
Epididymis	Normal
Seminal vesicle	Normal
Mammary gland	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]
SEX : MALE GROUP : 1 LEVEL(mg/kg/day) : 0 ANIMAL NO. : 1437008
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Cardiomyopathy/(2)
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Normal
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Normal
Kidney	Normal
Urinary bladder	Normal
Testis	Normal
Prostate	Inflammation/(2)
Epididymis	Normal
Seminal vesicle	Normal
Mammary gland	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE GROUP : 1 LEVEL(mg/kg/day) : 0 ANIMAL NO. : 1437009
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Cardiomyopathy/(2)
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Persistence of Rathke's pouch
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Normal
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Necrosis, multifocal/(2)
Kidney	Normal
Urinary bladder	Normal
Testis	Normal
Prostate	Normal
Epididymis	Normal
Seminal vesicle	Normal
Mammary gland	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE GROUP : 1 LEVEL(mg/kg/day) : 0 ANIMAL NO. : 1437010
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Cardiomyopathy/(2)
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Persistence of Rathke's pouch
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Normal
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Normal
Kidney	Normal
Urinary bladder	Normal
Testis	Normal
Prostate	Infiltrate, inflammatory cell, lymphocytic/(3)
Epididymis	Normal
Seminal vesicle	Normal
Mammary gland	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE	GROUP : 2	LEVEL(mg/kg/day) : 80	ANIMAL NO. : 1437011
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE	GROUP : 2	LEVEL(mg/kg/day) : 80	ANIMAL NO. : 1437012
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL HISTOPATHOLOGICAL DATA

STUDY NO. [redacted]

SEX : MALE GROUP : 2 LEVEL(mg/kg/day) : 80 ANIMAL NO. : 1437013

FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE	GROUP : 2	LEVEL(mg/kg/day) : 80	ANIMAL NO. : 1437014
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL HISTOPATHOLOGICAL DATA

STUDY NO. [redacted]

SEX : MALE GROUP : 2 LEVEL(mg/kg/day) : 80 ANIMAL NO. : 1437015

FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL HISTOPATHOLOGICAL DATA

STUDY NO. [redacted]

SEX : MALE GROUP : 2 LEVEL(mg/kg/day) : 80 ANIMAL NO. : 1437016

FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE	GROUP : 2	LEVEL(mg/kg/day) : 80	ANIMAL NO. : 1437017
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL HISTOPATHOLOGICAL DATA

STUDY NO. [redacted]

SEX : MALE GROUP : 2 LEVEL(mg/kg/day) : 80 ANIMAL NO. : 1437018

FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE	GROUP : 2	LEVEL(mg/kg/day) : 80	ANIMAL NO. : 1437019
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE	GROUP : 2	LEVEL(mg/kg/day) : 80	ANIMAL NO. : 1437020
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE	GROUP : 3	LEVEL(mg/kg/day) : 250	ANIMAL NO. : 1437021
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE	GROUP : 3	LEVEL(mg/kg/day) : 250	ANIMAL NO. : 1437022
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE	GROUP : 3	LEVEL(mg/kg/day) : 250	ANIMAL NO. : 1437023a
FATE : Found dead		WEEK AT DEATH : 5	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Lung/bronchial	Hemorrhage, alveoli/(5)
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe
a : Data was omitted from the evaluation and not reflected to TABLE 13.

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE GROUP : 3 LEVEL(mg/kg/day) : 250 ANIMAL NO. : 1437024
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE	GROUP : 3	LEVEL(mg/kg/day) : 250	ANIMAL NO. : 1437025
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE	GROUP : 3	LEVEL(mg/kg/day) : 250	ANIMAL NO. : 1437026
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Cyst, forestomach/(2)
	Hyperplasia, limiting ridge/(2)

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE	GROUP : 3	LEVEL(mg/kg/day) : 250	ANIMAL NO. : 1437027
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE	GROUP : 3	LEVEL(mg/kg/day) : 250	ANIMAL NO. : 1437028
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal
Abdominal fat	Necrosis/(2)

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE	GROUP : 3	LEVEL(mg/kg/day) : 250	ANIMAL NO. : 1437029
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE	GROUP : 3	LEVEL(mg/kg/day) : 250	ANIMAL NO. : 1437030
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE GROUP : 4 LEVEL(mg/kg/day) : 800 ANIMAL NO. : 1437031
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Hyperplasia, limiting ridge/(2)
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Normal
Kidney	Normal
Urinary bladder	Normal
Testis	Normal
Prostate	Normal
Epididymis	Normal
Seminal vesicle	Normal
Mammary gland	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE GROUP : 4 LEVEL(mg/kg/day) : 800 ANIMAL NO. : 1437032
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Cardiomyopathy/(2)
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Persistence of Rathke's pouch
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Hyperplasia, limiting ridge/(2)
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Normal
Kidney	Normal
Urinary bladder	Normal
Testis	Normal
Prostate	Normal
Epididymis	Normal
Seminal vesicle	Normal
Mammary gland	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE GROUP : 4 LEVEL(mg/kg/day) : 800 ANIMAL NO. : 1437033
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Hyperplasia, limiting ridge/(2)
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Tension lipidosis/(2)
Kidney	Normal
Urinary bladder	Normal
Testis	Normal
Prostate	Infiltrate, inflammatory cell, lymphocytic/(2)
Epididymis	Normal
Seminal vesicle	Normal
Mammary gland	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE GROUP : 4 LEVEL(mg/kg/day) : 800 ANIMAL NO. : 1437034
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Hyperplasia, limiting ridge/(2)
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Infarction/(3)
Kidney	Normal
Urinary bladder	Normal
Testis	Atrophy, tubular/(4)
Prostate	Infiltrate, inflammatory cell, lymphocytic/(1)
Epididymis	Atrophy, ductal/(3)
	Reduced sperm, luminal/(4)
Seminal vesicle	Normal
Mammary gland	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE GROUP : 4 LEVEL(mg/kg/day) : 800 ANIMAL NO. : 1437035
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Cardiomyopathy/(1)
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Hyperplasia, limiting ridge/(2)
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Normal
Kidney	Normal
Urinary bladder	Normal
Testis	Normal
Prostate	Normal
Epididymis	Normal
Seminal vesicle	Normal
Mammary gland	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE GROUP : 4 LEVEL(mg/kg/day) : 800 ANIMAL NO. : 1437036
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Hyperplasia, limiting ridge/(2)
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Tension lipidosis/(2)
Kidney	Normal
Urinary bladder	Normal
Testis	Normal
Prostate	Infiltrate, inflammatory cell, lymphocytic/(2)
Epididymis	Normal
Seminal vesicle	Normal
Mammary gland	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE GROUP : 4 LEVEL(mg/kg/day) : 800 ANIMAL NO. : 1437037
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Hyperplasia, limiting ridge/(2)
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Normal
Kidney	Normal
Urinary bladder	Normal
Testis	Normal
Prostate	Normal
Epididymis	Normal
Seminal vesicle	Normal
Mammary gland	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE	GROUP : 4	LEVEL(mg/kg/day) : 800	ANIMAL NO. : 1437038
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Hyperplasia, limiting ridge/(2)
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Normal
Kidney	Normal
Urinary bladder	Normal
Testis	Normal
Prostate	Normal
Epididymis	Normal
Seminal vesicle	Normal
Mammary gland	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE GROUP : 4 LEVEL(mg/kg/day) : 800 ANIMAL NO. : 1437039
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Persistence of Rathke's pouch
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Hyperplasia, limiting ridge/(2)
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Normal
Kidney	Normal
Urinary bladder	Normal
Testis	Normal
Prostate	Normal
Epididymis	Normal
Seminal vesicle	Normal
Mammary gland	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : MALE GROUP : 4 LEVEL(mg/kg/day) : 800 ANIMAL NO. : 1437040
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Persistence of Rathke's pouch
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Hyperplasia, limiting ridge/(2)
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Normal
Kidney	Normal
Urinary bladder	Normal
Testis	Normal
Prostate	Infiltrate, inflammatory cell, lymphocytic/(2)
Epididymis	Normal
Seminal vesicle	Normal
Mammary gland	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE GROUP : 5 LEVEL(mg/kg/day) : 0 ANIMAL NO. : 1437041
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Normal
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Fatty change/(1)
Kidney	Normal
Urinary bladder	Normal
Mammary gland	Normal
Ovary	Normal
Oviduct	Normal
Uterus	Dilatation, lumen/(2)
Vagina	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE GROUP : 5 LEVEL(mg/kg/day) : 0 ANIMAL NO. : 1437042
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Ultimobranchial rest
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Normal
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Infiltration, mononuclear/(2)
	Tension lipidosis/(2)
Kidney	Normal
Urinary bladder	Normal
Mammary gland	Normal
Ovary	Normal
Oviduct	Normal
Uterus	Normal
Vagina	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE GROUP : 5 LEVEL(mg/kg/day) : 0 ANIMAL NO. : 1437043
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Normal
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Fatty change/(3)
	Infiltration, mononuclear/(2)
Kidney	Normal
Urinary bladder	Normal
Mammary gland	Normal
Ovary	Normal
Oviduct	Normal
Uterus	Normal
Vagina	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE GROUP : 5 LEVEL(mg/kg/day) : 0 ANIMAL NO. : 1437044
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Normal
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Fatty change/(1)
	Tension lipidosis/(2)
Kidney	Normal
Urinary bladder	Normal
Mammary gland	Normal
Ovary	Normal
Oviduct	Normal
Uterus	Normal
Vagina	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE GROUP : 5 LEVEL(mg/kg/day) : 0 ANIMAL NO. : 1437045
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Normal
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Infiltration, mononuclear/(1)
Kidney	Normal
Urinary bladder	Normal
Mammary gland	Normal
Ovary	Normal
Oviduct	Normal
Uterus	Dilatation, lumen/(3)
Vagina	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE GROUP : 5 LEVEL(mg/kg/day) : 0 ANIMAL NO. : 1437046
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Normal
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Normal
Kidney	Normal
Urinary bladder	Normal
Mammary gland	Normal
Ovary	Cyst, bursal/(2)
Oviduct	Normal
Uterus	Normal
Vagina	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE	GROUP : 5	LEVEL(mg/kg/day) : 0	ANIMAL NO. : 1437047
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Ultimobranchial rest
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Normal
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Normal
Kidney	Normal
Urinary bladder	Normal
Mammary gland	Normal
Ovary	Normal
Oviduct	Normal
Uterus	Dilatation, lumen/(2)
Vagina	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE GROUP : 5 LEVEL(mg/kg/day) : 0 ANIMAL NO. : 1437048
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Persistence of Rathke's pouch
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Normal
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Fatty change/(3)
	Infiltration, mononuclear/(2)
Kidney	Normal
Urinary bladder	Normal
Mammary gland	Normal
Ovary	Normal
Oviduct	Normal
Uterus	Normal
Vagina	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE GROUP : 5 LEVEL(mg/kg/day) : 0 ANIMAL NO. : 1437049
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Ultimobranchial rest
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Normal
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Fatty change/(2)
	Infiltration, mononuclear/(1)
Kidney	Normal
Urinary bladder	Normal
Mammary gland	Normal
Ovary	Normal
Oviduct	Normal
Uterus	Normal
Vagina	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]
SEX : FEMALE GROUP : 5 LEVEL(mg/kg/day) : 0 ANIMAL NO. : 1437050
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Ultimobranchial rest
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Normal
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Fatty change/(2)
	Infiltration, mononuclear/(1)
Kidney	Normal
Urinary bladder	Normal
Mammary gland	Normal
Ovary	Cyst, bursal/(2)
Oviduct	Normal
Uterus	Normal
Vagina	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Cellular infiltration, lymphocyte/(1)
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE	GROUP : 6	LEVEL(mg/kg/day) : 80	ANIMAL NO. : 1437051
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE	GROUP : 6	LEVEL(mg/kg/day) : 80	ANIMAL NO. : 1437052
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE	GROUP : 6	LEVEL(mg/kg/day) : 80	ANIMAL NO. : 1437053
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE	GROUP : 6	LEVEL(mg/kg/day) : 80	ANIMAL NO. : 1437054
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE	GROUP : 6	LEVEL(mg/kg/day) : 80	ANIMAL NO. : 1437055
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE	GROUP : 6	LEVEL(mg/kg/day) : 80	ANIMAL NO. : 1437056
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL HISTOPATHOLOGICAL DATA

STUDY NO. [redacted]

SEX : FEMALE GROUP : 6 LEVEL(mg/kg/day) : 80 ANIMAL NO. : 1437057

FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE	GROUP : 6	LEVEL(mg/kg/day) : 80	ANIMAL NO. : 1437058
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE	GROUP : 6	LEVEL(mg/kg/day) : 80	ANIMAL NO. : 1437059
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE	GROUP : 6	LEVEL(mg/kg/day) : 80	ANIMAL NO. : 1437060
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE	GROUP : 7	LEVEL(mg/kg/day) : 250	ANIMAL NO. : 1437061
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE	GROUP : 7	LEVEL(mg/kg/day) : 250	ANIMAL NO. : 1437062
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Thymus	Hemorrhage/(1)
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE	GROUP : 7	LEVEL(mg/kg/day) : 250	ANIMAL NO. : 1437063
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE	GROUP : 7	LEVEL(mg/kg/day) : 250	ANIMAL NO. : 1437064
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal
Liver	Hepatodiaphragmatic nodule

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE GROUP : 7 LEVEL(mg/kg/day) : 250 ANIMAL NO. : 1437065
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Pituitary	Cyst
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE	GROUP : 7	LEVEL(mg/kg/day) : 250	ANIMAL NO. : 1437066
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE GROUP : 7 LEVEL(mg/kg/day) : 250 ANIMAL NO. : 1437067
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE	GROUP : 7	LEVEL(mg/kg/day) : 250	ANIMAL NO. : 1437068
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE GROUP : 7 LEVEL(mg/kg/day) : 250 ANIMAL NO. : 1437069
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE GROUP : 7 LEVEL(mg/kg/day) : 250 ANIMAL NO. : 1437070
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Stomach	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE GROUP : 8 LEVEL(mg/kg/day) : 800 ANIMAL NO. : 1437071
FATE : Found dead WEEK AT DEATH : 10

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Atrophy/(5)
	Pigmentation/(3)
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Inflammation/(2)
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Erosion, forestomach/(3)
	Hyperplasia, forestomach/(3)
	Hyperplasia, limiting ridge/(2)
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Normal
Kidney	Normal
Urinary bladder	Normal
Mammary gland	Normal
Ovary	Normal
Oviduct	Normal
Uterus	Normal
Vagina	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE GROUP : 8 LEVEL(mg/kg/day) : 800 ANIMAL NO. : 1437072
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Hyperplasia, limiting ridge/(2)
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Normal
Kidney	Normal
Urinary bladder	Normal
Mammary gland	Normal
Ovary	Normal
Oviduct	Normal
Uterus	Dilatation, lumen/(2)
Vagina	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE GROUP : 8 LEVEL(mg/kg/day) : 800 ANIMAL NO. : 1437073
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Hyperplasia, limiting ridge/(2)
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Normal
Kidney	Normal
Urinary bladder	Normal
Mammary gland	Normal
Ovary	Normal
Oviduct	Normal
Uterus	Normal
Vagina	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE GROUP : 8 LEVEL(mg/kg/day) : 800 ANIMAL NO. : 1437074
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Hyperplasia, limiting ridge/(2)
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Fatty change/(2)
	Infiltration, mononuclear/(2)
Kidney	Normal
Urinary bladder	Normal
Mammary gland	Normal
Ovary	Normal
Oviduct	Normal
Uterus	Normal
Vagina	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE GROUP : 8 LEVEL(mg/kg/day) : 800 ANIMAL NO. : 1437075
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Hyperplasia, limiting ridge/(2)
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Normal
Kidney	Normal
Urinary bladder	Normal
Mammary gland	Normal
Ovary	Normal
Oviduct	Normal
Uterus	Normal
Vagina	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE GROUP : 8 LEVEL(mg/kg/day) : 800 ANIMAL NO. : 1437076
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Hyperplasia, limiting ridge/(2)
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Normal
Kidney	Normal
Urinary bladder	Normal
Mammary gland	Normal
Ovary	Normal
Oviduct	Normal
Uterus	Normal
Vagina	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE	GROUP : 8	LEVEL(mg/kg/day) : 800	ANIMAL NO. : 1437077
FATE : Terminal sacrifice		WEEK AT DEATH : 14	

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Hyperplasia, limiting ridge/(2)
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Normal
Kidney	Normal
Urinary bladder	Normal
Mammary gland	Normal
Ovary	Normal
Oviduct	Normal
Uterus	Dilatation, lumen/(3)
Vagina	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L

REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS

INDIVIDUAL HISTOPATHOLOGICAL DATA

STUDY NO. [redacted]

SEX : FEMALE GROUP : 8 LEVEL(mg/kg/day) : 800 ANIMAL NO. : 1437078

FATE : Found dead WEEK AT DEATH : 11

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Hyperplasia, limiting ridge/(2)
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Normal
Kidney	Normal
Urinary bladder	Normal
Mammary gland	Normal
Ovary	Normal
Oviduct	Normal
Uterus	Normal
Vagina	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE GROUP : 8 LEVEL(mg/kg/day) : 800 ANIMAL NO. : 1437079
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Persistence of Rathke's pouch
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Hyperplasia, limiting ridge/(2)
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Fatty change/(1)
	Infiltration, mononuclear/(2)
Kidney	Normal
Urinary bladder	Normal
Mammary gland	Normal
Ovary	Normal
Oviduct	Normal
Uterus	Dilatation, lumen/(2)
Vagina	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

APPENDIX L
REPEATED DOSE 90-DAY ORAL TOXICITY STUDY OF 2-METHYLBUTYRIC ACID IN RATS
INDIVIDUAL HISTOPATHOLOGICAL DATA
STUDY NO. [redacted]

SEX : FEMALE GROUP : 8 LEVEL(mg/kg/day) : 800 ANIMAL NO. : 1437080
FATE : Terminal sacrifice WEEK AT DEATH : 14

ORGAN	HISTOPATHOLOGICAL FINDINGS
Heart	Normal
Aorta	Normal
Mandibular lymph node	Normal
Mesenteric lymph node	Normal
Spleen	Normal
Bone marrow	Normal
Thymus	Normal
Pituitary	Normal
Thyroid	Normal
Parathyroid	Normal
Adrenal	Normal
Nasal cavity	Normal
Trachea	Normal
Lung/bronchial	Normal
Tongue	Normal
Salivary gland	Normal
Esophagus	Normal
Stomach	Hyperplasia, limiting ridge/(2)
Duodenum	Normal
Jejunum	Normal
Ileum	Normal
Cecum	Normal
Colon	Normal
Rectum	Normal
Pancreas	Normal
Liver	Fatty change/(2)
Kidney	Normal
Urinary bladder	Normal
Mammary gland	Normal
Ovary	Normal
Oviduct	Normal
Uterus	Normal
Vagina	Normal
Femur	Normal
Sternum	Normal
Musculature	Normal
Skin/subcutis	Normal
Zymbal's gland	Normal
Eye	Normal
Harderian gland	Normal
Brain	Normal
Spinal cord	Normal
Sciatic nerve	Normal

Numbers in parenthesis indicate the grades of lesion : (1) Minimal (2) Slight (3) Moderate (4) Marked (5) Severe

9　添付資料

9.1　床敷中汚染物質分析試験成績書

9　添付資料

9.2　飼料中汚染物質分析試験成績書

9　添付資料

9.3　飲料水試験検査成績書

10　信頼性保証陳述書

信頼性保証陳述書

試 験 名　指定添加物の安全性に関する試験（2-メチルブチリックアシドに関する 90 日間反復投与毒性試験）

試験番号　[redacted]

本試験は適用 GLP 及び当施設の信頼性保証部門に関する標準操作手順書（SOP）に従って下記の調査を実施しました。その結果、試験計画書及び SOP に従って試験が適正に実施されており、最終報告書には試験した方法、手順が正確に記載され、かつ試験の生データを正確に反映していることを認めます。

適用 GLP：医薬品の安全性に関する非臨床試験の実施の基準に関する省令（平成 9 年 3 月 26 日厚生省令第 21 号、一部改正、平成 20 年 6 月 13 日厚生労働省令第 114 号）

調査の内容	QAU 調査日	運営管理者並びに試験責任者への報告日
試験計画書 変更書 01 変更書 02	[redacted]	
動物入荷 予備飼育・検疫（一般状態・体重を含む） 群分け・個体識別 被験物質に関する記録 被験物質の調製・サンプリング 被験物質投与液の分析 被験物質の投与 一般状態 体重・摂餌量・摂水量測定 尿検査（定性） 尿検査（pH） 尿検査（電解質） 眼科学的検査		

途中死亡動物の解剖 解剖 器官重量 器官重量（固定後） 血液学的検査 血液生化学的検査 病理標本の作製　　（切り出し） （骨整形） （包埋） （薄切） （染色・封入・照合） （照合） 病理組織学的検査	[redacted]	
帳票の確認		
帳票の再確認		
記録類		
記録類の再調査		
最終報告書草稿		
最終報告書		

[redacted]

信頼性保証担当者：[redacted]

信頼性保証部門責任者：