

[Redacted]

[Redacted]

最終報告書

4-エテニル-2-メトキシフェノール：ラットを用いた
90日間反復経口投与毒性試験

試験番号： [Redacted]

試験期間： [Redacted]

試験施設

[Redacted]

試験委託者

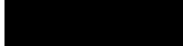
国立医薬品食品衛生研究所

[Redacted]

[Redacted]



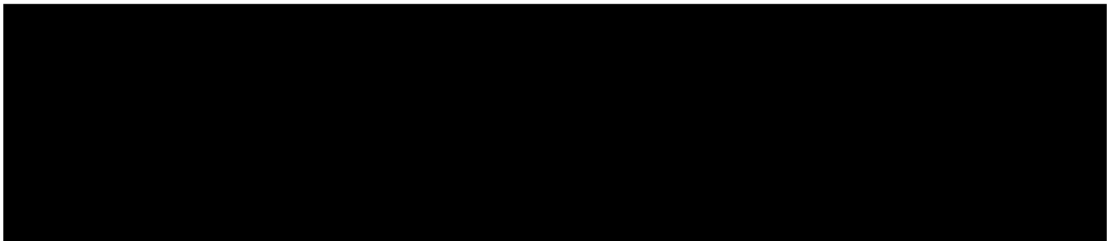
1. GLP 陳述書

試験番号 : 

試験表題 : 4-エテニル-2-メトキシフェノール：ラットを用いた
90日間反復経口投与毒性試験

本試験は以下に示す GLP 基準を遵守して実施したものであります。

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



2. 目次

1.	GLP 陳述書	2
2.	目次	3
3.	試験実施概要	6
3.1	試験番号	6
3.2	試験表題	6
3.3	試験目的	6
3.4	試験委託者	6
3.5	試験受託者	6
3.6	試験施設	6
3.7	試験日程	6
3.8	試験責任者	7
3.9	試験担当者	7
3.10	試験成績の信頼性に影響を及ぼしたと思われる環境要因	7
3.11	資料の保存	7
3.12	試験責任者の署名	7
4.	要約	8
5.	緒言	10
6.	試験材料及び方法	11
6.1	被験物質及び媒体	11
6.1.1	被験物質	11
6.1.2	媒体	11
6.2	投与液の調製	11
6.2.1	対照群液の分注	11
6.2.2	被験液の調製	12
6.2.2.1	調製頻度	12
6.2.2.2	投与液の保存方法	12
6.2.2.3	被験液の安定性	12
6.2.2.4	被験液の濃度確認	12
6.3	試験動物種及び系統の選択理由	14
6.4	試験動物及び群分け	14
6.5	飼育条件	15
6.6	飼料、床敷及び飲料水中の混入物質の分析	15
6.7	動物の識別及びケージへの表示	16
6.8	投与経路、投与期間、投与方法及び投与回数とそれらの選択理由	16
6.9	投与量及びその設定根拠並びに群構成	16
6.10	観察及び検査の方法	17

6.10.1	一般状態の観察	17
6.10.2	体重測定	17
6.10.3	摂餌量測定	17
6.10.4	眼科学検査	17
6.10.5	尿検査	18
6.10.6	血液学検査	19
6.10.7	血液化学検査	20
6.10.8	病理学検査	20
6.10.8.1	剖検	20
6.10.8.2	器官重量測定	20
6.10.8.3	病理組織学検査	21
6.11	データ採取に使用したコンピュータシステム	21
6.12	統計解析	22
7.	試験結果	23
7.1	一般状態	23
7.2	体重	23
7.3	摂餌量	23
7.4	眼科学検査	23
7.5	尿検査	23
7.6	血液学検査	23
7.7	血液化学検査	24
7.8	器官重量	24
7.9	剖検	25
7.10	病理組織学検査	25
8.	考察	27
9.	文献	29

添付資料

Attachment 1	試験成績書 (4-エテニル-2-メトキシフェノールの特性)	30
Attachment 2	試験成績書 (被験液中 4-エテニル-2-メトキシフェノールの安定性)	33
Attachment 3	分析結果 (被験液の濃度)	36

図

Fig. 1、2	体重	38
Fig. 3、4	摂餌量	40

表

Table 1-1~1-14	一般状態	42
Table 2-1~2-4	体重	56
Table 3-1~3-4	摂餌量	60
Table 4-1、4-2	眼科学検査	64
Table 5-1~5-16	尿検査	66
Table 6-1~6-8	血液学検査	82
Table 7-1~7-6	血液化学検査	90
Table 8-1~8-4	器官重量（絶対重量）	96
Table 9-1~9-4	器官重量（相対重量）	100
Table 10-1、10-2	剖検所見	104
Table 11-1~11-8	病理組織所見	106

付表

Appendix 1-1~1-56	個体別一般状態	114
Appendix 2-1~2-8	個体別体重	170
Appendix 3-1~3-8	個体別摂餌量	178
Appendix 4-1~4-8	個体別眼科学検査	186
Appendix 5-1~5-16	個体別尿検査	194
Appendix 6-1~6-24	個体別血液学検査	210
Appendix 7-1~7-16	個体別血液化学検査	234
Appendix 8-1~8-24	個体別器官重量（絶対重量）	250
Appendix 9-1~9-24	個体別器官重量（相対重量）	274
Appendix 10-1~10-80	個体別剖検及び病理組織所見	298

信頼性保証書	378
--------------	-----

3. 試験実施概要

3.1 試験番号

3.2 試験表題

4-エテニル-2-メトキシフェノール：ラットを用いた90日間反復経口投与毒性試験

3.3 試験目的

被験物質をラットに91日間反復経口投与し、明らかな毒性変化を惹起する用量とその変化の内容及び毒性変化の認められない用量を求める。

3.4 試験委託者

国立医薬品食品衛生研究所 安全性生物試験研究センター

3.5 試験受託者

3.6 試験施設

3.7 試験日程

試験開始日	:	
被験物質受領日 ^注	:	
被験物質の試験責任者入手日	:	
動物入荷日（実験開始日）	:	
投与開始日	:	
投与終了日	:	
投与終了剖検日	:	



病理組織学検査終了日（実験終了日）

:



試験終了日 :

注：被験物質受領から試験責任者入手日までの期間は、被験物質管理責任者が保存・管理した。

3.8 試験責任者



3.9 試験担当者

被験物質管理責任者 :



試験主担当者 :

臨床検査責任者 :

病理検査責任者 :

理化学分析責任者 :

濃度分析責任者 :

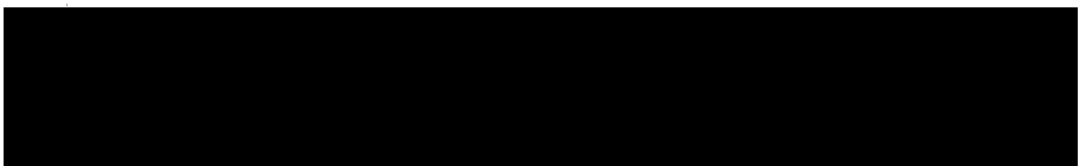
3.10 試験成績の信頼性に影響を及ぼしたと思われる環境要因

、蒸気減圧弁の不具合による飼育室内の湿度の逸脱（最低値：24%、約 15 分間）がみられた。逸脱時間は短時間であり、動物にも異常は認められていないことから、試験成績への影響は無いと判断した。

3.11 資料の保存

試験計画書（試験計画書変更書も含む）原本、記録文書、生データ、報告書類（最終報告書の原本を含む）及び標本（被験物質保存サンプル含む）は に保存する。なお、その期間は最終報告書作成後 5 年間とする。期間終了後の保存については、国立医薬品食品衛生研究所と 間で協議し、その処置を決定する。ただし、長期保存に耐えられない生体試料（尿、血漿）については、試験終了後に廃棄する。

3.12 試験責任者の署名



4. 要約

4-エテニル-2-メトキシフェノールをラットに 90 日間反復投与した時の毒性を検討した。投与量は、0 (コーン油)、100、300 及び 1000 mg/kg とし、Sprague-Dawley 系ラット [CrI:CD(SD)、10 匹/性/群、投与開始時 6 週齢] に 91 日間強制経口投与した。

1) 一般状態

1000 mg/kg 投与群の雌雄で、すべての投与日の投与直後のみに自発運動の減少がみられた。

2) 体重

1000 mg/kg 投与群の雄で投与 84 及び 91 日、雌で投与 63 日に有意な低値が認められた。

3) 摂餌量

1000 mg/kg 投与群の雄で投与 7 日、雌で投与 49 日に有意な低値が認められた。

4) 眼科学検査、尿検査及び血液学検査

すべての被験物質投与群で被験物質投与に起因する異常はみられなかった。

5) 血液化学検査

1000 mg/kg 投与群の雌雄で ALT 活性、総コレステロール及びリン脂質の有意な高値、300 mg/kg 以上の投与群の雌雄で γ -GTP 活性の有意な高値が認められた。

6) 器官重量

肝臓の絶対及び相対重量の有意な高値が 1000 mg/kg 投与群の雌に、相対重量の有意な高値が 1000 mg/kg 投与群の雄にみられた。

7) 病理学検査

胃では前胃の扁平上皮細胞の過形成及び過角化が 100 mg/kg 以上の投与群の雌雄に、腺胃の胃底腺の拡張が 300 mg/kg 以上の投与群の雌雄に、前胃の扁平上皮細胞の結節性過形成が 1000 mg/kg 投与群の雄にみられた。肝臓では肝細胞の空胞化の程度/頻度の減少が 300 mg/kg 以上の投与群の雄及び 1000 mg/kg 投与群の雌にみられた。鼻腔では呼吸上皮の細胞浸潤及び配列不整、嗅上皮の細胞浸潤、のう胞、萎縮及び配列不整、嗅腺の萎縮及び限局性過形成が 1000 mg/kg 投与群の雌雄に、呼吸上皮ののう胞及び鼻腺の拡張が 1000 mg/kg 投与群の雄にみられた。

以上の如く、4-エテニル-2-メトキシフェノールをラットに 90 日間反復投与した結

果、胃への影響が 100 mg/kg 以上の投与群の雌雄、肝臓への影響が 300 mg/kg 以上の投与群の雄及び 1000 mg/kg 投与群の雌に、鼻腔への影響が 1000 mg/kg 投与群の雌雄にみられた。したがって、本試験における無毒性量は雌雄ともに 100 mg/kg 未満と推定された。

5. 緒言

食品添加物として使用される「4-エテニル-2-メトキシフェノール」の安全性評価のため、90日間反復経口投与毒性試験を実施したので、その成績を報告する。当試験は国立医薬品食品衛生研究所の依頼により [REDACTED] で実施した。遵守した基準及び準拠したガイドラインなどは以下の通りである。

1) GLP

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

2) 毒性試験ガイドライン

- 「食品添加物の指定及び使用基準改正に関する指針について」
(衛化第 29 号：平成 8 年 3 月 22 日付厚生省生活衛生局長通知)

3) 動物の福祉

- 「動物の愛護及び管理に関する法律」
(昭和 48 年 10 月 1 日法律第 105 号)
- 「実験動物の飼養及び保管並びに苦痛の軽減に関する基準」
(平成 18 年 4 月 28 日環境省告示第 88 号)
- 「動物実験の適正な実施に向けたガイドライン」
(日本学術会議、平成 18 年 6 月 1 日)

本試験は、[REDACTED] 動物実験委員会の承認を受けて実施した
(承認番号：T170090)。

6. 試験材料及び方法

6.1 被験物質及び媒体

6.1.1 被験物質

使用した被験物質のロット番号及び性状などは以下の通りである。

供給者	:	国立医薬品食品衛生研究所
名称	:	4-エテニル-2-メトキシフェノール (英名 : 4-ethenyl-2-methoxyphenol)
CAS No.	:	7786-61-0
メーカー	:	██████████
ロット番号	:	██████████
純度 (GC 法) *	:	99.8%
性状*	:	液体、無色~淡黄色、特有の香気
安定性	:	当試験の一部として被験物質の使用前及び使用後に分析を行い、使用期間中安定であったことを確認した (Attachment 1)。
保存条件	:	冷蔵 (許容範囲 : 1~10°C、実測値 : 2.8~6.9°C)、遮光
保存場所	:	██████████ ██████████
保存サンプル	:	被験物質 1.01 g を保存サンプルとして保存した。
残余品の処理	:	試験終了後、残余被験物質の一部 (管理番号 : TU170231-3) を試験委託者へ返却し、残りの残余被験物質は予備試験使用分も含め廃棄する。

* : 非 GLP 下で分析された結果に基づく

6.1.2 媒体

名称	:	コーン油
規格	:	試薬 (生化学用)
ロット番号	:	██████████ ██████████
メーカー	:	和光純薬工業株式会社
保存方法	:	室温
保存場所	:	██████████ ██████████

6.2 投与液の調製

6.2.1 対照群液の分注

被験物質を秤量する前に、対照群の投与液として最大 7 日必要量のコーン油を褐色ガラス瓶に 1 日分ずつ分注した。

6.2.2 被験液の調製

高用量群液（200 mg/mL 液）の調製に必要な量の被験物質を秤量してコーン油に溶解し、更にコーン油を加えて規定量とした。中及び低用量群液（60 及び 20 mg/mL 液）は、高用量群液をコーン油で希釈して調製した。

6.2.2.1 調製頻度

最大 7 日分を一括して調製し、調製後 7 日以内に使用した。

6.2.2.2 投与液の保存方法

投与液（対照群投与液を含む）は、投与に使用するまで褐色ガラス瓶（遮光）に入れて冷蔵庫内（許容範囲：2~8°C、実測温度：2.8~6.9°C）に保存した。

6.2.2.3 被験液の安定性

4-エテニル-2-メトキシフェノールの 1 及び 200 mg/mL 溶液（媒体：コーン油）は褐色ガラス瓶に入れて冷蔵（冷蔵庫内、許容範囲：2~8°C）・遮光下 7 日後、室温・遮光下 24 時間保存した時の安定性が、[REDACTED] で確認されている（試験番号：[REDACTED]、Attachment 2）。

6.2.2.4 被験液の濃度確認

投与 1 日及び投与 13 週の投与に用いる各濃度の被験液について、その濃度を [REDACTED] で HPLC 法を用いて確認した。その結果、表示値に対する割合は 96.5~104.5%（許容範囲：表示値に対する割合 100±10%以内）であり、許容範囲内であった（Attachment 3）。分析法の概略を次に示す。

1 濃度当たりの採取本数及び採取量

	:	1 濃度当たり 1 本（約 30 mL を採取）
測定対象物質	:	4-エテニル-2-メトキシフェノール
標準物質	:	
名称	:	4-エテニル-2-メトキシフェノール
ロット番号	:	[REDACTED]
保存条件	:	冷蔵（許容範囲：1~10°C）、遮光
保存場所	:	[REDACTED] の冷蔵庫、[REDACTED] の冷蔵庫及び [REDACTED] の冷凍冷蔵庫の冷蔵庫部分（いずれも許容範囲：2~8°C、実測値：2.8~6.9°C）

濃度測定用試料溶液の調製：

以下の表に従い、各測定試料を無作為に n=3 で正確に採取し、エタノールで希釈した濃度測定用試料溶液を用時調製した。

濃度 (mg/mL)	1次希釈		2次希釈		希釈率
	採取量 (mL)	定容量 (mL)	採取量 (mL)	定容量 (mL)	
20	1	100	1	10	1000
60	1	100	1	30	3000
200	1	100	1	100	10000

HPLC システム

機器名及び型式		メーカー
HPLC	e2695 セパレーションモジュール	Waters Corporation
検出器	2489 デュアルλUV/VIS 検出器	
データ処理ソフト	Empower 3	

HPLC 測定条件

検出 : UV (測定波長 260 nm)
 カラム : YMC Pack Pro C18 RS
 (4.6 mm I.D. × 150 mm、粒子径 5 μm、株式会社ワイ
 エムシィ)

カラム恒温槽設定温度

: 40°C
 移動相 : 純水/アセトニトリル混液 (3:2)
 ニードル洗浄液 : 純水/アセトニトリル混液 (3:2)
 流量 : 1.0 mL/min
 試料注入量 : 10 μL
 オートサンプラー内設定温度
 : 10°C
 測定時間 : 10 分間
 測定の構成 :

注入 順序	注入 回数	注入内容	注入目的
1	6	標準溶液	システム適合性
2	1	標準溶液	濃度
3	1	20 mg/mL 被験液-1 の 濃度測定用試料溶液	
4	1	20 mg/mL 被験液-2 の 濃度測定用試料溶液	
5	1	20 mg/mL 被験液-3 の 濃度測定用試料溶液	
6	1	60 mg/mL 被験液-1 の 濃度測定用試料溶液	
7	1	60 mg/mL 被験液-2 の 濃度測定用試料溶液	
8	1	標準溶液	
9	1	60 mg/mL 被験液-3 の 濃度測定用試料溶液	



10	1	200 mg/mL 被験液-1 の 濃度測定用試料溶液	
11	1	200 mg/mL 被験液-2 の 濃度測定用試料溶液	
12	1	200 mg/mL 被験液-3 の 濃度測定用試料溶液	
13	1	標準溶液	

6.3 試験動物種及び系統の選択理由

毒性試験ガイドラインによりげっ歯類を用いた試験が必要とされている。ラットは医薬品などの安全性試験に広く用いられており、この試験に使用される Sprague-Dawley 系統のラットは特性がよく知られ、背景資料が豊富であることから選択した。

6.4 試験動物及び群分け

- 動物種 : ラット (SPF)
- 系統 : Sprague-Dawley [CrI:CD(SD)]
- 生産所 : 日本チャールス・リバー株式会社、厚木飼育センター
- 購入時週齢 : 5 週齢
- 購入匹数 : 雌雄各 50 匹
- 検疫・馴化期間 : 9 (雄) 又は 10 (雌) 日間 (4 日間の検疫期間を含む)
- 投与開始時週齢 : 6 週齢
- 供試動物数 : 雌雄各 40 匹
- 検疫・馴化期間中の飼育観察 : 体重測定 (3 回)、体外表、栄養状態、姿勢、行動及び排泄物の異常などの一般状態観察 (1 回/日) 及び眼科学検査を実施した^注。
- 供試動物の選択 : 体重増加 (検疫初回の体重~群分け時の体重) が順調で一般状態に異常がなく健康と思われる動物を選択した。なお、検疫・馴化期間中の一般状態及び体重推移に異常を示す動物はみられなかった。
- 群分け : 群分け当日 (雄は投与開始の 2 日前、雌は投与開始の 3 日前) の体重に基づいて、各群の平均体重ができるだけ均等となるよう各群を構成した。個体の割付けはコンピュータを用いたブロック配置法及び無作為抽出法の組合せにより行った。
- 投与開始時の体重範囲 : 投与開始時の体重範囲は雄で 183~216 g (平均値 198 g)、雌で 144~195 g (平均値 162 g) であった。

雄は平均値±20%（雄：159~237 g）以内であったが、雌1例〔動物番号4104（195 g）〕で平均値±20%（雌：130~194 g）以内から逸脱が認められた。しかし、同動物の逸脱の程度は非常に軽微であったことから、試験群として使用した。

残余動物の処置 : 投与開始日に試験から除外し、教育・研究用に有効利用した。

注： 投与開始前の検査で硝子体動脈遺残、硝子体出血、限局性網膜ひだ、虹彩出血及び癒着による中間透光体及び眼底観察不能がみられた雌雄各6例については、試験評価に悪影響を及ぼす可能性があるとして判断し、群分け対象から除外した。

6.5 飼育条件

飼育室の環境 : 温度 $23 \pm 3^{\circ}\text{C}$ （実測値：20.2~23.6 $^{\circ}\text{C}$ ）、相対湿度 $50 \pm 20\%$ （実測値：24~56%）^註、換気回数1時間当たり10~20回、照明1日12時間（07:00~19:00）の動物飼育室（飼育室番号：[REDACTED] [REDACTED]）。床敷（アルファドライ：Shepherd Specialty Papers, Inc、ロット番号：[REDACTED] [REDACTED] [REDACTED]）を入れたプラスチックケージ（W 280 × D 440 × H 210 mm：日本クレア株式会社）に、同性2匹ずつ収容。

飼料 : 固型飼料 CR-LPF（放射線滅菌、オリエンタル酵母工業株式会社、ロット番号：[REDACTED] [REDACTED] [REDACTED]）を自由に摂取させた。

飲料水 : [REDACTED] 水道水を給水瓶により自由に摂取させた。

環境エンリッチメント : ステンレス棒（ケージの蓋から吊り下げた玩具）を与えた。

注： 「3.10 試験成績の信頼性に影響を及ぼしたと思われる環境要因」参照

6.6 飼料、床敷及び飲料水中の混入物質の分析

混入物質の分析に関する下記の分析報告書を入手し、基準内であることを確認した。

- 供試飼料についての分析報告書（Eurofins Food and Product Testing Japan K.K.、供試ロット）
- 供試床敷についての分析報告書（N·P Analytical Laboratories、供試ロット）
- 水道法に準拠する水質の分析報告書（株式会社 江東微生物研究所）

6.7 動物の識別及びケージへの表示

- 小動物用耳標 : 入荷時に装着した。
- 動物番号 : 群分け後は、試験群、性及び群内の個体番号が区別できるよう、4桁の数字を割り当てた（表1の群構成表参照）。各飼育ケージに投与量（群）ごとに色分けしたケージラベルをつけ、試験番号、投与経路、投与量、性、動物番号、耳標番号及び剖検予定日を明記した。

6.8 投与経路、投与期間、投与方法及び投与回数とそれらの選択理由

本被験物質は食品添加物として使用されることから、毒性試験における投与方法は混餌投与による経口投与が望ましい。しかし、被験物質の性状から、混餌飼料の調製が困難であること、また、本被験物質は香料として使用されていることから、対照群への影響も考慮し、げっ歯類の毒性試験の一般的な投与方法である強制経口投与を選択した。投与期間は13週間（91日間）とした。投与回数は反復投与試験で一般的に行われている1日1回（7回/週）とした。投与容量は5 mL/kg体重とし、フレキシブル胃ゾンデを用いて強制経口投与した（08:01~12:09の間）。対照群には媒体（コーン油）を同様に投与した。動物ごとの投与液量は最新の体重を基準に算出した（表示単位：0.1 mL）。

6.9 投与量及びその設定根拠並びに群構成

で実施した4-エテニル-2-メトキシフェノールのラットを用いた14日間反復経口投与毒性試験（予備試験、試験番号：、投与量：100、300、1000 mg/kg¹⁾において、一般状態では1000 mg/kg投与群の雌雄で投与直後に自発運動の減少、血液化学検査では1000 mg/kg投与群の雌雄で総コレステロールの有意な高値、器官重量では1000 mg/kg投与群の雌で肝臓重量の有意な高値がみられた。これらの結果と投与期間を考慮して、1000 mg/kgを高用量とし、以下公比3で減じて300及び100 mg/kgを中及び低用量に設定し、これに対照群を加え、計4群を設けた。1群当たりの動物は雌雄各10匹とした。群構成表を表1に示す。

表1 群構成

試験群	投与量 (mg/kg)	濃度 (mg/mL)	投与容量 (mL/kg)	性	動物数	動物番号
対照群	0	0	5	雄	10	1001~1010
				雌	10	1101~1110
低用量群	100	20	5	雄	10	2001~2010
				雌	10	2101~2110
中用量群	300	60	5	雄	10	3001~3010
				雌	10	3101~3110
高用量群	1000	200	5	雄	10	4001~4010
				雌	10	4101~4110

6.10 観察及び検査の方法

投与期間中、試験群の全動物について次の観察及び検査を行った。試験日の起算については以下の通りである。

投与 1 日 (Day 1 of administration) : 投与開始日

投与 1 週 (Week 1 of administration) : 投与 1 から投与 7 日

6.10.1 一般状態の観察

全動物について、体外表、栄養状態、姿勢、行動及び排泄物の異常などの一般状態を 1 日 3 回 (投与前、投与直後及び投与 1~3 時間後、ただし、雌の投与 2 日を除いて土曜及び休日は投与前と投与直後の 2 回)、剖検日は剖検のための動物搬出前に 1 回、観察した。

6.10.2 体重測定

全動物について、投与 1 週は投与 1、4 及び 7 日の 3 回、その後は 7 日ごとに毎週 1 回、測定当日の投与前に体重を測定した (08:21~11:00 の間)。剖検日には相対器官重量算出のため、前日から約 16 時間絶食させた後の体重を測定した。

6.10.3 摂餌量測定

全ケージについて、投与開始日の測定は前日からの 1 日量を、投与 7 日は 6 日間の累積摂取量を、その後は 7 日ごとに 7 日間の累積摂取量を測定日の投与前 (08:58~11:19 の間) に測定し、1 匹 1 日量 (ケージごと) を算出した。

6.10.4 眼科学検査

投与 13 週 (投与後、雄 : 投与 89 日、雌 : 投与 88 日) に各群の雌雄各 5 匹 (群内番号 1~5 番) について検査を実施した。

前眼部以下の観察に先立って、ミドリン P 点眼液 (参天製薬株式会社、ロット番号 : XXXXXXXXXX) を点眼した後、前眼部、中間透光体及び眼底について倒像検眼鏡 (OMEGA 500: Heine Optotechnik GmbH & Co. KG) を用いて検査した。観察の際には、28D の非球面レンズを併用した。

6.10.5 尿検査

検査は投与 13 週（雄：投与 86~87 日^{注1}、雌：85~86 日）に行った。

全動物について、検査当日の投与後にそれぞれ採尿器をセットしたケージに個別に収容し、絶食・自由摂水下で 4 時間尿を、次いで自由摂食・自由摂水下でその後の 20 時間尿を採取し、表 2 に記載した項目及び方法により検査を行った。

注 1： 雄 1 例（動物番号 2007）は投与 86~87 日に採尿した 20 時間尿をこぼしてしまったため、投与 88~89 日に 20 時間尿を再採尿し、その尿を検査に用いた。

表 2 尿検査の項目、測定法及び使用機器など

1) 4 時間尿についての検査	
検査項目	測定方法
pH	マルティステイックス試験紙 ^{a)}
タンパク質	マルティステイックス試験紙 ^{a)}
ケトン体	マルティステイックス試験紙 ^{a)}
グルコース	マルティステイックス試験紙 ^{a)}
潜血	マルティステイックス試験紙 ^{a)}
ビリルビン	マルティステイックス試験紙 ^{a)}
ウロビリノーゲン	マルティステイックス試験紙 ^{a)}
色調	肉眼観察
沈渣	鏡検法
尿量（4 時間量） ^{注2}	容量測定（単位：mL）
2) 20 時間尿についての検査	
検査項目	測定方法
尿量（20 時間量） ^{注2}	容量測定（単位：mL）
浸透圧	氷点降下法 ^{b)} （単位：mOsm/kg）
ナトリウム ^{注3}	イオン選択電極法 ^{c)} （単位：mmol/24h）
カリウム ^{注3}	イオン選択電極法 ^{c)} （単位：mmol/24h）
塩素 ^{注3}	イオン選択電極法 ^{c)} （単位：mmol/24h）
使用測定機器	
a)：尿自動分析装置 Clinitek Advantus TM (Siemens Healthcare Diagnostics Inc.)	
b)：自動浸透圧測定装置 オズモステーション OM-6060 (株式会社アークレイ)	
c)：臨床化学自動分析装置 TBA-120FR [キヤノンメディカルシステムズ株式会社 (旧社名：東芝メディカルシステムズ株式会社)]	

注 2： 4 時間の尿量と 20 時間の尿量を合計して 24 時間の尿量（mL/24h）を算出した。

注 3： 20 時間尿について濃度を測定し、測定濃度と 24 時間の尿量から 1 日当たりの排泄量を算出した。

6.10.6 血液学検査

投与期間終了の翌日の計画剖検時に、前日から一夜（約 16~19 時間）絶食させた全動物についてイソフルラン麻酔下で開腹し、腹大動脈から EDTA-2K 加採血瓶（SB-41：シスメックス株式会社）に血液（約 1 mL）を採取した。得られた血液について表 3-1) に記載した項目及び方法により検査した。更に、血液（0.9 mL）を 3.2% クエン酸ナトリウム溶液加採血管（インセパック II-W、0.9 mL 採血用：積水メディカル株式会社）に採取し、遠心分離（設定：23°C、2,380 × g、10 分間）により得られた血漿について表 3-2) に記載した項目及び方法により検査した。なお、鏡検による確認に備え、全例について May-Grünwald-Giemsa 染色法による血液塗抹標本を作製したが、いずれの動物も測定結果に問題はなかったため、観察は実施しなかった。

表 3 血液学検査の項目、測定法及び使用機器など

1) EDTA-2K 加血液についての検査		
検査項目	測定方法	単位
赤血球数 (RBC) 注 ¹	2 角度レーザーフローサイトメトリー法 ^{a)}	10 ⁴ (E4)/μL
ヘモグロビン濃度 (HGB)	シアンメトヘモグロビン変法 ^{a)}	g/dL
ヘマトクリット値 (HCT)	赤血球数及び平均赤血球容積から算出 ^{a)}	%
平均赤血球容積 (MCV)	2 角度レーザーフローサイトメトリー法 ^{a)}	fL
平均赤血球ヘモグロビン量 (MCH)	赤血球数及びヘモグロビン濃度から算出 ^{a)}	pg
平均赤血球ヘモグロビン濃度 (MCHC)	ヘモグロビン濃度及びヘマトクリット値から算出 ^{a)}	g/dL
網赤血球数 (Retic)	RNA 染色によるレーザーフローサイトメトリー法で求めた網赤血球率及び赤血球数から算出 ^{a)}	10 ⁹ (E9)/L
血小板数 (PLT)	2 角度レーザーフローサイトメトリー法 ^{a)}	10 ⁴ (E4)/μL
白血球数 (WBC)	2 角度レーザーフローサイトメトリー法 ^{a)}	10 ² (E2)/μL
白血球分類注 ²	ペルオキシダーゼ染色によるフローサイトメトリー法+2 角度レーザーフローサイトメトリー法で求めた百分率及び白血球数から算出 ^{a)}	10 ² (E2)/μL
2) クエン酸ナトリウム加血液から分離した血漿についての検査		
検査項目	測定方法	単位
プロトロンビン時間 (PT)	Coagulometric test ^{b)}	s
活性化部分トロンボプラスチン時間 (APTT)	Coagulometric test ^{b)}	s
フィブリノゲン量 (FIB)	Coagulometric test ^{b)}	mg/dL
使用測定機器		
a): 総合血液学検査装置 ADVIA2120i (Siemens Healthcare Diagnostics Inc.)		
b): 血液凝固自動分析装置 ACL Elite Pro (Instrumentation Laboratory Inc.)		

注 1：雌 1 例（動物番号 1107）で、赤血球系測定不良の可能性を示すエラーがみられたため、SOP に従って再測定を実施した。その結果、エラー表示が認められなかったため、再測定値を採用した。

注 2：リンパ球 (LYMP)、好中球 (NEUT)、好酸球 (EOS)、好塩基球 (BASO)、単球 (MONO) 及び大型非染色球 (LUC)

6.10.7 血液化学検査

血液学検査のための採血と同時にヘパリン加試験管（ベノジェクト II ヘパリンナトリウム、5 mL 採血用：テルモ株式会社）に採取した血液（約 4 mL）を遠心分離（設定：23°C、2,380×g、10 分間）して得られた血漿について表 4 に記載の項目及び方法により検査した。

表 4 血液化学検査の項目、測定法及び使用機器など

検査項目	測定方法	単位
AST	UV-rate 法 ^{a)}	IU/L
ALT	UV-rate 法 ^{a)}	IU/L
LDH	UV-rate 法 ^{a)}	IU/L
γ-GTP	L-γ-グルタミル-3-カルボキシ-4-ニトロアニリド法 ^{a)}	IU/L
ALP	Bessey-Lowry 法 ^{a)}	IU/L
総コレステロール (T-CHO)	CEH-COD-POD 法 ^{a)}	mg/dL
トリグリセライド (TG)	LPL-GK-GPO-POD 法 ^{a)}	mg/dL
リン脂質 (PL)	PLD-ChOD-POD 法 ^{a)}	mg/dL
総ビリルビン (T-BIL)	ビリルビンオキシダーゼ法 ^{a)}	mg/dL
グルコース (GLU)	グルコースデヒドロゲナーゼ法 ^{a)}	mg/dL
尿素窒素 (BUN)	Urease-LEDH 法 ^{a)}	mg/dL
クレアチニン (CRNN)	Creatininase-creatinase-sarcosine oxidase-POD 法 ^{a)}	mg/dL
ナトリウム (Na)	イオン選択電極法 ^{a)}	mmol/L
カリウム (K)	イオン選択電極法 ^{a)}	mmol/L
塩素 (Cl)	イオン選択電極法 ^{a)}	mmol/L
カルシウム (Ca)	OCPC 法 ^{a)}	mg/dL
無機リン (P)	モリブデン酸法 ^{a)}	mg/dL
総タンパク質 (TP)	Biuret 法 ^{a)}	g/dL
アルブミン (ALB)	BCG 法 ^{a)}	g/dL
A/G 比 (A/G)	総タンパク質及びアルブミンから算出	
使用測定機器		
a)：臨床化学自動分析装置 TBA-120FR [キヤノンメディカルシステムズ株式会社 (旧社名：東芝メディカルシステムズ株式会社)]		

6.10.8 病理学検査

6.10.8.1 剖検

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

6.10.8.2 器官重量測定

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

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

脳、下垂体、甲状腺（上皮小体を含む）*、副腎*、胸腺、脾臓、心臓、肺（気管支を含む）、唾液腺（顎下腺及び舌下腺）*、肝臓、腎臓*、精巣*、前立腺、精嚢（凝固腺を含む）、卵巣*及び子宮

6.10.8.3 病理組織学検査

全ての動物について次に示す器官/組織を採取し、10%リン酸緩衝ホルマリン液で固定した。ただし、眼球及び視神経は3%グルタルアルデヒド・2.5%ホルマリン液で、また、精巣及び精巣上体はブアン液でそれぞれ固定したのち、10%リン酸緩衝ホルマリン液で保存した。その後、全動物の全器官/組織をパラフィン包埋後切片とし、ヘマトキシリン・エオジン染色標本（H・E）を作製した。このうち、先ず、対照群及び高用量群の全ての器官/組織について鏡検した。その結果、高用量群で被験物質投与による影響が疑われた鼻腔（雌雄）、肝臓（雌雄）及び胃（雌雄）については低及び中用量群のすべての動物についても鏡検した。*で示した両側性器官については両側を摘出し、片側のみを鏡検したが、他の両側性器官は両側を鏡検した。**で示した上皮小体は微小な器官であるため両側の標本作製を試み、片側（左側を優先）を鏡検した。各群80%以上の動物で鏡検が可能であったため、標本の再作製は行わなかった。

大脳、小脳、脊髄（胸部）、坐骨神経*、眼球、視神経、ハーダー腺、下垂体、甲状腺、上皮小体**、副腎、胸腺、脾臓、顎下リンパ節*、腸間膜リンパ節、心臓、胸大動脈、気管、肺（気管支を含む）、舌、食道、胃、十二指腸、空腸、回腸（パイエル板を含む）、盲腸、結腸、直腸、顎下腺、舌下腺、肝臓、膵臓、腎臓、膀胱、精巣、精巣上体、前立腺、精嚢（凝固腺を含む）*、卵巣、卵管、子宮、膣、乳腺（鼠径部）*、胸骨（骨髄を含む）、大腿骨（膝関節及び骨髄を含む）*、大腿部骨格筋*、皮膚（鼠径部）*、鼻腔及びジンバル腺*
他に、喉頭及び個体識別部位（耳介）を摘出して保存した。

病理組織学検査において対照群の雌雄各1例（動物番号1005及び1104）及び1000 mg/kg投与群の雄1例（動物番号4004）で、上皮小体（両側）の病理組織学検査標本作製することができなかった。しかし、評価に十分な例数が確保できており、高用量群の鏡検で上皮小体に被験物質投与による影響が認められていないことから、試験評価への影響はないものと判断した。

6.11 データ採取に使用したコンピュータシステム

MiTOX-BOZO システム（Version 7.6.1、三井造船システム技研株式会社）

Pathos5 システム（Pathology Operating Systems Ltd.）



6.12 統計解析

計量データ（体重、摂餌量、尿検査の定量的項目、血液学検査、血液化学検査及び器官重量）について、対照群と被験物質投与群との間で統計解析を行った。

各群の平均値±標準偏差を算出し、Bartlett法²⁾により分散性の検定を行った（有意水準：1%）。分散が等しい場合はDunnett法^{3),4)}を用いて、不等分散の場合はSteelの検定⁵⁾を用いて、対照群と各投与群との間で検定を行った（有意水準：5及び1%、両側）。検定には、統計パッケージSAS Release Ver. 9.1.3（SAS Institute Inc.）を使用した。

また、相対器官重量算出のためのみに行った剖検日の体重は統計解析の対象としなかった。

7. 試験結果

7.1 一般状態

成績を Table 1-1~1-14 並びに Appendix 1-1~1-56 に示した。

1000 mg/kg 投与群の雌雄で、すべての投与日の投与直後のみに 1~5 例で自発運動の減少がみられた。

300 mg/kg 以下の投与群の雌雄では、いずれの動物にも異常はみられなかった。

7.2 体重

成績を Fig. 1、2 及び Table 2-1~2-4 並びに Appendix 2-1~2-8 に示した。

1000 mg/kg 投与群の雄で投与 84 及び 91 日、雌で投与 63 日に有意な低値が認められた。

300 mg/kg 以下の投与群の雌雄では、対照群とほぼ同様に推移した。

7.3 摂餌量

成績を Fig. 3、4 及び Table 3-1~3-4 並びに Appendix 3-1~3-8 に示した。

1000 mg/kg 投与群の雄で投与 7 日に有意な低値が認められたが、投与 7 日以降は対照群との間に有意差はみられなかった。雌では、投与 49 日に有意な低値が認められたものの、それ以外は対照群との間に有意差はみられなかった。

300 mg/kg 以下の投与群の雌雄では、対照群とほぼ同様に推移した。

7.4 眼科学検査

成績を Table 4-1 及び 4-2 並びに Appendix 4-1~4-8 に示した。

雌雄ともに被験物質投与に起因する変化は認められなかった。

なお、対照群の雌で認められた所見は、この種の動物にみられる変化であり、またその発生状況から偶発性の変化と判断した。

7.5 尿検査

成績を Table 5-1~5-16 及び Appendix 5-1~5-16 に示した。

1000 mg/kg 投与群の雄で pH の低下傾向、尿量、ナトリウム及び塩素排泄量の有意な高値並びに浸透圧の有意な低値がみられた。

その他に、300 mg/kg 投与群の雌で尿量の有意な高値及び浸透圧の有意な低値がみられたが、用量に関連した変化でないことから、偶発性の変化と考えられた。

7.6 血液学検査

成績を Table 6-1~6-8 及び Appendix 6-1~6-24 に示した。

雌雄ともに被験物質投与に起因する変化は認められなかった。

100 mg/kg 投与群の雌でフィブリノゲン量の有意な高値がみられたが、用量に関連

した変化でないことから、偶発性の変化と考えられた。

7.7 血液化学検査

成績を Table 7-1~7-6 及び Appendix 7-1~7-16 に、結果の総括を次の表 5 に示した。

表 5 血液化学検査の総括

性	雄				雌			
	0	100	300	1000	0	100	300	1000
投与量 (mg/kg)	0	100	300	1000	0	100	300	1000
動物数	10	10	10	10	10	10	10	10
ALT (IU/L)	41	37	39	51* (+24%)	37	38	39	50* (+35%)
γ-GTP (IU/L)	0	0	1*	1**	0	0	1**	1**
T-CHO (mg/dL)	72	65	69	92** (+28%)	77	76	85	123** (+60%)
PL (mg/dL)	109	103	108	139** (+28%)	150	150	155	214** (+43%)
BUN (mg/dL)	16	13	13	14	19	17	17	14* (-26%)
K (mmol/L)	4.0	3.9	3.9	4.1	3.4	3.3	3.5	3.7** (+9%)

表中の値は各群の平均を示す。

() の値は対照群平均に対する増減率を示す (- : 減少、+ : 増加)

* : $p \leq 0.05$ 、** : $p \leq 0.01$ (対照群と比べ有意差あり)

1000 mg/kg 投与群の雄で ALT 活性、γ-GTP 活性、総コレステロール及びリン脂質の有意な高値が認められ、雌では ALT 活性、γ-GTP 活性、総コレステロール、リン脂質及びカリウムの有意な高値並びに尿素窒素の有意な低値がみられた。

300 mg/kg 投与群の雌雄で、γ-GTP 活性の有意な高値が認められた。

7.8 器官重量

成績を Table 8-1~8-4 及び Appendix 8-1~8-24 (絶対重量) 並びに Table 9-1~9-4 及び Appendix 9-1~9-24 (相対重量) に示した。

肝臓 : 絶対及び相対重量の有意な高値が 1000 mg/kg 投与群の雌に、相対重量の有意な高値が 1000 mg/kg 投与群の雄にみられた。

なお、前立腺の絶対重量の有意な低値、精巣及び雄の腎臓の相対重量の有意な高値が 1000 mg/kg 投与群にみられたが、体重減少に伴う変化と考えられた。卵巣の絶対及び相対重量の有意な高値が 300 mg/kg 投与群に認められたが、用量に関連した変化でないことから、偶発性の変化と考えられた。

7.9 剖検

成績を Table 10-1 及び 10-2 並びに Appendix 10-1~10-80 に示した。

胃 : 前胃の肥厚及び隆起巣が 1000 mg/kg 投与群の雌雄各 5 例及び雄 1 例にみられた。

その他の Table 及び Appendix に示す所見は、出現状況よりいずれも偶発性の変化と考えられた。

7.10 病理組織学検査

成績を Table 11-1~11-8 及び Appendix 10-1~10-80 に、結果の総括を次の表 6 に示した。

表 6 病理組織学検査の総括

性 投与量 (mg/kg) 動物数	雄				雌			
	0	100	300	1000	0	100	300	1000
動物数	10	10	10	10	10	10	10	10
肝臓								
肝細胞の空胞化	9	8	5	0	6	3	4	0
軽微	4	6	5	0	6	3	4	0
軽度	5	2	0	0	0	0	0	0
胃								
前胃の扁平上皮細胞の過形成	0	5	10	10	0	7	8	10
軽微	0	5	7	1	0	7	7	4
軽度	0	0	3	8	0	0	1	6
中等度	0	0	0	1	0	0	0	0
前胃の扁平上皮細胞の結節性過形成	0	0	0	1	0	0	0	0
中等度	0	0	0	1	0	0	0	0
前胃の過角化	0	5	10	10	0	7	8	10
軽微	0	5	7	1	0	7	7	4
軽度	0	0	3	6	0	0	1	5
中等度	0	0	0	3	0	0	0	1
腺胃の胃底腺の拡張	0	0	1	4	0	0	1	1
軽微	0	0	1	4	0	0	1	1
鼻腔								
呼吸上皮の細胞浸潤	0	0	0	1	0	0	0	2
軽微	0	0	0	0	0	0	0	2
軽度	0	0	0	1	0	0	0	0
呼吸上皮ののう胞	0	0	0	2	0	0	0	0
軽微	0	0	0	2	0	0	0	0
呼吸上皮の配列不整	0	0	0	6	0	0	0	2
軽微	0	0	0	6	0	0	0	2
嗅上皮の細胞浸潤	0	0	0	2	0	0	0	1
軽微	0	0	0	1	0	0	0	1
軽度	0	0	0	1	0	0	0	0
嗅上皮ののう胞	0	0	0	2	0	0	0	1
軽微	0	0	0	2	0	0	0	1



嗅上皮の萎縮	0	0	0	2	0	0	0	2
軽微	0	0	0	1	0	0	0	1
軽度	0	0	0	1	0	0	0	1
嗅上皮の配列不整	0	0	0	4	0	0	0	5
軽微	0	0	0	4	0	0	0	5
嗅腺の萎縮	0	0	0	10	0	0	0	10
軽度	0	0	0	0	0	0	0	1
中等度	0	0	0	10	0	0	0	9
嗅腺の限局性過形成	0	0	0	2	0	0	0	2
軽微	0	0	0	2	0	0	0	2
鼻腺の拡張	0	0	0	2	0	0	0	0
軽微	0	0	0	2	0	0	0	0

表中の数値は出現例数を示す。

- 肝臓 : 肝細胞の空胞化が対照群の雌雄からみられたが、300 mg/kg 以上の投与群の雄及び 1000 mg/kg 投与群の雌で程度/頻度が減少した。
- 胃 : 前胃の扁平上皮細胞の過形成及び過角化が 100 mg/kg 以上の投与群の雌雄に、腺胃の胃底腺の拡張が 300 mg/kg 以上の投与群の雌雄に、前胃の扁平上皮細胞の結節性過形成が 1000 mg/kg 投与群の雄にみられた。
- 鼻腔 : 呼吸上皮の細胞浸潤及び配列不整、嗅上皮の細胞浸潤、のう胞、萎縮及び配列不整、嗅腺の萎縮及び限局性過形成が 1000 mg/kg 投与群の雌雄に、呼吸上皮ののう胞及び鼻腺の拡張が 1000 mg/kg 投与の雄にみられた。

その他、Table 及び Appendix に示す所見が認められたが、その出現状況からいずれも偶発性の変化と考えられた。

8. 考察

4-エテニル-2-メトキシフェノールをラットに 90 日間反復投与した時の毒性を検討した。投与量は、0 (コーン油)、100、300 及び 1000 mg/kg とし、Sprague-Dawley 系ラット [CrI:CD(SD)、10 匹/性/群、投与開始時 6 週齢] に 91 日間強制経口投与した。

眼科学検査及び血液学検査では、被験物質投与による変化は認められなかった。

一般状態では、1000 mg/kg 投与群の雌雄で、すべての投与日の投与直後のみに自発運動の減少がみられたことから、被験物質投与による毒性変化と考えられた。

体重では、1000 mg/kg 投与群の雄で投与 84 及び 91 日、雌で投与 63 日に有意な低値が認められた。

摂餌量では、1000 mg/kg 投与群の雄で投与 7 日、雌で投与 49 日に有意な低値が認められた。

尿検査では、1000 mg/kg 投与群の雄で pH の低下傾向、尿量、ナトリウム及び塩素排泄量の有意な高値並びに浸透圧の有意な低値がみられたが、血液化学検査において血漿中電解質に変動はなく、腎臓の病理学検査にも異常が認められていないことから、毒性学的意義の乏しい変化と考えられた。

血液化学検査では、1000 mg/kg 投与群の雌雄で ALT 活性、総コレステロール及びリン脂質の有意な高値、300 mg/kg 以上の投与群の雌雄で γ -GTP 活性の有意な高値が認められ、病理学検査では 1000 mg/kg 投与群の雌雄で肝細胞の空胞化の程度/頻度の減少が認められたことから、被験物質の肝臓への毒性変化と考えられた。1000 mg/kg 投与群の雌で、カリウムの有意な高値及び尿素窒素の有意な低値がみられたが、尿検査及び腎臓の病理学検査で異常が認められていないことから、毒性学的意義の乏しい変化と考えられた。

病理学検査では、胃 (前胃及び腺胃)、肝臓及び鼻腔に被験物質投与による毒性変化がみられた。胃では、100 mg/kg 以上の投与群の雌雄で前胃の扁平上皮細胞の過形成及び過角化、300 mg/kg 以上の投与群の雌雄で腺胃の胃底腺の拡張、1000 mg/kg 投与群の雄で前胃の扁平上皮細胞の結節性過形成がみられた。扁平上皮細胞の過形成及び過角化は前胃にびまん性にみられたが、食道ではこのような変化がみられていないことから、被験物質と胃粘膜上皮が長時間接触したことにより惹起された変化であると推察された。扁平上皮細胞の結節性過形成は、粘膜下組織に軽度な浮腫や血管拡張を伴っていたことから、前胃粘膜傷害に対する反応性変化の可能性が考えられたが、詳細は不明であった。なお、剖検時に肉眼的にみられた前胃の肥厚及び隆起巣は、扁平上皮細胞の過形成/結節性過形成及び過角化に関連した変化と考えられた。また、腺胃では、300 mg/kg 以上の投与群の雌雄で胃底腺の拡張がみられ、投与との関連が疑われたが、原因は不明であった。

肝臓では、肝細胞の空胞化が対照群からみられた。空胞は媒体であるコーン油の投与に関連した変化と考えられた。本変化の程度/頻度は 300 mg/kg 以上の投与群の雄及

び 1000 mg/kg 投与群の雌で減少し、血液化学検査では 1000 mg/kg 投与群の雌雄で総コレステロール及びリン脂質の有意な高値がみられていたことから、被験物質の肝機能（脂質代謝）に対する影響が疑われた。なお、1000 mg/kg 投与群の雌雄において肝臓重量の増加がみられていたが、それに相当する明らかな組織学変化はみられなかった。

鼻腔では、1000 mg/kg 投与群の雌雄で、呼吸上皮に細胞浸潤及び配列不整、嗅上皮に細胞浸潤、のう胞、萎縮及び配列不整、嗅腺に萎縮及び限局性過形成がみられた。加えて、1000 mg/kg 投与群の雄では、呼吸上皮ののう胞及び鼻腺の拡張がみられた。嗅上皮の配列不整は傷害後の再生でみられることが知られていることから⁶⁾、呼吸上皮及び嗅上皮においてみられた諸々の変化は、粘膜上皮の傷害及びその再生に関連した変化と考えられた。嗅腺の萎縮は嗅上皮の変化がない部位においてもみられていることから、嗅腺に対する被験物質の直接的な影響の可能性が疑われた。また、嗅腺の限局性過形成は再生性変化と推察された。

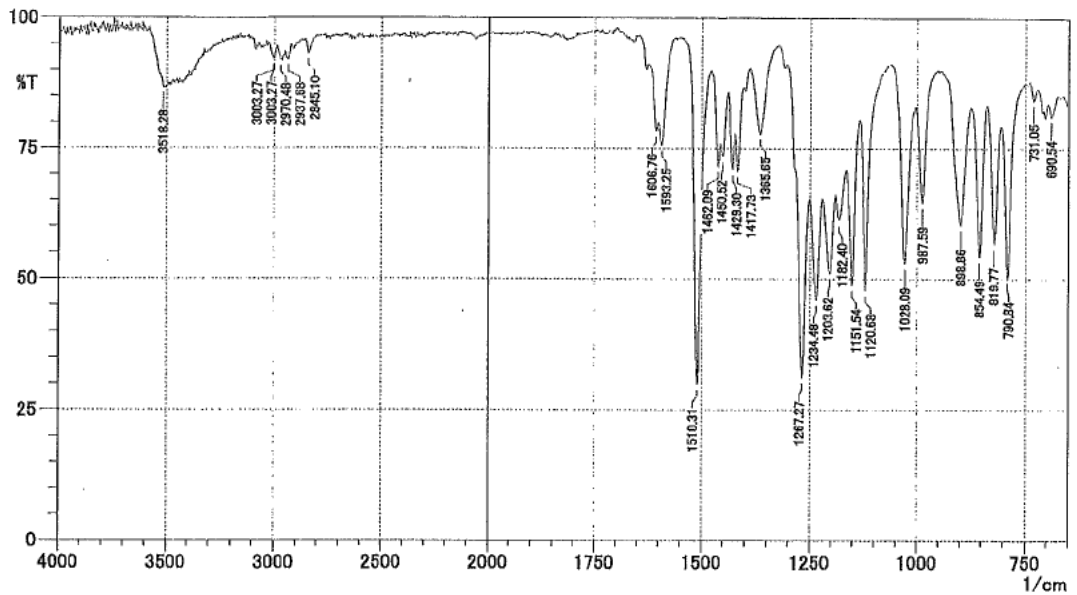
以上の如く、4-エテニル-2-メトキシフェノールをラットに 90 日間反復投与した結果、胃への影響が 100 mg/kg 以上の投与群の雌雄、肝臓への影響が 300 mg/kg 以上の投与群の雄及び 1000 mg/kg 投与群の雌に、鼻腔への影響が 1000 mg/kg 投与群の雌雄にみられた。したがって、本試験における無毒性量は雌雄ともに 100 mg/kg 未満と推定された。

9. 文献

- 1) ████████ : 4-エテニル-2-メトキシフェノール : ラットを用いた 14 日間反復経口投与毒性試験 (予備試験) (██████████, 試験番号 : ████████、2018 年)
- 2) Snedecor GW, Cochran WG. Statistical methods, 8th ed. Ames: Iowa State University Press; 1989.
- 3) Dunnett CW. A multiple comparison procedure for comparing several treatments with a control. J Am Stat Assoc 1955; 50: 1096-121.
- 4) Dunnett CW. New tables for multiple comparisons with a control. Biometrics. 1964; 20: 482-91.
- 5) Steel RGD. A multiple comparison rank sum test: Treatments versus control. Biometrics 1959; 15: 560-72.
- 6) 長野嘉介、今井田克己、相磯茂敏 (2017) : 呼吸器系、新毒性病理組織学(日本毒性病理学会 編)、pp. 99、西村書店、東京

試験成績書
(4-エテニル-2-メトキシフェノールの特性)

試験番号 : [REDACTED]
ステージ : 被験物質の使用前
測定日 : [REDACTED]
被験物質 : 4-エテニル-2-メトキシフェノール
(ロット番号; [REDACTED])
試験項目 : 赤外吸収スペクトルの確認 (ATR 法)
結果 : 特性のスペクトルを以下に示す。



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

分析結果
(4-エテニル-2-メトキシフェノールの安定性)

試験番号 : [REDACTED]

ステージ : 投与期間終了後

測定日 : [REDACTED]

被験物質 : 4-エテニル-2-メトキシフェノール (Lot No. ; [REDACTED])

測定項目 : 被験物質の安定性

判定基準 : 安定性のスペクトルを特性のスペクトル ([REDACTED]) と比較するとき、同一波数のところに同様の強度の吸収を認める。ただし、 2300 cm^{-1} 付近に吸収が観られた場合、この吸収は二酸化炭素の影響であるため、評価対象としない。

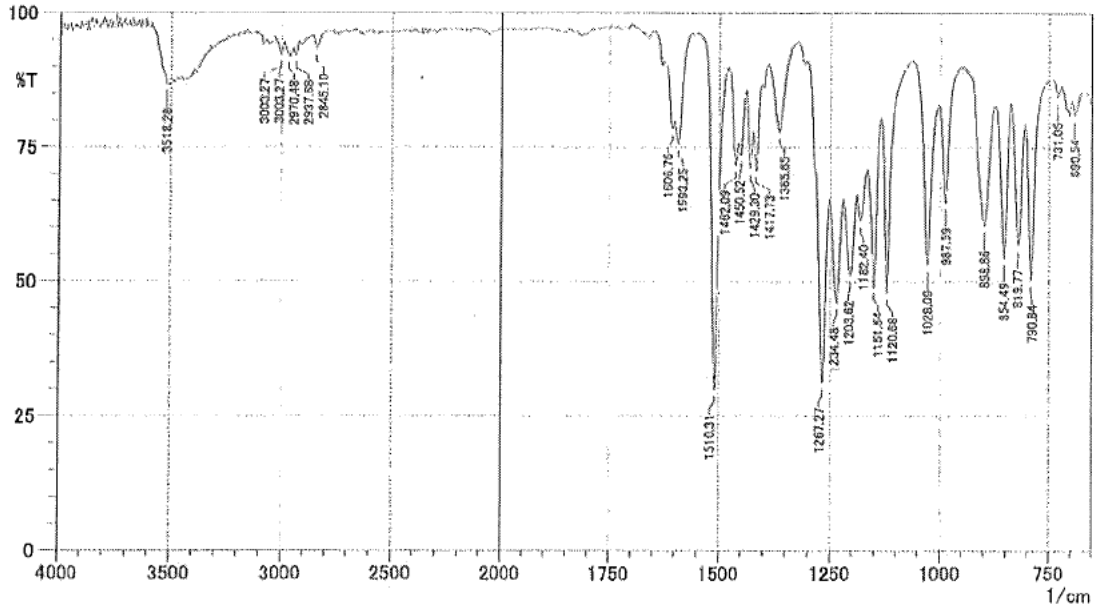
結果 : 安定性のスペクトルを特性のスペクトルと比較したとき、同一波数のところに同様の強度の吸収を認めた。なお、赤外吸収スペクトルは次のページに示す。

判定 : 適

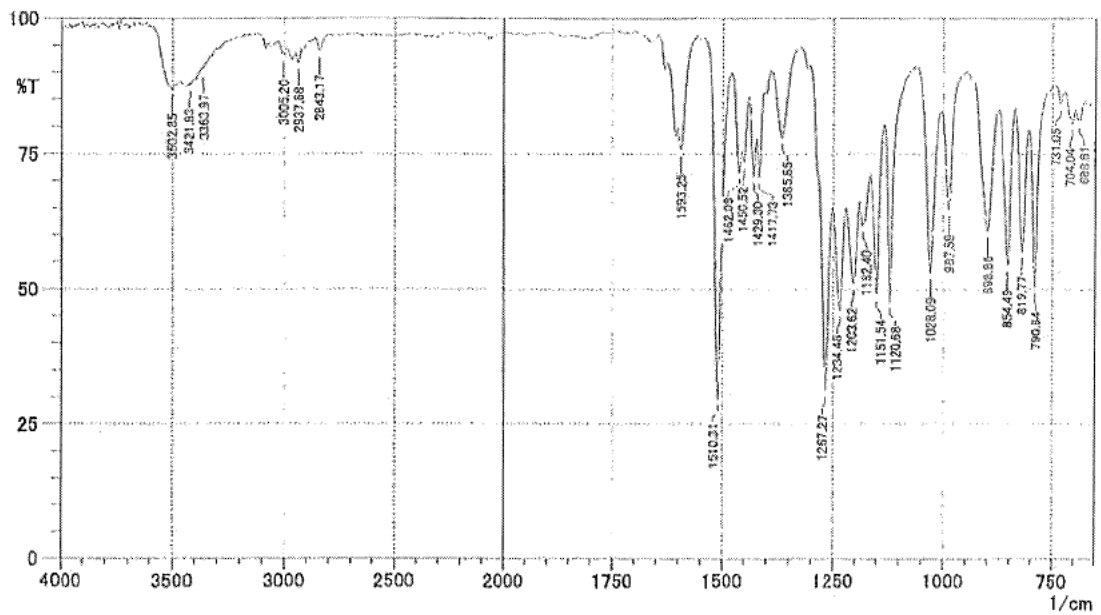
分析結果
(4-エテニル-2-メトキシフェノールの安定性)

試験番号 : [REDACTED]
ステージ : 投与期間終了後
結果 :

特性 [REDACTED] 試験番号 : [REDACTED]





安定性



試験成績書

(被験液中 4-エテニル-2-メトキシフェノールの安定性)

試験番号 : 

被験物質 : 4-エテニル-2-メトキシフェノール
(ロット番号 : 

媒体 : コーン油
形態 : 溶液

測定対象物質 : 4-エテニル-2-メトキシフェノール

保存条件 : 褐色ガラス瓶にて、冷蔵(冷蔵庫内、許容範囲:2~8°C)
及び室温保存、遮光

保存期間 : 冷蔵・遮光下で7日間保存した後、室温・遮光下で24
時間保存

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

結果 : 次ページに記載

判定 : 適

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

試験成績書
(被験液中 4-エテニル-2-メトキシフェノールの安定性)

試験番号 : [REDACTED]

結果 :

調製濃度 (mg/mL)	測定濃度 (mg/mL)	
	調製直後	冷蔵 7 日間及び 室温 24 時間保存後
1.00	1.02	1.01
	0.972	1.00
	1.00	0.996
平均値 残存率 (%)	0.997 (100)	1.00 100.3
200	196	193
	205	192
	193	187
平均値 残存率 (%)	198 (100)	191 96.5

試験成績書訂正書
(被験液中 4-エテニル-2-メトキシフェノールの安定性)

試験番号 : XXXXXXXXXX

結果の表において記載漏れ、記載誤りがあったため、以下の通り下線部を追加、訂正する。

[訂正前]

結果 :

調製濃度 (mg/mL)	測定濃度 (mg/mL)	
	調製直後	冷蔵 7 日間及び 室温 24 時間保存後
<u>1.00</u>	1.02	1.01
	0.972	1.00
	1.00	0.996
平均值	0.997	1.00
残存率 (%)	(100)	100.3
<u>200</u>	196	193
	205	192
	193	187
平均值	198	191
残存率 (%)	(100)	96.5

[訂正後]

結果 :

濃度 (mg/mL)	調製濃度 (mg/mL)	測定濃度 (mg/mL)	
		調製直後	冷蔵 7 日間及び 室温 24 時間保存後
<u>1</u>	<u>0.993</u>	1.02	1.01
		0.972	1.00
		1.00	0.996
平均值	0.997	1.00	
残存率 (%)	(100)	100.3	
<u>200</u>	<u>200</u>	196	193
		205	192
		193	187
平均值	198	191	
残存率 (%)	(100)	96.5	

分析結果

試験番号 : [REDACTED]
 測定項目 : 濃度
 ステージ : 投与 1 日
 測定期間 : [REDACTED]

測定試料
 被験物質 : 4-エテニル-2-メトキシフェノール (Lot No. ; [REDACTED])
 形態 : 溶液
 媒体 : コーン油
 調製日 : [REDACTED]

測定対象物質 : 4-エテニル-2-メトキシフェノール

判定基準
 濃度 : 表示値に対する割合 ; 100±10%以内 (平均値で評価)

結果 :

表示値 (mg/mL)	測定濃度 (mg/mL)	平均値	表示値に 対する割合 (%)
20	20.9	20.9	104.5
	20.9		
	20.8		
60	61.7	62.0	103.3
	62.4		
	61.9		
200	207	207	103.5
	206		
	207		

判定 : 適

分析結果

試験番号 : [REDACTED]
 測定項目 : 濃度
 ステージ : 投与 13 週
 測定期間 : [REDACTED]

測定試料
 被験物質 : 4-エテニル-2-メトキシフェノール (Lot No. ; [REDACTED])
 形態 : 溶液
 媒体 : コーン油
 調製日 : [REDACTED]

測定対象物質 : 4-エテニル-2-メトキシフェノール

判定基準
 濃度 : 表示値に対する割合 ; 100±10%以内 (平均値で評価)

結果 :

表示値 (mg/mL)	測定濃度 (mg/mL)	平均値	表示値に 対する割合 (%)
20	20.3	20.1	100.5
	20.0		
	19.9		
60	58.4	59.3	98.8
	59.7		
	59.8		
200	195	193	96.5
	191		
	192		

判定 : 適

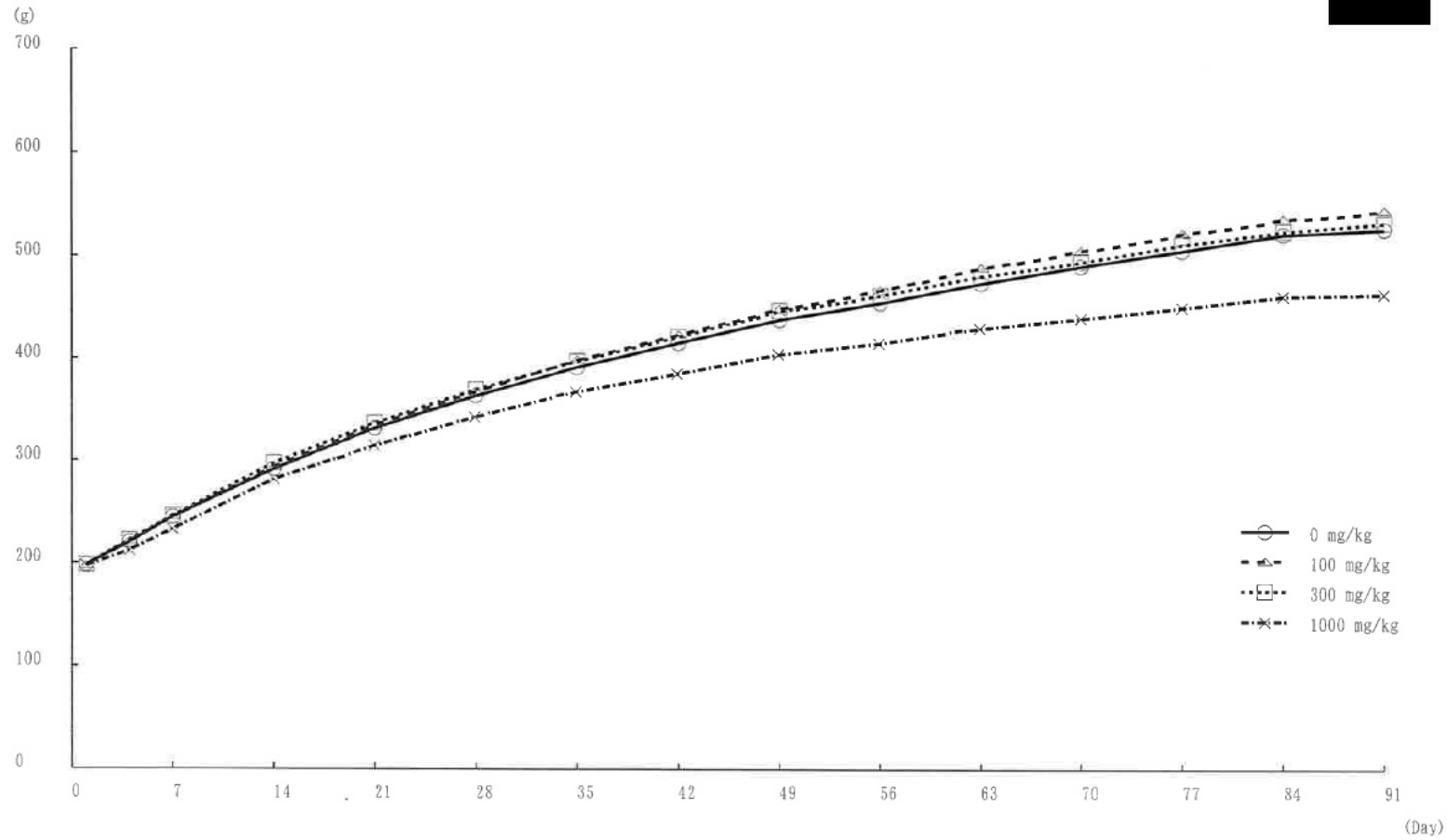


Fig. 1 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats
Body Weight - Male (Drug Admi. 1 - Drug Admi. 91)

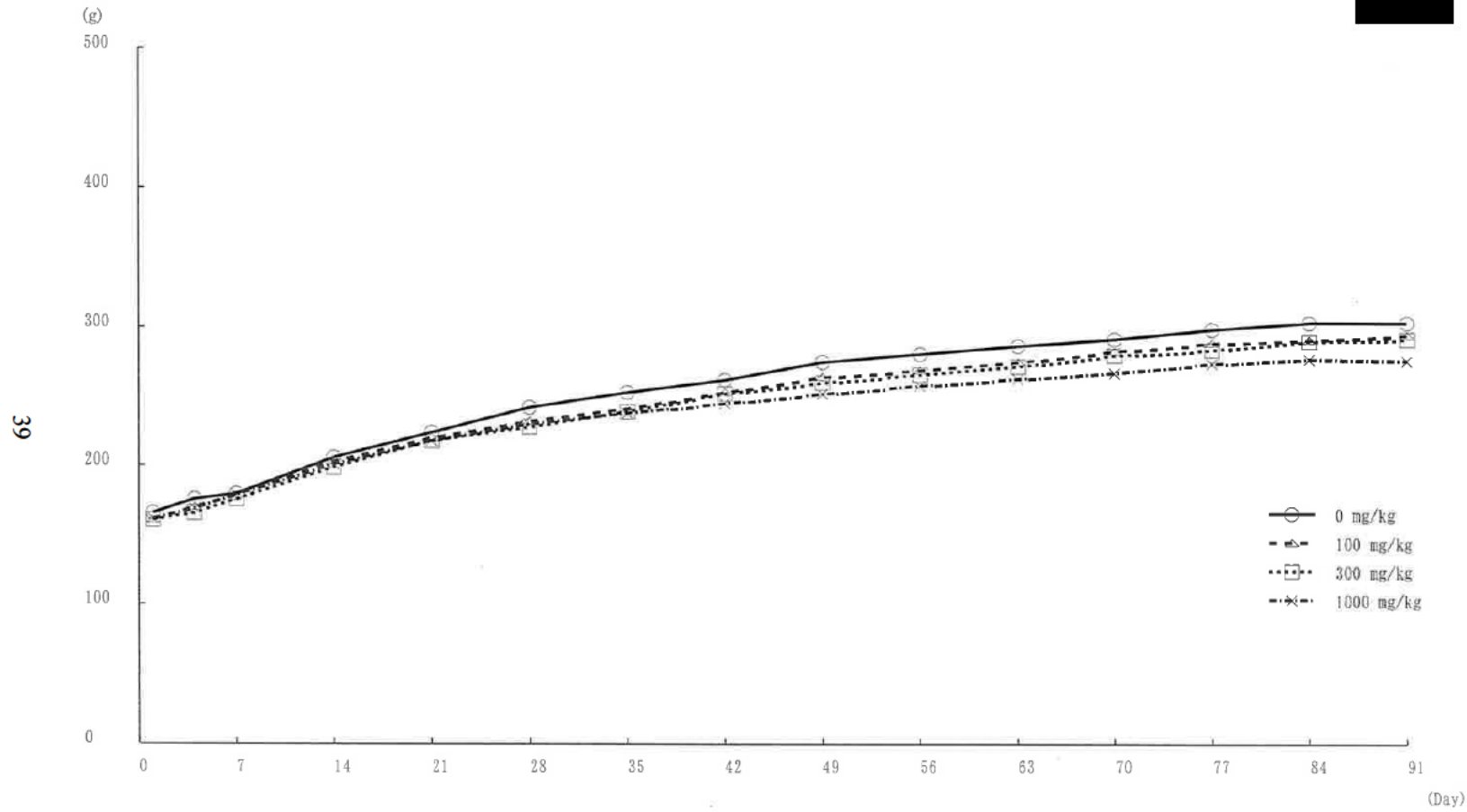


Fig. 2 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Body Weight - Female (Drug Admi. 1 - Drug Admi. 91)

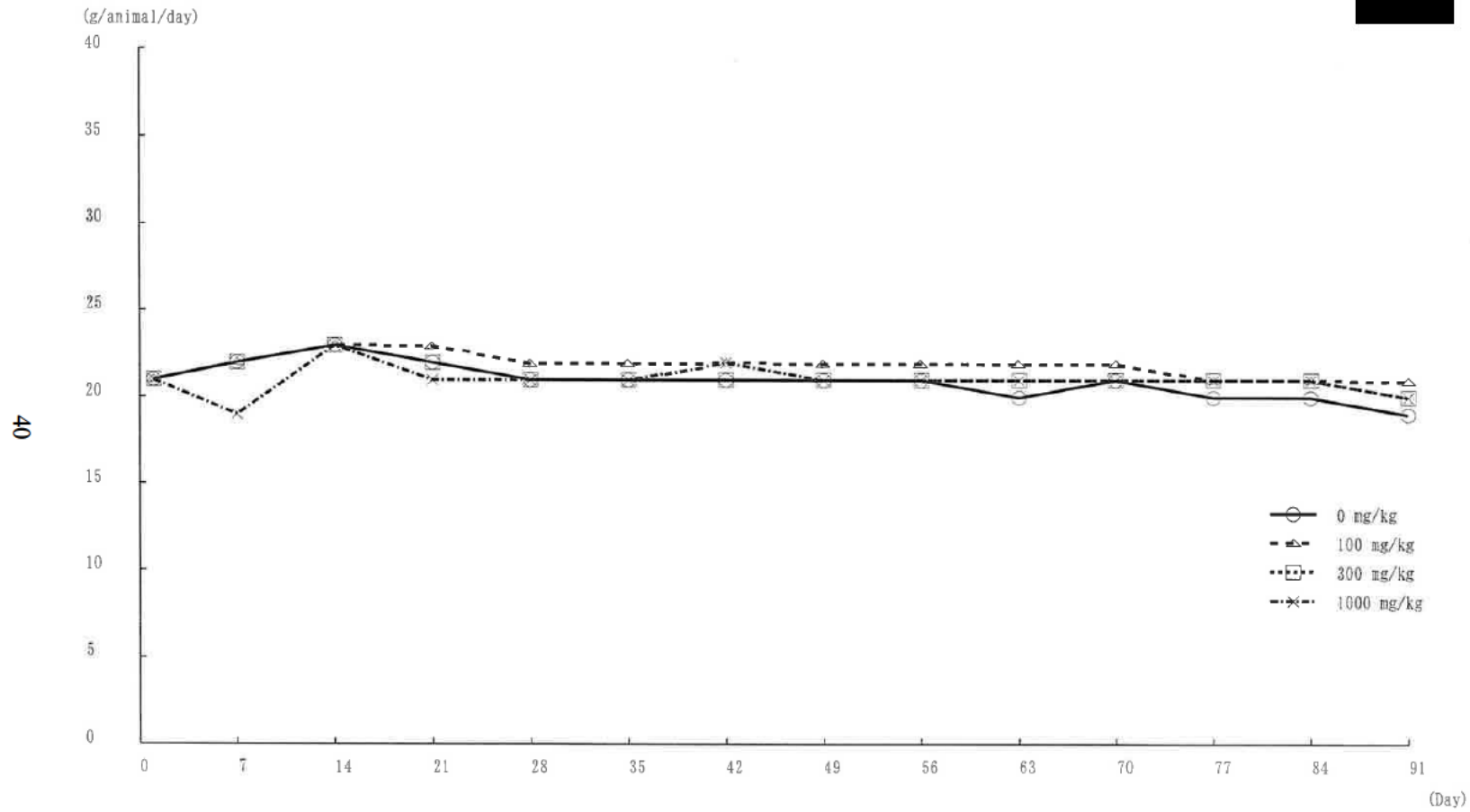


Fig. 3 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Food Consumption - Male (Drug Admi. 1 - Drug Admi. 91)

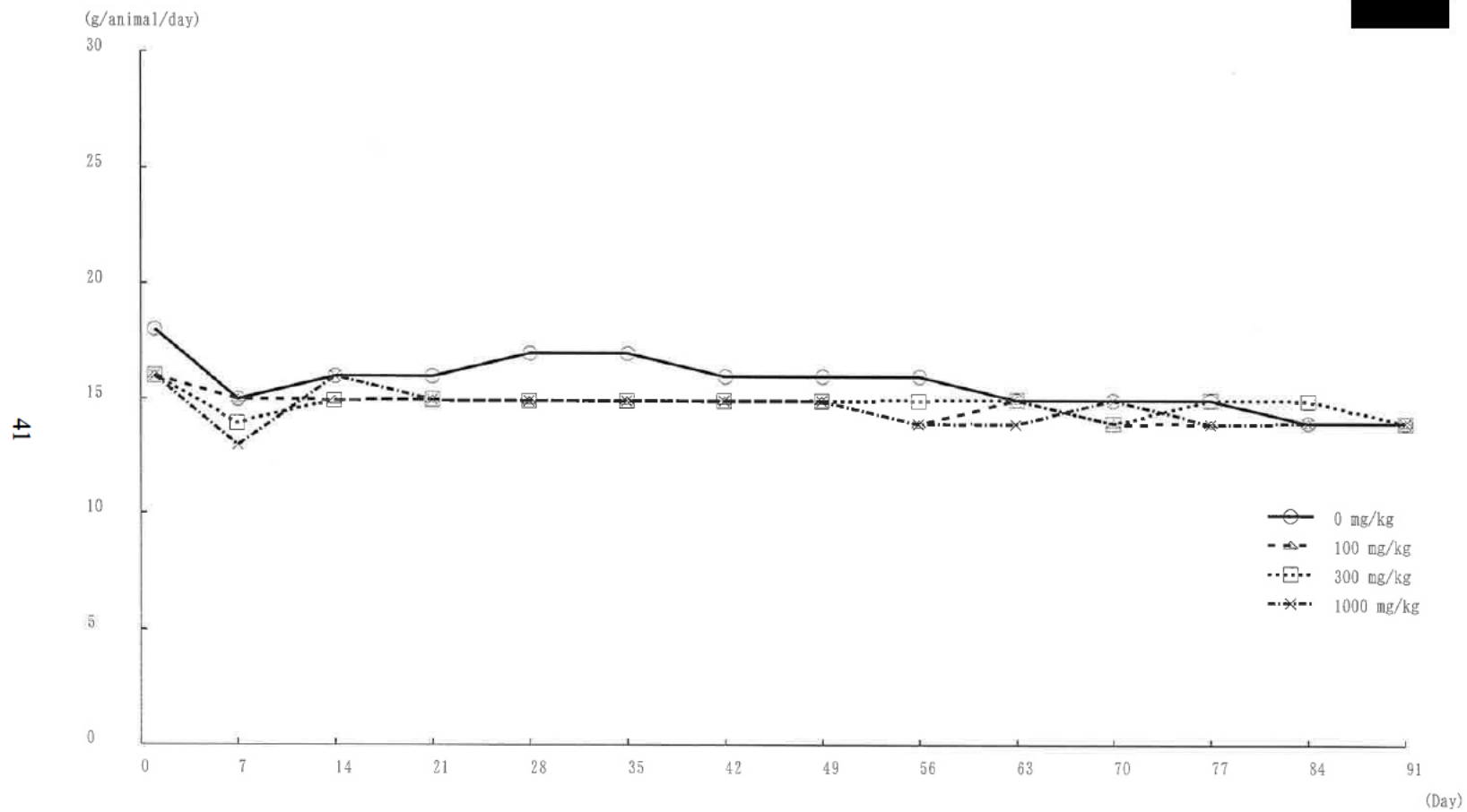


Fig. 4 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats
 Food Consumption - Female (Drug Admi. 1 - Drug Admi. 91)

Table 1-1 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Clinical signs
Male

Dose mg/kg	Findings	Day of administration													
		1	2	3	4	5	6	7	8	9	10	11	12	13	14
0	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
100	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
300	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
1000	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	9	5	6	5	5	6	6	7	7	8	8	9	9	5
	Decrease, spontaneous movement	1	5	4	5	5	4	4	3	3	2	2	1	1	5

Table 1-2 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Clinical signs
Male

Dose mg/kg	Findings	Day of administration													
		15	16	17	18	19	20	21	22	23	24	25	26	27	28
0	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
100	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
300	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
1000	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	7	8	6	7	7	6	7	8	7	8	8	7	7	5
	Decrease, spontaneous movement	3	2	4	3	3	4	3	2	3	2	2	3	3	5

Table 1-3 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Clinical signs
Male

Dose mg/kg	Findings	Day of administration													
		29	30	31	32	33	34	35	36	37	38	39	40	41	42
0	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
100	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
300	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
1000	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	5	5	8	7	7	8	6	7	7	7	7	8	7	6
	Decrease, spontaneous movement	5	5	2	3	3	2	4	3	3	3	3	2	3	4

Table 1-4 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Clinical signs
Male

Dose mg/kg	Findings	Day of administration													
		43	44	45	46	47	48	49	50	51	52	53	54	55	56
0	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
100	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
300	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
1000	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	6	9	7	6	7	7	5	6	6	8	8	8	7	8
	Decrease, spontaneous movement	4	1	3	4	3	3	5	4	4	2	2	2	3	2

Table 1-5 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Clinical signs
Male

Dose mg/kg	Findings	Day of administration													
		57	58	59	60	61	62	63	64	65	66	67	68	69	70
0	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
100	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
300	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
1000	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	8	8	8	8	6	7	5	7	8	8	8	7	7	6
	Decrease, spontaneous movement	2	2	2	2	4	3	5	3	2	2	2	3	3	4

Table 1-6 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Clinical signs
Male

Dose mg/kg	Findings	Day of administration													
		71	72	73	74	75	76	77	78	79	80	81	82	83	84
0	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
100	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
300	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
1000	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	7	7	6	7	7	7	7	7	7	7	7	7	6	8
	Decrease, spontaneous movement	3	3	4	3	3	3	3	3	3	3	3	3	4	2

Table 1-7 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Clinical signs
Male

Dose mg/kg	Findings	Day of administration							92#
		85	86	87	88	89	90	91	
0	n	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10
100	n	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10
300	n	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10
1000	n	10	10	10	10	10	10	10	10
	No abnormal findings	7	8	8	8	8	7	7	10
	Decrease, spontaneous movement	3	2	2	2	2	3	3	0

Day of necropsy

Table 1-8 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Clinical signs
Female

Dose mg/kg	Findings	Day of administration													
		1	2	3	4	5	6	7	8	9	10	11	12	13	14
0	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
100	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
300	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
1000	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	9	6	7	7	6	5	6	6	6	5	7	6	7	7
	Decrease, spontaneous movement	1	4	3	3	4	5	4	4	4	5	3	4	3	3

Table 1-9

4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Clinical signs
Female

Dose mg/kg	Findings	Day of administration													
		15	16	17	18	19	20	21	22	23	24	25	26	27	28
0	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
100	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
300	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
1000	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	8	7	6	8	6	6	7	6	7	7	7	7	8	7
	Decrease, spontaneous movement	2	3	4	2	4	4	3	4	3	3	3	3	2	3

Table 1-10 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Clinical signs
Female

Dose mg/kg	Findings	Day of administration													
		29	30	31	32	33	34	35	36	37	38	39	40	41	42
0	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
100	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
300	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
1000	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	7	7	7	7	7	7	6	7	7	8	7	7	7	7
	Decrease, spontaneous movement	3	3	3	3	3	3	3	4	3	3	2	3	3	3

Table 1-11 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Clinical signs
Female

Dose mg/kg	Findings	Day of administration													
		43	44	45	46	47	48	49	50	51	52	53	54	55	56
0	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
100	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
300	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
1000	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	7	7	8	7	7	7	5	6	6	7	8	8	6	6
	Decrease, spontaneous movement	3	3	2	3	3	3	5	4	4	3	2	2	4	4

Table 1-12 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Clinical signs
Female

Dose mg/kg	Findings	Day of administration													
		57	58	59	60	61	62	63	64	65	66	67	68	69	70
0	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
100	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
300	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
1000	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	7	7	7	7	7	7	5	7	7	7	6	7	7	6
	Decrease, spontaneous movement	3	3	3	3	3	3	3	5	3	3	3	4	3	3

Table 1-13 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Clinical signs
Female

Dose mg/kg	Findings	Day of administration													
		71	72	73	74	75	76	77	78	79	80	81	82	83	84
0	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
100	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
300	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10	10	10	10	10	10	10
1000	n	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No abnormal findings	6	6	7	7	7	7	7	7	7	8	7	7	8	8
	Decrease, spontaneous movement	4	4	3	3	3	3	3	3	3	2	3	3	2	2

Table 1-14 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Clinical signs
Female

Dose mg/kg	Findings	Day of administration							92#
		85	86	87	88	89	90	91	
0	n	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10
100	n	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10
300	n	10	10	10	10	10	10	10	10
	No abnormal findings	10	10	10	10	10	10	10	10
1000	n	10	10	10	10	10	10	10	10
	No abnormal findings	9	9	7	8	8	7	7	10
	Decrease, spontaneous movement	1	1	3	2	2	3	3	0

Day of necropsy

Table 2 - 1 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Body weight
Sex : Male

Unit : g

Test Article	Day	1	4	7	14	21	28	35	42	49
Dose										
0 mg/kg	Mean	198	220	245	292	332	364	392	416	439
	S.D.	8	9	11	16	21	25	29	32	34
	n	10	10	10	10	10	10	10	10	10
100 mg/kg	Mean	197	221	245	294	335	368	399	424	450
	S.D.	8	9	13	24	32	37	41	48	54
	n	10	10	10	10	10	10	10	10	10
300 mg/kg	Mean	198	222	246	298	337	370	398	422	448
	S.D.	8	7	8	9	10	13	15	18	20
	n	10	10	10	10	10	10	10	10	10
1000 mg/kg	Mean	197	212	233	282	315	344	369	387	406
	S.D.	8	10	13	16	24	31	36	40	41
	n	10	10	10	10	10	10	10	10	10

No significant difference in any treated groups from control group.

Table 2 - 2 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Body weight
Sex : Male

Unit : g

Test Article	Day	56	63	70	77	84	91
Dose							
0 mg/kg	Mean	456	475	492	507	523	528
	S.D.	35	39	41	43	43	46
	n	10	10	10	10	10	10
100 mg/kg	Mean	468	490	507	524	538	546
	S.D.	58	62	69	74	76	82
	n	10	10	10	10	10	10
300 mg/kg	Mean	463	482	496	513	526	534
	S.D.	20	24	24	26	26	30
	n	10	10	10	10	10	10
1000 mg/kg	Mean	417	432	442	453	464 D2*	466 D2*
	S.D.	41	44	45	46	50	49
	n	10	10	10	10	10	10

Significantly different from control : * P<0.05
D2:Dunnett Test Two-Side

Table 2 - 3 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Body weight
Sex : Female

Unit : g

Test Article	Day	1	4	7	14	21	28	35	42	49
Dose										
0 mg/kg	Mean	166	176	180	206	224	242	253	262	275
	S.D.	7	7	7	14	16	17	17	23	18
	n	10	10	10	10	10	10	10	10	10
100 mg/kg	Mean	161	170	179	203	220	232	241	253	264
	S.D.	11	10	13	21	23	24	22	26	27
	n	10	10	10	10	10	10	10	10	10
300 mg/kg	Mean	161	166	176	199	218	228	239	252	260
	S.D.	7	9	7	10	11	13	11	12	15
	n	10	10	10	10	10	10	10	10	10
1000 mg/kg	Mean	162	169	179	201	218	230	238	245	252
	S.D.	15	17	16	16	20	22	25	24	27
	n	10	10	10	10	10	10	10	10	10

No significant difference in any treated groups from control group.

Table 2 - 4 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Body weight
Sex : Female

Unit : g

Test Article	Day	56	63	70	77	84	91
Dose							
0 mg/kg	Mean	281	287	292	299	304	304
	S.D.	21	18	22	20	22	22
	n	10	10	10	10	10	10
100 mg/kg	Mean	269	275	283	289	292	295
	S.D.	24	24	26	29	27	25
	n	10	10	10	10	10	10
300 mg/kg	Mean	266	272	280	284	291	292
	S.D.	16	14	16	19	21	20
	n	10	10	10	10	10	10
1000 mg/kg	Mean	258	263 D2*	268	274	278	277
	S.D.	27	29	28	30	32	32
	n	10	10	10	10	10	10

Significantly different from control : * P<0.05
D2:Dunnett Test Two-Side

Table 3 - 1 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Food consumption
Sex : Male

Unit : g/animal/day

Test Article	Day	1	7	14	21	28	35	42	49	56
Dose										
0 mg/kg	Mean	21	22	23	22	21	21	21	21	21
	S.D.	1	0	1	1	1	1	1	1	1
	n	5	5	5	5	5	5	5	5	5
100 mg/kg	Mean	21	22	23	23	22	22	22	22	22
	S.D.	1	1	1	0	1	1	1	1	1
	n	5	5	5	5	5	5	5	5	5
300 mg/kg	Mean	21	22	23	22	21	21	21	21	21
	S.D.	1	1	1	1	1	1	2	2	2
	n	5	5	5	5	5	5	5	5	5
1000 mg/kg	Mean	21	19 D2**	23	21	21	21	22	21	21
	S.D.	1	1	1	1	2	2	2	2	2
	n	5	5	5	5	5	5	5	5	5

Significantly different from control : ** P≤0.01
D2:Dunnett Test Two-Side

Table 3 - 2 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Food consumption
Sex : Male

Unit : g/animal/day

Test Article	Day	63	70	77	84	91
Dose						
0 mg/kg	Mean	20	21	20	20	19
	S.D.	2	2	2	2	2
	n	5	5	5	5	5
100 mg/kg	Mean	22	22	21	21	21
	S.D.	2	1	1	1	1
	n	5	5	5	5	5
300 mg/kg	Mean	21	21	21	21	20
	S.D.	2	2	2	2	2
	n	5	5	5	5	5
1000 mg/kg	Mean	21	21	21	21	20
	S.D.	2	2	2	2	1
	n	5	5	5	5	5

No significant difference in any treated groups from control group.

Table 3 - 3 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Food consumption
Sex : Female

Unit : g/animal/day

Test Article	Day	1	7	14	21	28	35	42	49	56
Dose										
0 mg/kg	Mean	18	15	16	16	17	17	16	16	16
	S.D.	1	1	1	2	2	2	2	1	1
	n	5	5	5	5	5	5	5	5	5
100 mg/kg	Mean	16	15	15	15	15	15	15	15	14
	S.D.	2	2	2	1	1	1	1	1	1
	n	5	5	5	5	5	5	5	5	5
300 mg/kg	Mean	16	14	15	15	15	15	15	15	15
	S.D.	1	1	1	1	1	1	1	1	1
	n	5	5	5	5	5	5	5	5	5
1000 mg/kg	Mean	16	13	16	15	15	15	15	15 D2*	14
	S.D.	1	1	1	2	1	1	2	2	1
	n	5	5	5	5	5	5	5	5	5

Significantly different from control : * P<0.05
D2:Dunnett Test Two-Side

Table 3 - 4 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Food consumption
Sex : Female

Unit : g/animal/day

Test Article	Day	63	70	77	84	91
Dose						
0 mg/kg	Mean	15	15	15	14	14
	S.D.	1	1	1	1	1
	n	5	5	5	5	5
100 mg/kg	Mean	15	14	14	14	14
	S.D.	1	1	1	1	1
	n	5	5	5	5	5
300 mg/kg	Mean	15	14	15	15	14
	S.D.	1	1	1	1	1
	n	5	5	5	5	5
1000 mg/kg	Mean	14	15	14	14	14
	S.D.	1	1	1	2	1
	n	5	5	5	5	5

No significant difference in any treated groups from control group.

Table 4 - 1 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Ophthalmology (Week 13)
Sex : Male

Findings	Dose (mg/kg)	0	100	300	1000
	No. of animals	5	5	5	5
Ophthalmoscopy					
No abnormality		5	5	5	5

Table 4 - 2 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Ophthalmology (Week 13)
 Sex : Female

Findings	Dose (mg/kg) No. of animals	0 5	100 5	300 5	1000 5
Ophthalmoscopy					
No abnormality		4	5	5	5
Fundus oculi					
Hyperreflectivity in fundus, focal					
Unilateral		1	0	0	0

Table 5 - 1 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Urinalysis
Sex : Male

Stage : Week 13

Test Article Dose	pH	pH										Protein				
		5.0	5.5	6.0	6.5	7.0	7.5	8.0	8.5	9.0≤	-	+/-	1+	2+	3+	
0 mg/kg	Mean															
	S.D. n	10	0	0	1	1	1	0	2	4	1	10	0	0	0	10
100 mg/kg	Mean															
	S.D. n	10	0	0	0	1	0	0	2	7	0	10	0	0	3	6
300 mg/kg	Mean															
	S.D. n	10	1	0	1	1	3	0	0	2	2	10	0	2	2	5
1000 mg/kg	Mean															
	S.D. n	10	0	1	0	5	4	0	0	0	0	10	1	0	1	8

Protein) -:Negative, +/-:15, 1+:30, 2+:100, 3+:≥300 mg/dL

Table 5 - 2 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Urinalysis
Sex : Male

Stage : Week 13

Test Article Dose	Ketones	Ketones					Glucose	Glucose					
		-	+/-	1+	2+	3+		-	1+	2+	3+	4+	
0 mg/kg	Mean S.D. n	10	0	0	7	3	0	10	5	5	0	0	0
100 mg/kg	Mean S.D. n	10	0	0	10	0	0	10	9	1	0	0	0
300 mg/kg	Mean S.D. n	10	1	3	5	1	0	10	10	0	0	0	0
1000 mg/kg	Mean S.D. n	10	3	6	1	0	0	10	10	0	0	0	0

Ketones) -:Negative, +/-:5, 1+:15, 2+:40, 3+:80 mg/dL
Glucose) -:Negative, 1+:100, 2+:250, 3+:500, 4+:≥1000 mg/dL

Table 5 - 3 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Urinalysis
Sex : Male

Stage : Week 13

Test Article Dose	Oc.Blood	Urobili.					Urobili. +/-	Bilirubin								
		-	+/-	1+	2+	3+		-	1+	2+	3+					
0 mg/kg	Mean S.D. n	10	10	0	0	0	10	10	0	0	0	10	4	6	0	0
100 mg/kg	Mean S.D. n	10	9	1	0	0	10	10	0	0	0	10	7	3	0	0
300 mg/kg	Mean S.D. n	10	9	1	0	0	10	10	0	0	0	10	6	3	1	0
1000 mg/kg	Mean S.D. n	10	10	0	0	0	10	10	0	0	0	10	9	1	0	0

Oc.Blood) -:Negative, +/-:0.015, 1+:0.062, 2+:0.135, 3+:0.405 mg/dL

Urobili.) +/-:0.1-1.0, 1+:2.0, 2+:4.0, 3+:≥8.0 Ehrlich U/dL

Bilirubin) -:Negative, 1+:0.8, 2+:1.6, 3+:3.2 mg/dL

Oc.Blood : Occult blood Urobili. : Urobilinogen

Table 5 - 4 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Urinalysis
Sex : Male

Stage : Week 13

Test Article Dose	Color	Color				RBC	RBC					
		LY	Y	DY	Other		-	+/-	1+	2+	3+	
0 mg/kg	Mean											
	S.D. n	10	0	10	0	0	10	10	0	0	0	0
100 mg/kg	Mean											
	S.D. n	10	0	10	0	0	10	10	0	0	0	0
300 mg/kg	Mean											
	S.D. n	10	0	10	0	0	10	10	0	0	0	0
1000 mg/kg	Mean											
	S.D. n	10	0	10	0	0	10	10	0	0	0	0

Color) LY:Light yellow, Y:Yellow, DY:Dark yellow, Other:Other color
RBC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Table 5 - 5 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Urinalysis
Sex : Male

Stage : Week 13

Test Article Dose	WBC	WBC					Ep.SEC	Ep.SEC				
		-	+/-	1+	2+	3+		-	+/-	1+	2+	3+
0 mg/kg	Mean S.D. n	10	10	0	0	0	10	2	8	0	0	0
100 mg/kg	Mean S.D. n	10	10	0	0	0	10	3	7	0	0	0
300 mg/kg	Mean S.D. n	10	10	0	0	0	10	2	8	0	0	0
1000 mg/kg	Mean S.D. n	10	10	0	0	0	10	3	7	0	0	0

WBC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe
Ep.SEC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe
Ep.SEC : Squamous epithelial cells

Table 5 - 6 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Urinalysis
Sex : Male

Stage : Week 13

Test Article Dose	Ep.SREC	Ep.SREC					Cast	Cast				
		-	+/-	1+	2+	3+		-	+/-	1+	2+	3+
0 mg/kg	Mean											
	S.D.											
	n	10	10	0	0	0	10	10	0	0	0	
100 mg/kg	Mean											
	S.D.											
	n	10	10	0	0	0	10	10	0	0	0	
300 mg/kg	Mean											
	S.D.											
	n	10	10	0	0	0	10	10	0	0	0	
1000 mg/kg	Mean											
	S.D.											
	n	10	10	0	0	0	10	10	0	0	0	

Ep.SREC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Cast) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Ep.SREC : Small round epithelial cells

Table 5 - 7 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Urinalysis
Sex : Male

Stage : Week 13

Test Article Dose	Cr.PS						Cr.CO						Uri.Vol. mL/24h	Osmotic P. mOsm/kg
		-	+/-	1+	2+	3+		-	+/-	1+	2+	3+		
0 mg/kg	Mean												7.0	1861
	S.D.												2.2	319
	n	10	10	0	0	0	10	10	0	0	0	0	10	10
100 mg/kg	Mean												7.3	1808
	S.D.												3.5	364
	n	10	10	0	0	0	10	10	0	0	0	0	10	10
300 mg/kg	Mean												8.3	1789
	S.D.												2.5	352
	n	10	10	0	0	0	10	10	0	0	0	0	10	10
1000 mg/kg	Mean												14.7 S2**	1419 D2*
	S.D.												8.0	387
	n	10	9	0	1	0	10	10	0	0	0	0	10	10

Cr.PS) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Cr.CO) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Cr.PS : Crystal phosphate salts Cr.CO : Crystal calcium oxalate Uri.Vol. : Urine volume Osmotic P. : Osmotic Pressure

Significantly different from control : * P≤0.05, ** P≤0.01

D2:Dunnett Test Two-Side, S2:Steel Test Two-Side

Table 5 - 8 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Urinalysis
Sex : Male

Stage : Week 13

Test Article Dose		U-Na mmol/24h	U-K mmol/24h	U-Cl mmol/24h
0 mg/kg	Mean	1.1	2.3	1.7
	S.D.	0.2	0.4	0.3
	n	10	10	10
100 mg/kg	Mean	1.0	2.2	1.6
	S.D.	0.3	0.7	0.5
	n	10	10	10
300 mg/kg	Mean	1.3	2.2	2.1
	S.D.	0.4	0.4	0.5
	n	10	10	10
1000 mg/kg	Mean	1.4 D2*	2.7	2.6 D2**
	S.D.	0.3	0.4	0.3
	n	10	10	10

Significantly different from control : * P≤0.05, ** P≤0.01
D2:Dunnett Test Two-Side

Table 5 - 9 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Urinalysis
Sex : Female

Stage : Week 13

Test Article Dose	pH	pH										Protein	-	+/-	1+	2+	3+
		5.0	5.5	6.0	6.5	7.0	7.5	8.0	8.5	9.0≤							
0 mg/kg	Mean																
	S.D.																
	n	10	0	1	4	2	1	1	0	1	0	10	1	2	2	4	1
100 mg/kg	Mean																
	S.D.																
	n	10	0	2	6	0	0	1	0	1	0	10	3	6	1	0	0
300 mg/kg	Mean																
	S.D.																
	n	10	0	0	0	4	3	1	1	1	0	10	5	0	1	4	0
1000 mg/kg	Mean																
	S.D.																
	n	10	4	1	0	3	1	1	0	0	0	10	3	0	2	5	0

Protein) -:Negative, +/-:15, 1+:30, 2+:100, 3+:≥300 mg/dL

Table 5 - 10 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Urinalysis
Sex : Female

Stage : Week 13

Test Article Dose	Ketones	Ketones					Glucose	Glucose					
		-	+/-	1+	2+	3+		-	1+	2+	3+	4+	
0 mg/kg	Mean S.D. n	10	1	5	4	0	0	10	9	1	0	0	0
100 mg/kg	Mean S.D. n	10	6	4	0	0	0	10	10	0	0	0	0
300 mg/kg	Mean S.D. n	10	5	4	1	0	0	10	10	0	0	0	0
1000 mg/kg	Mean S.D. n	10	9	1	0	0	0	10	9	0	1	0	0

Ketones) -:Negative, +/-:5, 1+:15, 2+:40, 3+:80 mg/dL
Glucose) -:Negative, 1+:100, 2+:250, 3+:500, 4+:≥1000 mg/dL

Table 5 - 11 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Urinalysis
Sex : Female

Stage : Week 13

Test Article Dose	Oc.Blood	Urobili.					Bilirubin									
		-	+/-	1+	2+	3+	+/-	1+	2+	3+						
0 mg/kg	Mean S.D. n	10	10	0	0	0	10	10	0	0	0	10	6	4	0	0
100 mg/kg	Mean S.D. n	10	10	0	0	0	10	10	0	0	0	10	9	1	0	0
300 mg/kg	Mean S.D. n	10	10	0	0	0	10	10	0	0	0	10	9	1	0	0
1000 mg/kg	Mean S.D. n	10	10	0	0	0	10	10	0	0	0	10	9	1	0	0

Oc.Blood) -:Negative, +/-:0.015, 1+:0.062, 2+:0.135, 3+:0.405 mg/dL

Urobili.) +/-:0.1-1.0, 1+:2.0, 2+:4.0, 3+:≥8.0 Ehrlich U/dL

Bilirubin) -:Negative, 1+:0.8, 2+:1.6, 3+:3.2 mg/dL

Oc.Blood : Occult blood Urobili. : Urobilinogen

Table 5 - 12 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Urinalysis
Sex : Female

Stage : Week 13

Test Article Dose	Color	Color				RBC	RBC					
		LY	Y	DY	Other		-	+/-	1+	2+	3+	
0 mg/kg	Mean											
	S.D. n	10	0	10	0	0	10	10	0	0	0	0
100 mg/kg	Mean											
	S.D. n	10	0	10	0	0	10	10	0	0	0	0
300 mg/kg	Mean											
	S.D. n	10	0	10	0	0	10	10	0	0	0	0
1000 mg/kg	Mean											
	S.D. n	10	0	10	0	0	10	10	0	0	0	0

Color) LY:Light yellow, Y:Yellow, DY:Dark yellow, Other:Other color
RBC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Table 5 - 13 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Urinalysis
Sex : Female

Stage : Week 13

Test Article Dose	WBC	WBC					Ep.SEC	Ep.SEC				
		-	+/-	1+	2+	3+		-	+/-	1+	2+	3+
0 mg/kg	Mean											
	S.D.											
	n	10	10	0	0	0	10	0	10	0	0	0
100 mg/kg	Mean											
	S.D.											
	n	10	10	0	0	0	10	0	10	0	0	0
300 mg/kg	Mean											
	S.D.											
	n	10	10	0	0	0	10	2	8	0	0	0
1000 mg/kg	Mean											
	S.D.											
	n	10	10	0	0	0	10	0	10	0	0	0

WBC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe
 Ep.SEC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe
 Ep.SEC : Squamous epithelial cells

Table 5 - 14 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Urinalysis
Sex : Female

Stage : Week 13

Test Article Dose	Ep.SREC	Ep.SREC					Cast	Cast				
		-	+/-	1+	2+	3+		-	+/-	1+	2+	3+
0 mg/kg	Mean											
	S.D.											
	n	10	10	0	0	0	10	10	0	0	0	
100 mg/kg	Mean											
	S.D.											
	n	10	10	0	0	0	10	10	0	0	0	
300 mg/kg	Mean											
	S.D.											
	n	10	10	0	0	0	10	10	0	0	0	
1000 mg/kg	Mean											
	S.D.											
	n	10	10	0	0	0	10	10	0	0	0	

Ep.SREC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Cast) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Ep.SREC : Small round epithelial cells

Table 5 - 15 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Urinalysis
Sex : Female

Stage : Week 13

Test Article Dose	Cr.PS	Cr.CO					Cr.CO	Cr.CO					Uri.Vol. mL/24h	Osmotic P. mOsm/kg
		-	+/-	1+	2+	3+		-	+/-	1+	2+	3+		
0 mg/kg	Mean												5.1	1947
	S.D.												2.6	519
	n	10	8	2	0	0	0	10	10	0	0	0	0	10
100 mg/kg	Mean												6.5	1594
	S.D.												2.8	527
	n	10	10	0	0	0	0	10	10	0	0	0	0	10
300 mg/kg	Mean												9.6 D2*	1226 D2**
	S.D.												5.7	317
	n	10	10	0	0	0	0	10	7	0	0	1	2	10
1000 mg/kg	Mean												7.6	1588
	S.D.												3.0	274
	n	10	8	1	1	0	0	10	10	0	0	0	0	10

Cr.PS) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Cr.CO) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Cr.PS : Crystal phosphate salts Cr.CO : Crystal calcium oxalate Uri.Vol. : Urine volume Osmotic P. : Osmotic Pressure

Significantly different from control : * P≤0.05, ** P≤0.01

D2:Dunnett Test Two-Side

Table 5 - 16 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Urinalysis
Sex : Female

Stage : Week 13

Test Article		U-Na	U-K	U-Cl
Dose		mmol/24h	mmol/24h	mmol/24h
0 mg/kg	Mean	0.7	1.6	1.2
	S.D.	0.2	0.5	0.4
	n	10	10	10
100 mg/kg	Mean	0.8	1.6	1.3
	S.D.	0.3	0.4	0.3
	n	10	10	10
300 mg/kg	Mean	1.0	1.8	1.5
	S.D.	0.5	0.6	0.6
	n	10	10	10
1000 mg/kg	Mean	1.1	1.7	1.6
	S.D.	0.4	0.5	0.5
	n	10	10	10

No significant difference in any treated groups from control group.

Table 6 - 1 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Hematology
Sex : Male

Stage : Week 13

Test Article		RBC	HGB	HCT	MCV	MCH	MCHC
Dose		10E4/ μ L	g/dL	%	fL	pg	g/dL
0 mg/kg	Mean	822	14.7	42.4	51.6	17.9	34.6
	S.D.	33	0.4	1.3	1.4	0.6	0.5
	n	10	10	10	10	10	10
100 mg/kg	Mean	814	14.9	43.0	52.8	18.3	34.6
	S.D.	33	0.5	1.4	1.6	0.7	0.6
	n	10	10	10	10	10	10
300 mg/kg	Mean	818	14.9	43.0	52.7	18.2	34.5
	S.D.	21	0.4	1.4	1.4	0.6	0.7
	n	10	10	10	10	10	10
1000 mg/kg	Mean	818	14.7	42.8	52.4	18.0	34.4
	S.D.	36	0.5	1.3	1.7	0.7	0.6
	n	10	10	10	10	10	10

No significant difference in any treated groups from control group.

Table 6 - 2 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Hematology
Sex : Male

Stage : Week 13

Test Article		Retic	PLT	WBC	LYMP	NEUT	EOS
Dose		10E9/L	10E4/ μ L	10E2/ μ L	10E2/ μ L	10E2/ μ L	10E2/ μ L
0 mg/kg	Mean	133.5	87.4	84.1	63.8	16.8	0.9
	S.D.	23.2	7.7	16.0	14.4	4.9	0.2
	n	10	10	10	10	10	10
100 mg/kg	Mean	126.0	83.8	92.4	71.0	16.6	1.0
	S.D.	19.7	4.8	21.3	19.3	3.9	0.3
	n	10	10	10	10	10	10
300 mg/kg	Mean	119.2	88.7	93.8	75.2	13.7	1.0
	S.D.	15.1	6.3	16.5	12.4	5.4	0.4
	n	10	10	10	10	10	10
1000 mg/kg	Mean	130.3	95.9	93.4	71.4	16.6	1.1
	S.D.	27.5	12.9	35.6	29.8	7.4	0.7
	n	10	10	10	10	10	10

No significant difference in any treated groups from control group.

Retic : Reticulocyte

Table 6 - 3 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Hematology
Sex : Male

Stage : Week 13

Test Article		BASO	MONO	LUC
Dose		10E2/ μ L	10E2/ μ L	10E2/ μ L
0 mg/kg	Mean	0.3	2.0	0.4
	S.D.	0.2	0.4	0.2
	n	10	10	10
100 mg/kg	Mean	0.4	3.0	0.5
	S.D.	0.1	1.1	0.3
	n	10	10	10
300 mg/kg	Mean	0.4	3.0	0.5
	S.D.	0.1	1.5	0.2
	n	10	10	10
1000 mg/kg	Mean	0.4	3.1	0.7
	S.D.	0.2	1.2	0.7
	n	10	10	10

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

Table 6 - 4 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Hematology
Sex : Male

Stage : Week 13

Test Article Dose		PT s	APTT s	FIB mg/dL
0 mg/kg	Mean	12.9	13.0	307
	S.D.	1.0	1.9	31
	n	10	10	10
100 mg/kg	Mean	12.8	13.4	298
	S.D.	1.2	2.6	16
	n	10	10	10
300 mg/kg	Mean	13.5	13.4	290
	S.D.	1.2	1.9	24
	n	10	10	10
1000 mg/kg	Mean	12.7	12.6	304
	S.D.	1.2	2.5	26
	n	10	10	10

No significant difference in any treated groups from control group.

Table 6 - 5 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Hematology
Sex : Female

Stage : Week 13

Test Article		RBC	HGB	HCT	MCV	MCH	MCHC
Dose		10E4/ μ L	g/dL	%	fL	pg	g/dL
0 mg/kg	Mean	764	14.3	40.9	53.5	18.7	35.0
	S.D.	23	0.3	1.1	1.6	0.6	0.4
	n	10	10	10	10	10	10
100 mg/kg	Mean	770	14.7	41.7	54.2	19.0	35.1
	S.D.	29	0.5	1.5	1.9	0.8	0.4
	n	10	10	10	10	10	10
300 mg/kg	Mean	760	14.6	41.3	54.4	19.2	35.3
	S.D.	39	0.6	1.5	1.6	0.6	0.4
	n	10	10	10	10	10	10
1000 mg/kg	Mean	759	14.5	41.7	55.0	19.1	34.6
	S.D.	34	0.4	1.3	1.8	0.7	0.4
	n	10	10	10	10	10	10

No significant difference in any treated groups from control group.

Table 6 - 6 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Hematology
Sex : Female

Stage : Week 13

Test Article		Retic	PLT	WBC	LYMP	NEUT	EOS
Dose		10E9/L	10E4/ μ L	10E2/ μ L	10E2/ μ L	10E2/ μ L	10E2/ μ L
0 mg/kg	Mean	110.5	94.7	60.0	47.4	9.2	0.9
	S.D.	24.8	5.7	15.7	15.0	1.6	0.4
	n	10	10	10	10	10	10
100 mg/kg	Mean	127.4	91.9	52.4	40.0	9.5	0.8
	S.D.	21.9	9.4	7.5	5.7	3.0	0.4
	n	10	10	10	10	10	10
300 mg/kg	Mean	136.9	98.1	63.4	48.5	11.4	0.8
	S.D.	22.5	11.6	13.6	10.9	4.7	0.3
	n	10	10	10	10	10	10
1000 mg/kg	Mean	130.9	102.3	63.2	49.7	10.2	0.8
	S.D.	37.9	12.5	10.9	9.3	4.1	0.3
	n	10	10	10	10	10	10

No significant difference in any treated groups from control group.

Retic : Reticulocyte

Table 6 - 7 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Hematology
Sex : Female

Stage : Week 13

Test Article		BASO	MONO	LUC
Dose		10E2/ μ L	10E2/ μ L	10E2/ μ L
0 mg/kg	Mean	0.3	1.8	0.4
	S.D.	0.1	0.9	0.2
	n	10	10	10
100 mg/kg	Mean	0.3	1.5	0.3
	S.D.	0.1	0.7	0.2
	n	10	10	10
300 mg/kg	Mean	0.4	1.9	0.5
	S.D.	0.1	0.5	0.2
	n	10	10	10
1000 mg/kg	Mean	0.3	1.8	0.4
	S.D.	0.1	0.7	0.2
	n	10	10	10

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

Table 6 - 8 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Hematology
Sex : Female

Stage : Week 13

Test Article Dose		PT s	APTT s	FIB mg/dL
0 mg/kg	Mean	12.5	10.8	210
	S.D.	1.4	2.0	9
	n	10	10	10
100 mg/kg	Mean	12.3	10.6	221 S2*
	S.D.	1.2	2.0	11
	n	10	10	10
300 mg/kg	Mean	12.1	11.2	215
	S.D.	0.9	1.1	15
	n	10	10	10
1000 mg/kg	Mean	11.8	10.9	236
	S.D.	0.9	1.9	50
	n	10	10	10

Significantly different from control : * P<0.05
S2:Steel Test Two-Side

Table 7 - 1 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Blood chemistry
Sex : Male

Stage : Week 13

Test Article		AST	ALT	LDH	ALP	r-GTP	T-CHO
Dose		IU/L	IU/L	IU/L	IU/L	IU/L	mg/dL
0 mg/kg	Mean	57	41	59	411	0	72
	S.D.	5	7	19	137	0	13
	n	10	10	10	10	10	10
100 mg/kg	Mean	62	37	63	431	0	65
	S.D.	8	6	21	153	0	17
	n	10	10	10	10	10	10
300 mg/kg	Mean	57	39	52	388	1 S2*	69
	S.D.	5	6	6	76	1	14
	n	10	10	10	10	10	10
1000 mg/kg	Mean	57	51 D2*	70	516	1 S2**	92 D2**
	S.D.	10	11	57	153	0	8
	n	10	10	10	10	10	10

Significantly different from control : * P<0.05, ** P<0.01
D2:Dunnnett Test Two-Side, S2:Steel Test Two-Side

Table 7 - 2 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Blood chemistry
Sex : Male

Stage : Week 13

Test Article		TG	PL	T-BIL	GLU	BUN	CRNN
Dose		mg/dL	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL
0 mg/kg	Mean	47	109	0.1	159	16	0.31
	S.D.	24	15	0.0	27	2	0.03
	n	10	10	10	10	10	10
100 mg/kg	Mean	65	103	0.1	158	13	0.29
	S.D.	29	22	0.0	18	2	0.04
	n	10	10	10	10	10	10
300 mg/kg	Mean	55	108	0.1	150	13	0.29
	S.D.	25	18	0.0	13	4	0.03
	n	10	10	10	10	10	10
1000 mg/kg	Mean	57	139 D2**	0.1	144	14	0.28
	S.D.	28	11	0.0	15	4	0.05
	n	10	10	10	10	10	10

Significantly different from control : ** P<0.01
D2:Dunnett Test Two-Side

Table 7 - 3 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Blood chemistry
Sex : Male

Stage : Week 13

Test Article		Na	K	Cl	Ca	P	TP	ALB	A/G
Dose		mmol/L	mmol/L	mmol/L	mg/dL	mg/dL	g/dL	g/dL	
0 mg/kg	Mean	144	4.0	106	10.2	5.1	6.3	2.7	0.7
	S.D.	2	0.2	2	0.2	0.4	0.3	0.1	0.0
	n	10	10	10	10	10	10	10	10
100 mg/kg	Mean	144	3.9	106	10.1	5.0	6.2	2.7	0.8
	S.D.	1	0.3	2	0.3	0.5	0.3	0.1	0.1
	n	10	10	10	10	10	10	10	10
300 mg/kg	Mean	144	3.9	106	10.1	5.0	6.3	2.7	0.7
	S.D.	1	0.2	1	0.3	0.3	0.2	0.1	0.1
	n	10	10	10	10	10	10	10	10
1000 mg/kg	Mean	143	4.1	106	10.1	5.0	6.4	2.7	0.7
	S.D.	1	0.2	2	0.2	0.5	0.3	0.1	0.0
	n	10	10	10	10	10	10	10	10

No significant difference in any treated groups from control group.

Table 7 - 4 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Blood chemistry
Sex : Female

Stage : Week 13

Test Article		AST	ALT	LDH	ALP	r-GTP	T-CHO
Dose		IU/L	IU/L	IU/L	IU/L	IU/L	mg/dL
0 mg/kg	Mean	63	37	67	190	0	77
	S.D.	17	9	26	53	0	17
	n	10	10	10	10	10	10
100 mg/kg	Mean	60	38	70	215	0	76
	S.D.	8	14	37	86	0	16
	n	10	10	10	10	10	10
300 mg/kg	Mean	57	39	52	210	1 S2**	85
	S.D.	9	13	8	100	1	18
	n	10	10	10	10	10	10
1000 mg/kg	Mean	57	50 D2*	69	190	1 S2**	123 D2**
	S.D.	5	9	25	51	0	19
	n	10	10	10	10	10	10

Significantly different from control : * P<0.05, ** P<0.01
D2:Dunnnett Test Two-Side, S2:Steel Test Two-Side

Table 7 - 5 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Blood chemistry
Sex : Female

Stage : Week 13

Test Article		TG	PL	T-BIL	GLU	BUN	CRNN
Dose		mg/dL	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL
0 mg/kg	Mean	56	150	0.1	122	19	0.35
	S.D.	20	28	0.0	14	5	0.06
	n	10	10	10	10	10	10
100 mg/kg	Mean	49	150	0.1	127	17	0.37
	S.D.	23	28	0.0	10	4	0.05
	n	10	10	10	10	10	10
300 mg/kg	Mean	34	155	0.1	124	17	0.36
	S.D.	11	28	0.0	8	5	0.06
	n	10	10	10	10	10	10
1000 mg/kg	Mean	63	214 D2**	0.1	127	14 D2*	0.31
	S.D.	32	30	0.1	12	4	0.04
	n	10	10	10	10	10	10

Significantly different from control : * P≤0.05, ** P≤0.01
D2:Dunnett Test Two-Side

Table 7 - 6 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Blood chemistry
Sex : Female

Stage : Week 13

Test Article		Na	K	Cl	Ca	P	TP	ALB	A/G
Dose		mmol/L	mmol/L	mmol/L	mg/dL	mg/dL	g/dL	g/dL	
0 mg/kg	Mean	144	3.4	107	10.2	3.6	6.8	3.2	0.9
	S.D.	2	0.2	1	0.3	0.8	0.3	0.2	0.1
	n	10	10	10	10	10	10	10	10
100 mg/kg	Mean	144	3.3	108	10.2	3.3	6.8	3.2	0.9
	S.D.	1	0.2	1	0.4	0.8	0.4	0.3	0.1
	n	10	10	10	10	10	10	10	10
300 mg/kg	Mean	143	3.5	107	10.3	3.7	6.8	3.2	0.9
	S.D.	2	0.1	2	0.2	0.4	0.4	0.1	0.0
	n	10	10	10	10	10	10	10	10
1000 mg/kg	Mean	142	3.7 D2**	108	10.4	3.6	7.0	3.3	0.9
	S.D.	1	0.2	2	0.4	0.6	0.4	0.2	0.1
	n	10	10	10	10	10	10	10	10

Significantly different from control : ** P<0.01
D2:Dunnett Test Two-Side

Table 8 - 1 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Absolute organ weight
Sex : Male

Stage : Week 13

Test Article		F.B.W.@@	Brain	Pituitary	Thyroid-RL	Sa.G.-RL	Thymus	Heart	Lung
Dose		g	g	mg	mg	mg	mg	g	g
0 mg/kg	Mean	518	2.15	12.8	22.5	749	265	1.44	1.50
	S.D.	42	0.10	1.4	4.3	84	66	0.11	0.13
	n	10	10	10	10	10	10	10	10
100 mg/kg	Mean	535	2.16	12.1	25.2	734	280	1.49	1.55
	S.D.	80	0.08	1.3	6.4	75	80	0.24	0.15
	n	10	10	10	10	10	10	10	10
300 mg/kg	Mean	520	2.20	13.0	22.6	737	255	1.46	1.51
	S.D.	27	0.08	1.6	6.7	51	51	0.10	0.09
	n	10	10	10	10	10	10	10	10
1000 mg/kg	Mean	454	2.11	11.9	21.8	676	217	1.30	1.40
	S.D.	47	0.12	2.0	3.3	98	54	0.14	0.14
	n	10	10	10	10	10	10	10	10

Statistical analysis was not done : @@
No significant difference in any treated groups from control group.
Sa.G. : Salivary gland

Table 8 - 2 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Absolute organ weight
Sex : Male

Stage : Week 13

Test Article Dose		Liver g	Spleen g	Kidney-RL g	Adrenal-RL mg	Testis-RL g	Prostate g	Sem.Ves. g
0 mg/kg	Mean	13.53	0.73	3.12	55	3.25	1.48	1.94
	S.D.	1.67	0.09	0.32	9	0.24	0.20	0.36
	n	10	10	10	10	10	10	10
100 mg/kg	Mean	13.89	0.71	3.17	53	3.42	1.44	1.89
	S.D.	3.07	0.15	0.39	9	0.28	0.21	0.26
	n	10	10	10	10	10	10	10
300 mg/kg	Mean	13.68	0.72	3.29	50	3.38	1.28	1.94
	S.D.	1.37	0.06	0.20	9	0.29	0.17	0.27
	n	10	10	10	10	10	10	10
1000 mg/kg	Mean	12.97	0.62	3.14	46	3.36	1.24 D2*	1.69
	S.D.	1.69	0.13	0.44	7	0.24	0.17	0.19
	n	10	10	10	10	10	10	10

Significantly different from control : * $P \leq 0.05$
D2:Dunnett Test Two-Side
Sem.Ves. : Seminal vesicle

Table 8 - 3 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Absolute organ weight
Sex : Female

Stage : Week 13

Test Article Dose		F.B.W.@@ g	Brain g	Pituitary mg	Thyroid-RL mg	Sa.G.-RL mg	Thymus mg	Heart g	Lung g
0 mg/kg	Mean	296	2.02	16.2	17.7	449	243	0.92	1.15
	S.D.	20	0.08	2.8	3.2	38	66	0.08	0.09
	n	10	10	10	10	10	10	10	10
100 mg/kg	Mean	285	2.01	15.9	18.3	448	228	0.90	1.11
	S.D.	25	0.09	2.3	4.6	46	57	0.08	0.08
	n	10	10	10	10	10	10	10	10
300 mg/kg	Mean	284	2.03	15.6	20.4	442	222	0.87	1.12
	S.D.	19	0.07	1.9	4.6	33	46	0.08	0.07
	n	10	10	10	10	10	10	10	10
1000 mg/kg	Mean	270	1.94	16.2	15.9	443	217	0.85	1.08
	S.D.	32	0.12	2.6	3.0	73	67	0.11	0.13
	n	10	10	10	10	10	10	10	10

Statistical analysis was not done : @@
No significant difference in any treated groups from control group.
Sa.G. : Salivary gland

Table 8 - 4 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Absolute organ weight
Sex : Female

Stage : Week 13

Test Article		Liver	Spleen	Kidney-RL	Adrenal-RL	Ovary-RL	Uterus
Dose		g	g	g	mg	mg	mg
0 mg/kg	Mean	7.19	0.49	1.95	59	71.5	525
	S.D.	0.48	0.04	0.16	7	14.0	119
	n	10	10	10	10	10	10
100 mg/kg	Mean	6.89	0.45	1.80	56	78.5	608
	S.D.	0.56	0.09	0.24	7	8.7	122
	n	10	10	10	10	10	10
300 mg/kg	Mean	7.35	0.47	1.85	64	90.1 D2**	647
	S.D.	0.60	0.06	0.15	11	9.4	206
	n	10	10	10	10	10	10
1000 mg/kg	Mean	8.41 D2**	0.45	1.88	59	72.5	577
	S.D.	1.14	0.09	0.18	10	15.5	178
	n	10	10	10	10	10	10

Significantly different from control : ** P<0.01
D2:Dunnett Test Two-Side

Table 9 - 1 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Relative organ weight
Sex : Male

Stage : Week 13

Test Article Dose		F.B.W.@@ g	Brain g/100g	Pituitary mg/100g	Thyroid-RL mg/100g	Sa.G.-RL mg/100g	Thymus mg/100g	Heart g/100g	Lung g/100g
0 mg/kg	Mean	518	0.42	2.5	4.4	145	51	0.28	0.29
	S.D.	42	0.03	0.3	0.9	18	13	0.01	0.02
	n	10	10	10	10	10	10	10	10
100 mg/kg	Mean	535	0.41	2.3	4.8	140	52	0.28	0.29
	S.D.	80	0.07	0.3	1.2	24	13	0.02	0.02
	n	10	10	10	10	10	10	10	10
300 mg/kg	Mean	520	0.43	2.5	4.4	142	49	0.28	0.29
	S.D.	27	0.03	0.3	1.3	10	9	0.01	0.01
	n	10	10	10	10	10	10	10	10
1000 mg/kg	Mean	454	0.47	2.6	4.8	149	48	0.29	0.31
	S.D.	47	0.04	0.3	0.7	18	11	0.02	0.01
	n	10	10	10	10	10	10	10	10

Statistical analysis was not done : @@
No significant difference in any treated groups from control group.
Sa.G. : Salivary gland

Table 9 - 2 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Relative organ weight
Sex : Male

Stage : Week 13

Test Article Dose		Liver g/100g	Spleen g/100g	Kidney-RL g/100g	Adrenal-RL mg/100g	Testis-RL g/100g	Prostate g/100g	Sem.Ves. g/100g
0 mg/kg	Mean	2.61	0.14	0.60	11	0.63	0.29	0.38
	S.D.	0.18	0.01	0.05	2	0.07	0.04	0.08
	n	10	10	10	10	10	10	10
100 mg/kg	Mean	2.58	0.13	0.60	10	0.65	0.27	0.36
	S.D.	0.28	0.02	0.05	1	0.08	0.04	0.05
	n	10	10	10	10	10	10	10
300 mg/kg	Mean	2.63	0.14	0.63	9	0.65	0.24	0.37
	S.D.	0.19	0.01	0.05	2	0.07	0.03	0.06
	n	10	10	10	10	10	10	10
1000 mg/kg	Mean	2.85 D2*	0.14	0.69 D2**	10	0.75 D2**	0.28	0.38
	S.D.	0.18	0.02	0.04	2	0.09	0.04	0.06
	n	10	10	10	10	10	10	10

Significantly different from control : * P≤0.05, ** P≤0.01
D2:Dunnett Test Two-Side
Sem.Ves. : Seminal vesicle

Table 9 - 3 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Relative organ weight
Sex : Female

Stage : Week 13

Test Article Dose		F.B.W.@@ g	Brain g/100g	Pituitary mg/100g	Thyroid-RL mg/100g	Sa.G.-RL mg/100g	Thymus mg/100g	Heart g/100g	Lung g/100g
0 mg/kg	Mean	296	0.69	5.5	6.0	152	82	0.31	0.39
	S.D.	20	0.04	0.9	1.0	14	22	0.02	0.03
	n	10	10	10	10	10	10	10	10
100 mg/kg	Mean	285	0.71	5.6	6.4	158	79	0.32	0.39
	S.D.	25	0.06	0.7	1.5	8	15	0.02	0.02
	n	10	10	10	10	10	10	10	10
300 mg/kg	Mean	284	0.72	5.5	7.2	156	78	0.31	0.40
	S.D.	19	0.04	0.8	1.7	12	14	0.02	0.02
	n	10	10	10	10	10	10	10	10
1000 mg/kg	Mean	270	0.73	6.1	6.0	164	80	0.32	0.40
	S.D.	32	0.05	1.2	1.4	14	17	0.02	0.02
	n	10	10	10	10	10	10	10	10

Statistical analysis was not done : @@
No significant difference in any treated groups from control group.
Sa.G. : Salivary gland

Table 9 - 4 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Relative organ weight
Sex : Female

Stage : Week 13

Test Article		Liver	Spleen	Kidney-RL	Adrenal-RL	Ovary-RL	Uterus
Dose		g/100g	g/100g	g/100g	mg/100g	mg/100g	mg/100g
0 mg/kg	Mean	2.44	0.16	0.66	20	24.3	177
	S.D.	0.10	0.02	0.06	3	5.2	38
	n	10	10	10	10	10	10
100 mg/kg	Mean	2.43	0.16	0.63	20	27.6	216
	S.D.	0.17	0.02	0.05	2	2.6	55
	n	10	10	10	10	10	10
300 mg/kg	Mean	2.59	0.17	0.66	23	31.8 D2**	229
	S.D.	0.19	0.02	0.05	5	3.3	72
	n	10	10	10	10	10	10
1000 mg/kg	Mean	3.12 D2**	0.17	0.70	22	27.0	217
	S.D.	0.16	0.02	0.06	4	5.4	69
	n	10	10	10	10	10	10

Significantly different from control : ** P<0.01
D2:Dunnett Test Two-Side

Table 10-1 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats
Gross pathological findings

Organs	Sex:	M	M	M	M
Findings	Dose (mg/kg) :	0	100	300	1000
	Number:	10	10	10	10
Stomach					
Focus, dark red, glandular stomach		0	0	2	0
Focus, raised, forestomach		0	0	0	1
Thickening, forestomach		0	0	0	5
Testis					
Small		0	0	1	0

M : Male

Table 10-2 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats
Gross pathological findings

Organs	Sex:	F	F	F	F
Findings	Dose (mg/kg):	0	100	300	1000
	Number:	10	10	10	10
Stomach					
Focus, dark red, glandular stomach		1	0	0	0
Thickening, forestomach		0	0	0	5
Uterus					
Cyst		0	0	0	1

F : Female

Table 11-1 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats
 Histopathological findings

Organs	Sex:	M	M	M	M
Findings	Dose (mg/kg) :	0	100	300	1000
	Number:	10	10	10	10
Adrenal					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Aorta, thoracic					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Bone, femoral (knee joint)					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Bone marrow, femoral					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Bone, sternal					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Bone marrow, sternal					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Cerebellum					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Cerebrum					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Coagulating gland					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Epididymis					
Number examined		10	0	0	10
Not remarkable		9	0	0	9
Cell infiltration, interstitium		1	0	0	1
minimal		1	0	0	1
Esophagus					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Eye					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Harderian gland					
Number examined		10	0	0	10
Not remarkable		10	0	0	9
Cell infiltration, interstitium		0	0	0	1
minimal		0	0	0	1
Heart					
Number examined		10	0	0	10
Not remarkable		10	0	0	9
Cell infiltration, myocardium		0	0	0	1
minimal		0	0	0	1
Intestine, duodenum					
Number examined		10	0	0	10
Not remarkable		10	0	0	10

M : Male

Table 11-2 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats
 Histopathological findings

Organs	Sex:	M	M	M	M
	Dose (mg/kg) :	0	100	300	1000
Findings	Number:	10	10	10	10
Intestine, jejunum					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Intestine, ileum (Peyer's patch)					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Intestine, cecum					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Intestine, colon					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Intestine, rectum					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Kidney					
Number examined		10	0	0	10
Not remarkable		7	0	0	8
Basophilia, tubule		3	0	0	2
minimal		3	0	0	2
Urinary cast, hyaline		1	0	0	0
minimal		1	0	0	0
Liver					
Number examined		10	10	10	10
Not remarkable		0	0	2	5
Cell infiltration, focal		8	7	7	5
minimal		8	7	7	5
Vacuolation, hepatocyte		9	8	5	0
minimal		4	6	5	0
mild		5	2	0	0
Lung (bronchus)					
Number examined		10	0	0	10
Not remarkable		9	0	0	10
Aggregation, alveolar macrophage		1	0	0	0
minimal		1	0	0	0
Lymph node, mesenteric					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Lymph node, submandibular					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Mammary gland, inguinal					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Nasal cavity					
Number examined		10	10	10	10
Not remarkable		10	10	10	0
Cell infiltration, respiratory epithelium		0	0	0	1
mild		0	0	0	1
Cell infiltration, olfactory epithelium		0	0	0	2
minimal		0	0	0	1
mild		0	0	0	1

M : Male

Table 11-3 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats
 Histopathological findings

Organs	Sex:	M	M	M	M
Findings	Dose (mg/kg) :	0	100	300	1000
	Number:	10	10	10	10
Nasal cavity (continued)					
Cyst, respiratory epithelium		0	0	0	2
minimal		0	0	0	2
Cyst, olfactory epithelium		0	0	0	2
minimal		0	0	0	2
Atrophy, olfactory epithelium		0	0	0	2
minimal		0	0	0	1
mild		0	0	0	1
Disarrangement, respiratory epithelium		0	0	0	6
minimal		0	0	0	6
Disarrangement, olfactory epithelium		0	0	0	4
minimal		0	0	0	4
Hyperplasia, olfactory gland, focal		0	0	0	2
minimal		0	0	0	2
Dilatation, nasal gland		0	0	0	2
minimal		0	0	0	2
Atrophy, olfactory gland		0	0	0	10
moderate		0	0	0	10
Optic nerve					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Pancreas					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Parathyroid					
Number examined		9	0	0	9
Not remarkable		9	0	0	9
No sample		1	0	0	1
Pituitary					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Prostate					
Number examined		10	0	0	10
Not remarkable		7	0	0	7
Cell infiltration, interstitium		3	0	0	3
minimal		3	0	0	3
Salivary gland, submandibular					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Salivary gland, sublingual					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Sciatic nerve					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Seminal vesicle					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Skeletal muscle, femoral					
Number examined		10	0	0	10
Not remarkable		10	0	0	9
Degeneration, muscle		0	0	0	1
minimal		0	0	0	1

M : Male

Table 11-4 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats
 Histopathological findings

Organs	Sex:	M	M	M	M
Findings	Dose (mg/kg) :	0	100	300	1000
	Number:	10	10	10	10
Skin, inguinal					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Spinal cord, thoracic					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Spleen					
Number examined		10	0	0	10
Not remarkable		9	0	0	9
Hematopoiesis, extramedullary		1	0	0	1
minimal		1	0	0	1
Stomach					
Number examined		10	10	10	10
Not remarkable		10	5	0	0
Dilatation, gland, glandular stomach		0	0	1	4
minimal		0	0	1	4
Erosion/Ulcer, glandular stomach		0	0	1	0
minimal		0	0	1	0
Hyperplasia, squamous cell, forestomach		0	5	10	10
minimal		0	5	7	1
mild		0	0	3	8
moderate		0	0	0	1
Nodular hyperplasia, squamous cell, forestomach		0	0	0	1
moderate		0	0	0	1
Hyperkeratosis, forestomach		0	5	10	10
minimal		0	5	7	1
mild		0	0	3	6
moderate		0	0	0	3
Testis					
Number examined		10	0	0	10
Not remarkable		10	0	0	9
Atrophy, tubule		0	0	0	1
minimal		0	0	0	1
Thymus					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Thyroid					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Tongue					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Trachea					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Urinary bladder					
Number examined		10	0	0	10
Not remarkable		8	0	0	9
Cell infiltration, submucosa		2	0	0	1
minimal		2	0	0	1
Zymbal gland					
Number examined		10	0	0	10
Not remarkable		10	0	0	10

M : Male

Table 11-5 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats
 Histopathological findings

Organs	Sex:	F	F	F	F
	Dose (mg/kg) :	0	100	300	1000
Findings	Number:	10	10	10	10
Adrenal					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Aorta, thoracic					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Bone, femoral (knee joint)					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Bone marrow, femoral					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Bone, sternal					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Bone marrow, sternal					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Cerebellum					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Cerebrum					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Esophagus					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Eye					
Number examined		10	0	0	10
Not remarkable		10	0	0	9
Dysplasia, retina		0	0	0	1
minimal		0	0	0	1
Harderian gland					
Number examined		10	0	0	10
Not remarkable		10	0	0	9
Cell infiltration, interstitium		0	0	0	1
minimal		0	0	0	1
Heart					
Number examined		10	0	0	10
Not remarkable		10	0	0	9
Cell infiltration, myocardium		0	0	0	1
minimal		0	0	0	1
Intestine, duodenum					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Intestine, jejunum					
Number examined		10	0	0	10
Not remarkable		10	0	0	10

F : Female

Table 11-6 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats
 Histopathological findings

Organs	Sex:	F	F	F	F
Findings	Dose (mg/kg) : Number:	0 10	100 10	300 10	1000 10
Intestine, ileum (Peyer's patch)					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Intestine, cecum					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Intestine, colon					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Intestine, rectum					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Kidney					
Number examined		10	0	0	10
Not remarkable		9	0	0	9
Cyst		1	0	0	1
minimal		1	0	0	1
Liver					
Number examined		10	10	10	10
Not remarkable		2	3	3	5
Cell infiltration, focal		7	6	4	5
minimal		7	6	4	5
Vacuolation, hepatocyte		6	3	4	0
minimal		6	3	4	0
Lung (bronchus)					
Number examined		10	0	0	10
Not remarkable		9	0	0	9
Aggregation, alveolar macrophage		1	0	0	1
minimal		1	0	0	1
Lymph node, mesenteric					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Lymph node, submandibular					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Mammary gland, inguinal					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Nasal cavity					
Number examined		10	10	10	10
Not remarkable		10	10	10	0
Cell infiltration, respiratory epithelium		0	0	0	2
minimal		0	0	0	2
Cell infiltration, olfactory epithelium		0	0	0	1
minimal		0	0	0	1
Cyst, olfactory epithelium		0	0	0	1
minimal		0	0	0	1
Atrophy, olfactory epithelium		0	0	0	2
minimal		0	0	0	1
mild		0	0	0	1
Disarrangement, respiratory epithelium		0	0	0	2
minimal		0	0	0	2
Disarrangement, olfactory epithelium		0	0	0	5

F : Female

Table 11-7 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats
 Histopathological findings

Organs	Sex:	F	F	F	F
Findings	Dose (mg/kg) :	0	100	300	1000
	Number:	10	10	10	10
Nasal cavity (continued)					
Disarrangement,olfactory epithelium (continued)					
minimal		0	0	0	5
Hyperplasia,olfactory gland,focal		0	0	0	2
minimal		0	0	0	2
Atrophy,olfactory gland		0	0	0	10
mild		0	0	0	1
moderate		0	0	0	9
Optic nerve					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Ovary					
Number examined		10	0	0	10
Not remarkable		9	0	0	9
Atrophy		1	0	0	1
mild		0	0	0	1
moderate		1	0	0	0
Oviduct					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Pancreas					
Number examined		10	0	0	10
Not remarkable		9	0	0	10
Hemorrhage,focal		1	0	0	0
minimal		1	0	0	0
Parathyroid					
Number examined		9	0	0	10
Not remarkable		9	0	0	10
No sample		1	0	0	0
Pituitary					
Number examined		10	0	0	10
Not remarkable		10	0	0	9
Aberrant craniopharyngeal tissue		0	0	0	1
minimal		0	0	0	1
Salivary gland,submandibular					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Salivary gland,sublingual					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Sciatic nerve					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Skeletal muscle,femoral					
Number examined		10	0	0	10
Not remarkable		9	0	0	10
Degeneration,muscle		1	0	0	0
minimal		1	0	0	0
Skin,inguinal					
Number examined		10	0	0	10
Not remarkable		10	0	0	10

F : Female

Table 11-8 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats
 Histopathological findings

Organs	Sex:	F	F	F	F
Findings	Dose (mg/kg) :	0	100	300	1000
	Number:	10	10	10	10
Spinal cord, thoracic					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Spleen					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Stomach					
Number examined		10	10	10	10
Not remarkable		10	3	1	0
Dilatation, gland, glandular stomach		0	0	1	1
minimal		0	0	1	1
Hyperplasia, squamous cell, forestomach		0	7	8	10
minimal		0	7	7	4
mild		0	0	1	6
Hyperkeratosis, forestomach		0	7	8	10
minimal		0	7	7	4
mild		0	0	1	5
moderate		0	0	0	1
Thymus					
Number examined		10	0	0	10
Not remarkable		10	0	0	9
Hyperplasia, epithelium		0	0	0	1
minimal		0	0	0	1
Thyroid					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Tongue					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Trachea					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Urinary bladder					
Number examined		10	0	0	10
Not remarkable		10	0	0	9
Cell infiltration, submucosa		0	0	0	1
minimal		0	0	0	1
Uterus					
Number examined		10	0	0	10
Not remarkable		10	0	0	9
Cyst, squamous		0	0	0	1
minimal		0	0	0	1
Vagina					
Number examined		10	0	0	10
Not remarkable		10	0	0	10
Zymbal gland					
Number examined		10	0	0	10
Not remarkable		10	0	0	10

F : Female



Individual clinical signs

Dose (mg/kg) : 0

Sex : Male

Animal No.	Day of administration													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1010	-	-	-	-	-	-	-	-	-	-	-	-	-	-

--No abnormal findings

Appendix 1-2

4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Individual clinical signs

Dose (mg/kg) : 0

Sex : Male

Animal No.	Day of administration													
	15	16	17	18	19	20	21	22	23	24	25	26	27	28
1001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1010	-	-	-	-	-	-	-	-	-	-	-	-	-	-

--No abnormal findings



Individual clinical signs

Dose (mg/kg) : 0

Sex : Male

Animal No.	Day of administration													
	29	30	31	32	33	34	35	36	37	38	39	40	41	42
1001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1010	-	-	-	-	-	-	-	-	-	-	-	-	-	-

--No abnormal findings



Individual clinical signs

Dose (mg/kg) : 0

Sex : Male

Animal No.	Day of administration													
	43	44	45	46	47	48	49	50	51	52	53	54	55	56
1001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1010	-	-	-	-	-	-	-	-	-	-	-	-	-	-

--No abnormal findings



Individual clinical signs

Dose (mg/kg) : 0

Sex : Male

Animal No.	Day of administration													
	57	58	59	60	61	62	63	64	65	66	67	68	69	70
1001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1010	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-:No abnormal findings



Individual clinical signs

Dose (mg/kg) : 0

Sex : Male

Animal No.	Day of administration													
	71	72	73	74	75	76	77	78	79	80	81	82	83	84
1001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1010	-	-	-	-	-	-	-	-	-	-	-	-	-	-

--No abnormal findings



Individual clinical signs

Dose (mg/kg) : 0

Sex : Male

Animal No.	Day of administration							92#
	85	86	87	88	89	90	91	
1001	-	-	-	-	-	-	-	-
1002	-	-	-	-	-	-	-	-
1003	-	-	-	-	-	-	-	-
1004	-	-	-	-	-	-	-	-
1005	-	-	-	-	-	-	-	-
1006	-	-	-	-	-	-	-	-
1007	-	-	-	-	-	-	-	-
1008	-	-	-	-	-	-	-	-
1009	-	-	-	-	-	-	-	-
1010	-	-	-	-	-	-	-	-

Day of necropsy

-:No abnormal findings



Individual clinical signs

Dose (mg/kg) : 100

Sex : Male

Animal No.	Day of administration													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
2001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2010	-	-	-	-	-	-	-	-	-	-	-	-	-	-

--No abnormal findings



Individual clinical signs

Dose (mg/kg) : 100

Sex : Male

Animal No.	Day of administration													
	15	16	17	18	19	20	21	22	23	24	25	26	27	28
2001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2010	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-:No abnormal findings



Individual clinical signs

Dose (mg/kg) : 100

Sex : Male

Animal No.	Day of administration													
	29	30	31	32	33	34	35	36	37	38	39	40	41	42
2001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2010	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-:No abnormal findings



Individual clinical signs

Dose (mg/kg) : 100

Sex : Male

Animal No.	Day of administration													
	43	44	45	46	47	48	49	50	51	52	53	54	55	56
2001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2010	-	-	-	-	-	-	-	-	-	-	-	-	-	-

--No abnormal findings



Individual clinical signs

Dose (mg/kg) : 100

Sex : Male

Animal No.	Day of administration													
	57	58	59	60	61	62	63	64	65	66	67	68	69	70
2001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2010	-	-	-	-	-	-	-	-	-	-	-	-	-	-

--No abnormal findings



Individual clinical signs

Dose (mg/kg) : 100

Sex : Male

Animal No.	Day of administration													
	71	72	73	74	75	76	77	78	79	80	81	82	83	84
2001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2010	-	-	-	-	-	-	-	-	-	-	-	-	-	-

--No abnormal findings

Appendix 1-14 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Individual clinical signs

Dose (mg/kg) : 100

Sex : Male

Animal No.	Day of administration							92#
	85	86	87	88	89	90	91	
2001	-	-	-	-	-	-	-	-
2002	-	-	-	-	-	-	-	-
2003	-	-	-	-	-	-	-	-
2004	-	-	-	-	-	-	-	-
2005	-	-	-	-	-	-	-	-
2006	-	-	-	-	-	-	-	-
2007	-	-	-	-	-	-	-	-
2008	-	-	-	-	-	-	-	-
2009	-	-	-	-	-	-	-	-
2010	-	-	-	-	-	-	-	-

Day of necropsy

--:No abnormal findings



Individual clinical signs

Dose (mg/kg) : 300

Sex : Male

Animal No.	Day of administration													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
3001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3010	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-:No abnormal findings



Individual clinical signs

Dose (mg/kg) : 300

Sex : Male

Animal No.	Day of administration													
	15	16	17	18	19	20	21	22	23	24	25	26	27	28
3001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3010	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-:No abnormal findings



Individual clinical signs

Dose (mg/kg) : 300

Sex : Male

Animal No.	Day of administration													
	29	30	31	32	33	34	35	36	37	38	39	40	41	42
3001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3010	-	-	-	-	-	-	-	-	-	-	-	-	-	-

--No abnormal findings



Individual clinical signs

Dose (mg/kg) : 300

Sex : Male

Animal No.	Day of administration													
	43	44	45	46	47	48	49	50	51	52	53	54	55	56
3001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3010	-	-	-	-	-	-	-	-	-	-	-	-	-	-

--No abnormal findings

Appendix 1-19 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Individual clinical signs

Dose (mg/kg) : 300

Sex : Male

Animal No.	Day of administration													
	57	58	59	60	61	62	63	64	65	66	67	68	69	70
3001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3010	-	-	-	-	-	-	-	-	-	-	-	-	-	-

--No abnormal findings



Individual clinical signs

Dose (mg/kg) : 300

Sex : Male

Animal No.	Day of administration													
	71	72	73	74	75	76	77	78	79	80	81	82	83	84
3001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3010	-	-	-	-	-	-	-	-	-	-	-	-	-	-

--No abnormal findings



Individual clinical signs

Dose (mg/kg) : 300

Sex : Male

Animal No.	Day of administration							92#
	85	86	87	88	89	90	91	
3001	-	-	-	-	-	-	-	-
3002	-	-	-	-	-	-	-	-
3003	-	-	-	-	-	-	-	-
3004	-	-	-	-	-	-	-	-
3005	-	-	-	-	-	-	-	-
3006	-	-	-	-	-	-	-	-
3007	-	-	-	-	-	-	-	-
3008	-	-	-	-	-	-	-	-
3009	-	-	-	-	-	-	-	-
3010	-	-	-	-	-	-	-	-

Day of necropsy

-:No abnormal findings



Individual clinical signs
Dose (mg/kg) : 1000

Sex : Male

Animal No.	Day of administration													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
4001	-	-	-	A	-	A	-	-	A	A	A	-	-	-
4002	-	-	-	-	A	-	-	-	-	-	-	-	-	A
4003	-	-	A	A	A	-	-	A	A	A	A	-	A	-
4004	-	A	-	A	-	A	A	-	A	-	-	-	-	A
4005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4006	A	A	-	-	A	-	-	-	-	-	-	-	-	-
4007	-	A	A	A	-	-	A	-	-	-	-	-	-	A
4008	-	A	-	-	A	-	-	-	-	-	-	-	-	A
4009	-	A	A	-	A	A	A	A	-	-	-	A	-	-
4010	-	-	A	A	-	A	A	A	-	-	-	-	-	A

-:No abnormal findings
A:Decrease, spontaneous movement



Individual clinical signs

Dose (mg/kg) : 1000

Sex : Male

Animal No.	Day of administration													
	15	16	17	18	19	20	21	22	23	24	25	26	27	28
4001	-	A	-	-	A	A	A	-	A	A	A	A	-	A
4002	-	-	A	A	-	-	-	-	-	-	-	-	-	-
4003	A	A	A	A	A	A	-	A	A	A	A	A	A	A
4004	A	-	-	A	-	-	A	-	-	-	-	-	-	A
4005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4008	-	-	A	-	-	A	-	-	-	-	-	-	A	-
4009	A	-	-	-	A	-	A	A	-	-	-	A	-	A
4010	-	-	A	-	-	A	-	-	A	-	-	-	A	A

-:No abnormal findings

A:Decrease, spontaneous movement



Individual clinical signs

Dose (mg/kg) : 1000

Sex : Male

Animal No.	Day of administration													
	29	30	31	32	33	34	35	36	37	38	39	40	41	42
4001	-	A	-	-	A	A	A	-	A	A	-	-	-	A
4002	-	-	-	-	-	-	-	-	A	A	-	-	-	-
4003	A	A	A	A	-	-	A	A	-	-	A	A	-	A
4004	A	A	A	A	A	A	A	-	A	-	-	A	-	-
4005	A	-	-	-	-	-	-	-	-	-	-	-	-	-
4006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4007	-	-	-	-	-	-	A	A	-	-	-	-	-	A
4008	-	A	-	A	A	-	-	-	-	A	A	-	A	-
4009	A	A	-	-	-	-	-	A	-	-	A	-	A	A
4010	A	-	-	-	-	-	-	-	-	-	-	-	A	-

-:No abnormal findings

A:Decrease, spontaneous movement



Individual clinical signs

Dose (mg/kg) : 1000

Sex : Male

Animal No.	Day of administration													
	43	44	45	46	47	48	49	50	51	52	53	54	55	56
4001	A	-	A	A	A	-	A	-	-	A	-	-	A	A
4002	A	A	-	-	-	-	-	-	-	-	A	-	-	-
4003	A	-	A	A	-	A	A	A	A	A	A	-	-	A
4004	-	-	-	A	-	A	A	A	A	-	-	A	A	-
4005	-	-	-	-	A	-	-	-	-	-	-	-	A	-
4006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4007	-	-	-	-	-	A	-	-	-	-	-	A	-	-
4008	-	-	-	-	-	-	-	A	A	-	-	-	-	-
4009	-	-	A	A	A	-	A	A	A	-	-	-	-	-
4010	A	-	-	-	-	-	A	-	-	-	-	-	-	-

-:No abnormal findings

A:Decrease, spontaneous movement



Individual clinical signs

Dose (mg/kg) : 1000

Sex : Male

Animal No.	Day of administration													
	57	58	59	60	61	62	63	64	65	66	67	68	69	70
4001	-	A	-	-	-	-	-	-	-	-	-	-	-	-
4002	-	-	-	-	A	A	A	A	-	-	-	A	A	-
4003	-	A	-	A	A	A	A	A	A	-	A	A	A	A
4004	A	-	-	-	-	-	A	-	-	-	-	-	-	A
4005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4007	-	-	-	-	-	-	-	A	-	A	-	-	-	A
4008	A	-	A	-	A	A	-	-	A	-	-	-	A	-
4009	-	-	-	-	A	-	A	-	-	A	-	A	-	A
4010	-	-	A	A	-	-	A	-	-	-	A	-	-	-

-:No abnormal findings

A:Decrease, spontaneous movement



Individual clinical signs

Dose (mg/kg) : 1000

Sex : Male

Animal No.	Day of administration													
	71	72	73	74	75	76	77	78	79	80	81	82	83	84
4001	-	A	-	-	-	-	-	-	A	-	-	-	A	A
4002	-	A	A	-	A	-	-	A	-	-	-	-	-	-
4003	A	-	A	A	-	A	-	A	-	A	A	A	A	A
4004	-	-	-	A	A	-	A	-	-	-	A	-	-	-
4005	A	-	-	-	-	-	-	-	A	-	-	-	-	-
4006	-	-	-	-	-	-	-	-	-	A	-	-	-	-
4007	A	-	A	-	A	-	A	A	-	-	-	A	A	-
4008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4009	-	A	-	-	-	A	A	-	-	-	-	A	-	-
4010	-	-	A	A	-	A	-	-	A	A	A	-	A	-

-:No abnormal findings

A:Decrease, spontaneous movement



Individual clinical signs

Dose (mg/kg) : 1000

Sex : Male

Animal No.	Day of administration							
	85	86	87	88	89	90	91	92#
4001	-	A	-	-	A	A	-	-
4002	-	-	-	-	-	-	-	-
4003	-	-	-	-	-	A	A	-
4004	-	-	-	A	-	A	-	-
4005	-	-	A	-	-	-	-	-
4006	-	-	A	A	-	-	-	-
4007	A	-	-	-	-	-	A	-
4008	-	-	-	-	-	-	-	-
4009	A	A	-	-	A	-	-	-
4010	A	-	-	-	-	-	A	-

Day of necropsy

-:No abnormal findings

A:Decrease, spontaneous movement



Individual clinical signs

Dose (mg/kg) : 0

Sex : Female

Animal No.	Day of administration													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1101	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1102	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1103	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1104	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1106	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1107	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1108	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1109	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1110	-	-	-	-	-	-	-	-	-	-	-	-	-	-

--No abnormal findings



Individual clinical signs

Dose (mg/kg) : 0

Sex : Female

Animal No.	Day of administration													
	15	16	17	18	19	20	21	22	23	24	25	26	27	28
1101	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1102	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1103	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1104	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1106	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1107	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1108	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1109	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1110	-	-	-	-	-	-	-	-	-	-	-	-	-	-

--No abnormal findings



Individual clinical signs

Dose (mg/kg) : 0

Sex : Female

Animal No.	Day of administration													
	29	30	31	32	33	34	35	36	37	38	39	40	41	42
1101	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1102	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1103	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1104	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1106	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1107	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1108	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1109	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1110	-	-	-	-	-	-	-	-	-	-	-	-	-	-

--No abnormal findings



Individual clinical signs
Dose (mg/kg) : 0

Sex : Female

Animal No.	Day of administration													
	43	44	45	46	47	48	49	50	51	52	53	54	55	56
1101	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1102	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1103	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1104	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1106	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1107	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1108	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1109	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1110	-	-	-	-	-	-	-	-	-	-	-	-	-	-

--No abnormal findings



Individual clinical signs

Dose (mg/kg) : 0

Sex : Female

Animal No.	Day of administration													
	57	58	59	60	61	62	63	64	65	66	67	68	69	70
1101	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1102	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1103	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1104	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1106	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1107	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1108	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1109	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1110	-	-	-	-	-	-	-	-	-	-	-	-	-	-

--No abnormal findings



Individual clinical signs

Dose (mg/kg) : 0

Sex : Female

Animal No.	Day of administration													
	71	72	73	74	75	76	77	78	79	80	81	82	83	84
1101	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1102	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1103	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1104	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1106	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1107	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1108	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1109	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1110	-	-	-	-	-	-	-	-	-	-	-	-	-	-

--No abnormal findings



Individual clinical signs

Dose (mg/kg) : 0

Sex : Female

Animal No.	Day of administration							92#
	85	86	87	88	89	90	91	
1101	-	-	-	-	-	-	-	-
1102	-	-	-	-	-	-	-	-
1103	-	-	-	-	-	-	-	-
1104	-	-	-	-	-	-	-	-
1105	-	-	-	-	-	-	-	-
1106	-	-	-	-	-	-	-	-
1107	-	-	-	-	-	-	-	-
1108	-	-	-	-	-	-	-	-
1109	-	-	-	-	-	-	-	-
1110	-	-	-	-	-	-	-	-

Day of necropsy

-:No abnormal findings



Individual clinical signs

Dose (mg/kg) : 100

Sex : Female

Animal No.	Day of administration													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
2101	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2102	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2103	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2104	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2106	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2107	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2108	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2109	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2110	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-:No abnormal findings



Individual clinical signs

Dose (mg/kg) : 100

Sex : Female

Animal No.	Day of administration													
	15	16	17	18	19	20	21	22	23	24	25	26	27	28
2101	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2102	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2103	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2104	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2106	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2107	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2108	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2109	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2110	-	-	-	-	-	-	-	-	-	-	-	-	-	-

--No abnormal findings



Individual clinical signs

Dose (mg/kg) : 100

Sex : Female

Animal No.	Day of administration													
	29	30	31	32	33	34	35	36	37	38	39	40	41	42
2101	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2102	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2103	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2104	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2106	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2107	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2108	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2109	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2110	-	-	-	-	-	-	-	-	-	-	-	-	-	-

--No abnormal findings



Individual clinical signs

Dose (mg/kg) : 100

Sex : Female

Animal No.	Day of administration													
	43	44	45	46	47	48	49	50	51	52	53	54	55	56
2101	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2102	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2103	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2104	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2106	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2107	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2108	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2109	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2110	-	-	-	-	-	-	-	-	-	-	-	-	-	-

--No abnormal findings



Individual clinical signs

Dose (mg/kg) : 100

Sex : Female

Animal No.	Day of administration													
	57	58	59	60	61	62	63	64	65	66	67	68	69	70
2101	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2102	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2103	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2104	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2106	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2107	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2108	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2109	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2110	-	-	-	-	-	-	-	-	-	-	-	-	-	-

--No abnormal findings



Individual clinical signs

Dose (mg/kg) : 100

Sex : Female

Animal No.	Day of administration													
	71	72	73	74	75	76	77	78	79	80	81	82	83	84
2101	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2102	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2103	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2104	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2106	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2107	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2108	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2109	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2110	-	-	-	-	-	-	-	-	-	-	-	-	-	-

--No abnormal findings



Individual clinical signs

Dose (mg/kg) : 100

Sex : Female

Animal No.	Day of administration							92#
	85	86	87	88	89	90	91	
2101	-	-	-	-	-	-	-	-
2102	-	-	-	-	-	-	-	-
2103	-	-	-	-	-	-	-	-
2104	-	-	-	-	-	-	-	-
2105	-	-	-	-	-	-	-	-
2106	-	-	-	-	-	-	-	-
2107	-	-	-	-	-	-	-	-
2108	-	-	-	-	-	-	-	-
2109	-	-	-	-	-	-	-	-
2110	-	-	-	-	-	-	-	-

Day of necropsy

-:No abnormal findings



Individual clinical signs

Dose (mg/kg) : 300

Sex : Female

Animal No.	Day of administration													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
3101	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3102	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3103	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3104	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3106	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3107	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3108	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3109	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3110	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-:No abnormal findings



Individual clinical signs

Dose (mg/kg) : 300

Sex : Female

Animal No.	Day of administration													
	15	16	17	18	19	20	21	22	23	24	25	26	27	28
3101	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3102	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3103	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3104	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3106	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3107	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3108	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3109	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3110	-	-	-	-	-	-	-	-	-	-	-	-	-	-

--No abnormal findings



Individual clinical signs

Dose (mg/kg) : 300

Sex : Female

Animal No.	Day of administration													
	29	30	31	32	33	34	35	36	37	38	39	40	41	42
3101	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3102	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3103	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3104	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3106	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3107	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3108	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3109	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3110	-	-	-	-	-	-	-	-	-	-	-	-	-	-

--No abnormal findings



Individual clinical signs

Dose (mg/kg) : 300

Sex : Female

Animal No.	Day of administration													
	43	44	45	46	47	48	49	50	51	52	53	54	55	56
3101	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3102	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3103	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3104	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3106	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3107	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3108	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3109	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3110	-	-	-	-	-	-	-	-	-	-	-	-	-	-

--No abnormal findings



Individual clinical signs

Dose (mg/kg) : 300

Sex : Female

Animal No.	Day of administration													
	57	58	59	60	61	62	63	64	65	66	67	68	69	70
3101	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3102	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3103	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3104	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3106	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3107	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3108	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3109	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3110	-	-	-	-	-	-	-	-	-	-	-	-	-	-

--No abnormal findings



Individual clinical signs

Dose (mg/kg) : 300

Sex : Female

Animal No.	Day of administration													
	71	72	73	74	75	76	77	78	79	80	81	82	83	84
3101	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3102	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3103	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3104	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3106	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3107	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3108	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3109	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3110	-	-	-	-	-	-	-	-	-	-	-	-	-	-

--No abnormal findings



Individual clinical signs

Dose (mg/kg) : 300

Sex : Female

Animal No.	Day of administration							92#
	85	86	87	88	89	90	91	
3101	-	-	-	-	-	-	-	-
3102	-	-	-	-	-	-	-	-
3103	-	-	-	-	-	-	-	-
3104	-	-	-	-	-	-	-	-
3105	-	-	-	-	-	-	-	-
3106	-	-	-	-	-	-	-	-
3107	-	-	-	-	-	-	-	-
3108	-	-	-	-	-	-	-	-
3109	-	-	-	-	-	-	-	-
3110	-	-	-	-	-	-	-	-

Day of necropsy

-:No abnormal findings



Individual clinical signs

Dose (mg/kg) : 1000

Sex : Female

Animal No.	Day of administration													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
4101	-	-	-	-	-	-	-	A	-	A	-	-	-	-
4102	-	-	-	-	A	A	-	A	A	-	-	-	-	A
4103	-	A	-	A	A	A	A	A	A	A	A	A	A	A
4104	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4106	-	A	A	A	-	-	A	-	A	A	A	A	-	-
4107	-	-	-	-	A	A	-	-	-	-	A	-	A	-
4108	A	A	A	-	-	A	A	-	-	A	-	A	A	A
4109	-	A	A	A	A	A	A	A	A	A	-	A	-	-
4110	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-:No abnormal findings

A:Decrease, spontaneous movement



Individual clinical signs

Dose (mg/kg) : 1000

Sex : Female

Animal No.	Day of administration													
	15	16	17	18	19	20	21	22	23	24	25	26	27	28
4101	A	-	-	-	-	A	A	A	A	A	-	A	-	A
4102	-	-	-	A	A	A	-	-	-	-	A	A	-	A
4103	-	-	-	A	A	-	-	-	-	-	-	-	-	-
4104	-	-	-	-	-	-	-	A	-	-	-	-	-	-
4105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4106	A	A	-	-	-	A	A	-	-	-	-	-	-	-
4107	-	-	A	-	-	-	-	-	-	-	-	-	-	-
4108	-	-	A	-	A	-	A	A	A	A	A	-	A	A
4109	-	A	A	-	A	A	-	A	A	A	A	A	A	-
4110	-	A	A	-	-	-	-	-	-	-	-	-	-	-

-:No abnormal findings

A:Decrease, spontaneous movement



Individual clinical signs
Dose (mg/kg) : 1000

Sex : Female

Animal No.	Day of administration													
	29	30	31	32	33	34	35	36	37	38	39	40	41	42
4101	A	-	A	A	-	-	A	A	-	-	-	-	-	-
4102	-	A	-	-	-	A	A	-	A	A	A	-	A	A
4103	-	-	A	A	A	-	A	-	-	-	A	A	A	A
4104	-	-	-	-	A	-	-	-	-	-	-	-	-	-
4105	-	-	A	-	-	-	-	-	-	-	-	-	-	-
4106	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4107	-	A	-	-	-	-	-	-	-	-	-	-	-	A
4108	-	A	-	A	-	A	A	A	A	A	-	A	A	-
4109	A	-	-	-	A	A	-	A	A	-	A	-	-	-
4110	A	-	-	-	-	-	-	-	-	-	-	A	-	-

--No abnormal findings
A:Decrease, spontaneous movement



Individual clinical signs

Dose (mg/kg) : 1000

Sex : Female

Animal No.	Day of administration													
	43	44	45	46	47	48	49	50	51	52	53	54	55	56
4101	A	-	-	-	A	-	A	A	-	-	A	A	A	-
4102	A	A	-	A	-	-	A	A	A	A	-	A	-	-
4103	-	A	-	A	A	A	-	-	A	A	-	-	A	-
4104	-	-	-	-	-	-	-	-	-	-	-	-	-	A
4105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4106	-	-	A	-	-	-	A	A	-	-	-	-	-	-
4107	-	-	-	-	-	-	-	-	-	-	-	-	-	A
4108	-	-	A	-	A	A	A	A	A	-	A	-	-	A
4109	A	A	-	A	-	A	-	-	A	A	-	-	A	A
4110	-	-	-	-	-	-	A	-	-	-	-	-	A	-

-:No abnormal findings

A:Decrease, spontaneous movement



Individual clinical signs

Dose (mg/kg) : 1000

Sex : Female

Animal No.	Day of administration													
	57	58	59	60	61	62	63	64	65	66	67	68	69	70
4101	A	A	A	A	A	A	A	A	-	A	A	-	A	A
4102	-	A	A	-	A	-	A	-	-	-	-	A	A	A
4103	-	-	-	A	-	-	A	-	A	-	A	-	-	-
4104	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4105	-	-	-	-	-	-	-	-	-	-	-	-	A	-
4106	A	-	-	-	A	-	-	-	-	-	-	-	-	A
4107	-	-	-	-	-	-	-	-	A	-	-	-	-	-
4108	A	-	A	A	-	A	A	A	A	A	A	A	-	-
4109	-	A	-	-	-	A	A	A	-	A	A	A	-	A
4110	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-:No abnormal findings

A:Decrease, spontaneous movement



Individual clinical signs

Dose (mg/kg) : 1000

Sex : Female

Animal No.	Day of administration													
	71	72	73	74	75	76	77	78	79	80	81	82	83	84
4101	A	A	A	-	-	A	A	A	-	-	A	A	A	-
4102	A	A	-	A	A	-	-	-	A	A	A	A	-	A
4103	-	-	-	-	-	-	-	-	A	A	-	-	-	-
4104	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4105	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4106	-	A	A	A	A	-	A	-	-	-	-	-	-	-
4107	-	-	-	-	-	-	-	-	-	-	-	A	-	-
4108	A	A	A	A	A	A	A	A	A	-	A	-	A	A
4109	A	-	-	-	-	A	-	A	-	-	-	-	-	-
4110	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-:No abnormal findings

A:Decrease, spontaneous movement



Individual clinical signs

Dose (mg/kg) : 1000

Sex : Female

Animal No.	Day of administration							92#
	85	86	87	88	89	90	91	
4101	A	-	A	-	A	-	A	-
4102	-	-	A	-	-	A	A	-
4103	-	-	-	A	-	-	-	-
4104	-	-	-	-	-	-	-	-
4105	-	-	-	-	-	-	-	-
4106	-	-	-	-	-	A	-	-
4107	-	-	-	-	-	-	-	-
4108	-	A	A	-	A	A	A	-
4109	-	-	-	A	-	-	-	-
4110	-	-	-	-	-	-	-	-

Day of necropsy

-:No abnormal findings

A:Decrease, spontaneous movement

Appendix 2 - 1 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual body weight
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 0 mg/kg Unit : g

Animal No.	Day	1	4	7	14	21	28	35	42	49	56	63	70	77	84	91
1001		203	228	251	299	342	369	399	421	438	447	461	468	482	496	497
1002		188	213	239	288	330	364	394	426	444	461	480	492	505	520	522
1003		190	210	232	272	301	330	347	366	391	407	422	439	453	464	468
1004		195	219	244	295	337	370	395	419	444	456	476	489	508	520	530
1005		211	234	263	323	373	418	448	479	510	531	561	587	610	624	639
1006		197	216	240	276	304	330	355	375	400	416	436	460	477	495	502
1007		208	232	261	311	345	373	411	429	454	475	495	509	519	535	535
1008		188	208	230	274	315	348	376	398	413	437	449	470	480	498	512
1009		197	215	240	285	334	369	402	429	459	473	500	518	537	555	559
1010		204	225	251	295	335	367	394	416	439	459	473	491	502	523	520
Mean		198	220	245	292	332	364	392	416	439	456	475	492	507	523	528
S.D.		8	9	11	16	21	25	29	32	34	35	39	41	43	43	46
S.E.		3	3	4	5	7	8	9	10	11	11	12	13	14	14	15
n		10	10	10	10	10	10	10	10	10	10	10	10	10	10	10

Appendix 2 - 2 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual body weight
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 100 mg/kg Unit : g

Animal No.	Day	1	4	7	14	21	28	35	42	49	56	63	70	77	84	91
2001		202	230	255	314	353	389	419	448	473	498	522	540	555	574	582
2002		199	224	245	284	322	349	380	398	426	443	475	487	503	519	533
2003		196	221	237	277	305	337	372	397	424	437	454	470	486	494	503
2004		201	225	251	304	345	380	409	432	453	472	491	506	521	534	541
2005		212	235	262	330	381	425	454	493	523	542	563	586	606	622	635
2006		187	204	219	249	275	300	318	333	346	354	367	372	381	392	390
2007		183	208	227	269	307	335	360	375	394	407	420	428	440	451	447
2008		198	223	254	314	365	400	440	473	511	530	561	591	620	636	655
2009		196	217	247	297	342	377	413	443	471	494	518	542	560	580	586
2010		199	224	249	302	352	389	422	451	478	500	527	547	566	577	586
Mean		197	221	245	294	335	368	399	424	450	468	490	507	524	538	546
S.D.		8	9	13	24	32	37	41	48	54	58	62	69	74	76	82
S.E.		3	3	4	8	10	12	13	15	17	18	20	22	23	24	26
n		10	10	10	10	10	10	10	10	10	10	10	10	10	10	10

Appendix 2 - 3 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual body weight
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 300 mg/kg Unit : g

Animal No.	Day	1	4	7	14	21	28	35	42	49	56	63	70	77	84	91
3001		200	223	244	297	335	366	395	420	444	463	482	496	510	525	529
3002		201	227	258	314	354	397	429	455	479	497	517	528	546	564	568
3003		186	213	237	288	322	351	376	393	412	430	437	452	470	483	488
3004		209	232	256	308	339	367	385	406	424	436	450	460	472	489	489
3005		194	218	239	294	334	367	392	418	446	465	493	505	522	541	549
3006		192	216	240	296	343	379	411	435	463	475	496	515	532	546	554
3007		198	221	243	291	324	355	385	410	445	456	485	502	522	538	554
3008		189	212	237	288	330	367	397	421	452	467	480	491	502	510	514
3009		203	226	249	297	341	381	408	438	467	484	506	519	541	549	566
3010		208	230	253	303	345	369	403	426	443	455	478	492	512	518	524
Mean		198	222	246	298	337	370	398	422	448	463	482	496	513	526	534
S.D.		8	7	8	9	10	13	15	18	20	20	24	24	26	26	30
S.E.		2	2	2	3	3	4	5	6	6	6	8	8	8	8	9
n		10	10	10	10	10	10	10	10	10	10	10	10	10	10	10

Appendix 2 - 4 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Individual body weight
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 1000 mg/kg Unit : g

Animal No.	Day	1	4	7	14	21	28	35	42	49	56	63	70	77	84	91
4001		192	203	227	277	320	351	384	404	431	446	460	469	484	495	491
4002		195	210	230	274	295	308	336	354	375	389	414	423	439	455	453
4003		188	204	213	269	305	329	347	356	373	379	385	388	398	401	406
4004		196	216	237	288	321	346	363	377	396	411	420	433	446	467	469
4005		200	211	227	267	283	301	319	331	340	349	359	367	379	380	387
4006		194	212	237	287	320	355	380	403	424	431	443	455	463	472	473
4007		199	216	245	298	339	377	416	441	463	475	495	509	524	532	531
4008		187	206	227	270	289	318	342	356	375	390	404	416	421	426	431
4009		203	207	223	275	313	346	371	396	414	424	443	458	470	490	488
4010		216	236	262	318	365	404	436	454	464	474	493	497	508	524	534
Mean		197	212	233	282	315	344	369	387	406	417	432	442	453	464	466
S.D.		8	10	13	16	24	31	36	40	41	41	44	45	46	50	49
S.E.		3	3	4	5	8	10	11	13	13	13	14	14	15	16	15
n		10	10	10	10	10	10	10	10	10	10	10	10	10	10	10

Appendix 2 - 5 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual body weight
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 0 mg/kg Unit : g

Animal No.	Day	1	4	7	14	21	28	35	42	49	56	63	70	77	84	91
1101		160	176	177	213	236	250	270	284	285	301	307	318	323	332	329
1102		169	177	181	190	215	230	240	243	263	271	276	270	283	289	286
1103		167	167	182	203	217	227	247	245	261	267	271	270	280	281	276
1104		160	165	168	198	212	229	237	254	269	271	276	286	291	298	292
1105		170	183	191	211	242	262	278	287	302	311	319	317	323	330	328
1106		177	190	188	230	255	274	279	299	310	311	306	322	329	329	329
1107		178	182	183	217	235	255	259	281	276	295	293	312	309	321	329
1108		161	176	171	201	212	228	240	235	261	253	273	276	284	278	288
1109		160	172	175	183	208	228	238	242	259	264	271	268	280	287	284
1110		162	175	181	209	212	236	239	253	261	264	276	282	288	295	296
Mean		166	176	180	206	224	242	253	262	275	281	287	292	299	304	304
S.D.		7	7	7	14	16	17	17	23	18	21	18	22	20	22	22
S.E.		2	2	2	4	5	5	5	7	6	7	6	7	6	7	7
n		10	10	10	10	10	10	10	10	10	10	10	10	10	10	10

Appendix 2 - 6 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual body weight
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 100 mg/kg Unit : g

Animal No.	Day	1	4	7	14	21	28	35	42	49	56	63	70	77	84	91
2101		156	164	162	195	214	227	234	253	264	269	271	282	289	296	289
2102		156	161	171	179	207	210	225	225	247	248	246	257	256	263	266
2103		165	166	184	207	222	228	241	253	262	263	268	277	283	281	287
2104		171	180	203	250	262	275	278	300	314	312	318	338	348	345	341
2105		146	160	166	183	198	203	219	229	227	240	246	248	247	257	259
2106		153	169	172	198	206	232	238	246	257	268	275	280	291	294	297
2107		161	169	184	199	225	233	250	251	266	273	280	287	291	288	299
2108		183	194	198	227	249	262	261	282	293	293	291	303	309	314	305
2109		153	167	171	188	185	201	205	219	232	239	254	262	267	270	279
2110		166	173	183	204	228	250	256	276	281	289	301	299	309	315	325
Mean		161	170	179	203	220	232	241	253	264	269	275	283	289	292	295
S.D.		11	10	13	21	23	24	22	26	27	24	24	26	29	27	25
S.E.		3	3	4	7	7	8	7	8	8	7	7	8	9	9	8
n		10	10	10	10	10	10	10	10	10	10	10	10	10	10	10

Appendix 2 - 7 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual body weight
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 300 mg/kg Unit : g

Animal No.	Day	1	4	7	14	21	28	35	42	49	56	63	70	77	84	91
3101		162	173	178	213	234	248	255	271	287	290	297	308	319	327	321
3102		161	159	179	197	211	219	236	247	257	255	272	277	280	282	286
3103		160	174	180	200	217	220	238	249	247	266	278	284	284	302	307
3104		156	166	165	190	205	217	224	237	248	250	256	265	268	270	270
3105		157	162	172	188	212	218	233	243	247	262	258	264	272	275	266
3106		162	168	180	199	216	233	250	259	262	275	275	278	282	293	300
3107		152	151	169	189	206	211	225	237	243	240	251	258	256	257	262
3108		179	182	185	215	234	248	251	270	280	287	285	303	310	315	310
3109		156	159	164	195	214	233	234	249	263	268	269	278	288	294	292
3110		161	166	183	207	226	232	245	253	262	265	277	281	284	294	306
Mean		161	166	176	199	218	228	239	252	260	266	272	280	284	291	292
S.D.		7	9	7	10	11	13	11	12	15	16	14	16	19	21	20
S.E.		2	3	2	3	3	4	3	4	5	5	4	5	6	7	6
n		10	10	10	10	10	10	10	10	10	10	10	10	10	10	10

Appendix 2 - 8 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual body weight
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 1000 mg/kg Unit : g

Animal No.	Day	1	4	7	14	21	28	35	42	49	56	63	70	77	84	91
4101		165	173	185	206	222	237	245	249	252	251	265	272	276	271	276
4102		157	166	178	192	211	227	233	235	244	252	259	260	266	269	267
4103		156	166	179	198	219	231	235	239	251	258	258	259	272	280	274
4104		195	209	216	237	266	286	302	307	321	327	336	339	348	360	358
4105		152	154	161	184	194	207	214	220	225	228	226	234	235	240	234
4106		174	182	190	213	226	229	233	247	256	261	263	274	275	282	280
4107		168	174	182	208	222	231	245	252	255	269	272	275	275	284	284
4108		144	147	161	187	209	217	223	236	247	249	258	270	280	280	285
4109		150	159	169	190	201	214	223	227	227	241	242	243	251	259	256
4110		155	164	170	192	206	216	224	233	241	243	248	255	259	259	260
Mean		162	169	179	201	218	230	238	245	252	258	263	268	274	278	277
S.D.		15	17	16	16	20	22	25	24	27	27	29	28	30	32	32
S.E.		5	5	5	5	6	7	8	8	8	8	9	9	9	10	10
n		10	10	10	10	10	10	10	10	10	10	10	10	10	10	10

Appendix 3 - 1 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual food consumption
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 0 mg/kg Unit : g/animal/day

Animal No.	Day	1	7	14	21	28	35	42	49	56	63	70	77	84	91
1001		21	22	23	23	22	22	21	21	21	20	20	20	19	18
1002															
1003		21	21	22	21	20	19	20	19	19	19	19	19	19	18
1004															
1005		22	22	24	23	22	21	21	23	23	23	23	23	23	22
1006															
1007		21	22	21	21	20	21	20	20	20	19	20	19	19	19
1008															
1009		22	22	23	22	22	22	21	21	21	21	21	20	21	20
1010															
Mean		21	22	23	22	21	21	21	21	21	20	21	20	20	19
S.D.		1	0	1	1	1	1	1	1	1	2	2	2	2	2
S.E.		0	0	1	0	0	1	0	1	1	1	1	1	1	1
n		5	5	5	5	5	5	5	5	5	5	5	5	5	5

Appendix 3 - 2 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual food consumption
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 100 mg/kg Unit : g/animal/day

Animal No.	Day	1	7	14	21	28	35	42	49	56	63	70	77	84	91
2001		20	22	24	23	22	23	23	23	24	24	23	23	23	21
2002															
2003		21	23	23	22	21	21	22	22	21	20	21	20	20	20
2004															
2005		22	21	23	23	22	22	22	22	22	21	22	21	21	21
2006															
2007		20	21	23	23	22	21	21	21	21	21	21	21	21	20
2008															
2009		22	23	24	23	23	23	23	23	23	23	23	22	22	21
2010															
Mean		21	22	23	23	22	22	22	22	22	22	22	21	21	21
S.D.		1	1	1	0	1	1	1	1	1	2	1	1	1	1
S.E.		0	0	0	0	0	0	0	0	1	1	0	1	1	0
n		5	5	5	5	5	5	5	5	5	5	5	5	5	5

Appendix 3 - 3 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual food consumption
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 300 mg/kg Unit : g/animal/day

Animal No.	Day	1	7	14	21	28	35	42	49	56	63	70	77	84	91
3001		21	23	24	22	21	22	22	22	22	22	22	22	22	21
3002															
3003		21	21	23	21	20	20	19	19	19	18	18	18	19	18
3004															
3005		21	22	25	24	23	22	23	23	23	23	23	23	23	22
3006															
3007		21	21	22	21	20	20	20	21	21	20	20	20	20	19
3008															
3009		23	22	23	23	21	22	23	22	22	22	22	23	22	21
3010															
Mean		21	22	23	22	21	21	21	21	21	21	21	21	21	20
S.D.		1	1	1	1	1	1	2	2	2	2	2	2	2	2
S.E.		0	0	1	1	1	0	1	1	1	1	1	1	1	1
n		5	5	5	5	5	5	5	5	5	5	5	5	5	5

Appendix 3 - 4 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual food consumption
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 1000 mg/kg Unit : g/animal/day

Animal No.	Day	1	7	14	21	28	35	42	49	56	63	70	77	84	91
4001		21	18	22	21	21	21	22	22	22	22	22	22	22	20
4002															
4003		19	19	22	21	20	20	19	18	19	18	19	18	19	19
4004															
4005		21	21	22	20	20	20	21	21	20	20	20	19	18	20
4006															
4007		22	20	23	21	23	23	23	23	23	22	23	22	21	20
4008															
4009		22	19	24	23	23	23	23	22	22	22	22	22	23	22
4010															
Mean		21	19	23	21	21	21	22	21	21	21	21	21	21	20
S.D.		1	1	1	1	2	2	2	2	2	2	2	2	2	1
S.E.		1	1	0	0	1	1	1	1	1	1	1	1	1	0
n		5	5	5	5	5	5	5	5	5	5	5	5	5	5

Appendix 3 - 5 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual food consumption
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 0 mg/kg Unit : g/animal/day

Animal No.	Day	1	7	14	21	28	35	42	49	56	63	70	77	84	91
1101		18	14	15	16	16	15	15	16	16	14	15	15	14	13
1102															
1103		18	15	15	15	15	16	15	16	15	15	14	13	13	13
1104															
1105		19	17	18	19	20	20	20	18	17	16	16	15	15	14
1106															
1107		18	15	16	16	17	17	16	17	17	17	17	16	16	16
1108															
1109		17	14	15	15	15	15	15	15	14	14	14	14	14	13
1110															
Mean		18	15	16	16	17	17	16	16	16	15	15	15	14	14
S.D.		1	1	1	2	2	2	2	1	1	1	1	1	1	1
S.E.		0	1	1	1	1	1	1	1	1	1	1	1	1	1
n		5	5	5	5	5	5	5	5	5	5	5	5	5	5

Appendix 3 - 6 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual food consumption
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 100 mg/kg Unit : g/animal/day

Animal No.	Day	1	7	14	21	28	35	42	49	56	63	70	77	84	91
2101		16	13	14	15	15	15	15	15	14	14	14	14	14	13
2102															
2103		17	16	18	17	16	16	16	16	16	16	16	15	14	14
2104															
2105		12	13	14	14	14	14	13	14	14	14	13	14	13	14
2106															
2107		18	16	15	16	15	15	15	15	13	14	14	14	13	14
2108															
2109		17	15	15	14	15	14	15	16	15	16	15	15	15	15
2110															
Mean		16	15	15	15	15	15	15	15	14	15	14	14	14	14
S.D.		2	2	2	1	1	1	1	1	1	1	1	1	1	1
S.E.		1	1	1	1	0	0	0	0	1	0	1	0	0	0
n		5	5	5	5	5	5	5	5	5	5	5	5	5	5

Appendix 3 - 7 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual food consumption
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 300 mg/kg Unit : g/animal/day

Animal No.	Day	1	7	14	21	28	35	42	49	56	63	70	77	84	91
3101		17	15	15	15	16	16	15	15	15	15	15	15	15	15
3102															
3103		14	13	14	14	14	15	14	15	15	14	14	15	15	14
3104															
3105		16	14	14	16	16	16	16	16	17	15	15	16	16	14
3106															
3107		16	14	15	14	14	14	15	14	13	14	14	13	13	13
3108															
3109		17	14	15	15	15	15	15	15	15	15	13	15	15	14
3110															
Mean		16	14	15	15	15	15	15	15	15	15	14	15	15	14
S.D.		1	1	1	1	1	1	1	1	1	1	1	1	1	1
S.E.		1	0	0	0	0	0	0	1	0	0	0	0	0	0
n		5	5	5	5	5	5	5	5	5	5	5	5	5	5

Appendix 3 - 8 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual food consumption
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 1000 mg/kg Unit : g/animal/day

Animal No.	Day	1	7	14	21	28	35	42	49	56	63	70	77	84	91
4101		16	14	15	15	15	15	14	14	14	14	14	14	13	14
4102															
4103		18	15	18	18	17	17	17	17	16	16	16	16	16	14
4104															
4105		17	13	15	14	14	14	13	14	13	13	13	12	12	12
4106															
4107		14	12	16	15	15	15	15	15	15	15	16	15	15	14
4108															
4109		16	13	15	15	15	14	14	13	14	13	14	14	13	14
4110															
Mean		16	13	16	15	15	15	15	15	14	14	15	14	14	14
S.D.		1	1	1	2	1	1	2	2	1	1	1	1	2	1
S.E.		1	1	1	1	0	1	1	1	1	1	1	1	1	0
n		5	5	5	5	5	5	5	5	5	5	5	5	5	5

Appendix 4 - 1 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual ophthalmology (Week 13)

Dose (mg/kg) : 0

Sex	Animal No.	Ophthalmoscopy					
		Anterior portion		Transparent body		Fundus oculi	
		Right	Left	Right	Left	Right	Left
Male	1001	-	-	-	-	-	-
	1002	-	-	-	-	-	-
	1003	-	-	-	-	-	-
	1004	-	-	-	-	-	-
	1005	-	-	-	-	-	-

-: No abnormality

Appendix 4 - 2 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual ophthalmology (Week 13)

Dose (mg/kg) : 100

Sex	Animal No.	Ophthalmoscopy					
		Anterior portion		Transparent body		Fundus oculi	
		Right	Left	Right	Left	Right	Left
Male	2001	-	-	-	-	-	-
	2002	-	-	-	-	-	-
	2003	-	-	-	-	-	-
	2004	-	-	-	-	-	-
	2005	-	-	-	-	-	-

-: No abnormality

Appendix 4 - 3 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual ophthalmology (Week 13)

Dose (mg/kg) : 300

Sex	Animal No.	Ophthalmoscopy					
		Anterior portion		Transparent body		Fundus oculi	
		Right	Left	Right	Left	Right	Left
Male	3001	-	-	-	-	-	-
	3002	-	-	-	-	-	-
	3003	-	-	-	-	-	-
	3004	-	-	-	-	-	-
	3005	-	-	-	-	-	-

-: No abnormality

Appendix 4 - 4 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual ophthalmology (Week 13)

Dose (mg/kg) : 1000

Sex	Animal No.	Ophthalmoscopy					
		Anterior portion		Transparent body		Fundus oculi	
		Right	Left	Right	Left	Right	Left
Male	4001	-	-	-	-	-	-
	4002	-	-	-	-	-	-
	4003	-	-	-	-	-	-
	4004	-	-	-	-	-	-
	4005	-	-	-	-	-	-

- : No abnormality

Appendix 4 - 5 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual ophthalmology (Week 13)

Dose (mg/kg) : 0

Sex	Animal No.	Ophthalmoscopy					
		Anterior portion		Transparent body		Fundus oculi	
		Right	Left	Right	Left	Right	Left
Female	1101	-	-	-	-	-	-
	1102	-	-	-	-	-	-
	1103	-	-	-	-	-	-
	1104	-	-	-	-	-	A
	1105	-	-	-	-	-	-

- : No abnormality

A: Hyperreflectivity in fundus, focal

Appendix 4 - 6 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual ophthalmology (Week 13)

Dose (mg/kg) : 100

Sex	Animal No.	Ophthalmoscopy					
		Anterior portion		Transparent body		Fundus oculi	
		Right	Left	Right	Left	Right	Left
Female	2101	-	-	-	-	-	-
	2102	-	-	-	-	-	-
	2103	-	-	-	-	-	-
	2104	-	-	-	-	-	-
	2105	-	-	-	-	-	-

-: No abnormality

Appendix 4 - 7 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual ophthalmology (Week 13)

Dose (mg/kg) : 300

Sex	Animal No.	Ophthalmoscopy					
		Anterior portion		Transparent body		Fundus oculi	
		Right	Left	Right	Left	Right	Left
Female	3101	-	-	-	-	-	-
	3102	-	-	-	-	-	-
	3103	-	-	-	-	-	-
	3104	-	-	-	-	-	-
	3105	-	-	-	-	-	-

- : No abnormality

Appendix 4 - 8 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual ophthalmology (Week 13)

Dose (mg/kg) : 1000

Sex	Animal No.	Ophthalmoscopy					
		Anterior portion		Transparent body		Fundus oculi	
		Right	Left	Right	Left	Right	Left
Female	4101	-	-	-	-	-	-
	4102	-	-	-	-	-	-
	4103	-	-	-	-	-	-
	4104	-	-	-	-	-	-
	4105	-	-	-	-	-	-

-: No abnormality

Appendix 5 - 1 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual urinalysis Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 0 mg/kg

Animal No.	pH	Protein	Ketones	Glucose	Oc.Blood	Urobili.	Bilirubin	Color	RBC	WBC
1001	7.0	2 +	1 +	-	-	+/-	1 +	Y	-	-
1002	8.5	2 +	2 +	-	-	+/-	1 +	Y	-	-
1003	6.5	2 +	1 +	1 +	-	+/-	1 +	Y	-	-
1004	6.0	2 +	1 +	1 +	-	+/-	-	Y	-	-
1005	8.5	2 +	1 +	1 +	-	+/-	-	Y	-	-
1006	8.0	2 +	1 +	-	-	+/-	-	Y	-	-
1007	8.5	2 +	2 +	1 +	-	+/-	1 +	Y	-	-
1008	8.0	2 +	2 +	1 +	-	+/-	1 +	Y	-	-
1009	9.0 ^u	2 +	1 +	-	-	+/-	-	Y	-	-
1010	8.5	2 +	1 +	-	-	+/-	1 +	Y	-	-
Mean										
S.D.										
S.E.										
n	10	10	10	10	10	10	10	10	10	10

Protein) -:Negative, +/-:15, 1+:30, 2+:100, 3+:≥300 mg/dL
 Ketones) -:Negative, +/-:5, 1+:15, 2+:40, 3+:80 mg/dL
 Glucose) -:Negative, 1+:100, 2+:250, 3+:500, 4+:≥1000 mg/dL
 Oc.Blood) -:Negative, +/-:0.015, 1+:0.062, 2+:0.135, 3+:0.405 mg/dL
 Urobili.) +/-:0.1-1.0, 1+:2.0, 2+:4.0, 3+:≥8.0 Ehrlich U/dL
 Bilirubin) -:Negative, 1+:0.8, 2+:1.6, 3+:3.2 mg/dL
 Color) LY:Light yellow, Y:Yellow, DY:Dark yellow, Other:Other color
 RBC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe
 WBC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe
 Oc.Blood : Occult blood Urobili. : Urobilinogen

Appendix 5 - 2 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual urinalysis Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 0 mg/kg

Animal No.	Ep.SEC	Ep.SREC	Cast	Cr.PS	Cr.CO	Uri.Vol. mL/24h	Osmotic P. mOsm/kg	U-Na mmol/24h	U-K mmol/24h	U-Cl mmol/24h
1001	+/-	-	-	-	-	7.4	1830	1.2	2.4	2.0
1002	+/-	-	-	-	-	4.8	1946	0.9	1.9	1.5
1003	+/-	-	-	-	-	6.2	1692	1.3	1.9	1.5
1004	+/-	-	-	-	-	6.1	2074	1.1	2.5	1.7
1005	+/-	-	-	-	-	11.1	1474	1.1	3.2	2.1
1006	+/-	-	-	-	-	5.4	2236	1.3	2.2	1.7
1007	-	-	-	-	-	8.1	1760	1.1	2.7	1.7
1008	-	-	-	-	-	3.6	2462	0.8	1.7	1.2
1009	+/-	-	-	-	-	7.9	1588	0.9	2.2	1.7
1010	+/-	-	-	-	-	8.9	1550	1.2	2.6	1.8
Mean						7.0	1861	1.1	2.3	1.7
S.D.						2.2	319	0.2	0.4	0.3
S.E.						0.7	101	0.1	0.1	0.1
n	10	10	10	10	10	10	10	10	10	10

Ep.SEC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Ep.SREC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Cast) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Cr.PS) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Cr.CO) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Ep.SEC : Squamous epithelial cells Ep.SREC : Small round epithelial cells Cr.PS : Crystal phosphate salts
 Cr.CO : Crystal calcium oxalate Uri.Vol. : Urine volume Osmotic P. : Osmotic Pressure

Appendix 5 - 3 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual urinalysis Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 100 mg/kg

Animal No.	pH	Protein	Ketones	Glucose	Oc.Blood	Urobili.	Bilirubin	Color	RBC	WBC
2001	8.5	3 +	1 +	-	+/-	+/-	1 +	Y	-	-
2002	8.5	2 +	1 +	1 +	-	+/-	1 +	Y	-	-
2003	8.5	1 +	1 +	-	-	+/-	-	Y	-	-
2004	8.5	1 +	1 +	-	-	+/-	-	Y	-	-
2005	8.5	2 +	1 +	-	-	+/-	-	Y	-	-
2006	6.5	2 +	1 +	-	-	+/-	-	Y	-	-
2007	8.0	1 +	1 +	-	-	+/-	-	Y	-	-
2008	8.5	2 +	1 +	-	-	+/-	1 +	Y	-	-
2009	8.0	2 +	1 +	-	-	+/-	-	Y	-	-
2010	8.5	2 +	1 +	-	-	+/-	-	Y	-	-
Mean										
S.D.										
S.E.										
n	10	10	10	10	10	10	10	10	10	10

Protein) -:Negative, +/-:15, 1+:30, 2+:100, 3+:≥300 mg/dL
 Ketones) -:Negative, +/-:5, 1+:15, 2+:40, 3+:80 mg/dL
 Glucose) -:Negative, 1+:100, 2+:250, 3+:500, 4+:≥1000 mg/dL
 Oc.Blood) -:Negative, +/-:0.015, 1+:0.062, 2+:0.135, 3+:0.405 mg/dL
 Urobili.) +/-:0.1-1.0, 1+:2.0, 2+:4.0, 3+:≥8.0 Ehrlich U/dL
 Bilirubin) -:Negative, 1+:0.8, 2+:1.6, 3+:3.2 mg/dL
 Color) LY:Light yellow, Y:Yellow, DY:Dark yellow, Other:Other color
 RBC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe
 WBC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe
 Oc.Blood : Occult blood Urobili. : Urobilinogen

Appendix 5 - 4 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual urinalysis Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 100 mg/kg

Animal No.	Ep.SEC	Ep.SREC	Cast	Cr.PS	Cr.CO	Uri.Vol. mL/24h	Osmotic P. mOsm/kg	U-Na mmol/24h	U-K mmol/24h	U-Cl mmol/24h
2001	+/-	-	-	-	-	5.7	2472	1.2	2.4	2.0
2002	-	-	-	-	-	6.5	1730	0.9	1.9	1.5
2003	+/-	-	-	-	-	9.0	1728	1.1	2.8	1.9
2004	+/-	-	-	-	-	5.5	1744	0.8	1.8	1.3
2005	+/-	-	-	-	-	6.9	2046	1.3	2.5	2.0
2006	+/-	-	-	-	-	2.6	2022	0.3	0.8	0.5
2007	-	-	-	-	-	5.3	1684	0.7	1.6	1.0
2008	+/-	-	-	-	-	7.4	1876	1.1	2.6	1.8
2009	-	-	-	-	-	16.0	1026	1.3	3.0	2.0
2010	+/-	-	-	-	-	8.5	1756	1.4	2.7	2.1
Mean						7.3	1808	1.0	2.2	1.6
S.D.						3.5	364	0.3	0.7	0.5
S.E.						1.1	115	0.1	0.2	0.2
n	10	10	10	10	10	10	10	10	10	10

Ep.SEC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe
 Ep.SREC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe
 Cast) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe
 Cr.PS) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe
 Cr.CO) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe
 Ep.SEC : Squamous epithelial cells Ep.SREC : Small round epithelial cells Cr.PS : Crystal phosphate salts
 Cr.CO : Crystal calcium oxalate Uri.Vol. : Urine volume Osmotic P. : Osmotic Pressure

Appendix 5 - 5 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual urinalysis Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 300 mg/kg

Animal No.	pH	Protein	Ketones	Glucose	Oc.Blood	Urobili.	Bilirubin	Color	RBC	WBC
3001	7.0	+/-	1 +	-	-	+/-	-	Y	-	-
3002	7.0	2 +	1 +	-	-	+/-	1 +	Y	-	-
3003	6.5	1 +	+/-	-	-	+/-	-	Y	-	-
3004	9.0 ^{MI}	2 +	1 +	-	+/-	+/-	1 +	Y	-	-
3005	9.0 ^{MI}	2 +	+/-	-	-	+/-	-	Y	-	-
3006	8.5	2 +	1 +	-	-	+/-	-	Y	-	-
3007	6.0	+/-	-	-	-	+/-	-	Y	-	-
3008	7.0	2 +	1 +	-	-	+/-	1 +	Y	-	-
3009	5.0	1 +	+/-	-	-	+/-	-	Y	-	-
3010	8.5	3 +	2 +	-	-	+/-	2 +	Y	-	-
Mean										
S.D.										
S.E.										
n	10	10	10	10	10	10	10	10	10	10

Protein) -:Negative, +/-:15, 1+:30, 2+:100, 3+:≥300 mg/dL
 Ketones) -:Negative, +/-:5, 1+:15, 2+:40, 3+:80 mg/dL
 Glucose) -:Negative, 1+:100, 2+:250, 3+:500, 4+:≥1000 mg/dL
 Oc.Blood) -:Negative, +/-:0.015, 1+:0.062, 2+:0.135, 3+:0.405 mg/dL
 Urobili.) +/-:0.1-1.0, 1+:2.0, 2+:4.0, 3+:≥8.0 Ehrlich U/dL
 Bilirubin) -:Negative, 1+:0.8, 2+:1.6, 3+:3.2 mg/dL
 Color) LY:Light yellow, Y:Yellow, DY:Dark yellow, Other:Other color
 RBC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe
 WBC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe
 Oc.Blood : Occult blood Urobili. : Urobilinogen

Appendix 5 - 6 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Individual urinalysis Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 300 mg/kg

Animal No.	Ep.SEC	Ep.SREC	Cast	Cr.PS	Cr.CO	Uri.Vol. mL/24h	Osmotic P. mOsm/kg	U-Na mmol/24h	U-K mmol/24h	U-Cl mmol/24h
3001	+/-	-	-	-	-	8.5	1432	0.8	1.8	1.5
3002	-	-	-	-	-	11.9	1378	1.7	2.5	2.4
3003	+/-	-	-	-	-	6.0	1906	0.9	1.9	1.7
3004	+/-	-	-	-	-	6.2	1924	1.1	1.8	1.7
3005	+/-	-	-	-	-	12.2	1394	1.5	2.9	2.5
3006	+/-	-	-	-	-	8.0	1872	1.4	2.2	2.1
3007	+/-	-	-	-	-	10.3	1496	1.5	2.4	2.4
3008	-	-	-	-	-	5.3	1914	0.9	1.6	1.3
3009	+/-	-	-	-	-	7.1	2392	1.8	2.7	2.8
3010	+/-	-	-	-	-	7.0	2184	1.4	2.3	2.1
Mean						8.3	1789	1.3	2.2	2.1
S.D.						2.5	352	0.4	0.4	0.5
S.E.						0.8	111	0.1	0.1	0.2
n	10	10	10	10	10	10	10	10	10	10

Ep.SEC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Ep.SREC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Cast) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Cr.PS) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Cr.CO) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Ep.SEC : Squamous epithelial cells Ep.SREC : Small round epithelial cells Cr.PS : Crystal phosphate salts
 Cr.CO : Crystal calcium oxalate Uri.Vol. : Urine volume Osmotic P. : Osmotic Pressure

Appendix 5 - 7 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual urinalysis Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 1000 mg/kg

Animal No.	pH	Protein	Ketones	Glucose	Oc.Blood	Urobili.	Bilirubin	Color	RBC	WBC
4001	7.0	2 +	+/-	-	-	+/-	1 +	Y	-	-
4002	7.0	2 +	+/-	-	-	+/-	-	Y	-	-
4003	6.5	2 +	-	-	-	+/-	-	Y	-	-
4004	7.0	2 +	+/-	-	-	+/-	-	Y	-	-
4005	5.5	-	-	-	-	+/-	-	Y	-	-
4006	6.5	2 +	1 +	-	-	+/-	-	Y	-	-
4007	6.5	2 +	+/-	-	-	+/-	-	Y	-	-
4008	6.5	1 +	+/-	-	-	+/-	-	Y	-	-
4009	6.5	2 +	+/-	-	-	+/-	-	Y	-	-
4010	7.0	2 +	-	-	-	+/-	-	Y	-	-
Mean										
S.D.										
S.E.										
n	10	10	10	10	10	10	10	10	10	10

Protein) -:Negative, +/-:15, 1+:30, 2+:100, 3+:≥300 mg/dL
 Ketones) -:Negative, +/-:5, 1+:15, 2+:40, 3+:80 mg/dL
 Glucose) -:Negative, 1+:100, 2+:250, 3+:500, 4+:≥1000 mg/dL
 Oc.Blood) -:Negative, +/-:0.015, 1+:0.062, 2+:0.135, 3+:0.405 mg/dL
 Urobili.) +/-:0.1-1.0, 1+:2.0, 2+:4.0, 3+:≥8.0 Ehrlich U/dL
 Bilirubin) -:Negative, 1+:0.8, 2+:1.6, 3+:3.2 mg/dL
 Color) LY:Light yellow, Y:Yellow, DY:Dark yellow, Other:Other color
 RBC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe
 WBC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe
 Oc.Blood : Occult blood Urobili. : Urobilinogen

Appendix 5 - 8 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual urinalysis Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 1000 mg/kg

Animal No.	Ep.SEC	Ep.SREC	Cast	Cr.PS	Cr.CO	Uri.Vol. mL/24h	Osmotic P. mOsm/kg	U-Na mmol/24h	U-K mmol/24h	U-Cl mmol/24h
4001	-	-	-	-	-	9.1	1764	1.2	2.1	2.1
4002	-	-	-	-	-	18.5	1002	1.6	2.7	2.8
4003	+/-	-	-	-	-	9.5	1704	1.3	2.4	2.4
4004	+/-	-	-	1 +	-	11.1	1650	1.6	2.7	2.6
4005	+/-	-	-	-	-	35.8	574	1.8	3.5	2.8
4006	+/-	-	-	-	-	9.2	1842	1.3	2.3	2.2
4007	-	-	-	-	-	10.9	1558	1.2	2.3	2.6
4008	+/-	-	-	-	-	14.5	1358	1.1	3.1	2.7
4009	+/-	-	-	-	-	13.5	1382	1.4	2.7	2.6
4010	+/-	-	-	-	-	14.7	1356	1.8	3.1	2.9
Mean						14.7	1419	1.4	2.7	2.6
S.D.						8.0	387	0.3	0.4	0.3
S.E.						2.5	122	0.1	0.1	0.1
n	10	10	10	10	10	10	10	10	10	10

Ep.SEC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Ep.SREC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Cast) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Cr.PS) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Cr.CO) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Ep.SEC : Squamous epithelial cells Ep.SREC : Small round epithelial cells Cr.PS : Crystal phosphate salts
 Cr.CO : Crystal calcium oxalate Uri.Vol. : Urine volume Osmotic P. : Osmotic Pressure

Appendix 5 - 9 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual urinalysis Stage : Week 13
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 0 mg/kg

Animal No.	pH	Protein	Ketones	Glucose	Oc.Blood	Urobili.	Bilirubin	Color	RBC	WBC
1101	7.0	2 +	+/-	1 +	-	+/-	1 +	Y	-	-
1102	8.5	+/-	+/-	-	-	+/-	-	Y	-	-
1103	6.5	2 +	1 +	-	-	+/-	1 +	Y	-	-
1104	6.0	1 +	1 +	-	-	+/-	-	Y	-	-
1105	7.5	1 +	+/-	-	-	+/-	-	Y	-	-
1106	6.0	3 +	1 +	-	-	+/-	1 +	Y	-	-
1107	6.5	2 +	1 +	-	-	+/-	1 +	Y	-	-
1108	6.0	+/-	+/-	-	-	+/-	-	Y	-	-
1109	6.0	-	-	-	-	+/-	-	Y	-	-
1110	5.5	2 +	+/-	-	-	+/-	-	Y	-	-
Mean										
S.D.										
S.E.										
n	10	10	10	10	10	10	10	10	10	10

Protein) -:Negative, +/-:15, 1+:30, 2+:100, 3+:≥300 mg/dL
 Ketones) -:Negative, +/-:5, 1+:15, 2+:40, 3+:80 mg/dL
 Glucose) -:Negative, 1+:100, 2+:250, 3+:500, 4+:≥1000 mg/dL
 Oc.Blood) -:Negative, +/-:0.015, 1+:0.062, 2+:0.135, 3+:0.405 mg/dL
 Urobili.) +/-:0.1-1.0, 1+:2.0, 2+:4.0, 3+:≥8.0 Ehrlich U/dL
 Bilirubin) -:Negative, 1+:0.8, 2+:1.6, 3+:3.2 mg/dL
 Color) LY:Light yellow, Y:Yellow, DY:Dark yellow, Other:Other color
 RBC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe
 WBC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe
 Oc.Blood : Occult blood Urobili. : Urobilinogen

Appendix 5 - 10 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Individual urinalysis Stage : Week 13
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 0 mg/kg

Animal No.	Ep.SEC	Ep.SREC	Cast	Cr.PS	Cr.CO	Uri.Vol. mL/24h	Osmotic P. mOsm/kg	U-Na mmol/24h	U-K mmol/24h	U-Cl mmol/24h
1101	+/-	-	-	-	-	5.2	1976	0.8	1.9	1.3
1102	+/-	-	-	+/-	-	2.8	1956	0.4	1.0	0.7
1103	+/-	-	-	-	-	3.6	1660	0.6	1.0	0.8
1104	+/-	-	-	-	-	4.4	1658	0.6	1.5	1.1
1105	+/-	-	-	+/-	-	4.6	2340	0.8	2.0	1.4
1106	+/-	-	-	-	-	6.6	1786	0.9	2.2	1.6
1107	+/-	-	-	-	-	4.1	2350	0.7	1.7	1.2
1108	+/-	-	-	-	-	6.7	1856	1.1	2.3	1.7
1109	+/-	-	-	-	-	1.7	2920	0.3	0.9	0.6
1110	+/-	-	-	-	-	11.0	966	0.9	1.9	1.4
Mean						5.1	1947	0.7	1.6	1.2
S.D.						2.6	519	0.2	0.5	0.4
S.E.						0.8	164	0.1	0.2	0.1
n	10	10	10	10	10	10	10	10	10	10

Ep.SEC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Ep.SREC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Cast) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Cr.PS) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Cr.CO) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Ep.SEC : Squamous epithelial cells Ep.SREC : Small round epithelial cells Cr.PS : Crystal phosphate salts
 Cr.CO : Crystal calcium oxalate Uri.Vol. : Urine volume Osmotic P. : Osmotic Pressure

Appendix 5 - 11 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual urinalysis Stage : Week 13
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 100 mg/kg

Animal No.	pH	Protein	Ketones	Glucose	Oc.Blood	Urobili.	Bilirubin	Color	RBC	WBC
2101	6.0	-	-	-	-	+/-	-	Y	-	-
2102	6.0	-	-	-	-	+/-	-	Y	-	-
2103	6.0	-	+/-	-	-	+/-	-	Y	-	-
2104	8.5	1 +	+/-	-	-	+/-	1 +	Y	-	-
2105	6.0	+/-	+/-	-	-	+/-	-	Y	-	-
2106	7.5	+/-	-	-	-	+/-	-	Y	-	-
2107	6.0	+/-	-	-	-	+/-	-	Y	-	-
2108	6.0	+/-	+/-	-	-	+/-	-	Y	-	-
2109	5.5	+/-	-	-	-	+/-	-	Y	-	-
2110	5.5	+/-	-	-	-	+/-	-	Y	-	-
Mean										
S.D.										
S.E.										
n	10	10	10	10	10	10	10	10	10	10

Protein) -:Negative, +/-:15, 1+:30, 2+:100, 3+:≥300 mg/dL
 Ketones) -:Negative, +/-:5, 1+:15, 2+:40, 3+:80 mg/dL
 Glucose) -:Negative, 1+:100, 2+:250, 3+:500, 4+:≥1000 mg/dL
 Oc.Blood) -:Negative, +/-:0.015, 1+:0.062, 2+:0.135, 3+:0.405 mg/dL
 Urobili.) +/-:0.1-1.0, 1+:2.0, 2+:4.0, 3+:≥8.0 Ehrlich U/dL
 Bilirubin) -:Negative, 1+:0.8, 2+:1.6, 3+:3.2 mg/dL
 Color) LY:Light yellow, Y:Yellow, DY:Dark yellow, Other:Other color
 RBC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe
 WBC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe
 Oc.Blood : Occult blood Urobili. : Urobilinogen

Appendix 5 - 12 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Individual urinalysis Stage : Week 13
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 100 mg/kg

Animal No.	Ep.SEC	Ep.SREC	Cast	Cr.PS	Cr.CO	Uri.Vol. mL/24h	Osmotic P. mOsm/kg	U-Na mmol/24h	U-K mmol/24h	U-Cl mmol/24h
2101	+/-	-	-	-	-	1.8	2806	0.4	0.9	0.8
2102	+/-	-	-	-	-	5.4	1252	0.6	1.2	0.9
2103	+/-	-	-	-	-	11.3	1114	1.3	2.2	1.8
2104	+/-	-	-	-	-	8.8	1138	0.8	1.7	1.3
2105	+/-	-	-	-	-	6.5	1640	1.0	1.9	1.5
2106	+/-	-	-	-	-	7.1	1468	0.8	2.0	1.4
2107	+/-	-	-	-	-	4.1	2160	0.6	1.6	1.2
2108	+/-	-	-	-	-	5.0	1396	0.7	1.3	1.1
2109	+/-	-	-	-	-	5.4	1674	0.7	1.6	1.3
2110	+/-	-	-	-	-	9.2	1294	1.1	1.9	1.7
Mean						6.5	1594	0.8	1.6	1.3
S.D.						2.8	527	0.3	0.4	0.3
S.E.						0.9	167	0.1	0.1	0.1
n	10	10	10	10	10	10	10	10	10	10

Ep.SEC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Ep.SREC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Cast) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Cr.PS) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Cr.CO) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Ep.SEC : Squamous epithelial cells Ep.SREC : Small round epithelial cells Cr.PS : Crystal phosphate salts
 Cr.CO : Crystal calcium oxalate Uri.Vol. : Urine volume Osmotic P. : Osmotic Pressure

Appendix 5 - 13 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual urinalysis Stage : Week 13
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 300 mg/kg

Animal No.	pH	Protein	Ketones	Glucose	Oc.Blood	Urobili.	Bilirubin	Color	RBC	WBC
3101	8.5	1 +	+/-	-	-	+/-	1 +	Y	-	-
3102	6.5	2 +	+/-	-	-	+/-	-	Y	-	-
3103	6.5	2 +	+/-	-	-	+/-	-	Y	-	-
3104	6.5	2 +	+/-	-	-	+/-	-	Y	-	-
3105	7.0	-	-	-	-	+/-	-	Y	-	-
3106	7.0	-	-	-	-	+/-	-	Y	-	-
3107	7.5	-	-	-	-	+/-	-	Y	-	-
3108	6.5	2 +	1 +	-	-	+/-	-	Y	-	-
3109	8.0	-	-	-	-	+/-	-	Y	-	-
3110	7.0	-	-	-	-	+/-	-	Y	-	-
Mean										
S.D.										
S.E.										
n	10	10	10	10	10	10	10	10	10	10

Protein) -:Negative, +/-:15, 1+:30, 2+:100, 3+:≥300 mg/dL
 Ketones) -:Negative, +/-:5, 1+:15, 2+:40, 3+:80 mg/dL
 Glucose) -:Negative, 1+:100, 2+:250, 3+:500, 4+:≥1000 mg/dL
 Oc.Blood) -:Negative, +/-:0.015, 1+:0.062, 2+:0.135, 3+:0.405 mg/dL
 Urobili.) +/-:0.1-1.0, 1+:2.0, 2+:4.0, 3+:≥8.0 Ehrlich U/dL
 Bilirubin) -:Negative, 1+:0.8, 2+:1.6, 3+:3.2 mg/dL
 Color) LY:Light yellow, Y:Yellow, DY:Dark yellow, Other:Other color
 RBC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe
 WBC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe
 Oc.Blood : Occult blood Urobili. : Urobilinogen

Appendix 5 - 14 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Individual urinalysis Stage : Week 13
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 300 mg/kg

Animal No.	Ep.SEC	Ep.SREC	Cast	Cr.PS	Cr.CO	Uri.Vol. mL/24h	Osmotic P. mOsm/kg	U-Na mmol/24h	U-K mmol/24h	U-Cl mmol/24h
3101	+/-	-	-	-	3 +	22.4	680	1.3	2.7	2.1
3102	-	-	-	-	-	10.5	1466	1.4	2.6	2.2
3103	+/-	-	-	-	-	6.6	1318	0.9	1.3	1.2
3104	-	-	-	-	2 +	6.9	986	0.5	1.1	0.8
3105	+/-	-	-	-	3 +	5.6	1256	0.6	1.3	1.0
3106	+/-	-	-	-	-	15.9	1018	1.9	2.6	2.4
3107	+/-	-	-	-	-	4.9	1716	0.7	1.3	1.1
3108	+/-	-	-	-	-	5.2	1624	0.7	1.5	1.3
3109	+/-	-	-	-	-	6.9	1162	0.6	1.4	1.2
3110	+/-	-	-	-	-	11.1	1034	1.2	1.8	1.6
Mean						9.6	1226	1.0	1.8	1.5
S.D.						5.7	317	0.5	0.6	0.6
S.E.						1.8	100	0.1	0.2	0.2
n	10	10	10	10	10	10	10	10	10	10

Ep.SEC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Ep.SREC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Cast) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Cr.PS) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Cr.CO) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Ep.SEC : Squamous epithelial cells Ep.SREC : Small round epithelial cells Cr.PS : Crystal phosphate salts
 Cr.CO : Crystal calcium oxalate Uri.Vol. : Urine volume Osmotic P. : Osmotic Pressure

Appendix 5 - 15 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual urinalysis Stage : Week 13
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 1000 mg/kg

Animal No.	pH	Protein	Ketones	Glucose	Oc.Blood	Urobili.	Bilirubin	Color	RBC	WBC
4101	5.5	-	-	2 +	-	+/-	-	Y	-	-
4102	5.0	2 +	-	-	-	+/-	-	Y	-	-
4103	5.0	1 +	-	-	-	+/-	-	Y	-	-
4104	6.5	2 +	-	-	-	+/-	-	Y	-	-
4105	7.5	-	-	-	-	+/-	-	Y	-	-
4106	7.0	-	-	-	-	+/-	-	Y	-	-
4107	6.5	2 +	-	-	-	+/-	1 +	Y	-	-
4108	5.0	2 +	-	-	-	+/-	-	Y	-	-
4109	6.5	2 +	+/-	-	-	+/-	-	Y	-	-
4110	5.0	1 +	-	-	-	+/-	-	Y	-	-
Mean										
S.D.										
S.E.										
n	10	10	10	10	10	10	10	10	10	10

Protein) -:Negative, +/-:15, 1+:30, 2+:100, 3+:≥300 mg/dL
 Ketones) -:Negative, +/-:5, 1+:15, 2+:40, 3+:80 mg/dL
 Glucose) -:Negative, 1+:100, 2+:250, 3+:500, 4+:≥1000 mg/dL
 Oc.Blood) -:Negative, +/-:0.015, 1+:0.062, 2+:0.135, 3+:0.405 mg/dL
 Urobili.) +/-:0.1-1.0, 1+:2.0, 2+:4.0, 3+:≥8.0 Ehrlich U/dL
 Bilirubin) -:Negative, 1+:0.8, 2+:1.6, 3+:3.2 mg/dL
 Color) LY:Light yellow, Y:Yellow, DY:Dark yellow, Other:Other color
 RBC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe
 WBC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe
 Oc.Blood : Occult blood Urobili. : Urobilinogen

Appendix 5 - 16 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats

Item : Individual urinalysis Stage : Week 13
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 1000 mg/kg

Animal No.	Ep.SEC	Ep.SREC	Cast	Cr.PS	Cr.CO	Uri.Vol. mL/24h	Osmotic P. mOsm/kg	U-Na mmol/24h	U-K mmol/24h	U-Cl mmol/24h
4101	+/-	-	-	-	-	7.1	1642	1.2	1.8	1.5
4102	+/-	-	-	-	-	5.9	1686	1.0	1.5	1.5
4103	+/-	-	-	-	-	4.6	1640	0.5	1.1	0.8
4104	+/-	-	-	-	-	5.3	2154	1.0	1.5	1.6
4105	+/-	-	-	-	-	10.3	1218	1.2	1.7	1.9
4106	+/-	-	-	-	-	14.7	1224	2.0	2.9	2.7
4107	+/-	-	-	+/-	-	5.1	1804	0.8	1.3	1.2
4108	+/-	-	-	1+	-	8.0	1512	1.0	1.6	1.6
4109	+/-	-	-	-	-	6.7	1504	1.0	1.5	1.5
4110	+/-	-	-	-	-	7.9	1492	0.8	1.9	1.3
Mean						7.6	1588	1.1	1.7	1.6
S.D.						3.0	274	0.4	0.5	0.5
S.E.						1.0	87	0.1	0.2	0.2
n	10	10	10	10	10	10	10	10	10	10

Ep.SEC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Ep.SREC) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Cast) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Cr.PS) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Cr.CO) -:Negative, +/-:Slight, 1+:Mild, 2+:Moderate, 3+:Severe

Ep.SEC : Squamous epithelial cells Ep.SREC : Small round epithelial cells Cr.PS : Crystal phosphate salts
 Cr.CO : Crystal calcium oxalate Uri.Vol. : Urine volume Osmotic P. : Osmotic Pressure

Appendix 6 - 1 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual hematology Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 0 mg/kg

Animal No.	RBC 10E4/ μ L	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic 10E9/L	PLT 10E4/ μ L	WBC 10E2/ μ L	LYMP 10E2/ μ L
1001	836	15.0	42.5	50.9	17.9	35.2	108.4	92.0	93.2	72.4
1002	824	14.8	42.8	52.0	17.9	34.5	113.6	91.6	76.6	55.6
1003	836	14.9	42.1	50.3	17.8	35.4	106.1	85.1	107.2	82.9
1004	758	13.8	40.0	52.7	18.2	34.4	142.4	88.3	75.9	62.4
1005	827	15.2	44.6	53.9	18.4	34.1	153.7	90.9	84.1	61.7
1006	835	14.7	43.1	51.6	17.7	34.2	118.0	71.8	73.7	54.9
1007	886	14.7	43.3	48.9	16.6	34.0	147.6	93.6	100.4	69.4
1008	815	14.3	41.7	51.1	17.6	34.4	178.6	81.3	63.8	41.9
1009	802	14.3	41.0	51.2	17.9	34.9	125.5	98.2	103.0	87.1
1010	805	15.1	42.7	53.1	18.7	35.2	140.8	80.9	63.5	49.3
Mean	822	14.7	42.4	51.6	17.9	34.6	133.5	87.4	84.1	63.8
S.D.	33	0.4	1.3	1.4	0.6	0.5	23.2	7.7	16.0	14.4
S.E.	10	0.1	0.4	0.5	0.2	0.2	7.3	2.4	5.1	4.5
n	10	10	10	10	10	10	10	10	10	10

Retic : Reticulocyte

Appendix 6 - 2 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual hematology Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 0 mg/kg

Animal No.	NEUT 10E2/ μ L	EOS 10E2/ μ L	BASO 10E2/ μ L	MONO 10E2/ μ L	LUC 10E2/ μ L
1001	17.4	0.7	0.6	1.8	0.3
1002	17.5	0.9	0.2	2.2	0.2
1003	20.2	0.9	0.5	2.3	0.5
1004	11.1	0.7	0.3	1.2	0.3
1005	17.6	1.3	0.4	2.5	0.5
1006	16.1	0.8	0.2	1.5	0.2
1007	27.2	1.0	0.2	2.3	0.3
1008	18.1	1.1	0.2	1.9	0.4
1009	11.4	0.8	0.6	2.4	0.7
1010	11.3	0.8	0.2	1.7	0.2
Mean	16.8	0.9	0.3	2.0	0.4
S.D.	4.9	0.2	0.2	0.4	0.2
S.E.	1.5	0.1	0.1	0.1	0.1
n	10	10	10	10	10

LUC : Large unstained cells

Appendix 6 - 3 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual hematology Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 0 mg/kg

Animal No.	PT s	APTT s	FIB mg/dL
1001	11.4	10.7	346
1002	12.6	13.1	266
1003	12.7	11.5	276
1004	11.8	11.3	308
1005	13.3	15.1	290
1006	12.7	11.4	285
1007	12.7	12.9	365
1008	14.3	13.5	301
1009	13.0	13.5	331
1010	14.9	16.9	305
Mean	12.9	13.0	307
S.D.	1.0	1.9	31
S.E.	0.3	0.6	10
n	10	10	10

Appendix 6 - 4 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual hematology Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 100 mg/kg

Animal No.	RBC 10E4/ μ L	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic 10E9/L	PLT 10E4/ μ L	WBC 10E2/ μ L	LYMP 10E2/ μ L
2001	793	13.7	40.5	51.0	17.3	33.9	127.0	80.7	115.1	95.0
2002	848	15.1	44.5	52.5	17.8	34.0	139.5	87.3	92.3	77.1
2003	824	15.5	45.1	54.8	18.8	34.4	94.6	82.0	90.6	71.8
2004	770	14.7	42.1	54.7	19.2	35.0	116.4	81.3	91.8	66.6
2005	819	14.4	42.8	52.3	17.6	33.6	163.5	89.1	72.9	47.2
2006	826	15.1	43.2	52.4	18.2	34.8	111.4	81.9	43.5	31.2
2007	808	15.4	43.8	54.3	19.0	35.1	113.9	78.1	94.1	73.7
2008	794	14.9	42.7	53.8	18.8	35.0	136.7	77.8	108.4	82.0
2009	779	14.7	41.2	52.9	18.9	35.6	141.3	88.0	113.7	92.0
2010	881	15.3	43.8	49.7	17.4	34.9	115.5	91.4	102.0	73.3
Mean	814	14.9	43.0	52.8	18.3	34.6	126.0	83.8	92.4	71.0
S.D.	33	0.5	1.4	1.6	0.7	0.6	19.7	4.8	21.3	19.3
S.E.	11	0.2	0.5	0.5	0.2	0.2	6.2	1.5	6.7	6.1
n	10	10	10	10	10	10	10	10	10	10

Retic : Reticulocyte

Appendix 6 - 5 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual hematology Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 100 mg/kg

Animal No.	NEUT 10E2/ μ L	EOS 10E2/ μ L	BASO 10E2/ μ L	MONO 10E2/ μ L	LUC 10E2/ μ L
2001	15.6	0.8	0.4	2.7	0.7
2002	11.9	0.8	0.5	1.8	0.2
2003	15.1	0.5	0.4	2.5	0.2
2004	20.7	0.8	0.3	3.2	0.3
2005	20.4	1.3	0.3	3.1	0.6
2006	9.8	0.7	0.2	1.5	0.2
2007	16.2	1.1	0.5	2.2	0.3
2008	19.8	1.4	0.5	4.0	0.7
2009	15.1	0.7	0.6	4.4	0.9
2010	21.5	1.5	0.6	4.5	0.5
Mean	16.6	1.0	0.4	3.0	0.5
S.D.	3.9	0.3	0.1	1.1	0.3
S.E.	1.2	0.1	0.0	0.3	0.1
n	10	10	10	10	10

LUC : Large unstained cells

Appendix 6 - 6 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual hematology Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 100 mg/kg

Animal No.	PT s	APTT s	FIB mg/dL
2001	10.5	11.9	289
2002	13.5	16.2	315
2003	13.1	11.4	278
2004	11.6	11.9	275
2005	12.2	11.3	305
2006	12.5	12.9	315
2007	12.5	11.8	286
2008	14.5	16.0	295
2009	12.7	11.4	300
2010	14.5	18.7	321
Mean	12.8	13.4	298
S.D.	1.2	2.6	16
S.E.	0.4	0.8	5
n	10	10	10

Appendix 6 - 7 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual hematology Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 300 mg/kg

Animal No.	RBC 10E4/ μ L	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic 10E9/L	PLT 10E4/ μ L	WBC 10E2/ μ L	LYMP 10E2/ μ L
3001	793	15.1	42.2	53.3	19.1	35.8	107.2	82.9	110.9	95.5
3002	841	15.8	46.4	55.1	18.8	34.1	132.8	96.6	104.4	82.3
3003	841	14.7	44.2	52.6	17.5	33.2	117.9	82.5	91.3	73.8
3004	804	14.8	42.7	53.1	18.4	34.6	126.2	90.8	71.0	58.3
3005	805	14.8	43.3	53.8	18.4	34.2	102.0	96.5	86.3	70.9
3006	790	14.7	42.4	53.7	18.7	34.8	127.8	84.8	117.1	82.0
3007	809	14.4	41.7	51.5	17.8	34.6	127.2	81.5	113.1	90.6
3008	838	15.0	43.0	51.4	17.9	34.9	136.4	95.6	85.2	66.7
3009	815	14.6	42.2	51.8	17.9	34.6	125.3	83.3	74.0	59.2
3010	841	14.6	42.2	50.2	17.4	34.6	89.0	92.5	84.8	73.0
Mean	818	14.9	43.0	52.7	18.2	34.5	119.2	88.7	93.8	75.2
S.D.	21	0.4	1.4	1.4	0.6	0.7	15.1	6.3	16.5	12.4
S.E.	7	0.1	0.4	0.5	0.2	0.2	4.8	2.0	5.2	3.9
n	10	10	10	10	10	10	10	10	10	10

Retic : Reticulocyte

Appendix 6 - 8 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual hematology Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 300 mg/kg

Animal No.	NEUT 10E2/ μ L	EOS 10E2/ μ L	BASO 10E2/ μ L	MONO 10E2/ μ L	LUC 10E2/ μ L
3001	11.1	1.0	0.4	2.2	0.7
3002	18.3	1.2	0.4	1.8	0.3
3003	12.4	0.8	0.4	3.5	0.5
3004	9.8	0.6	0.2	2.0	0.1
3005	9.8	1.0	0.3	3.6	0.6
3006	26.8	1.5	0.6	5.4	0.9
3007	14.6	1.2	0.4	5.7	0.6
3008	14.2	1.7	0.2	2.1	0.3
3009	11.7	0.4	0.3	2.2	0.2
3010	8.3	1.0	0.5	1.6	0.4
Mean	13.7	1.0	0.4	3.0	0.5
S.D.	5.4	0.4	0.1	1.5	0.2
S.E.	1.7	0.1	0.0	0.5	0.1
n	10	10	10	10	10

LUC : Large unstained cells

Appendix 6 - 9 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual hematology Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 300 mg/kg

Animal No.	PT s	APTT s	FIB mg/dL
3001	12.8	12.2	273
3002	13.4	13.8	282
3003	14.2	16.2	252
3004	12.7	11.5	260
3005	12.4	11.0	299
3006	14.7	14.9	297
3007	12.5	12.2	308
3008	13.2	13.5	314
3009	12.6	12.6	327
3010	16.0	16.2	288
Mean	13.5	13.4	290
S.D.	1.2	1.9	24
S.E.	0.4	0.6	8
n	10	10	10

Appendix 6 - 10 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual hematology Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 1000 mg/kg

Animal No.	RBC 10E4/ μ L	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic 10E9/L	PLT 10E4/ μ L	WBC 10E2/ μ L	LYMP 10E2/ μ L
4001	821	14.7	43.9	53.5	17.9	33.4	158.6	100.8	119.5	101.5
4002	871	15.0	44.0	50.5	17.2	34.0	122.5	118.7	139.7	109.3
4003	849	14.7	43.5	51.2	17.3	33.7	96.0	95.8	96.1	65.2
4004	860	15.6	44.8	52.1	18.2	34.8	123.2	88.2	64.4	49.1
4005	813	14.6	42.0	51.7	18.0	34.8	126.9	68.4	46.6	35.7
4006	779	14.5	42.7	54.9	18.6	34.0	184.5	96.5	55.4	39.7
4007	818	14.5	42.2	51.6	17.7	34.3	112.5	101.8	70.5	56.7
4008	779	13.8	40.3	51.6	17.7	34.3	117.7	88.1	84.3	65.5
4009	832	14.8	42.6	51.2	17.7	34.6	105.2	101.3	106.1	69.4
4010	762	15.1	42.4	55.7	19.8	35.6	156.3	98.9	151.2	122.3
Mean	818	14.7	42.8	52.4	18.0	34.4	130.3	95.9	93.4	71.4
S.D.	36	0.5	1.3	1.7	0.7	0.6	27.5	12.9	35.6	29.8
S.E.	12	0.1	0.4	0.5	0.2	0.2	8.7	4.1	11.3	9.4
n	10	10	10	10	10	10	10	10	10	10

Retic : Reticulocyte

Appendix 6 - 11 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual hematology Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 1000 mg/kg

Animal No.	NEUT 10E2/ μ L	EOS 10E2/ μ L	BASO 10E2/ μ L	MONO 10E2/ μ L	LUC 10E2/ μ L
4001	12.7	1.3	0.6	2.7	0.7
4002	24.1	0.9	0.6	3.9	0.9
4003	24.7	0.9	0.2	4.3	0.7
4004	12.0	0.2	0.3	2.5	0.2
4005	7.9	0.7	0.2	1.8	0.2
4006	12.3	0.9	0.2	2.1	0.2
4007	10.6	0.7	0.3	1.8	0.4
4008	12.9	1.3	0.3	3.7	0.6
4009	30.2	2.8	0.6	2.6	0.6
4010	18.7	1.6	0.8	5.2	2.6
Mean	16.6	1.1	0.4	3.1	0.7
S.D.	7.4	0.7	0.2	1.2	0.7
S.E.	2.3	0.2	0.1	0.4	0.2
n	10	10	10	10	10

LUC : Large unstained cells

Appendix 6 - 12 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual hematology Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 1000 mg/kg

Animal No.	PT s	APTT s	FIB mg/dL
4001	12.3	13.2	326
4002	11.0	11.3	305
4003	14.9	18.3	287
4004	11.5	10.2	344
4005	13.8	15.6	266
4006	13.5	11.5	307
4007	12.5	11.4	326
4008	12.2	11.3	264
4009	12.0	10.8	298
4010	13.7	12.5	316
Mean	12.7	12.6	304
S.D.	1.2	2.5	26
S.E.	0.4	0.8	8
n	10	10	10

Appendix 6 - 13 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual hematology Stage : Week 13
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 0 mg/kg

Animal No.	RBC 10E4/ μ L	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic 10E9/L	PLT 10E4/ μ L	WBC 10E2/ μ L	LYMP 10E2/ μ L
1101	730	13.9	39.3	53.9	19.0	35.3	94.9	100.9	55.3	46.5
1102	793	14.1	40.7	51.3	17.8	34.7	72.9	91.4	72.2	60.5
1103	765	14.7	41.3	54.0	19.2	35.6	109.5	89.3	49.7	38.5
1104	727	14.2	40.4	55.6	19.5	35.1	118.6	104.1	37.1	24.6
1105	784	14.4	41.2	52.6	18.4	35.0	127.8	94.5	86.5	69.6
1106	763	14.1	40.3	52.8	18.5	35.0	94.6	97.4	63.9	52.2
1107	748	14.1	40.6	54.3	18.9	34.8	161.5	92.5	72.1	59.8
1108	768	14.4	40.5	52.8	18.8	35.6	94.1	90.0	40.8	28.4
1109	774	15.0	43.5	56.2	19.4	34.6	128.1	99.8	70.7	57.8
1110	790	14.0	40.8	51.7	17.7	34.2	102.7	86.7	51.5	36.3
Mean	764	14.3	40.9	53.5	18.7	35.0	110.5	94.7	60.0	47.4
S.D.	23	0.3	1.1	1.6	0.6	0.4	24.8	5.7	15.7	15.0
S.E.	7	0.1	0.3	0.5	0.2	0.1	7.8	1.8	5.0	4.8
n	10	10	10	10	10	10	10	10	10	10

Retic : Reticulocyte

Appendix 6 - 14 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual hematology Stage : Week 13
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 0 mg/kg

Animal No.	NEUT 10E2/ μ L	EOS 10E2/ μ L	BASO 10E2/ μ L	MONO 10E2/ μ L	LUC 10E2/ μ L
1101	6.3	0.4	0.3	1.5	0.3
1102	8.0	1.6	0.3	1.6	0.3
1103	8.4	0.5	0.2	1.9	0.2
1104	9.9	1.3	0.1	1.1	0.1
1105	10.7	1.0	0.5	4.0	0.7
1106	8.8	1.0	0.4	1.1	0.4
1107	8.6	0.6	0.4	1.9	0.7
1108	10.0	1.1	0.2	0.9	0.2
1109	9.6	0.8	0.5	1.8	0.3
1110	12.0	0.9	0.2	1.7	0.4
Mean	9.2	0.9	0.3	1.8	0.4
S.D.	1.6	0.4	0.1	0.9	0.2
S.E.	0.5	0.1	0.0	0.3	0.1
n	10	10	10	10	10

LUC : Large unstained cells

Appendix 6 - 15 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual hematology Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 0 mg/kg

Animal No.	PT s	APTT s	FIB mg/dL
1101	10.0	9.3	199
1102	11.5	8.5	210
1103	12.4	11.0	203
1104	11.7	10.4	220
1105	11.9	11.1	222
1106	14.7	15.5	204
1107	12.3	10.9	209
1108	14.2	12.6	202
1109	13.5	9.4	224
1110	13.2	9.7	209
Mean	12.5	10.8	210
S.D.	1.4	2.0	9
S.E.	0.4	0.6	3
n	10	10	10

Appendix 6 - 16 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual hematology Stage : Week 13
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 100 mg/kg

Animal No.	RBC 10E4/ μ L	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic 10E9/L	PLT 10E4/ μ L	WBC 10E2/ μ L	LYMP 10E2/ μ L
2101	773	15.1	43.3	56.1	19.5	34.7	126.0	88.2	66.4	49.7
2102	800	14.7	42.1	52.6	18.3	34.8	114.7	100.4	42.7	33.8
2103	740	14.7	40.9	55.3	19.8	35.8	161.2	102.1	52.7	38.5
2104	762	15.5	44.0	57.7	20.4	35.3	108.2	100.5	59.5	46.9
2105	743	13.7	39.1	52.7	18.4	35.0	133.4	78.6	48.3	35.8
2106	735	14.1	40.0	54.5	19.1	35.1	108.8	93.6	52.7	35.0
2107	797	14.9	43.1	54.1	18.7	34.6	161.8	80.4	43.2	34.1
2108	823	14.8	42.1	51.2	17.9	35.1	95.6	85.0	48.5	40.2
2109	769	14.4	41.1	53.4	18.7	35.1	132.5	86.2	58.8	45.8
2110	757	14.6	41.3	54.6	19.3	35.4	132.0	103.5	51.0	40.5
Mean	770	14.7	41.7	54.2	19.0	35.1	127.4	91.9	52.4	40.0
S.D.	29	0.5	1.5	1.9	0.8	0.4	21.9	9.4	7.5	5.7
S.E.	9	0.2	0.5	0.6	0.2	0.1	6.9	3.0	2.4	1.8
n	10	10	10	10	10	10	10	10	10	10

Retic : Reticulocyte

Appendix 6 - 17 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual hematology Stage : Week 13
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 100 mg/kg

Animal No.	NEUT 10E2/ μ L	EOS 10E2/ μ L	BASO 10E2/ μ L	MONO 10E2/ μ L	LUC 10E2/ μ L
2101	10.9	1.6	0.3	3.3	0.5
2102	6.7	0.4	0.3	1.4	0.2
2103	12.0	0.7	0.3	1.0	0.2
2104	8.9	1.0	0.4	1.7	0.6
2105	10.7	0.5	0.3	0.9	0.1
2106	15.5	0.7	0.2	1.1	0.3
2107	5.9	0.8	0.3	1.7	0.3
2108	6.2	0.5	0.2	1.1	0.2
2109	9.0	1.1	0.3	1.8	0.8
2110	8.8	0.4	0.3	0.9	0.2
Mean	9.5	0.8	0.3	1.5	0.3
S.D.	3.0	0.4	0.1	0.7	0.2
S.E.	0.9	0.1	0.0	0.2	0.1
n	10	10	10	10	10

LUC : Large unstained cells

Appendix 6 - 18 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual hematology Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 100 mg/kg

Animal No.	PT s	APTT s	FIB mg/dL
2101	9.9	8.6	224
2102	13.9	9.4	213
2103	12.1	9.7	211
2104	13.4	14.0	205
2105	11.0	9.8	232
2106	12.7	11.2	228
2107	12.4	12.7	214
2108	11.9	9.2	239
2109	13.5	13.3	228
2110	11.7	8.5	211
Mean	12.3	10.6	221
S.D.	1.2	2.0	11
S.E.	0.4	0.6	4
n	10	10	10

Appendix 6 - 19 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual hematology Stage : Week 13
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 300 mg/kg

Animal No.	RBC 10E4/ μ L	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic 10E9/L	PLT 10E4/ μ L	WBC 10E2/ μ L	LYMP 10E2/ μ L
3101	761	14.1	40.1	52.7	18.5	35.1	143.0	93.7	65.8	51.9
3102	729	13.9	39.4	54.0	19.0	35.2	125.3	118.8	62.3	50.6
3103	768	14.6	41.8	54.4	19.0	34.9	153.2	104.1	70.5	52.3
3104	758	14.3	40.3	53.2	18.9	35.5	138.1	97.0	59.3	39.6
3105	748	14.6	40.9	54.7	19.5	35.7	94.4	87.9	61.1	48.6
3106	728	14.8	41.1	56.5	20.3	35.9	149.7	86.5	44.6	37.4
3107	740	14.3	41.1	55.5	19.3	34.8	159.5	86.9	40.3	30.6
3108	777	15.1	43.4	55.9	19.4	34.7	114.0	88.1	72.9	48.0
3109	860	15.8	44.4	51.6	18.3	35.5	124.1	105.2	87.2	69.6
3110	728	14.3	40.5	55.7	19.6	35.3	167.7	112.6	70.2	56.6
Mean	760	14.6	41.3	54.4	19.2	35.3	136.9	98.1	63.4	48.5
S.D.	39	0.6	1.5	1.6	0.6	0.4	22.5	11.6	13.6	10.9
S.E.	12	0.2	0.5	0.5	0.2	0.1	7.1	3.7	4.3	3.4
n	10	10	10	10	10	10	10	10	10	10

Retic : Reticulocyte

Appendix 6 - 20 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual hematology Stage : Week 13
Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 300 mg/kg

Animal No.	NEUT 10E2/ μ L	EOS 10E2/ μ L	BASO 10E2/ μ L	MONO 10E2/ μ L	LUC 10E2/ μ L
3101	9.8	1.2	0.3	2.1	0.4
3102	8.9	0.6	0.4	1.4	0.4
3103	14.6	0.9	0.5	1.8	0.4
3104	15.9	0.9	0.4	2.1	0.4
3105	8.3	0.6	0.5	2.6	0.5
3106	5.2	0.3	0.3	1.0	0.3
3107	7.2	0.7	0.1	1.4	0.3
3108	21.1	1.1	0.4	1.8	0.5
3109	12.7	1.0	0.5	2.7	0.8
3110	10.2	0.7	0.5	1.7	0.6
Mean	11.4	0.8	0.4	1.9	0.5
S.D.	4.7	0.3	0.1	0.5	0.2
S.E.	1.5	0.1	0.0	0.2	0.0
n	10	10	10	10	10

LUC : Large unstained cells

Appendix 6 - 21 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual hematology Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 300 mg/kg

Animal No.	PT s	APTT s	FIB mg/dL
3101	12.7	12.7	204
3102	11.7	11.3	217
3103	13.6	12.6	221
3104	10.4	9.9	198
3105	12.9	11.6	220
3106	12.5	11.0	196
3107	12.4	12.1	203
3108	11.3	10.9	224
3109	12.0	9.4	224
3110	11.8	10.8	244
Mean	12.1	11.2	215
S.D.	0.9	1.1	15
S.E.	0.3	0.3	5
n	10	10	10

Appendix 6 - 22 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual hematology Stage : Week 13
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 1000 mg/kg

Animal No.	RBC 10E4/ μ L	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic 10E9/L	PLT 10E4/ μ L	WBC 10E2/ μ L	LYMP 10E2/ μ L
4101	747	14.5	41.9	56.1	19.4	34.5	108.4	97.7	69.1	57.8
4102	694	14.1	40.7	58.7	20.3	34.6	123.8	105.3	62.1	54.2
4103	710	13.4	38.5	54.2	18.9	34.9	110.0	121.6	68.8	47.3
4104	771	14.5	41.7	54.1	18.8	34.8	117.0	98.3	63.5	46.7
4105	804	14.5	42.2	52.4	18.0	34.4	93.6	87.3	51.6	42.3
4106	787	14.8	42.6	54.1	18.8	34.7	90.0	125.8	63.5	53.8
4107	760	14.8	43.5	57.2	19.5	34.0	207.7	96.1	43.7	31.4
4108	784	14.4	42.2	53.8	18.3	34.0	164.7	89.7	81.3	63.9
4109	769	15.0	42.3	55.0	19.5	35.4	123.4	101.6	55.6	44.0
4110	768	14.5	41.8	54.5	19.0	34.8	170.4	99.3	73.2	55.6
Mean	759	14.5	41.7	55.0	19.1	34.6	130.9	102.3	63.2	49.7
S.D.	34	0.4	1.3	1.8	0.7	0.4	37.9	12.5	10.9	9.3
S.E.	11	0.1	0.4	0.6	0.2	0.1	12.0	3.9	3.4	2.9
n	10	10	10	10	10	10	10	10	10	10

Retic : Reticulocyte

Appendix 6 - 23 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual hematology Stage : Week 13
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 1000 mg/kg

Animal No.	NEUT 10E2/ μ L	EOS 10E2/ μ L	BASO 10E2/ μ L	MONO 10E2/ μ L	LUC 10E2/ μ L
4101	8.0	0.9	0.2	1.5	0.8
4102	4.2	0.6	0.3	2.3	0.4
4103	17.3	0.7	0.2	3.0	0.3
4104	14.1	0.7	0.3	1.6	0.2
4105	6.8	1.0	0.4	1.0	0.1
4106	6.6	0.7	0.3	1.8	0.3
4107	10.0	0.5	0.2	1.2	0.3
4108	12.6	0.9	0.4	2.8	0.7
4109	8.7	0.8	0.4	1.1	0.5
4110	14.0	1.4	0.4	1.5	0.5
Mean	10.2	0.8	0.3	1.8	0.4
S.D.	4.1	0.3	0.1	0.7	0.2
S.E.	1.3	0.1	0.0	0.2	0.1
n	10	10	10	10	10

LUC : Large unstained cells

Appendix 6 -24 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual hematology Stage : Week 13
Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 1000 mg/kg

Animal No.	PT s	APTT s	FIB mg/dL
4101	11.6	11.2	219
4102	11.8	13.2	188
4103	12.5	12.3	366
4104	11.8	12.2	216
4105	10.9	8.7	199
4106	12.6	11.5	237
4107	10.1	7.6	233
4108	12.9	11.2	252
4109	11.3	8.7	201
4110	12.9	12.6	245
Mean	11.8	10.9	236
S.D.	0.9	1.9	50
S.E.	0.3	0.6	16
n	10	10	10

Appendix 7 - 1 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual blood chemistry Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 0 mg/kg

Animal No.	AST IU/L	ALT IU/L	LDH IU/L	ALP IU/L	r-GTP IU/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
1001	62	55	67	757	0	61	18	98	0.1	142
1002	55	38	40	434	0	75	43	114	0.1	126
1003	51	44	94	357	0	58	27	94	0.1	137
1004	64	46	62	522	0	72	46	106	0.1	178
1005	60	33	70	372	0	79	100	127	0.1	149
1006	50	41	38	336	0	49	36	79	0.1	171
1007	59	38	41	339	0	77	42	111	0.1	148
1008	60	46	62	321	0	78	55	114	0.1	164
1009	57	40	77	365	0	93	70	130	0.1	222
1010	49	30	40	307	0	80	29	113	0.1	151
Mean	57	41	59	411	0	72	47	109	0.1	159
S.D.	5	7	19	137	0	13	24	15	0.0	27
S.E.	2	2	6	43	0	4	8	5	0.0	9
n	10	10	10	10	10	10	10	10	10	10

Appendix 7 - 2 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual blood chemistry Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 0 mg/kg

Animal No.	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
1001	18	0.30	141	3.8	105	10.2	5.3	6.4	2.7	0.7
1002	14	0.31	144	4.0	106	10.3	5.7	6.7	2.8	0.7
1003	19	0.34	143	3.9	107	10.3	4.6	6.3	2.7	0.8
1004	16	0.31	145	4.0	107	10.0	4.7	5.9	2.5	0.7
1005	15	0.33	146	4.1	107	10.4	5.2	6.4	2.7	0.7
1006	12	0.24	144	3.9	107	9.9	5.0	6.3	2.6	0.7
1007	16	0.35	144	3.7	106	10.2	5.4	6.6	2.7	0.7
1008	19	0.32	141	4.2	106	10.3	4.5	6.5	2.8	0.8
1009	17	0.29	142	3.8	102	10.3	5.6	5.9	2.6	0.8
1010	16	0.35	146	4.2	107	10.0	5.4	6.2	2.6	0.7
Mean	16	0.31	144	4.0	106	10.2	5.1	6.3	2.7	0.7
S.D.	2	0.03	2	0.2	2	0.2	0.4	0.3	0.1	0.0
S.E.	1	0.01	1	0.1	0	0.1	0.1	0.1	0.0	0.0
n	10	10	10	10	10	10	10	10	10	10

Appendix 7 - 3 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual blood chemistry Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 100 mg/kg

Animal No.	AST IU/L	ALT IU/L	LDH IU/L	ALP IU/L	r-GTP IU/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
2001	54	32	43	406	0	90	88	136	0.1	161
2002	57	36	49	453	0	65	105	108	0.1	143
2003	61	38	53	477	0	44	37	77	0.1	137
2004	54	31	52	369	0	77	29	107	0.1	143
2005	60	36	113	275	0	86	108	132	0.1	188
2006	60	38	58	353	0	44	46	72	0.1	179
2007	78	51	83	799	0	47	51	83	0.1	137
2008	74	36	72	332	0	62	87	103	0.1	167
2009	61	39	46	541	0	77	56	116	0.1	168
2010	56	30	59	300	0	59	42	98	0.1	160
Mean	62	37	63	431	0	65	65	103	0.1	158
S.D.	8	6	21	153	0	17	29	22	0.0	18
S.E.	3	2	7	49	0	5	9	7	0.0	6
n	10	10	10	10	10	10	10	10	10	10

Appendix 7 - 4 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual blood chemistry Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 100 mg/kg

Animal No.	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
2001	11	0.23	143	4.1	104	10.3	5.4	6.4	2.8	0.8
2002	13	0.27	144	4.0	106	10.3	4.8	6.6	2.7	0.7
2003	10	0.26	144	4.0	107	9.9	4.9	5.9	2.6	0.8
2004	11	0.31	145	3.7	107	9.9	4.6	6.3	2.6	0.7
2005	17	0.34	143	4.4	107	10.4	5.1	6.1	2.6	0.7
2006	13	0.27	145	4.1	109	9.4	4.0	5.8	2.5	0.8
2007	14	0.30	144	3.7	105	9.9	5.4	6.1	2.6	0.7
2008	14	0.33	144	3.7	105	10.2	5.6	6.3	2.8	0.8
2009	15	0.27	143	3.8	104	10.5	5.2	6.0	2.6	0.8
2010	15	0.32	143	3.4	104	10.2	4.6	6.6	2.7	0.7
Mean	13	0.29	144	3.9	106	10.1	5.0	6.2	2.7	0.8
S.D.	2	0.04	1	0.3	2	0.3	0.5	0.3	0.1	0.1
S.E.	1	0.01	0	0.1	1	0.1	0.2	0.1	0.0	0.0
n	10	10	10	10	10	10	10	10	10	10

Appendix 7 - 5 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual blood chemistry Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 300 mg/kg

Animal No.	AST IU/L	ALT IU/L	LDH IU/L	ALP IU/L	r-GTP IU/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
3001	61	34	54	462	1	72	57	112	0.1	144
3002	53	42	57	368	0	78	43	116	0.1	131
3003	51	38	53	303	1	62	43	99	0.1	148
3004	65	51	49	349	1	48	40	79	0.1	152
3005	49	36	45	401	0	63	37	95	0.1	174
3006	56	39	54	349	1	66	106	116	0.1	140
3007	57	32	53	542	0	79	96	132	0.1	149
3008	60	41	62	348	0	82	35	117	0.1	165
3009	59	44	56	451	1	88	56	129	0.1	157
3010	59	32	39	306	0	49	39	82	0.1	135
Mean	57	39	52	388	1	69	55	108	0.1	150
S.D.	5	6	6	76	1	14	25	18	0.0	13
S.E.	2	2	2	24	0	4	8	6	0.0	4
n	10	10	10	10	10	10	10	10	10	10

Appendix 7 - 6 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual blood chemistry Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 300 mg/kg

Animal No.	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
3001	11	0.29	143	3.8	106	10.1	5.1	6.4	2.7	0.7
3002	9	0.26	144	3.9	107	10.4	5.1	6.4	2.7	0.7
3003	14	0.26	144	4.0	106	10.2	5.3	6.4	2.8	0.8
3004	12	0.28	144	4.4	107	9.9	4.7	6.1	2.7	0.8
3005	13	0.32	145	3.9	106	9.8	4.5	5.9	2.6	0.8
3006	12	0.27	144	3.9	106	10.1	4.8	6.2	2.6	0.7
3007	15	0.28	144	3.8	106	10.4	5.5	6.1	2.7	0.8
3008	11	0.31	144	3.6	105	10.1	4.8	6.5	2.7	0.7
3009	22	0.32	142	3.7	103	10.6	5.0	6.4	2.6	0.7
3010	15	0.34	144	3.6	106	9.8	4.7	6.2	2.5	0.7
Mean	13	0.29	144	3.9	106	10.1	5.0	6.3	2.7	0.7
S.D.	4	0.03	1	0.2	1	0.3	0.3	0.2	0.1	0.1
S.E.	1	0.01	0	0.1	0	0.1	0.1	0.1	0.0	0.0
n	10	10	10	10	10	10	10	10	10	10

Appendix 7 - 7 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual blood chemistry Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 1000 mg/kg

Animal No.	AST IU/L	ALT IU/L	LDH IU/L	ALP IU/L	r-GTP IU/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
4001	47	44	49	473	1	92	87	152	0.1	129
4002	58	61	55	578	2	75	60	123	0.1	131
4003	66	73	62	724	1	89	25	134	0.1	131
4004	50	56	45	363	1	104	121	162	0.1	141
4005	50	44	45	556	1	90	66	141	0.1	139
4006	45	42	231	358	1	88	45	129	0.1	173
4007	53	49	52	787	1	95	41	135	0.1	163
4008	69	52	49	490	2	103	47	145	0.1	141
4009	74	53	68	325	1	94	34	136	0.1	137
4010	53	35	45	502	1	86	46	136	0.1	153
Mean	57	51	70	516	1	92	57	139	0.1	144
S.D.	10	11	57	153	0	8	28	11	0.0	15
S.E.	3	3	18	48	0	3	9	4	0.0	5
n	10	10	10	10	10	10	10	10	10	10

Appendix 7 - 8 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual blood chemistry Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 1000 mg/kg

Animal No.	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
4001	10	0.21	142	4.0	106	10.3	5.1	6.7	2.9	0.8
4002	11	0.25	142	3.9	106	10.1	4.6	6.4	2.7	0.7
4003	14	0.31	142	4.3	106	10.1	5.4	6.8	2.9	0.7
4004	12	0.26	142	4.3	106	10.4	5.2	6.6	2.7	0.7
4005	13	0.28	146	3.7	109	10.1	4.3	6.4	2.7	0.7
4006	13	0.31	142	4.1	108	9.6	4.6	6.1	2.6	0.7
4007	22	0.38	143	4.2	106	10.1	5.3	6.3	2.6	0.7
4008	14	0.26	144	3.7	104	9.8	4.7	6.0	2.6	0.8
4009	18	0.34	143	4.2	104	10.2	5.8	6.1	2.6	0.7
4010	11	0.24	143	4.2	107	9.9	4.8	6.3	2.7	0.8
Mean	14	0.28	143	4.1	106	10.1	5.0	6.4	2.7	0.7
S.D.	4	0.05	1	0.2	2	0.2	0.5	0.3	0.1	0.0
S.E.	1	0.02	0	0.1	0	0.1	0.1	0.1	0.0	0.0
n	10	10	10	10	10	10	10	10	10	10

Appendix 7 - 9 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual blood chemistry Stage : Week 13
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 0 mg/kg

Animal No.	AST IU/L	ALT IU/L	LDH IU/L	ALP IU/L	r-GTP IU/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
1101	43	29	60	130	0	90	82	170	0.1	129
1102	49	36	49	142	0	50	32	104	0.1	110
1103	62	35	63	220	0	70	34	140	0.1	112
1104	53	33	54	265	0	66	43	130	0.1	133
1105	62	33	62	183	1	108	89	185	0.1	133
1106	60	26	70	121	0	67	76	138	0.1	145
1107	61	33	45	241	0	70	43	141	0.1	130
1108	75	52	51	225	0	70	59	138	0.1	107
1109	58	36	82	140	0	81	44	152	0.1	103
1110	106	52	135	228	0	99	62	198	0.1	114
Mean	63	37	67	190	0	77	56	150	0.1	122
S.D.	17	9	26	53	0	17	20	28	0.0	14
S.E.	6	3	8	17	0	6	6	9	0.0	4
n	10	10	10	10	10	10	10	10	10	10

Appendix 7 - 10 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual blood chemistry Stage : Week 13
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 0 mg/kg

Animal No.	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
1101	16	0.31	140	3.5	106	10.4	4.1	6.8	3.3	0.9
1102	16	0.27	143	3.6	106	10.2	2.6	6.7	3.2	0.9
1103	14	0.32	143	3.4	107	10.0	3.7	6.7	3.2	0.9
1104	14	0.34	144	3.1	107	9.8	2.3	6.8	3.1	0.8
1105	27	0.48	143	3.2	106	10.2	3.5	6.6	3.0	0.8
1106	15	0.35	145	3.4	109	10.1	2.9	6.9	3.1	0.8
1107	20	0.32	144	3.3	108	9.9	3.6	6.5	3.1	0.9
1108	22	0.39	146	3.6	109	9.9	4.4	6.7	3.0	0.8
1109	22	0.38	145	3.5	109	10.6	4.5	7.0	3.3	0.9
1110	27	0.33	146	3.4	106	10.7	4.2	7.4	3.6	0.9
Mean	19	0.35	144	3.4	107	10.2	3.6	6.8	3.2	0.9
S.D.	5	0.06	2	0.2	1	0.3	0.8	0.3	0.2	0.1
S.E.	2	0.02	1	0.1	0	0.1	0.2	0.1	0.1	0.0
n	10	10	10	10	10	10	10	10	10	10

Appendix 7 - 11 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual blood chemistry Stage : Week 13
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 100 mg/kg

Animal No.	AST IU/L	ALT IU/L	LDH IU/L	ALP IU/L	r-GTP IU/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
2101	59	36	51	185	0	66	36	126	0.1	114
2102	62	55	72	156	0	54	89	129	0.1	121
2103	62	48	76	346	0	65	28	142	0.1	120
2104	70	34	42	381	0	75	32	134	0.2	140
2105	58	62	64	180	0	79	37	163	0.1	130
2106	70	23	169	149	0	69	42	138	0.1	145
2107	59	28	39	192	0	73	71	146	0.1	118
2108	65	38	69	263	0	81	47	146	0.1	134
2109	46	22	66	130	0	115	83	224	0.1	127
2110	51	29	52	171	0	85	25	152	0.1	125
Mean	60	38	70	215	0	76	49	150	0.1	127
S.D.	8	14	37	86	0	16	23	28	0.0	10
S.E.	2	4	12	27	0	5	7	9	0.0	3
n	10	10	10	10	10	10	10	10	10	10

Appendix 7 - 12 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual blood chemistry Stage : Week 13
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 100 mg/kg

Animal No.	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
2101	14	0.30	142	3.5	107	10.0	3.9	6.4	2.9	0.8
2102	23	0.39	143	3.5	108	10.2	2.9	6.8	3.2	0.9
2103	13	0.32	142	3.1	106	10.0	2.2	6.6	3.1	0.9
2104	14	0.38	143	2.9	108	9.9	2.6	6.5	2.9	0.8
2105	17	0.31	144	3.3	109	10.4	2.9	7.1	3.3	0.9
2106	16	0.39	143	3.4	107	9.4	3.3	6.6	2.9	0.8
2107	18	0.39	144	3.5	108	10.1	3.3	6.6	3.1	0.9
2108	24	0.45	144	3.5	107	10.3	3.2	6.8	3.1	0.8
2109	15	0.30	145	3.3	107	10.8	5.0	7.8	3.8	1.0
2110	19	0.43	146	3.4	110	10.4	3.9	6.8	3.3	0.9
Mean	17	0.37	144	3.3	108	10.2	3.3	6.8	3.2	0.9
S.D.	4	0.05	1	0.2	1	0.4	0.8	0.4	0.3	0.1
S.E.	1	0.02	0	0.1	0	0.1	0.3	0.1	0.1	0.0
n	10	10	10	10	10	10	10	10	10	10

Appendix 7 - 13 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual blood chemistry Stage : Week 13
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 300 mg/kg

Animal No.	AST IU/L	ALT IU/L	LDH IU/L	ALP IU/L	r-GTP IU/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
3101	51	29	46	104	1	72	40	137	0.1	122
3102	52	27	68	311	0	113	40	203	0.1	119
3103	63	56	53	396	2	83	24	153	0.1	129
3104	48	22	54	118	1	111	56	190	0.1	127
3105	56	37	51	169	1	70	35	129	0.1	136
3106	65	52	52	170	1	86	33	159	0.1	122
3107	53	42	39	173	0	79	42	154	0.1	134
3108	46	28	44	112	1	104	24	177	0.1	116
3109	75	56	60	235	1	62	26	117	0.2	109
3110	59	36	50	316	1	74	22	133	0.1	125
Mean	57	39	52	210	1	85	34	155	0.1	124
S.D.	9	13	8	100	1	18	11	28	0.0	8
S.E.	3	4	3	32	0	6	3	9	0.0	3
n	10	10	10	10	10	10	10	10	10	10

Appendix 7 - 14 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual blood chemistry Stage : Week 13
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 300 mg/kg

Animal No.	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
3101	13	0.31	142	3.4	104	10.0	3.6	6.6	3.1	0.9
3102	14	0.30	140	3.3	104	10.5	3.6	7.3	3.3	0.8
3103	15	0.33	143	3.6	109	10.3	3.1	6.9	3.2	0.9
3104	15	0.38	142	3.3	108	10.5	3.7	7.3	3.3	0.8
3105	13	0.30	143	3.4	107	9.8	3.4	6.3	3.0	0.9
3106	15	0.35	146	3.4	108	10.1	4.0	6.7	3.1	0.9
3107	21	0.43	145	3.5	110	10.3	3.1	6.7	3.2	0.9
3108	17	0.35	144	3.6	108	10.6	4.4	7.1	3.3	0.9
3109	23	0.38	143	3.6	107	10.2	4.2	6.3	2.9	0.9
3110	27	0.47	145	3.4	109	10.3	4.0	6.8	3.2	0.9
Mean	17	0.36	143	3.5	107	10.3	3.7	6.8	3.2	0.9
S.D.	5	0.06	2	0.1	2	0.2	0.4	0.4	0.1	0.0
S.E.	2	0.02	1	0.0	1	0.1	0.1	0.1	0.0	0.0
n	10	10	10	10	10	10	10	10	10	10

Appendix 7 - 15 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual blood chemistry Stage : Week 13
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 1000 mg/kg

Animal No.	AST IU/L	ALT IU/L	LDH IU/L	ALP IU/L	r-GTP IU/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
4101	58	57	58	296	2	130	36	208	0.1	137
4102	64	50	61	180	0	137	78	264	0.3	113
4103	55	56	104	190	1	143	42	244	0.1	132
4104	50	50	51	257	1	153	106	244	0.1	126
4105	63	63	98	138	1	119	53	218	0.2	141
4106	60	52	111	132	1	127	88	212	0.1	132
4107	51	36	53	187	1	103	33	166	0.1	141
4108	58	57	48	164	1	91	117	186	0.1	113
4109	54	42	45	155	1	115	42	195	0.1	115
4110	52	39	59	196	1	111	35	199	0.1	115
Mean	57	50	69	190	1	123	63	214	0.1	127
S.D.	5	9	25	51	0	19	32	30	0.1	12
S.E.	2	3	8	16	0	6	10	9	0.0	4
n	10	10	10	10	10	10	10	10	10	10

Appendix 7 - 16 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual blood chemistry Stage : Week 13
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 1000 mg/kg

Animal No.	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
4101	9	0.30	141	3.4	109	9.9	2.8	6.4	3.0	0.9
4102	12	0.28	141	3.9	106	11.0	3.9	7.5	3.7	1.0
4103	14	0.30	141	3.8	106	11.0	3.5	7.6	3.5	0.9
4104	15	0.31	143	3.4	106	10.5	3.2	7.3	3.3	0.8
4105	12	0.29	143	3.7	110	10.0	2.8	7.2	3.4	0.9
4106	16	0.36	142	4.0	107	10.2	3.5	6.4	3.1	0.9
4107	10	0.30	142	3.8	110	10.2	3.6	6.7	3.0	0.8
4108	21	0.33	143	3.7	108	10.4	4.6	6.7	3.2	0.9
4109	11	0.23	142	3.6	107	10.4	4.3	7.0	3.3	0.9
4110	20	0.36	145	3.6	111	10.3	3.9	6.9	3.2	0.9
Mean	14	0.31	142	3.7	108	10.4	3.6	7.0	3.3	0.9
S.D.	4	0.04	1	0.2	2	0.4	0.6	0.4	0.2	0.1
S.E.	1	0.01	0	0.1	1	0.1	0.2	0.1	0.1	0.0
n	10	10	10	10	10	10	10	10	10	10

Appendix 8 - 1 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual absolute organ weight Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 0 mg/kg

Animal No.	F.B.W. g	Brain g	Pituitary mg	Thyroid-R mg	Thyroid-L mg	Thyroid-RL mg	Sa.G.-R mg	Sa.G.-L mg	Sa.G.-RL mg	Thymus mg
1001	486	2.13	12.1	13.0	11.9	24.9	423	410	833	330
1002	513	2.18	12.1	13.1	8.6	21.7	337	326	663	246
1003	463	2.08	14.0	9.2	11.5	20.7	324	334	658	203
1004	519	2.22	11.3	8.3	10.1	18.4	443	481	924	212
1005	618	2.29	11.4	11.7	10.2	21.9	385	359	744	327
1006	493	2.07	12.8	13.5	13.3	26.8	392	365	757	376
1007	526	2.21	14.4	11.9	12.8	24.7	361	364	725	254
1008	501	2.00	12.7	10.2	9.1	19.3	344	316	660	186
1009	547	2.07	15.4	12.2	18.3	30.5	384	405	789	312
1010	509	2.27	11.8	8.1	7.8	15.9	369	363	732	207
Mean	518	2.15	12.8	11.1	11.4	22.5	376	372	749	265
S.D.	42	0.10	1.4	2.0	3.0	4.3	37	49	84	66
S.E.	13	0.03	0.4	0.6	1.0	1.4	12	15	27	21
n	10	10	10	10	10	10	10	10	10	10

Sa.G. : Salivary gland

Appendix 8 - 2 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual absolute organ weight Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 0 mg/kg

Animal No.	Heart g	Lung g	Liver g	Spleen g	Kidney-R g	Kidney-L g	Kidney-RL g	Adrenal-R mg	Adrenal-L mg	Adrenal-RL mg
1001	1.40	1.58	13.34	0.75	1.66	1.74	3.40	23	24	47
1002	1.37	1.41	13.43	0.58	1.45	1.48	2.93	25	26	51
1003	1.29	1.34	11.23	0.68	1.23	1.30	2.53	29	31	60
1004	1.35	1.44	11.74	0.69	1.45	1.43	2.88	19	22	41
1005	1.66	1.71	16.85	0.89	1.88	1.83	3.71	32	30	62
1006	1.43	1.54	13.13	0.77	1.52	1.54	3.06	27	31	58
1007	1.45	1.66	13.74	0.77	1.67	1.68	3.35	30	30	60
1008	1.39	1.34	13.56	0.67	1.60	1.60	3.20	23	23	46
1009	1.54	1.52	15.63	0.79	1.50	1.60	3.10	22	28	50
1010	1.51	1.49	12.63	0.67	1.51	1.50	3.01	35	36	71
Mean	1.44	1.50	13.53	0.73	1.55	1.57	3.12	27	28	55
S.D.	0.11	0.13	1.67	0.09	0.17	0.16	0.32	5	4	9
S.E.	0.03	0.04	0.53	0.03	0.05	0.05	0.10	2	1	3
n	10	10	10	10	10	10	10	10	10	10

Appendix 8 - 5 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual absolute organ weight Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 100 mg/kg

Animal No.	Heart g	Lung g	Liver g	Spleen g	Kidney-R g	Kidney-L g	Kidney-RL g	Adrenal-R mg	Adrenal-L mg	Adrenal-RL mg
2001	1.78	1.70	18.56	0.95	1.90	1.98	3.88	23	25	48
2002	1.46	1.51	14.00	0.73	1.57	1.65	3.22	26	28	54
2003	1.34	1.37	11.79	0.62	1.45	1.51	2.96	23	26	49
2004	1.48	1.55	13.57	0.57	1.47	1.48	2.95	27	27	54
2005	1.64	1.69	16.38	0.69	1.83	1.79	3.62	29	28	57
2006	0.98	1.33	9.08	0.45	1.32	1.32	2.64	22	23	45
2007	1.23	1.38	9.38	0.61	1.32	1.36	2.68	22	24	46
2008	1.68	1.74	16.40	0.81	1.65	1.77	3.42	37	37	74
2009	1.59	1.59	14.36	0.80	1.53	1.60	3.13	23	25	48
2010	1.67	1.61	15.41	0.83	1.56	1.64	3.20	29	29	58
Mean	1.49	1.55	13.89	0.71	1.56	1.61	3.17	26	27	53
S.D.	0.24	0.15	3.07	0.15	0.19	0.20	0.39	5	4	9
S.E.	0.08	0.05	0.97	0.05	0.06	0.06	0.12	1	1	3
n	10	10	10	10	10	10	10	10	10	10

Appendix 8 - 7 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual absolute organ weight Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 300 mg/kg

Animal No.	F.B.W. g	Brain g	Pituitary mg	Thyroid-R mg	Thyroid-L mg	Thyroid-RL mg	Sa.G.-R mg	Sa.G.-L mg	Sa.G.-RL mg	Thymus mg
3001	519	2.22	13.4	20.8	18.5	39.3	405	396	801	266
3002	549	2.20	14.6	10.9	12.5	23.4	346	357	703	233
3003	477	2.22	15.8	14.1	11.4	25.5	373	375	748	279
3004	479	2.31	11.5	8.7	9.6	18.3	321	328	649	202
3005	534	2.19	12.6	12.6	6.2	18.8	377	364	741	353
3006	541	2.10	13.6	10.1	8.5	18.6	394	381	775	218
3007	543	2.33	12.5	10.5	11.5	22.0	378	369	747	270
3008	505	2.24	11.5	8.3	6.4	14.7	333	326	659	232
3009	545	2.08	13.5	11.5	11.7	23.2	390	393	783	307
3010	512	2.15	10.5	10.7	11.3	22.0	393	373	766	186
Mean	520	2.20	13.0	11.8	10.8	22.6	371	366	737	255
S.D.	27	0.08	1.6	3.6	3.5	6.7	28	24	51	51
S.E.	8	0.03	0.5	1.1	1.1	2.1	9	8	16	16
n	10	10	10	10	10	10	10	10	10	10

Sa.G. : Salivary gland

Appendix 8 - 8 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual absolute organ weight Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 300 mg/kg

Animal No.	Heart g	Lung g	Liver g	Spleen g	Kidney-R g	Kidney-L g	Kidney-RL g	Adrenal-R mg	Adrenal-L mg	Adrenal-RL mg
3001	1.48	1.48	13.08	0.73	1.60	1.62	3.22	23	24	47
3002	1.51	1.55	14.24	0.69	1.73	1.85	3.58	26	27	53
3003	1.38	1.42	13.19	0.68	1.66	1.76	3.42	24	29	53
3004	1.33	1.33	11.63	0.64	1.56	1.71	3.27	23	26	49
3005	1.46	1.58	13.85	0.85	1.52	1.67	3.19	19	21	40
3006	1.51	1.50	13.79	0.75	1.44	1.58	3.02	23	25	48
3007	1.46	1.54	15.53	0.70	1.52	1.69	3.21	18	21	39
3008	1.30	1.44	13.40	0.73	1.49	1.50	2.99	20	22	42
3009	1.59	1.66	16.04	0.76	1.74	1.84	3.58	35	37	72
3010	1.61	1.56	12.04	0.68	1.64	1.73	3.37	24	29	53
Mean	1.46	1.51	13.68	0.72	1.59	1.70	3.29	24	26	50
S.D.	0.10	0.09	1.37	0.06	0.10	0.11	0.20	5	5	9
S.E.	0.03	0.03	0.43	0.02	0.03	0.03	0.06	2	2	3
n	10	10	10	10	10	10	10	10	10	10

Appendix 8 - 10 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual absolute organ weight Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 1000 mg/kg

Animal No.	F.B.W. g	Brain g	Pituitary mg	Thyroid-R mg	Thyroid-L mg	Thyroid-RL mg	Sa.G.-R mg	Sa.G.-L mg	Sa.G.-RL mg	Thymus mg
4001	479	2.06	12.7	12.0	12.8	24.8	358	336	694	205
4002	443	1.98	11.6	11.5	13.8	25.3	298	290	588	270
4003	394	2.06	10.2	13.0	9.7	22.7	308	314	622	159
4004	460	2.16	10.6	8.1	8.4	16.5	420	412	832	333
4005	380	1.94	9.2	9.7	7.6	17.3	304	286	590	173
4006	460	2.26	15.4	11.9	11.2	23.1	380	405	785	185
4007	520	2.01	13.9	11.9	14.3	26.2	327	339	666	179
4008	418	2.10	10.7	9.8	9.7	19.5	285	291	576	213
4009	473	2.22	10.8	9.7	11.3	21.0	309	296	605	194
4010	517	2.30	13.8	13.8	7.5	21.3	391	414	805	261
Mean	454	2.11	11.9	11.1	10.6	21.8	338	338	676	217
S.D.	47	0.12	2.0	1.8	2.5	3.3	46	53	98	54
S.E.	15	0.04	0.6	0.6	0.8	1.0	15	17	31	17
n	10	10	10	10	10	10	10	10	10	10

Sa.G. : Salivary gland

Appendix 8 - 19 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual absolute organ weight Stage : Week 13
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 300 mg/kg

Animal No.	F.B.W. g	Brain g	Pituitary mg	Thyroid-R mg	Thyroid-L mg	Thyroid-RL mg	Sa.G.-R mg	Sa.G.-L mg	Sa.G.-RL mg	Thymus mg
3101	314	2.11	13.2	14.2	10.7	24.9	215	216	431	218
3102	274	2.04	18.3	8.8	7.9	16.7	227	211	438	236
3103	294	2.19	16.7	7.7	7.0	14.7	233	223	456	235
3104	258	1.93	13.1	10.7	18.1	28.8	223	232	455	173
3105	269	1.96	14.0	8.4	8.7	17.1	194	200	394	165
3106	289	2.00	17.6	9.6	8.6	18.2	245	242	487	321
3107	255	2.05	16.6	8.3	8.8	17.1	193	201	394	175
3108	306	2.03	16.6	13.6	10.9	24.5	219	246	465	223
3109	285	2.00	14.1	8.9	10.3	19.2	244	237	481	215
3110	291	2.00	15.8	13.1	9.8	22.9	214	209	423	259
Mean	284	2.03	15.6	10.3	10.1	20.4	221	222	442	222
S.D.	19	0.07	1.9	2.4	3.1	4.6	18	17	33	46
S.E.	6	0.02	0.6	0.8	1.0	1.4	6	5	10	15
n	10	10	10	10	10	10	10	10	10	10

Sa.G. : Salivary gland

Appendix 8 - 20 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual absolute organ weight Stage : Week 13
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 300 mg/kg

Animal No.	Heart g	Lung g	Liver g	Spleen g	Kidney-R g	Kidney-L g	Kidney-RL g	Adrenal-R mg	Adrenal-L mg	Adrenal-RL mg
3101	1.00	1.14	7.80	0.55	0.86	0.92	1.78	26	25	51
3102	0.92	1.23	8.19	0.50	0.93	1.01	1.94	34	34	68
3103	0.85	1.15	7.57	0.47	0.95	0.96	1.91	27	28	55
3104	0.82	1.04	6.97	0.39	0.82	0.86	1.68	38	40	78
3105	0.79	1.04	6.98	0.38	0.90	0.96	1.86	36	40	76
3106	0.91	1.17	7.66	0.51	0.97	1.01	1.98	33	36	69
3107	0.76	1.00	6.60	0.46	0.81	0.76	1.57	24	24	48
3108	0.91	1.15	7.92	0.45	0.92	0.95	1.87	27	27	54
3109	0.75	1.10	6.32	0.41	0.92	0.92	1.84	29	31	60
3110	0.95	1.18	7.46	0.56	1.03	1.07	2.10	38	39	77
Mean	0.87	1.12	7.35	0.47	0.91	0.94	1.85	31	32	64
S.D.	0.08	0.07	0.60	0.06	0.07	0.09	0.15	5	6	11
S.E.	0.03	0.02	0.19	0.02	0.02	0.03	0.05	2	2	4
n	10	10	10	10	10	10	10	10	10	10

Appendix 8 - 22 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual absolute organ weight Stage : Week 13
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 1000 mg/kg

Animal No.	F.B.W. g	Brain g	Pituitary mg	Thyroid-R mg	Thyroid-L mg	Thyroid-RL mg	Sa.G.-R mg	Sa.G.-L mg	Sa.G.-RL mg	Thymus mg
4101	265	1.97	17.7	8.8	5.8	14.6	207	206	413	172
4102	264	1.88	20.7	9.1	8.5	17.6	190	194	384	216
4103	269	1.93	15.0	9.1	10.0	19.1	217	220	437	170
4104	348	2.17	15.2	6.8	7.7	14.5	307	312	619	361
4105	224	1.77	13.2	9.3	7.5	16.8	179	180	359	172
4106	272	2.05	14.7	10.1	10.2	20.3	206	198	404	252
4107	276	2.03	13.5	4.4	5.0	9.4	235	245	480	240
4108	279	1.84	16.0	8.9	6.9	15.8	238	218	456	261
4109	249	1.94	15.7	8.8	6.9	15.7	199	200	399	117
4110	250	1.86	20.6	8.5	6.3	14.8	238	236	474	212
Mean	270	1.94	16.2	8.4	7.5	15.9	222	221	443	217
S.D.	32	0.12	2.6	1.6	1.7	3.0	36	38	73	67
S.E.	10	0.04	0.8	0.5	0.5	0.9	11	12	23	21
n	10	10	10	10	10	10	10	10	10	10

Sa.G. : Salivary gland

Appendix 8 - 23 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual absolute organ weight Stage : Week 13
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 1000 mg/kg

Animal No.	Heart g	Lung g	Liver g	Spleen g	Kidney-R g	Kidney-L g	Kidney-RL g	Adrenal-R mg	Adrenal-L mg	Adrenal-RL mg
4101	0.74	1.09	8.07	0.43	0.90	0.87	1.77	27	29	56
4102	0.87	0.93	9.11	0.46	0.94	0.85	1.79	27	27	54
4103	0.90	1.10	8.97	0.52	0.99	1.05	2.04	22	26	48
4104	1.07	1.36	10.88	0.56	1.12	1.04	2.16	27	29	56
4105	0.68	0.90	6.68	0.30	0.80	0.78	1.58	23	23	46
4106	0.89	1.10	7.97	0.42	0.95	1.00	1.95	32	37	69
4107	0.81	1.17	8.73	0.58	0.88	0.88	1.76	30	37	67
4108	0.91	1.10	8.41	0.47	1.00	0.98	1.98	39	39	78
4109	0.80	1.03	7.76	0.34	1.03	1.03	2.06	31	30	61
4110	0.84	1.02	7.47	0.46	0.88	0.86	1.74	26	25	51
Mean	0.85	1.08	8.41	0.45	0.95	0.93	1.88	28	30	59
S.D.	0.11	0.13	1.14	0.09	0.09	0.10	0.18	5	6	10
S.E.	0.03	0.04	0.36	0.03	0.03	0.03	0.06	2	2	3
n	10	10	10	10	10	10	10	10	10	10

Appendix 9 - 1 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual relative organ weight Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 0 mg/kg

Animal No.	F.B.W. g	Brain g/100g	Pituitary mg/100g	Thyroid-R mg/100g	Thyroid-L mg/100g	Thyroid-RL mg/100g	Sa.G.-R mg/100g	Sa.G.-L mg/100g	Sa.G.-RL mg/100g	Thymus mg/100g
1001	486	0.44	2.5	2.7	2.4	5.1	87	84	171	68
1002	513	0.42	2.4	2.6	1.7	4.2	66	64	129	48
1003	463	0.45	3.0	2.0	2.5	4.5	70	72	142	44
1004	519	0.43	2.2	1.6	1.9	3.5	85	93	178	41
1005	618	0.37	1.8	1.9	1.7	3.5	62	58	120	53
1006	493	0.42	2.6	2.7	2.7	5.4	80	74	154	76
1007	526	0.42	2.7	2.3	2.4	4.7	69	69	138	48
1008	501	0.40	2.5	2.0	1.8	3.9	69	63	132	37
1009	547	0.38	2.8	2.2	3.3	5.6	70	74	144	57
1010	509	0.45	2.3	1.6	1.5	3.1	72	71	144	41
Mean	518	0.42	2.5	2.2	2.2	4.4	73	72	145	51
S.D.	42	0.03	0.3	0.4	0.6	0.9	8	10	18	13
S.E.	13	0.01	0.1	0.1	0.2	0.3	3	3	6	4
n	10	10	10	10	10	10	10	10	10	10

Sa.G. : Salivary gland

Appendix 9 - 2 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual relative organ weight Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 0 mg/kg

Animal No.	Heart g/100g	Lung g/100g	Liver g/100g	Spleen g/100g	Kidney-R g/100g	Kidney-L g/100g	Kidney-RL g/100g	Adrenal-R mg/100g	Adrenal-L mg/100g	Adrenal-RL mg/100g
1001	0.29	0.33	2.74	0.15	0.34	0.36	0.70	5	5	10
1002	0.27	0.27	2.62	0.11	0.28	0.29	0.57	5	5	10
1003	0.28	0.29	2.43	0.15	0.27	0.28	0.55	6	7	13
1004	0.26	0.28	2.26	0.13	0.28	0.28	0.55	4	4	8
1005	0.27	0.28	2.73	0.14	0.30	0.30	0.60	5	5	10
1006	0.29	0.31	2.66	0.16	0.31	0.31	0.62	5	6	12
1007	0.28	0.32	2.61	0.15	0.32	0.32	0.64	6	6	11
1008	0.28	0.27	2.71	0.13	0.32	0.32	0.64	5	5	9
1009	0.28	0.28	2.86	0.14	0.27	0.29	0.57	4	5	9
1010	0.30	0.29	2.48	0.13	0.30	0.29	0.59	7	7	14
Mean	0.28	0.29	2.61	0.14	0.30	0.30	0.60	5	6	11
S.D.	0.01	0.02	0.18	0.01	0.02	0.02	0.05	1	1	2
S.E.	0.00	0.01	0.06	0.00	0.01	0.01	0.02	0	0	1
n	10	10	10	10	10	10	10	10	10	10

Appendix 9 - 3 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual relative organ weight Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 0 mg/kg

Animal No.	Testis-R g/100g	Testis-L g/100g	Testis-RL g/100g	Prostate g/100g	Sem.Ves. g/100g
1001	0.33	0.33	0.66	0.35	0.44
1002	0.29	0.29	0.58	0.24	0.30
1003	0.40	0.39	0.78	0.32	0.36
1004	0.31	0.31	0.62	0.34	0.39
1005	0.27	0.27	0.54	0.27	0.25
1006	0.32	0.31	0.63	0.31	0.46
1007	0.33	0.33	0.66	0.28	0.49
1008	0.35	0.34	0.69	0.22	0.35
1009	0.29	0.29	0.58	0.28	0.30
1010	0.28	0.28	0.56	0.26	0.44
Mean	0.32	0.31	0.63	0.29	0.38
S.D.	0.04	0.04	0.07	0.04	0.08
S.E.	0.01	0.01	0.02	0.01	0.03
n	10	10	10	10	10

Sem.Ves. : Seminal vesicle

Appendix 9 - 4 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual relative organ weight Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 100 mg/kg

Animal No.	F.B.W. g	Brain g/100g	Pituitary mg/100g	Thyroid-R mg/100g	Thyroid-L mg/100g	Thyroid-RL mg/100g	Sa.G.-R mg/100g	Sa.G.-L mg/100g	Sa.G.-RL mg/100g	Thymus mg/100g
2001	577	0.38	2.1	1.5	2.8	4.2	67	69	136	44
2002	520	0.41	2.1	2.4	1.6	4.0	62	68	129	69
2003	487	0.41	2.0	2.5	2.4	5.0	73	73	146	54
2004	529	0.43	2.3	2.1	1.9	4.0	63	65	128	66
2005	628	0.32	2.2	1.5	2.0	3.6	58	60	118	40
2006	381	0.57	2.7	3.1	3.0	6.1	103	100	203	43
2007	442	0.50	2.8	2.4	2.9	5.3	73	72	145	41
2008	635	0.34	2.2	1.4	2.3	3.7	71	71	142	45
2009	573	0.37	2.1	2.5	2.1	4.6	65	65	130	74
2010	574	0.39	2.2	3.9	3.6	7.5	62	59	120	48
Mean	535	0.41	2.3	2.3	2.5	4.8	70	70	140	52
S.D.	80	0.07	0.3	0.8	0.6	1.2	13	11	24	13
S.E.	25	0.02	0.1	0.2	0.2	0.4	4	4	8	4
n	10	10	10	10	10	10	10	10	10	10

Sa.G. : Salivary gland

Appendix 9 - 5 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual relative organ weight Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 100 mg/kg

Animal No.	Heart g/100g	Lung g/100g	Liver g/100g	Spleen g/100g	Kidney-R g/100g	Kidney-L g/100g	Kidney-RL g/100g	Adrenal-R mg/100g	Adrenal-L mg/100g	Adrenal-RL mg/100g
2001	0.31	0.29	3.22	0.16	0.33	0.34	0.67	4	4	8
2002	0.28	0.29	2.69	0.14	0.30	0.32	0.62	5	5	10
2003	0.28	0.28	2.42	0.13	0.30	0.31	0.61	5	5	10
2004	0.28	0.29	2.57	0.11	0.28	0.28	0.56	5	5	10
2005	0.26	0.27	2.61	0.11	0.29	0.29	0.58	5	4	9
2006	0.26	0.35	2.38	0.12	0.35	0.35	0.69	6	6	12
2007	0.28	0.31	2.12	0.14	0.30	0.31	0.61	5	5	10
2008	0.26	0.27	2.58	0.13	0.26	0.28	0.54	6	6	12
2009	0.28	0.28	2.51	0.14	0.27	0.28	0.55	4	4	8
2010	0.29	0.28	2.68	0.14	0.27	0.29	0.56	5	5	10
Mean	0.28	0.29	2.58	0.13	0.30	0.31	0.60	5	5	10
S.D.	0.02	0.02	0.28	0.02	0.03	0.03	0.05	1	1	1
S.E.	0.00	0.01	0.09	0.00	0.01	0.01	0.02	0	0	0
n	10	10	10	10	10	10	10	10	10	10

Appendix 9 - 7 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual relative organ weight Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 300 mg/kg

Animal No.	F.B.W. g	Brain g/100g	Pituitary mg/100g	Thyroid-R mg/100g	Thyroid-L mg/100g	Thyroid-RL mg/100g	Sa.G.-R mg/100g	Sa.G.-L mg/100g	Sa.G.-RL mg/100g	Thymus mg/100g
3001	519	0.43	2.6	4.0	3.6	7.6	78	76	154	51
3002	549	0.40	2.7	2.0	2.3	4.3	63	65	128	42
3003	477	0.47	3.3	3.0	2.4	5.3	78	79	157	58
3004	479	0.48	2.4	1.8	2.0	3.8	67	68	135	42
3005	534	0.41	2.4	2.4	1.2	3.5	71	68	139	66
3006	541	0.39	2.5	1.9	1.6	3.4	73	70	143	40
3007	543	0.43	2.3	1.9	2.1	4.1	70	68	138	50
3008	505	0.44	2.3	1.6	1.3	2.9	66	65	130	46
3009	545	0.38	2.5	2.1	2.1	4.3	72	72	144	56
3010	512	0.42	2.1	2.1	2.2	4.3	77	73	150	36
Mean	520	0.43	2.5	2.3	2.1	4.4	72	70	142	49
S.D.	27	0.03	0.3	0.7	0.7	1.3	5	5	10	9
S.E.	8	0.01	0.1	0.2	0.2	0.4	2	1	3	3
n	10	10	10	10	10	10	10	10	10	10

Sa.G. : Salivary gland

Appendix 9 - 8 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual relative organ weight Stage : Week 13
 Sex : Male Test Article : 4-ethenyl-2-methoxyphenol Dose : 300 mg/kg

Animal No.	Heart g/100g	Lung g/100g	Liver g/100g	Spleen g/100g	Kidney-R g/100g	Kidney-L g/100g	Kidney-RL g/100g	Adrenal-R mg/100g	Adrenal-L mg/100g	Adrenal-RL mg/100g
3001	0.29	0.29	2.52	0.14	0.31	0.31	0.62	4	5	9
3002	0.28	0.28	2.59	0.13	0.32	0.34	0.65	5	5	10
3003	0.29	0.30	2.77	0.14	0.35	0.37	0.72	5	6	11
3004	0.28	0.28	2.43	0.13	0.33	0.36	0.68	5	5	10
3005	0.27	0.30	2.59	0.16	0.28	0.31	0.60	4	4	7
3006	0.28	0.28	2.55	0.14	0.27	0.29	0.56	4	5	9
3007	0.27	0.28	2.86	0.13	0.28	0.31	0.59	3	4	7
3008	0.26	0.29	2.65	0.14	0.30	0.30	0.59	4	4	8
3009	0.29	0.30	2.94	0.14	0.32	0.34	0.66	6	7	13
3010	0.31	0.30	2.35	0.13	0.32	0.34	0.66	5	6	10
Mean	0.28	0.29	2.63	0.14	0.31	0.33	0.63	5	5	9
S.D.	0.01	0.01	0.19	0.01	0.03	0.03	0.05	1	1	2
S.E.	0.00	0.00	0.06	0.00	0.01	0.01	0.02	0	0	1
n	10	10	10	10	10	10	10	10	10	10

Appendix 9 - 13 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual relative organ weight Stage : Week 13
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 0 mg/kg

Animal No.	F.B.W. g	Brain g/100g	Pituitary mg/100g	Thyroid-R mg/100g	Thyroid-L mg/100g	Thyroid-RL mg/100g	Sa.G.-R mg/100g	Sa.G.-L mg/100g	Sa.G.-RL mg/100g	Thymus mg/100g
1101	322	0.61	6.5	2.2	2.7	4.9	61	63	124	74
1102	276	0.75	6.1	2.0	2.9	4.9	80	78	159	116
1103	270	0.70	4.6	3.1	3.4	6.6	78	79	157	57
1104	286	0.69	6.5	2.7	2.7	5.4	78	80	158	92
1105	323	0.65	3.7	2.4	2.9	5.4	73	73	146	63
1106	317	0.68	4.7	3.6	3.6	7.2	72	69	141	85
1107	311	0.67	5.8	3.8	2.7	6.5	87	86	174	114
1108	282	0.70	5.4	2.8	2.4	5.2	80	84	164	53
1109	279	0.71	5.3	3.3	2.7	5.9	75	77	152	97
1110	292	0.69	6.0	4.6	3.0	7.7	74	73	148	71
Mean	296	0.69	5.5	3.1	2.9	6.0	76	76	152	82
S.D.	20	0.04	0.9	0.8	0.4	1.0	7	7	14	22
S.E.	6	0.01	0.3	0.3	0.1	0.3	2	2	4	7
n	10	10	10	10	10	10	10	10	10	10

Sa.G. : Salivary gland

Appendix 9 - 19 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual relative organ weight Stage : Week 13
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 300 mg/kg

Animal No.	F.B.W. g	Brain g/100g	Pituitary mg/100g	Thyroid-R mg/100g	Thyroid-L mg/100g	Thyroid-RL mg/100g	Sa.G.-R mg/100g	Sa.G.-L mg/100g	Sa.G.-RL mg/100g	Thymus mg/100g
3101	314	0.67	4.2	4.5	3.4	7.9	68	69	137	69
3102	274	0.74	6.7	3.2	2.9	6.1	83	77	160	86
3103	294	0.74	5.7	2.6	2.4	5.0	79	76	155	80
3104	258	0.75	5.1	4.1	7.0	11.2	86	90	176	67
3105	269	0.73	5.2	3.1	3.2	6.4	72	74	146	61
3106	289	0.69	6.1	3.3	3.0	6.3	85	84	169	111
3107	255	0.80	6.5	3.3	3.5	6.7	76	79	155	69
3108	306	0.66	5.4	4.4	3.6	8.0	72	80	152	73
3109	285	0.70	4.9	3.1	3.6	6.7	86	83	169	75
3110	291	0.69	5.4	4.5	3.4	7.9	74	72	145	89
Mean	284	0.72	5.5	3.6	3.6	7.2	78	78	156	78
S.D.	19	0.04	0.8	0.7	1.3	1.7	7	6	12	14
S.E.	6	0.01	0.2	0.2	0.4	0.5	2	2	4	5
n	10	10	10	10	10	10	10	10	10	10

Sa.G. : Salivary gland

Appendix 9 - 22 4-ethenyl-2-methoxyphenol: 90-day oral toxicity study in rats



Item : Individual relative organ weight Stage : Week 13
 Sex : Female Test Article : 4-ethenyl-2-methoxyphenol Dose : 1000 mg/kg

Animal No.	F.B.W. g	Brain g/100g	Pituitary mg/100g	Thyroid-R mg/100g	Thyroid-L mg/100g	Thyroid-RL mg/100g	Sa.G.-R mg/100g	Sa.G.-L mg/100g	Sa.G.-RL mg/100g	Thymus mg/100g
4101	265	0.74	6.7	3.3	2.2	5.5	78	78	156	65
4102	264	0.71	7.8	3.4	3.2	6.7	72	73	145	82
4103	269	0.72	5.6	3.4	3.7	7.1	81	82	162	63
4104	348	0.62	4.4	2.0	2.2	4.2	88	90	178	104
4105	224	0.79	5.9	4.2	3.3	7.5	80	80	160	77
4106	272	0.75	5.4	3.7	3.8	7.5	76	73	149	93
4107	276	0.74	4.9	1.6	1.8	3.4	85	89	174	87
4108	279	0.66	5.7	3.2	2.5	5.7	85	78	163	94
4109	249	0.78	6.3	3.5	2.8	6.3	80	80	160	47
4110	250	0.74	8.2	3.4	2.5	5.9	95	94	190	85
Mean	270	0.73	6.1	3.2	2.8	6.0	82	82	164	80
S.D.	32	0.05	1.2	0.8	0.7	1.4	7	7	14	17
S.E.	10	0.02	0.4	0.2	0.2	0.4	2	2	4	5
n	10	10	10	10	10	10	10	10	10	10

Sa.G. : Salivary gland

Appendix 10-1(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 1001 Male 0 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Epididymis Cell infiltration,interstitium: minimal, unilateral, lymphocytic

Liver Vacuolation,hepatocyte: minimal

Following tissues : Not remarkable

Adrenal, Aorta,thoracic, Bone marrow,femoral, Bone,sternal, Bone marrow,sternal
Cerebellum, Coagulating gland, Cerebrum, Esophagus, Eye
Bone,femoral(knee joint), Harderian gland, Heart, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Mammary gland,inguinal, Nasal cavity
Optic nerve, Parathyroid, Pancreas, Pituitary, Prostate
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Seminal vesicle
Spinal cord,thoracic, Testis, Thymus, Tongue, Trachea, Thyroid, Urinary bladder
Zymbal gland

Appendix 10-2(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 1002 Male 0 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Kidney Basophilia,tubule: minimal, bilateral

Liver Cell infiltration,focal: minimal, mononuclear
Vacuolation,hepatocyte: minimal

Lung(bronchus) Aggregation,alveolar macrophage: minimal

Urinary bladder Cell infiltration,submucosa: minimal, mononuclear

Following tissues : Not remarkable

Adrenal, Aorta, thoracic, Bone marrow, femoral, Bone, sternal, Bone marrow, sternal
Cerebellum, Coagulating gland, Cerebrum, Epididymis, Esophagus, Eye
Bone, femoral (knee joint), Harderian gland, Heart, Intestine, duodenum
Intestine, jejunum, Intestine, ileum (Peyer's patch), Intestine, cecum
Intestine, colon, Intestine, rectum, Lymph node, mesenteric
Lymph node, submandibular, Mammary gland, inguinal, Nasal cavity, Optic nerve
Parathyroid, Pancreas, Pituitary, Prostate, Salivary gland, submandibular
Salivary gland, sublingual, Skin, inguinal, Sciatic nerve, Spleen, Stomach
Skeletal muscle, femoral, Seminal vesicle, Spinal cord, thoracic, Testis, Thymus
Tongue, Trachea, Thyroid, Zymbal gland

Appendix 10-3(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 1003 Male 0 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear
Vacuolation,hepatocyte: minimal

Prostate Cell infiltration,interstitium: minimal, lymphocytic

Urinary bladder Cell infiltration,submucosa: minimal, mononuclear

Following tissues : Not remarkable

Adrenal, Aorta,thoracic, Bone marrow,femoral, Bone,sternal, Bone marrow,sternal
Cerebellum, Coagulating gland, Cerebrum, Epididymis, Esophagus, Eye
Bone,femoral(knee joint), Harderian gland, Heart, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Mammary gland,inguinal, Nasal cavity
Optic nerve, Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular
Salivary gland,sublingual, Skin,inguinal, Sciatic nerve, Spleen, Stomach
Skeletal muscle,femoral, Seminal vesicle, Spinal cord,thoracic, Testis, Thymus
Tongue, Trachea, Thyroid, Zymbal gland

Appendix 10-4(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 1004 Male 0 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear

Following tissues : Not remarkable

Adrenal, Aorta,thoracic, Bone marrow,femoral, Bone,sternal, Bone marrow,sternal
Cerebellum, Coagulating gland, Cerebrum, Epididymis, Esophagus, Eye
Bone,femoral(knee joint), Harderian gland, Heart, Intestine,duodenum
Intestine,jejenum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Mammary gland,inguinal, Nasal cavity
Optic nerve, Parathyroid, Pancreas, Pituitary, Prostate
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Seminal vesicle
Spinal cord,thoracic, Testis, Thymus, Tongue, Trachea, Thyroid, Urinary bladder
Zymbal gland

Appendix 10-5(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 1005 Male 0 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear
Vacuolation,hepatocyte: mild

Parathyroid No sample

Following tissues : Not remarkable

Adrenal, Aorta,thoracic, Bone marrow,femoral, Bone,sternal, Bone marrow,sternal
Cerebellum, Coagulating gland, Cerebrum, Epididymis, Esophagus, Eye
Bone,femoral(knee joint), Harderian gland, Heart, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Mammary gland,inguinal, Nasal cavity
Optic nerve, Pancreas, Pituitary, Prostate, Salivary gland,submandibular
Salivary gland,sublingual, Skin,inguinal, Sciatic nerve, Spleen, Stomach
Skeletal muscle,femoral, Seminal vesicle, Spinal cord,thoracic, Testis, Thymus
Tongue, Trachea, Thyroid, Urinary bladder, Zymbal gland

Appendix 10-6(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 1006 Male 0 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Kidney Basophilia,tubule: minimal, unilateral

Liver Cell infiltration,focal: minimal, mononuclear
Vacuolation,hepatocyte: mild

Following tissues : Not remarkable

Adrenal, Aorta,thoracic, Bone marrow,femoral, Bone,sternal, Bone marrow,sternal
Cerebellum, Coagulating gland, Cerebrum, Epididymis, Esophagus, Eye
Bone,femoral(knee joint), Harderian gland, Heart, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Mammary gland,inguinal, Nasal cavity
Optic nerve, Parathyroid, Pancreas, Pituitary, Prostate
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Seminal vesicle
Spinal cord,thoracic, Testis, Thymus, Tongue, Trachea, Thyroid, Urinary bladder
Zymbal gland

Appendix 10-7(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 1007 Male 0 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Kidney Basophilia,tubule: minimal, unilateral
Urinary cast,hyaline: minimal, unilateral

Liver Vacuolation,hepatocyte: mild

Prostate Cell infiltration,interstitium: minimal, lymphocytic

Following tissues : Not remarkable

Adrenal, Aorta,thoracic, Bone marrow,femoral, Bone,sternal, Bone marrow,sternal
Cerebellum, Coagulating gland, Cerebrum, Epididymis, Esophagus, Eye
Bone,femoral(knee joint), Harderian gland, Heart, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Mammary gland,inguinal, Nasal cavity
Optic nerve, Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular
Salivary gland,sublingual, Skin,inguinal, Sciatic nerve, Spleen, Stomach
Skeletal muscle,femoral, Seminal vesicle, Spinal cord,thoracic, Testis, Thymus
Tongue, Trachea, Thyroid, Urinary bladder, Zymbal gland

Appendix 10-8(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 1008 Male 0 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear
Vacuolation,hepatocyte: mild

Spleen Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Aorta,thoracic, Bone marrow,femoral, Bone,sternal, Bone marrow,sternal
Cerebellum, Coagulating gland, Cerebrum, Epididymis, Esophagus, Eye
Bone,femoral(knee joint), Harderian gland, Heart, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Mammary gland,inguinal, Nasal cavity
Optic nerve, Parathyroid, Pancreas, Pituitary, Prostate
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Stomach, Skeletal muscle,femoral, Seminal vesicle
Spinal cord,thoracic, Testis, Thymus, Tongue, Trachea, Thyroid, Urinary bladder
Zymbal gland

Appendix 10-9(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 1009 Male 0 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear
Vacuolation,hepatocyte: mild

Following tissues : Not remarkable

Adrenal, Aorta,thoracic, Bone marrow,femoral, Bone,sternal, Bone marrow,sternal
Cerebellum, Coagulating gland, Cerebrum, Epididymis, Esophagus, Eye
Bone,femoral(knee joint), Harderian gland, Heart, Intestine,duodenum
Intestine,jejenum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Mammary gland,inguinal, Nasal cavity
Optic nerve, Parathyroid, Pancreas, Pituitary, Prostate
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Seminal vesicle
Spinal cord,thoracic, Testis, Thymus, Tongue, Trachea, Thyroid, Urinary bladder
Zymbal gland

Appendix 10-10(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 1010 Male 0 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear
Vacuolation,hepatocyte: minimal

Prostate Cell infiltration,interstitium: minimal, lymphocytic

Following tissues : Not remarkable

Adrenal, Aorta,thoracic, Bone marrow,femoral, Bone,sternal, Bone marrow,sternal
Cerebellum, Coagulating gland, Cerebrum, Epididymis, Esophagus, Eye
Bone,femoral(knee joint), Harderian gland, Heart, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Mammary gland,inguinal, Nasal cavity
Optic nerve, Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular
Salivary gland,sublingual, Skin,inguinal, Sciatic nerve, Spleen, Stomach
Skeletal muscle,femoral, Seminal vesicle, Spinal cord,thoracic, Testis, Thymus
Tongue, Trachea, Thyroid, Urinary bladder, Zymbal gland

Appendix 10-11(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 2001 Male 100 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Vacuolation,hepatocyte: mild

Stomach Hyperplasia,squamous cell,forestomach: minimal
Hyperkeratosis,forestomach: minimal

Following tissues : Not remarkable

Nasal cavity

Appendix 10-12(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 2002 Male 100 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Vacuolation, hepatocyte: minimal

Following tissues : Not remarkable

Nasal cavity, Stomach

Appendix 10-13(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 2003 Male 100 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Vacuolation,hepatocyte: minimal

Stomach Hyperplasia,squamous cell,forestomach: minimal
Hyperkeratosis,forestomach: minimal

Following tissues : Not remarkable

Nasal cavity

Appendix 10-14(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 2004 Male 100 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear
Vacuolation,hepatocyte: minimal

Stomach Hyperplasia,squamous cell,forestomach: minimal
Hyperkeratosis,forestomach: minimal

Following tissues : Not remarkable

Nasal cavity

Appendix 10-15(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 2005 Male 100 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear
Vacuolation,hepatocyte: minimal

Following tissues : Not remarkable

Nasal cavity, Stomach

Appendix 10-16(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 2006 Male 100 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear

Stomach Hyperplasia,squamous cell,forestomach: minimal
Hyperkeratosis,forestomach: minimal

Following tissues : Not remarkable

Nasal cavity

Appendix 10-17(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 2007 Male 100 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear

Stomach Hyperplasia,squamous cell,forestomach: minimal
Hyperkeratosis,forestomach: minimal

Following tissues : Not remarkable

Nasal cavity

Appendix 10-18(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 2008 Male 100 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear
Vacuolation,hepatocyte: mild

Following tissues : Not remarkable

Nasal cavity, Stomach

Appendix 10-19(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 2009 Male 100 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear
Vacuolation,hepatocyte: minimal

Following tissues : Not remarkable

Nasal cavity, Stomach

Appendix 10-20(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 2010 Male 100 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear
Vacuolation,hepatocyte: minimal

Following tissues : Not remarkable

Nasal cavity, Stomach

Appendix 10-21(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 3001 Male 300 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear

Stomach Hyperplasia,squamous cell,forestomach: minimal
Hyperkeratosis,forestomach: minimal

Following tissues : Not remarkable

Nasal cavity

Appendix 10-22(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 3002 Male 300 mg/kg Day 92 End of administration period

Gross pathology:

Testis Small: mild, right

Other tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear
Vacuolation,hepatocyte: minimal

Stomach Hyperplasia,squamous cell,forestomach: minimal
Hyperkeratosis,forestomach: minimal

Following tissues : Not remarkable

Nasal cavity

Appendix 10-23(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 3003 Male 300 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear
Vacuolation,hepatocyte: minimal

Stomach Hyperplasia,squamous cell,forestomach: mild
Hyperkeratosis,forestomach: mild

Following tissues : Not remarkable

Nasal cavity

Appendix 10-24 (1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 3004 Male 300 mg/kg Day 92 End of administration period

Gross pathology:

Stomach Focus, dark red, glandular stomach: 1 present
2x1mm

Other tissues Not remarkable

Histopathology:

Liver Cell infiltration, focal: minimal, mononuclear
Vacuolation, hepatocyte: minimal

Stomach Hyperplasia, squamous cell, forestomach: mild
Hyperkeratosis, forestomach: mild

General Information Antemortem artifact:
dark red focus in the glandular stomach

Following tissues : Not remarkable

Nasal cavity

Appendix 10-25(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 3005 Male 300 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear

Stomach Hyperplasia,squamous cell,forestomach: minimal
Hyperkeratosis,forestomach: minimal

Following tissues : Not remarkable

Nasal cavity

Appendix 10-26(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 3006 Male 300 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Stomach Hyperplasia, squamous cell, forestomach: minimal
Hyperkeratosis, forestomach: mild

Following tissues : Not remarkable

Liver, Nasal cavity

Appendix 10-27(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 3007 Male 300 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Stomach Hyperplasia, squamous cell, forestomach: minimal
Hyperkeratosis, forestomach: minimal

Following tissues : Not remarkable

Liver, Nasal cavity

Appendix 10-28(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 3008 Male 300 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear
Vacuolation,hepatocyte: minimal

Stomach Hyperplasia,squamous cell,forestomach: mild
Hyperkeratosis,forestomach: minimal

Following tissues : Not remarkable

Nasal cavity

Appendix 10-29(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 3009 Male 300 mg/kg Day 92 End of administration period

Gross pathology:

Stomach Focus, dark red, glandular stomach: 1 present
1x2mm

Other tissues Not remarkable

Histopathology:

Liver Vacuolation, hepatocyte: minimal

Stomach Dilatation, gland, glandular stomach: minimal
Erosion/Ulcer, glandular stomach: minimal
Hyperplasia, squamous cell, forestomach: minimal
Hyperkeratosis, forestomach: minimal

Following tissues : Not remarkable

Nasal cavity

Appendix 10-30(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 3010 Male 300 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear

Stomach Hyperplasia,squamous cell,forestomach: minimal
Hyperkeratosis,forestomach: minimal

Following tissues : Not remarkable

Nasal cavity

Appendix 10-31(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 4001 Male 1000 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Epididymis	Cell infiltration,interstitium: minimal, unilateral, lymphocytic
Heart	Cell infiltration,myocardium: minimal, focal, mononuclear
Nasal cavity	Cell infiltration,respiratory epithelium: mild, inflammatory Level 1, Level 2, Level 3 Cell infiltration,olfactory epithelium: mild, inflammatory Level 2, Level 3 Atrophy,olfactory epithelium: mild, focal Level 2, Level 3 Disarrangement,respiratory epithelium: minimal with single cell necrosis, Level 1, Level 2, Level 3 Atrophy,olfactory gland: moderate Level 3
Prostate	Cell infiltration,interstitium: minimal, lymphocytic
Stomach	Dilatation,gland,glandular stomach: minimal Hyperplasia,squamous cell,forestomach: mild Hyperkeratosis,forestomach: mild
Testis	Atrophy,tubule: minimal, bilateral, focal

Following tissues : Not remarkable

Adrenal, Aorta,thoracic, Bone marrow,femoral, Bone,sternal, Bone marrow,sternal
Cerebellum, Coagulating gland, Cerebrum, Esophagus, Eye
Bone,femoral(knee joint), Harderian gland, Intestine,duodenum, Intestine,jejunum
Intestine,ileum(Peyer's patch), Intestine,cecum, Intestine,colon
Intestine,rectum, Kidney, Lymph node,mesenteric, Lymph node,submandibular, Liver
Lung(bronchus), Mammary gland,inguinal, Optic nerve, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Salivary gland,sublingual
Skin,inguinal, Sciatic nerve, Spleen, Skeletal muscle,femoral, Seminal vesicle
Spinal cord,thoracic, Thymus, Tongue, Trachea, Thyroid, Urinary bladder
Zymbal gland

Appendix 10-32(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 4002 Male 1000 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Nasal cavity Disarrangement, olfactory epithelium: minimal
with single cell necrosis,
Level 3
Atrophy, olfactory gland: moderate
Level 3

Prostate Cell infiltration, interstitium: minimal, lymphocytic

Stomach Hyperplasia, squamous cell, forestomach: moderate
Hyperkeratosis, forestomach: mild

Urinary bladder Cell infiltration, submucosa: minimal, mononuclear

Following tissues : Not remarkable

Adrenal, Aorta, thoracic, Bone marrow, femoral, Bone, sternal, Bone marrow, sternal
Cerebellum, Coagulating gland, Cerebrum, Epididymis, Esophagus, Eye
Bone, femoral (knee joint), Harderian gland, Heart, Intestine, duodenum
Intestine, jejunum, Intestine, ileum (Peyer's patch), Intestine, cecum
Intestine, colon, Intestine, rectum, Kidney, Lymph node, mesenteric
Lymph node, submandibular, Liver, Lung (bronchus), Mammary gland, inguinal
Optic nerve, Parathyroid, Pancreas, Pituitary, Salivary gland, submandibular
Salivary gland, sublingual, Skin, inguinal, Sciatic nerve, Spleen
Skeletal muscle, femoral, Seminal vesicle, Spinal cord, thoracic, Testis, Thymus
Tongue, Trachea, Thyroid, Zymbal gland

Appendix 10-33(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 4003 Male 1000 mg/kg Day 92 End of administration period

Gross pathology:

Stomach Focus,raised,forestomach: 1 present
10x10x10mm
Thickening,forestomach: mild

Other tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear

Nasal cavity Cyst,respiratory epithelium: minimal
Level 2
Cyst,olfactory epithelium: minimal
Level 3
Disarrangement,respiratory epithelium: minimal
Level 1
Dilatation,nasal gland: minimal
Level 2
Atrophy,olfactory gland: moderate
Level 3

Stomach Dilatation,gland,glandular stomach: minimal
Hyperplasia,squamous cell,forestomach: mild
Nodular hyperplasia,squamous cell,forestomach: moderate, focal
with hyperkeratosis, submucosal edema and submucosal
angiectasis
Hyperkeratosis,forestomach: moderate

Skeletal muscle,femoral Degeneration,muscle: minimal

Following tissues : Not remarkable

Adrenal, Aorta,thoracic, Bone marrow,femoral, Bone,sternal, Bone marrow,sternal
Cerebellum, Coagulating gland, Cerebrum, Epididymis, Esophagus, Eye
Bone,femoral(knee joint), Harderian gland, Heart, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Mammary gland,inguinal, Optic nerve
Parathyroid, Pancreas, Pituitary, Prostate, Salivary gland,submandibular
Salivary gland,sublingual, Skin,inguinal, Sciatic nerve, Spleen, Seminal vesicle
Spinal cord,thoracic, Testis, Thymus, Tongue, Trachea, Thyroid, Urinary bladder
Zymbal gland

Appendix 10-34 (1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 4004 Male 1000 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Kidney Basophilia,tubule: minimal, unilateral

Liver Cell infiltration,focal: minimal, mononuclear

Nasal cavity Disarrangement,respiratory epithelium: minimal
Level 1
Atrophy,olfactory gland: moderate
Level 3

Parathyroid No sample

Stomach Hyperplasia,squamous cell,forestomach: mild
Hyperkeratosis,forestomach: mild

Following tissues : Not remarkable

Adrenal, Aorta,thoracic, Bone marrow,femoral, Bone,sternal, Bone marrow,sternal
Cerebellum, Coagulating gland, Cerebrum, Epididymis, Esophagus, Eye
Bone,femoral(knee joint), Harderian gland, Heart, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Mammary gland,inguinal, Optic nerve
Pancreas, Pituitary, Prostate, Salivary gland,submandibular
Salivary gland,sublingual, Skin,inguinal, Sciatic nerve, Spleen
Skeletal muscle,femoral, Seminal vesicle, Spinal cord,thoracic, Testis, Thymus
Tongue, Trachea, Thyroid, Urinary bladder, Zymbal gland

Appendix 10-35(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 4005 Male 1000 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Nasal cavity Cell infiltration, olfactory epithelium: minimal, inflammatory
Level 3
Disarrangement, olfactory epithelium: minimal
with single cell necrosis,
Level 3
Hyperplasia, olfactory gland, focal: minimal
Level 3
Atrophy, olfactory gland: moderate
Level 3

Stomach Hyperplasia, squamous cell, forestomach: minimal
Hyperkeratosis, forestomach: minimal

Following tissues : Not remarkable

Adrenal, Aorta, thoracic, Bone marrow, femoral, Bone, sternal, Bone marrow, sternal
Cerebellum, Coagulating gland, Cerebrum, Epididymis, Esophagus, Eye
Bone, femoral (knee joint), Harderian gland, Heart, Intestine, duodenum
Intestine, jejunum, Intestine, ileum (Peyer's patch), Intestine, cecum
Intestine, colon, Intestine, rectum, Kidney, Lymph node, mesenteric
Lymph node, submandibular, Liver, Lung (bronchus), Mammary gland, inguinal
Optic nerve, Parathyroid, Pancreas, Pituitary, Prostate
Salivary gland, submandibular, Salivary gland, sublingual, Skin, inguinal
Sciatic nerve, Spleen, Skeletal muscle, femoral, Seminal vesicle
Spinal cord, thoracic, Testis, Thymus, Tongue, Trachea, Thyroid, Urinary bladder
Zymbal gland

Appendix 10-36(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 4006 Male 1000 mg/kg Day 92 End of administration period

Gross pathology:

Stomach Thickening,forestomach: mild

Other tissues Not remarkable

Histopathology:

Nasal cavity Atrophy,olfactory gland: moderate
Level 3

Prostate Cell infiltration,interstitium: minimal, lymphocytic

Spleen Hematopoiesis,extramedullary: minimal

Stomach Hyperplasia,squamous cell,forestomach: mild
Hyperkeratosis,forestomach: mild

Following tissues : Not remarkable

Adrenal, Aorta,thoracic, Bone marrow,femoral, Bone,sternal, Bone marrow,sternal
Cerebellum, Coagulating gland, Cerebrum, Epididymis, Esophagus, Eye
Bone,femoral(knee joint), Harderian gland, Heart, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Mammary gland,inguinal
Optic nerve, Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular
Salivary gland,sublingual, Skin,inguinal, Sciatic nerve, Skeletal muscle,femoral
Seminal vesicle, Spinal cord,thoracic, Testis, Thymus, Tongue, Trachea, Thyroid
Urinary bladder, Zymbal gland

Appendix 10-37(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 4007 Male 1000 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Harderian gland	Cell infiltration,interstitium: minimal, unilateral, lymphocytic
Liver	Cell infiltration,focal: minimal, mononuclear
Nasal cavity	Atrophy,olfactory epithelium: minimal, focal Level 3 Disarrangement,respiratory epithelium: minimal Level 1 Hyperplasia,olfactory gland,focal: minimal Level 3 Atrophy,olfactory gland: moderate Level 3
Stomach	Dilatation,gland,glandular stomach: minimal Hyperplasia,squamous cell,forestomach: mild Hyperkeratosis,forestomach: mild

Following tissues : Not remarkable

Adrenal, Aorta,thoracic, Bone marrow,femoral, Bone,sternal, Bone marrow,sternal
Cerebellum, Coagulating gland, Cerebrum, Epididymis, Esophagus, Eye
Bone,femoral(knee joint), Heart, Intestine,duodenum, Intestine,jejunum
Intestine,ileum(Peyer's patch), Intestine,cecum, Intestine,colon
Intestine,rectum, Kidney, Lymph node,mesenteric, Lymph node,submandibular
Lung(bronchus), Mammary gland,inguinal, Optic nerve, Parathyroid, Pancreas
Pituitary, Prostate, Salivary gland,submandibular, Salivary gland,sublingual
Skin,inguinal, Sciatic nerve, Spleen, Skeletal muscle,femoral, Seminal vesicle
Spinal cord,thoracic, Testis, Thymus, Tongue, Trachea, Thyroid, Urinary bladder
Zymbal gland

Appendix 10-38(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 4008 Male 1000 mg/kg Day 92 End of administration period

Gross pathology:

Stomach Thickening,forestomach: mild

Other tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear

Nasal cavity Disarrangement,respiratory epithelium: minimal
Level 1
Dilatation,nasal gland: minimal
Level 2
Atrophy,olfactory gland: moderate
Level 3

Stomach Hyperplasia,squamous cell,forestomach: mild
Hyperkeratosis,forestomach: mild

Following tissues : Not remarkable

Adrenal, Aorta,thoracic, Bone marrow,femoral, Bone,sternal, Bone marrow,sternal
Cerebellum, Coagulating gland, Cerebrum, Epididymis, Esophagus, Eye
Bone,femoral(knee joint), Harderian gland, Heart, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Mammary gland,inguinal, Optic nerve
Parathyroid, Pancreas, Pituitary, Prostate, Salivary gland,submandibular
Salivary gland,sublingual, Skin,inguinal, Sciatic nerve, Spleen
Skeletal muscle,femoral, Seminal vesicle, Spinal cord,thoracic, Testis, Thymus
Tongue, Trachea, Thyroid, Urinary bladder, Zymbal gland

Appendix 10-39(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 4009 Male 1000 mg/kg Day 92 End of administration period

Gross pathology:

Stomach Thickening,forestomach: mild

Other tissues Not remarkable

Histopathology:

Kidney Basophilia,tubule: minimal, unilateral

Liver Cell infiltration,focal: minimal, mononuclear

Nasal cavity Cyst,respiratory epithelium: minimal
Level 1
Cyst,olfactory epithelium: minimal
Level 3
Disarrangement,respiratory epithelium: minimal
Level 1
Disarrangement,olfactory epithelium: minimal
Level 3
Atrophy,olfactory gland: moderate
Level 3

Stomach Hyperplasia,squamous cell,forestomach: mild
Hyperkeratosis,forestomach: moderate

Following tissues : Not remarkable

Adrenal, Aorta,thoracic, Bone marrow,femoral, Bone,sternal, Bone marrow,sternal
Cerebellum, Coagulating gland, Cerebrum, Epididymis, Esophagus, Eye
Bone,femoral(knee joint), Harderian gland, Heart, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Mammary gland,inguinal, Optic nerve
Parathyroid, Pancreas, Pituitary, Prostate, Salivary gland,submandibular
Salivary gland,sublingual, Skin,inguinal, Sciatic nerve, Spleen
Skeletal muscle,femoral, Seminal vesicle, Spinal cord,thoracic, Testis, Thymus
Tongue, Trachea, Thyroid, Urinary bladder, Zymbal gland

Appendix 10-40(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 4010 Male 1000 mg/kg Day 92 End of administration period

Gross pathology:

Stomach Thickening,forestomach: mild

Other tissues Not remarkable

Histopathology:

Nasal cavity Disarrangement,olfactory epithelium: minimal
Level 3
Atrophy,olfactory gland: moderate
Level 3

Stomach Dilatation,gland,glandular stomach: minimal
Hyperplasia,squamous cell,forestomach: mild
Hyperkeratosis,forestomach: moderate

Following tissues : Not remarkable

Adrenal, Aorta,thoracic, Bone marrow,femoral, Bone,sternal, Bone marrow,sternal
Cerebellum, Coagulating gland, Cerebrum, Epididymis, Esophagus, Eye
Bone,femoral(knee joint), Harderian gland, Heart, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Mammary gland,inguinal
Optic nerve, Parathyroid, Pancreas, Pituitary, Prostate
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Skeletal muscle,femoral, Seminal vesicle
Spinal cord,thoracic, Testis, Thymus, Tongue, Trachea, Thyroid, Urinary bladder
Zymbal gland

Appendix 10-41(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 1101 Female 0 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Kidney Cyst: minimal, bilateral
with hyaline cast

Following tissues : Not remarkable

Adrenal, Aorta, thoracic, Bone marrow, femoral, Bone, sternal, Bone marrow, sternal
Cerebellum, Cerebrum, Esophagus, Eye, Bone, femoral (knee joint), Harderian gland
Heart, Intestine, duodenum, Intestine, jejunum, Intestine, ileum (Peyer's patch)
Intestine, cecum, Intestine, colon, Intestine, rectum, Lymph node, mesenteric
Lymph node, submandibular, Liver, Lung (bronchus), Mammary gland, inguinal
Nasal cavity, Oviduct, Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland, submandibular, Salivary gland, sublingual, Skin, inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle, femoral, Spinal cord, thoracic
Thymus, Tongue, Trachea, Thyroid, Urinary bladder, Uterus, Vagina, Zymbal gland

Appendix 10-42(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 1102 Female 0 mg/kg Day 92 End of administration period

Gross pathology:

Stomach Focus, dark red, glandular stomach: 1 present
2x1mm

Other tissues Not remarkable

Histopathology:

Liver Cell infiltration, focal: minimal, mononuclear

Skeletal muscle, femoral Degeneration, muscle: minimal

General Information Antemortem artifact:
dark red focus in the glandular stomach

Following tissues : Not remarkable

Adrenal, Aorta, thoracic, Bone marrow, femoral, Bone, sternal, Bone marrow, sternal
Cerebellum, Cerebrum, Esophagus, Eye, Bone, femoral (knee joint), Harderian gland
Heart, Intestine, duodenum, Intestine, jejunum, Intestine, ileum (Peyer's patch)
Intestine, cecum, Intestine, colon, Intestine, rectum, Kidney
Lymph node, mesenteric, Lymph node, submandibular, Lung (bronchus)
Mammary gland, inguinal, Nasal cavity, Oviduct, Optic nerve, Ovary, Parathyroid
Pancreas, Pituitary, Salivary gland, submandibular, Salivary gland, sublingual
Skin, inguinal, Sciatic nerve, Spleen, Stomach, Spinal cord, thoracic, Thymus
Tongue, Trachea, Thyroid, Urinary bladder, Uterus, Vagina, Zymbal gland

Appendix 10-43(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 1103 Female 0 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear
Vacuolation,hepatocyte: minimal

Lung(bronchus) Aggregation,alveolar macrophage: minimal

Pancreas Hemorrhage,focal: minimal
with mononuclear cell infiltration

Following tissues : Not remarkable

Adrenal, Aorta,thoracic, Bone marrow,femoral, Bone,sternal, Bone marrow,sternal
Cerebellum, Cerebrum, Esophagus, Eye, Bone,femoral(knee joint), Harderian gland
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Mammary gland,inguinal
Nasal cavity, Oviduct, Optic nerve, Ovary, Parathyroid, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Tongue, Trachea, Thyroid, Urinary bladder, Uterus, Vagina, Zymbal gland

Appendix 10-44 (1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 1104 Female 0 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear
Vacuolation,hepatocyte: minimal

Parathyroid No sample

Following tissues : Not remarkable

Adrenal, Aorta,thoracic, Bone marrow,femoral, Bone,sternal, Bone marrow,sternal
Cerebellum, Cerebrum, Esophagus, Eye, Bone,femoral(knee joint), Harderian gland
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus)
Mammary gland,inguinal, Nasal cavity, Oviduct, Optic nerve, Ovary, Pancreas
Pituitary, Salivary gland,submandibular, Salivary gland,sublingual
Skin,inguinal, Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral
Spinal cord,thoracic, Thymus, Tongue, Trachea, Thyroid, Urinary bladder, Uterus
Vagina, Zymbal gland

Appendix 10-45(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 1105 Female 0 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear

Following tissues : Not remarkable

Adrenal, Aorta,thoracic, Bone marrow,femoral, Bone,sternal, Bone marrow,sternal
Cerebellum, Cerebrum, Esophagus, Eye, Bone,femoral(knee joint), Harderian gland
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus)
Mammary gland,inguinal, Nasal cavity, Oviduct, Optic nerve, Ovary, Parathyroid
Pancreas, Pituitary, Salivary gland,submandibular, Salivary gland,sublingual
Skin,inguinal, Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral
Spinal cord,thoracic, Thymus, Tongue, Trachea, Thyroid, Urinary bladder, Uterus
Vagina, Zymbal gland

Appendix 10-46(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 1106 Female 0 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Vacuolation,hepatocyte: minimal

Following tissues : Not remarkable

Adrenal, Aorta,thoracic, Bone marrow,femoral, Bone,sternal, Bone marrow,sternal
Cerebellum, Cerebrum, Esophagus, Eye, Bone,femoral(knee joint), Harderian gland
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus)
Mammary gland,inguinal, Nasal cavity, Oviduct, Optic nerve, Ovary, Parathyroid
Pancreas, Pituitary, Salivary gland,submandibular, Salivary gland,sublingual
Skin,inguinal, Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral
Spinal cord,thoracic, Thymus, Tongue, Trachea, Thyroid, Urinary bladder, Uterus
Vagina, Zymbal gland

Appendix 10-47(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 1107 Female 0 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear
Vacuolation,hepatocyte: minimal

Following tissues : Not remarkable

Adrenal, Aorta,thoracic, Bone marrow,femoral, Bone,sternal, Bone marrow,sternal
Cerebellum, Cerebrum, Esophagus, Eye, Bone,femoral(knee joint), Harderian gland
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus)
Mammary gland,inguinal, Nasal cavity, Oviduct, Optic nerve, Ovary, Parathyroid
Pancreas, Pituitary, Salivary gland,submandibular, Salivary gland,sublingual
Skin,inguinal, Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral
Spinal cord,thoracic, Thymus, Tongue, Trachea, Thyroid, Urinary bladder, Uterus
Vagina, Zymbal gland

Appendix 10-48(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 1108 Female 0 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear
Vacuolation,hepatocyte: minimal

Following tissues : Not remarkable

Adrenal, Aorta,thoracic, Bone marrow,femoral, Bone,sternal, Bone marrow,sternal
Cerebellum, Cerebrum, Esophagus, Eye, Bone,femoral(knee joint), Harderian gland
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus)
Mammary gland,inguinal, Nasal cavity, Oviduct, Optic nerve, Ovary, Parathyroid
Pancreas, Pituitary, Salivary gland,submandibular, Salivary gland,sublingual
Skin,inguinal, Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral
Spinal cord,thoracic, Thymus, Tongue, Trachea, Thyroid, Urinary bladder, Uterus
Vagina, Zymbal gland

Appendix 10-49(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 1109 Female 0 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear
Vacuolation,hepatocyte: minimal

Following tissues : Not remarkable

Adrenal, Aorta,thoracic, Bone marrow,femoral, Bone,sternal, Bone marrow,sternal
Cerebellum, Cerebrum, Esophagus, Eye, Bone,femoral(knee joint), Harderian gland
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus)
Mammary gland,inguinal, Nasal cavity, Oviduct, Optic nerve, Ovary, Parathyroid
Pancreas, Pituitary, Salivary gland,submandibular, Salivary gland,sublingual
Skin,inguinal, Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral
Spinal cord,thoracic, Thymus, Tongue, Trachea, Thyroid, Urinary bladder, Uterus
Vagina, Zymbal gland

Appendix 10-50(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 1110 Female 0 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Ovary Atrophy: moderate, bilateral

Following tissues : Not remarkable

Adrenal, Aorta, thoracic, Bone marrow, femoral, Bone, sternal, Bone marrow, sternal
Cerebellum, Cerebrum, Esophagus, Eye, Bone, femoral (knee joint), Harderian gland
Heart, Intestine, duodenum, Intestine, jejunum, Intestine, ileum (Peyer's patch)
Intestine, cecum, Intestine, colon, Intestine, rectum, Kidney
Lymph node, mesenteric, Lymph node, submandibular, Liver, Lung (bronchus)
Mammary gland, inguinal, Nasal cavity, Oviduct, Optic nerve, Parathyroid
Pancreas, Pituitary, Salivary gland, submandibular, Salivary gland, sublingual
Skin, inguinal, Sciatic nerve, Spleen, Stomach, Skeletal muscle, femoral
Spinal cord, thoracic, Thymus, Tongue, Trachea, Thyroid, Urinary bladder, Uterus
Vagina, Zymbal gland

Appendix 10-51(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 2101 Female 100 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Vacuolation,hepatocyte: minimal

Stomach Hyperplasia,squamous cell,forestomach: minimal
Hyperkeratosis,forestomach: minimal

Following tissues : Not remarkable

Nasal cavity

Appendix 10-52(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 2102 Female 100 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear

Stomach Hyperplasia,squamous cell,forestomach: minimal
Hyperkeratosis,forestomach: minimal

Following tissues : Not remarkable

Nasal cavity

Appendix 10-53(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 2103 Female 100 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Liver, Nasal cavity, Stomach

Appendix 10-54(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 2104 Female 100 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear
Vacuolation,hepatocyte: minimal

Stomach Hyperplasia,squamous cell,forestomach: minimal
Hyperkeratosis,forestomach: minimal

Following tissues : Not remarkable

Nasal cavity

Appendix 10-55(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 2105 Female 100 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Stomach Hyperplasia, squamous cell, forestomach: minimal
Hyperkeratosis, forestomach: minimal

Following tissues : Not remarkable

Liver, Nasal cavity

Appendix 10-56(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 2106 Female 100 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear

Stomach Hyperplasia,squamous cell,forestomach: minimal
Hyperkeratosis,forestomach: minimal

Following tissues : Not remarkable

Nasal cavity

Appendix 10-57(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 2107 Female 100 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear

Stomach Hyperplasia,squamous cell,forestomach: minimal
Hyperkeratosis,forestomach: minimal

Following tissues : Not remarkable

Nasal cavity

Appendix 10-58(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 2108 Female 100 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear

Following tissues : Not remarkable

Nasal cavity, Stomach

Appendix 10-59(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 2109 Female 100 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Liver, Nasal cavity, Stomach

Appendix 10-60(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 2110 Female 100 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear
Vacuolation,hepatocyte: minimal

Stomach Hyperplasia,squamous cell,forestomach: minimal
Hyperkeratosis,forestomach: minimal

Following tissues : Not remarkable

Nasal cavity

Appendix 10-61(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 3101 Female 300 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear
Vacuolation,hepatocyte: minimal

Stomach Hyperplasia,squamous cell,forestomach: minimal
Hyperkeratosis,forestomach: minimal

Following tissues : Not remarkable

Nasal cavity

Appendix 10-62(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 3102 Female 300 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Stomach Hyperplasia, squamous cell, forestomach: minimal
Hyperkeratosis, forestomach: minimal

Following tissues : Not remarkable

Liver, Nasal cavity

Appendix 10-63(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 3103 Female 300 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear

Stomach Hyperplasia,squamous cell,forestomach: minimal
Hyperkeratosis,forestomach: minimal

Following tissues : Not remarkable

Nasal cavity

Appendix 10-64(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 3104 Female 300 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear

Stomach Hyperplasia,squamous cell,forestomach: minimal
Hyperkeratosis,forestomach: minimal

Following tissues : Not remarkable

Nasal cavity

Appendix 10-65(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 3105 Female 300 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Vacuolation,hepatocyte: minimal

Stomach Hyperplasia,squamous cell,forestomach: minimal
Hyperkeratosis,forestomach: minimal

Following tissues : Not remarkable

Nasal cavity

Appendix 10-66(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 3106 Female 300 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Vacuolation,hepatocyte: minimal

Stomach Hyperplasia,squamous cell,forestomach: mild
Hyperkeratosis,forestomach: mild

Following tissues : Not remarkable

Nasal cavity

Appendix 10-67(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 3107 Female 300 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Stomach Hyperplasia, squamous cell, forestomach: minimal
Hyperkeratosis, forestomach: minimal

Following tissues : Not remarkable

Liver, Nasal cavity

Appendix 10-68(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 3108 Female 300 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Liver, Nasal cavity, Stomach

Appendix 10-69(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 3109 Female 300 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Vacuolation,hepatocyte: minimal

Stomach Dilatation,gland,glandular stomach: minimal

Following tissues : Not remarkable

Nasal cavity

Appendix 10-70(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 3110 Female 300 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear

Stomach Hyperplasia,squamous cell,forestomach: minimal
Hyperkeratosis,forestomach: minimal

Following tissues : Not remarkable

Nasal cavity

Appendix 10-71(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 4101 Female 1000 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Nasal cavity Atrophy, olfactory epithelium: minimal, focal
Level 3
Disarrangement, respiratory epithelium: minimal
Level 1
Disarrangement, olfactory epithelium: minimal
Level 3
Atrophy, olfactory gland: moderate
Level 3

Stomach Dilatation, gland, glandular stomach: minimal
Hyperplasia, squamous cell, forestomach: minimal
Hyperkeratosis, forestomach: minimal

Following tissues : Not remarkable

Adrenal, Aorta, thoracic, Bone marrow, femoral, Bone, sternal, Bone marrow, sternal
Cerebellum, Cerebrum, Esophagus, Eye, Bone, femoral (knee joint), Harderian gland
Heart, Intestine, duodenum, Intestine, jejunum, Intestine, ileum (Peyer's patch)
Intestine, cecum, Intestine, colon, Intestine, rectum, Kidney
Lymph node, mesenteric, Lymph node, submandibular, Liver, Lung (bronchus)
Mammary gland, inguinal, Oviduct, Optic nerve, Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland, submandibular, Salivary gland, sublingual
Skin, inguinal, Sciatic nerve, Spleen, Skeletal muscle, femoral
Spinal cord, thoracic, Thymus, Tongue, Trachea, Thyroid, Urinary bladder, Uterus
Vagina, Zymbal gland

Appendix 10-72(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 4102 Female 1000 mg/kg Day 92 End of administration period

Gross pathology:

Uterus Cyst: 1 present
cervical, 3x2x2mm

Other tissues Not remarkable

Histopathology:

Nasal cavity Disarrangement, olfactory epithelium: minimal
with single cell necrosis,
Level 3
Hyperplasia, olfactory gland, focal: minimal
Level 3
Atrophy, olfactory gland: moderate
Level 3

Ovary Atrophy: mild, bilateral

Stomach Hyperplasia, squamous cell, forestomach: minimal
Hyperkeratosis, forestomach: minimal

Uterus Cyst, squamous: minimal, cervical

Following tissues : Not remarkable

Adrenal, Aorta, thoracic, Bone marrow, femoral, Bone, sternal, Bone marrow, sternal
Cerebellum, Cerebrum, Esophagus, Eye, Bone, femoral (knee joint), Harderian gland
Heart, Intestine, duodenum, Intestine, jejunum, Intestine, ileum (Peyer's patch)
Intestine, cecum, Intestine, colon, Intestine, rectum, Kidney
Lymph node, mesenteric, Lymph node, submandibular, Liver, Lung (bronchus)
Mammary gland, inguinal, Oviduct, Optic nerve, Parathyroid, Pancreas, Pituitary
Salivary gland, submandibular, Salivary gland, sublingual, Skin, inguinal
Sciatic nerve, Spleen, Skeletal muscle, femoral, Spinal cord, thoracic, Thymus
Tongue, Trachea, Thyroid, Urinary bladder, Vagina, Zymbal gland

Appendix 10-73(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 4103 Female 1000 mg/kg Day 92 End of administration period

Gross pathology:

Stomach Thickening,forestomach: mild

Other tissues Not remarkable

Histopathology:

Nasal cavity Cell infiltration,respiratory epithelium: minimal, inflammatory
Level 2
Cyst,olfactory epithelium: minimal
Level 2
Disarrangement,respiratory epithelium: minimal
with single cell necrosis,
Level 1, Level 2
Disarrangement,olfactory epithelium: minimal
with single cell necrosis,
Level 2
Atrophy,olfactory gland: moderate
Level 3

Stomach Hyperplasia,squamous cell,forestomach: mild
Hyperkeratosis,forestomach: moderate

Following tissues : Not remarkable

Adrenal, Aorta,thoracic, Bone marrow,femoral, Bone,sternal, Bone marrow,sternal
Cerebellum, Cerebrum, Esophagus, Eye, Bone,femoral(knee joint), Harderian gland
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Oviduct, Optic nerve, Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Salivary gland,sublingual
Skin,inguinal, Sciatic nerve, Spleen, Skeletal muscle,femoral
Spinal cord,thoracic, Thymus, Tongue, Trachea, Thyroid, Urinary bladder, Uterus
Vagina, Zymbal gland

Appendix 10-74 (1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 4104 Female 1000 mg/kg Day 92 End of administration period

Gross pathology:

Stomach Thickening, forestomach: mild

Other tissues Not remarkable

Histopathology:

Heart Cell infiltration, myocardium: minimal, focal, mononuclear

Liver Cell infiltration, focal: minimal, mononuclear

Nasal cavity Disarrangement, olfactory epithelium: minimal
Level 3
Atrophy, olfactory gland: mild
Level 3

Stomach Hyperplasia, squamous cell, forestomach: mild
Hyperkeratosis, forestomach: mild

Urinary bladder Cell infiltration, submucosa: minimal, mononuclear

Following tissues : Not remarkable

Adrenal, Aorta, thoracic, Bone marrow, femoral, Bone, sternal, Bone marrow, sternal
Cerebellum, Cerebrum, Esophagus, Eye, Bone, femoral (knee joint), Harderian gland
Intestine, duodenum, Intestine, jejunum, Intestine, ileum (Peyer's patch)
Intestine, cecum, Intestine, colon, Intestine, rectum, Kidney
Lymph node, mesenteric, Lymph node, submandibular, Lung (bronchus)
Mammary gland, inguinal, Oviduct, Optic nerve, Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland, submandibular, Salivary gland, sublingual
Skin, inguinal, Sciatic nerve, Spleen, Skeletal muscle, femoral
Spinal cord, thoracic, Thymus, Tongue, Trachea, Thyroid, Uterus, Vagina
Zymbal gland

Appendix 10-75(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 4105 Female 1000 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Kidney Cyst: minimal, unilateral

Liver Cell infiltration,focal: minimal, mononuclear

Nasal cavity Atrophy,olfactory gland: moderate
Level 3

Pituitary Aberrant craniopharyngeal tissue: minimal

Stomach Hyperplasia,squamous cell,forestomach: minimal
Hyperkeratosis,forestomach: minimal

Following tissues : Not remarkable

Adrenal, Aorta,thoracic, Bone marrow,femoral, Bone,sternal, Bone marrow,sternal
Cerebellum, Cerebrum, Esophagus, Eye, Bone,femoral(knee joint), Harderian gland
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Mammary gland,inguinal, Oviduct
Optic nerve, Ovary, Parathyroid, Pancreas, Salivary gland,submandibular
Salivary gland,sublingual, Skin,inguinal, Sciatic nerve, Spleen
Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Tongue, Trachea, Thyroid
Urinary bladder, Uterus, Vagina, Zymbal gland

Appendix 10-76 (1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 4106 Female 1000 mg/kg Day 92 End of administration period

Gross pathology:

Stomach Thickening, forestomach: mild

Other tissues Not remarkable

Histopathology:

Liver Cell infiltration, focal: minimal, mononuclear

Nasal cavity Cell infiltration, respiratory epithelium: minimal, inflammatory
Level 1
Disarrangement, olfactory epithelium: minimal
with single cell necrosis,
Level 2, Level 3
Hyperplasia, olfactory gland, focal: minimal
Level 3
Atrophy, olfactory gland: moderate
Level 3

Stomach Hyperplasia, squamous cell, forestomach: mild
Hyperkeratosis, forestomach: mild

Following tissues : Not remarkable

Adrenal, Aorta, thoracic, Bone marrow, femoral, Bone, sternal, Bone marrow, sternal
Cerebellum, Cerebrum, Esophagus, Eye, Bone, femoral (knee joint), Harderian gland
Heart, Intestine, duodenum, Intestine, jejunum, Intestine, ileum (Peyer's patch)
Intestine, cecum, Intestine, colon, Intestine, rectum, Kidney
Lymph node, mesenteric, Lymph node, submandibular, Lung (bronchus)
Mammary gland, inguinal, Oviduct, Optic nerve, Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland, submandibular, Salivary gland, sublingual
Skin, inguinal, Sciatic nerve, Spleen, Skeletal muscle, femoral
Spinal cord, thoracic, Thymus, Tongue, Trachea, Thyroid, Urinary bladder, Uterus
Vagina, Zymbal gland

Appendix 10-77(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 4107 Female 1000 mg/kg Day 92 End of administration period

Gross pathology:

Stomach Thickening,forestomach: mild

Other tissues Not remarkable

Histopathology:

Eye Dysplasia,retina: minimal, unilateral, focal

Liver Cell infiltration,focal: minimal, mononuclear

Nasal cavity Atrophy,olfactory gland: moderate
Level 3

Stomach Hyperplasia,squamous cell,forestomach: mild
Hyperkeratosis,forestomach: mild

Following tissues : Not remarkable

Adrenal, Aorta,thoracic, Bone marrow,femoral, Bone,sternal, Bone marrow,sternal
Cerebellum, Cerebrum, Esophagus, Bone,femoral(knee joint), Harderian gland
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus)
Mammary gland,inguinal, Oviduct, Optic nerve, Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Salivary gland,sublingual
Skin,inguinal, Sciatic nerve, Spleen, Skeletal muscle,femoral
Spinal cord,thoracic, Thymus, Tongue, Trachea, Thyroid, Urinary bladder, Uterus
Vagina, Zymbal gland

Appendix 10-78(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 4108 Female 1000 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Liver Cell infiltration,focal: minimal, mononuclear

Lung(bronchus) Aggregation,alveolar macrophage: minimal

Nasal cavity Cell infiltration,olfactory epithelium: minimal, inflammatory
Level 3
Atrophy,olfactory epithelium: mild, focal
Level 2, Level 3
Atrophy,olfactory gland: moderate
Level 3

Stomach Hyperplasia,squamous cell,forestomach: minimal
Hyperkeratosis,forestomach: minimal

Following tissues : Not remarkable

Adrenal, Aorta,thoracic, Bone marrow,femoral, Bone,sternal, Bone marrow,sternal
Cerebellum, Cerebrum, Esophagus, Eye, Bone,femoral(knee joint), Harderian gland
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Mammary gland,inguinal, Oviduct
Optic nerve, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Salivary gland,sublingual, Skin,inguinal
Sciatic nerve, Spleen, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus
Tongue, Trachea, Thyroid, Urinary bladder, Uterus, Vagina, Zymbal gland

Appendix 10-79(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 4109 Female 1000 mg/kg Day 92 End of administration period

Gross pathology:

Stomach Thickening,forestomach: mild

Other tissues Not remarkable

Histopathology:

Nasal cavity Atrophy,olfactory gland: moderate
Level 3

Stomach Hyperplasia,squamous cell,forestomach: mild
Hyperkeratosis,forestomach: mild

Thymus Hyperplasia,epithelium: minimal, focal

Following tissues : Not remarkable

Adrenal, Aorta,thoracic, Bone marrow,femoral, Bone,sternal, Bone marrow,sternal
Cerebellum, Cerebrum, Esophagus, Eye, Bone,femoral(knee joint), Harderian gland
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Oviduct, Optic nerve, Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Salivary gland,sublingual
Skin,inguinal, Sciatic nerve, Spleen, Skeletal muscle,femoral
Spinal cord,thoracic, Tongue, Trachea, Thyroid, Urinary bladder, Uterus, Vagina
Zymbal gland

Appendix 10-80(1/1) 4-ethenyl-2-methoxyphenol:90-day oral toxicity study in rats

Individual gross and histopathological findings

Animal No. 4110 Female 1000 mg/kg Day 92 End of administration period

Gross pathology:

All tissues Not remarkable

Histopathology:

Harderian gland Cell infiltration,interstitium: minimal, unilateral, lymphocytic

Nasal cavity Atrophy,olfactory gland: moderate
Level 3

Stomach Hyperplasia,squamous cell,forestomach: mild
Hyperkeratosis,forestomach: mild

Following tissues : Not remarkable

Adrenal, Aorta,thoracic, Bone marrow,femoral, Bone,sternal, Bone marrow,sternal
Cerebellum, Cerebrum, Esophagus, Eye, Bone,femoral(knee joint), Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Oviduct, Optic nerve, Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Salivary gland,sublingual
Skin,inguinal, Sciatic nerve, Spleen, Skeletal muscle,femoral
Spinal cord,thoracic, Thymus, Tongue, Trachea, Thyroid, Urinary bladder, Uterus
Vagina, Zymbal gland

信頼性保証書 (1/2)

試験番号 : [REDACTED]

試験表題 : 4-エテニル-2-メトキシフェノール:ラットを用いた90日間反復経口投与毒性試験

本試験は以下に示す基準に従って実施されたことを保証致します。

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

なお、調査は下記の通り実施し、報告致しました。

調査項目	調査担当者	調査日	試験責任者及び運営管理者への報告日
試験計画書	[REDACTED]	[REDACTED]	[REDACTED]
コンピュータプロトコール	[REDACTED]	[REDACTED]	[REDACTED]
動物入荷、検疫(入荷時)	[REDACTED]	[REDACTED]	[REDACTED]
被験液の調製・被験物質の保存	[REDACTED]	[REDACTED]	[REDACTED]
被験液の濃度確認	[REDACTED]	[REDACTED]	[REDACTED]
検疫(検疫終了)・馴化	[REDACTED]	[REDACTED]	[REDACTED]
眼科学検査	[REDACTED]	[REDACTED]	[REDACTED]
群分け	[REDACTED]	[REDACTED]	[REDACTED]
体重・摂餌量測定、投与・一般状態の観察	[REDACTED]	[REDACTED]	[REDACTED]
尿検査	[REDACTED]	[REDACTED]	[REDACTED]
血液学検査	[REDACTED]	[REDACTED]	[REDACTED]
血液化学検査	[REDACTED]	[REDACTED]	[REDACTED]
採血、剖検	[REDACTED]	[REDACTED]	[REDACTED]
病理組織学検査(切り出し)	[REDACTED]	[REDACTED]	[REDACTED]
被験物質の安定性測定	[REDACTED]	[REDACTED]	[REDACTED]



信頼性保証書 (2/2)

調査項目	調査担当者	調査日	試験責任者及び運営 管理者への報告日
病理組織学検査 (包埋)			
病理組織学検査 (薄切)			
病理組織学検査 (染色)			
最終報告書草案、生データ			
改善確認			
試験計画書変更書 (1)			
最終報告書			