

—最終報告書—

表 題:ポリオキシエチレン p-ノニルフェニルエーテルのラットにおける 28 日間反復経口投  
与毒性試験および 14 日間回復性試験

試験番号:SBL 79-02

当該資料は原本の正式な複写で  
あり, 原本と相違ないことを保証い  
たします。

00/年 3 月 30 日

試験施設

:株式会社 新日本科学 安全性研究所

鹿児島県鹿児島郡吉田町宮之浦 2438 番地(〒891-1394)

電話(099)294-2600, ファクシミリ(099)294-3619

:株式会社 新日本科学 安全性研究所 薬物代謝分析センター

和歌山県海南市南赤坂 16-1(〒642-0017)

電話(073)483-8881, ファクシミリ(073)483-7377

最終報告書の作成

表 題 : ポリオキシエチレン p-ノニルフェニルエーテルのラットにおける 28 日間反  
復経口投与毒性試験および 14 日間回復性試験

試験番号 : SBL 79-02

本試験の最終報告書は, 私の責任の下に作成しました.




2001年 3月 30日

本試験の各検査報告書は, 私達の責任の下に作成しました.



2001年 3月 30日



3月 30日

## 陳 述 書

表 題 : ポリオキシエチレン p-ノニルフェニルエーテルのラットにおける 28 日間反復経口投与毒性試験および 14 日間回復性試験

試験番号 : SBL 79-02

本試験は, OECD Principles of Good Laboratory Practice (revision in 1997) および OECD Guidelines for Testing of Chemicals 407 (Repeated Dose 28-day Oral Toxicity Study in Rodents, Adopted: 27th July 1995) に準拠して実施し, また, 最終報告書は試験の方法を正確に記載し, 生データを正確に反映したものに相違ありません.

試験責任者

(所属) 株式会社 新日本科学 安全性研究所



2000/年 3 月 30 日

## QAU 陳述書

表 題 : ポリオキシエチレンp-ノニルフェニルエーテルのラットにおける28日間  
反復経口投与毒性試験および14日間回復性試験

試験番号 : SBL 79-02

本試験は、OECD Principles of Good Laboratory Practice (revision in 1997) および OECD Guidelines for Testing of Chemicals 407 (Repeated Dose 28-day Oral Toxicity Study in Rodents, Adopted: 27th July 1995) に準拠して実施され、また、最終報告書は試験の方法を正確に記載し、生データを正確に反映したものに相違ありません。

| 査察項目                | 査察実施日                       | 試験責任者<br>への報告日 | 運営管理者<br>への報告日 |
|---------------------|-----------------------------|----------------|----------------|
| 試験計画書               | 2000年11月14日                 | 2000年11月14日    | 2000年11月14日    |
| 試験スケジュール            | 2000年11月14日                 | 2000年11月22日    | 2000年11月22日    |
| 試験計画書変更確認書(No. 1)   | 2000年11月22日                 | 2000年11月22日    | 2000年11月22日    |
| 試験スケジュール            | 2000年11月22日                 | 2000年11月22日    | 2000年11月22日    |
| 被験物質保管状態            | 2000年11月23日                 | 2000年12月1日     | 2000年12月1日     |
| 被験物質の調製             | 2000年11月23日                 | 2000年12月1日     | 2000年12月1日     |
| 調製液の濃度測定            | 2000年11月24日                 | 2000年12月1日     | 2000年12月1日     |
| 試験室                 | 2000年11月25日                 | 2000年12月1日     | 2000年12月1日     |
| 動物の飼育管理             | 2000年11月25日                 | 2000年12月1日     | 2000年12月1日     |
| 試験動物                | 2000年11月25日                 | 2000年12月1日     | 2000年12月1日     |
| 投与                  | 2000年11月25日                 | 2000年12月1日     | 2000年12月1日     |
| 一般状態観察              | 2000年11月25日                 | 2000年12月1日     | 2000年12月1日     |
| 行動薬理学的側面からの<br>行動観察 | 2000年11月25日                 | 2000年12月1日     | 2000年12月1日     |
| 摂餌量測定               | 2000年12月1日                  | 2000年12月1日     | 2000年12月1日     |
| 体重測定                | 2000年12月1日                  | 2000年12月1日     | 2000年12月1日     |
| 尿検査                 | 2000年12月20日                 | 2000年12月25日    | 2000年12月25日    |
| 眼科的検査               | 2000年12月21日                 | 2000年12月25日    | 2000年12月25日    |
| 血液学的検査              | 2000年12月23日                 | 2000年12月25日    | 2000年12月25日    |
| 血液生化学的検査            | 2000年12月23日、<br>2000年12月24日 | 2000年12月25日    | 2000年12月25日    |
| 剖検                  | 2000年12月23日                 | 2000年12月25日    | 2000年12月25日    |
| 器官重量測定              | 2000年12月23日                 | 2000年12月25日    | 2000年12月25日    |
| 剖検                  | 2001年1月6日                   | 2001年1月9日      | 2001年1月9日      |
| 器官重量測定              | 2001年1月6日                   | 2001年1月9日      | 2001年1月9日      |

SBL 79-02

| 査察項目              | 査察実施日                              | 試験責任者<br>への報告日  | 運営管理者<br>への報告日  |
|-------------------|------------------------------------|-----------------|-----------------|
| 試験計画書変更確認書(No. 2) | 2001 年 1 月 23 日                    | 2001 年 1 月 23 日 | 2001 年 1 月 23 日 |
| 病理組織学的検査          | 2001 年 2 月 13 日                    | 2001 年 2 月 16 日 | 2001 年 2 月 16 日 |
| 試験計画書変更確認書(No. 3) | 2001 年 2 月 27 日                    | 2001 年 2 月 27 日 | 2001 年 2 月 27 日 |
| 書類・生データ           | 2001 年 3 月 9 日,<br>2001 年 3 月 12 日 | 2001 年 3 月 12 日 | 2001 年 3 月 19 日 |
| 最終報告書草案           | 2001 年 3 月 9 日,<br>2001 年 3 月 12 日 | 2001 年 3 月 12 日 | 2001 年 3 月 19 日 |
| 最終報告書草案           | 2001 年 3 月 14 日                    | 2001 年 3 月 14 日 | 2001 年 3 月 19 日 |
| 試験計画書逸脱書(No. 1)   | 2001 年 3 月 29 日                    | 2001 年 3 月 29 日 | 2001 年 3 月 29 日 |
| 最終報告書             | 2001 年 3 月 30 日                    | 2001 年 3 月 30 日 | 2001 年 3 月 30 日 |

QAU 責任者  
(所属)株式会社新日本科学

2001 年 3 月 30 日

試験責任者, その他の試験に従事した研究者全員の氏名および業務分担

・試験責任者

〒891-1394 鹿児島県鹿児島郡吉田町宮之浦 2438 番地

・最終報告書の作成

〒891-1394 鹿児島県鹿児島郡吉田町宮之浦 2438 番地

・検疫

・被験物質の調製および分析

・投与

・一般状態観察

・行動薬理学的側面からの

行動観察

・摂餌量測定

・体重測定

・眼科的検査

・尿検査

・血液学的検査

・血液生化学的検査

・剖検

・器官重量測定

・病理組織学的検査

・統計解析

記録, 資料, 試料および標本の保存場所

株式会社新日本科学内のデータ資料室(記録および資料), 試験物質保管庫  
(保存用被験物質)および器官保管室(標本)

## 目 次

|   | 頁  |
|---|----|
| 要 約 .....   | 1  |
| 緒 言 .....   | 2  |
| 材料および方法 .....   | 3  |
| 1. 被験物質およびその調製法 .....                                   | 3  |
| 2. 試験動物および飼育条件 .....                                    | 3  |
| 3. 投与量の設定および投与方法 .....                                  | 4  |
| 4. 群構成 .....  | 5  |
| 5. 観察および検査項目 .....                                      | 5  |
| 1) 一般状態 .....   | 5  |
| 2) 行動薬理学的側面からの行動観察 .....                                | 5  |
| 3) 摂餌量 .....  | 6  |
| 4) 体重 .....   | 6  |
| 5) 眼科的検査 .....  | 6  |
| 6) 尿検査 .....  | 7  |
| 7) 血液学的検査 .....   | 7  |
| 8) 血液生化学的検査 .....                                       | 8  |
| 9) 剖検 .....   | 9  |
| 10) 器官重量(絶対および相対重量) .....                               | 9  |
| 11) 病理組織学的検査 .....                                      | 9  |
| 6. 統計学的手法 .....   | 10 |
| 7. 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および試験計画書に<br>従わなかったこと ..... | 10 |
| 結 果 .....   | 11 |
| 1. 一般状態 .....   | 11 |
| 2. 行動薬理学的側面からの行動観察 .....                                | 11 |
| 3. 摂餌量 .....  | 11 |
| 4. 体重 .....   | 11 |



|                   |      |
|-------------------|------|
| 5. 眼科的検査.....     | 11   |
| 6. 尿検査.....       | 11   |
| 7. 血液学的検査.....    | 12   |
| 8. 血液生化学的検査.....  | 12   |
| 9. 剖検.....        | 12   |
| 10. 器官重量.....     | 13   |
| 11. 病理組織学的検査..... | 13   |
| 考 察.....          | 15   |
| 文 献.....          | 17   |
| 別紙                | 1～3  |
| Figs.             | 1, 2 |
| Tables            | 1～11 |
| Appendices        | 1～11 |

## 要 約

ポリオキシエチレン p-ノニルフェニルエーテルの 0(対照), 20, 200 および 1000 mg/kg を各群雌雄各 5 例の Crj:CD(SD)IGS ラットに 1 日 1 回 28 日間反復経口投与し, さらに, 0(対照) および 1000 mg/kg 群にそれぞれ雌雄各 5 例の 2 週間回復試験例を設けて, その毒性と回復性を調べるとともに NOEL(no-observed-effect level)を求めた. 対照群には媒体の注射用水を被験物質群と同様の方法で投与した.

1. 投与および回復期間中, いずれの群においても死亡はみられず, 一般状態観察および行動薬理学的側面からの行動観察においても異常はみられなかった.
2. 摂餌量, 体重, 眼科的検査, 尿検査, 血液学的検査, 血液生化学的検査, 剖検, 器官重量および病理組織学的検査では, いずれの検査時期においても被験物質投与に起因した変化はみられなかった.

以上の結果, 本試験条件下では一般に反復投与毒性試験の投与量の上限とされる 1000 mg/kg を投与しても被験物質投与に起因する変化がみられなかったことから, ポリオキシエチレン p-ノニルフェニルエーテルの NOEL は雌雄ともに 1000 mg/kg/日を超える量と結論した.

## 緒 言

本試験の目的は、ポリオキシエチレン p-ノニルフェニルエーテルをラットに 28 日間毎日 1 回経口投与し、さらに 14 日間回復性試験を実施して、その毒性について調べることである。本試験は、OECD Principles of Good Laboratory Practice (revision in 1997) および OECD Guidelines for Testing of Chemicals 407 (Repeated Dose 28-day Oral Toxicity Study in Rodents, Adopted: 27th July 1995) に準拠して実施した。

試験開始日: 2000 年 11 月 14 日

実験開始日: 2000 年 11 月 25 日

実験終了日: 2001 年 2 月 26 日

試験終了日: 2001 年 3 月 30 日

試験委託者: 経済産業省(旧通商産業省) 製品評価技術センター

化学物質安全管理センター

〒151-0066 東京都渋谷区西原 2-49-10

## 材料および方法

## 1. 被験物質およびその調製法

被験物質は、経済産業省(旧通商産業省)製品評価技術センター化学物質安全管理センターから2000年9月25日に提供を受けたポリオキシエチレン p-ノニルフェニルエーテル(商品名 [REDACTED])を使用した。ポリオキシエチレン p-ノニルフェニルエーテルは、CAS 番号 9016-45-9, 示性式  $C_9H_{19}(C_6H_4)O(CH_2CH_2O)_nH$  ( $n=28.8$ ), 分子量 1488, 純度 100 wt%, 融点  $29.0^{\circ}C$  の白色固体である。溶解性は、水およびイソプロパノールに可溶である。被験物質の安定性は、投与終了後に株式会社新日本科学で純度を測定し、投与期間中の安定性を確認した(Stability of the Test Article, Certificate No.:790210-3, 別紙 1)。被験物質は、株式会社新日本科学試験物質保管所内の温度  $20 \pm 4^{\circ}C$  に設定した常温室[受領日～返却日(2000年9月25日～2001年3月29日):温度  $18.0 \sim 24.0^{\circ}C$ ]に遮光下で気密容器内に保存した。なお、残余被験物質は2001年3月29日に保存用被験物質(約 1 g)を除き全て試験委託者に返却した。

被験物質の調製は、ポリオキシエチレン p-ノニルフェニルエーテルを秤量し、2, 20 および 100 mg/mL になるように注射用水(ロット番号 0G76, 0I77, 0J74, 株式会社大塚製薬工場)を加えて溶解した。調製は週 1 回以上行い、1 日分毎に分注した後、使用時まで株式会社新日本科学試験物質保管所内の温度  $20 \pm 4^{\circ}C$  に設定した常温室[初回調製日～最終投与日(2000年11月23日～2000年12月22日):温度  $20.3 \sim 23.9^{\circ}C$ ]に遮光下で保存した。

ポリオキシエチレン p-ノニルフェニルエーテルの 0.1 および 200 mg/mL 濃度の調製液は、室温、遮光下 7 日間安定であることが株式会社新日本科学で確認されている(Stability of the Test Article in the Dosing Preparation, Certificate No.:790210-2, 別紙 2)。また、投与開始日および最終週の投与液について HPLC を用いて株式会社新日本科学で確認した結果、いずれも目標濃度の  $\pm 5\%$  以内であることが確認された(Concentration of the Test Article in the Dosing Preparation, Certificate No.:7902-1, 7902-2, 別紙 3-1, 3-2)。

## 2. 試験動物および飼育条件

試験動物は、4 週齢の Crj:CD(SD)IGS ラット(日本チャールス・リバー株式会社生産)雌雄

各 33 匹を 2000 年 11 月 16 日に入手し、検収時に体重測定を行った。その後、9 日間の検疫馴化期間中に、全例について一般状態観察を毎日 1 回、体重測定を検疫馴化終了日に 1 回、また、摂餌量測定および眼科的検査を各 1 回行い、異常のみられなかった雌雄各 30 匹(群分け時体重:雄 132~169 g, 雌 121~138 g)を使用した。

試験動物は、温度  $22 \pm 2^{\circ}\text{C}$  (実測値:  $18.7 \sim 23.4^{\circ}\text{C}$ )、湿度  $50 \pm 10\%$  (実測値:  $40 \sim 68\%$ )、換気回数 15 回/時間、人工照明 1 日 12 時間(午前 6 時~午後 6 時)に設定した SPF 施設 95 号室内で、サスペンド式ステンレス製ケージ[ $32.5 \text{ cm (D)} \times 19.5 \text{ cm (W)} \times 18 \text{ cm (H)}$ ]に個別飼育した。なお、温湿度は SOP の許容範囲内であった。室内は毎日清掃し、ケージは 4 週間に 1 回、オートクレーブ滅菌処理( $121^{\circ}\text{C}$ , 30 分間)済みのものと交換した。飼料はコバルト 60 照射滅菌済みの固型飼料(CE-2, ロット番号 E2090, E2100, 日本クレア株式会社)を与え、飲水は水道法水質基準に適合した水を自動給水装置(Edstrom Industries, Inc.)で自由に摂取させた。ただし、代謝ケージによる尿採取時には絶食および絶水とし、剖検前にも 16 時間以上絶食させた。なお、飼料はロットごとに、飲水は定期的に分析した結果、いずれも問題のないことが確認されている。

### 3. 投与量の設定および投与方法

先に実施した 14 日間反復投与毒性試験(試験番号: SBL79-02-20, 投与量: 0, 30, 100, 300, 1000 mg/kg)において、100 mg/kg 以上の群の雄で用量に依存していないもののトリグリセライドの高値がみられたが、そのほかには被験物質投与に起因すると考えられる変化はみられなかった。従って、本試験の投与量は、高用量を 1000 mg/kg とし、以下公比 5 または 10 で 200 および 20 mg/kg に設定した。

投与経路は OECD Guidelines for Testing of Chemicals 407 に従い経口とした。投与回数および期間についても OECD Guidelines for Testing of Chemicals 407 に従い 1 日 1 回 4 週間(計 28 日)連日投与とした。投与は 2000 年 11 月 25 日から 2000 年 12 月 22 日の午前 9 時~正午、ただし、尿検査日は午後 3 時~4 時の間に行い、ラット用胃ゾンデを用いて 10 mL/kg の容量で強制経口投与した。対照群には注射用水を被験物質群と同様の方法で投与した。

#### 4. 群構成

群構成は、対照群 1 群、被験物質群 3 群の計 4 群とし、各群には雌雄各 5 匹を配分した。さらに、対照群および高用量群には回復性試験のためにそれぞれ雌雄各 5 匹を加えた。群分けは投与開始前日の 2000 年 11 月 24 日に各群の平均体重がほぼ均一になるよう、体重の層別無作為化によって行った。

各個体は耳パンチ法で、ケージはカラーケージカード(試験番号、群、投与量、性および動物番号記載)でそれぞれ識別した。

試験群の構成を次の表に示した。

| 群 | 試験物質                       | 投与量<br>(mg/kg/日) | 投与容量<br>(mL/kg/日) | 動物数(動物番号)     |               |
|---|----------------------------|------------------|-------------------|---------------|---------------|
|   |                            |                  |                   | 雄             | 雌             |
| 1 | 媒体                         | 0                | 10                | 5+5 * (1~10)  | 5+5 * (11~20) |
| 2 | ポリオキシエチレン<br>p-ノニルフェニルエーテル | 20               | 10                | 5 (21~25)     | 5 (26~30)     |
| 3 | ポリオキシエチレン<br>p-ノニルフェニルエーテル | 200              | 10                | 5 (31~35)     | 5 (36~40)     |
| 4 | ポリオキシエチレン<br>p-ノニルフェニルエーテル | 1000             | 10                | 5+5 * (41~50) | 5+5 * (51~60) |

\*: 回復試験例(動物番号: 1~5, 11~15, 41~45, 51~55)

#### 5. 観察および検査項目

投与開始日を投与 0 日、投与期間終了の翌日を回復 0 日、また、投与あるいは回復開始週を投与あるいは回復 1 週と起算した。なお、回復期間は 2 週間(14 日間)とした。

##### 1) 一般状態

投与期間中は毎日 3 回(投与前、投与後 1~2 時間、投与後 4~6 時間)、回復期間中は毎日 1 回および剖検日に 1 回、全例について動物の生死と併せて観察した。

##### 2) 行動薬理学的側面からの行動観察

投与 0 日目の投与前および投与後 2~4 時間、投与 27 日目の投与後 2~4 時間および回復 2 週に各 1 回、各群の雌雄とも動物番号の小さいほうから各 5 例について Irwin 法を参考にした方法で行動観察を行った。また、1 分間にみられた立ち上がり動作をカウントした。検査

項目を次に示した。

- 行動的側面 ; 認知力(警戒性, 視覚による位置認知, 受動性, 常同反応), 気分(身づくろい, 鳴啼, 落ち着きのなさ, 被刺激性の亢進, 恐怖), 運動性(反応性, 自発運動, 触反応, 疼痛反応), 立ち上がり動作
- 神経学的側面 ; 中枢興奮(驚愕反応, 挙尾反応, 振戦, 攣縮, 痙攣), 協調運動障害(体姿勢, 四肢の位置, よろめき歩行, 異常歩行, 正向反射), 筋緊張度(四肢筋緊張度, 握力, 軀幹筋緊張度, 腹筋緊張度), 反射(耳介反射, 角膜反射, 同側屈曲反射)
- 自律神経的側面 ; 眼徴候(瞳孔径, 眼裂, 眼球突出), 分泌徴候(排尿, 流涎), 一般徴候(もだえ反応, 立毛, 体温下降, 皮膚色, 心拍数, 呼吸数)

### 3) 摂餌量

投与開始前 1 回, 投与および回復期間中週 1 回, 全例について給餌量を電子天秤(FY-3000, 株式会社エー・アンド・デイ)で測定し, その翌日に残余量を測定して 1 日あたりの摂餌量を算出した。

### 4) 体重

投与開始前日に 1 回, 投与および回復期間中週 1 回および剖検日に 1 回, 全例について電子天秤(FY-3000, 株式会社エー・アンド・デイ)を用いて測定した。また, 測定時ごとの体重の増加量を求めた。

### 5) 眼科的検査

投与開始前, 投与 4 週目および回復 2 週目に各 1 回, 全例についてペンライトを用いて前眼部および中間透光体を詳細に観察した。また, 眼底カメラ(RC-2, 興和株式会社)を用いて眼底を検査した。なお, 中間透光体および眼底の検査時には散瞳剤(Mydrin<sup>®</sup>-P, ロット番号 MP0659, 参天製薬株式会社)を使用した。眼底に異常が認められなかったため写真撮影は実施しなかった。

## 6) 尿検査

投与 4 週(投与前)および回復 2 週に各 1 回, 全例について強制採尿法により新鮮尿を採取し, 肉眼的に尿の色を確認するとともに, 尿試験紙(マルティスティックス®, バイエル・三共株式会社)および自動尿分析器(Clinitek 200+, Miles Labs., Inc.)を用いて次の項目を測定した.

pH, 蛋白, 糖, ケトン体, ビリルビン, 潜血, ウロビリノーゲン(いずれも試験紙法)

新鮮尿の採取後, 各群の雌雄とも動物番号の小さい方から各 5 例について代謝ケージにより 4 時間の蓄尿を採取し, 尿量をメスシリンダーで, 比重を尿比重屈折計(ユリコーン-JE, 株式会社アタゴ)を用いてそれぞれ測定した. また, 遠心分離(1500 r.p.m., 5 分間, 多本架遠心機, KUBOTA KS-3000P, 株式会社久保田製作所)して得た沈渣を, Sternheimer - Malbin 染色して赤血球, 白血球, 結晶, 上皮細胞, 細菌, 尿円柱, 精子およびその他を鏡検した.

## 7) 血液学的検査

各剖検時に, 全例についてペントバルビタールナトリウム(東京化成工業株式会社)水溶液(6.48 mg/mL, 5 mL/kg)の腹腔内投与による麻酔下で, 後大静脈腹部から注射器を用いて 1 mL 採血し, EDTA-2K で抗凝固処理した. その後別途 3.8w/v%クエン酸ナトリウム溶液を入れた注射器で 1 mL 採血し, 遠心分離(3000 r.p.m., 15 分間, ユニバーサル冷却遠心機 5910, 5920, KUBOTA 5800, 株式会社久保田製作所)して血漿を得た.

EDTA-2K で抗凝固処理した血液については, 多項目自動血球計数装置(E-4000, シスメックス株式会社)を用いて次の項目を測定あるいは算出した.

赤血球数, 白血球数, 血小板数(いずれも電気抵抗検出方式)

ヘマトクリット値(パルス検出方式)

ヘモグロビン濃度(ラウリル硫酸ナトリウムヘモグロビン法)

MCV, MCH, MCHC(いずれも計算式により算出)

また, 血液細胞自動分析装置(MICROX HEG-120A, 株式会社オムロン)を用いて次の項目を測定した.

網状赤血球数(Brecher 法)

白血球百分率(Wright 染色法)



3.8 w/v%クエン酸ナトリウム溶液で抗凝固処理後遠心分離して得た血漿については、全自動血液凝固測定装置(CA-5000, シスメックス株式会社)を用いて次の項目を測定した。

プロトロンビン時間、活性化部分トロンボプラスチン時間(いずれも光散乱法)

#### 8) 血液生化学的検査

各剖検時に、全例について血液学的検査用に採血後、腹大動脈から注射器を用いて可能な限り採血し、室温で40～60分間静置した後、遠心分離(3000 r.p.m., 15分間, 多本架遠心機, KUBOTA KS-3000P, 株式会社久保田製作所)して得た血清について、自動分析装置(Clinalyzer RX-10, 日本電子株式会社)を用いて次の項目を測定した。

ASAT, ALAT(いずれもJSCC準拠処方, UV法)

ALP(p-ニトロフェニルリン酸基質法)

LDH(UV Rate 法)

コリンエステラーゼ(DTNB 法)

γ-GTP(包接 L-γ-グルタミル-p-ニトロアニリド基質法)

総ビリルビン(アルカリアゾビリルビン法)

総蛋白(ビウレット法)

アルブミン(BCG 法)

A/G 比(計算式により算出)

総コレステロール(COD-HDAOS 法)

トリグリセライド(GPO-HDAOS 法)

糖(G1cK・G-6-PDH 法)

尿素窒素(ウレアーゼ-GIDH 法)

クレアチニン(Jaffé 法)

無機リン(モリブデン酸直接法)

Ca(OCPC 法)

Na, K(いずれも電極法)

Cl(電量滴定法)

## 9) 剖検

全例について、最終投与あるいは回復期間終了の翌日(絶食 16～18 時間後)に体重測定し、ペントバルビタールナトリウム(東京化成工業株式会社)水溶液(6.48 mg/mL, 5 mL/kg)の腹腔内投与による麻酔下で検査用の血液を採取後、放血致死させ、器官および組織を観察した。なお、被験物質投与に起因したと考えられる変化がみられなかったため写真撮影は実施しなかった。

## 10) 器官重量(絶対および相対重量)

全例について、脳(小脳および脳幹を含む)、心臓、肝臓、腎臓(左右)、副腎(左右)、脾臓、胸腺、精巣(左右)、精巣上体(左右)および卵巣(左右)を電子天秤(ER-60A, 株式会社エー・アンド・デイ)を用いて測定するとともに、絶対重量および剖検日の体重から相対重量を算出した。

## 11) 病理組織学的検査

全例について、大脳、小脳、脳幹、下垂体、ハーダー腺\*、顎下リンパ節\*\*、甲状腺\*、上皮小体(可能な限り)\*、気管、肺(気管支を含む)\*、胸腺、心臓、骨髄および骨(大腿骨、胸骨：脱灰標本)、脊髄(胸部)、胃(前胃、腺胃)、小腸(十二指腸、空腸、回腸)、大腸(盲腸、結腸、直腸)、腸間膜リンパ節、肝臓、膀胱、脾臓、副腎\*、腎臓\*、精巣上体\*、精囊、前立腺、卵巣\*、子宮、膣および坐骨神経\*\*を10%中性緩衝ホルマリンで、眼球(視神経を含む)\*をホルムアルデヒド・グルタルアルデヒド混合液で、精巣\*をブアン液でそれぞれ固定し、真空パック後保存した。\*及び\*\*を付した器官および組織は左右両側を採取した。

対照群および高用量群の全例の上記器官および組織について、株式会社新日本科学安全性研究所で常法に従い切り出しされた組織を、株式会社新日本科学安全性研究所薬物代謝分析センターの毒性病理部和歌山グループに送付し、パラフィン包埋、薄切を行い、H.E.染色、封入および鏡検を行った。なお、上記器官および組織のうち、\*を付した器官および組織は左右両側を、\*\*を付した器官および組織は左側を検査した。被験物質に起因したと考えられる変化がみられなかったため、写真撮影は実施しなかった。

## 6. 統計学的手法

各群の摂餌量, 体重, 尿検査の定量データ, 血液学的検査, 血液生化学的検査, 器官重量(絶対および相対重量)のデータについては, まず, Bartlett 法により等分散性の検定を行い, 等分散の場合は, 一元配置法により分散分析を行った. その結果, 群間に有意性が認められた場合, Dunnett 法により対照群に対する被験物質各群の平均値の一对比較検定を行った. Bartlett 法により等分散性が認められない場合は順位変換を行い, Kruskal-Wallis の H 検定を行った. その結果, 有意性が認められた場合, Dunnett 型の平均順位の一对比較検定を行った. 定量データ以外の尿検査, 眼科的検査, 剖検および病理組織学的検査については, 評価段階付きのデータは Exact rank sum test, 評価段階なしのデータは Fisher 検定を対照群と被験物質各群の間で実施した. これらの検定および計算には COMPUTER (AlphaServer 1000, DEC)を用い, 有意水準は 5%とした. なお, 一般状態および行動薬理学的側面からの行動観察のデータについては検定は実施しなかった.

## 7. 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および試験計画書に従わなかったこと

試験計画書では, 行動薬理学的側面からの行動観察は検疫馴化期間中にも 1 回行うと記載されていたが, 投与 0 日目の投与前および投与後 2~4 時間, 投与 27 日目の投与後 2~4 時間および回復 2 週に各 1 回行い, 検疫馴化期間中には行わなかった. 検疫馴化期間中の検査は投与開始前の状態を確認することが目的であり, また, 2000 年 11 月 22 日付試験計画書変更確認書(No.1)に従い, 投与 0 日目の投与前に実施していることから試験成績への影響はないものと判断した.

なお, 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および上述以外の試験計画書に従わなかったことはなかった.

## 結 果

## 1. 一般状態 (Tables 1-1～1-4, Appendices 1-1, 1-2)

投与および回復期間中、いずれの群においても死亡はみられず、一般状態観察においても全例で異常はみられなかった。

## 2. 行動薬理学的側面からの行動観察 (Tables 2-1～2-16, Appendices 2-1～2-16)

投与 0 日の投与前および投与後 2～4 時間、投与 27 日の投与後 2～4 時間、ならびに回復 2 週の観察では、いずれの群においても全例で異常はみられなかった。

## 3. 摂餌量 (Fig. 1, Tables 3-1, 3-2, Appendices 3-1, 3-2)

1000 mg/kg 群では、回復 2 週に雌で摂餌量の低値がみられたが、個別値は対照群の個別値の範囲内であった。投与期間中は雌雄ともに異常はみられなかった。

200 mg/kg 群では、投与 2 週に雄で摂餌量の低値がみられた。

20 mg/kg 群では、雌雄ともに異常はみられなかった。

## 4. 体重 (Fig. 2, Tables 4-1～4-4, Appendices 4-1～4-4)

投与および回復期間中、いずれの群においても異常はみられなかった。

## 5. 眼科的検査 (Tables 5-1～5-4, Appendices 5-1～5-4)

投与 4 週および回復 2 週の検査では、いずれの群においても全例で異常はみられなかった。

## 6. 尿検査 (Tables 6-1～6-16, Appendices 6-1～6-12)

1000 および 200 mg/kg 群では、投与 4 週および回復 2 週の検査において雌雄ともに異常はみられなかった。

20 mg/kg 群では、投与 4 週の検査において雌で蛋白の高値がみられたが、個別値は背景値<sup>1)</sup>の範囲内であった。

## 7. 血液学的検査 (Tables 7-1～7-4, Appendices 7-1～7-8)

1000 mg/kg 群では、回復期間終了時の検査において雄でプロトロンビン時間の延長がみられたが、個別値は1例を除き、背景値<sup>1)</sup>の範囲内であった。投与期間終了時の検査においては雌雄ともに異常はみられなかった。

200 および 20 mg/kg 群では、投与期間終了時の検査において雌雄ともに異常はみられなかった。

## 8. 血液生化学的検査 (Tables 8-1～8-4, Appendices 8-1～8-8)

1000 mg/kg 群では、回復期間終了時の検査において雄でNaの高値がみられたが、個別値は背景値<sup>1)</sup>の範囲内であった。投与期間終了時の検査においては雌雄ともに異常はみられなかった。

200 mg/kg 群では、投与期間終了時の検査において雌雄ともに異常はみられなかった。

20 mg/kg 群では、投与期間終了時の検査において雌で糖の低値がみられたが、個別値は背景値<sup>1)</sup>の範囲内であった。

## 9. 剖検 (Tables 9-1～9-4, Appendices 9-1～9-4)

1000 mg/kg 群では、投与期間終了時の剖検において肺の赤色巣あるいは黒色巣が雄2例、肝臓の白色巣が雌2例、回復期間終了時の剖検において肺の黒色巣が雌1例、肝臓の白色巣が雄1例および雌2例、副腎の左右不対称が雄1例でみられた。

200 mg/kg 群では、投与期間終了時の剖検において肺の赤色巣が雄1例、肝臓の白色巣が雌雄各1例、腎臓の嚢胞が雌1例でみられた。

20 mg/kg 群では、投与期間終了時の剖検において肺の赤色巣が雄1例、肝臓の白色巣が雄1例、腎臓の嚢胞が雄1例でみられた。

対照群では、投与期間終了時の剖検において肺の赤色巣あるいは黒色巣が雄2例および雌1例、肝臓の白色巣が雌2例、回復期間終了時の剖検において肺の黒色巣が雄1例、肝臓の白色巣が雄2例および雌1例でみられた。

## 10. 器官重量 (Tables 10-1～10-8, Appendices 10-1～10-12)

1000 mg/kg 群では、回復期間終了時の測定において雌で副腎の絶対および相対重量の高値、脾臓および腎臓の絶対重量の低値がみられたが、これらの個別値はいずれも背景値<sup>1)</sup>の範囲内であった。投与期間終了時の測定においては雌雄ともに異常はみられなかった。

200 mg/kg 群では、投与期間終了時の測定において雄で胸腺の相対重量の低値がみられたが、個別値は背景値<sup>1)</sup>の範囲内であった。

20 mg/kg 群では、投与期間終了時の測定において雌雄ともに異常はみられなかった。

## 11. 病理組織学的検査 (Tables 11-1～11-9, Appendices 11-1～11-9)

1000 mg/kg 群では、投与期間終了時の検査において脾臓の髄外造血が雄 4 例および雌 1 例、顎下リンパ節の形質細胞過形成が雌雄各 1 例、肺の肺胞泡沫細胞集簇が雄 2 例、肝臓の門脈領域の肝細胞微細空胞が雌 1 例、単核細胞浸潤が雄 5 例および雌 4 例、腎臓の尿細管鉍質沈着が雌 3 例、尿細管好酸性小体が雄 4 例、尿細管の塩基性変化が雄 2 例および雌 3 例、拡張尿細管の尿円柱が雄 1 例、卵巢の単核細胞浸潤が雌 1 例、子宮の内腔拡張が雌 1 例、副腎の皮質嚢胞が雄 1 例、副腎の皮質細胞の限局性過形成が雄 2 例および雌 1 例、甲状腺の鰓嚢遺残が雄 2 例、大腿骨の骨膜への褐色色素が雄 2 例、回復期間終了時の検査において脾臓の髄外造血が雄 2 例、肺の骨化生が雌 1 例、肺胞泡沫細胞集簇が雌 2 例、限局性出血が雄 1 例、肺動脈鉍質沈着が雌雄各 1 例、肝臓の単核細胞浸潤が雄 3 例および雌 4 例、限局性壊死が雄 1 例、腎臓の尿細管好酸性小体が雄 5 例、尿細管の塩基性変化が雄 2 例、副腎の皮質細胞の限局性過形成が雌 1 例、前立腺の単核細胞浸潤が雄 1 例、甲状腺の異所性胸腺が雄 1 例、鰓嚢遺残が雄 1 例および雌 3 例、大腿骨の骨膜への褐色色素が雄 5 例および雌 4 例、骨膜の出血が雄 2 例でみられた。

対照群では、投与期間終了時の検査において心臓の限局性心筋変性が雌雄各 1 例、脾臓の髄外造血が雄 2 例、顎下リンパ節の形質細胞過形成が雄 1 例、肺の肺胞泡沫細胞集簇が雄 1 例、気管の粘膜単核細胞浸潤が雄 1 例、肝臓の門脈領域の肝細胞微細空胞が雌 3 例、単核細胞浸潤が雄 3 例、腎臓の尿細管鉍質沈着が雌雄各 2 例、尿細管の塩基性変化が雌 3 例、単核細胞浸潤が雄 2 例、精巣の萎縮が雄 1 例、精巣上体の片側性精子不在が雄 1 例、副腎の皮質細胞の限局性過形成が雌雄各 2 例、甲状腺の鰓嚢遺残が雄 2 例および雌 3 例、

大腿骨の骨膜への褐色色素が雄 1 例, 回復期間終了時の検査において心臓の単核細胞浸潤が雌 1 例, 脾臓の髄外造血が雄 1 例および雌 3 例, 肺の骨化生が雄 1 例, 肺胞泡沫細胞集簇が雄 2 例, 肺動脈鉍質沈着が雄 1 例, 肝臓の門脈領域の肝細胞微細空胞が雄 1 例, 単核細胞浸潤が雄 4 例および雌 5 例, 限局性壊死が雌 1 例, 腎臓の尿細管好酸性小体が雄 3 例, 尿細管の塩基性変化が雄 1 例, 尿細管鉍質沈着が雌 1 例, 副腎の皮質細胞の限局性過形成が雌 1 例, 甲状腺の異所性胸腺が雌 1 例, 鰓囊遺残が雄 3 例, 大腿骨の骨膜への褐色色素が雄 4 例および雌 5 例, 骨膜の出血が雄 2 例でみられた.



## 考 察

ポリオキシエチレン p-ノニルフェニルエーテルの 0(対照), 20, 200 および 1000 mg/kg を各群雌雄各 5 例の Crj:CD(SD)IGS ラットに 1 日 1 回 28 日間反復経口投与し, さらに, 0(対照) および 1000 mg/kg 群にそれぞれ雌雄各 5 例の 2 週間回復試験例を設けて, その毒性と回復性を調べるとともに NOEL(no-observed-effect level)を求めた. 対照群には媒体の注射用水を被験物質群と同様の方法で投与した.

投与および回復期間中, いずれの群においても死亡はみられず, 一般状態観察および行動薬理学的側面からの行動観察においても全例で異常はみられなかった.

摂餌量では, 投与 2 週に 200 mg/kg 群の雄で摂餌量の低値がみられたが, 一過性の用量に依存しない変化であることから, 被験物質投与に起因した変化ではないと判断した. また, 回復 2 週に 1000 mg/kg 群の雌でみられた摂餌量の低値は, 個別値が対照群の個別値の範囲内であり, 投与および回復期間を通して一定の傾向がみられないことから偶発的変化と判断した.

体重および眼科的検査では, いずれの群においても異常はみられなかった.

尿検査では, 投与 4 週の検査において 20 mg/kg 群の雌で蛋白の高値がみられたが, 個別値は背景値<sup>1)</sup>の範囲内であり, 用量に依存しない変化であることから, 被験物質投与に起因した変化ではないと判断した. 回復 2 週の検査においては異常はみられなかった.

血液学的検査では, 投与期間終了時の検査においていずれの群においても異常はみられなかった. 回復期間終了時の検査において 1000 mg/kg 群の雄でみられたプロトロンビン時間の延長は, 個別値が 1 例を除き背景値<sup>1)</sup>の範囲内であり, 投与期間終了時の検査でみられていない変化であることから, 偶発的変化と判断した.

血液生化学的検査では, 投与期間終了時の検査において 20 mg/kg 群の雌で糖の低値がみられたが, 個別値は背景値<sup>1)</sup>の範囲内であり, 用量に依存しない変化であることから, 被験物質投与に起因した変化ではないと判断した. 回復期間終了時の検査において 1000 mg/kg 群の雄でみられた Na の高値は, 個別値が背景値<sup>1)</sup>の範囲内であり, 投与期間終了時の検査でみられていない変化であることから, 偶発的変化と判断した.

剖検では, 投与あるいは回復期間終了時において被験物質群で肺の赤色巣あるいは黒色



巢, 肝臓の白色巢, 腎臓の嚢胞, 副腎の左右不対称がみられたが, 当該器官の病理組織学的検査で被験物質投与に起因した変化がみられず, 対照群にもみられる変化, 用量に依存しない変化, あるいは, 投与期間終了時にみられていない 1 例のみの変化であることから, いずれも偶発的变化と判断した。

器官重量では, 投与期間終了時の測定において 200 mg/kg 群の雄で胸腺の相対重量の低値がみられたが, 当該器官の病理組織学的検査で被験物質投与に起因した変化がみられず, 個別値は背景値<sup>1)</sup>の範囲内であり, 相対重量のみの変化であることから, 被験物質投与に起因した変化ではないと判断した。回復期間終了時の測定において 1000 mg/kg 群の雌でみられた副腎の絶対および相対重量の高値, 脾臓および腎臓の絶対重量の低値は, 当該器官の病理組織学的検査で被験物質投与に起因した変化がみられず, 個別値が背景値<sup>1)</sup>の範囲内であり, 投与期間終了時の検査でみられていない変化であること, あるいは, 絶対重量のみの変化であることから, いずれも偶発的变化と判断した。

病理組織学的検査では, 投与あるいは回復期間終了時において 1000 mg/kg 群で脾臓の髄外造血, 顎下リンパ節の形質細胞過形成, 肺の骨化生, 肺胞泡沫細胞集簇, 限局性出血, 肺動脈鉍質沈着, 肝臓の門脈領域の肝細胞微細空胞, 単核細胞浸潤, 限局性壊死, 腎臓の尿細管鉍質沈着, 尿細管好酸性小体, 尿細管の塩基性変化, 拡張尿細管の尿円柱, 前立腺の単核細胞浸潤, 卵巣の単核細胞浸潤, 子宮の内腔拡張, 副腎の皮質嚢胞, 皮質細胞の限局性過形成, 甲状腺の異所性胸腺, 鰓嚢遺残, 大腿骨の骨膜への褐色色素, 骨膜の出血がみられたが, 対照群あるいは背景データ<sup>1)</sup>にみられる変化, あるいは, 1 例のみの変化であることから, いずれも偶発的变化と判断した。

以上の結果, 本試験条件下では一般に反復投与毒性試験の投与量の上限とされる 1000 mg/kg を投与しても被験物質投与に起因する変化がみられなかったことから, ポリオキシエチレン p-ニルフェニルエーテルの NOEL は雌雄ともに 1000 mg/kg/日を超える量と結論した。

文 献

1. SNBL Control Background Data (Crj:CD(SD)IGS), Vol. 47, 株式会社新日本科学社内資料(2000)

## Stability of the Test Article

### (1) Experimental

Test Article (Lot No.) : Polyoxethylene *p*-nonylphenyl ether [REDACTED]  
Appearance : White solid  
Sampling Size : 20 mg  
Storage Conditions : Airtight container at room temperature under light protected conditions

### (2) Results

| Container               | Time Point   | Assay * |
|-------------------------|--------------|---------|
|                         |              | (%)     |
| Glass bottle<br>(amber) | Initial      | 99.26   |
|                         | End of Study | 99.14   |

\* % of total area (mean of 2 values).

Dates of analysis : October 10, 2000 and February 9, 2001

[REDACTED]

[REDACTED]

[REDACTED]

## Stability of the Test Article in the Dosing Preparation

## (1) Experimental

Test Article (Lot No.) : Polyoxethylene *p*-nonylphenyl ether [REDACTED]  
Vehicle : Water for injection  
Form : Solution  
Sampling Size : 2.5 mL

## (2) Results

| Storage Conditions      |                                    | Stability*               |       |
|-------------------------|------------------------------------|--------------------------|-------|
| Container               | Temperature and Duration           | Conc. of Analyte (mg/mL) |       |
|                         |                                    | 0.1                      | 200   |
| Glass bottle<br>(amber) | Initial                            | 100.0                    | 100.0 |
|                         | After 24 hours at room temperature | 101.1                    | 97.5  |
|                         | After 7 days at room temperature   | 102.4                    | 99.9  |

Remaining % (mean of 2 values). Acceptable range:  $100 \pm 5$  %

Data of analysis : October 10, 2000 - October 17, 2000

Analyst [REDACTED]

Analyst [REDACTED]

Superv [REDACTED]

(Respo [REDACTED])

(Shin Nippon Biomedical Laboratories, Ltd.)

試験結果報告書の内容に関するお問い合わせには応じかねますので御了承下さい。

## Concentration of the Test Article in the Dosing Preparation

## (1) Experimental

Test Article (Lot No.) : Polyoxyethylenc *p*-nonylphenyl ether [REDACTED]  
Vehicle : Water for injection  
Form : Solution  
Sampling Size : 1 mL

## (2) Results

| Date of Preparation | Date of Analysis  | Target Conc.<br>(mg/mL) | Found Conc.<br>(mg/mL) | Found/Target*<br>(%) |
|---------------------|-------------------|-------------------------|------------------------|----------------------|
| November 23, 2000   | November 24, 2000 | 2                       | 2.008                  | 100.4                |
|                     |                   | 20                      | 19.756                 | 98.8                 |
|                     |                   | 100                     | 98.720                 | 98.7                 |

Data are the mean values of 2 injections of 1 determination.

\*Acceptable range :  $100 \pm 5\%$ .

Analys [REDACTED]

Super [REDACTED]

(Respo [REDACTED])

(Shin Nippon Biomedical Laboratories, Ltd.)

試験結果報告書の内容に関するお問い合わせには応じかねますので御了承下さい。

## Concentration of the Test Article in the Dosing Preparation

### (1) Experimental

Test Article (Lot No.) : Polyoxyethylene *p*-nonylphenyl ether [REDACTED]  
Vehicle : Water for injection  
Form : Solution  
Sampling Size : 1 mL

### (2) Results

| Date of Preparation | Date of Analysis  | Target Conc. (mg/mL) | Found Conc. (mg/mL) | Found/Target* (%) |
|---------------------|-------------------|----------------------|---------------------|-------------------|
|                     |                   | 2                    | 2.006               | 100.3             |
| December 19, 2000   | December 20, 2000 | 20                   | 20.530              | 102.7             |
|                     |                   | 100                  | 100.955             | 101.0             |

Data are the mean values of 2 injections of 1 determination.

\*Acceptable range :  $100 \pm 5\%$ .

(Shin Nippon Biomedical Laboratories, Ltd.)

[様式 1]

ほ乳類を用いる 28 日間の反復投与毒性試験結果報告書

1. 一般的事項

|                             |   |                |                 |            |
|-----------------------------|---|----------------|-----------------|------------|
| 新規化学物質の名称<br>(IUPAC 命名法による) | ポリオキシエチレンp-ノニルフェニルエーテル  |                |                 |            |
| 別 名                         | —   | 物理化<br>的性<br>状 | 分 子 式           | —          |
|                             |   |                | 分 子 量           | 1488       |
| 構造式又は示性式                    | $C_9H_{19}(C_6H_4)O(CH_2CH_2O)_nH$<br>(n=28.8)  |                | 常温における性状        | 白色固体       |
| 試験に供した新規化学物質の純度             | 100 wt%<br>(ロット番号: <span style="background-color: black; color: black;">XXXXXXXXXX</span> ) |                | 安 定 性           | 常温, 遮光下で安定 |
|                             |   |                | 融 点             | 29.0°C     |
|                             |   |                | 沸 点             | —          |
|                             |   |                | 蒸 気 圧           | —          |
|                             |   |                | 分 配 係 数         | —          |
|                             |   |                | 溶 解 性           | —          |
| 不純物の名称及び濃度                  | —   |                | 溶 解 度           | —          |
|                             |   |                | 水               | 可溶         |
|                             |   |                | DMSO            | —          |
|                             |   |                | アセトン            | —          |
|                             |   |                | その他<br>イソプロパノール | 可溶         |

## 2. 急性毒性試験

| 試験 No. | 試験の種類<br>及び期間   | 動物種                 | 1 群当りの<br>動物数  | 投与経路 | 投与量<br>(mg/kg)                                 | LD50 値又は NOEL<br>(mg/kg)  | 実験場所          |
|--------|---|---------------------|----------------|------|--|---|---------------|
| 1      | 急性毒性試験<br><br>2000 年 10 月 12 日<br>～<br>2000 年 10 月 26 日             | ラット<br>Cj:CD(SD)IGS | 雄 5 匹<br>雌 5 匹 | 経口   | 2000<br>1414<br>1000<br>707<br>500             | 雄 LD50 2000<<br>雌 LD50 2000<  | 株式会社<br>新日本科学 |
| 2      | 投与量設定試験<br>(14 日間)<br><br>2000 年 10 月 31 日<br>～<br>2000 年 11 月 14 日 | ラット<br>Cj:CD(SD)IGS | 雄 3 匹<br>雌 3 匹 | 経口   | 1000<br><br>300<br><br>100<br><br>30<br>媒体対照群* | 血液生化学的検査:<br>トリグリセライド↓♂<br>血液生化学的検査:<br>トリグリセライド↓♂<br>血液生化学的検査:<br>トリグリセライド↓♂<br>—<br>—<br><br>雄 NOEL 30<br>雌 NOEL 1000<<br><br>〔観察項目〕<br>一般状態, 体重,<br>眼科的検査,<br>血液学的検査,<br>血液生化学的検査,<br>剖検, 器官重量 | 株式会社<br>新日本科学 |

\* 媒体: 注射用水



## 3. 28 日間反復投与毒性試験

| 被験物質投与期間           |             | 自平成 12 年 11 月 25 日  |              |   |            | 至平成 12 年 12 月 22 日                             |             |   |              |   |     |   |   |   |   |
|--------------------|-------------|---|--------------|---|------------|--|-------------|---|--------------|---|-----|---|---|---|---|
| 使用動物種・系統           |             | ラット, Crj:CD(SD)IGS  |              |   |            | 1 群当りの動物数                                      |             |   |              |   |     |   |   |   |   |
| 投 与 経 路            |             | 強制経口投与(媒体:注射用水)   |              |   |            | 雄: 5 匹 雌: 5 匹<br>(対照群および高用量群には回復例の雌雄各 5 匹を加えた) |             |   |              |   |     |   |   |   |   |
| 被験物質の純度<br>100 wt% | 投<br>与<br>量 | (mg/kg)   | 対照群<br>0     |   | 低用量群<br>20 |  | 中用量群<br>200 |   | 高用量群<br>1000 |   | 回復群 |   |   |   |   |
|                    |             |   | ♂            | ♀ | ♂          | ♀  | ♂           | ♀ | ♂            | ♀ | ♂   | ♀ | ♂ | ♀ |   |
| 死亡                 |             |   | —            | — | —          | —  | —           | — | —            | — | —   | — | — | — |   |
| 体重                 |             |   | —            | — | —          | —  | —           | — | —            | — | —   | — | — | — |   |
| 体重増加量              |             |   | —            | — | —          | —  | —           | — | —            | — | —   | — | — | — |   |
| 摂餌量                |             |   | —            | — | —          | —  | ▽           | — | —            | — | —   | — | — | ▽ |   |
| 一般症状               |             |   | —            | — | —          | —  | —           | — | —            | — | —   | — | — | — |   |
| 行動観察               |             |   | —            | — | —          | —  | —           | — | —            | — | —   | — | — | — |   |
| 眼科学的検査             |             |   | —            | — | —          | —  | —           | — | —            | — | —   | — | — | — |   |
| 血液形態学的検査           |             |   | —            | — | —          | —  | —           | — | —            | — | —   | — | — | — |   |
| 生化学的検査             |             |   | 糖            |   | —          | ▼  | —           | — | —            | — |     |   | — | — |   |
|                    |             |   | Na           |   | —          | —  | —           | — | —            | — |     |   | △ | — |   |
| 血液凝固系検査            |             |   | PT           |   | —          | —  | —           | — | —            | — |     |   | △ | — |   |
| 尿検査                |             |   | 蛋白           |   | —          | △  | —           | — | —            | — |     |   | — | — |   |
| 臓器重量(絶対重量)         |             |   | 副腎(両側)       |   | —          | —  | —           | — | —            | — |     |   | — | △ |   |
|                    |             |   | 脾臓           |   | —          | —  | —           | — | —            | — |     |   | — | ▽ |   |
|                    |             |   | 腎臓(左, 両側)    |   | —          | —  | —           | — | —            | — |     |   | — | ▽ |   |
| 臓器重量(相対重量)         |             |   | 胸腺           |   | —          | —  | ▽           | — | —            | — |     |   | — | — |   |
|                    |             |   | 副腎(左右)       |   | —          | —  | —           | — | —            | — |     |   | — | △ |   |
|                    |             |   | 副腎(両側)       |   | —          | —  | —           | — | —            | — |     |   | — | ▲ |   |
| 剖検所見               |             |   |              |   |            |  |             |   |              |   |     |   |   |   |   |
| 肺                  |             |   | 赤色果あるいは黒色果   | 2 | 1          | 1  | —           | 1 | —            | 2 | —   | 1 | — | — | 1 |
| 肝臓                 |             |   | 白色果          | — | 2          | 1  | —           | 1 | 1            | — | 2   | 2 | 1 | 1 | 2 |
| 腎臓                 |             |   | 嚢胞           | — | —          | 1  | —           | — | 1            | — | —   | — | — | — | — |
| 副腎                 |             |   | 左右不対称        | — | —          | —  | —           | — | —            | — | —   | — | 1 | — | — |
| 組織学的所見             |             |   |              |   |            |  |             |   |              |   |     |   |   |   |   |
| 心臓                 |             |   | 限局性心筋変性      | 1 | 1          | *  | *           | * | *            | — | —   | — | — | — | — |
|                    |             |   | 単核細胞浸潤       | — | —          | *  | *           | * | *            | — | —   | — | 1 | — | — |
| 脾臓                 |             |   | 髓外造血         | 2 | —          | *  | *           | * | *            | 4 | 1   | 1 | 3 | 2 | — |
| 顎下リンパ節             |             |   | 形質細胞過形成      | 1 | —          | *  | *           | * | *            | 1 | 1   | — | — | — | — |
| 肺                  |             |   | 肺胞泡沫細胞集簇     | 1 | —          | *  | *           | * | *            | 2 | —   | 2 | — | — | 2 |
|                    |             |   | 限局性出血        | — | —          | *  | *           | * | *            | — | —   | — | — | 1 | — |
|                    |             |   | 骨化生          | — | —          | *  | *           | * | *            | — | —   | 1 | — | — | 1 |
|                    |             |   | 肺動脈鉍質沈着      | — | —          | *  | *           | * | *            | — | —   | 1 | — | 1 | 1 |
| 気管                 |             |   | 粘膜単核細胞浸潤     | 1 | —          | *  | *           | * | *            | — | —   | — | — | — | — |
| 肝臓                 |             |   | 単核細胞浸潤       | 3 | —          | *  | *           | * | *            | 5 | 4   | 4 | 5 | 3 | 4 |
|                    |             |   | 門脈領域の肝細胞微細空胞 | — | 3          | *  | *           | * | *            | — | 1   | 1 | — | — | — |
|                    |             |   | 限局性壊死        | — | —          | *  | *           | * | *            | — | —   | — | 1 | 1 | — |
| 腎臓                 |             |   | 尿細管好酸性小体     | — | —          | *  | *           | * | *            | 4 | —   | 3 | — | 5 | — |
|                    |             |   | 尿細管鉍質沈着      | 2 | 2          | *  | *           | * | *            | — | 3   | — | 1 | — | — |
|                    |             |   | 尿細管の塩基性変化    | — | 3          | *  | *           | * | *            | 2 | 3   | 1 | — | 2 | — |
|                    |             |   | 拡張尿細管の尿円柱    | — | —          | *  | *           | * | *            | 1 | —   | — | — | — | — |
|                    |             |   | 単核細胞浸潤       | 2 | —          | *  | *           | * | *            | — | 2   | — | — | — | — |
| 精巣                 |             |   | 萎縮           | 1 | *          | *  | *           | * | *            | — | *   | — | * | — | * |
| 精巣上体               |             |   | 片側性精子不在      | 1 | *          | *  | *           | * | *            | — | *   | — | * | — | * |
| 前立腺                |             |   | 単核細胞浸潤       | — | —          | *  | *           | * | *            | — | *   | — | * | 1 | * |
| 卵巣                 |             |   | 単核細胞浸潤       | * | —          | *  | *           | * | *            | 1 | *   | — | * | — | — |
| 子宮                 |             |   | 内腔拡張         | * | —          | *  | *           | * | *            | 1 | *   | — | * | — | — |
| 副腎                 |             |   | 皮質嚢胞         | — | —          | *  | *           | * | *            | 1 | —   | — | — | — | — |
|                    |             |   | 皮質細胞の限局性過形成  | 2 | 2          | *  | *           | * | *            | 2 | 1   | — | 1 | — | 1 |
| 甲状腺                |             |   | 嚢嚢遺残         | 2 | 3          | *  | *           | * | *            | 2 | —   | 3 | — | 1 | 3 |
|                    |             |   | 異所性胸腺        | — | —          | *  | *           | * | *            | — | —   | — | 1 | 1 | — |
| 大腿骨                |             |   | 骨膜への褐色色素     | 1 | —          | *  | *           | * | *            | 2 | —   | 4 | 5 | 5 | 4 |
|                    |             |   | 骨膜の出血        | — | —          | *  | *           | * | *            | — | —   | 2 | — | 2 | — |
| NOEL(mg/kg)        |             | >1000   |              |   |            |  |             |   |              |   |     |   |   |   |   |
| NOEL の推定根拠とした変化    |             | 反復投与毒性試験の投与量の上限とされる1000 mg/kgを投与しても被験物質投与に起因する変化がみられなかったことから、ポリオキシエチレンp-ノニルフェニルエーテルのNOELは雌雄ともに1000 mg/kg/日を超える量と推定した。 |              |   |            |  |             |   |              |   |     |   |   |   |   |

\*: 検査せず

—: 異常(変化)なし

△: 対照群に比べ有意に増加(p&lt;0.05) ▲: 対照群に比べ有意に増加(p&lt;0.01)

▽: 対照群に比べ有意に減少(p&lt;0.05) ▼: 対照群に比べ有意に減少(p&lt;0.01)

試験結果報告書の内容に関するお問い合わせには応じかねますので御了承下さい。

4. その他

|                      |                   |                                   |
|----------------------|-------------------|-----------------------------------|
| 反復投与<br>毒性試験<br>実施機関 | 名 称               | 株式会社 新日本科学                        |
|                      | 所 在 地             | 〒 891-1394 鹿児島県鹿児島郡吉田町宮之浦 2438 番地 |
| 試験責任者                | 職 氏 名             |                                   |
| 試験実施年月日              | 平成 12 年 11 月 14 日 |                                   |

## REPEATED DOSE TOXICITY

### TEST SUBSTANCE

- **Identity:** Polyoxyethylene p-nonylphenylether (CAS No. 9016-45-9)
- **Remarks:** Source: Chemical Substances Safety Management Center  
National Institute of Technology and Evaluation Ministry of  
Economy, Trade and Industry. Purity: 100 wt%. Stability  
during use confirmed by high performance liquid  
chromatography.

### METHOD

- **Method/guideline:** OECD Guidelines for Testing of Chemicals 407
- **Test type:** Repeated Dose 28-day Oral Toxicity Study in Rodents
- **GLP:** Yes
- **Year:** 2000 to 2001
- **Species:** Rat
- **Strain:** Crj: CD (SD) IGS
- **Route of administration:** Oral (by gavage)
- **Doses/ concentration levels:** 0, 20, 200, 1000 mg/kg/day (in water for injection)
- **Sex:** Male & Female
- **Exposure period:** November 25, 2000 to December 22, 2000
- **Frequency of treatment:** Once daily, seven times weekly, for 28 consecutive days
- **Control group and treatment:** Concurrent vehicle
- **Post exposure observation period:** 14 Days
- **Statistical methods:** Food consumption, body weight, quantitative data from

urinalysis, hematology, blood chemistry and organ weight (absolute and relative) data were first analyzed for homogeneity of variance by Bartlett's test. When homogeneity of variance existed, a one way analysis of variance was applied. When significance was achieved, Dunnett's test was applied to compare the means between the treatment and control groups. When no homogeneity of variance existed by Bartlett's test, the order of the data was converted and analyzed by the Kruskal-Wallis H test. When the result was significant, a non-parametric Dunnett's test was applied to compare the mean ranks.

For non-quantitative data from urinalysis, ophthalmology, gross pathology and histopathology, gradeable data was analyzed by the Exact rank sum test, and non-gradeable values was analyzed by Fisher's exact test between the treatment and control groups.

The level of significance was set at 5%.

## REMARKS FIELD FOR TEST CONDITIONS

### • Test Subjects:

**Age at study initiation:** Five weeks

**Weight at study initiation:** Male; 132 to 169 g, female; 121 to 138 g

**No. of animals per sex per dose:**

| Group          | Number of Animals |        |
|----------------|-------------------|--------|
|                | Male              | Female |
| Control        | 5+5 *             | 5+5 *  |
| 20 mg/kg/day   | 5                 | 5      |
| 200 mg/kg/day  | 5                 | 5      |
| 1000 mg/kg/day | 5+5 *             | 5+5 *  |

\*: Recovery animal

### • Study Design:

**Vehicle:** Water for injection

**Satellite groups and reasons they were added:**

1 control group and 1 test article group

In order to evaluate the reversibility of the toxicity followed by a 14-day recovery period.

**Clinical observations performed and frequency:**

The first day of dosing was designated as Day 0 of the dosing period. The day following the end of the dosing period was designated as Day 0 of the recovery period. The first week of dosing or recovery periods were designated as Week 1 of the dosing and recovery periods, respectively.

Clinical signs; All animals were observed for mortality and clinical signs 3 times daily, once daily during the recovery period and once on the days of autopsy.

General behavioral observations; General behavior, neurologic and autonomic profile were observed according to the Irwin method once on Days 0 and 27 of the dosing period, and once Week 2 of the recovery period in five males and five females in each group.

Food consumption; Food consumption was weighed once prior to the initiation of dosing and once weekly during the dosing and recovery periods in all animals.

Body weight; All animals were weighed once prior to the initiation of dosing, once weekly during the dosing and recovery periods. Body weight gain was calculated at each measurement.

Ophthalmology; Gross observation and fundus examination were observed once prior to the initiation of dosing, once at Week 4 of the dosing period and Week 2 of the recovery period in all animals.

Urinalysis; All animals were examined at Week 4 of the dosing period and Week 2 the recovery period.

Hematology and biochemistry; All animals were examined at each gross pathology.

**Organs examines at necropsy:**

Organ Weight; Brain, heart, liver, kidneys, adrenals,

spleen, thymus, testes, epididymis and ovaries in all animals

Microscopic; Cerebrum, cerebellum, brain stem, pituitary, eye balls, harderian glands, submandibular lymph node, thyroids, parathyroids, trachea, lungs, thymus, heart, bone and bone marrow, spinal cord, stomach, small intestine, large intestine, mesenteric lymph node, liver, urinary bladder, spleen, adrenals, kidneys, testes, epididymides, seminal vesicles, prostate, ovaries, uterus, vagina and sciatic nerve in all animals in the control and 500 mg/kg groups

## **RESULTS**

- **NOAEL (NOEL):** Male; >1000 mg/kg/day  
Female; >1000 mg/kg/day
- **LOAEL (LOEL):** Male; >1000 mg/kg/day  
Female; >1000 mg/kg/day

## **REMARKS FIELD FOR RESULTS**

- **Clinical signs (description, severity, time of onset and duration):**

No animals died in any group during the dosing or recovery period. No abnormalities were observed in any animal during the dosing or recovery period.

- **General behavioral observations:**

No abnormalities were observed in any animal during the dosing or recovery period.

- **Food consumption:**

Low food consumption was noted in males in the 200 mg/kg group at Week 2 of the dosing period and in females in the 1000 mg/kg group at Week 2 of the recovery period. However, they were judged not to be test article related changes.

- **Body weight:**

No abnormalities were noted in any group during the dosing or recovery period.

- **Ophthalmology:**

No abnormalities were observed in any animal during the dosing or recovery period.

- **Urinalysis:**

High protein in females in the 20 mg/kg group was noted at Week 4 of the dosing period. However, it was judged not to be test article related changes. No abnormalities were noted at Week 2 of the recovery period.

- **Hematology:**

No abnormalities were noted at the end of the dosing period. The prolongation of APTT in males in the 1000 mg/kg group was noted at the end of the recovery period. However, it was judged to be incidental.

- **Biochemistry:**

Low glucose was noted in females in the 20 mg/kg group at the end of the dosing period. High Na was noted in males in the 1000 mg/kg at the end of the recovery period. However, they were judged not to be test article related changes.

- **Mortality and time to death:**

None

- **Gross pathology incidence and severity:**

The following changes were observed in the test article groups at the end of dosing or recovery period: red or black focus in the lung, white foci in the liver, cysts in the kidneys and asymmetry in the size of the adrenals. However, they were judged to be incidental.

- **Organ weight changes:**

Low relative thymic weight was noted in males in the 200 mg/kg group at the end of the dosing period. High absolute and relative weights of the adrenal and low absolute weight of the spleen and kidney were noted in females in the 1000 mg/kg group at the end of the recovery period. However, they were judged not to be test article related changes.

- **Histopathology (incidence and severity):**

The following changes were observed in the 1000 mg/kg group at the end of the dosing or recovery period: extramedullary hematopoiesis, hyperplasia in the plasma cells of the submandibular lymph nodes, osseous metaplasia in the lung, foamy cell aggregation in the alveoli of the lungs, focal hemorrhage of the lung, mineralization in the pulmonary artery, microvacuolization in hepatocytes of the periportal liver, mononuclear cell infiltration in the liver, focal necrosis in the liver, mineralization of the renal tubules, eosinophilic bodies in the renal tubules, basophilic change in the renal tubules, hyaline casts in the dilated tubules of the kidney, mononuclear cell infiltration in the prostate, mononuclear cell infiltration in the ovary, dilatation in the lumen of the uterus, cysts in the cortex of the adrenal, focal hypertrophy in the cortical cells of the adrenal, ectopic thymus in the thyroid, ultimobranchial bodies in the

thyroid, brown pigment and hemorrhage in the periosteum of the femur. However, they were judged to be incidental.

## **CONCLUTIONS**

During the dosing and recovery period, no animals died in any group. No abnormalities were observed in clinical signs or in general behavioral observations.

No test article related changes were noted in food consumption, body weight, ophthalmology, urinalysis, hematology, blood biochemistry, gross pathology, organ weight or histopathology.

It was concluded from these results that under the conditions of this study, the no-observed-effect level (NOEL) of polyoxyethylene p-nonylphenyl ether was greater than 1000 mg/kg/day in both males and females.

## **DATA QUALITY**

- **Reliabilities:** Valid without restriction

### **Remarks field for Data Reliability**

Well conducted study, carried out by Shin Nippon Biomedical Laboratories, Ltd.  
(Kagoshima, Japan)

## **REFERENCES (Free Text)**

1. SNBL Control Background Data - Crj: CD (SD) IGS, Vol. 47, Shin Nippon Biomedical Laboratories, Ltd. In-house data, 2000

## **GENERAL REMAERKS**

None.



ポリオキシエチレン p-ノニルフェニルエーテルのラットにおけ  
る28日間反復経口投与毒性試験および14日間回復性試験

試験結果報告書の内容に関するお問い合わせには応じかねますので御了承下さい。

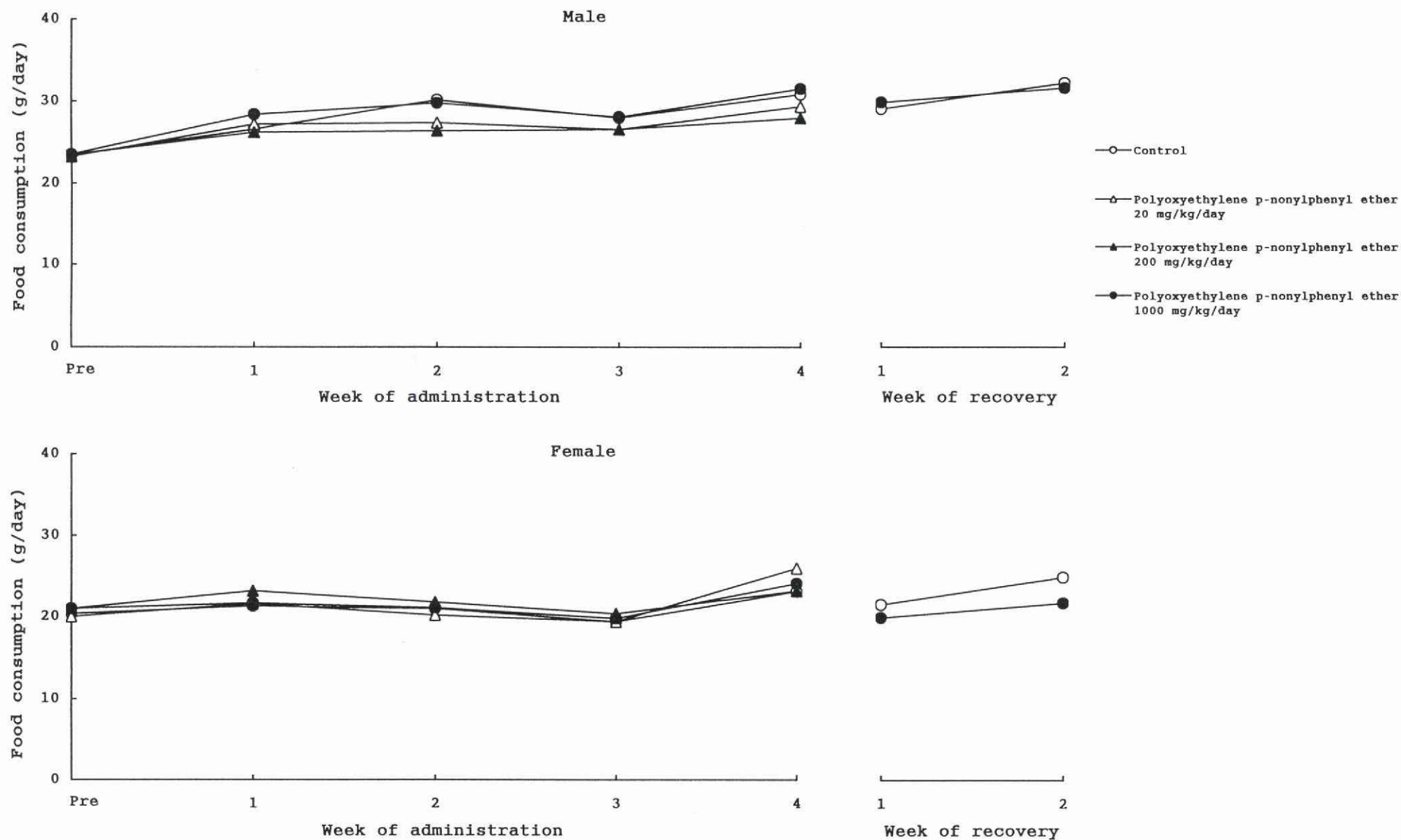


Fig. 1 Changes of food consumption in rats

試験結果報告書の内容に関するお問い合わせには応じかねますので御了承下さい。

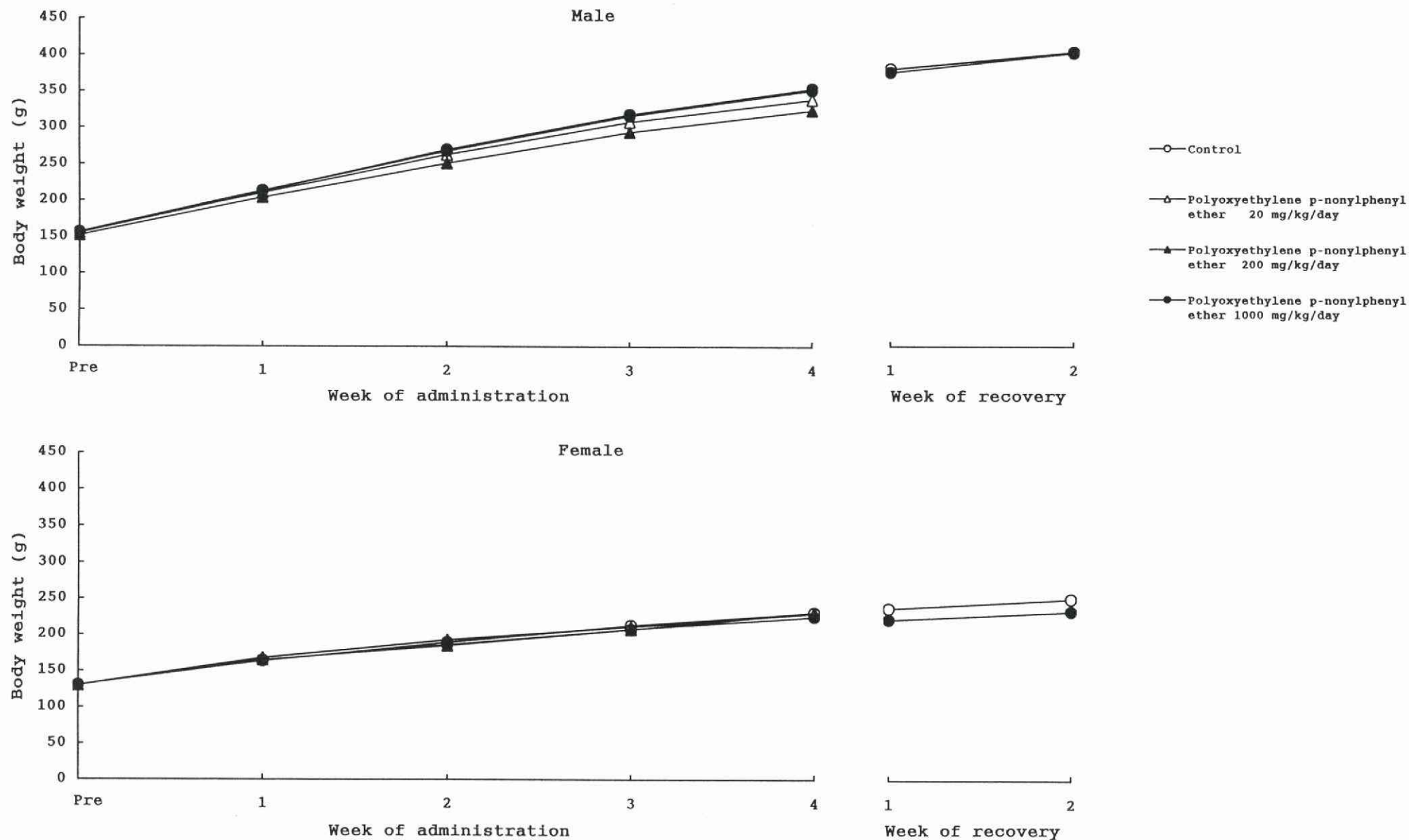


Fig. 2 Changes of body weight in rats

Clinical Sign

Grade

- 0 : No abnormal signs
- 1 : Slight
- 2 : Moderate
- 3 : Severe
- + : Non-graded clinical signs

Table 1-1 Clinical signs in male rats

Study No. : SBL79-02

| Group            |                   | Control |    |   |   |   | Polyoxyethylene p-nonylphenyl ether |    |   |   |   |   |     |   |   |   |   |      |   |   |   |   |
|------------------|-------------------|---------|----|---|---|---|-------------------------------------|----|---|---|---|---|-----|---|---|---|---|------|---|---|---|---|
| Dose (mg/kg/day) |                   | Grade   |    |   |   |   |                                     | 20 |   |   |   |   | 200 |   |   |   |   | 1000 |   |   |   |   |
|                  |                   |         | 0  | 1 | 2 | 3 | +                                   | 0  | 1 | 2 | 3 | + | 0   | 1 | 2 | 3 | + | 0    | 1 | 2 | 3 | + |
| Day              | Item              |         |    |   |   |   |                                     |    |   |   |   |   |     |   |   |   |   |      |   |   |   |   |
| 0                | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 1                | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 2                | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 3                | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 4                | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 5                | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 6                | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 7                | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 8                | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 9                | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 10               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 11               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 12               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 13               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 14               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 15               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 16               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 17               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 18               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 19               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 20               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 21               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 22               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 23               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |

Numerals represent the number of animals.

Table 1-2

Clinical signs in male rats

Study No. : SBL79-02

| Group            |                   | Control |    |   |   |   | Polyoxyethylene p-nonylphenyl ether |    |   |   |   |   |     |   |   |   |   |      |   |   |   |   |
|------------------|-------------------|---------|----|---|---|---|-------------------------------------|----|---|---|---|---|-----|---|---|---|---|------|---|---|---|---|
| Dose (mg/kg/day) |                   | Grade   |    |   |   |   |                                     | 20 |   |   |   |   | 200 |   |   |   |   | 1000 |   |   |   |   |
|                  |                   |         | 0  | 1 | 2 | 3 | +                                   | 0  | 1 | 2 | 3 | + | 0   | 1 | 2 | 3 | + | 0    | 1 | 2 | 3 | + |
| Day              | Item              |         |    |   |   |   |                                     |    |   |   |   |   |     |   |   |   |   |      |   |   |   |   |
| 24               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 25               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 26               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 27               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 28               | No abnormal signs |         | 5  |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 5    |   |   |   |   |
| R:0              | No abnormal signs |         | 5  |   |   |   |                                     |    |   |   |   |   |     |   |   |   |   | 5    |   |   |   |   |
| R:1              | No abnormal signs |         | 5  |   |   |   |                                     |    |   |   |   |   |     |   |   |   |   | 5    |   |   |   |   |
| R:2              | No abnormal signs |         | 5  |   |   |   |                                     |    |   |   |   |   |     |   |   |   |   | 5    |   |   |   |   |
| R:3              | No abnormal signs |         | 5  |   |   |   |                                     |    |   |   |   |   |     |   |   |   |   | 5    |   |   |   |   |
| R:4              | No abnormal signs |         | 5  |   |   |   |                                     |    |   |   |   |   |     |   |   |   |   | 5    |   |   |   |   |
| R:5              | No abnormal signs |         | 5  |   |   |   |                                     |    |   |   |   |   |     |   |   |   |   | 5    |   |   |   |   |
| R:6              | No abnormal signs |         | 5  |   |   |   |                                     |    |   |   |   |   |     |   |   |   |   | 5    |   |   |   |   |
| R:7              | No abnormal signs |         | 5  |   |   |   |                                     |    |   |   |   |   |     |   |   |   |   | 5    |   |   |   |   |
| R:8              | No abnormal signs |         | 5  |   |   |   |                                     |    |   |   |   |   |     |   |   |   |   | 5    |   |   |   |   |
| R:9              | No abnormal signs |         | 5  |   |   |   |                                     |    |   |   |   |   |     |   |   |   |   | 5    |   |   |   |   |
| R:10             | No abnormal signs |         | 5  |   |   |   |                                     |    |   |   |   |   |     |   |   |   |   | 5    |   |   |   |   |
| R:11             | No abnormal signs |         | 5  |   |   |   |                                     |    |   |   |   |   |     |   |   |   |   | 5    |   |   |   |   |
| R:12             | No abnormal signs |         | 5  |   |   |   |                                     |    |   |   |   |   |     |   |   |   |   | 5    |   |   |   |   |
| R:13             | No abnormal signs |         | 5  |   |   |   |                                     |    |   |   |   |   |     |   |   |   |   | 5    |   |   |   |   |
| R:14             | No abnormal signs |         | 5  |   |   |   |                                     |    |   |   |   |   |     |   |   |   |   | 5    |   |   |   |   |

Numerals represent the number of animals.

Table 1-3 Clinical signs in female rats

Study No. : SBL79-02

| Group            |                   | Control |    |   |   |   | Polyoxyethylene p-nonylphenyl ether |    |   |   |   |   |     |   |   |   |   |      |   |   |   |   |
|------------------|-------------------|---------|----|---|---|---|-------------------------------------|----|---|---|---|---|-----|---|---|---|---|------|---|---|---|---|
| Dose (mg/kg/day) |                   | Grade   |    |   |   |   |                                     | 20 |   |   |   |   | 200 |   |   |   |   | 1000 |   |   |   |   |
|                  |                   |         | 0  | 1 | 2 | 3 | +                                   | 0  | 1 | 2 | 3 | + | 0   | 1 | 2 | 3 | + | 0    | 1 | 2 | 3 | + |
| Day              | Item              |         |    |   |   |   |                                     |    |   |   |   |   |     |   |   |   |   |      |   |   |   |   |
| 0                | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 1                | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 2                | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 3                | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 4                | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 5                | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 6                | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 7                | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 8                | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 9                | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 10               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 11               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 12               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 13               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 14               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 15               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 16               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 17               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 18               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 19               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 20               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 21               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 22               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |
| 23               | No abnormal signs |         | 10 |   |   |   |                                     | 5  |   |   |   |   | 5   |   |   |   |   | 10   |   |   |   |   |

Numerals represent the number of animals.

Table 1-4 Clinical signs in female rats

Study No. : SBL79-02

| Group           |                   | Control |   |   |   |   | Polyoxyethylene p-nonylphenyl ether |    |   |   |   |   |     |   |   |   |    |      |   |   |   |   |
|-----------------|-------------------|---------|---|---|---|---|-------------------------------------|----|---|---|---|---|-----|---|---|---|----|------|---|---|---|---|
| Dose(mg/kg/day) |                   | Grade   |   |   |   |   |                                     | 20 |   |   |   |   | 200 |   |   |   |    | 1000 |   |   |   |   |
|                 |                   |         | 0 | 1 | 2 | 3 | +                                   | 0  | 1 | 2 | 3 | + | 0   | 1 | 2 | 3 | +  | 0    | 1 | 2 | 3 | + |
| Day             | Item              |         |   |   |   |   |                                     |    |   |   |   |   |     |   |   |   |    |      |   |   |   |   |
| 24              | No abnormal signs | 10      |   |   |   |   | 5                                   |    |   |   |   | 5 |     |   |   |   | 10 |      |   |   |   |   |
| 25              | No abnormal signs | 10      |   |   |   |   | 5                                   |    |   |   |   | 5 |     |   |   |   | 10 |      |   |   |   |   |
| 26              | No abnormal signs | 10      |   |   |   |   | 5                                   |    |   |   |   | 5 |     |   |   |   | 10 |      |   |   |   |   |
| 27              | No abnormal signs | 10      |   |   |   |   | 5                                   |    |   |   |   | 5 |     |   |   |   | 10 |      |   |   |   |   |
| 28              | No abnormal signs | 5       |   |   |   |   | 5                                   |    |   |   |   | 5 |     |   |   |   | 5  |      |   |   |   |   |
| R:0             | No abnormal signs | 5       |   |   |   |   |                                     |    |   |   |   |   |     |   |   |   | 5  |      |   |   |   |   |
| R:1             | No abnormal signs | 5       |   |   |   |   |                                     |    |   |   |   |   |     |   |   |   | 5  |      |   |   |   |   |
| R:2             | No abnormal signs | 5       |   |   |   |   |                                     |    |   |   |   |   |     |   |   |   | 5  |      |   |   |   |   |
| R:3             | No abnormal signs | 5       |   |   |   |   |                                     |    |   |   |   |   |     |   |   |   | 5  |      |   |   |   |   |
| R:4             | No abnormal signs | 5       |   |   |   |   |                                     |    |   |   |   |   |     |   |   |   | 5  |      |   |   |   |   |
| R:5             | No abnormal signs | 5       |   |   |   |   |                                     |    |   |   |   |   |     |   |   |   | 5  |      |   |   |   |   |
| R:6             | No abnormal signs | 5       |   |   |   |   |                                     |    |   |   |   |   |     |   |   |   | 5  |      |   |   |   |   |
| R:7             | No abnormal signs | 5       |   |   |   |   |                                     |    |   |   |   |   |     |   |   |   | 5  |      |   |   |   |   |
| R:8             | No abnormal signs | 5       |   |   |   |   |                                     |    |   |   |   |   |     |   |   |   | 5  |      |   |   |   |   |
| R:9             | No abnormal signs | 5       |   |   |   |   |                                     |    |   |   |   |   |     |   |   |   | 5  |      |   |   |   |   |
| R:10            | No abnormal signs | 5       |   |   |   |   |                                     |    |   |   |   |   |     |   |   |   | 5  |      |   |   |   |   |
| R:11            | No abnormal signs | 5       |   |   |   |   |                                     |    |   |   |   |   |     |   |   |   | 5  |      |   |   |   |   |
| R:12            | No abnormal signs | 5       |   |   |   |   |                                     |    |   |   |   |   |     |   |   |   | 5  |      |   |   |   |   |
| R:13            | No abnormal signs | 5       |   |   |   |   |                                     |    |   |   |   |   |     |   |   |   | 5  |      |   |   |   |   |
| R:14            | No abnormal signs | 5       |   |   |   |   |                                     |    |   |   |   |   |     |   |   |   | 5  |      |   |   |   |   |

Numerals represent the number of animals.



Table 2-1 Effects of Polyoxyethylene p-nonylphenyl ether on the general behavior in male rats (Prior to administration on Day 0)

Study No. : SBL79-02

| General behavior     | Group |                  | Control | Polyoxyethylene p-nonylphenyl ether |     |      |
|----------------------|-------|------------------|---------|-------------------------------------|-----|------|
|                      | Grade | Dose (mg/kg/day) |         | 20                                  | 200 | 1000 |
| Awareness            |       |                  |         |                                     |     |      |
| Alertness            | N     |                  | 5       | 5                                   | 5   | 5    |
| Visual Placing       | N     |                  | 5       | 5                                   | 5   | 5    |
| Stereotypy           | N     |                  | 5       | 5                                   | 5   | 5    |
| Passivity            | N     |                  | 5       | 5                                   | 5   | 5    |
| Mood                 |       |                  |         |                                     |     |      |
| Grooming             | N     |                  | 5       | 5                                   | 5   | 5    |
| Vocalization         | N     |                  | 5       | 5                                   | 5   | 5    |
| Restlessness         | N     |                  | 5       | 5                                   | 5   | 5    |
| Irritability         | N     |                  | 5       | 5                                   | 5   | 5    |
| Fearfulness          | N     |                  | 5       | 5                                   | 5   | 5    |
| Motor Activity       |       |                  |         |                                     |     |      |
| Reactivity           | N     |                  | 5       | 5                                   | 5   | 5    |
| Spontaneous Activity | N     |                  | 5       | 5                                   | 5   | 5    |
| Touch Response       | N     |                  | 5       | 5                                   | 5   | 5    |
| Pain Response        | N     |                  | 5       | 5                                   | 5   | 5    |
| CNS Excitation       |       |                  |         |                                     |     |      |
| Startle Response     | N     |                  | 5       | 5                                   | 5   | 5    |
| Straub Tail          | N     |                  | 5       | 5                                   | 5   | 5    |
| Tremors              | N     |                  | 5       | 5                                   | 5   | 5    |
| Twitches             | N     |                  | 5       | 5                                   | 5   | 5    |
| Convulsions          | N     |                  | 5       | 5                                   | 5   | 5    |
| Posture              |       |                  |         |                                     |     |      |
| Body Posture         | N     |                  | 5       | 5                                   | 5   | 5    |
| Limb Posture         | N     |                  | 5       | 5                                   | 5   | 5    |
| Motor Incoordination |       |                  |         |                                     |     |      |
| Staggering Gait      | N     |                  | 5       | 5                                   | 5   | 5    |
| Abnormal Gait        | N     |                  | 5       | 5                                   | 5   | 5    |
| Righting Reflex      | N     |                  | 5       | 5                                   | 5   | 5    |

Notes) N : Normal sign

Numerals represent the number of animals.

Table 2-2 Effects of Polyoxyethylene p-nonylphenyl ether on the general behavior in male rats (Prior to administration on Day 0)

Study No. : SBL79-02

| General behavior  | Group |                  | Control | Polyoxyethylene p-nonylphenyl ether |     |      |
|-------------------|-------|------------------|---------|-------------------------------------|-----|------|
|                   | Grade | Dose (mg/kg/day) |         | 20                                  | 200 | 1000 |
| Muscle Tone       |       |                  |         |                                     |     |      |
| Limb Tone         | N     |                  | 5       | 5                                   | 5   | 5    |
| Grip Strength     | N     |                  | 5       | 5                                   | 5   | 5    |
| Body Tone         | N     |                  | 5       | 5                                   | 5   | 5    |
| Abdominal Tone    | N     |                  | 5       | 5                                   | 5   | 5    |
| Reflex            |       |                  |         |                                     |     |      |
| Pinna Reflex      | N     |                  | 5       | 5                                   | 5   | 5    |
| Corneal Reflex    | N     |                  | 5       | 5                                   | 5   | 5    |
| IPR               | N     |                  | 5       | 5                                   | 5   | 5    |
| Autonomic Profile |       |                  |         |                                     |     |      |
| Writhing          | N     |                  | 5       | 5                                   | 5   | 5    |
| Palpebral Opening | N     |                  | 5       | 5                                   | 5   | 5    |
| Exophthalmos      | N     |                  | 5       | 5                                   | 5   | 5    |
| Urination         | N     |                  | 5       | 5                                   | 5   | 5    |
| Salivation        | N     |                  | 5       | 5                                   | 5   | 5    |
| Piloerection      | N     |                  | 5       | 5                                   | 5   | 5    |
| Hypothermia       | N     |                  | 5       | 5                                   | 5   | 5    |
| Skin Color        | N     |                  | 5       | 5                                   | 5   | 5    |
| Heart Rate        | N     |                  | 5       | 5                                   | 5   | 5    |
| Respiratory Rate  | N     |                  | 5       | 5                                   | 5   | 5    |
| Pupil Size        | N     |                  | 5       | 5                                   | 5   | 5    |
| Rearing*          | 0     |                  | 5       | 5                                   | 5   | 5    |

Notes) N : Normal sign

\* : Numerals represent the count of rearing

Numerals represent the number of animals.

Table 2-3 Effects of Polyoxyethylene p-nonylphenyl ether on the general behavior in male rats (2 - 4 hours after administration on Day 0)

Study No. : SBL79-02

| General behavior     | Group |                  | Control | Polyoxyethylene <i>p</i> -nonylphenyl ether |     |      |
|----------------------|-------|------------------|---------|---|-----|------|
|                      | Grade | Dose (mg/kg/day) |         | 20  | 200 | 1000 |
| Awareness            |       |                  |         |   |     |      |
| Alertness            | N     |                  | 5       | 5   | 5   | 5    |
| Visual Placing       | N     |                  | 5       | 5   | 5   | 5    |
| Stereotypy           | N     |                  | 5       | 5   | 5   | 5    |
| Passivity            | N     |                  | 5       | 5   | 5   | 5    |
| Mood                 |       |                  |         |   |     |      |
| Grooming             | N     |                  | 5       | 5   | 5   | 5    |
| Vocalization         | N     |                  | 5       | 5   | 5   | 5    |
| Restlessness         | N     |                  | 5       | 5   | 5   | 5    |
| Irritability         | N     |                  | 5       | 5   | 5   | 5    |
| Fearfulness          | N     |                  | 5       | 5   | 5   | 5    |
| Motor Activity       |       |                  |         |   |     |      |
| Reactivity           | N     |                  | 5       | 5   | 5   | 5    |
| Spontaneous Activity | N     |                  | 5       | 5   | 5   | 5    |
| Touch Response       | N     |                  | 5       | 5   | 5   | 5    |
| Pain Response        | N     |                  | 5       | 5   | 5   | 5    |
| CNS Excitation       |       |                  |         |   |     |      |
| Startle Response     | N     |                  | 5       | 5   | 5   | 5    |
| Straub Tail          | N     |                  | 5       | 5   | 5   | 5    |
| Tremors              | N     |                  | 5       | 5   | 5   | 5    |
| Twitches             | N     |                  | 5       | 5   | 5   | 5    |
| Convulsions          | N     |                  | 5       | 5   | 5   | 5    |
| Posture              |       |                  |         |   |     |      |
| Body Posture         | N     |                  | 5       | 5   | 5   | 5    |
| Limb Posture         | N     |                  | 5       | 5   | 5   | 5    |
| Motor Incoordination |       |                  |         |   |     |      |
| Staggering Gait      | N     |                  | 5       | 5   | 5   | 5    |
| Abnormal Gait        | N     |                  | 5       | 5   | 5   | 5    |
| Righting Reflex      | N     |                  | 5       | 5   | 5   | 5    |

Notes) N : Normal sign

Numerals represent the number of animals.

Table 2-4 Effects of Polyoxyethylene p-nonylphenyl ether on the general behavior in male rats (2 - 4 hours after administration on Day 0)

Study No. : SBL79-02

| General behavior  | Group |                  | Control | Polyoxyethylene p-nonylphenyl ether |     |      |
|-------------------|-------|------------------|---------|-------------------------------------|-----|------|
|                   | Grade | Dose (mg/kg/day) |         | 20                                  | 200 | 1000 |
| Muscle Tone       |       |                  |         |                                     |     |      |
| Limb Tone         | N     |                  | 5       | 5                                   | 5   | 5    |
| Grip Strength     | N     |                  | 5       | 5                                   | 5   | 5    |
| Body Tone         | N     |                  | 5       | 5                                   | 5   | 5    |
| Abdominal Tone    | N     |                  | 5       | 5                                   | 5   | 5    |
| Reflex            |       |                  |         |                                     |     |      |
| Pinna Reflex      | N     |                  | 5       | 5                                   | 5   | 5    |
| Corneal Reflex    | N     |                  | 5       | 5                                   | 5   | 5    |
| IPR               | N     |                  | 5       | 5                                   | 5   | 5    |
| Autonomic Profile |       |                  |         |                                     |     |      |
| Writhing          | N     |                  | 5       | 5                                   | 5   | 5    |
| Palpebral Opening | N     |                  | 5       | 5                                   | 5   | 5    |
| Exophthalmos      | N     |                  | 5       | 5                                   | 5   | 5    |
| Urination         | N     |                  | 5       | 5                                   | 5   | 5    |
| Salivation        | N     |                  | 5       | 5                                   | 5   | 5    |
| Piloerection      | N     |                  | 5       | 5                                   | 5   | 5    |
| Hypothermia       | N     |                  | 5       | 5                                   | 5   | 5    |
| Skin Color        | N     |                  | 5       | 5                                   | 5   | 5    |
| Heart Rate        | N     |                  | 5       | 5                                   | 5   | 5    |
| Respiratory Rate  | N     |                  | 5       | 5                                   | 5   | 5    |
| Pupil Size        | N     |                  | 5       | 5                                   | 5   | 5    |
| Rearing*          | 0     |                  | 4       | 5                                   | 5   | 5    |
|                   | 1     |                  | 1       | 0                                   | 0   | 0    |

Notes) N : Normal sign

\* : Numerals represent the count of rearing

Numerals represent the number of animals.

Table 2-5 Effects of Polyoxyethylene p-nonylphenyl ether on the general behavior in male rats (2 - 4 hours after administration on Day 27)

Study No. : SBL79-02

| General behavior     | Grade | Group<br>Dose (mg/kg/day) | Control | Polyoxyethylene p-nonylphenyl ether |     |      |
|----------------------|-------|---------------------------|---------|-------------------------------------|-----|------|
|                      |       |                           |         | 20                                  | 200 | 1000 |
| Awareness            |       |                           |         |                                     |     |      |
| Alertness            | N     |                           | 5       | 5                                   | 5   | 5    |
| Visual Placing       | N     |                           | 5       | 5                                   | 5   | 5    |
| Stereotypy           | N     |                           | 5       | 5                                   | 5   | 5    |
| Passivity            | N     |                           | 5       | 5                                   | 5   | 5    |
| Mood                 |       |                           |         |                                     |     |      |
| Grooming             | N     |                           | 5       | 5                                   | 5   | 5    |
| Vocalization         | N     |                           | 5       | 5                                   | 5   | 5    |
| Restlessness         | N     |                           | 5       | 5                                   | 5   | 5    |
| Irritability         | N     |                           | 5       | 5                                   | 5   | 5    |
| Fearfulness          | N     |                           | 5       | 5                                   | 5   | 5    |
| Motor Activity       |       |                           |         |                                     |     |      |
| Reactivity           | N     |                           | 5       | 5                                   | 5   | 5    |
| Spontaneous Activity | N     |                           | 5       | 5                                   | 5   | 5    |
| Touch Response       | N     |                           | 5       | 5                                   | 5   | 5    |
| Pain Response        | N     |                           | 5       | 5                                   | 5   | 5    |
| CNS Excitation       |       |                           |         |                                     |     |      |
| Startle Response     | N     |                           | 5       | 5                                   | 5   | 5    |
| Straub Tail          | N     |                           | 5       | 5                                   | 5   | 5    |
| Tremors              | N     |                           | 5       | 5                                   | 5   | 5    |
| Twitches             | N     |                           | 5       | 5                                   | 5   | 5    |
| Convulsions          | N     |                           | 5       | 5                                   | 5   | 5    |
| Posture              |       |                           |         |                                     |     |      |
| Body Posture         | N     |                           | 5       | 5                                   | 5   | 5    |
| Limb Posture         | N     |                           | 5       | 5                                   | 5   | 5    |
| Motor Incoordination |       |                           |         |                                     |     |      |
| Staggering Gait      | N     |                           | 5       | 5                                   | 5   | 5    |
| Abnormal Gait        | N     |                           | 5       | 5                                   | 5   | 5    |
| Righting Reflex      | N     |                           | 5       | 5                                   | 5   | 5    |

Notes) N : Normal sign

Numerals represent the number of animals.

Table 2-6 Effects of Polyoxyethylene p-nonylphenyl ether on the general behavior in male rats (2 - 4 hours after administration on Day 27)

Study No. : SBL79-02

| General behavior  | Group |                  | Control | Polyoxyethylene p-nonylphenyl ether |     |      |
|-------------------|-------|------------------|---------|-------------------------------------|-----|------|
|                   | Grade | Dose (mg/kg/day) |         | 20                                  | 200 | 1000 |
| Muscle Tone       |       |                  |         |                                     |     |      |
| Limb Tone         | N     |                  | 5       | 5                                   | 5   | 5    |
| Grip Strength     | N     |                  | 5       | 5                                   | 5   | 5    |
| Body Tone         | N     |                  | 5       | 5                                   | 5   | 5    |
| Abdominal Tone    | N     |                  | 5       | 5                                   | 5   | 5    |
| Reflex            |       |                  |         |                                     |     |      |
| Pinna Reflex      | N     |                  | 5       | 5                                   | 5   | 5    |
| Corneal Reflex    | N     |                  | 5       | 5                                   | 5   | 5    |
| IPR               | N     |                  | 5       | 5                                   | 5   | 5    |
| Autonomic Profile |       |                  |         |                                     |     |      |
| Writhing          | N     |                  | 5       | 5                                   | 5   | 5    |
| Palpebral Opening | N     |                  | 5       | 5                                   | 5   | 5    |
| Exophthalmos      | N     |                  | 5       | 5                                   | 5   | 5    |
| Urination         | N     |                  | 5       | 5                                   | 5   | 5    |
| Salivation        | N     |                  | 5       | 5                                   | 5   | 5    |
| Piloerection      | N     |                  | 5       | 5                                   | 5   | 5    |
| Hypothermia       | N     |                  | 5       | 5                                   | 5   | 5    |
| Skin Color        | N     |                  | 5       | 5                                   | 5   | 5    |
| Heart Rate        | N     |                  | 5       | 5                                   | 5   | 5    |
| Respiratory Rate  | N     |                  | 5       | 5                                   | 5   | 5    |
| Pupil Size        | N     |                  | 5       | 5                                   | 5   | 5    |
| Rearing*          | 0     |                  | 5       | 5                                   | 5   | 5    |

Notes) N : Normal sign

\* : Numerals represent the count of rearing

Numerals represent the number of animals.

Table 2-7 Effects of Polyoxyethylene p-nonylphenyl ether on the general behavior in male rats (Week 2 of recovery period)

Study No. : SBL79-02

| General behavior     | Group |                  | Control | Polyoxyethylene <i>p</i> -nonylphenyl ether |     |      |
|----------------------|-------|------------------|---------|---|-----|------|
|                      | Grade | Dose (mg/kg/day) |         | 20  | 200 | 1000 |
| Awareness            |       |                  |         |   |     |      |
| Alertness            | N     |                  | 5       |   |     | 5    |
| Visual Placing       | N     |                  | 5       |   |     | 5    |
| Stereotypy           | N     |                  | 5       |   |     | 5    |
| Passivity            | N     |                  | 5       |   |     | 5    |
| Hood                 |       |                  |         |   |     |      |
| Grooming             | N     |                  | 5       |   |     | 5    |
| Vocalization         | N     |                  | 5       |   |     | 5    |
| Restlessness         | N     |                  | 5       |   |     | 5    |
| Irritability         | N     |                  | 5       |   |     | 5    |
| Fearfulness          | N     |                  | 5       |   |     | 5    |
| Motor Activity       |       |                  |         |   |     |      |
| Reactivity           | N     |                  | 5       |   |     | 5    |
| Spontaneous Activity | N     |                  | 5       |   |     | 5    |
| Touch Response       | N     |                  | 5       |   |     | 5    |
| Pain Response        | N     |                  | 5       |   |     | 5    |
| CNS Excitation       |       |                  |         |   |     |      |
| Startle Response     | N     |                  | 5       |   |     | 5    |
| Straub Tail          | N     |                  | 5       |   |     | 5    |
| Tremors              | N     |                  | 5       |   |     | 5    |
| Twitches             | N     |                  | 5       |   |     | 5    |
| Convulsions          | N     |                  | 5       |   |     | 5    |
| Posture              |       |                  |         |   |     |      |
| Body Posture         | N     |                  | 5       |   |     | 5    |
| Limb Posture         | N     |                  | 5       |   |     | 5    |
| Motor Incoordination |       |                  |         |   |     |      |
| Staggering Gait      | N     |                  | 5       |   |     | 5    |
| Abnormal Gait        | N     |                  | 5       |   |     | 5    |
| Righting Reflex      | N     |                  | 5       |   |     | 5    |

Notes) N : Normal sign

Numerals represent the number of animals.

Table 2-8 Effects of Polyoxyethylene p-nonylphenyl ether on the general behavior in male rats (Week 2 of recovery period)

Study No. : SBL79-02

| General behavior         | Group |                  | Control | Polyoxyethylene p-nonylphenyl ether |     |      |
|--------------------------|-------|------------------|---------|-------------------------------------|-----|------|
|                          | Grade | Dose (mg/kg/day) |         | 20                                  | 200 | 1000 |
| <b>Muscle Tone</b>       |       |                  |         |                                     |     |      |
| Limb Tone                | N     |                  | 5       |                                     |     | 5    |
| Grip Strength            | N     |                  | 5       |                                     |     | 5    |
| Body Tone                | N     |                  | 5       |                                     |     | 5    |
| Abdominal Tone           | N     |                  | 5       |                                     |     | 5    |
| <b>Reflex</b>            |       |                  |         |                                     |     |      |
| Pinna Reflex             | N     |                  | 5       |                                     |     | 5    |
| Corneal Reflex           | N     |                  | 5       |                                     |     | 5    |
| IPR                      | N     |                  | 5       |                                     |     | 5    |
| <b>Autonomic Profile</b> |       |                  |         |                                     |     |      |
| Writhing                 | N     |                  | 5       |                                     |     | 5    |
| Palpebral Opening        | N     |                  | 5       |                                     |     | 5    |
| Exophthalmos             | N     |                  | 5       |                                     |     | 5    |
| Urination                | N     |                  | 5       |                                     |     | 5    |
| Salivation               | N     |                  | 5       |                                     |     | 5    |
| Piloerection             | N     |                  | 5       |                                     |     | 5    |
| Hypothermia              | N     |                  | 5       |                                     |     | 5    |
| Skin Color               | N     |                  | 5       |                                     |     | 5    |
| Heart Rate               | N     |                  | 5       |                                     |     | 5    |
| Respiratory Rate         | N     |                  | 5       |                                     |     | 5    |
| Pupil Size               | N     |                  | 5       |                                     |     | 5    |
| Rearing*                 | 0     |                  | 5       |                                     |     | 5    |

Notes) N : Normal sign

\* : Numerals represent the count of rearing

Numerals represent the number of animals.



Table 2-9 Effects of Polyoxyethylene p-nonylphenyl ether on the general behavior in female rats (Prior to administration on Day 0)

Study No. : SBL79-02

| General behavior     | Group |                  | Control | Polyoxyethylene p-nonylphenyl ether |     |      |
|----------------------|-------|------------------|---------|-------------------------------------|-----|------|
|                      | Grade | Dose (mg/kg/day) |         | 20                                  | 200 | 1000 |
| Awareness            |       |                  |         |                                     |     |      |
| Alertness            | N     |                  | 5       | 5                                   | 5   | 5    |
| Visual Placing       | N     |                  | 5       | 5                                   | 5   | 5    |
| Stereotypy           | N     |                  | 5       | 5                                   | 5   | 5    |
| Passivity            | N     |                  | 5       | 5                                   | 5   | 5    |
| Mood                 |       |                  |         |                                     |     |      |
| Grooming             | N     |                  | 5       | 5                                   | 5   | 5    |
| Vocalization         | N     |                  | 5       | 5                                   | 5   | 5    |
| Restlessness         | N     |                  | 5       | 5                                   | 5   | 5    |
| Irritability         | N     |                  | 5       | 5                                   | 5   | 5    |
| Fearfulness          | N     |                  | 5       | 5                                   | 5   | 5    |
| Motor Activity       |       |                  |         |                                     |     |      |
| Reactivity           | N     |                  | 5       | 5                                   | 5   | 5    |
| Spontaneous Activity | N     |                  | 5       | 5                                   | 5   | 5    |
| Touch Response       | N     |                  | 5       | 5                                   | 5   | 5    |
| Pain Response        | N     |                  | 5       | 5                                   | 5   | 5    |
| CNS Excitation       |       |                  |         |                                     |     |      |
| Startle Response     | N     |                  | 5       | 5                                   | 5   | 5    |
| Straub Tail          | N     |                  | 5       | 5                                   | 5   | 5    |
| Tremors              | N     |                  | 5       | 5                                   | 5   | 5    |
| Twitches             | N     |                  | 5       | 5                                   | 5   | 5    |
| Convulsions          | N     |                  | 5       | 5                                   | 5   | 5    |
| Posture              |       |                  |         |                                     |     |      |
| Body Posture         | N     |                  | 5       | 5                                   | 5   | 5    |
| Limb Posture         | N     |                  | 5       | 5                                   | 5   | 5    |
| Motor Incoordination |       |                  |         |                                     |     |      |
| Staggering Gait      | N     |                  | 5       | 5                                   | 5   | 5    |
| Abnormal Gait        | N     |                  | 5       | 5                                   | 5   | 5    |
| Righting Reflex      | N     |                  | 5       | 5                                   | 5   | 5    |

Notes) N : Normal sign

Numerals represent the number of animals.

Table 2-10 Effects of Polyoxyethylene p-nonylphenyl ether on the general behavior in female rats (Prior to administration on Day 0)

Study No. : SBL79-02

| General behavior  | Group |                  | Control | Polyoxyethylene p-nonylphenyl ether |     |      |
|-------------------|-------|------------------|---------|-------------------------------------|-----|------|
|                   | Grade | Dose (mg/kg/day) |         | 20                                  | 200 | 1000 |
| Muscle Tone       |       |                  |         |                                     |     |      |
| Limb Tone         | N     |                  | 5       | 5                                   | 5   | 5    |
| Grip Strength     | N     |                  | 5       | 5                                   | 5   | 5    |
| Body Tone         | N     |                  | 5       | 5                                   | 5   | 5    |
| Abdominal Tone    | N     |                  | 5       | 5                                   | 5   | 5    |
| Reflex            |       |                  |         |                                     |     |      |
| Pinna Reflex      | N     |                  | 5       | 5                                   | 5   | 5    |
| Corneal Reflex    | N     |                  | 5       | 5                                   | 5   | 5    |
| IPR               | N     |                  | 5       | 5                                   | 5   | 5    |
| Autonomic Profile |       |                  |         |                                     |     |      |
| Writhing          | N     |                  | 5       | 5                                   | 5   | 5    |
| Palpebral Opening | N     |                  | 5       | 5                                   | 5   | 5    |
| Exophthalmos      | N     |                  | 5       | 5                                   | 5   | 5    |
| Urination         | N     |                  | 5       | 5                                   | 5   | 5    |
| Salivation        | N     |                  | 5       | 5                                   | 5   | 5    |
| Piloerection      | N     |                  | 5       | 5                                   | 5   | 5    |
| Hypothermia       | N     |                  | 5       | 5                                   | 5   | 5    |
| Skin Color        | N     |                  | 5       | 5                                   | 5   | 5    |
| Heart Rate        | N     |                  | 5       | 5                                   | 5   | 5    |
| Respiratory Rate  | N     |                  | 5       | 5                                   | 5   | 5    |
| Pupil Size        | N     |                  | 5       | 5                                   | 5   | 5    |
| Rearing*          | 0     |                  | 4       | 5                                   | 4   | 5    |
|                   | 1     |                  | 1       | 0                                   | 1   | 0    |

Notes) N : Normal sign

\* : Numerals represent the count of rearing

Numerals represent the number of animals.

Table 2-11 Effects of Polyoxyethylene p-nonylphenyl ether on the general behavior in female rats (2 - 4 hours after administration on Day 0)

Study No. : SBL79-02

| General behavior     | Group |                  | Control | Polyoxyethylene p-nonylphenyl ether |     |      |
|----------------------|-------|------------------|---------|-------------------------------------|-----|------|
|                      | Grade | Dose (mg/kg/day) |         | 20                                  | 200 | 1000 |
| Awareness            |       |                  |         |                                     |     |      |
| Alertness            | N     |                  | 5       | 5                                   | 5   | 5    |
| Visual Placing       | N     |                  | 5       | 5                                   | 5   | 5    |
| Stereotypy           | N     |                  | 5       | 5                                   | 5   | 5    |
| Passivity            | N     |                  | 5       | 5                                   | 5   | 5    |
| Mood                 |       |                  |         |                                     |     |      |
| Grooming             | N     |                  | 5       | 5                                   | 5   | 5    |
| Vocalization         | N     |                  | 5       | 5                                   | 5   | 5    |
| Restlessness         | N     |                  | 5       | 5                                   | 5   | 5    |
| Irritability         | N     |                  | 5       | 5                                   | 5   | 5    |
| Fearfulness          | N     |                  | 5       | 5                                   | 5   | 5    |
| Motor Activity       |       |                  |         |                                     |     |      |
| Reactivity           | N     |                  | 5       | 5                                   | 5   | 5    |
| Spontaneous Activity | N     |                  | 5       | 5                                   | 5   | 5    |
| Touch Response       | N     |                  | 5       | 5                                   | 5   | 5    |
| Pain Response        | N     |                  | 5       | 5                                   | 5   | 5    |
| CNS Excitation       |       |                  |         |                                     |     |      |
| Startle Response     | N     |                  | 5       | 5                                   | 5   | 5    |
| Straub Tail          | N     |                  | 5       | 5                                   | 5   | 5    |
| Tremors              | N     |                  | 5       | 5                                   | 5   | 5    |
| Twitches             | N     |                  | 5       | 5                                   | 5   | 5    |
| Convulsions          | N     |                  | 5       | 5                                   | 5   | 5    |
| Posture              |       |                  |         |                                     |     |      |
| Body Posture         | N     |                  | 5       | 5                                   | 5   | 5    |
| Limb Posture         | N     |                  | 5       | 5                                   | 5   | 5    |
| Motor Incoordination |       |                  |         |                                     |     |      |
| Staggering Gait      | N     |                  | 5       | 5                                   | 5   | 5    |
| Abnormal Gait        | N     |                  | 5       | 5                                   | 5   | 5    |
| Righting Reflex      | N     |                  | 5       | 5                                   | 5   | 5    |

Notes) N : Normal sign

Numerals represent the number of animals.

Table 2-12 Effects of Polyoxyethylene p-nonylphenyl ether on the general behavior in female rats (2 - 4 hours after administration on Day 0)

Study No. : SBL79-02

| General behavior  | Group |                  | Control | Polyoxyethylene p-nonylphenyl ether |     |      |
|-------------------|-------|------------------|---------|-------------------------------------|-----|------|
|                   | Grade | Dose (mg/kg/day) |         | 20                                  | 200 | 1000 |
| Muscle Tone       |       |                  |         |                                     |     |      |
| Limb Tone         | N     |                  | 5       | 5                                   | 5   | 5    |
| Grip Strength     | N     |                  | 5       | 5                                   | 5   | 5    |
| Body Tone         | N     |                  | 5       | 5                                   | 5   | 5    |
| Abdominal Tone    | N     |                  | 5       | 5                                   | 5   | 5    |
| Reflex            |       |                  |         |                                     |     |      |
| Pinna Reflex      | N     |                  | 5       | 5                                   | 5   | 5    |
| Corneal Reflex    | N     |                  | 5       | 5                                   | 5   | 5    |
| IPR               | N     |                  | 5       | 5                                   | 5   | 5    |
| Autonomic Profile |       |                  |         |                                     |     |      |
| Writhing          | N     |                  | 5       | 5                                   | 5   | 5    |
| Palpebral Opening | N     |                  | 5       | 5                                   | 5   | 5    |
| Exophthalmos      | N     |                  | 5       | 5                                   | 5   | 5    |
| Urination         | N     |                  | 5       | 5                                   | 5   | 5    |
| Salivation        | N     |                  | 5       | 5                                   | 5   | 5    |
| Piloerection      | N     |                  | 5       | 5                                   | 5   | 5    |
| Hypothermia       | N     |                  | 5       | 5                                   | 5   | 5    |
| Skin Color        | N     |                  | 5       | 5                                   | 5   | 5    |
| Heart Rate        | N     |                  | 5       | 5                                   | 5   | 5    |
| Respiratory Rate  | N     |                  | 5       | 5                                   | 5   | 5    |
| Pupil Size        | N     |                  | 5       | 5                                   | 5   | 5    |
| Rearing*          | 0     |                  | 5       | 5                                   | 5   | 4    |
|                   | 1     |                  | 0       | 0                                   | 0   | 1    |

Notes) N : Normal sign

\* : Numerals represent the count of rearing

Numerals represent the number of animals.

Table 2-13 Effects of Polyoxyethylene p-nonylphenyl ether on the general behavior in female rats (2 - 4 hours after administration on Day 27)

Study No. : SBL79-02

| General behavior     | Group |                  | Control | Polyoxyethylene p-nonylphenyl ether |     |      |
|----------------------|-------|------------------|---------|-------------------------------------|-----|------|
|                      | Grade | Dose (mg/kg/day) |         | 20                                  | 200 | 1000 |
| Awareness            |       |                  |         |                                     |     |      |
| Alertness            | N     |                  | 5       | 5                                   | 5   | 5    |
| Visual Placing       | N     |                  | 5       | 5                                   | 5   | 5    |
| Stereotypy           | N     |                  | 5       | 5                                   | 5   | 5    |
| Passivity            | N     |                  | 5       | 5                                   | 5   | 5    |
| Mood                 |       |                  |         |                                     |     |      |
| Grooming             | N     |                  | 5       | 5                                   | 5   | 5    |
| Vocalization         | N     |                  | 5       | 5                                   | 5   | 5    |
| Restlessness         | N     |                  | 5       | 5                                   | 5   | 5    |
| Irritability         | N     |                  | 5       | 5                                   | 5   | 5    |
| Fearfulness          | N     |                  | 5       | 5                                   | 5   | 5    |
| Motor Activity       |       |                  |         |                                     |     |      |
| Reactivity           | N     |                  | 5       | 5                                   | 5   | 5    |
| Spontaneous Activity | N     |                  | 5       | 5                                   | 5   | 5    |
| Touch Response       | N     |                  | 5       | 5                                   | 5   | 5    |
| Pain Response        | N     |                  | 5       | 5                                   | 5   | 5    |
| CNS Excitation       |       |                  |         |                                     |     |      |
| Startle Response     | N     |                  | 5       | 5                                   | 5   | 5    |
| Straub Tail          | N     |                  | 5       | 5                                   | 5   | 5    |
| Tremors              | N     |                  | 5       | 5                                   | 5   | 5    |
| Twitches             | N     |                  | 5       | 5                                   | 5   | 5    |
| Convulsions          | N     |                  | 5       | 5                                   | 5   | 5    |
| Posture              |       |                  |         |                                     |     |      |
| Body Posture         | N     |                  | 5       | 5                                   | 5   | 5    |
| Limb Posture         | N     |                  | 5       | 5                                   | 5   | 5    |
| Motor Incoordination |       |                  |         |                                     |     |      |
| Staggering Gait      | N     |                  | 5       | 5                                   | 5   | 5    |
| Abnormal Gait        | N     |                  | 5       | 5                                   | 5   | 5    |
| Righting Reflex      | N     |                  | 5       | 5                                   | 5   | 5    |

Notes) N : Normal sign

Numerals represent the number of animals.

Table 2-14 Effects of Polyoxyethylene p-nonylphenyl ether on the general behavior in female rats (2 - 4 hours after administration on Day 27) Study No. : SBL79-02

| General behavior         | Group |                  | Control | Polyoxyethylene p-nonylphenyl ether |     |      |
|--------------------------|-------|------------------|---------|-------------------------------------|-----|------|
|                          | Grade | Dose (mg/kg/day) |         | 20                                  | 200 | 1000 |
| <b>Muscle Tone</b>       |       |                  |         |                                     |     |      |
| Limb Tone                | N     |                  | 5       | 5                                   | 5   | 5    |
| Grip Strength            | N     |                  | 5       | 5                                   | 5   | 5    |
| Body Tone                | N     |                  | 5       | 5                                   | 5   | 5    |
| Abdominal Tone           | N     |                  | 5       | 5                                   | 5   | 5    |
| <b>Reflex</b>            |       |                  |         |                                     |     |      |
| Pinna Reflex             | N     |                  | 5       | 5                                   | 5   | 5    |
| Corneal Reflex           | N     |                  | 5       | 5                                   | 5   | 5    |
| IPR                      | N     |                  | 5       | 5                                   | 5   | 5    |
| <b>Autonomic Profile</b> |       |                  |         |                                     |     |      |
| Writhing                 | N     |                  | 5       | 5                                   | 5   | 5    |
| Palpebral Opening        | N     |                  | 5       | 5                                   | 5   | 5    |
| Exophthalmos             | N     |                  | 5       | 5                                   | 5   | 5    |
| Urination                | N     |                  | 5       | 5                                   | 5   | 5    |
| Salivation               | N     |                  | 5       | 5                                   | 5   | 5    |
| Piloerection             | N     |                  | 5       | 5                                   | 5   | 5    |
| Hypothermia              | N     |                  | 5       | 5                                   | 5   | 5    |
| Skin Color               | N     |                  | 5       | 5                                   | 5   | 5    |
| Heart Rate               | N     |                  | 5       | 5                                   | 5   | 5    |
| Respiratory Rate         | N     |                  | 5       | 5                                   | 5   | 5    |
| Pupil Size               | N     |                  | 5       | 5                                   | 5   | 5    |
| Rearing†                 | 0     |                  | 3       | 5                                   | 5   | 3    |
|                          | 1     |                  | 1       | 0                                   | 0   | 2    |
|                          | 2     |                  | 1       | 0                                   | 0   | 0    |

Notes) N : Normal sign

\* : Numerals represent the count of rearing

Numerals represent the number of animals.

Table 2-15 Effects of Polyoxyethylene p-nonylphenyl ether on the general behavior in female rats (Week 2 of recovery period)

Study No. : SBL79-02

| General behavior     | Group |                  | Control | Polyoxyethylene <i>p</i> -nonylphenyl ether |     |      |
|----------------------|-------|------------------|---------|---|-----|------|
|                      | Grade | Dose (mg/kg/day) |         | 20  | 200 | 1000 |
| Awareness            |       |                  |         |   |     |      |
| Alertness            | N     |                  | 5       |   |     | 5    |
| Visual Placing       | N     |                  | 5       |   |     | 5    |
| Stereotypy           | N     |                  | 5       |   |     | 5    |
| Passivity            | N     |                  | 5       |   |     | 5    |
| Mood                 |       |                  |         |   |     |      |
| Grooming             | N     |                  | 5       |   |     | 5    |
| Vocalization         | N     |                  | 5       |   |     | 5    |
| Restlessness         | N     |                  | 5       |   |     | 5    |
| Irritability         | N     |                  | 5       |   |     | 5    |
| Fearfulness          | N     |                  | 5       |   |     | 5    |
| Motor Activity       |       |                  |         |   |     |      |
| Reactivity           | N     |                  | 5       |   |     | 5    |
| Spontaneous Activity | N     |                  | 5       |   |     | 5    |
| Touch Response       | N     |                  | 5       |   |     | 5    |
| Pain Response        | N     |                  | 5       |   |     | 5    |
| CNS Excitation       |       |                  |         |   |     |      |
| Startle Response     | N     |                  | 5       |   |     | 5    |
| Straub Tail          | N     |                  | 5       |   |     | 5    |
| Tremors              | N     |                  | 5       |   |     | 5    |
| Twitches             | N     |                  | 5       |   |     | 5    |
| Convulsions          | N     |                  | 5       |   |     | 5    |
| Posture              |       |                  |         |   |     |      |
| Body Posture         | N     |                  | 5       |   |     | 5    |
| Limb Posture         | N     |                  | 5       |   |     | 5    |
| Motor Incoordination |       |                  |         |   |     |      |
| Staggering Gait      | N     |                  | 5       |   |     | 5    |
| Abnormal Gait        | N     |                  | 5       |   |     | 5    |
| Righting Reflex      | N     |                  | 5       |   |     | 5    |

Notes) N : Normal sign

Numerals represent the number of animals.

Table 2-16 Effects of Polyoxyethylene p-nonylphenyl ether on the general behavior in female rats (Week 2 of recovery period)

Study No. : SBL79-02

| General behavior  | Group |                  | Control | Polyoxyethylene p-nonylphenyl ether |     |      |
|-------------------|-------|------------------|---------|-------------------------------------|-----|------|
|                   | Grade | Dose (mg/kg/day) |         | 20                                  | 200 | 1000 |
| Muscle Tone       |       |                  |         |                                     |     |      |
| Limb Tone         | N     |                  | 5       |                                     |     | 5    |
| Grip Strength     | N     |                  | 5       |                                     |     | 5    |
| Body Tone         | N     |                  | 5       |                                     |     | 5    |
| Abdominal Tone    | N     |                  | 5       |                                     |     | 5    |
| Reflex            |       |                  |         |                                     |     |      |
| Pinna Reflex      | N     |                  | 5       |                                     |     | 5    |
| Corneal Reflex    | N     |                  | 5       |                                     |     | 5    |
| IPR               | N     |                  | 5       |                                     |     | 5    |
| Autonomic Profile |       |                  |         |                                     |     |      |
| Writhing          | N     |                  | 5       |                                     |     | 5    |
| Palpebral Opening | N     |                  | 5       |                                     |     | 5    |
| Exophthalmos      | N     |                  | 5       |                                     |     | 5    |
| Urination         | N     |                  | 5       |                                     |     | 5    |
| Salivation        | N     |                  | 5       |                                     |     | 5    |
| Piloerection      | N     |                  | 5       |                                     |     | 5    |
| Hypothermia       | N     |                  | 5       |                                     |     | 5    |
| Skin Color        | N     |                  | 5       |                                     |     | 5    |
| Heart Rate        | N     |                  | 5       |                                     |     | 5    |
| Respiratory Rate  | N     |                  | 5       |                                     |     | 5    |
| Pupil Size        | N     |                  | 5       |                                     |     | 5    |
| Rearing*          | 0     |                  | 5       |                                     |     | 3    |
|                   | 1     |                  | 0       |                                     |     | 2    |

Notes) N : Normal sign

\* : Numerals represent the count of rearing

Numerals represent the number of animals.



Table 3-1 Food consumption ( g/day ) in male rats

Study No. : SBL79-02

| Group | Control            | Polyoxyethylene p-nonylphenyl ether |                     |                    |
|-------|--------------------|-------------------------------------|---------------------|--------------------|
|       |                    | 20                                  | 200                 | 1000               |
| Pre   | 23.4 $\pm$ 1.3(10) | 23.2 $\pm$ 1.9( 5)                  | 23.4 $\pm$ 3.2( 5)  | 23.5 $\pm$ 1.9(10) |
| 1w    | 26.6 $\pm$ 2.9(10) | 27.2 $\pm$ 3.0( 5)                  | 26.2 $\pm$ 3.1( 5)  | 28.4 $\pm$ 1.6(10) |
| 2w    | 30.2 $\pm$ 2.5(10) | 27.4 $\pm$ 2.3( 5)                  | 26.4 $\pm$ 3.4( 5)* | 29.8 $\pm$ 2.8(10) |
| 3w    | 28.0 $\pm$ 3.1(10) | 26.6 $\pm$ 2.6( 5)                  | 26.6 $\pm$ 2.7( 5)  | 28.1 $\pm$ 3.3(10) |
| 4w    | 30.9 $\pm$ 3.0(10) | 29.4 $\pm$ 3.4( 5)                  | 28.0 $\pm$ 2.7( 5)  | 31.6 $\pm$ 4.2(10) |
| R:1w  | 29.2 $\pm$ 4.3( 5) |                                     |                     | 30.0 $\pm$ 2.1( 5) |
| R:2w  | 32.4 $\pm$ 3.1( 5) |                                     |                     | 31.8 $\pm$ 4.1( 5) |

Values are expressed as the mean  $\pm$  S.D. (N).

\* P&lt;0.05 : Significantly different from control.

Table 3-2 Food consumption ( g/day ) in female rats

Study No. : SBL79-02

| Group | Control            | Polyoxyethylene p-nonylphenyl ether |                    |                     |
|-------|--------------------|-------------------------------------|--------------------|---------------------|
|       |                    | 20                                  | 200                | 1000                |
| Pre   | 20.4 $\pm$ 1.6(10) | 20.0 $\pm$ 1.4( 5)                  | 21.0 $\pm$ 1.6( 5) | 21.0 $\pm$ 1.2(10)  |
| 1w    | 21.3 $\pm$ 2.1(10) | 21.6 $\pm$ 2.2( 5)                  | 23.2 $\pm$ 2.8( 5) | 21.7 $\pm$ 1.9(10)  |
| 2w    | 21.0 $\pm$ 2.8(10) | 20.2 $\pm$ 1.9( 5)                  | 21.8 $\pm$ 2.6( 5) | 21.1 $\pm$ 2.3(10)  |
| 3w    | 19.4 $\pm$ 3.0(10) | 19.4 $\pm$ 2.1( 5)                  | 20.4 $\pm$ 2.6( 5) | 19.8 $\pm$ 3.2(10)  |
| 4w    | 23.1 $\pm$ 3.2(10) | 26.0 $\pm$ 2.3( 5)                  | 23.2 $\pm$ 3.5( 5) | 24.1 $\pm$ 5.0(10)  |
| R:1w  | 21.6 $\pm$ 3.2( 5) |                                     |                    | 20.0 $\pm$ 5.7( 5)  |
| R:2w  | 25.0 $\pm$ 1.7( 5) |                                     |                    | 21.8 $\pm$ 1.3( 5)* |

Values are expressed as the mean  $\pm$  S.D. (N).

\* P&lt;0.05 : Significantly different from control.

Table 4-1 Body weight ( g ) in male rats

Study No. : SBL79-02

| Group | Control        | Polyoxyethylene p-nonylphenyl ether |                |                |
|-------|----------------|-------------------------------------|----------------|----------------|
|       |                | 20                                  | 200            | 1000           |
| Pre   | 156.5± 7.3(10) | 155.6± 7.3( 5)                      | 151.8±12.9( 5) | 156.1±10.1(10) |
| 1w    | 213.0±14.8(10) | 210.6±14.4( 5)                      | 204.0±23.3( 5) | 213.7±13.3(10) |
| 2w    | 270.0±23.6(10) | 263.2±17.0( 5)                      | 251.4±29.6( 5) | 268.1±17.3(10) |
| 3w    | 318.5±32.3(10) | 308.2±17.6( 5)                      | 294.2±33.7( 5) | 316.4±25.4(10) |
| 4w    | 354.3±37.7(10) | 339.2±23.0( 5)                      | 324.4±36.4( 5) | 352.0±34.2(10) |
| R:1w  | 383.2±34.2( 5) |                                     |                | 378.6±31.6( 5) |
| R:2w  | 407.4±38.9( 5) |                                     |                | 406.0±35.6( 5) |

Values are expressed as the mean + S.D. (N).  
Not significantly different from control.

Table 4-2 Body weight ( g ) in female rats

Study No. : SBL79-02

| Group | Control              | Polyoxyethylene p-nonylphenyl ether |                      |                      |
|-------|----------------------|-------------------------------------|----------------------|----------------------|
|       |                      | 20                                  | 200                  | 1000                 |
| Pre   | 130.4 $\pm$ 4.4(10)  | 130.2 $\pm$ 6.1( 5)                 | 130.2 $\pm$ 6.8( 5)  | 130.0 $\pm$ 4.8(10)  |
| 1w    | 163.5 $\pm$ 5.9(10)  | 165.2 $\pm$ 10.1( 5)                | 168.2 $\pm$ 10.8( 5) | 164.8 $\pm$ 6.2(10)  |
| 2w    | 189.3 $\pm$ 10.9(10) | 184.8 $\pm$ 12.5( 5)                | 193.0 $\pm$ 14.8( 5) | 185.9 $\pm$ 10.3(10) |
| 3w    | 212.7 $\pm$ 18.8(10) | 207.2 $\pm$ 13.8( 5)                | 211.4 $\pm$ 22.3( 5) | 207.4 $\pm$ 14.5(10) |
| 4w    | 230.5 $\pm$ 19.4(10) | 231.2 $\pm$ 14.2( 5)                | 229.8 $\pm$ 24.4( 5) | 224.7 $\pm$ 19.1(10) |
| R:1w  | 238.0 $\pm$ 12.2( 5) |                                     |                      | 222.4 $\pm$ 10.5( 5) |
| R:2w  | 251.4 $\pm$ 13.2( 5) |                                     |                      | 233.8 $\pm$ 15.1( 5) |

Values are expressed as the mean  $\pm$  S.D. (N).  
Not significantly different from control.

Table 4-3 Body weight gain ( g ) in male rats

Study No. : SBL79-02

| Group | Control             | Polyoxyethylene p-nonylphenyl ether |                     |                     |
|-------|---------------------|-------------------------------------|---------------------|---------------------|
|       |                     | 20                                  | 200                 | 1000                |
| 1w    | 56.5 $\pm$ 8.9(10)  | 55.0 $\pm$ 7.3( 5)                  | 52.2 $\pm$ 10.8( 5) | 57.6 $\pm$ 4.7(10)  |
| 2w    | 57.0 $\pm$ 9.6(10)  | 52.6 $\pm$ 4.2( 5)                  | 47.4 $\pm$ 7.2( 5)  | 54.4 $\pm$ 5.5(10)  |
| 3w    | 48.5 $\pm$ 10.0(10) | 45.0 $\pm$ 2.9( 5)                  | 42.8 $\pm$ 7.6( 5)  | 48.3 $\pm$ 9.5(10)  |
| 4w    | 35.8 $\pm$ 7.3(10)  | 31.0 $\pm$ 6.2( 5)                  | 30.2 $\pm$ 5.8( 5)  | 35.6 $\pm$ 10.1(10) |
| R:1w  | 34.6 $\pm$ 5.6( 5)  |                                     |                     | 35.0 $\pm$ 4.3( 5)  |
| R:2w  | 24.2 $\pm$ 9.2( 5)  |                                     |                     | 27.4 $\pm$ 5.1( 5)  |

Values are expressed as the mean  $\pm$  S.D. (N).  
Not significantly different from control.

Table 4-4 Body weight gain ( g ) in female rats

Study No. : SBL79-02

| Group | Control            | Polyoxyethylene p-nonylphenyl ether |                     |                    |
|-------|--------------------|-------------------------------------|---------------------|--------------------|
|       |                    | 20                                  | 200                 | 1000               |
| 1w    | 33.1 $\pm$ 5.0(10) | 35.0 $\pm$ 5.1( 5)                  | 38.0 $\pm$ 4.7( 5)  | 34.8 $\pm$ 3.2(10) |
| 2w    | 25.8 $\pm$ 7.0(10) | 19.6 $\pm$ 4.5( 5)                  | 24.8 $\pm$ 11.6( 5) | 21.1 $\pm$ 5.2(10) |
| 3w    | 23.4 $\pm$ 9.1(10) | 22.4 $\pm$ 4.6( 5)                  | 18.4 $\pm$ 8.1( 5)  | 21.5 $\pm$ 5.9(10) |
| 4w    | 17.8 $\pm$ 6.2(10) | 24.0 $\pm$ 4.0( 5)                  | 18.4 $\pm$ 3.7( 5)  | 17.3 $\pm$ 8.5(10) |
| R:1w  | 18.4 $\pm$ 4.8( 5) |                                     |                     | 13.4 $\pm$ 4.0( 5) |
| R:2w  | 13.4 $\pm$ 1.1( 5) |                                     |                     | 11.4 $\pm$ 8.1( 5) |

Values are expressed as the mean  $\pm$  S.D. (N).  
Not significantly different from control.

Gross ophthalmological examination

Grade

- 0 : No abnormal changes
- 1 : Slight
- 2 : Moderate
- 3 : Severe
- P : Non-graded change
- U : Unexamined

Table 5-1 Gross ophthalmological examination in male rats

Study No. : SBL79-02

| Group            |                     | Control | Polyoxyethylene p-nonylphenyl ether |     |      |
|------------------|---------------------|---------|-------------------------------------|-----|------|
| Dose (mg/kg/day) |                     |         | 20                                  | 200 | 1000 |
| Week             | Item                | Grade   |                                     |     |      |
| Pre              | No abnormal changes | 10      | 5                                   | 5   | 10   |
| 4w               | No abnormal changes | 10      | 5                                   | 5   | 10   |
| R:2w             | No abnormal changes | 5       |                                     |     | 5    |

Numerals represent the number of animals.



Table 5-2

Gross ophthalmological examination in female rats

Study No. : SBL79-02

| Group           |                     | Control | Polyoxyethylene p-nonylphenyl ether |     |      |
|-----------------|---------------------|---------|-------------------------------------|-----|------|
| Dose(mg/kg/day) |                     |         | 20                                  | 200 | 1000 |
| Week            | Item                | Grade   |                                     |     |      |
| Pre             | No abnormal changes | 10      | 5                                   | 5   | 10   |
| 4w              | No abnormal changes | 10      | 5                                   | 5   | 10   |
| R:2w            | No abnormal changes | 5       |                                     |     | 5    |

Numerals represent the number of animals.

Funduscopy examination

Grade

- 0 : No abnormal changes
- 1 : Slight
- 2 : Moderate
- 3 : Severe
- P : Non-graded change
- U : Unexamined

Table 5-3 Fundusoscopic examination in male rats

Study No. : SBL79-02

| Group            |                     | Control | Polyoxyethylene p-nonylphenyl ether |     |      |
|------------------|---------------------|---------|-------------------------------------|-----|------|
| Dose (mg/kg/day) |                     |         | 20                                  | 200 | 1000 |
| Week             | Item                | Grade   |                                     |     |      |
| Pre              | No abnormal changes | 10      | 5                                   | 5   | 10   |
| 4w               | No abnormal changes | 10      | 5                                   | 5   | 10   |
| R:2w             | No abnormal changes | 5       |                                     |     | 5    |

Numerals represent the number of animals.

Table 5-4 Fundusoscopic examination in female rats

Study No. : SBL79-02

| Group           |                     | Control | Polyoxyethylene p-nonylphenyl ether |     |      |
|-----------------|---------------------|---------|-------------------------------------|-----|------|
| Dose(mg/kg/day) |                     |         | 20                                  | 200 | 1000 |
| Week            | Item                | Grade   |                                     |     |      |
| Pre             | No abnormal changes | 10      | 5                                   | 5   | 10   |
| 4w              | No abnormal changes | 10      | 5                                   | 5   | 10   |
| R:2w            | No abnormal changes | 5       |                                     |     | 5    |

Numerals represent the number of animals.

## Number of Animals

Study No. : SBL79-02

Item : Urinalysis  
Sex : Male

| Group                           | Control | Polyoxyethylene p-nonylphenyl ether |     |      |
|---------------------------------|---------|-------------------------------------|-----|------|
|                                 |         | 20                                  | 200 | 1000 |
| Dose (mg/kg/day)                |         |                                     |     |      |
| 4w                              | 10      | 5                                   | 5   | 10   |
| R:2w                            | 5       |                                     |     | 5    |
| Urine volume & Specific gravity |         |                                     |     |      |
| 4w                              | 5       | 5                                   | 5   | 5    |
| R:2w                            | 5       |                                     |     | 5    |

## Number of Animals

Study No. : SBL79-02

Item : Urinalysis  
Sex : Female

| Group                           | Control | Polyoxyethylene p-nonylphenyl ether |     |      |
|---------------------------------|---------|-------------------------------------|-----|------|
|                                 |         | 20                                  | 200 | 1000 |
| Dose(mg/kg/day)                 |         |                                     |     |      |
| 4w                              | 10      | 5                                   | 5   | 10   |
| R:2w                            | 5       |                                     |     | 5    |
| Urine volume & Specific gravity |         |                                     |     |      |
| 4w                              | 5       | 5                                   | 5   | 5    |
| R:2w                            | 5       |                                     |     | 5    |

# Standard Urinalysis

|                              |                    |           |          |                   |              |          |        |
|------------------------------|--------------------|-----------|----------|-------------------|--------------|----------|--------|
| Color                        | 0 : Normal color   | Protein   | 0 : -    | (mg/dl)           | Glucose      | 0 : -    | (g/dl) |
|                              | 1 : Abnormal color |           | 1 : +    |                   |              | 1 : +    |        |
|                              |                    |           | 2 : +    | 30                |              | 2 : +    | 0.1    |
|                              |                    |           | 3 : ++   | 100               |              | 3 : ++   | 0.25   |
|                              |                    |           | 4 : +++  | 300               |              | 4 : +++  | 0.5    |
|                              |                    |           | 5 : ++++ | 1000              |              | 5 : ++++ | 1      |
|                              |                    |           |          |                   |              |          | 2      |
| Ketone body                  | 0 : -              | Bilirubin | 0 : -    | (mg/dl)           | Occult blood | 0 : -    |        |
|                              | 1 : +              |           | 1 : +    |                   |              | 1 : +    |        |
|                              | 2 : +              |           | 2 : ++   |                   |              | 2 : +    |        |
|                              | 3 : ++             |           | 3 : +++  |                   |              | 3 : ++   |        |
|                              | 4 : +++            |           |          |                   |              | 4 : +++  |        |
|                              | 5 : ++++           |           |          |                   |              |          |        |
|                              |                    |           |          |                   |              |          |        |
| Urobilinogen                 | 0 : +              |           |          | (Ehrlich unit/dl) |              |          |        |
|                              | 1 : +              |           |          |                   |              |          |        |
|                              | 2 : ++             |           |          |                   |              |          |        |
|                              | 3 : +++            |           |          |                   |              |          |        |
|                              | 4 : ++++           |           |          |                   |              |          |        |
|                              | 5 : +++++          |           |          |                   |              |          |        |
|                              |                    |           |          |                   |              |          |        |
| Urine volume (U.Volume)      |                    |           |          |                   |              |          |        |
| Specific gravity (S.Gravity) |                    |           |          |                   |              |          |        |

Table 6-1 Urinalysis in male rats

Study No. : SBL79-02

| Group            | Control |     | Polyoxyethylene p-nonylphenyl ether |     |      |
|------------------|---------|-----|-------------------------------------|-----|------|
|                  |         |     | 20                                  | 200 | 1000 |
| Dose (mg/kg/day) | Grade   |     |                                     |     |      |
| Color            | 4w      | 0   | 5                                   | 5   | 10   |
|                  |         | 1   |                                     |     |      |
|                  | R:2w    | 0   |                                     |     | 5    |
|                  |         | 1   |                                     |     |      |
| pH               | 4w      | 5   |                                     |     |      |
|                  |         | 5.5 |                                     |     |      |
|                  |         | 6   | 1                                   |     |      |
|                  |         | 6.5 | 2                                   |     | 1    |
|                  |         | 7   | 4                                   | 1   | 2    |
|                  |         | 7.5 | 1                                   | 2   | 4    |
|                  |         | 8   | 2                                   | 2   | 3    |
|                  |         | 8.5 |                                     |     |      |
|                  |         | 9   |                                     |     |      |
|                  | R:2w    | 5   |                                     |     |      |
|                  |         | 5.5 |                                     |     |      |
|                  |         | 6   |                                     |     |      |
|                  |         | 6.5 |                                     |     |      |
|                  |         | 7   |                                     |     | 2    |
|                  |         | 7.5 | 3                                   |     | 3    |
|                  |         | 8   | 2                                   |     |      |
|                  |         | 8.5 |                                     |     |      |
|                  |         | 9   |                                     |     |      |

Numerals represent the number of animals.  
 Not significantly different from control.



Table 6-2

Urinalysis in male rats

Study No. : SBL79-02

| Group            | Control |   | Polyoxyethylene p-nonylphenyl ether |     |      |    |
|------------------|---------|---|-------------------------------------|-----|------|----|
| Dose (mg/kg/day) | Grade   |   | 20                                  | 200 | 1000 |    |
| Protein          | 4w      | 0 | 1                                   |     |      |    |
|                  |         | 1 | 1                                   |     |      |    |
|                  |         | 2 | 4                                   | 2   | 3    | 5  |
|                  |         | 3 | 6                                   | 1   | 2    | 5  |
|                  |         | 4 |                                     |     |      |    |
|                  | 5       |   |                                     |     |      |    |
|                  | R:2w    | 0 | 1                                   |     |      |    |
|                  |         | 1 |                                     |     |      |    |
|                  |         | 2 | 1                                   |     |      | 4  |
|                  |         | 3 | 3                                   |     |      | 1  |
|                  |         | 4 |                                     |     |      |    |
|                  | 5       |   |                                     |     |      |    |
| Glucose          | 4w      | 0 | 10                                  | 5   | 5    | 10 |
|                  |         | 1 |                                     |     |      |    |
|                  |         | 2 |                                     |     |      |    |
|                  |         | 3 |                                     |     |      |    |
|                  |         | 4 |                                     |     |      |    |
|                  | 5       |   |                                     |     |      |    |
|                  | R:2w    | 0 | 5                                   |     |      | 5  |
|                  |         | 1 |                                     |     |      |    |
|                  |         | 2 |                                     |     |      |    |
|                  |         | 3 |                                     |     |      |    |
|                  |         | 4 |                                     |     |      |    |
|                  | 5       |   |                                     |     |      |    |

Numerals represent the number of animals.  
 Not significantly different from control.

Table 6-3 Urinalysis in male rats

Study No. : SBL79-02

| Group           | Control |   | Polyoxyethylene p-nonylphenyl ether |     |      |    |
|-----------------|---------|---|-------------------------------------|-----|------|----|
| Dose(mg/kg/day) |         |   | 20                                  | 200 | 1000 |    |
|                 | Grade   |   |                                     |     |      |    |
| Ketone body     | 4w      | 0 | 1                                   | 1   |      |    |
|                 |         | 1 | 7                                   | 3   | 4    | 7  |
|                 |         | 2 | 2                                   | 1   |      | 3  |
|                 |         | 3 |                                     |     |      |    |
|                 |         | 4 |                                     |     |      |    |
|                 |         | 5 |                                     |     |      |    |
|                 | R:2w    | 0 |                                     |     |      | 1  |
|                 |         | 1 | 5                                   |     |      | 2  |
|                 |         | 2 |                                     |     |      | 2  |
|                 |         | 3 |                                     |     |      |    |
|                 |         | 4 |                                     |     |      |    |
|                 |         | 5 |                                     |     |      |    |
| Bilirubin       | 4w      | 0 | 10                                  | 4   | 5    | 10 |
|                 |         | 1 |                                     | 1   |      |    |
|                 |         | 2 |                                     |     |      |    |
|                 |         | 3 |                                     |     |      |    |
|                 | R:2w    | 0 | 5                                   |     |      | 5  |
|                 |         | 1 |                                     |     |      |    |
|                 |         | 2 |                                     |     |      |    |
|                 |         | 3 |                                     |     |      |    |

Numerals represent the number of animals.  
 Not significantly different from control.

Table 6-4 Urinalysis in male rats

Study No. : SBL79-02

| Group            | Control |   | Polyoxyethylene p-nonylphenyl ether |     |      |   |
|------------------|---------|---|-------------------------------------|-----|------|---|
| Dose (mg/kg/day) | Grade   |   | 20                                  | 200 | 1000 |   |
| Occult blood     | 4w      | 0 | 6                                   | 5   | 4    | 9 |
|                  |         | 1 | 2                                   |     | 1    | 1 |
|                  |         | 2 | 2                                   |     |      |   |
|                  |         | 3 |                                     |     |      |   |
|                  |         | 4 |                                     |     |      |   |
|                  | R:2w    | 0 | 4                                   |     |      | 5 |
|                  |         | 1 |                                     |     |      |   |
|                  |         | 2 | 1                                   |     |      |   |
|                  |         | 3 |                                     |     |      |   |
|                  |         | 4 |                                     |     |      |   |
| Urobilinogen     | 4w      | 0 | 10                                  | 5   | 4    | 9 |
|                  |         | 1 |                                     |     | 1    | 1 |
|                  |         | 2 |                                     |     |      |   |
|                  |         | 3 |                                     |     |      |   |
|                  |         | 4 |                                     |     |      |   |
|                  |         | 5 |                                     |     |      |   |
|                  | R:2w    | 0 | 4                                   |     |      | 5 |
|                  |         | 1 | 1                                   |     |      |   |
|                  |         | 2 |                                     |     |      |   |
|                  |         | 3 |                                     |     |      |   |
| 4                |         |   |                                     |     |      |   |
| 5                |         |   |                                     |     |      |   |

Numerals represent the number of animals.  
 Not significantly different from control.

Table 6-5

Urinalysis in male rats

Study No. : SBL79-02

| Group           |      | Control       | Polyoxyethylene p-nonylphenyl ether |               |               |
|-----------------|------|---------------|-------------------------------------|---------------|---------------|
| Dose(mg/kg/day) |      |               | 20                                  | 200           | 1000          |
| U.Volume (mL)   | 4w   | 2.44+0.97     | 3.68+1.37                           | 3.14+1.28     | 1.44+0.88     |
|                 | R:2w | 2.40+1.15     |                                     |               | 2.58+0.84     |
| S.Gravity       | 4w   | 1.0338+0.0137 | 1.0268+0.0060                       | 1.0322+0.0149 | 1.0404+0.0201 |
|                 | R:2w | 1.0426+0.0184 |                                     |               | 1.0360+0.0115 |

Values are expressed as the mean + S.D.  
Not significantly different from Control.

Table 6-6 Urinalysis in female rats

Study No. : SBL79-02

| Group | Control          |   | Polyoxyethylene p-nonylphenyl ether |             |                  |
|-------|------------------|---|-------------------------------------|-------------|------------------|
|       | Dose (mg/kg/day) |   | 20                                  | 200         | 1000             |
|       | Grade            |   |                                     |             |                  |
| Color | 4w               | 0<br>1  | 5                                   | 5           | 10               |
|       | R:2w             | 0<br>1  |                                     |             | 5                |
| pH    | 4w               | 5<br>5.5<br>6<br>6.5<br>7<br>7.5<br>8<br>8.5<br>9 |                                     |             |                  |
|       |                  |   | 2<br>2<br>1                         | 3<br>1<br>1 | 1<br>1<br>7<br>1 |
|       | R:2w             | 5<br>5.5<br>6<br>6.5<br>7<br>7.5<br>8<br>8.5<br>9 |                                     |             |                  |
|       |                  |   |                                     |             | 2<br>1<br>2      |

Numerals represent the number of animals.  
Not significantly different from control.

Table 6-7 Urinalysis in female rats

Study No. : SBL79-02

| Group           | Control |   | Polyoxyethylene p-nonylphenyl ether |     |      |    |
|-----------------|---------|---|-------------------------------------|-----|------|----|
| Dose(mg/kg/day) | Grade   |   | 20                                  | 200 | 1000 |    |
| Protein         | 4w      | 0 | 6                                   | *   | 3    | 4  |
|                 |         | 1 | 2                                   | 1   |      |    |
|                 |         | 2 | 2                                   | 4   | 2    | 5  |
|                 |         | 3 |                                     |     |      | 1  |
|                 |         | 4 |                                     |     |      |    |
|                 |         | 5 |                                     |     |      |    |
|                 | R:2w    | 0 | 3                                   |     |      | 3  |
|                 |         | 1 |                                     |     |      | 2  |
|                 |         | 2 | 2                                   |     |      |    |
|                 |         | 3 |                                     |     |      |    |
|                 |         | 4 |                                     |     |      |    |
|                 |         | 5 |                                     |     |      |    |
| Glucose         | 4w      | 0 | 10                                  | 5   | 5    | 10 |
|                 |         | 1 |                                     |     |      |    |
|                 |         | 2 |                                     |     |      |    |
|                 |         | 3 |                                     |     |      |    |
|                 |         | 4 |                                     |     |      |    |
|                 |         | 5 |                                     |     |      |    |
|                 | R:2w    | 0 | 5                                   |     |      | 5  |
|                 |         | 1 |                                     |     |      |    |
|                 |         | 2 |                                     |     |      |    |
|                 |         | 3 |                                     |     |      |    |
|                 |         | 4 |                                     |     |      |    |
|                 |         | 5 |                                     |     |      |    |

Numerals represent the number of animals.

\* P&lt;0.05 : Significantly different from control.

Table 6-8 Urinalysis in female rats

Study No. : SBL79-02

| Group           | Control |   | Polyoxyethylene p-nonylphenyl ether |     |      |
|-----------------|---------|---|-------------------------------------|-----|------|
|                 |         |   | 20                                  | 200 | 1000 |
| Dose(mg/kg/day) | Grade   |   |                                     |     |      |
| Ketone body     | 4w      | 0 | 9                                   | 4   | 5    |
|                 |         | 1 | 1                                   | 5   | 4    |
|                 |         | 2 |                                     |     | 1    |
|                 |         | 3 |                                     |     |      |
|                 |         | 4 |                                     |     |      |
|                 |         | 5 |                                     |     |      |
|                 | R:2w    | 0 | 4                                   |     | 4    |
|                 |         | 1 | 1                                   |     | 1    |
|                 |         | 2 |                                     |     |      |
|                 |         | 3 |                                     |     |      |
|                 |         | 4 |                                     |     |      |
|                 |         | 5 |                                     |     |      |
| Bilirubin       | 4w      | 0 | 10                                  | 5   | 10   |
|                 |         | 1 |                                     |     |      |
|                 |         | 2 |                                     |     |      |
|                 |         | 3 |                                     |     |      |
|                 | R:2w    | 0 | 5                                   |     | 5    |
|                 |         | 1 |                                     |     |      |
|                 |         | 2 |                                     |     |      |
|                 |         | 3 |                                     |     |      |
|                 |         |   |                                     |     |      |
|                 |         |   |                                     |     |      |

Numerals represent the number of animals.  
 Not significantly different from control.

Table 6-9 Urinalysis in female rats

Study No. : SBL79-02

| Group        | Control |   | Polyoxyethylene p-nonylphenyl ether |     |      |
|--------------|---------|---|-------------------------------------|-----|------|
|              | Grade   |   | 20                                  | 200 | 1000 |
| Occult blood | 4w      | 0 | 4                                   | 5   | 8    |
|              |         | 1 |                                     |     | 1    |
|              |         | 2 | 1                                   |     | 1    |
|              |         | 3 |                                     |     |      |
|              |         | 4 |                                     |     |      |
|              | R:2w    | 0 |                                     |     | 5    |
|              |         | 1 |                                     |     |      |
|              |         | 2 | 1                                   |     |      |
|              |         | 3 |                                     |     |      |
|              |         | 4 |                                     |     |      |
| Urobilinogen | 4w      | 0 | 8                                   | 5   | 7    |
|              |         | 1 | 2                                   |     | 3    |
|              |         | 2 |                                     |     |      |
|              |         | 3 |                                     |     |      |
|              |         | 4 |                                     |     |      |
|              |         | 5 |                                     |     |      |
|              | R:2w    | 0 | 3                                   |     | 5    |
|              |         | 1 | 2                                   |     |      |
|              |         | 2 |                                     |     |      |
|              |         | 3 |                                     |     |      |
|              |         | 4 |                                     |     |      |
|              |         | 5 |                                     |     |      |

Numerals represent the number of animals.  
 Not significantly different from control.



Table 6-10 Urinalysis in female rats

Study No. : SBL79-02

| Group           |      | Control             | Polyoxyethylene p-nonylphenyl ether |                     |                     |
|-----------------|------|---------------------|-------------------------------------|---------------------|---------------------|
| Dose(mg/kg/day) |      |                     | 20                                  | 200                 | 1000                |
| U.Volume (mL)   | 4w   | 2.68 $\pm$ 1.45     | 3.94 $\pm$ 1.29                     | 2.94 $\pm$ 1.55     | 1.76 $\pm$ 0.67     |
|                 | R:2w | 2.50 $\pm$ 0.79     |                                     |                     | 2.26 $\pm$ 0.91     |
| S.Gravity       | 4w   | 1.0242 $\pm$ 0.0159 | 1.0160 $\pm$ 0.0019                 | 1.0300 $\pm$ 0.0193 | 1.0246 $\pm$ 0.0074 |
|                 | R:2w | 1.0262 $\pm$ 0.0110 |                                     |                     | 1.0214 $\pm$ 0.0040 |

Values are expressed as the mean + S.D.  
Not significantly different from Control.

# Urinary Sediment

RBC  
 0 : -  
 1 : 1 - 4 /HPF  
 2 : 5 -10 /HPF  
 3 :10 < /HPF

WBC  
 0 : -  
 1 : 1 - 5 /HPF  
 2 : 6 -20 /HPF  
 3 :20 < /HPF

Phosphate crystal  
 (Phosphate) 0 : -  
 1 : 1 -10 /HPF  
 2 :11 -20 /HPF  
 3 :20 < /HPF

Urate crystal  
 (Urate) 0 : -  
 1 : 1 -10 /HPF  
 2 :11 -20 /HPF  
 3 :20 < /HPF

Oxalate crystal  
 (Oxalate) 0 : -  
 1 : 1 -10 /HPF  
 2 :11 -20 /HPF  
 3 :20 < /HPF

Other crystal  
 (Other c.) 0 : -  
 1 : 1 -10 /HPF  
 2 :11 -20 /HPF  
 3 :20 < /HPF

Epithelial cell  
 (Epith.) 0 : -  
 1 : 1 - 5 /HPF  
 2 : 6 -20 /HPF  
 3 :20 < /HPF

Bacteria  
 0 : -  
 1 : +

Cast  
 0 : -  
 1 : Hyaline Cast  
 2 : Waxy Cast  
 3 : Erythrocytic Cast

Sperm  
 0 : -  
 1 : +

Others  
 0 : -  
 1 : +

HPF : High power field

Table 6-11 Urinary sediments in male rats

Study No. : SBL79-02

| Group           |      |                  | Control | Polyoxyethylene p-nonylphenyl ether |             |             |
|-----------------|------|------------------|---------|-------------------------------------|-------------|-------------|
|                 |      |                  |         | 20                                  | 200         | 1000        |
| Dose(mg/kg/day) |      | Grade            |         |                                     |             |             |
| RBC             | 4w   | 0<br>1<br>2<br>3 | 5       | 5                                   | 5           | 5           |
|                 | R:2w | 0<br>1<br>2<br>3 | 5       |                                     |             | 5           |
| WBC             | 4w   | 0<br>1<br>2<br>3 | 5       | 5                                   | 5           | 5           |
|                 | R:2w | 0<br>1<br>2<br>3 | 5       |                                     |             | 5           |
| Phosphate       | 4w   | 0<br>1<br>2<br>3 | 3<br>2  | 3<br>2                              | 2<br>1<br>2 | 1<br>1<br>3 |
|                 | R:2w | 0<br>1<br>2<br>3 | 1<br>4  |                                     |             | 1<br>4      |
| Urate           | 4w   | 0<br>1<br>2<br>3 | 5       | 5                                   | 5           | 5           |
|                 | R:2w | 0<br>1<br>2<br>3 | 5       |                                     |             | 5           |

Numerals represent the number of animals.  
Not significantly different from control.

Table 6-12 Urinary sediments in male rats

Study No. : SBL79-02

| Group           | Control |   | Polyoxyethylene p-nonylphenyl ether |     |      |
|-----------------|---------|---|-------------------------------------|-----|------|
|                 |         |   | 20                                  | 200 | 1000 |
| Dose(mg/kg/day) | Grade   |   |                                     |     |      |
| Oxalate         | 4w      | 0 | 5                                   | 5   | 5    |
|                 |         | 1 |                                     |     |      |
|                 |         | 2 |                                     |     |      |
|                 |         | 3 |                                     |     |      |
|                 | R:2w    | 0 | 5                                   |     | 5    |
|                 |         | 1 |                                     |     |      |
|                 |         | 2 |                                     |     |      |
|                 |         | 3 |                                     |     |      |
| Other c.        | 4w      | 0 | 5                                   | 5   | 5    |
|                 |         | 1 |                                     |     |      |
|                 |         | 2 |                                     |     |      |
|                 |         | 3 |                                     |     |      |
|                 | R:2w    | 0 | 5                                   |     | 5    |
|                 |         | 1 |                                     |     |      |
|                 |         | 2 |                                     |     |      |
|                 |         | 3 |                                     |     |      |
| Epith.          | 4w      | 0 | 5                                   | 5   | 5    |
|                 |         | 1 |                                     |     |      |
|                 |         | 2 |                                     |     |      |
|                 |         | 3 |                                     |     |      |
|                 | R:2w    | 0 | 5                                   |     | 5    |
|                 |         | 1 |                                     |     |      |
|                 |         | 2 |                                     |     |      |
|                 |         | 3 |                                     |     |      |
| Bacteria        | 4w      | 0 | 5                                   | 5   | 5    |
|                 |         | 1 |                                     |     |      |
|                 |         |   |                                     |     |      |
|                 |         |   |                                     |     |      |
|                 | R:2w    | 0 | 5                                   |     | 5    |
|                 |         | 1 |                                     |     |      |

Numerals represent the number of animals.  
 Not significantly different from control.

Table 6-13 Urinary sediments in male rats

Study No. : SBL79-02

| Group            |      | Control | Polyoxyethylene p-nonylphenyl ether |     |      |
|------------------|------|---------|-------------------------------------|-----|------|
| Dose (mg/kg/day) |      |         | 20                                  | 200 | 1000 |
| Grade            |      |         |                                     |     |      |
| Cast             | 4w   | 0       | 5                                   | 5   | 5    |
|                  |      | 1       |                                     |     |      |
|                  |      | 2       |                                     |     |      |
|                  |      | 3       |                                     |     |      |
| R:2w             |      | 0       | 5                                   |     | 5    |
|                  |      | 1       |                                     |     |      |
|                  |      | 2       |                                     |     |      |
|                  |      | 3       |                                     |     |      |
| Sperm            | 4w   | 0       | 3                                   | 5   | 4    |
|                  |      | 1       | 2                                   |     | 1    |
|                  | R:2w | 0       | 3                                   |     | 3    |
|                  |      | 1       | 2                                   |     | 2    |
| Others           | 4w   | 0       | 5                                   | 5   | 5    |
|                  |      | 1       |                                     |     |      |
|                  | R:2w | 0       | 5                                   |     | 5    |
|                  |      | 1       |                                     |     |      |

Numerals represent the number of animals.  
 Not significantly different from control.

Table 6-14 Urinary sediments in female rats

Study No. : SBL79-02

| Group           | Control |   | Polyoxyethylene p-nonylphenyl ether |     |      |
|-----------------|---------|---|-------------------------------------|-----|------|
|                 |         |   | 20                                  | 200 | 1000 |
| Dose(mg/kg/day) | Grade   |   |                                     |     |      |
| RBC             | 4w      | 0 | 5                                   | 5   | 5    |
|                 |         | 1 |                                     |     |      |
|                 |         | 2 |                                     |     |      |
|                 |         | 3 |                                     |     |      |
|                 | R:2w    | 0 | 5                                   |     | 5    |
|                 |         | 1 |                                     |     |      |
|                 |         | 2 |                                     |     |      |
|                 |         | 3 |                                     |     |      |
| WBC             | 4w      | 0 | 5                                   | 5   | 5    |
|                 |         | 1 |                                     |     |      |
|                 |         | 2 |                                     |     |      |
|                 |         | 3 |                                     |     |      |
|                 | R:2w    | 0 | 5                                   |     | 5    |
|                 |         | 1 |                                     |     |      |
|                 |         | 2 |                                     |     |      |
|                 |         | 3 |                                     |     |      |
| Phosphate       | 4w      | 0 | 5                                   | 5   | 2    |
|                 |         | 1 |                                     |     | 2    |
|                 |         | 2 |                                     | 2   | 1    |
|                 |         | 3 |                                     |     |      |
|                 | R:2w    | 0 | 3                                   |     | 4    |
|                 |         | 1 | 2                                   |     | 1    |
|                 |         | 2 |                                     |     |      |
|                 |         | 3 |                                     |     |      |
| Urate           | 4w      | 0 | 5                                   | 5   | 5    |
|                 |         | 1 |                                     |     |      |
|                 |         | 2 |                                     |     |      |
|                 |         | 3 |                                     |     |      |
|                 | R:2w    | 0 | 5                                   |     | 5    |
|                 |         | 1 |                                     |     |      |
|                 |         | 2 |                                     |     |      |
|                 |         | 3 |                                     |     |      |

Numerals represent the number of animals.  
Not significantly different from control.

Table 6-15 Urinary sediments in female rats

Study No. : SBL79-02

| Group            | Control |   | Polyoxyethylene p-nonylphenyl ether |     |      |
|------------------|---------|---|-------------------------------------|-----|------|
|                  |         |   | 20                                  | 200 | 1000 |
| Dose (mg/kg/day) | Grade   |   |                                     |     |      |
| Oxalate          | 4w      | 0 | 5                                   | 5   | 5    |
|                  |         | 1 |                                     |     |      |
|                  |         | 2 |                                     |     |      |
|                  |         | 3 |                                     |     |      |
|                  | R:2w    | 0 | 5                                   |     | 5    |
|                  |         | 1 |                                     |     |      |
|                  |         | 2 |                                     |     |      |
|                  |         | 3 |                                     |     |      |
| Other c.         | 4w      | 0 | 5                                   | 5   | 5    |
|                  |         | 1 |                                     |     |      |
|                  |         | 2 |                                     |     |      |
|                  |         | 3 |                                     |     |      |
|                  | R:2w    | 0 | 5                                   |     | 5    |
|                  |         | 1 |                                     |     |      |
|                  |         | 2 |                                     |     |      |
|                  |         | 3 |                                     |     |      |
| Epith.           | 4w      | 0 | 5                                   | 5   | 5    |
|                  |         | 1 |                                     |     |      |
|                  |         | 2 |                                     |     |      |
|                  |         | 3 |                                     |     |      |
|                  | R:2w    | 0 | 5                                   |     | 5    |
|                  |         | 1 |                                     |     |      |
|                  |         | 2 |                                     |     |      |
|                  |         | 3 |                                     |     |      |
| Bacteria         | 4w      | 0 | 5                                   | 5   | 5    |
|                  |         | 1 |                                     |     |      |
|                  |         |   |                                     |     |      |
|                  |         |   |                                     |     |      |
|                  | R:2w    | 0 | 5                                   |     | 5    |
|                  |         | 1 |                                     |     |      |

Numerals represent the number of animals.  
Not significantly different from control.

Table 6-16 Urinary sediments in female rats

Study No. : SBL79-02

| Group           |      | Control | Polyoxyethylene p-nonylphenyl ether |     |      |
|-----------------|------|---------|-------------------------------------|-----|------|
| Dose(mg/kg/day) |      |         | 20                                  | 200 | 1000 |
| Grade           |      |         |                                     |     |      |
| Cast            | 4w   | 0       | 5                                   | 5   | 5    |
|                 |      | 1       |                                     |     |      |
|                 |      | 2       |                                     |     |      |
|                 |      | 3       |                                     |     |      |
| R:2w            |      | 0       | 5                                   |     | 5    |
|                 |      | 1       |                                     |     |      |
|                 |      | 2       |                                     |     |      |
|                 |      | 3       |                                     |     |      |
| Sperm           | 4w   | 0       | 5                                   | 5   | 5    |
|                 |      | 1       |                                     |     |      |
|                 | R:2w | 0       | 5                                   |     | 5    |
|                 |      | 1       |                                     |     |      |
| Others          | 4w   | 0       | 5                                   | 5   | 5    |
|                 |      | 1       |                                     |     |      |
|                 | R:2w | 0       | 5                                   |     | 5    |
|                 |      | 1       |                                     |     |      |

Numerals represent the number of animals.  
Not significantly different from control.



# Hematology

|                        |                        |   |
|------------------------|------------------------|---|
| RBC                    | ( $10^4/\text{mm}^3$ ) | Number of red blood cells                   |
| WBC                    | ( $10^2/\text{mm}^3$ ) | Number of white blood cells                 |
| Ht                     | (%)                    | Hematocrit value                            |
| Hb                     | (g/dL)                 | Hemoglobin concentration                    |
| Plat.                  | ( $10^4/\text{mm}^3$ ) | Number of blood platelets                   |
| MCV                    | (fl)                   | Mean corpuscular volume                     |
| MCH                    | (pg)                   | Mean corpuscular hemoglobin                 |
| MCHC                   | (%)                    | Mean corpuscular hemoglobin concentration   |
| Ret.                   | ( $10^{-1}\%$ )        | Number of reticulocytes                     |
| Hemogram               |                        |   |
| N-Stab                 | ( $10^2/\text{mm}^3$ ) | Number of stab-form neutrophilic leukocytes |
| N-Stab                 | (%)                    | Stab-form neutrophilic leukocyte ratio      |
| N-Seg.                 | ( $10^2/\text{mm}^3$ ) | Number of segmented neutrophilic leukocytes |
| N-Seg.                 | (%)                    | Segmented neutrophilic leukocyte ratio      |
| Eosino.                | ( $10^2/\text{mm}^3$ ) | Number of eosinophilic leukocytes           |
| Eosino.                | (%)                    | Eosinophilic leukocyte ratio                |
| Baso.                  | ( $10^2/\text{mm}^3$ ) | Number of basophilic leukocytes             |
| Baso.                  | (%)                    | Basophilic leukocyte ratio                  |
| Mono.                  | ( $10^2/\text{mm}^3$ ) | Number of monocytes                         |
| Mono.                  | (%)                    | Monocyte ratio                              |
| Lymph.                 | ( $10^2/\text{mm}^3$ ) | Number of lymphocytes                       |
| Lymph.                 | (%)                    | Lymphocyte ratio                            |
| Blood coagulation test |                        |   |
| PT                     | (Sec)                  | Prothrombin time                            |
| APTT                   | (Sec)                  | Activated partial thromboplastin time       |

Table 7-1 Hematology in male rats (End of drug administration)

Study No. : SBL79-02

| Group           |                        | Control           | Polyoxyethylene p-nonylphenyl ether |                   |                    |  |
|-----------------|------------------------|-------------------|-------------------------------------|-------------------|--------------------|--|
| Dose(mg/kg/day) |                        |                   | 20                                  | 200               | 1000               |  |
| N               |                        | 5                 | 5                                   | 5                 | 5                  |  |
| RBC             | ( $10^4/\text{mm}^3$ ) | 776.8 $\pm$ 38.8  | 773.4 $\pm$ 45.3                    | 800.0 $\pm$ 38.0  | 752.6 $\pm$ 58.0   |  |
| WBC             | ( $10^2/\text{mm}^3$ ) | 105.8 $\pm$ 45.5  | 64.0 $\pm$ 23.6                     | 72.8 $\pm$ 15.6   | 78.6 $\pm$ 23.3    |  |
| Ht              | (%)                    | 44.26 $\pm$ 1.89  | 43.84 $\pm$ 2.45                    | 44.80 $\pm$ 1.90  | 42.46 $\pm$ 2.74   |  |
| Hb              | (g/dL)                 | 15.66 $\pm$ 1.07  | 15.20 $\pm$ 0.64                    | 15.70 $\pm$ 0.64  | 15.20 $\pm$ 0.80   |  |
| Plat.           | ( $10^4/\text{mm}^3$ ) | 131.62 $\pm$ 8.54 | 105.64 $\pm$ 20.12                  | 120.30 $\pm$ 7.02 | 123.82 $\pm$ 25.80 |  |
| MCV             | (fL)                   | 57.0 $\pm$ 3.2    | 56.8 $\pm$ 1.1                      | 56.0 $\pm$ 1.2    | 56.4 $\pm$ 1.1     |  |
| MCH             | (pg)                   | 20.20 $\pm$ 1.66  | 19.68 $\pm$ 0.51                    | 19.64 $\pm$ 0.44  | 20.22 $\pm$ 0.84   |  |
| MCHC            | (%)                    | 35.36 $\pm$ 1.22  | 34.70 $\pm$ 0.89                    | 35.08 $\pm$ 1.16  | 35.86 $\pm$ 1.40   |  |
| Ret.            | ( $10^{-1}\%$ )        | 15.2 $\pm$ 3.7    | 18.8 $\pm$ 2.6                      | 14.6 $\pm$ 3.2    | 18.0 $\pm$ 5.6     |  |
| N-Stab          | ( $10^2/\text{mm}^3$ ) | 0.00 $\pm$ 0.00   | 0.00 $\pm$ 0.00                     | 0.00 $\pm$ 0.00   | 0.00 $\pm$ 0.00    |  |
| N-Stab          | (%)                    | 0.0 $\pm$ 0.0     | 0.0 $\pm$ 0.0                       | 0.0 $\pm$ 0.0     | 0.0 $\pm$ 0.0      |  |
| N-Seg.          | ( $10^2/\text{mm}^3$ ) | 5.32 $\pm$ 2.76   | 2.28 $\pm$ 0.43                     | 8.52 $\pm$ 6.68   | 6.10 $\pm$ 3.79    |  |
| N-Seg.          | (%)                    | 5.0 $\pm$ 2.2     | 4.0 $\pm$ 1.6                       | 11.4 $\pm$ 7.0    | 7.6 $\pm$ 3.8      |  |
| Eosino.         | ( $10^2/\text{mm}^3$ ) | 0.00 $\pm$ 0.00   | 0.00 $\pm$ 0.00                     | 0.18 $\pm$ 0.40   | 0.14 $\pm$ 0.31    |  |
| Eosino.         | (%)                    | 0.0 $\pm$ 0.0     | 0.0 $\pm$ 0.0                       | 0.2 $\pm$ 0.4     | 0.2 $\pm$ 0.4      |  |
| Baso.           | ( $10^2/\text{mm}^3$ ) | 0.00 $\pm$ 0.00   | 0.00 $\pm$ 0.00                     | 0.00 $\pm$ 0.00   | 0.00 $\pm$ 0.00    |  |
| Baso.           | (%)                    | 0.0 $\pm$ 0.0     | 0.0 $\pm$ 0.0                       | 0.0 $\pm$ 0.0     | 0.0 $\pm$ 0.0      |  |
| Mono.           | ( $10^2/\text{mm}^3$ ) | 2.30 $\pm$ 2.85   | 0.82 $\pm$ 0.95                     | 0.56 $\pm$ 0.82   | 1.08 $\pm$ 0.93    |  |
| Mono.           | (%)                    | 1.8 $\pm$ 1.6     | 1.4 $\pm$ 1.3                       | 0.8 $\pm$ 1.1     | 1.2 $\pm$ 0.8      |  |
| Lymph.          | ( $10^2/\text{mm}^3$ ) | 98.22 $\pm$ 41.16 | 60.92 $\pm$ 23.72                   | 63.56 $\pm$ 12.94 | 71.34 $\pm$ 19.95  |  |
| Lymph.          | (%)                    | 93.2 $\pm$ 1.8    | 94.6 $\pm$ 2.2                      | 87.6 $\pm$ 8.4    | 91.0 $\pm$ 3.9     |  |
| PT              | (Sec)                  | 11.84 $\pm$ 2.25  | 15.14 $\pm$ 2.02                    | 15.24 $\pm$ 2.97  | 13.42 $\pm$ 3.45   |  |
| APTT            | (Sec)                  | 22.40 $\pm$ 1.68  | 23.94 $\pm$ 1.80                    | 22.36 $\pm$ 2.22  | 23.64 $\pm$ 1.97   |  |

Values are expressed as the mean  $\pm$  S.D.  
 Not significantly different from Control.

Table 7-2

Hematology in female rats (End of drug administration)

Study No. : SBL79-02

| Group            |                        | Control            | Polyoxyethylene p-nonylphenyl ether |                   |                    |  |
|------------------|------------------------|--------------------|-------------------------------------|-------------------|--------------------|--|
| Dose (mg/kg/day) |                        |                    | 20                                  | 200               | 1000               |  |
| N                |                        | 5                  | 5                                   | 5                 | 5                  |  |
| RBC              | ( $10^4/\text{mm}^3$ ) | 747.8 $\pm$ 52.1   | 768.0 $\pm$ 25.2                    | 778.0 $\pm$ 46.7  | 750.2 $\pm$ 13.4   |  |
| WBC              | ( $10^2/\text{mm}^3$ ) | 43.8 $\pm$ 7.3     | 48.0 $\pm$ 6.3                      | 53.4 $\pm$ 12.3   | 60.0 $\pm$ 19.4    |  |
| Ht               | (%)                    | 42.32 $\pm$ 2.75   | 43.64 $\pm$ 1.79                    | 44.58 $\pm$ 2.40  | 42.92 $\pm$ 0.87   |  |
| Hb               | (g/dL)                 | 14.88 $\pm$ 0.81   | 15.24 $\pm$ 0.67                    | 15.26 $\pm$ 0.61  | 14.92 $\pm$ 0.29   |  |
| Plat.            | ( $10^4/\text{mm}^3$ ) | 102.96 $\pm$ 21.76 | 124.82 $\pm$ 11.63                  | 98.84 $\pm$ 20.47 | 113.62 $\pm$ 28.29 |  |
| MCV              | (fl)                   | 56.8 $\pm$ 1.3     | 56.8 $\pm$ 1.3                      | 57.2 $\pm$ 4.4    | 57.2 $\pm$ 0.8     |  |
| MCH              | (pg)                   | 19.94 $\pm$ 0.46   | 19.86 $\pm$ 0.51                    | 19.64 $\pm$ 0.60  | 19.90 $\pm$ 0.41   |  |
| MCHC             | (%)                    | 35.18 $\pm$ 0.54   | 34.94 $\pm$ 0.38                    | 34.28 $\pm$ 1.56  | 34.78 $\pm$ 0.72   |  |
| Ret.             | ( $10^{-1}\%$ )        | 12.4 $\pm$ 2.3     | 12.8 $\pm$ 5.3                      | 15.8 $\pm$ 5.9    | 17.6 $\pm$ 4.4     |  |
| N-Stab           | ( $10^2/\text{mm}^3$ ) | 0.00 $\pm$ 0.00    | 0.00 $\pm$ 0.00                     | 0.00 $\pm$ 0.00   | 0.00 $\pm$ 0.00    |  |
| N-Stab           | (%)                    | 0.0 $\pm$ 0.0      | 0.0 $\pm$ 0.0                       | 0.0 $\pm$ 0.0     | 0.0 $\pm$ 0.0      |  |
| N-Seg.           | ( $10^2/\text{mm}^3$ ) | 2.12 $\pm$ 1.45    | 1.76 $\pm$ 0.98                     | 3.02 $\pm$ 0.95   | 2.60 $\pm$ 1.55    |  |
| N-Seg.           | (%)                    | 4.8 $\pm$ 3.1      | 3.6 $\pm$ 1.8                       | 6.0 $\pm$ 2.3     | 4.4 $\pm$ 2.6      |  |
| Eosino.          | ( $10^2/\text{mm}^3$ ) | 0.40 $\pm$ 0.28    | 0.10 $\pm$ 0.22                     | 0.32 $\pm$ 0.31   | 0.32 $\pm$ 0.30    |  |
| Eosino.          | (%)                    | 1.0 $\pm$ 0.7      | 0.2 $\pm$ 0.4                       | 0.6 $\pm$ 0.5     | 0.6 $\pm$ 0.5      |  |
| Baso.            | ( $10^2/\text{mm}^3$ ) | 0.00 $\pm$ 0.00    | 0.00 $\pm$ 0.00                     | 0.00 $\pm$ 0.00   | 0.00 $\pm$ 0.00    |  |
| Baso.            | (%)                    | 0.0 $\pm$ 0.0      | 0.0 $\pm$ 0.0                       | 0.0 $\pm$ 0.0     | 0.0 $\pm$ 0.0      |  |
| Mono.            | ( $10^2/\text{mm}^3$ ) | 0.34 $\pm$ 0.33    | 0.60 $\pm$ 0.28                     | 0.38 $\pm$ 0.65   | 0.68 $\pm$ 0.48    |  |
| Mono.            | (%)                    | 0.8 $\pm$ 0.8      | 1.2 $\pm$ 0.4                       | 0.8 $\pm$ 1.3     | 1.4 $\pm$ 1.1      |  |
| Lymph.           | ( $10^2/\text{mm}^3$ ) | 40.92 $\pm$ 6.97   | 45.58 $\pm$ 5.64                    | 49.68 $\pm$ 12.95 | 56.38 $\pm$ 19.33  |  |
| Lymph.           | (%)                    | 93.4 $\pm$ 3.2     | 95.0 $\pm$ 2.1                      | 92.6 $\pm$ 3.0    | 93.6 $\pm$ 2.9     |  |
| PT               | (Sec)                  | 7.66 $\pm$ 0.15    | 7.40 $\pm$ 0.25                     | 7.44 $\pm$ 0.43   | 7.26 $\pm$ 0.11    |  |
| APTT             | (Sec)                  | 17.38 $\pm$ 0.24   | 16.90 $\pm$ 1.65                    | 16.36 $\pm$ 1.58  | 16.54 $\pm$ 1.39   |  |

Values are expressed as the mean  $\pm$  S.D.  
 Not significantly different from Control.

Table 7-3

Hematology in male rats (End of recovery test)

Study No. : SBL79-02

| Group            |                        | Control            | Polyoxyethylene p-nonylphenyl ether |     |                    |
|------------------|------------------------|--------------------|-------------------------------------|-----|--------------------|
| Dose (mg/kg/day) |                        |                    | 20                                  | 200 | 1000               |
| N                |                        | 5                  | 0                                   | 0   | 5                  |
| RBC              | ( $10^4/\text{mm}^3$ ) | 848.2 $\pm$ 21.4   |                                     |     | 823.4 $\pm$ 33.2   |
| WBC              | ( $10^2/\text{mm}^3$ ) | 85.2 $\pm$ 27.3    |                                     |     | 93.4 $\pm$ 25.8    |
| Ht               | (%)                    | 45.92 $\pm$ 1.66   |                                     |     | 44.32 $\pm$ 1.41   |
| Hb               | (g/dL)                 | 16.24 $\pm$ 0.58   |                                     |     | 15.72 $\pm$ 0.36   |
| Plat.            | ( $10^4/\text{mm}^3$ ) | 117.90 $\pm$ 10.84 |                                     |     | 126.72 $\pm$ 18.20 |
| MCV              | (fl)                   | 54.0 $\pm$ 1.2     |                                     |     | 53.8 $\pm$ 1.5     |
| MCH              | (pg)                   | 19.14 $\pm$ 0.40   |                                     |     | 19.10 $\pm$ 0.61   |
| MCHC             | (%)                    | 35.38 $\pm$ 0.16   |                                     |     | 35.50 $\pm$ 1.29   |
| Ret.             | ( $10^{-1}\%$ )        | 15.6 $\pm$ 5.0     |                                     |     | 18.4 $\pm$ 4.9     |
| N-Stab           | ( $10^2/\text{mm}^3$ ) | 0.00 $\pm$ 0.00    |                                     |     | 0.00 $\pm$ 0.00    |
| N-Stab           | (%)                    | 0.0 $\pm$ 0.0      |                                     |     | 0.0 $\pm$ 0.0      |
| N-Seg.           | ( $10^2/\text{mm}^3$ ) | 2.30 $\pm$ 2.36    |                                     |     | 5.72 $\pm$ 5.64    |
| N-Seg.           | (%)                    | 2.4 $\pm$ 1.5      |                                     |     | 6.0 $\pm$ 5.1      |
| Eosino.          | ( $10^2/\text{mm}^3$ ) | 0.18 $\pm$ 0.40    |                                     |     | 0.84 $\pm$ 1.17    |
| Eosino.          | (%)                    | 0.2 $\pm$ 0.4      |                                     |     | 0.8 $\pm$ 1.1      |
| Baso.            | ( $10^2/\text{mm}^3$ ) | 0.00 $\pm$ 0.00    |                                     |     | 0.00 $\pm$ 0.00    |
| Baso.            | (%)                    | 0.0 $\pm$ 0.0      |                                     |     | 0.0 $\pm$ 0.0      |
| Mono.            | ( $10^2/\text{mm}^3$ ) | 1.22 $\pm$ 1.11    |                                     |     | 1.14 $\pm$ 1.13    |
| Mono.            | (%)                    | 1.8 $\pm$ 1.9      |                                     |     | 1.4 $\pm$ 1.5      |
| Lymph.           | ( $10^2/\text{mm}^3$ ) | 81.52 $\pm$ 26.15  |                                     |     | 85.72 $\pm$ 24.47  |
| Lymph.           | (%)                    | 95.6 $\pm$ 1.7     |                                     |     | 91.8 $\pm$ 6.3     |
| PT               | (Sec)                  | 12.66 $\pm$ 2.00   |                                     |     | 16.00 $\pm$ 2.28*  |
| APTT             | (Sec)                  | 20.52 $\pm$ 1.40   |                                     |     | 21.44 $\pm$ 1.37   |

Values are expressed as the mean  $\pm$  S.D.\*  $P < 0.05$  : Significantly different from control.

Table 7-4

Hematology in female rats (End of recovery test)

Study No. : SBL79-02

| Group            |                        | Control            | Polyoxyethylene p-nonylphenyl ether |     |                   |
|------------------|------------------------|--------------------|-------------------------------------|-----|-------------------|
| Dose (mg/kg/day) |                        |                    | 20                                  | 200 | 1000              |
| N                |                        | 5                  | 0                                   | 0   | 5                 |
| RBC              | ( $10^4/\text{mm}^3$ ) | 772.2 $\pm$ 20.8   |                                     |     | 764.0 $\pm$ 40.8  |
| WBC              | ( $10^2/\text{mm}^3$ ) | 41.6 $\pm$ 3.3     |                                     |     | 36.6 $\pm$ 12.3   |
| Ht               | (%)                    | 42.86 $\pm$ 1.04   |                                     |     | 42.10 $\pm$ 2.15  |
| Hb               | (g/dL)                 | 15.24 $\pm$ 0.58   |                                     |     | 15.08 $\pm$ 0.85  |
| Plat.            | ( $10^4/\text{mm}^3$ ) | 117.26 $\pm$ 16.83 |                                     |     | 90.82 $\pm$ 21.91 |
| MCV              | (fl)                   | 55.4 $\pm$ 1.1     |                                     |     | 55.0 $\pm$ 1.9    |
| MCH              | (pg)                   | 19.72 $\pm$ 0.48   |                                     |     | 19.76 $\pm$ 0.59  |
| MCHC             | (%)                    | 35.54 $\pm$ 0.75   |                                     |     | 35.82 $\pm$ 0.47  |
| Ret.             | ( $10^{-1}\%$ )        | 11.2 $\pm$ 6.1     |                                     |     | 17.6 $\pm$ 5.5    |
| N-Stab           | ( $10^2/\text{mm}^3$ ) | 0.00 $\pm$ 0.00    |                                     |     | 0.00 $\pm$ 0.00   |
| N-Stab           | (%)                    | 0.0 $\pm$ 0.0      |                                     |     | 0.0 $\pm$ 0.0     |
| N-Seg.           | ( $10^2/\text{mm}^3$ ) | 3.26 $\pm$ 2.74    |                                     |     | 3.18 $\pm$ 1.31   |
| N-Seg.           | (%)                    | 8.2 $\pm$ 7.3      |                                     |     | 8.8 $\pm$ 2.9     |
| Eosino.          | ( $10^2/\text{mm}^3$ ) | 0.24 $\pm$ 0.36    |                                     |     | 0.20 $\pm$ 0.19   |
| Eosino.          | (%)                    | 0.6 $\pm$ 0.9      |                                     |     | 0.6 $\pm$ 0.5     |
| Baso.            | ( $10^2/\text{mm}^3$ ) | 0.00 $\pm$ 0.00    |                                     |     | 0.00 $\pm$ 0.00   |
| Baso.            | (%)                    | 0.0 $\pm$ 0.0      |                                     |     | 0.0 $\pm$ 0.0     |
| Mono.            | ( $10^2/\text{mm}^3$ ) | 0.72 $\pm$ 0.90    |                                     |     | 0.54 $\pm$ 0.23   |
| Mono.            | (%)                    | 1.6 $\pm$ 1.9      |                                     |     | 1.6 $\pm$ 0.9     |
| Lymph.           | ( $10^2/\text{mm}^3$ ) | 37.46 $\pm$ 5.56   |                                     |     | 32.70 $\pm$ 11.42 |
| Lymph.           | (%)                    | 89.6 $\pm$ 6.7     |                                     |     | 89.0 $\pm$ 2.9    |
| PT               | (Sec)                  | 7.80 $\pm$ 0.10    |                                     |     | 7.70 $\pm$ 0.25   |
| APTT             | (Sec)                  | 16.98 $\pm$ 0.93   |                                     |     | 17.34 $\pm$ 1.13  |

Values are expressed as the mean  $\pm$  S.D.  
 Not significantly different from Control.

# Blood Chemistry

|         |         |                                 |
|---------|---------|---------------------------------|
| ASAT    | (IU/L)  | Aspartate aminotransferase      |
| ALAT    | (IU/L)  | Alanine aminotransferase        |
| ALP     | (IU/L)  | Alkaline phosphatase            |
| LDH     | (IU/L)  | Lactate dehydrogenase           |
| G-GTP   | (IU/L)  | Gamma - glutamyl transpeptidase |
| T.Bil.  | (mg/dL) | Total bilirubin                 |
| T.Prot. | (g/dL)  | Total protein                   |
| Albumin | (g/dL)  | Albumin                         |
| A/G     |         | Albumin / Globulin              |
| T.Chol. | (mg/dL) | Total cholesterol               |
| TGL     | (mg/dL) | Triglyceride                    |
| Glucose | (mg/dL) | Glucose                         |
| BUN     | (mg/dL) | Blood urea nitrogen             |
| Creat.  | (mg/dL) | Creatinine                      |
| ChE     | (IU/L)  | Cholinesterase                  |
| IP      | (mg/dL) | Inorganic phosphorus            |
| Ca      | (mg/dL) | Calcium                         |
| Na      | (mEq/L) | Sodium                          |
| K       | (mEq/L) | Potassium                       |
| Cl      | (mEq/L) | Chloride                        |

Table 8-1

Blood chemistry in male rats (End of drug administration)

Study No. : SBL79-02

| Group            |         | Control     | Polyoxyethylene p-nonylphenyl ether |              |             |
|------------------|---------|-------------|-------------------------------------|--------------|-------------|
| Dose (mg/kg/day) |         |             | 20                                  | 200          | 1000        |
| N                |         | 5           | 5                                   | 5            | 5           |
| ASAT             | (IU/L)  | 81.0±15.3   | 80.6±7.7                            | 85.0±7.2     | 87.6±20.2   |
| ALAT             | (IU/L)  | 30.0±3.7    | 31.2±5.1                            | 31.2±2.8     | 32.0±5.5    |
| ALP              | (IU/L)  | 311.2±38.3  | 329.6±59.9                          | 327.4±50.9   | 296.8±43.0  |
| LDH              | (IU/L)  | 882.8±493.8 | 747.0±209.2                         | 1375.0±357.7 | 961.8±431.1 |
| G-GTP            | (IU/L)  | 0.72±0.38   | 0.36±0.21                           | 0.46±0.11    | 0.58±0.31   |
| T.Bil.           | (mg/dL) | 0.102±0.015 | 0.098±0.016                         | 0.084±0.005  | 0.094±0.011 |
| T.Prot.          | (g/dL)  | 5.84±0.25   | 5.68±0.22                           | 5.76±0.29    | 5.74±0.26   |
| Albumin          | (g/dL)  | 4.22±0.13   | 4.14±0.09                           | 4.28±0.19    | 4.12±0.13   |
| A/G              |         | 2.570±0.232 | 2.706±0.258                         | 2.904±0.340  | 2.568±0.246 |
| T.Chol.          | (mg/dL) | 53.6±4.7    | 46.0±6.4                            | 56.0±4.1     | 44.2±10.9   |
| TGL              | (mg/dL) | 33.4±13.5   | 24.6±7.1                            | 33.8±12.1    | 23.0±6.1    |
| Glucose          | (mg/dL) | 150.6±10.2  | 149.0±17.1                          | 135.6±6.7    | 138.2±25.4  |
| BUN              | (mg/dL) | 19.48±1.55  | 17.50±2.08                          | 19.28±1.41   | 18.70±3.97  |
| Creat.           | (mg/dL) | 0.514±0.094 | 0.474±0.056                         | 0.448±0.027  | 0.456±0.039 |
| ChE              | (IU/L)  | 476.2±126.0 | 351.2±65.8                          | 414.4±86.1   | 406.6±28.8  |
| IP               | (mg/dL) | 8.944±0.447 | 9.420±0.392                         | 9.590±0.647  | 9.618±0.220 |
| Ca               | (mg/dL) | 10.40±0.28  | 10.26±0.32                          | 10.14±0.58   | 10.58±0.30  |
| Na               | (mEq/L) | 142.8±2.2   | 144.8±0.8                           | 145.0±1.2    | 144.2±1.5   |
| K                | (mEq/L) | 3.90±0.33   | 3.86±0.21                           | 4.10±0.24    | 4.02±0.31   |
| Cl               | (mEq/L) | 101.4±1.5   | 103.8±1.8                           | 104.0±1.4    | 103.4±2.3   |

Values are expressed as the mean ± S.D.  
 Not significantly different from Control.

Table 8-2

Blood chemistry in female rats (End of drug administration)

Study No. : SBL79-02

| Group           |         | Control      | Polyoxyethylene p-nonylphenyl ether |              |              |
|-----------------|---------|--------------|-------------------------------------|--------------|--------------|
| Dose(mg/kg/day) |         |              | 20                                  | 200          | 1000         |
| N               |         | 5            | 5                                   | 5            | 5            |
| ASAT            | (IU/L)  | 96.6±24.7    | 105.6±14.1                          | 100.6±9.3    | 81.2±13.1    |
| ALAT            | (IU/L)  | 20.8±4.6     | 22.0±5.0                            | 25.2±3.8     | 19.6±1.1     |
| ALP             | (IU/L)  | 215.0±50.1   | 220.4±31.0                          | 241.4±62.5   | 189.2±35.4   |
| LDH             | (IU/L)  | 2009.4±808.2 | 2425.8±647.3                        | 1625.4±524.0 | 1355.4±685.8 |
| G-GTP           | (IU/L)  | 0.86±0.13    | 0.90±0.50                           | 1.06±0.47    | 0.72±0.36    |
| T.Bil.          | (mg/dL) | 0.100±0.010  | 0.102±0.013                         | 0.082±0.018  | 0.086±0.023  |
| T.Prot.         | (g/dL)  | 5.74±0.19    | 5.96±0.42                           | 5.84±0.57    | 6.00±0.30    |
| Albumin         | (g/dL)  | 4.28±0.13    | 4.38±0.27                           | 4.30±0.34    | 4.50±0.19    |
| A/G             |         | 3.010±0.209  | 2.854±0.202                         | 2.914±0.419  | 3.058±0.375  |
| T.Chol.         | (mg/dL) | 55.4±10.3    | 60.2±7.5                            | 62.0±11.8    | 70.8±10.0    |
| TGL             | (mg/dL) | 13.2±4.5     | 10.6±4.2                            | 12.2±1.8     | 15.2±1.9     |
| Glucose         | (mg/dL) | 148.0±11.8   | 124.8±4.4**                         | 147.6±6.9    | 137.8±9.7    |
| BUN             | (mg/dL) | 22.94±2.35   | 20.96±1.68                          | 22.46±3.08   | 25.08±4.69   |
| Creat.          | (mg/dL) | 0.526±0.051  | 0.476±0.034                         | 0.548±0.050  | 0.546±0.097  |
| ChE             | (IU/L)  | 1517.8±289.5 | 1781.4±466.8                        | 1406.8±466.0 | 1533.4±338.0 |
| IP              | (mg/dL) | 7.858±0.491  | 8.490±0.793                         | 7.796±0.584  | 8.912±0.813  |
| Ca              | (mg/dL) | 9.92±0.31    | 10.22±0.31                          | 10.32±0.36   | 10.46±0.23   |
| Na              | (mEq/L) | 144.0±0.7    | 145.4±1.1                           | 144.6±1.1    | 145.0±2.5    |
| K               | (mEq/L) | 3.82±0.19    | 3.74±0.25                           | 3.80±0.20    | 3.84±0.17    |
| Cl              | (mEq/L) | 105.4±0.9    | 106.6±1.1                           | 106.8±1.3    | 107.8±1.9    |

Values are expressed as the mean + S.D.

\*\* P&lt;0.01 : Significantly different from control.



Table 8-3

Blood chemistry in male rats (End of recovery test)

Study No. : SBL79-02

| Group            |         | Control       | Polyoxyethylene p-nonylphenyl ether |     |             |
|------------------|---------|---------------|-------------------------------------|-----|-------------|
| Dose (mg/kg/day) |         |               | 20                                  | 200 | 1000        |
| N                |         | 5             | 0                                   | 0   | 5           |
| ASAT             | (IU/L)  | 86.4±24.0     |                                     |     | 78.2±9.9    |
| ALAT             | (IU/L)  | 33.6±4.1      |                                     |     | 30.6±6.9    |
| ALP              | (IU/L)  | 243.0±48.5    |                                     |     | 278.0±60.7  |
| LDH              | (IU/L)  | 1502.6±1353.2 |                                     |     | 915.2±379.9 |
| G-GTP            | (IU/L)  | 0.36±0.15     |                                     |     | 0.46±0.40   |
| T.Bil.           | (mg/dL) | 0.154±0.021   |                                     |     | 0.160±0.012 |
| T.Prot.          | (g/dL)  | 5.70±0.12     |                                     |     | 5.72±0.36   |
| Albumin          | (g/dL)  | 4.14±0.11     |                                     |     | 4.00±0.20   |
| A/G              |         | 2.632±0.264   |                                     |     | 2.330±0.146 |
| T.Chol.          | (mg/dL) | 47.2±8.6      |                                     |     | 50.6±14.4   |
| TGL              | (mg/dL) | 38.4±13.1     |                                     |     | 26.2±8.1    |
| Glucose          | (mg/dL) | 168.0±15.2    |                                     |     | 162.2±9.7   |
| BUN              | (mg/dL) | 17.38±2.41    |                                     |     | 19.42±4.33  |
| Creat.           | (mg/dL) | 0.508±0.034   |                                     |     | 0.558±0.074 |
| ChE              | (IU/L)  | 367.8±43.8    |                                     |     | 382.0±106.7 |
| IP               | (mg/dL) | 7.522±0.542   |                                     |     | 8.064±0.536 |
| Ca               | (mg/dL) | 9.82±0.26     |                                     |     | 9.98±0.29   |
| Na               | (mEq/L) | 141.2±1.1     |                                     |     | 143.2±0.8*  |
| K                | (mEq/L) | 3.86±0.09     |                                     |     | 3.82±0.22   |
| Cl               | (mEq/L) | 102.0±1.0     |                                     |     | 101.2±0.4   |

Values are expressed as the mean + S.D.

\* P&lt;0.05 : Significantly different from control.

Table 8-4 Blood chemistry in female rats (End of recovery test)

Study No. : SBL79-02

| Group           |         | Control      | Polyoxyethylene p-nonylphenyl ether |     |              |
|-----------------|---------|--------------|-------------------------------------|-----|--------------|
| Dose(mg/kg/day) |         |              | 20                                  | 200 | 1000         |
| N               |         | 5            | 0                                   | 0   | 5            |
| ASAT            | (IU/L)  | 80.6±18.1    |                                     |     | 96.0±15.3    |
| ALAT            | (IU/L)  | 25.0±2.7     |                                     |     | 30.2±10.2    |
| ALP             | (IU/L)  | 173.4±49.2   |                                     |     | 201.8±35.1   |
| LDH             | (IU/L)  | 1560.2±858.4 |                                     |     | 1335.6±764.2 |
| G-GTP           | (IU/L)  | 0.92±0.50    |                                     |     | 0.82±0.46    |
| T.Bil.          | (mg/dL) | 0.174±0.018  |                                     |     | 0.178±0.019  |
| T.Prot.         | (g/dL)  | 5.96±0.42    |                                     |     | 6.24±0.32    |
| Albumin         | (g/dL)  | 4.32±0.26    |                                     |     | 4.36±0.13    |
| A/G             |         | 2.632±0.268  |                                     |     | 2.324±0.233  |
| T.Chol.         | (mg/dL) | 57.4±12.2    |                                     |     | 63.2±10.7    |
| TGL             | (mg/dL) | 11.0±9.1     |                                     |     | 7.2±3.3      |
| Glucose         | (mg/dL) | 137.2±22.8   |                                     |     | 130.4±15.3   |
| BUN             | (mg/dL) | 17.38±2.39   |                                     |     | 18.98±1.55   |
| Creat.          | (mg/dL) | 0.534±0.053  |                                     |     | 0.590±0.058  |
| ChE             | (IU/L)  | 1551.8±567.7 |                                     |     | 1600.8±266.9 |
| IP              | (mg/dL) | 5.896±1.277  |                                     |     | 6.244±0.553  |
| Ca              | (mg/dL) | 9.90±0.20    |                                     |     | 9.80±0.19    |
| Na              | (mEq/L) | 142.4±1.5    |                                     |     | 143.0±1.4    |
| K               | (mEq/L) | 3.80±0.25    |                                     |     | 3.52±0.34    |
| Cl              | (mEq/L) | 105.0±1.9    |                                     |     | 105.6±1.3    |

Values are expressed as the mean + S.D.  
 Not significantly different from Control.

Gross Autopsy Findings

Grade

- 0 : No abnormal changes
- 1 : Slight
- 2 : Moderate
- 3 : Marked
- P : Non-graded changes

Table 9-1 Gross autopsy findings in male rats (End of drug administration)

Study No. : SBL79-02

| Findings             | Group<br>Dose(mg/kg/day)<br>Grade | Control |   |   |   |   | Polyoxyethylene p-nonylphenyl ether |   |   |   |   |     |   |   |   |   |      |   |   |   |   |
|----------------------|-----------------------------------|---------|---|---|---|---|-------------------------------------|---|---|---|---|-----|---|---|---|---|------|---|---|---|---|
|                      |                                   |         |   |   |   |   | 20                                  |   |   |   |   | 200 |   |   |   |   | 1000 |   |   |   |   |
|                      |                                   | 0       | 1 | 2 | 3 | P | 0                                   | 1 | 2 | 3 | P | 0   | 1 | 2 | 3 | P | 0    | 1 | 2 | 3 | P |
| Lung                 |                                   |         |   |   |   |   |                                     |   |   |   |   |     |   |   |   |   |      |   |   |   |   |
| Black focus, single  |                                   | 4       |   |   |   | 1 | 5                                   |   |   |   | 0 | 5   |   |   |   | 0 | 5    |   |   |   | 0 |
| Black focus, several |                                   | 5       |   |   |   | 0 | 5                                   |   |   |   | 0 | 5   |   |   |   | 0 | 4    |   |   |   | 1 |
| Red focus, several   |                                   | 4       |   |   |   | 1 | 5                                   |   |   |   | 0 | 5   |   |   |   | 0 | 5    |   |   |   | 0 |
| Red focus, single    |                                   | 5       |   |   |   | 0 | 4                                   |   |   |   | 1 | 4   |   |   |   | 1 | 4    |   |   |   | 1 |
| Liver                |                                   |         |   |   |   |   |                                     |   |   |   |   |     |   |   |   |   |      |   |   |   |   |
| White focus, single  |                                   | 5       |   |   |   | 0 | 4                                   |   |   |   | 1 | 4   |   |   |   | 1 | 5    |   |   |   | 0 |
| Kidney               |                                   |         |   |   |   |   |                                     |   |   |   |   |     |   |   |   |   |      |   |   |   |   |
| Cyst, single, right  |                                   | 5       |   |   |   | 0 | 4                                   |   |   |   | 1 | 5   |   |   |   | 0 | 5    |   |   |   | 0 |

Numerals represent the number of animals.  
Not significantly different from control.

Table 9-2 Gross autopsy findings in female rats (End of drug administration)

Study No. : SBL79-02

| Findings            | Group<br>Dose(mg/kg/day)<br>Grade | Control |   |   |   |   | Polyoxyethylene p-nonylphenyl ether |   |   |   |   |     |   |   |   |   |      |   |   |   |   |
|---------------------|-----------------------------------|---------|---|---|---|---|-------------------------------------|---|---|---|---|-----|---|---|---|---|------|---|---|---|---|
|                     |                                   |         |   |   |   |   | 20                                  |   |   |   |   | 200 |   |   |   |   | 1000 |   |   |   |   |
|                     |                                   | 0       | 1 | 2 | 3 | P | 0                                   | 1 | 2 | 3 | P | 0   | 1 | 2 | 3 | P | 0    | 1 | 2 | 3 | P |
| Lung                |                                   |         |   |   |   |   |                                     |   |   |   |   |     |   |   |   |   |      |   |   |   |   |
| Red focus, single   |                                   | 4       |   |   |   | 1 | 5                                   |   |   |   | 0 | 5   |   |   |   | 0 | 5    |   |   |   | 0 |
| Liver               |                                   |         |   |   |   |   |                                     |   |   |   |   |     |   |   |   |   |      |   |   |   |   |
| White focus, single |                                   | 3       |   |   |   | 2 | 5                                   |   |   |   | 0 | 4   |   |   |   | 1 | 3    |   |   |   | 2 |
| Kidney              |                                   |         |   |   |   |   |                                     |   |   |   |   |     |   |   |   |   |      |   |   |   |   |
| Cyst, single, right |                                   | 5       |   |   |   | 0 | 5                                   |   |   |   | 0 | 4   |   |   |   | 1 | 5    |   |   |   | 0 |

Numerals represent the number of animals.  
Not significantly different from control.

Table 9-3

Gross autopsy findings in male rats (End of recovery test)

Study No. : SBL79-02

| Findings             | Group<br>Dose(mg/kg/day)<br>Grade | Control |   |   |   |   | Polyoxyethylene p-nonylphenyl ether |   |   |   |   |     |   |   |   |   |      |   |   |   |   |
|----------------------|-----------------------------------|---------|---|---|---|---|-------------------------------------|---|---|---|---|-----|---|---|---|---|------|---|---|---|---|
|                      |                                   |         |   |   |   |   | 20                                  |   |   |   |   | 200 |   |   |   |   | 1000 |   |   |   |   |
|                      |                                   | 0       | 1 | 2 | 3 | P | 0                                   | 1 | 2 | 3 | P | 0   | 1 | 2 | 3 | P | 0    | 1 | 2 | 3 | P |
| Lung                 |                                   |         |   |   |   |   |                                     |   |   |   |   |     |   |   |   |   |      |   |   |   |   |
| Black focus, several |                                   | 4       |   |   |   | 1 |                                     |   |   |   |   |     |   |   |   |   | 5    |   |   |   | 0 |
| Liver                |                                   |         |   |   |   |   |                                     |   |   |   |   |     |   |   |   |   |      |   |   |   |   |
| White focus, single  |                                   | 3       |   |   |   | 2 |                                     |   |   |   |   |     |   |   |   |   | 4    |   |   |   | 1 |
| Adrenal              |                                   |         |   |   |   |   |                                     |   |   |   |   |     |   |   |   |   |      |   |   |   |   |
| Asymmetry, size      |                                   | 5       |   |   |   | 0 |                                     |   |   |   |   |     |   |   |   |   | 4    |   |   |   | 1 |

Numerals represent the number of animals.  
Not significantly different from control.

Table 9-4 Gross autopsy findings in female rats (End of recovery test)

Study No. : SBL79-02

| Findings             | Group<br>Dose(mg/kg/day)<br>Grade | Control |   |   |   |   | Polyoxyethylene p-nonylphenyl ether |   |   |   |   |     |   |   |   |   |      |   |   |   |   |
|----------------------|-----------------------------------|---------|---|---|---|---|-------------------------------------|---|---|---|---|-----|---|---|---|---|------|---|---|---|---|
|                      |                                   | 0       | 1 | 2 | 3 | P | 20                                  |   |   |   |   | 200 |   |   |   |   | 1000 |   |   |   |   |
|                      |                                   |         |   |   |   |   | 0                                   | 1 | 2 | 3 | P | 0   | 1 | 2 | 3 | P | 0    | 1 | 2 | 3 | P |
| Lung                 |                                   |         |   |   |   |   |                                     |   |   |   |   |     |   |   |   |   |      |   |   |   |   |
| Black focus, several |                                   | 5       |   |   |   | 0 |                                     |   |   |   |   |     |   |   |   |   | 4    |   |   |   | 1 |
| Liver                |                                   |         |   |   |   |   |                                     |   |   |   |   |     |   |   |   |   |      |   |   |   |   |
| White focus, single  |                                   | 4       |   |   |   | 1 |                                     |   |   |   |   |     |   |   |   |   | 3    |   |   |   | 2 |

Numerals represent the number of animals.  
Not significantly different from control.

Organ weight

| Epididy. | Epididymis       |
|----------|------------------|
| -R       | (Right)          |
| -L       | (Left)           |
| -R&L     | (Right and Left) |



Table 10-1 Organ weight in male rats (End of drug administration)

Study No. : SBL79-02

| Group            |      | Control      | Polyoxyethylene p-nonylphenyl ether |              |              |  |
|------------------|------|--------------|-------------------------------------|--------------|--------------|--|
| Dose (mg/kg/day) |      |              | 20                                  | 200          | 1000         |  |
| N                |      | 5            | 5                                   | 5            | 5            |  |
| Adrenal-R        | (mg) | 29.32±6.70   | 25.96±2.52                          | 27.60±1.63   | 31.98±6.91   |  |
| Adrenal-L        | (mg) | 29.44±6.08   | 28.14±3.84                          | 30.46±2.33   | 32.32±5.51   |  |
| Adrenal-R&L      | (mg) | 58.76±12.71  | 54.10±5.89                          | 58.06±3.03   | 64.30±12.03  |  |
| Testis-R         | (mg) | 1359.6±244.4 | 1460.8±108.0                        | 1268.8±376.9 | 1387.4±174.8 |  |
| Testis-L         | (mg) | 1435.8±124.0 | 1443.2±92.7                         | 1273.0±360.2 | 1406.6±139.6 |  |
| Testis-R&L       | (mg) | 2795.4±348.9 | 2904.0±198.5                        | 2541.8±737.0 | 2794.0±313.9 |  |
| Thymus           | (mg) | 554.4±108.4  | 497.2±88.0                          | 396.0±32.9   | 593.6±170.2  |  |
| Spleen           | (mg) | 672.2±170.5  | 652.0±63.5                          | 629.8±116.6  | 734.0±137.0  |  |
| Brain            | (mg) | 1959.0±118.4 | 1941.4±83.1                         | 1951.6±70.9  | 1908.2±122.0 |  |
| Heart            | (mg) | 1142.6±197.6 | 1106.4±20.5                         | 1133.0±104.5 | 1103.6±92.5  |  |
| Liver            | (g)  | 10.786±2.096 | 9.642±0.723                         | 9.550±1.404  | 11.190±1.886 |  |
| Kidney-R         | (mg) | 1400.4±226.9 | 1330.2±58.8                         | 1231.2±154.3 | 1436.8±166.2 |  |
| Kidney-L         | (mg) | 1351.0±203.7 | 1315.6±90.6                         | 1217.2±181.5 | 1443.2±150.8 |  |
| Kidney-R&L       | (mg) | 2751.4±428.0 | 2645.8±132.4                        | 2448.4±335.6 | 2880.0±313.7 |  |
| Epididy.-R       | (mg) | 339.2±80.6   | 399.0±15.2                          | 370.8±45.3   | 371.8±40.6   |  |
| Epididy.-L       | (mg) | 353.6±54.5   | 380.8±26.0                          | 370.6±48.2   | 368.0±42.5   |  |
| Epididy.-R&L     | (mg) | 692.8±133.3  | 779.8±39.5                          | 741.4±91.9   | 739.8±80.7   |  |

Values are expressed as the mean + S.D.  
 Not significantly different from Control.

Table 10-2

Organ weight in female rats (End of drug administration)

Study No. : SBL79-02

| Group            |      | Control      | Polyoxyethylene p-nonylphenyl ether |              |              |
|------------------|------|--------------|-------------------------------------|--------------|--------------|
| Dose (mg/kg/day) |      |              | 20                                  | 200          | 1000         |
| N                |      | 5            | 5                                   | 5            | 5            |
| Adrenal-R        | (mg) | 29.48±4.84   | 32.80±4.49                          | 34.96±2.59   | 33.36±4.81   |
| Adrenal-L        | (mg) | 32.34±4.68   | 35.14±6.67                          | 39.00±2.63   | 34.94±6.32   |
| Adrenal-R&L      | (mg) | 61.82±9.34   | 67.94±10.52                         | 73.96±3.25   | 68.30±10.84  |
| Ovary-R          | (mg) | 45.48±8.45   | 45.34±11.30                         | 42.76±9.84   | 39.90±9.16   |
| Ovary-L          | (mg) | 42.96±4.19   | 43.30±7.20                          | 45.32±7.11   | 42.82±11.02  |
| Ovary-R&L        | (mg) | 88.44±12.38  | 88.64±18.11                         | 88.08±12.07  | 82.72±17.25  |
| Thymus           | (mg) | 522.6±112.9  | 518.2±44.1                          | 387.0±76.2   | 522.6±100.6  |
| Spleen           | (mg) | 512.0±81.0   | 477.4±62.0                          | 457.0±56.6   | 444.4±27.4   |
| Brain            | (mg) | 1852.0±79.7  | 1858.8±67.7                         | 1842.8±138.8 | 1781.2±55.2  |
| Heart            | (mg) | 824.4±92.6   | 748.0±55.4                          | 837.6±75.8   | 816.8±44.4   |
| Liver            | (g)  | 7.040±0.925  | 6.632±0.646                         | 6.740±0.874  | 7.044±0.377  |
| Kidney-R         | (mg) | 939.4±99.2   | 918.2±103.9                         | 923.2±130.4  | 882.0±60.7   |
| Kidney-L         | (mg) | 923.4±108.7  | 904.4±126.4                         | 909.6±152.5  | 879.4±63.2   |
| Kidney-R&L       | (mg) | 1862.8±197.3 | 1822.6±229.4                        | 1832.8±282.1 | 1761.4±120.7 |

Values are expressed as the mean + S.D.  
 Not significantly different from Control.

Table 10-3 Organ weight in male rats (End of recovery test)

Study No. : SBL79-02

| Group           |      | Control      | Polyoxyethylene p-nonylphenyl ether |     |              |
|-----------------|------|--------------|-------------------------------------|-----|--------------|
| Dose(mg/kg/day) |      |              | 20                                  | 200 | 1000         |
| N               |      | 5            | 0                                   | 0   | 5            |
| Adrenal-R       | (mg) | 30.26±3.76   |                                     |     | 26.68±8.31   |
| Adrenal-L       | (mg) | 32.66±4.39   |                                     |     | 31.86±5.84   |
| Adrenal-R&L     | (mg) | 62.92±8.13   |                                     |     | 58.54±12.14  |
| Testis-R        | (mg) | 1429.0±93.3  |                                     |     | 1525.0±162.4 |
| Testis-L        | (mg) | 1436.6±95.1  |                                     |     | 1529.8±160.8 |
| Testis-R&L      | (mg) | 2865.6±187.1 |                                     |     | 3054.8±322.5 |
| Thymus          | (mg) | 534.4±93.8   |                                     |     | 464.0±62.1   |
| Spleen          | (mg) | 708.8±119.6  |                                     |     | 711.2±109.6  |
| Brain           | (mg) | 1967.4±57.1  |                                     |     | 2004.2±108.7 |
| Heart           | (mg) | 1325.4±156.7 |                                     |     | 1304.4±69.7  |
| Liver           | (g)  | 12.114±2.147 |                                     |     | 11.650±1.656 |
| Kidney-R        | (mg) | 1502.6±169.2 |                                     |     | 1474.6±231.9 |
| Kidney-L        | (mg) | 1484.8±156.1 |                                     |     | 1521.4±255.3 |
| Kidney-R&L      | (mg) | 2987.4±321.5 |                                     |     | 2996.0±486.6 |
| Epididym.-R     | (mg) | 529.6±14.9   |                                     |     | 507.2±66.2   |
| Epididym.-L     | (mg) | 520.0±29.8   |                                     |     | 511.0±74.7   |
| Epididym.-R&L   | (mg) | 1049.6±43.0  |                                     |     | 1018.2±138.4 |

Values are expressed as the mean ± S.D.  
 Not significantly different from Control.

Table 10-4

Organ weight in female rats (End of recovery test)

Study No. : SBL79-02

| Group            |      | Control      | Polyoxyethylene p-nonylphenyl ether |     |               |
|------------------|------|--------------|-------------------------------------|-----|---------------|
| Dose (mg/kg/day) |      |              | 20                                  | 200 | 1000          |
| N                |      | 5            | 0                                   | 0   | 5             |
| Adrenal-R        | (mg) | 28.68±5.07   |                                     |     | 33.40±2.05    |
| Adrenal-L        | (mg) | 30.26±3.71   |                                     |     | 35.34±3.40    |
| Adrenal-R&L      | (mg) | 58.94±8.09   |                                     |     | 68.74±3.71*   |
| Ovary-R          | (mg) | 43.38±12.18  |                                     |     | 49.18±12.32   |
| Ovary-L          | (mg) | 46.06±8.09   |                                     |     | 41.00±6.84    |
| Ovary-R&L        | (mg) | 89.44±18.46  |                                     |     | 90.18±18.87   |
| Thymus           | (mg) | 405.0±72.0   |                                     |     | 406.8±87.0    |
| Spleen           | (mg) | 540.8±46.1   |                                     |     | 448.0±75.6*   |
| Brain            | (mg) | 1876.0±69.8  |                                     |     | 1845.2±25.5   |
| Heart            | (mg) | 821.0±73.2   |                                     |     | 814.8±30.6    |
| Liver            | (g)  | 6.856±0.993  |                                     |     | 6.366±0.596   |
| Kidney-R         | (mg) | 968.4±60.6   |                                     |     | 893.4±59.9    |
| Kidney-L         | (mg) | 972.4±71.9   |                                     |     | 862.2±60.6*   |
| Kidney-R&L       | (mg) | 1940.8±131.0 |                                     |     | 1755.6±117.8* |

Values are expressed as the mean + S.D.

\* P&lt;0.05 : Significantly different from control.

Table 10-5

Relative organ weight in male rats (End of drug administration)

Study No. : SBL79-02

| Group                     | Dose(mg/kg/day)<br>N | Control<br>5 | Polyoxyethylene p-nonylphenyl ether |             |             |
|---------------------------|----------------------|--------------|-------------------------------------|-------------|-------------|
|                           |                      |              | 20<br>5                             | 200<br>5    | 1000<br>5   |
| Body weight (g)           |                      | 330.4±42.1   | 312.8±20.7                          | 298.2±35.8  | 327.0±37.5  |
| Adrenal-R (mg/100gBW)     |                      | 8.78±1.08    | 8.32±0.69                           | 9.38±1.39   | 9.98±2.99   |
| Adrenal-L (mg/100gBW)     |                      | 8.82±0.87    | 9.02±1.34                           | 10.34±1.48  | 10.14±2.98  |
| Adrenal-R&L (mg/100gBW)   |                      | 17.60±1.89   | 17.34±1.94                          | 19.72±2.76  | 20.12±5.89  |
| Testis-R (mg/100gBW)      |                      | 419.4±98.0   | 468.4±43.3                          | 437.6±155.3 | 431.0±86.2  |
| Testis-L (mg/100gBW)      |                      | 440.0±63.4   | 462.4±36.2                          | 438.6±150.0 | 436.4±76.3  |
| Testis-R&L (mg/100gBW)    |                      | 859.4±158.3  | 930.8±78.6                          | 876.4±304.8 | 867.4±162.5 |
| Thymus (mg/100gBW)        |                      | 167.2±22.8   | 158.0±17.6                          | 133.4±6.3*  | 180.0±45.3  |
| Spleen (mg/100gBW)        |                      | 202.2±30.9   | 209.4±28.3                          | 210.0±21.0  | 223.4±19.1  |
| Brain (mg/100gBW)         |                      | 597.6±48.5   | 622.0±30.7                          | 660.8±69.3  | 589.4±69.4  |
| Heart (mg/100gBW)         |                      | 344.8±26.5   | 354.6±21.3                          | 382.4±38.5  | 339.0±22.1  |
| Liver (g/100gBW)          |                      | 3.242±0.296  | 3.080±0.072                         | 3.196±0.162 | 3.406±0.230 |
| Kidney-R (mg/100gBW)      |                      | 422.6±21.0   | 426.2±26.2                          | 412.8±12.9  | 441.2±42.1  |
| Kidney-L (mg/100gBW)      |                      | 407.8±15.5   | 421.4±34.2                          | 407.0±22.5  | 443.4±38.5  |
| Kidney-R&L (mg/100gBW)    |                      | 830.4±33.9   | 847.8±55.7                          | 819.8±34.8  | 884.6±79.3  |
| Epididym.-R (mg/100gBW)   |                      | 104.4±27.5   | 127.8±8.8                           | 125.8±19.8  | 115.8±23.3  |
| Epididym.-L (mg/100gBW)   |                      | 108.6±20.5   | 122.0±11.9                          | 126.2±22.7  | 114.2±20.5  |
| Epididym.-R&L (mg/100gBW) |                      | 213.0±48.2   | 250.2±20.6                          | 251.6±42.4  | 229.8±43.2  |

Values are expressed as the mean + S.D.

\* P&lt;0.05 : Significantly different from control.

Table 10-6 Relative organ weight in female rats (End of drug administration)

Study No. : SBL79-02

| Group                   | Control     | Polyoxyethylene p-nonylphenyl ether |             |             |
|-------------------------|-------------|-------------------------------------|-------------|-------------|
| Dose (mg/kg/day)        |             | 20                                  | 200         | 1000        |
| N                       | 5           | 5                                   | 5           | 5           |
| Body weight (g)         | 221.4±19.4  | 210.4±12.6                          | 210.8±22.8  | 219.4±10.4  |
| Adrenal-R (mg/100gBW)   | 13.26±1.22  | 15.56±1.60                          | 16.76±2.44  | 15.26±2.58  |
| Adrenal-L (mg/100gBW)   | 14.56±1.21  | 16.62±2.37                          | 18.58±0.90  | 16.04±3.43  |
| Adrenal-R&L (mg/100gBW) | 27.84±2.30  | 32.20±3.59                          | 35.36±3.17  | 31.28±5.93  |
| Ovary-R (mg/100gBW)     | 20.48±2.95  | 21.52±4.84                          | 20.24±4.35  | 18.26±4.31  |
| Ovary-L (mg/100gBW)     | 19.44±1.38  | 20.62±3.46                          | 21.62±3.34  | 19.64±5.39  |
| Ovary-R&L (mg/100gBW)   | 39.90±4.02  | 42.12±7.93                          | 41.88±4.61  | 37.90±8.45  |
| Thymus (mg/100gBW)      | 235.0±39.4  | 246.4±18.0                          | 182.4±19.1  | 238.4±46.5  |
| Spleen (mg/100gBW)      | 231.2±29.4  | 227.0±27.5                          | 218.6±34.9  | 202.8±14.0  |
| Brain (mg/100gBW)       | 843.0±96.8  | 885.2±43.9                          | 881.2±104.3 | 813.2±43.1  |
| Heart (mg/100gBW)       | 372.0±17.9  | 355.4±8.8                           | 398.4±21.5  | 373.2±30.3  |
| Liver (g/100gBW)        | 3.170±0.161 | 3.146±0.139                         | 3.192±0.083 | 3.210±0.098 |
| Kidney-R (mg/100gBW)    | 424.4±22.4  | 435.4±27.1                          | 437.4±31.1  | 402.0±24.0  |
| Kidney-L (mg/100gBW)    | 416.4±20.7  | 428.4±39.6                          | 430.0±39.8  | 401.4±32.0  |
| Kidney-R&L (mg/100gBW)  | 840.6±29.6  | 864.2±66.3                          | 867.6±70.1  | 803.4±55.6  |

Values are expressed as the mean ± S.D.  
 Not significantly different from Control.

Table 10-7

Relative organ weight in male rats (End of recovery test)

Study No. : SBL79-02

| Group                     | Control     | Polyoxyethylene p-nonylphenyl ether |     |             |
|---------------------------|-------------|-------------------------------------|-----|-------------|
|                           |             | 20                                  | 200 | 1000        |
| Dose(mg/kg/day)           |             |                                     |     |             |
| N                         | 5           | 0                                   | 0   | 5           |
| Body weight (g)           | 379.8±38.8  |                                     |     | 378.2±33.5  |
| Adrenal-R (mg/100gBW)     | 8.08±1.45   |                                     |     | 7.16±2.35   |
| Adrenal-L (mg/100gBW)     | 8.72±1.66   |                                     |     | 8.44±1.48   |
| Adrenal-R&L (mg/100gBW)   | 16.72±3.11  |                                     |     | 15.62±3.45  |
| Testis-R (mg/100gBW)      | 380.6±58.1  |                                     |     | 402.8±12.3  |
| Testis-L (mg/100gBW)      | 382.6±58.8  |                                     |     | 404.0±14.9  |
| Testis-R&L (mg/100gBW)    | 763.6±116.7 |                                     |     | 807.0±26.4  |
| Thymus (mg/100gBW)        | 140.6±18.9  |                                     |     | 122.4±9.6   |
| Spleen (mg/100gBW)        | 185.8±14.9  |                                     |     | 187.6±19.3  |
| Brain (mg/100gBW)         | 521.2±39.6  |                                     |     | 532.4±45.3  |
| Heart (mg/100gBW)         | 349.8±37.6  |                                     |     | 346.2±24.3  |
| Liver (g/100gBW)          | 3.170±0.236 |                                     |     | 3.070±0.189 |
| Kidney-R (mg/100gBW)      | 395.4±12.5  |                                     |     | 388.6±37.3  |
| Kidney-L (mg/100gBW)      | 391.2±13.1  |                                     |     | 400.4±43.9  |
| Kidney-R&L (mg/100gBW)    | 786.4±21.5  |                                     |     | 788.8±81.3  |
| Epididym.-R (mg/100gBW)   | 140.8±15.8  |                                     |     | 134.0±8.2   |
| Epididym.-L (mg/100gBW)   | 138.2±16.8  |                                     |     | 134.8±8.9   |
| Epididym.-R&L (mg/100gBW) | 278.8±32.8  |                                     |     | 268.8±15.5  |

Values are expressed as the mean + S.D.  
 Not significantly different from Control.

Table 10-8 Relative organ weight in female rats (End of recovery test)

Study No. : SBL79-02

| Group                   | Control     | Polyoxyethylene p-nonylphenyl ether |     |              |
|-------------------------|-------------|-------------------------------------|-----|--------------|
|                         |             | 20                                  | 200 | 1000         |
| Dose (mg/kg/day)        |             |                                     |     |              |
| N                       | 5           | 0                                   | 0   | 5            |
| Body weight (g)         | 231.8±13.8  |                                     |     | 216.2±12.0   |
| Adrenal-R (mg/100gBW)   | 12.32±1.65  |                                     |     | 15.48±1.37*  |
| Adrenal-L (mg/100gBW)   | 13.02±0.96  |                                     |     | 16.44±2.34*  |
| Adrenal-R&L (mg/100gBW) | 25.36±2.10  |                                     |     | 31.94±3.29** |
| Ovary-R (mg/100gBW)     | 18.70±5.15  |                                     |     | 22.72±5.34   |
| Ovary-L (mg/100gBW)     | 19.84±3.20  |                                     |     | 19.00±3.17   |
| Ovary-R&L (mg/100gBW)   | 38.54±7.49  |                                     |     | 41.70±8.29   |
| Thymus (mg/100gBW)      | 174.0±20.5  |                                     |     | 187.6±36.0   |
| Spleen (mg/100gBW)      | 233.4±17.4  |                                     |     | 207.4±33.2   |
| Brain (mg/100gBW)       | 811.2±54.9  |                                     |     | 855.8±49.7   |
| Heart (mg/100gBW)       | 354.0±23.7  |                                     |     | 377.4±16.5   |
| Liver (g/100gBW)        | 2.948±0.244 |                                     |     | 2.938±0.138  |
| Kidney-R (mg/100gBW)    | 418.0±17.7  |                                     |     | 413.2±12.3   |
| Kidney-L (mg/100gBW)    | 419.4±18.5  |                                     |     | 398.8±20.5   |
| Kidney-R&L (mg/100gBW)  | 837.6±35.0  |                                     |     | 812.0±32.1   |

Values are expressed as the mean + S.D.

\* P&lt;0.05 , \*\* P&lt;0.01 : Significantly different from control.



# Histopathological Findings

## Grade

- 0 : No abnormal changes
- 1 : Very slight
- 2 : Slight
- 3 : Moderate
- 4 : Marked
- P : Non-graded change
- U : Unexamined

Table 11-1 Histopathological findings in male rats (End of drug administration) - [H.E STAINING]

Study No. : SBL79-02

| Findings | Group<br>Dose(mg/kg/day)<br>Grade | Control |   |   |   |   |   |   | Polyoxyethylene p-nonylphenyl ether |   |   |   |   |   |   |     |   |   |   |   |   |   |      |   |   |   |   |   |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    |
|----------|-----------------------------------|---------|---|---|---|---|---|---|-------------------------------------|---|---|---|---|---|---|-----|---|---|---|---|---|---|------|---|---|---|---|---|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|----|
|          |                                   | 0       | 1 | 2 | 3 | 4 | P | U | 20                                  |   |   |   |   |   |   | 200 |   |   |   |   |   |   | 1000 |   |   |   |   |   |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    |
|          |                                   |         |   |   |   |   |   |   | 0                                   | 1 | 2 | 3 | 4 | P | U | 0   | 1 | 2 | 3 | 4 | P | U | 0    | 1 | 2 | 3 | 4 | P | U |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |    |
| Heart    |                                   |         |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   |      |   |   |   |   |   |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | </ |

Numerals represent the number of animals.  
Not significantly different from control.

Table 11-2

Histopathological findings in male rats (End of drug administration) - [H.E STAINING]

Study No. : SBL79-02

| Findings                                | Group           | Control |   |   |   |   |   |   | Polyoxyethylene p-nonylphenyl ether |   |   |   |   |   |   |     |   |   |   |   |   |   |      |   |   |   |   |   |   |  |  |  |
|---|-----------------|---------|---|---|---|---|---|---|-------------------------------------|---|---|---|---|---|---|-----|---|---|---|---|---|---|------|---|---|---|---|---|---|--|--|--|
|   | Dose(mg/kg/day) |         |   |   |   |   |   |   | 20                                  |   |   |   |   |   |   | 200 |   |   |   |   |   |   | 1000 |   |   |   |   |   |   |  |  |  |
|   | Grade           | 0       | 1 | 2 | 3 | 4 | P | U | 0                                   | 1 | 2 | 3 | 4 | P | U | 0   | 1 | 2 | 3 | 4 | P | U | 0    | 1 | 2 | 3 | 4 | P | U |  |  |  |
| Kidney                                  |                 |         |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   |      |   |   |   |   |   |   |  |  |  |
| Hyaline cast, dilated tubule            |                 | 5       | 0 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 4    | 1 | 0 | 0 | 0 |   |   |  |  |  |
| Mononuclear cell infiltration           |                 | 3       | 2 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    | 0 | 0 | 0 | 0 |   |   |  |  |  |
| Urinary bladder                         |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |  |  |  |
| Testis                                  |                 |         |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   |      |   |   |   |   |   |   |  |  |  |
| Atrophy, seminiferous tubule, bilateral |                 | 4       | 0 | 0 | 1 | 0 |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    | 0 | 0 | 0 | 0 |   |   |  |  |  |
| Epididymis                              |                 |         |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   |      |   |   |   |   |   |   |  |  |  |
| Absence, sperm, unilateral              |                 | 4       |   |   |   |   |   | 1 |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   | 0 |   |  |  |  |
| Seminal vesicle                         |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |  |  |  |
| Prostate                                |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |  |  |  |
| Pituitary                               |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |  |  |  |
| Adrenal                                 |                 |         |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   |      |   |   |   |   |   |   |  |  |  |
| Cyst, cortex                            |                 | 5       | 0 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 4    | 1 | 0 | 0 | 0 |   |   |  |  |  |
| Hypertrophy, cortical cell, focal       |                 | 3       | 2 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 3    | 2 | 0 | 0 | 0 |   |   |  |  |  |
| Thyroid                                 |                 |         |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   |      |   |   |   |   |   |   |  |  |  |
| Ultimobranchial body                    |                 | 3       |   |   |   |   |   | 2 |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 3    |   |   |   |   | 2 |   |  |  |  |
| Parathyroid                             |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |  |  |  |
| Cerebrum                                |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |  |  |  |
| Cerebellum                              |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |  |  |  |
| Sciatic nerve                           |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |  |  |  |
| Brain stem                              |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |  |  |  |
| Spinal cord (Thoracic)                  |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |  |  |  |
| Eyeball (Optic n.)                      |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |  |  |  |
| Harderian gland                         |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |  |  |  |
| Femur                                   |                 |         |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   |      |   |   |   |   |   |   |  |  |  |
| Brown pigment, periosteum               |                 | 4       | 1 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 3    | 2 | 0 | 0 | 0 |   |   |  |  |  |
| Sternum                                 |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |  |  |  |

Numerals represent the number of animals.  
Not significantly different from control.

Table 11-3

Histopathological findings in female rats (End of drug administration) - [H.E STAINING]

Study No. : SBL79-02

| Findings                                   | Group           | Control |   |   |   |   |   |   | Polyoxyethylene p-nonylphenyl ether |   |   |   |   |   |   |     |   |   |   |   |   |   |      |   |   |   |   |   |   |
|--|-----------------|---------|---|---|---|---|---|---|-------------------------------------|---|---|---|---|---|---|-----|---|---|---|---|---|---|------|---|---|---|---|---|---|
|  | Dose(mg/kg/day) |         |   |   |   |   |   |   | 20                                  |   |   |   |   |   |   | 200 |   |   |   |   |   |   | 1000 |   |   |   |   |   |   |
|  | Grade           | 0       | 1 | 2 | 3 | 4 | P | U | 0                                   | 1 | 2 | 3 | 4 | P | U | 0   | 1 | 2 | 3 | 4 | P | U | 0    | 1 | 2 | 3 | 4 | P | U |
| Heart                                      |                 |         |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   |      |   |   |   |   |   |   |
| Myocardial degeneration, focal             |                 | 4       | 1 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    | 0 | 0 | 0 | 0 |   |   |
| Spleen                                     |                 |         |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   |      |   |   |   |   |   |   |
| Extramedullary hematopoiesis               |                 | 4       | 1 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 4    | 1 | 0 | 0 | 0 |   |   |
| Thymus                                     |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Femoral bone marrow                        |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Sternal bone marrow                        |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Lymph node (Mesenteric)                    |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Lymph node (Submandibular)                 |                 |         |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   |      |   |   |   |   |   |   |
| Hyperplasia, plasma cell                   |                 | 5       | 0 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 4    | 1 | 0 | 0 | 0 |   |   |
| Lung                                       |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Trachea                                    |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Bronchus/Bronchiole                        |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Stomach                                    |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Duodenum                                   |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Jejunum                                    |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Ileum                                      |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Cecum                                      |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Colon                                      |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Rectum                                     |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Liver                                      |                 |         |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   |      |   |   |   |   |   |   |
| Microvacuolization, hepatocyte, periportal |                 | 2       | 3 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 4    | 1 | 0 | 0 | 0 |   |   |
| Mononuclear cell infiltration              |                 | 1       | 4 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 1    | 4 | 0 | 0 | 0 |   |   |
| Kidney                                     |                 |         |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   |      |   |   |   |   |   |   |
| Mineralization, renal tubule               |                 | 3       | 2 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 2    | 3 | 0 | 0 | 0 |   |   |
| Basophilic change, renal tubule            |                 | 2       | 3 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 2    | 3 | 0 | 0 | 0 |   |   |

Numerals represent the number of animals.  
Not significantly different from control.

Table 11-4

Histopathological findings in female rats (End of drug administration) - [H.E STAINING]

Study No. : SBL79-02

| Findings                          | Group           | Control |   |   |   |   |   |   | Polyoxyethylene p-nonylphenyl ether |   |   |   |   |   |   |   |     |   |   |   |   |   |   |   |      |   |   |   |   |  |  |  |
|-----------------------------------|-----------------|---------|---|---|---|---|---|---|-------------------------------------|---|---|---|---|---|---|---|-----|---|---|---|---|---|---|---|------|---|---|---|---|--|--|--|
|                                   | Dose(mg/kg/day) |         |   |   |   |   |   |   | 20                                  |   |   |   |   |   |   |   | 200 |   |   |   |   |   |   |   | 1000 |   |   |   |   |  |  |  |
|                                   | Grade           | 0       | 1 | 2 | 3 | 4 | P | U | 0                                   | 1 | 2 | 3 | 4 | P | U | 0 | 1   | 2 | 3 | 4 | P | U | 0 | 1 | 2    | 3 | 4 | P | U |  |  |  |
| Kidney                            |                 |         |   |   |   |   |   |   |                                     |   |   |   |   |   |   |   |     |   |   |   |   |   |   |   |      |   |   |   |   |  |  |  |
| Mononuclear cell infiltration     |                 | 5       | 0 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |   |     |   |   |   |   |   | 3 | 2 | 0    | 0 | 0 |   |   |  |  |  |
| Urinary bladder                   |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |   |     |   |   |   |   |   | 5 |   |      |   |   |   |   |  |  |  |
| Ovary                             |                 |         |   |   |   |   |   |   |                                     |   |   |   |   |   |   |   |     |   |   |   |   |   |   |   |      |   |   |   |   |  |  |  |
| Mononuclear cell infiltration     |                 | 5       | 0 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |   |     |   |   |   |   |   | 4 | 1 | 0    | 0 | 0 |   |   |  |  |  |
| Uterus                            |                 |         |   |   |   |   |   |   |                                     |   |   |   |   |   |   |   |     |   |   |   |   |   |   |   |      |   |   |   |   |  |  |  |
| Dilatation, lumen                 |                 | 5       | 0 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |   |     |   |   |   |   |   | 4 | 1 | 0    | 0 | 0 |   |   |  |  |  |
| Vagina                            |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |   |     |   |   |   |   |   | 5 |   |      |   |   |   |   |  |  |  |
| Pituitary                         |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |   |     |   |   |   |   |   | 5 |   |      |   |   |   |   |  |  |  |
| Adrenal                           |                 |         |   |   |   |   |   |   |                                     |   |   |   |   |   |   |   |     |   |   |   |   |   |   |   |      |   |   |   |   |  |  |  |
| Hypertrophy, cortical cell, focal |                 | 3       | 2 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |   |     |   |   |   |   |   | 4 | 1 | 0    | 0 | 0 |   |   |  |  |  |
| Thyroid                           |                 |         |   |   |   |   |   |   |                                     |   |   |   |   |   |   |   |     |   |   |   |   |   |   |   |      |   |   |   |   |  |  |  |
| Ultimobranchial body              |                 | 2       |   |   |   |   |   | 3 |                                     |   |   |   |   |   |   |   |     |   |   |   |   |   | 5 |   |      |   |   | 0 |   |  |  |  |
| Parathyroid                       |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |   |     |   |   |   |   |   | 5 |   |      |   |   |   |   |  |  |  |
| Cerebrum                          |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |   |     |   |   |   |   |   | 5 |   |      |   |   |   |   |  |  |  |
| Cerebellum                        |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |   |     |   |   |   |   |   | 5 |   |      |   |   |   |   |  |  |  |
| Sciatic nerve                     |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |   |     |   |   |   |   |   | 5 |   |      |   |   |   |   |  |  |  |
| Brain stem                        |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |   |     |   |   |   |   |   | 5 |   |      |   |   |   |   |  |  |  |
| Spinal cord (Thoracic)            |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |   |     |   |   |   |   |   | 5 |   |      |   |   |   |   |  |  |  |
| Eyeball (Optic n.)                |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |   |     |   |   |   |   |   | 5 |   |      |   |   |   |   |  |  |  |
| Harderian gland                   |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |   |     |   |   |   |   |   | 5 |   |      |   |   |   |   |  |  |  |
| Femur                             |                 |         |   |   |   |   |   |   |                                     |   |   |   |   |   |   |   |     |   |   |   |   |   |   |   |      |   |   |   |   |  |  |  |
| Brown pigment, periosteum         |                 | 5       | 0 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |   |     |   |   |   |   |   | 4 | 1 | 0    | 0 | 0 |   |   |  |  |  |
| Sternum                           |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |   |     |   |   |   |   |   | 5 |   |      |   |   |   |   |  |  |  |

Numerals represent the number of animals.  
Not significantly different from control.

Table 11-5 Histopathological findings in male rats (End of recovery test) - [H.E STAINING]

Study No. : SBL79-02

| Findings                                   | Group           | Control |   |   |   |   |   |   | Polyoxyethylene p-nonylphenyl ether |   |   |   |   |   |   |     |   |   |   |   |   |   |      |   |   |   |   |   |   |
|--|-----------------|---------|---|---|---|---|---|---|-------------------------------------|---|---|---|---|---|---|-----|---|---|---|---|---|---|------|---|---|---|---|---|---|
|  | Dose(mg/kg/day) |         |   |   |   |   |   |   | 20                                  |   |   |   |   |   |   | 200 |   |   |   |   |   |   | 1000 |   |   |   |   |   |   |
|  | Grade           | 0       | 1 | 2 | 3 | 4 | P | U | 0                                   | 1 | 2 | 3 | 4 | P | U | 0   | 1 | 2 | 3 | 4 | P | U | 0    | 1 | 2 | 3 | 4 | P | U |
| Heart                                      |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Spleen                                     |                 |         |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   |      |   |   |   |   |   |   |
| Extramedullary hematopoiesis               |                 | 4       | 1 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 3    | 2 | 0 | 0 | 0 |   |   |
| Thymus                                     |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Femoral bone marrow                        |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Sternal bone marrow                        |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Lymph node (Mesenteric)                    |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Lymph node (Submandibular)                 |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Lung                                       |                 |         |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   |      |   |   |   |   |   |   |
| Hemorrhage, focal                          |                 | 5       | 0 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 4    | 1 | 0 | 0 | 0 |   |   |
| Osseous metaplasia                         |                 | 4       | 1 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    | 0 | 0 | 0 | 0 |   |   |
| Foamy cell aggregation, alveolus           |                 | 3       | 2 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    | 0 | 0 | 0 | 0 |   |   |
| Mineralization, pulmonary artery           |                 | 4       | 1 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 4    | 1 | 0 | 0 | 0 |   |   |
| Trachea                                    |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Bronchus/Bronchiole                        |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Stomach                                    |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Duodenum                                   |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Jejunum                                    |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Ileum                                      |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Cecum                                      |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Colon                                      |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Rectum                                     |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Liver                                      |                 |         |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   |      |   |   |   |   |   |   |
| Microvacuolization, hepatocyte, periportal |                 | 4       | 1 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    | 0 | 0 | 0 | 0 |   |   |
| Mononuclear cell infiltration              |                 | 1       | 4 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 2    | 3 | 0 | 0 | 0 |   |   |

Numerals represent the number of animals.  
Not significantly different from control.

Table 11-6

Histopathological findings in male rats (End of recovery test) - [H.E STAINING]

Study No. : SBL79-02

| Findings | Group<br>Dose(mg/kg/day)<br>Grade | Control |   |   |   |   |   |   | Polyoxyethylene p-nonylphenyl ether |   |   |   |   |   |     |   |   |   |   |   |      |   |   |   |   |   |   |   |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|----------|-----------------------------------|---------|---|---|---|---|---|---|-------------------------------------|---|---|---|---|---|-----|---|---|---|---|---|------|---|---|---|---|---|---|---|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
|          |                                   | 0       | 1 | 2 | 3 | 4 | P | U | 20                                  |   |   |   |   |   | 200 |   |   |   |   |   | 1000 |   |   |   |   |   |   |   |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|          |                                   |         |   |   |   |   |   |   | 0                                   | 1 | 2 | 3 | 4 | P | U   | 0 | 1 | 2 | 3 | 4 | P    | U | 0 | 1 | 2 | 3 | 4 | P | U |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Liver    |                                   |         |   |   |   |   |   |   |                                     |   |   |   |   |   |     |   |   |   |   |   |      |   |   |   |   |   |   |   |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

Numerals represent the number of animals.  
Not significantly different from control.

Table 11-7

Histopathological findings in male rats (End of recovery test) - [H.E STAINING]

Study No. : SBL79-02

| Findings | Group            | Control |   |   |   |   |   |   |   | Polyoxyethylene p-nonylphenyl ether |   |   |   |   |   |   |   |     |   |   |   |   |   |   |   |      |   |   |   |   |  |  |  |
|----------|------------------|---------|---|---|---|---|---|---|---|-------------------------------------|---|---|---|---|---|---|---|-----|---|---|---|---|---|---|---|------|---|---|---|---|--|--|--|
|          | Dose (mg/kg/day) |         |   |   |   |   |   |   |   | 20                                  |   |   |   |   |   |   |   | 200 |   |   |   |   |   |   |   | 1000 |   |   |   |   |  |  |  |
|          | Grade            | 0       | 1 | 2 | 3 | 4 | P | U | 0 | 1                                   | 2 | 3 | 4 | P | U | 0 | 1 | 2   | 3 | 4 | P | U | 0 | 1 | 2 | 3    | 4 | P | U |   |  |  |  |
| Sternum  |                  | 5       |   |   |   |   |   |   |   |                                     |   |   |   |   |   |   |   |     |   |   |   |   |   |   |   |      |   |   |   | 5 |  |  |  |

Numerals represent the number of animals.  
 Not significantly different from control.



Table 11-8

Histopathological findings in female rats (End of recovery test) - [H.E STAINING]

Study No. : SBL79-02

| Findings                         | Group           | Control |   |   |   |   |   |   | Polyoxyethylene p-nonylphenyl ether |   |   |   |   |   |   |     |   |   |   |   |   |   |      |   |   |   |   |   |   |
|----------------------------------|-----------------|---------|---|---|---|---|---|---|-------------------------------------|---|---|---|---|---|---|-----|---|---|---|---|---|---|------|---|---|---|---|---|---|
|                                  | Dose(mg/kg/day) |         |   |   |   |   |   |   | 20                                  |   |   |   |   |   |   | 200 |   |   |   |   |   |   | 1000 |   |   |   |   |   |   |
|                                  | Grade           | 0       | 1 | 2 | 3 | 4 | P | U | 0                                   | 1 | 2 | 3 | 4 | P | U | 0   | 1 | 2 | 3 | 4 | P | U | 0    | 1 | 2 | 3 | 4 | P | U |
| Heart                            |                 |         |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   |      |   |   |   |   |   |   |
| Mononuclear cell infiltration    |                 | 4       | 1 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    | 0 | 0 | 0 | 0 |   |   |
| Spleen                           |                 |         |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   |      |   |   |   |   |   |   |
| Extramedullary hematopoiesis     |                 | 2       | 3 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    | 0 | 0 | 0 | 0 |   |   |
| Thymus                           |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Femoral bone marrow              |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Sternal bone marrow              |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Lymph node (Mesenteric)          |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Lymph node (Submandibular)       |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Lung                             |                 |         |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   |      |   |   |   |   |   |   |
| Osseous metaplasia               |                 | 5       | 0 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 4    | 1 | 0 | 0 | 0 |   |   |
| Foamy cell aggregation, alveolus |                 | 5       | 0 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 3    | 2 | 0 | 0 | 0 |   |   |
| Mineralization, pulmonary artery |                 | 5       | 0 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 4    | 1 | 0 | 0 | 0 |   |   |
| Inflammation, perivascular       |                 | 5       | 0 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 4    | 0 | 1 | 0 | 0 |   |   |
| Trachea                          |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Bronchus/Bronchiole              |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Stomach                          |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Duodenum                         |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Jejunum                          |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Ileum                            |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Cecum                            |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Colon                            |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Rectum                           |                 | 5       |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    |   |   |   |   |   |   |
| Liver                            |                 |         |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   |      |   |   |   |   |   |   |
| Mononuclear cell infiltration    |                 | 0       | 5 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 1    | 4 | 0 | 0 | 0 |   |   |
| Necrosis, focal                  |                 | 4       | 1 | 0 | 0 | 0 |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   | 5    | 0 | 0 | 0 | 0 |   |   |

Numerals represent the number of animals.  
Not significantly different from control.

試験結果報告書の内容に関するお問い合わせには応じかねますので御了承下さい。

Table 11-9

Histopathological findings in female rats (End of recovery test) - [H.E STAINING]

Study No. : SBL79-02

| Findings | Group                     | Control |   |   |   |   |   |   | Polyoxyethylene p-nonylphenyl ether |   |   |   |   |   |   |     |   |   |   |   |   |   |      |   |   |   |   |   |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|----------|---------------------------|---------|---|---|---|---|---|---|-------------------------------------|---|---|---|---|---|---|-----|---|---|---|---|---|---|------|---|---|---|---|---|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
|          | Dose (mg/kg/day)<br>Grade | 0       | 1 | 2 | 3 | 4 | P | U | 20                                  |   |   |   |   |   |   | 200 |   |   |   |   |   |   | 1000 |   |   |   |   |   |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|          |                           |         |   |   |   |   |   |   | 0                                   | 1 | 2 | 3 | 4 | P | U | 0   | 1 | 2 | 3 | 4 | P | U | 0    | 1 | 2 | 3 | 4 | P | U |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Kidney   |                           |         |   |   |   |   |   |   |                                     |   |   |   |   |   |   |     |   |   |   |   |   |   |      |   |   |   |   |   |   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

Numerals represent the number of animals.  
Not significantly different from control.

Clinical Sign

Grade

- 1 : Slight
- 2 : Moderate
- 3 : Severe
- + : Non-graded clinical signs

Time

- Pre: Before administration
- S1 : 1-2 hours after administration
- S2 : 4-6 hours after administration

| Group                               | Anim.No. | Item              | Grade | Time | Day |
|-------------------------------------|----------|-------------------|-------|------|-----|
| Control                             |          |                   |       |      |     |
|                                     | 1        | No abnormal signs |       |      |     |
|                                     | 2        | No abnormal signs |       |      |     |
|                                     | 3        | No abnormal signs |       |      |     |
|                                     | 4        | No abnormal signs |       |      |     |
|                                     | 5        | No abnormal signs |       |      |     |
|                                     | 6        | No abnormal signs |       |      |     |
|                                     | 7        | No abnormal signs |       |      |     |
|                                     | 8        | No abnormal signs |       |      |     |
|                                     | 9        | No abnormal signs |       |      |     |
|                                     | 10       | No abnormal signs |       |      |     |
| Polyoxyethylene p-nonylphenyl ether |          |                   |       |      |     |
| 20 (mg/kg/day)                      | 21       | No abnormal signs |       |      |     |
|                                     | 22       | No abnormal signs |       |      |     |
|                                     | 23       | No abnormal signs |       |      |     |
|                                     | 24       | No abnormal signs |       |      |     |
|                                     | 25       | No abnormal signs |       |      |     |
| Polyoxyethylene p-nonylphenyl ether |          |                   |       |      |     |
| 200 (mg/kg/day)                     | 31       | No abnormal signs |       |      |     |
|                                     | 32       | No abnormal signs |       |      |     |
|                                     | 33       | No abnormal signs |       |      |     |
|                                     | 34       | No abnormal signs |       |      |     |
|                                     | 35       | No abnormal signs |       |      |     |
| Polyoxyethylene p-nonylphenyl ether |          |                   |       |      |     |
| 1000 (mg/kg/day)                    | 41       | No abnormal signs |       |      |     |
|                                     | 42       | No abnormal signs |       |      |     |
|                                     | 43       | No abnormal signs |       |      |     |
|                                     | 44       | No abnormal signs |       |      |     |
|                                     | 45       | No abnormal signs |       |      |     |
|                                     | 46       | No abnormal signs |       |      |     |
|                                     | 47       | No abnormal signs |       |      |     |
|                                     | 48       | No abnormal signs |       |      |     |
|                                     | 49       | No abnormal signs |       |      |     |
|                                     | 50       | No abnormal signs |       |      |     |

| Group   | Anim.No. | Item              | Grade | Time | Day |
|---|----------|-------------------|-------|------|-----|
| Control   |          |                   |       |      |     |
|   | 11       | No abnormal signs |       |      |     |
|   | 12       | No abnormal signs |       |      |     |
|   | 13       | No abnormal signs |       |      |     |
|   | 14       | No abnormal signs |       |      |     |
|   | 15       | No abnormal signs |       |      |     |
|   | 16       | No abnormal signs |       |      |     |
|   | 17       | No abnormal signs |       |      |     |
|   | 18       | No abnormal signs |       |      |     |
|   | 19       | No abnormal signs |       |      |     |
|   | 20       | No abnormal signs |       |      |     |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |                   |       |      |     |
|   | 26       | No abnormal signs |       |      |     |
|   | 27       | No abnormal signs |       |      |     |
|   | 28       | No abnormal signs |       |      |     |
|   | 29       | No abnormal signs |       |      |     |
|   | 30       | No abnormal signs |       |      |     |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |                   |       |      |     |
|   | 36       | No abnormal signs |       |      |     |
|   | 37       | No abnormal signs |       |      |     |
|   | 38       | No abnormal signs |       |      |     |
|   | 39       | No abnormal signs |       |      |     |
|   | 40       | No abnormal signs |       |      |     |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |                   |       |      |     |
|   | 51       | No abnormal signs |       |      |     |
|   | 52       | No abnormal signs |       |      |     |
|   | 53       | No abnormal signs |       |      |     |
|   | 54       | No abnormal signs |       |      |     |
|   | 55       | No abnormal signs |       |      |     |
|   | 56       | No abnormal signs |       |      |     |
|   | 57       | No abnormal signs |       |      |     |
|   | 58       | No abnormal signs |       |      |     |
|   | 59       | No abnormal signs |       |      |     |
|   | 60       | No abnormal signs |       |      |     |

| General behavior            | Group           | Control |   |   |   |   | Polyoxyethylene p-nonylphenyl ether |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
|-----------------------------|-----------------|---------|---|---|---|---|-------------------------------------|----|----|----|----|-----|----|----|----|----|------|----|----|----|----|
|                             | Dose(mg/kg/day) |         |   |   |   |   | 20                                  |    |    |    |    | 200 |    |    |    |    | 1000 |    |    |    |    |
|                             | Animal No.      | 1       | 2 | 3 | 4 | 5 | 21                                  | 22 | 23 | 24 | 25 | 31  | 32 | 33 | 34 | 35 | 41   | 42 | 43 | 44 | 45 |
| <b>Awareness</b>            |                 |         |   |   |   |   |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Alertness                   |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Visual Placing              |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Stereotypy                  |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Passivity                   |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| <b>Mood</b>                 |                 |         |   |   |   |   |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Grooming                    |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Vocalization                |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Restlessness                |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Irritability                |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Fearfulness                 |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| <b>Motor Activity</b>       |                 |         |   |   |   |   |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Reactivity                  |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Spontaneous Activity        |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Touch Response              |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Pain Response               |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| <b>CNS Excitation</b>       |                 |         |   |   |   |   |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Startle Response            |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Straub Tail                 |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Tremors                     |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Twitches                    |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Convulsions                 |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| <b>Posture</b>              |                 |         |   |   |   |   |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Body Posture                |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Limb Posture                |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| <b>Motor Incoordination</b> |                 |         |   |   |   |   |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Staggering Gait             |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Abnormal Gait               |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Righting Reflex             |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |

Note) - : Normal sign

## Appendix 2-2 Effects of Polyoxyethylene p-nonylphenyl ether on the general behavior in male rats (Prior to administration on Day 0)

Study No. : SBL79-02

| General behavior  | Group           | Control |   |   |   |   | Polyoxyethylene p-nonylphenyl ether |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
|-------------------|-----------------|---------|---|---|---|---|-------------------------------------|----|----|----|----|-----|----|----|----|----|------|----|----|----|----|
|                   | Dose(mg/kg/day) |         |   |   |   |   | 20                                  |    |    |    |    | 200 |    |    |    |    | 1000 |    |    |    |    |
|                   | Animal No.      | 1       | 2 | 3 | 4 | 5 | 21                                  | 22 | 23 | 24 | 25 | 31  | 32 | 33 | 34 | 35 | 41   | 42 | 43 | 44 | 45 |
| Muscle Tone       |                 |         |   |   |   |   |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Limb Tone         |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Grip Strength     |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Body Tone         |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Abdominal Tone    |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Reflex            |                 |         |   |   |   |   |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Pinna Reflex      |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Corneal Reflex    |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| IPR               |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Autonomic Profile |                 |         |   |   |   |   |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Writhing          |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Palpebral Opening |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Exophthalmos      |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Urination         |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Salivation        |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Piloerection      |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Hypothermia       |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Skin Color        |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Heart Rate        |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Respiratory Rate  |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Pupil Size        |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Rearing*          |                 | 0       | 0 | 0 | 0 | 0 | 0                                   | 0  | 0  | 0  | 0  | 0   | 0  | 0  | 0  | 0  | 0    | 0  | 0  | 0  | 0  |

Notes) - : Normal sign

\* : Numerals represent the count of rearing

Appendix 2-3 Effects of Polyoxyethylene p-nonylphenyl ether on the general behavior in male rats (2 - 4 hours after administration on Day 0)

Study No. : SBL79-02

| General behavior            | Group           | Control |   |   |   |   | Polyoxyethylene p-nonylphenyl ether |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
|-----------------------------|-----------------|---------|---|---|---|---|-------------------------------------|----|----|----|----|-----|----|----|----|----|------|----|----|----|----|
|                             | Dose(mg/kg/day) |         |   |   |   |   | 20                                  |    |    |    |    | 200 |    |    |    |    | 1000 |    |    |    |    |
|                             | Animal No.      | 1       | 2 | 3 | 4 | 5 | 21                                  | 22 | 23 | 24 | 25 | 31  | 32 | 33 | 34 | 35 | 41   | 42 | 43 | 44 | 45 |
| <b>Awareness</b>            |                 |         |   |   |   |   |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Alertness                   |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Visual Placing              |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Stereotypy                  |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Passivity                   |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| <b>Mood</b>                 |                 |         |   |   |   |   |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Grooming                    |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Vocalization                |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Restlessness                |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Irritability                |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Fearfulness                 |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| <b>Motor Activity</b>       |                 |         |   |   |   |   |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Reactivity                  |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Spontaneous Activity        |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Touch Response              |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Pain Response               |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| <b>CNS Excitation</b>       |                 |         |   |   |   |   |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Startle Response            |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Straub Tail                 |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Tremors                     |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Twitches                    |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Convulsions                 |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| <b>Posture</b>              |                 |         |   |   |   |   |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Body Posture                |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Limb Posture                |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| <b>Motor Incoordination</b> |                 |         |   |   |   |   |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Staggering Gait             |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Abnormal Gait               |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Righting Reflex             |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |

Note) - : Normal sign



Appendix 2-4 Effects of Polyoxyethylene p-nonylphenyl ether on the general behavior in male rats (2 - 4 hours after administration on Day 0)

Study No. : SBL79-02

| General behavior  | Group<br>Dose(mg/kg/day)<br>Animal No. | Control |   |   |   |   | Polyoxyethylene p-nonylphenyl ether |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
|-------------------|--|---------|---|---|---|---|-------------------------------------|----|----|----|----|-----|----|----|----|----|------|----|----|----|----|
|                   |  |         |   |   |   |   | 20                                  |    |    |    |    | 200 |    |    |    |    | 1000 |    |    |    |    |
|                   |  | 1       | 2 | 3 | 4 | 5 | 21                                  | 22 | 23 | 24 | 25 | 31  | 32 | 33 | 34 | 35 | 41   | 42 | 43 | 44 | 45 |
| Muscle Tone       |  |         |   |   |   |   |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Limb Tone         |  | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Grip Strength     |  | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Body Tone         |  | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Abdominal Tone    |  | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Reflex            |  |         |   |   |   |   |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Pinna Reflex      |  | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Corneal Reflex    |  | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| IFR               |  | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Autonomic Profile |  |         |   |   |   |   |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Writhing          |  | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Palpebral Opening |  | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Exophthalmos      |  | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Urination         |  | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Salivation        |  | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Piloerection      |  | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Hypothermia       |  | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Skin Color        |  | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Heart Rate        |  | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Respiratory Rate  |  | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Pupil Size        |  | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Rearing*          |  | 0       | 0 | 0 | 0 | 1 | 0                                   | 0  | 0  | 0  | 0  | 0   | 0  | 0  | 0  | 0  | 0    | 0  | 0  | 0  | 0  |

Notes) - : Normal sign

\* : Numerals represent the count of rearing

Appendix 2-5 Effects of Polyoxyethylene p-nonylphenyl ether on the general behavior in male rats (2 - 4 hours after administration on Day 27)

Study No. : SBL79-02

| General behavior            | Group           | Control |   |   |   |   | Polyoxyethylene p-nonylphenyl ether |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
|-----------------------------|-----------------|---------|---|---|---|---|-------------------------------------|----|----|----|----|-----|----|----|----|----|------|----|----|----|----|
|                             | Dose(mg/kg/day) |         |   |   |   |   | 20                                  |    |    |    |    | 200 |    |    |    |    | 1000 |    |    |    |    |
|                             | Animal No.      | 1       | 2 | 3 | 4 | 5 | 21                                  | 22 | 23 | 24 | 25 | 31  | 32 | 33 | 34 | 35 | 41   | 42 | 43 | 44 | 45 |
| <b>Awareness</b>            |                 |         |   |   |   |   |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Alertness                   |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Visual Placing              |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Stereotypy                  |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Passivity                   |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| <b>Mood</b>                 |                 |         |   |   |   |   |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Grooming                    |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Vocalization                |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Restlessness                |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Irritability                |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Fearfulness                 |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| <b>Motor Activity</b>       |                 |         |   |   |   |   |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Reactivity                  |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Spontaneous Activity        |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Touch Response              |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Pain Response               |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| <b>CNS Excitation</b>       |                 |         |   |   |   |   |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Startle Response            |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Straub Tail                 |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Tremors                     |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Twitches                    |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Convulsions                 |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| <b>Posture</b>              |                 |         |   |   |   |   |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Body Posture                |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Limb Posture                |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| <b>Motor Incoordination</b> |                 |         |   |   |   |   |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Staggering Gait             |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Abnormal Gait               |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Righting Reflex             |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |

Note) - : Normal sign

Appendix 2-6 Effects of Polyoxyethylene p-nonylphenyl ether on the general behavior in male rats (2 - 4 hours after administration on Day 27)

Study No. : SBL79-02

| General behavior  | Group           | Control |   |   |   |   | Polyoxyethylene p-nonylphenyl ether |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
|-------------------|-----------------|---------|---|---|---|---|-------------------------------------|----|----|----|----|-----|----|----|----|----|------|----|----|----|----|
|                   | Dose(mg/kg/day) |         |   |   |   |   | 20                                  |    |    |    |    | 200 |    |    |    |    | 1000 |    |    |    |    |
|                   | Animal No.      | 1       | 2 | 3 | 4 | 5 | 21                                  | 22 | 23 | 24 | 25 | 31  | 32 | 33 | 34 | 35 | 41   | 42 | 43 | 44 | 45 |
| Muscle Tone       |                 |         |   |   |   |   |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Limb Tone         |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Grip Strength     |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Body Tone         |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Abdominal Tone    |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Reflex            |                 |         |   |   |   |   |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Pinna Reflex      |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Corneal Reflex    |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| IFR               |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Autonomic Profile |                 |         |   |   |   |   |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Writhing          |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Palpebral Opening |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Exophthalmos      |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Urination         |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Salivation        |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Piloerection      |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Hypothermia       |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Skin Color        |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Heart Rate        |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Respiratory Rate  |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Pupil Size        |                 | -       | - | - | - | - | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Rearing*          |                 | 0       | 0 | 0 | 0 | 0 | 0                                   | 0  | 0  | 0  | 0  | 0   | 0  | 0  | 0  | 0  | 0    | 0  | 0  | 0  | 0  |

Notes) - : Normal sign

\* : Numerals represent the count of rearing

| General behavior     | Group           | Control |   |   |   |   | Polyoxyethylene p-nonylphenyl ether |  |     |  |  |      |    |    |    |    |
|----------------------|-----------------|---------|---|---|---|---|-------------------------------------|--|-----|--|--|------|----|----|----|----|
|                      | Dose(mg/kg/day) |         |   |   |   |   | 20                                  |  | 200 |  |  | 1000 |    |    |    |    |
|                      | Animal No.      | 1       | 2 | 3 | 4 | 5 |                                     |  |     |  |  | 41   | 42 | 43 | 44 | 45 |
| Awareness            |                 |         |   |   |   |   |                                     |  |     |  |  |      |    |    |    |    |
| Alertness            |                 | -       | - | - | - | - |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Visual Placing       |                 | -       | - | - | - | - |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Stereotypy           |                 | -       | - | - | - | - |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Passivity            |                 | -       | - | - | - | - |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Mood                 |                 |         |   |   |   |   |                                     |  |     |  |  |      |    |    |    |    |
| Grooming             |                 | -       | - | - | - | - |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Vocalization         |                 | -       | - | - | - | - |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Restlessness         |                 | -       | - | - | - | - |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Irritability         |                 | -       | - | - | - | - |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Fearfulness          |                 | -       | - | - | - | - |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Motor Activity       |                 |         |   |   |   |   |                                     |  |     |  |  |      |    |    |    |    |
| Reactivity           |                 | -       | - | - | - | - |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Spontaneous Activity |                 | -       | - | - | - | - |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Touch Response       |                 | -       | - | - | - | - |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Pain Response        |                 | -       | - | - | - | - |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| CNS Excitation       |                 |         |   |   |   |   |                                     |  |     |  |  |      |    |    |    |    |
| Startle Response     |                 | -       | - | - | - | - |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Straub Tail          |                 | -       | - | - | - | - |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Tremors              |                 | -       | - | - | - | - |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Twitches             |                 | -       | - | - | - | - |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Convulsions          |                 | -       | - | - | - | - |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Posture              |                 |         |   |   |   |   |                                     |  |     |  |  |      |    |    |    |    |
| Body Posture         |                 | -       | - | - | - | - |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Limb Posture         |                 | -       | - | - | - | - |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Motor Incoordination |                 |         |   |   |   |   |                                     |  |     |  |  |      |    |    |    |    |
| Staggering Gait      |                 | -       | - | - | - | - |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Abnormal Gait        |                 | -       | - | - | - | - |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Righting Reflex      |                 | -       | - | - | - | - |                                     |  |     |  |  | -    | -  | -  | -  | -  |

Note) - : Normal sign

| General behavior  | Group<br>Dose(mg/kg/day)<br>Animal No. | Control |   |   |   |   | Polyoxyethylene p-nonylphenyl ether |  |     |  |      |    |    |    |    |  |
|-------------------|--|---------|---|---|---|---|-------------------------------------|--|-----|--|------|----|----|----|----|--|
|                   |  |         |   |   |   |   | 20                                  |  | 200 |  | 1000 |    |    |    |    |  |
|                   |  | 1       | 2 | 3 | 4 | 5 |                                     |  |     |  | 41   | 42 | 43 | 44 | 45 |  |
| Muscle Tone       |  |         |   |   |   |   |                                     |  |     |  |      |    |    |    |    |  |
| Limb Tone         |  | -       | - | - | - | - |                                     |  |     |  | -    | -  | -  | -  | -  |  |
| Grip Strength     |  | -       | - | - | - | - |                                     |  |     |  | -    | -  | -  | -  | -  |  |
| Body Tone         |  | -       | - | - | - | - |                                     |  |     |  | -    | -  | -  | -  | -  |  |
| Abdominal Tone    |  | -       | - | - | - | - |                                     |  |     |  | -    | -  | -  | -  | -  |  |
| Reflex            |  |         |   |   |   |   |                                     |  |     |  |      |    |    |    |    |  |
| Pinna Reflex      |  | -       | - | - | - | - |                                     |  |     |  | -    | -  | -  | -  | -  |  |
| Corneal Reflex    |  | -       | - | - | - | - |                                     |  |     |  | -    | -  | -  | -  | -  |  |
| IFR               |  | -       | - | - | - | - |                                     |  |     |  | -    | -  | -  | -  | -  |  |
| Autonomic Profile |  |         |   |   |   |   |                                     |  |     |  |      |    |    |    |    |  |
| Writhing          |  | -       | - | - | - | - |                                     |  |     |  | -    | -  | -  | -  | -  |  |
| Palpebral Opening |  | -       | - | - | - | - |                                     |  |     |  | -    | -  | -  | -  | -  |  |
| Exophthalmos      |  | -       | - | - | - | - |                                     |  |     |  | -    | -  | -  | -  | -  |  |
| Urination         |  | -       | - | - | - | - |                                     |  |     |  | -    | -  | -  | -  | -  |  |
| Salivation        |  | -       | - | - | - | - |                                     |  |     |  | -    | -  | -  | -  | -  |  |
| Piloerection      |  | -       | - | - | - | - |                                     |  |     |  | -    | -  | -  | -  | -  |  |
| Hypothermia       |  | -       | - | - | - | - |                                     |  |     |  | -    | -  | -  | -  | -  |  |
| Skin Color        |  | -       | - | - | - | - |                                     |  |     |  | -    | -  | -  | -  | -  |  |
| Heart Rate        |  | -       | - | - | - | - |                                     |  |     |  | -    | -  | -  | -  | -  |  |
| Respiratory Rate  |  | -       | - | - | - | - |                                     |  |     |  | -    | -  | -  | -  | -  |  |
| Pupil Size        |  | -       | - | - | - | - |                                     |  |     |  | -    | -  | -  | -  | -  |  |
| Rearing*          |  | 0       | 0 | 0 | 0 | 0 |                                     |  |     |  | 0    | 0  | 0  | 0  | 0  |  |

Notes) - : Normal sign

\* : Numerals represent the count of rearing

| General behavior            | Group<br>Dose(mg/kg/day)<br>Animal No. | Control |    |    |    |    | Polyoxyethylene p-nonylphenyl ether |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
|-----------------------------|--|---------|----|----|----|----|-------------------------------------|----|----|----|----|-----|----|----|----|----|------|----|----|----|----|
|                             |  |         |    |    |    |    | 20                                  |    |    |    |    | 200 |    |    |    |    | 1000 |    |    |    |    |
|                             |  | 11      | 12 | 13 | 14 | 15 | 26                                  | 27 | 28 | 29 | 30 | 36  | 37 | 38 | 39 | 40 | 51   | 52 | 53 | 54 | 55 |
| <b>Awareness</b>            |  |         |    |    |    |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Alertness                   |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Visual Placing              |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Stereotypy                  |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Passivity                   |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| <b>Mood</b>                 |  |         |    |    |    |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Grooming                    |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Vocalization                |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Restlessness                |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Irritability                |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Fearfulness                 |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| <b>Motor Activity</b>       |  |         |    |    |    |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Reactivity                  |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Spontaneous Activity        |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Touch Response              |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Pain Response               |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| <b>CNS Excitation</b>       |  |         |    |    |    |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Startle Response            |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Straub Tail                 |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Tremors                     |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Twitches                    |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Convulsions                 |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| <b>Posture</b>              |  |         |    |    |    |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Body Posture                |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Limb Posture                |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| <b>Motor Incoordination</b> |  |         |    |    |    |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Staggering Gait             |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Abnormal Gait               |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Righting Reflex             |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |

Note) - : Normal sign

| General behavior  | Group<br>Dose(mg/kg/day)<br>Animal No. | Control |    |    |    |    | Polyoxyethylene p-nonylphenyl ether |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
|-------------------|--|---------|----|----|----|----|-------------------------------------|----|----|----|----|-----|----|----|----|----|------|----|----|----|----|
|                   |  |         |    |    |    |    | 20                                  |    |    |    |    | 200 |    |    |    |    | 1000 |    |    |    |    |
|                   |  | 11      | 12 | 13 | 14 | 15 | 26                                  | 27 | 28 | 29 | 30 | 36  | 37 | 38 | 39 | 40 | 51   | 52 | 53 | 54 | 55 |
| Muscle Tone       |  |         |    |    |    |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Limb Tone         |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Grip Strength     |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Body Tone         |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Abdominal Tone    |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Reflex            |  |         |    |    |    |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Pinna Reflex      |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Corneal Reflex    |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| IFR               |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Autonomic Profile |  |         |    |    |    |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Writhing          |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Palpebral Opening |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Exophthalmos      |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Urination         |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Salivation        |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Piloerection      |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Hypothermia       |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Skin Color        |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Heart Rate        |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Respiratory Rate  |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Pupil Size        |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Rearing*          |  | 0       | 0  | 0  | 0  | 1  | 0                                   | 0  | 0  | 0  | 0  | 1   | 0  | 0  | 0  | 0  | 0    | 0  | 0  | 0  | 0  |

Notes) - : Normal sign

\* : Numerals represent the count of rearing

Appendix 2-11 Effects of Polyoxyethylene p-nonylphenyl ether on the general behavior in female rats (2 - 4 hours after administration on Day 0)

Study No. : SBL79-02

| General behavior            | Group           | Control |    |    |    |    | Polyoxyethylene p-nonylphenyl ether |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
|-----------------------------|-----------------|---------|----|----|----|----|-------------------------------------|----|----|----|----|-----|----|----|----|----|------|----|----|----|----|
|                             | Dose(mg/kg/day) |         |    |    |    |    | 20                                  |    |    |    |    | 200 |    |    |    |    | 1000 |    |    |    |    |
|                             | Animal No.      | 11      | 12 | 13 | 14 | 15 | 26                                  | 27 | 28 | 29 | 30 | 36  | 37 | 38 | 39 | 40 | 51   | 52 | 53 | 54 | 55 |
| <b>Awareness</b>            |                 |         |    |    |    |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Alertness                   |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Visual Placing              |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Stereotypy                  |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Passivity                   |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| <b>Hood</b>                 |                 |         |    |    |    |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Grooming                    |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Vocalization                |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Restlessness                |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Irritability                |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Fearfulness                 |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| <b>Motor Activity</b>       |                 |         |    |    |    |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Reactivity                  |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Spontaneous Activity        |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Touch Response              |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Pain Response               |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| <b>CNS Excitation</b>       |                 |         |    |    |    |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Startle Response            |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Straub Tail                 |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Tremors                     |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Twitches                    |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Convulsions                 |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| <b>Posture</b>              |                 |         |    |    |    |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Body Posture                |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Limb Posture                |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| <b>Motor Incoordination</b> |                 |         |    |    |    |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Staggering Gait             |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Abnormal Gait               |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Righting Reflex             |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |

Note) - : Normal sign



Appendix 2-12 Effects of Polyoxyethylene p-nonylphenyl ether on the general behavior in female rats (2 - 4 hours after administration on Day 0)

Study No. : SBL79-02

| General behavior  | Group           | Control |    |    |    |    | Polyoxyethylene p-nonylphenyl ether |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
|-------------------|-----------------|---------|----|----|----|----|-------------------------------------|----|----|----|----|-----|----|----|----|----|------|----|----|----|----|
|                   | Dose(mg/kg/day) |         |    |    |    |    | 20                                  |    |    |    |    | 200 |    |    |    |    | 1000 |    |    |    |    |
|                   | Animal No.      | 11      | 12 | 13 | 14 | 15 | 26                                  | 27 | 28 | 29 | 30 | 36  | 37 | 38 | 39 | 40 | 51   | 52 | 53 | 54 | 55 |
|                   |                 |         |    |    |    |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Muscle Tone       |                 |         |    |    |    |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Limb Tone         |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Grip Strength     |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Body Tone         |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Abdominal Tone    |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Reflex            |                 |         |    |    |    |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Pinna Reflex      |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Corneal Reflex    |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| IFR               |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Autonomic Profile |                 |         |    |    |    |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Writhing          |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Palpebral Opening |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Exophthalmos      |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Urination         |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Salivation        |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Piloerection      |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Hypothermia       |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Skin Color        |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Heart Rate        |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Respiratory Rate  |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Pupil Size        |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Rearing*          |                 | 0       | 0  | 0  | 0  | 0  | 0                                   | 0  | 0  | 0  | 0  | 0   | 0  | 0  | 0  | 0  | 1    | 0  | 0  | 0  | 0  |

Notes) - : Normal sign

\* : Numerals represent the count of rearing

Appendix 2-13 Effects of Polyoxyethylene p-nonylphenyl ether on the general behavior in female rats (2 - 4 hours after administration on Day 27)

Study No. : SBL79-02

| General behavior            | Group           | Control |    |    |    |    | Polyoxyethylene p-nonylphenyl ether |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
|-----------------------------|-----------------|---------|----|----|----|----|-------------------------------------|----|----|----|----|-----|----|----|----|----|------|----|----|----|----|
|                             | Dose(mg/kg/day) |         |    |    |    |    | 20                                  |    |    |    |    | 200 |    |    |    |    | 1000 |    |    |    |    |
|                             | Animal No.      | 11      | 12 | 13 | 14 | 15 | 26                                  | 27 | 28 | 29 | 30 | 36  | 37 | 38 | 39 | 40 | 51   | 52 | 53 | 54 | 55 |
| <b>Awareness</b>            |                 |         |    |    |    |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Alertness                   |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Visual Placing              |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Stereotypy                  |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Passivity                   |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| <b>Mood</b>                 |                 |         |    |    |    |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Grooming                    |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Vocalization                |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Restlessness                |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Irritability                |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Fearfulness                 |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| <b>Motor Activity</b>       |                 |         |    |    |    |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Reactivity                  |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Spontaneous Activity        |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Touch Response              |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Pain Response               |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| <b>CNS Excitation</b>       |                 |         |    |    |    |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Startle Response            |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Straub Tail                 |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Tremors                     |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Twitches                    |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Convulsions                 |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| <b>Posture</b>              |                 |         |    |    |    |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Body Posture                |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Limb Posture                |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| <b>Motor Incoordination</b> |                 |         |    |    |    |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Staggering Gait             |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Abnormal Gait               |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Righting Reflex             |                 | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |

Note) - : Normal sign

Appendix 2-14 Effects of Polyoxyethylene p-nonylphenyl ether on the general behavior in female rats (2 - 4 hours after administration on Day 27)

Study No. : SBL79-02

| General behavior  | Group<br>Dose(mg/kg/day)<br>Animal No. | Control |    |    |    |    | Polyoxyethylene p-nonylphenyl ether |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
|-------------------|--|---------|----|----|----|----|-------------------------------------|----|----|----|----|-----|----|----|----|----|------|----|----|----|----|
|                   |  |         |    |    |    |    | 20                                  |    |    |    |    | 200 |    |    |    |    | 1000 |    |    |    |    |
|                   |  | 11      | 12 | 13 | 14 | 15 | 26                                  | 27 | 28 | 29 | 30 | 36  | 37 | 38 | 39 | 40 | 51   | 52 | 53 | 54 | 55 |
| Muscle Tone       |  |         |    |    |    |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Limb Tone         |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Grip Strength     |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Body Tone         |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Abdominal Tone    |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Reflex            |  |         |    |    |    |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Pinna Reflex      |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Corneal Reflex    |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| IPR               |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Autonomic Profile |  |         |    |    |    |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Writhing          |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Palpebral Opening |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Exophthalmos      |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Urination         |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Salivation        |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Piloerection      |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Hypothermia       |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Skin Color        |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Heart Rate        |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Respiratory Rate  |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Pupil Size        |  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Rearing*          |  | 0       | 1  | 0  | 0  | 2  | 0                                   | 0  | 0  | 0  | 0  | 0   | 0  | 0  | 0  | 0  | 0    | 1  | 1  | 0  | 0  |

Notes) - : Normal sign

\* : Numerals represent the count of rearing

| General behavior     | Group           | Control |    |    |    |    | Polyoxyethylene p-nonylphenyl ether |  |     |  |  |  |      |    |    |    |    |
|----------------------|-----------------|---------|----|----|----|----|-------------------------------------|--|-----|--|--|--|------|----|----|----|----|
|                      | Dose(mg/kg/day) |         |    |    |    |    | 20                                  |  | 200 |  |  |  | 1000 |    |    |    |    |
|                      | Animal No.      | 11      | 12 | 13 | 14 | 15 |                                     |  |     |  |  |  | 51   | 52 | 53 | 54 | 55 |
| Awareness            |                 |         |    |    |    |    |                                     |  |     |  |  |  |      |    |    |    |    |
| Alertness            |                 | -       | -  | -  | -  | -  |                                     |  |     |  |  |  | -    | -  | -  | -  | -  |
| Visual Placing       |                 | -       | -  | -  | -  | -  |                                     |  |     |  |  |  | -    | -  | -  | -  | -  |
| Stereotypy           |                 | -       | -  | -  | -  | -  |                                     |  |     |  |  |  | -    | -  | -  | -  | -  |
| Passivity            |                 | -       | -  | -  | -  | -  |                                     |  |     |  |  |  | -    | -  | -  | -  | -  |
| Hood                 |                 |         |    |    |    |    |                                     |  |     |  |  |  |      |    |    |    |    |
| Grooming             |                 | -       | -  | -  | -  | -  |                                     |  |     |  |  |  | -    | -  | -  | -  | -  |
| Vocalization         |                 | -       | -  | -  | -  | -  |                                     |  |     |  |  |  | -    | -  | -  | -  | -  |
| Restlessness         |                 | -       | -  | -  | -  | -  |                                     |  |     |  |  |  | -    | -  | -  | -  | -  |
| Irritability         |                 | -       | -  | -  | -  | -  |                                     |  |     |  |  |  | -    | -  | -  | -  | -  |
| Fearfulness          |                 | -       | -  | -  | -  | -  |                                     |  |     |  |  |  | -    | -  | -  | -  | -  |
| Motor Activity       |                 |         |    |    |    |    |                                     |  |     |  |  |  |      |    |    |    |    |
| Reactivity           |                 | -       | -  | -  | -  | -  |                                     |  |     |  |  |  | -    | -  | -  | -  | -  |
| Spontaneous Activity |                 | -       | -  | -  | -  | -  |                                     |  |     |  |  |  | -    | -  | -  | -  | -  |
| Touch Response       |                 | -       | -  | -  | -  | -  |                                     |  |     |  |  |  | -    | -  | -  | -  | -  |
| Pain Response        |                 | -       | -  | -  | -  | -  |                                     |  |     |  |  |  | -    | -  | -  | -  | -  |
| CNS Excitation       |                 |         |    |    |    |    |                                     |  |     |  |  |  |      |    |    |    |    |
| Startle Response     |                 | -       | -  | -  | -  | -  |                                     |  |     |  |  |  | -    | -  | -  | -  | -  |
| Straub Tail          |                 | -       | -  | -  | -  | -  |                                     |  |     |  |  |  | -    | -  | -  | -  | -  |
| Tremors              |                 | -       | -  | -  | -  | -  |                                     |  |     |  |  |  | -    | -  | -  | -  | -  |
| Twitches             |                 | -       | -  | -  | -  | -  |                                     |  |     |  |  |  | -    | -  | -  | -  | -  |
| Convulsions          |                 | -       | -  | -  | -  | -  |                                     |  |     |  |  |  | -    | -  | -  | -  | -  |
| Posture              |                 |         |    |    |    |    |                                     |  |     |  |  |  |      |    |    |    |    |
| Body Posture         |                 | -       | -  | -  | -  | -  |                                     |  |     |  |  |  | -    | -  | -  | -  | -  |
| Limb Posture         |                 | -       | -  | -  | -  | -  |                                     |  |     |  |  |  | -    | -  | -  | -  | -  |
| Motor Incoordination |                 |         |    |    |    |    |                                     |  |     |  |  |  |      |    |    |    |    |
| Staggering Gait      |                 | -       | -  | -  | -  | -  |                                     |  |     |  |  |  | -    | -  | -  | -  | -  |
| Abnormal Gait        |                 | -       | -  | -  | -  | -  |                                     |  |     |  |  |  | -    | -  | -  | -  | -  |
| Righting Reflex      |                 | -       | -  | -  | -  | -  |                                     |  |     |  |  |  | -    | -  | -  | -  | -  |

Note) - : Normal sign

| General behavior  | Group<br>Dose(mg/kg/day)<br>Animal No. | Control |    |    |    |    | Polyoxyethylene p-nonylphenyl ether |  |     |  |  |      |    |    |    |    |
|-------------------|--|---------|----|----|----|----|-------------------------------------|--|-----|--|--|------|----|----|----|----|
|                   |  |         |    |    |    |    | 20                                  |  | 200 |  |  | 1000 |    |    |    |    |
|                   |  | 11      | 12 | 13 | 14 | 15 |                                     |  |     |  |  | 51   | 52 | 53 | 54 | 55 |
| Muscle Tone       |  |         |    |    |    |    |                                     |  |     |  |  |      |    |    |    |    |
| Limb Tone         |  | -       | -  | -  | -  | -  |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Grip Strength     |  | -       | -  | -  | -  | -  |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Body Tone         |  | -       | -  | -  | -  | -  |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Abdominal Tone    |  | -       | -  | -  | -  | -  |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Reflex            |  |         |    |    |    |    |                                     |  |     |  |  |      |    |    |    |    |
| Pinna Reflex      |  | -       | -  | -  | -  | -  |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Corneal Reflex    |  | -       | -  | -  | -  | -  |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| IPR               |  | -       | -  | -  | -  | -  |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Autonomic Profile |  |         |    |    |    |    |                                     |  |     |  |  |      |    |    |    |    |
| Writhing          |  | -       | -  | -  | -  | -  |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Palpebral Opening |  | -       | -  | -  | -  | -  |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Exophthalmos      |  | -       | -  | -  | -  | -  |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Urination         |  | -       | -  | -  | -  | -  |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Salivation        |  | -       | -  | -  | -  | -  |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Piloerection      |  | -       | -  | -  | -  | -  |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Hypothermia       |  | -       | -  | -  | -  | -  |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Skin Color        |  | -       | -  | -  | -  | -  |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Heart Rate        |  | -       | -  | -  | -  | -  |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Respiratory Rate  |  | -       | -  | -  | -  | -  |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Pupil Size        |  | -       | -  | -  | -  | -  |                                     |  |     |  |  | -    | -  | -  | -  | -  |
| Rearing*          |  | 0       | 0  | 0  | 0  | 0  |                                     |  |     |  |  | 0    | 1  | 1  | 0  | 0  |

Notes) - : Normal sign

\* : Numerals represent the count of rearing

## Appendix 3-1 Food consumption ( g/day ) in male rats

Study No. : SBL79-02

| Group   | Anim.No. | Pre  | 1w   | 2w   | 3w   | 4w   | R:1w | R:2w |
|---|----------|------|------|------|------|------|------|------|
| Control   |          |      |      |      |      |      |      |      |
|   | 1        | 23   | 26   | 32   | 28   | 31   | 30   | 31   |
|   | 2        | 26   | 26   | 31   | 26   | 31   | 28   | 29   |
|   | 3        | 21   | 26   | 31   | 27   | 28   | 30   | 34   |
|   | 4        | 24   | 32   | 33   | 33   | 36   | 35   | 37   |
|   | 5        | 23   | 25   | 29   | 29   | 30   | 23   | 31   |
|   | 6        | 22   | 22   | 25   | 22   | 25   |      |      |
|   | 7        | 24   | 31   | 31   | 29   | 33   |      |      |
|   | 8        | 24   | 26   | 32   | 27   | 30   |      |      |
|   | 9        | 23   | 26   | 31   | 27   | 33   |      |      |
|   | 10       | 24   | 26   | 27   | 32   | 32   |      |      |
|   | Mean     | 23.4 | 26.6 | 30.2 | 28.0 | 30.9 | 29.2 | 32.4 |
|   | +S.D.    | 1.3  | 2.9  | 2.5  | 3.1  | 3.0  | 4.3  | 3.1  |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |      |      |      |      |      |      |      |
|   | 21       | 22   | 24   | 24   | 26   | 27   |      |      |
|   | 22       | 24   | 30   | 27   | 26   | 30   |      |      |
|   | 23       | 21   | 24   | 27   | 23   | 25   |      |      |
|   | 24       | 23   | 30   | 30   | 30   | 33   |      |      |
|   | 25       | 26   | 28   | 29   | 28   | 32   |      |      |
|   | Mean     | 23.2 | 27.2 | 27.4 | 26.6 | 29.4 |      |      |
|   | +S.D.    | 1.9  | 3.0  | 2.3  | 2.6  | 3.4  |      |      |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |      |      |      |      |      |      |      |
|   | 31       | 22   | 27   | 25   | 27   | 25   |      |      |
|   | 32       | 26   | 29   | 30   | 31   | 32   |      |      |
|   | 33       | 27   | 29   | 30   | 26   | 29   |      |      |
|   | 34       | 23   | 24   | 24   | 25   | 28   |      |      |
|   | 35       | 19   | 22   | 23   | 24   | 26   |      |      |
|   | Mean     | 23.4 | 26.2 | 26.4 | 26.6 | 28.0 |      |      |
|   | +S.D.    | 3.2  | 3.1  | 3.4  | 2.7  | 2.7  |      |      |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |      |      |      |      |      |      |      |
|   | 41       | 21   | 26   | 24   | 23   | 25   | 28   | 25   |
|   | 42       | 24   | 29   | 30   | 29   | 35   | 33   | 36   |
|   | 43       | 23   | 29   | 29   | 26   | 29   | 28   | 33   |
|   | 44       | 24   | 29   | 30   | 29   | 30   | 30   | 33   |
|   | 45       | 22   | 29   | 32   | 29   | 31   | 31   | 32   |
|   | 46       | 25   | 27   | 28   | 28   | 37   |      |      |
|   | 47       | 23   | 30   | 32   | 32   | 34   |      |      |
|   | 48       | 25   | 28   | 28   | 27   | 32   |      |      |
|   | 49       | 27   | 31   | 34   | 34   | 37   |      |      |
|   | 50       | 21   | 26   | 31   | 24   | 26   |      |      |
|   | Mean     | 23.5 | 28.4 | 29.8 | 28.1 | 31.6 | 30.0 | 31.8 |
|   | +S.D.    | 1.9  | 1.6  | 2.8  | 3.3  | 4.2  | 2.1  | 4.1  |

## Appendix 3-2 Food consumption ( g/day ) in female rats

Study No. : SBL79-02

| Group   | Anim.No. | Pre  | 1w   | 2w   | 3w   | 4w   | R:1w | R:2w |
|---|----------|------|------|------|------|------|------|------|
| Control   |          |      |      |      |      |      |      |      |
|   | 11       | 20   | 22   | 19   | 15   | 23   | 19   | 26   |
|   | 12       | 21   | 17   | 23   | 20   | 24   | 23   | 26   |
|   | 13       | 19   | 21   | 21   | 20   | 21   | 26   | 25   |
|   | 14       | 23   | 22   | 20   | 20   | 21   | 18   | 26   |
|   | 15       | 18   | 19   | 16   | 15   | 21   | 22   | 22   |
|   | 16       | 21   | 21   | 26   | 24   | 23   |      |      |
|   | 17       | 22   | 23   | 23   | 23   | 30   |      |      |
|   | 18       | 19   | 21   | 19   | 18   | 21   |      |      |
|   | 19       | 19   | 23   | 20   | 18   | 20   |      |      |
|   | 20       | 22   | 24   | 23   | 21   | 27   |      |      |
|   |          |      |      |      |      |      |      |      |
| Mean  |          | 20.4 | 21.3 | 21.0 | 19.4 | 23.1 | 21.6 | 25.0 |
| +S.D.   |          | 1.6  | 2.1  | 2.8  | 3.0  | 3.2  | 3.2  | 1.7  |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |      |      |      |      |      |      |      |
|   | 26       | 19   | 18   | 18   | 16   | 24   |      |      |
|   | 27       | 21   | 22   | 23   | 21   | 28   |      |      |
|   | 28       | 18   | 22   | 20   | 21   | 25   |      |      |
|   | 29       | 21   | 24   | 19   | 19   | 24   |      |      |
|   | 30       | 21   | 22   | 21   | 20   | 29   |      |      |
|   |          |      |      |      |      |      |      |      |
| Mean  |          | 20.0 | 21.6 | 20.2 | 19.4 | 26.0 |      |      |
| +S.D.   |          | 1.4  | 2.2  | 1.9  | 2.1  | 2.3  |      |      |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |      |      |      |      |      |      |      |
|   | 36       | 20   | 20   | 19   | 20   | 21   |      |      |
|   | 37       | 21   | 27   | 24   | 22   | 20   |      |      |
|   | 38       | 22   | 25   | 21   | 22   | 27   |      |      |
|   | 39       | 19   | 22   | 20   | 16   | 21   |      |      |
|   | 40       | 23   | 22   | 25   | 22   | 27   |      |      |
|   |          |      |      |      |      |      |      |      |
| Mean  |          | 21.0 | 23.2 | 21.8 | 20.4 | 23.2 |      |      |
| +S.D.   |          | 1.6  | 2.8  | 2.6  | 2.6  | 3.5  |      |      |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |      |      |      |      |      |      |      |
|   | 51       | 22   | 20   | 17   | 16   | 21   | 18   | 20   |
|   | 52       | 21   | 22   | 22   | 18   | 33   | 11   | 23   |
|   | 53       | 19   | 19   | 19   | 15   | 17   | 25   | 23   |
|   | 54       | 22   | 22   | 24   | 20   | 19   | 24   | 21   |
|   | 55       | 21   | 23   | 23   | 25   | 30   | 22   | 22   |
|   | 56       | 22   | 20   | 21   | 22   | 26   |      |      |
|   | 57       | 19   | 25   | 23   | 23   | 26   |      |      |
|   | 58       | 21   | 23   | 23   | 19   | 20   |      |      |
|   | 59       | 21   | 23   | 20   | 18   | 25   |      |      |
|   | 60       | 22   | 20   | 19   | 22   | 24   |      |      |
|   |          |      |      |      |      |      |      |      |
| Mean  |          | 21.0 | 21.7 | 21.1 | 19.8 | 24.1 | 20.0 | 21.8 |
| +S.D.   |          | 1.2  | 1.9  | 2.3  | 3.2  | 5.0  | 5.7  | 1.3  |

## Appendix 4-1 Body weight ( g ) in male rats

Study No. : SBL79-02

| Group   | Anim.No. | Pre   | 1w    | 2w    | 3w    | 4w    | R:1w  | R:2w  |
|---|----------|-------|-------|-------|-------|-------|-------|-------|
| Control   |          |       |       |       |       |       |       |       |
|   | 1        | 155   | 214   | 270   | 324   | 372   | 409   | 429   |
|   | 2        | 153   | 207   | 262   | 306   | 341   | 371   | 388   |
|   | 3        | 144   | 198   | 256   | 292   | 317   | 353   | 385   |
|   | 4        | 166   | 226   | 294   | 349   | 387   | 429   | 465   |
|   | 5        | 150   | 202   | 251   | 296   | 326   | 354   | 370   |
|   | 6        | 151   | 189   | 225   | 257   | 286   |       |       |
|   | 7        | 167   | 239   | 307   | 372   | 416   |       |       |
|   | 8        | 158   | 219   | 283   | 330   | 360   |       |       |
|   | 9        | 161   | 224   | 285   | 334   | 375   |       |       |
|   | 10       | 160   | 212   | 267   | 325   | 363   |       |       |
| Mean  |          | 156.5 | 213.0 | 270.0 | 318.5 | 354.3 | 383.2 | 407.4 |
| +S.D.   |          | 7.3   | 14.8  | 23.6  | 32.3  | 37.7  | 34.2  | 38.9  |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |       |       |       |       |       |       |       |
|   | 21       | 151   | 201   | 248   | 293   | 323   |       |       |
|   | 22       | 165   | 229   | 285   | 328   | 368   |       |       |
|   | 23       | 146   | 192   | 245   | 289   | 314   |       |       |
|   | 24       | 157   | 217   | 274   | 324   | 358   |       |       |
|   | 25       | 159   | 214   | 264   | 307   | 333   |       |       |
| Mean  |          | 155.6 | 210.6 | 263.2 | 308.2 | 339.2 |       |       |
| +S.D.   |          | 7.3   | 14.4  | 17.0  | 17.6  | 23.0  |       |       |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |       |       |       |       |       |       |       |
|   | 31       | 154   | 213   | 258   | 298   | 323   |       |       |
|   | 32       | 163   | 219   | 275   | 329   | 365   |       |       |
|   | 33       | 163   | 225   | 279   | 323   | 353   |       |       |
|   | 34       | 147   | 196   | 238   | 271   | 307   |       |       |
|   | 35       | 132   | 167   | 207   | 250   | 274   |       |       |
| Mean  |          | 151.8 | 204.0 | 251.4 | 294.2 | 324.4 |       |       |
| +S.D.   |          | 12.9  | 23.3  | 29.6  | 33.7  | 36.4  |       |       |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |       |       |       |       |       |       |       |
|   | 41       | 137   | 188   | 234   | 272   | 299   | 331   | 352   |
|   | 42       | 159   | 222   | 285   | 334   | 378   | 419   | 452   |
|   | 43       | 154   | 208   | 262   | 307   | 344   | 381   | 411   |
|   | 44       | 160   | 224   | 278   | 321   | 345   | 375   | 405   |
|   | 45       | 147   | 207   | 267   | 320   | 352   | 387   | 410   |
|   | 46       | 157   | 210   | 264   | 314   | 351   |       |       |
|   | 47       | 163   | 225   | 282   | 341   | 389   |       |       |
|   | 48       | 168   | 224   | 276   | 332   | 376   |       |       |
|   | 49       | 169   | 229   | 287   | 347   | 392   |       |       |
|   | 50       | 147   | 200   | 246   | 276   | 294   |       |       |
| Mean  |          | 156.1 | 213.7 | 268.1 | 316.4 | 352.0 | 378.6 | 406.0 |
| +S.D.   |          | 10.1  | 13.3  | 17.3  | 25.4  | 34.2  | 31.6  | 35.6  |



## Appendix 4-2 Body weight ( g ) in female rats

Study No. : SBL79-02

| Group   | Anim.No. | Pre   | 1w    | 2w    | 3w    | 4w    | R:1w  | R:2w  |
|---|----------|-------|-------|-------|-------|-------|-------|-------|
| Control   |          |       |       |       |       |       |       |       |
|   | 11       | 131   | 162   | 183   | 195   | 216   | 235   | 248   |
|   | 12       | 130   | 157   | 184   | 205   | 225   | 235   | 248   |
|   | 13       | 129   | 163   | 192   | 216   | 237   | 259   | 274   |
|   | 14       | 134   | 162   | 184   | 201   | 213   | 234   | 248   |
|   | 15       | 124   | 155   | 170   | 183   | 207   | 227   | 239   |
|   | 16       | 135   | 164   | 204   | 241   | 251   |       |       |
|   | 17       | 133   | 176   | 204   | 243   | 271   |       |       |
|   | 18       | 122   | 161   | 184   | 209   | 221   |       |       |
|   | 19       | 131   | 166   | 187   | 214   | 225   |       |       |
|   | 20       | 135   | 169   | 201   | 220   | 239   |       |       |
| Mean  |          | 130.4 | 163.5 | 189.3 | 212.7 | 230.5 | 238.0 | 251.4 |
| +S.D.   |          | 4.4   | 5.9   | 10.9  | 18.8  | 19.4  | 12.2  | 13.2  |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |       |       |       |       |       |       |       |
|   | 26       | 121   | 150   | 168   | 186   | 207   |       |       |
|   | 27       | 135   | 166   | 184   | 213   | 239   |       |       |
|   | 28       | 127   | 162   | 182   | 207   | 236   |       |       |
|   | 29       | 133   | 172   | 187   | 206   | 231   |       |       |
|   | 30       | 135   | 176   | 203   | 224   | 243   |       |       |
| Mean  |          | 130.2 | 165.2 | 184.8 | 207.2 | 231.2 |       |       |
| +S.D.   |          | 6.1   | 10.1  | 12.5  | 13.8  | 14.2  |       |       |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |       |       |       |       |       |       |       |
|   | 36       | 133   | 167   | 191   | 212   | 235   |       |       |
|   | 37       | 134   | 176   | 187   | 196   | 215   |       |       |
|   | 38       | 138   | 182   | 214   | 242   | 262   |       |       |
|   | 39       | 123   | 157   | 174   | 185   | 198   |       |       |
|   | 40       | 123   | 159   | 199   | 222   | 239   |       |       |
| Mean  |          | 130.2 | 168.2 | 193.0 | 211.4 | 229.8 |       |       |
| +S.D.   |          | 6.8   | 10.8  | 14.8  | 22.3  | 24.4  |       |       |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |       |       |       |       |       |       |       |
|   | 51       | 128   | 158   | 177   | 196   | 208   | 220   | 228   |
|   | 52       | 129   | 163   | 180   | 198   | 208   | 216   | 233   |
|   | 53       | 121   | 155   | 171   | 183   | 199   | 212   | 223   |
|   | 54       | 137   | 174   | 193   | 209   | 210   | 225   | 225   |
|   | 55       | 130   | 160   | 178   | 204   | 220   | 239   | 260   |
|   | 56       | 135   | 172   | 201   | 234   | 260   |       |       |
|   | 57       | 125   | 165   | 191   | 214   | 232   |       |       |
|   | 58       | 134   | 171   | 201   | 225   | 244   |       |       |
|   | 59       | 132   | 166   | 185   | 204   | 234   |       |       |
|   | 60       | 129   | 164   | 182   | 207   | 232   |       |       |
| Mean  |          | 130.0 | 164.8 | 185.9 | 207.4 | 224.7 | 222.4 | 233.8 |
| +S.D.   |          | 4.8   | 6.2   | 10.3  | 14.5  | 19.1  | 10.5  | 15.1  |

## Appendix 4-3 Body weight gain ( g ) in male rats

Study No. : SBL79-02

| Group   | Anim.No. | 1w   | 2w   | 3w   | 4w   | R:1w | R:2w |
|---|----------|------|------|------|------|------|------|
| Control   |          |      |      |      |      |      |      |
|   | 1        | 59   | 56   | 54   | 48   | 37   | 20   |
|   | 2        | 54   | 55   | 44   | 35   | 30   | 17   |
|   | 3        | 54   | 58   | 36   | 25   | 36   | 32   |
|   | 4        | 60   | 68   | 55   | 38   | 42   | 36   |
|   | 5        | 52   | 49   | 45   | 30   | 28   | 16   |
|   | 6        | 38   | 36   | 32   | 29   |      |      |
|   | 7        | 72   | 68   | 65   | 44   |      |      |
|   | 8        | 61   | 64   | 47   | 30   |      |      |
|   | 9        | 63   | 61   | 49   | 41   |      |      |
|   | 10       | 52   | 55   | 58   | 38   |      |      |
|   | Mean     | 56.5 | 57.0 | 48.5 | 35.8 | 34.6 | 24.2 |
|   | +S.D.    | 8.9  | 9.6  | 10.0 | 7.3  | 5.6  | 9.2  |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |      |      |      |      |      |      |
|   | 21       | 50   | 47   | 45   | 30   |      |      |
|   | 22       | 64   | 56   | 43   | 40   |      |      |
|   | 23       | 46   | 53   | 44   | 25   |      |      |
|   | 24       | 60   | 57   | 50   | 34   |      |      |
|   | 25       | 55   | 50   | 43   | 26   |      |      |
|   | Mean     | 55.0 | 52.6 | 45.0 | 31.0 |      |      |
|   | +S.D.    | 7.3  | 4.2  | 2.9  | 6.2  |      |      |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |      |      |      |      |      |      |
|   | 31       | 59   | 45   | 40   | 25   |      |      |
|   | 32       | 56   | 56   | 54   | 36   |      |      |
|   | 33       | 62   | 54   | 44   | 30   |      |      |
|   | 34       | 49   | 42   | 33   | 36   |      |      |
|   | 35       | 35   | 40   | 43   | 24   |      |      |
|   | Mean     | 52.2 | 47.4 | 42.8 | 30.2 |      |      |
|   | +S.D.    | 10.8 | 7.2  | 7.6  | 5.8  |      |      |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |      |      |      |      |      |      |
|   | 41       | 51   | 46   | 38   | 27   | 32   | 21   |
|   | 42       | 63   | 63   | 49   | 44   | 41   | 33   |
|   | 43       | 54   | 54   | 45   | 37   | 37   | 30   |
|   | 44       | 64   | 54   | 43   | 24   | 30   | 30   |
|   | 45       | 60   | 60   | 53   | 32   | 35   | 23   |
|   | 46       | 53   | 54   | 50   | 37   |      |      |
|   | 47       | 62   | 57   | 59   | 48   |      |      |
|   | 48       | 56   | 52   | 56   | 44   |      |      |
|   | 49       | 60   | 58   | 60   | 45   |      |      |
|   | 50       | 53   | 46   | 30   | 18   |      |      |
|   | Mean     | 57.6 | 54.4 | 48.3 | 35.6 | 35.0 | 27.4 |
|   | +S.D.    | 4.7  | 5.5  | 9.5  | 10.1 | 4.3  | 5.1  |

## Appendix 4-4 Body weight gain ( g ) in female rats

Study No. : SBL79-02

| Group   | Anim.No. | 1w   | 2w   | 3w   | 4w   | R:1w | R:2w |
|---|----------|------|------|------|------|------|------|
| Control   |          |      |      |      |      |      |      |
|   | 11       | 31   | 21   | 12   | 21   | 19   | 13   |
|   | 12       | 27   | 27   | 21   | 20   | 10   | 13   |
|   | 13       | 34   | 29   | 24   | 21   | 22   | 15   |
|   | 14       | 28   | 22   | 17   | 12   | 21   | 14   |
|   | 15       | 31   | 15   | 13   | 24   | 20   | 12   |
|   | 16       | 29   | 40   | 37   | 10   |      |      |
|   | 17       | 43   | 28   | 39   | 28   |      |      |
|   | 18       | 39   | 23   | 25   | 12   |      |      |
|   | 19       | 35   | 21   | 27   | 11   |      |      |
|   | 20       | 34   | 32   | 19   | 19   |      |      |
| Mean  |          | 33.1 | 25.8 | 23.4 | 17.8 | 18.4 | 13.4 |
| +S.D.   |          | 5.0  | 7.0  | 9.1  | 6.2  | 4.8  | 1.1  |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |      |      |      |      |      |      |
|   | 26       | 29   | 18   | 18   | 21   |      |      |
|   | 27       | 31   | 18   | 29   | 26   |      |      |
|   | 28       | 35   | 20   | 25   | 29   |      |      |
|   | 29       | 39   | 15   | 19   | 25   |      |      |
|   | 30       | 41   | 27   | 21   | 19   |      |      |
| Mean  |          | 35.0 | 19.6 | 22.4 | 24.0 |      |      |
| +S.D.   |          | 5.1  | 4.5  | 4.6  | 4.0  |      |      |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |      |      |      |      |      |      |
|   | 36       | 34   | 24   | 21   | 23   |      |      |
|   | 37       | 42   | 11   | 9    | 19   |      |      |
|   | 38       | 44   | 32   | 28   | 20   |      |      |
|   | 39       | 34   | 17   | 11   | 13   |      |      |
|   | 40       | 36   | 40   | 23   | 17   |      |      |
| Mean  |          | 38.0 | 24.8 | 18.4 | 18.4 |      |      |
| +S.D.   |          | 4.7  | 11.6 | 8.1  | 3.7  |      |      |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |      |      |      |      |      |      |
|   | 51       | 30   | 19   | 19   | 12   | 12   | 8    |
|   | 52       | 34   | 17   | 18   | 10   | 8    | 17   |
|   | 53       | 34   | 16   | 12   | 16   | 13   | 11   |
|   | 54       | 37   | 19   | 16   | 1    | 15   | 0    |
|   | 55       | 30   | 18   | 26   | 16   | 19   | 21   |
|   | 56       | 37   | 29   | 33   | 26   |      |      |
|   | 57       | 40   | 26   | 23   | 18   |      |      |
|   | 58       | 37   | 30   | 24   | 19   |      |      |
|   | 59       | 34   | 19   | 19   | 30   |      |      |
|   | 60       | 35   | 18   | 25   | 25   |      |      |
| Mean  |          | 34.8 | 21.1 | 21.5 | 17.3 | 13.4 | 11.4 |
| +S.D.   |          | 3.2  | 5.2  | 5.9  | 8.5  | 4.0  | 8.1  |

Gross ophthalmological examination

Grade

- 1 : slight
- 2 : Moderate
- 3 : Severe
- P : Non-graded change
- N : No abnormal changes
- U : Unexamined

| Group                               | Anim.No. | Item | Pre | 4w | R:2w |
|-------------------------------------|----------|------|-----|----|------|
| Control                             | 1        |      | N   | N  | N    |
|                                     | 2        |      | N   | N  | N    |
|                                     | 3        |      | N   | N  | N    |
|                                     | 4        |      | N   | N  | N    |
|                                     | 5        |      | N   | N  | N    |
|                                     | 6        |      | N   | N  |      |
|                                     | 7        |      | N   | N  |      |
|                                     | 8        |      | N   | N  |      |
|                                     | 9        |      | N   | N  |      |
|                                     | 10       |      | N   | N  |      |
| Polyoxyethylene p-nonylphenyl ether |          |      |     |    |      |
| 20 (mg/kg/day)                      |          |      |     |    |      |
|                                     | 21       |      | N   | N  |      |
|                                     | 22       |      | N   | N  |      |
|                                     | 23       |      | N   | N  |      |
|                                     | 24       |      | N   | N  |      |
|                                     | 25       |      | N   | N  |      |
| Polyoxyethylene p-nonylphenyl ether |          |      |     |    |      |
| 200 (mg/kg/day)                     |          |      |     |    |      |
|                                     | 31       |      | N   | N  |      |
|                                     | 32       |      | N   | N  |      |
|                                     | 33       |      | N   | N  |      |
|                                     | 34       |      | N   | N  |      |
|                                     | 35       |      | N   | N  |      |
| Polyoxyethylene p-nonylphenyl ether |          |      |     |    |      |
| 1000 (mg/kg/day)                    |          |      |     |    |      |
|                                     | 41       |      | N   | N  | N    |
|                                     | 42       |      | N   | N  | N    |
|                                     | 43       |      | N   | N  | N    |
|                                     | 44       |      | N   | N  | N    |
|                                     | 45       |      | N   | N  | N    |
|                                     | 46       |      | N   | N  |      |
|                                     | 47       |      | N   | N  |      |
|                                     | 48       |      | N   | N  |      |
|                                     | 49       |      | N   | N  |      |
|                                     | 50       |      | N   | N  |      |

| Group   | Anim.No. | Item | Pre | 4w | R:2w |
|---|----------|------|-----|----|------|
| Control   |          |      |     |    |      |
|   | 11       |      | N   | N  | N    |
|   | 12       |      | N   | N  | N    |
|   | 13       |      | N   | N  | N    |
|   | 14       |      | N   | N  | N    |
|   | 15       |      | N   | N  | N    |
|   | 16       |      | N   | N  |      |
|   | 17       |      | N   | N  |      |
|   | 18       |      | N   | N  |      |
|   | 19       |      | N   | N  |      |
|   | 20       |      | N   | N  |      |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |      |     |    |      |
|   | 26       |      | N   | N  |      |
|   | 27       |      | N   | N  |      |
|   | 28       |      | N   | N  |      |
|   | 29       |      | N   | N  |      |
|   | 30       |      | N   | N  |      |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |      |     |    |      |
|   | 36       |      | N   | N  |      |
|   | 37       |      | N   | N  |      |
|   | 38       |      | N   | N  |      |
|   | 39       |      | N   | N  |      |
|   | 40       |      | N   | N  |      |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |      |     |    |      |
|   | 51       |      | N   | N  | N    |
|   | 52       |      | N   | N  | N    |
|   | 53       |      | N   | N  | N    |
|   | 54       |      | N   | N  | N    |
|   | 55       |      | N   | N  | N    |
|   | 56       |      | N   | N  |      |
|   | 57       |      | N   | N  |      |
|   | 58       |      | N   | N  |      |
|   | 59       |      | N   | N  |      |
|   | 60       |      | N   | N  |      |

Funduscopy examination

Grade

- 1 : Slight
- 2 : Moderate
- 3 : Severe
- P : Non-graded change
- N : No abnormal changes
- U : Unexamined

| Group   | Anim.No. | Item | Pre | 4w | R:2w |
|---|----------|------|-----|----|------|
| Control   |          |      |     |    |      |
|   | 1        |      | N   | N  | N    |
|   | 2        |      | N   | N  | N    |
|   | 3        |      | N   | N  | N    |
|   | 4        |      | N   | N  | N    |
|   | 5        |      | N   | N  | N    |
|   | 6        |      | N   | N  |      |
|   | 7        |      | N   | N  |      |
|   | 8        |      | N   | N  |      |
|   | 9        |      | N   | N  |      |
|   | 10       |      | N   | N  |      |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |      |     |    |      |
|   | 21       |      | N   | N  |      |
|   | 22       |      | N   | N  |      |
|   | 23       |      | N   | N  |      |
|   | 24       |      | N   | N  |      |
|   | 25       |      | N   | N  |      |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |      |     |    |      |
|   | 31       |      | N   | N  |      |
|   | 32       |      | N   | N  |      |
|   | 33       |      | N   | N  |      |
|   | 34       |      | N   | N  |      |
|   | 35       |      | N   | N  |      |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |      |     |    |      |
|   | 41       |      | N   | N  | N    |
|   | 42       |      | N   | N  | N    |
|   | 43       |      | N   | N  | N    |
|   | 44       |      | N   | N  | N    |
|   | 45       |      | N   | N  | N    |
|   | 46       |      | N   | N  |      |
|   | 47       |      | N   | N  |      |
|   | 48       |      | N   | N  |      |
|   | 49       |      | N   | N  |      |
|   | 50       |      | N   | N  |      |



| Group   | Anim.No. | Item | Pre | 4w | R:2w |
|---|----------|------|-----|----|------|
| Control   |          |      |     |    |      |
|   | 11       |      | N   | N  | N    |
|   | 12       |      | N   | N  | N    |
|   | 13       |      | N   | N  | N    |
|   | 14       |      | N   | N  | N    |
|   | 15       |      | N   | N  | N    |
|   | 16       |      | N   | N  |      |
|   | 17       |      | N   | N  |      |
|   | 18       |      | N   | N  |      |
|   | 19       |      | N   | N  |      |
|   | 20       |      | N   | N  |      |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |      |     |    |      |
|   | 26       |      | N   | N  |      |
|   | 27       |      | N   | N  |      |
|   | 28       |      | N   | N  |      |
|   | 29       |      | N   | N  |      |
|   | 30       |      | N   | N  |      |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |      |     |    |      |
|   | 36       |      | N   | N  |      |
|   | 37       |      | N   | N  |      |
|   | 38       |      | N   | N  |      |
|   | 39       |      | N   | N  |      |
|   | 40       |      | N   | N  |      |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |      |     |    |      |
|   | 51       |      | N   | N  | N    |
|   | 52       |      | N   | N  | N    |
|   | 53       |      | N   | N  | N    |
|   | 54       |      | N   | N  | N    |
|   | 55       |      | N   | N  | N    |
|   | 56       |      | N   | N  |      |
|   | 57       |      | N   | N  |      |
|   | 58       |      | N   | N  |      |
|   | 59       |      | N   | N  |      |
|   | 60       |      | N   | N  |      |

# Standard Urinalysis

Color 0 : Normal color  
1 : Abnormal color

Protein 0 : - (mg/dL)  
1 : +  
2 :  $\overline{+}$  30  
3 : ++ 100  
4 : +++ 300  
5 : ++++ 1000

Glucose 0 : - (g/dL)  
1 : + 0.1  
2 :  $\overline{+}$  0.25  
3 : ++ 0.5  
4 : +++ 1  
5 : ++++ 2

Ketone body 0 : - (mg/dL)  
(Ketone) 1 : + 5  
2 :  $\overline{+}$  15  
3 : ++ 40  
4 : +++ 80  
5 : ++++ 160

Bilirubin 0 : -  
(Bil.) 1 : +  
2 : ++  
3 : +++

Occult blood 0 : -  
(Oc.Bld.) 1 : +  
2 :  $\overline{+}$   
3 : ++  
4 : +++

Urobilinogen 0 : + (Ehrlich unit/dL) 0.1  
(Urobil.) 1 :  $\overline{+}$  1  
2 : ++ 2  
3 : +++ 4  
4 : ++++ 8  
5 : +++++ 12

Urine volume (U.Vol.)

Specific gravity (S.Grav.)

## Appendix 6-1 Urinalysis in male rats

Study No. : SBL79-02

| Group  | Anim.No. | Color |      | pH  |      | Protein |      | Glucose |      | Ketone |      | Bil. |      |
|--|----------|-------|------|-----|------|---------|------|---------|------|--------|------|------|------|
|  |          | 4w    | R:2w | 4w  | R:2w | 4w      | R:2w | 4w      | R:2w | 4w     | R:2w | 4w   | R:2w |
| Control  |          |       |      |     |      |         |      |         |      |        |      |      |      |
|  | 1        | 0     | 0    | 8   | 8    | 2       | 2    | 0       | 0    | 2      | 1    | 0    | 0    |
|  | 2        | 0     | 0    | 6.5 | 7.5  | 2       | 3    | 0       | 0    | 0      | 1    | 0    | 0    |
|  | 3        | 0     | 0    | 7   | 7.5  | 3       | 3    | 0       | 0    | 1      | 1    | 0    | 0    |
|  | 4        | 0     | 0    | 6   | 8    | 2       | 3    | 0       | 0    | 1      | 1    | 0    | 0    |
|  | 5        | 0     | 0    | 6.5 | 7.5  | 3       | 0    | 0       | 0    | 1      | 1    | 0    | 0    |
|  | 6        | 0     |      | 7.5 |      | 3       |      | 0       |      | 2      |      | 0    |      |
|  | 7        | 0     |      | 8   |      | 3       |      | 0       |      | 1      |      | 0    |      |
|  | 8        | 0     |      | 7   |      | 3       |      | 0       |      | 1      |      | 0    |      |
|  | 9        | 0     |      | 7   |      | 3       |      | 0       |      | 1      |      | 0    |      |
|  | 10       | 0     |      | 7   |      | 2       |      | 0       |      | 1      |      | 0    |      |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)  |          |       |      |     |      |         |      |         |      |        |      |      |      |
|  | 21       | 0     |      | 7   |      | 3       |      | 0       |      | 0      |      | 0    |      |
|  | 22       | 0     |      | 7   |      | 2       |      | 0       |      | 2      |      | 0    |      |
|  | 23       | 0     |      | 6   |      | 0       |      | 0       |      | 1      |      | 1    |      |
|  | 24       | 0     |      | 6.5 |      | 1       |      | 0       |      | 1      |      | 0    |      |
|  | 25       | 0     |      | 7.5 |      | 2       |      | 0       |      | 1      |      | 0    |      |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day) |          |       |      |     |      |         |      |         |      |        |      |      |      |
|  | 31       | 0     |      | 7.5 |      | 3       |      | 0       |      | 0      |      | 0    |      |
|  | 32       | 0     |      | 7   |      | 2       |      | 0       |      | 1      |      | 0    |      |
|  | 33       | 0     |      | 8   |      | 3       |      | 0       |      | 1      |      | 0    |      |
|  | 34       | 0     |      | 8   |      | 2       |      | 0       |      | 1      |      | 0    |      |
|  | 35       | 0     |      | 7.5 |      | 2       |      | 0       |      | 1      |      | 0    |      |

| Group   | Anim.No. | Color |      | pH  |      | Protein |      | Glucose |      | Ketone |      | Bil. |      |
|---|----------|-------|------|-----|------|---------|------|---------|------|--------|------|------|------|
|   |          | 4w    | R:2w | 4w  | R:2w | 4w      | R:2w | 4w      | R:2w | 4w     | R:2w | 4w   | R:2w |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |       |      |     |      |         |      |         |      |        |      |      |      |
|   | 41       | 0     | 0    | 7.5 | 7    | 3       | 3    | 0       | 0    | 2      | 2    | 0    | 0    |
|   | 42       | 0     | 0    | 7.5 | 7.5  | 3       | 2    | 0       | 0    | 2      | 1    | 0    | 0    |
|   | 43       | 0     | 0    | 7.5 | 7.5  | 2       | 2    | 0       | 0    | 1      | 1    | 0    | 0    |
|   | 44       | 0     | 0    | 7   | 7.5  | 3       | 2    | 0       | 0    | 1      | 2    | 0    | 0    |
|   | 45       | 0     | 0    | 8   | 7    | 2       | 2    | 0       | 0    | 1      | 0    | 0    | 0    |
|   | 46       | 0     |      | 8   |      | 3       |      | 0       |      | 1      |      | 0    |      |
|   | 47       | 0     |      | 6.5 |      | 2       |      | 0       |      | 1      |      | 0    |      |
|   | 48       | 0     |      | 7.5 |      | 2       |      | 0       |      | 1      |      | 0    |      |
|   | 49       | 0     |      | 8   |      | 3       |      | 0       |      | 1      |      | 0    |      |
|   | 50       | 0     |      | 7   |      | 2       |      | 0       |      | 2      |      | 0    |      |

| Group  | Anim.No. | Oc.Bld. |      | Urobil. |      | U.Vol.<br>(mL) |      | S.Grav. |        |
|--|----------|---------|------|---------|------|----------------|------|---------|--------|
|  |          | 4w      | R:2w | 4w      | R:2w | 4w             | R:2w | 4w      | R:2w   |
| Control  |          |         |      |         |      |                |      |         |        |
|  | 1        | 0       | 0    | 0       | 1    | 2.6            | 3.2  | 1.034   | 1.035  |
|  | 2        | 1       | 0    | 0       | 0    | 2.7            | 1.6  | 1.030   | 1.024  |
|  | 3        | 2       | 0    | 0       | 0    | 1.2            | 0.8  | 1.022   | 1.071  |
|  | 4        | 0       | 2    | 0       | 0    | 1.9            | 2.9  | 1.057   | 1.050  |
|  | 5        | 0       | 0    | 0       | 0    | 3.8            | 3.5  | 1.026   | 1.033  |
|  | 6        | 0       |      | 0       |      |                |      |         |        |
|  | 7        | 0       |      | 0       |      |                |      |         |        |
|  | 8        | 2       |      | 0       |      |                |      |         |        |
|  | 9        | 0       |      | 0       |      |                |      |         |        |
|  | 10       | 1       |      | 0       |      |                |      |         |        |
|  | Mean     |         |      |         |      | 2.44           | 2.40 | 1.0338  | 1.0426 |
|  | +S.D.    |         |      |         |      | 0.97           | 1.15 | 0.0137  | 0.0184 |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)  |          |         |      |         |      |                |      |         |        |
|  | 21       | 0       |      | 0       |      | 2.1            |      | 1.034   |        |
|  | 22       | 0       |      | 0       |      | 3.4            |      | 1.032   |        |
|  | 23       | 0       |      | 0       |      | 3.1            |      | 1.025   |        |
|  | 24       | 0       |      | 0       |      | 4.0            |      | 1.023   |        |
|  | 25       | 0       |      | 0       |      | 5.8            |      | 1.020   |        |
|  | Mean     |         |      |         |      | 3.68           |      | 1.0268  |        |
|  | +S.D.    |         |      |         |      | 1.37           |      | 0.0060  |        |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day) |          |         |      |         |      |                |      |         |        |
|  | 31       | 0       |      | 0       |      | 1.6            |      | 1.045   |        |
|  | 32       | 1       |      | 1       |      | 2.4            |      | 1.050   |        |
|  | 33       | 0       |      | 0       |      | 3.2            |      | 1.022   |        |
|  | 34       | 0       |      | 0       |      | 3.5            |      | 1.029   |        |
|  | 35       | 0       |      | 0       |      | 5.0            |      | 1.015   |        |
|  | Mean     |         |      |         |      | 3.14           |      | 1.0322  |        |
|  | +S.D.    |         |      |         |      | 1.28           |      | 0.0149  |        |

## Appendix 6-4 Urinalysis in male rats

Study No. : SBL79-02

| Group   | Anim.No. | Oc.Bld. |      | Urobil. |      | U.Vol.<br>(mL) |      | S.Grav. |        |
|---|----------|---------|------|---------|------|----------------|------|---------|--------|
|   |          | 4w      | R:2w | 4w      | R:2w | 4w             | R:2w | 4w      | R:2w   |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |         |      |         |      |                |      |         |        |
|   | 41       | 0       | 0    | 1       | 0    | 2.4            | 1.9  | 1.026   | 1.024  |
|   | 42       | 0       | 0    | 0       | 0    | 2.2            | 3.2  | 1.045   | 1.035  |
|   | 43       | 0       | 0    | 0       | 0    | 1.4            | 1.6  | 1.043   | 1.055  |
|   | 44       | 0       | 0    | 0       | 0    | 0.3            | 2.6  | 1.070   | 1.034  |
|   | 45       | 0       | 0    | 0       | 0    | 0.9            | 3.6  | 1.018   | 1.032  |
|   | 46       | 0       |      | 0       |      |                |      |         |        |
|   | 47       | 0       |      | 0       |      |                |      |         |        |
|   | 48       | 1       |      | 0       |      |                |      |         |        |
|   | 49       | 0       |      | 0       |      |                |      |         |        |
|   | 50       | 0       |      | 0       |      |                |      |         |        |
|   | Mean     |         |      |         |      | 1.44           | 2.58 | 1.0404  | 1.0360 |
|   | +S.D.    |         |      |         |      | 0.88           | 0.84 | 0.0201  | 0.0115 |

| Group  | Anim.No. | Color |      | pH  |      | Protein |      | Glucose |      | Ketone |      | Bil. |      |
|--|----------|-------|------|-----|------|---------|------|---------|------|--------|------|------|------|
|  |          | 4w    | R:2w | 4w  | R:2w | 4w      | R:2w | 4w      | R:2w | 4w     | R:2w | 4w   | R:2w |
| Control  |          |       |      |     |      |         |      |         |      |        |      |      |      |
|  | 11       | 0     | 0    | 6.5 | 7    | 0       | 0    | 0       | 0    | 0      | 0    | 0    | 0    |
|  | 12       | 0     | 0    | 8   | 6.5  | 1       | 0    | 0       | 0    | 0      | 0    | 0    | 0    |
|  | 13       | 0     | 0    | 8   | 7    | 0       | 2    | 0       | 0    | 0      | 1    | 0    | 0    |
|  | 14       | 0     | 0    | 8   | 7.5  | 0       | 0    | 0       | 0    | 0      | 0    | 0    | 0    |
|  | 15       | 0     | 0    | 6.5 | 8    | 2       | 2    | 0       | 0    | 1      | 0    | 0    | 0    |
|  | 16       | 0     |      | 7.5 |      | 1       |      | 0       |      | 0      |      | 0    |      |
|  | 17       | 0     |      | 7.5 |      | 0       |      | 0       |      | 0      |      | 0    |      |
|  | 18       | 0     |      | 8   |      | 2       |      | 0       |      | 0      |      | 0    |      |
|  | 19       | 0     |      | 6   |      | 0       |      | 0       |      | 0      |      | 0    |      |
|  | 20       | 0     |      | 6.5 |      | 0       |      | 0       |      | 0      |      | 0    |      |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)  |          |       |      |     |      |         |      |         |      |        |      |      |      |
|  | 26       | 0     |      | 6.5 |      | 2       |      | 0       |      | 0      |      | 0    |      |
|  | 27       | 0     |      | 7   |      | 2       |      | 0       |      | 0      |      | 0    |      |
|  | 28       | 0     |      | 7.5 |      | 2       |      | 0       |      | 1      |      | 0    |      |
|  | 29       | 0     |      | 6.5 |      | 1       |      | 0       |      | 0      |      | 0    |      |
|  | 30       | 0     |      | 7   |      | 2       |      | 0       |      | 0      |      | 0    |      |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day) |          |       |      |     |      |         |      |         |      |        |      |      |      |
|  | 36       | 0     |      | 7   |      | 0       |      | 0       |      | 0      |      | 0    |      |
|  | 37       | 0     |      | 7.5 |      | 2       |      | 0       |      | 0      |      | 0    |      |
|  | 38       | 0     |      | 7   |      | 2       |      | 0       |      | 0      |      | 0    |      |
|  | 39       | 0     |      | 7   |      | 0       |      | 0       |      | 0      |      | 0    |      |
|  | 40       | 0     |      | 8   |      | 0       |      | 0       |      | 0      |      | 0    |      |

| Group   | Anim.No. | Color |      | pH  |      | Protein |      | Glucose |      | Ketone |      | Bil. |      |
|---|----------|-------|------|-----|------|---------|------|---------|------|--------|------|------|------|
|   |          | 4w    | R:2w | 4w  | R:2w | 4w      | R:2w | 4w      | R:2w | 4w     | R:2w | 4w   | R:2w |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |       |      |     |      |         |      |         |      |        |      |      |      |
|   | 51       | 0     | 0    | 6.5 | 7    | 2       | 1    | 0       | 0    | 1      | 1    | 0    | 0    |
|   | 52       | 0     | 0    | 7.5 | 7.5  | 2       | 0    | 0       | 0    | 2      | 0    | 0    | 0    |
|   | 53       | 0     | 0    | 8   | 7    | 2       | 1    | 0       | 0    | 0      | 0    | 0    | 0    |
|   | 54       | 0     | 0    | 7.5 | 8    | 3       | 0    | 0       | 0    | 1      | 0    | 0    | 0    |
|   | 55       | 0     | 0    | 7.5 | 8    | 2       | 0    | 0       | 0    | 1      | 0    | 0    | 0    |
|   | 56       | 0     |      | 7.5 |      | 0       |      | 0       |      | 0      |      | 0    |      |
|   | 57       | 0     |      | 7.5 |      | 0       |      | 0       |      | 0      |      | 0    |      |
|   | 58       | 0     |      | 7.5 |      | 2       |      | 0       |      | 1      |      | 0    |      |
|   | 59       | 0     |      | 7.5 |      | 0       |      | 0       |      | 0      |      | 0    |      |
|   | 60       | 0     |      | 7   |      | 0       |      | 0       |      | 0      |      | 0    |      |



| Group  | Anim.No. | Oc.Bld. |      | Urobil. |      | U.Vol.<br>{mL} |      | S.Grav. |        |
|--|----------|---------|------|---------|------|----------------|------|---------|--------|
|  |          | 4w      | R:2w | 4w      | R:2w | 4w             | R:2w | 4w      | R:2w   |
| Control  |          |         |      |         |      |                |      |         |        |
|  | 11       | 0       | 0    | 0       | 0    | 3.5            | 3.4  | 1.021   | 1.015  |
|  | 12       | 0       | 2    | 0       | 0    | 4.2            | 2.0  | 1.013   | 1.018  |
|  | 13       | 0       | 0    | 0       | 1    | 3.0            | 2.9  | 1.020   | 1.026  |
|  | 14       | 0       | 0    | 0       | 0    | 2.3            | 2.8  | 1.015   | 1.029  |
|  | 15       | 0       | 0    | 1       | 1    | 0.4            | 1.4  | 1.052   | 1.043  |
|  | 16       | 0       |      | 0       |      |                |      |         |        |
|  | 17       | 0       |      | 0       |      |                |      |         |        |
|  | 18       | 0       |      | 1       |      |                |      |         |        |
|  | 19       | 0       |      | 0       |      |                |      |         |        |
|  | 20       | 0       |      | 0       |      |                |      |         |        |
|  | Mean     |         |      |         |      | 2.68           | 2.50 | 1.0242  | 1.0262 |
|  | +S.D.    |         |      |         |      | 1.45           | 0.79 | 0.0159  | 0.0110 |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)  |          |         |      |         |      |                |      |         |        |
|  | 26       | 2       |      | 0       |      | 1.9            |      | 1.016   |        |
|  | 27       | 0       |      | 0       |      | 5.4            |      | 1.013   |        |
|  | 28       | 0       |      | 0       |      | 4.0            |      | 1.018   |        |
|  | 29       | 0       |      | 0       |      | 3.9            |      | 1.016   |        |
|  | 30       | 0       |      | 0       |      | 4.5            |      | 1.017   |        |
|  | Mean     |         |      |         |      | 3.94           |      | 1.0160  |        |
|  | +S.D.    |         |      |         |      | 1.29           |      | 0.0019  |        |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day) |          |         |      |         |      |                |      |         |        |
|  | 36       | 0       |      | 0       |      | 3.2            |      | 1.028   |        |
|  | 37       | 0       |      | 0       |      | 2.4            |      | 1.019   |        |
|  | 38       | 0       |      | 0       |      | 1.2            |      | 1.063   |        |
|  | 39       | 0       |      | 0       |      | 2.5            |      | 1.026   |        |
|  | 40       | 0       |      | 0       |      | 5.4            |      | 1.014   |        |
|  | Mean     |         |      |         |      | 2.94           |      | 1.0300  |        |
|  | +S.D.    |         |      |         |      | 1.55           |      | 0.0193  |        |

| Group   | Anim.No. | Oc.Bld. |      | Urobil. |      | U.Vol.<br>{mL} |      | S.Grav. |        |
|---|----------|---------|------|---------|------|----------------|------|---------|--------|
|   |          | 4w      | R:2w | 4w      | R:2w | 4w             | R:2w | 4w      | R:2w   |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |         |      |         |      |                |      |         |        |
|   | 51       | 0       | 0    | 0       | 0    | 2.8            | 3.0  | 1.024   | 1.023  |
|   | 52       | 0       | 0    | 0       | 0    | 1.1            | 3.1  | 1.037   | 1.021  |
|   | 53       | 0       | 0    | 1       | 0    | 2.0            | 1.1  | 1.024   | 1.022  |
|   | 54       | 0       | 0    | 1       | 0    | 1.3            | 1.5  | 1.020   | 1.015  |
|   | 55       | 0       | 0    | 1       | 0    | 1.6            | 2.6  | 1.018   | 1.026  |
|   | 56       | 0       |      | 0       |      |                |      |         |        |
|   | 57       | 1       |      | 0       |      |                |      |         |        |
|   | 58       | 0       |      | 0       |      |                |      |         |        |
|   | 59       | 0       |      | 0       |      |                |      |         |        |
|   | 60       | 2       |      | 0       |      |                |      |         |        |
|   | Mean     |         |      |         |      | 1.76           | 2.26 | 1.0246  | 1.0214 |
|   | +S.D.    |         |      |         |      | 0.67           | 0.91 | 0.0074  | 0.0040 |

# Urinary Sediment

RBC  
 0 : -  
 1 : 1 - 4 /HPF  
 2 : 5 -10 /HPF  
 3 :10 < /HPF

WBC  
 0 : -  
 1 : 1 - 5 /HPF  
 2 : 6 -20 /HPF  
 3 :20 < /HPF

Phosphate crystal  
 (Phosphate) 0 : -  
 1 : 1 -10 /HPF  
 2 :11 -20 /HPF  
 3 :20 < /HPF

Urate crystal  
 (Urate) 0 : -  
 1 : 1 -10 /HPF  
 2 :11 -20 /HPF  
 3 :20 < /HPF

Oxalate crystal  
 (Oxalate) 0 : -  
 1 : 1 -10 /HPF  
 2 :11 -20 /HPF  
 3 :20 < /HPF

Other crystal  
 (Other c.) 0 : -  
 1 : 1 -10 /HPF  
 2 :11 -20 /HPF  
 3 :20 < /HPF

Epithelial cell  
 (Epith.) 0 : -  
 1 : 1 - 5 /HPF  
 2 : 6 -20 /HPF  
 3 :20 < /HPF

Bacteria  
 0 : -  
 1 : +

Cast  
 0 : -  
 1 : Hyaline Cast  
 2 : Waxy Cast  
 3 : Erythrocytic Cast

Sperm  
 0 : -  
 1 : +

Others  
 0 : -  
 1 : +

HPF : High power field

| Group   | Anim.No. | RBC |      | WBC |      | Phosphate |      | Urate |      | Oxalate |      | Other c. |      |
|---|----------|-----|------|-----|------|-----------|------|-------|------|---------|------|----------|------|
|   |          | 4w  | R:2w | 4w  | R:2w | 4w        | R:2w | 4w    | R:2w | 4w      | R:2w | 4w       | R:2w |
| Control   |          |     |      |     |      |           |      |       |      |         |      |          |      |
|   | 1        | 0   | 0    | 0   | 0    | 0         | 1    | 0     | 0    | 0       | 0    | 0        | 0    |
|   | 2        | 0   | 0    | 0   | 0    | 0         | 1    | 0     | 0    | 0       | 0    | 0        | 0    |
|   | 3        | 0   | 0    | 0   | 0    | 0         | 1    | 0     | 0    | 0       | 0    | 0        | 0    |
|   | 4        | 0   | 0    | 0   | 0    | 1         | 1    | 0     | 0    | 0       | 0    | 0        | 0    |
|   | 5        | 0   | 0    | 0   | 0    | 1         | 0    | 0     | 0    | 0       | 0    | 0        | 0    |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |     |      |     |      |           |      |       |      |         |      |          |      |
|   | 21       | 0   |      | 0   |      | 0         |      | 0     |      | 0       |      | 0        |      |
|   | 22       | 0   |      | 0   |      | 1         |      | 0     |      | 0       |      | 0        |      |
|   | 23       | 0   |      | 0   |      | 0         |      | 0     |      | 0       |      | 0        |      |
|   | 24       | 0   |      | 0   |      | 0         |      | 0     |      | 0       |      | 0        |      |
|   | 25       | 0   |      | 0   |      | 1         |      | 0     |      | 0       |      | 0        |      |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |     |      |     |      |           |      |       |      |         |      |          |      |
|   | 31       | 0   |      | 0   |      | 2         |      | 0     |      | 0       |      | 0        |      |
|   | 32       | 0   |      | 0   |      | 1         |      | 0     |      | 0       |      | 0        |      |
|   | 33       | 0   |      | 0   |      | 0         |      | 0     |      | 0       |      | 0        |      |
|   | 34       | 0   |      | 0   |      | 2         |      | 0     |      | 0       |      | 0        |      |
|   | 35       | 0   |      | 0   |      | 0         |      | 0     |      | 0       |      | 0        |      |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |     |      |     |      |           |      |       |      |         |      |          |      |
|   | 41       | 0   | 0    | 0   | 0    | 2         | 0    | 0     | 0    | 0       | 0    | 0        | 0    |
|   | 42       | 0   | 0    | 0   | 0    | 2         | 1    | 0     | 0    | 0       | 0    | 0        | 0    |
|   | 43       | 0   | 0    | 0   | 0    | 2         | 1    | 0     | 0    | 0       | 0    | 0        | 0    |
|   | 44       | 0   | 0    | 0   | 0    | 0         | 1    | 0     | 0    | 0       | 0    | 0        | 0    |
|   | 45       | 0   | 0    | 0   | 0    | 1         | 1    | 0     | 0    | 0       | 0    | 0        | 0    |

| Group   | Anim.No. | Epith. |      | Bacteria |      | Cast |      | Sperm |      | Others |      |
|---|----------|--------|------|----------|------|------|------|-------|------|--------|------|
|   |          | 4w     | R:2w | 4w       | R:2w | 4w   | R:2w | 4w    | R:2w | 4w     | R:2w |
| Control   |          |        |      |          |      |      |      |       |      |        |      |
|   | 1        | 0      | 0    | 0        | 0    | 0    | 0    | 0     | 1    | 0      | 0    |
|   | 2        | 0      | 0    | 0        | 0    | 0    | 0    | 1     | 0    | 0      | 0    |
|   | 3        | 0      | 0    | 0        | 0    | 0    | 0    | 1     | 1    | 0      | 0    |
|   | 4        | 0      | 0    | 0        | 0    | 0    | 0    | 0     | 0    | 0      | 0    |
|   | 5        | 0      | 0    | 0        | 0    | 0    | 0    | 0     | 0    | 0      | 0    |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |        |      |          |      |      |      |       |      |        |      |
|   | 21       | 0      |      | 0        |      | 0    |      | 0     |      | 0      |      |
|   | 22       | 0      |      | 0        |      | 0    |      | 1     |      | 0      |      |
|   | 23       | 0      |      | 0        |      | 0    |      | 0     |      | 0      |      |
|   | 24       | 0      |      | 0        |      | 0    |      | 0     |      | 0      |      |
|   | 25       | 0      |      | 0        |      | 0    |      | 1     |      | 0      |      |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |        |      |          |      |      |      |       |      |        |      |
|   | 31       | 0      |      | 0        |      | 0    |      | 0     |      | 0      |      |
|   | 32       | 0      |      | 0        |      | 0    |      | 0     |      | 0      |      |
|   | 33       | 0      |      | 0        |      | 0    |      | 0     |      | 0      |      |
|   | 34       | 0      |      | 0        |      | 0    |      | 0     |      | 0      |      |
|   | 35       | 0      |      | 0        |      | 0    |      | 0     |      | 0      |      |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |        |      |          |      |      |      |       |      |        |      |
|   | 41       | 0      | 0    | 0        | 0    | 0    | 0    | 0     | 0    | 0      | 0    |
|   | 42       | 0      | 0    | 0        | 0    | 0    | 0    | 1     | 1    | 0      | 0    |
|   | 43       | 0      | 0    | 0        | 0    | 0    | 0    | 0     | 1    | 0      | 0    |
|   | 44       | 0      | 0    | 0        | 0    | 0    | 0    | 0     | 0    | 0      | 0    |
|   | 45       | 0      | 0    | 0        | 0    | 0    | 0    | 0     | 0    | 0      | 0    |

| Group   | Anim.No. | RBC |      | WBC |      | Phosphate |      | Urate |      | Oxalate |      | Other c. |      |
|---|----------|-----|------|-----|------|-----------|------|-------|------|---------|------|----------|------|
|   |          | 4w  | R:2w | 4w  | R:2w | 4w        | R:2w | 4w    | R:2w | 4w      | R:2w | 4w       | R:2w |
| Control   |          |     |      |     |      |           |      |       |      |         |      |          |      |
|   | 11       | 0   | 0    | 0   | 0    | 0         | 0    | 0     | 0    | 0       | 0    | 0        | 0    |
|   | 12       | 0   | 0    | 0   | 0    | 0         | 0    | 0     | 0    | 0       | 0    | 0        | 0    |
|   | 13       | 0   | 0    | 0   | 0    | 0         | 1    | 0     | 0    | 0       | 0    | 0        | 0    |
|   | 14       | 0   | 0    | 0   | 0    | 0         | 1    | 0     | 0    | 0       | 0    | 0        | 0    |
|   | 15       | 0   | 0    | 0   | 0    | 0         | 0    | 0     | 0    | 0       | 0    | 0        | 0    |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |     |      |     |      |           |      |       |      |         |      |          |      |
|   | 26       | 0   |      | 0   |      | 0         |      | 0     |      | 0       |      | 0        |      |
|   | 27       | 0   |      | 0   |      | 0         |      | 0     |      | 0       |      | 0        |      |
|   | 28       | 0   |      | 0   |      | 0         |      | 0     |      | 0       |      | 0        |      |
|   | 29       | 0   |      | 0   |      | 0         |      | 0     |      | 0       |      | 0        |      |
|   | 30       | 0   |      | 0   |      | 0         |      | 0     |      | 0       |      | 0        |      |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |     |      |     |      |           |      |       |      |         |      |          |      |
|   | 36       | 0   |      | 0   |      | 1         |      | 0     |      | 0       |      | 0        |      |
|   | 37       | 0   |      | 0   |      | 0         |      | 0     |      | 0       |      | 0        |      |
|   | 38       | 0   |      | 0   |      | 1         |      | 0     |      | 0       |      | 0        |      |
|   | 39       | 0   |      | 0   |      | 2         |      | 0     |      | 0       |      | 0        |      |
|   | 40       | 0   |      | 0   |      | 0         |      | 0     |      | 0       |      | 0        |      |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |     |      |     |      |           |      |       |      |         |      |          |      |
|   | 51       | 0   | 0    | 0   | 0    | 0         | 0    | 0     | 0    | 0       | 0    | 0        | 0    |
|   | 52       | 0   | 0    | 0   | 0    | 1         | 1    | 0     | 0    | 0       | 0    | 0        | 0    |
|   | 53       | 0   | 0    | 0   | 0    | 1         | 0    | 0     | 0    | 0       | 0    | 0        | 0    |
|   | 54       | 0   | 0    | 0   | 0    | 0         | 0    | 0     | 0    | 0       | 0    | 0        | 0    |
|   | 55       | 0   | 0    | 0   | 0    | 0         | 0    | 0     | 0    | 0       | 0    | 0        | 0    |

| Group   | Anim.No. | Epith. |      | Bacteria |      | Cast |      | Sperm |      | Others |      |
|---|----------|--------|------|----------|------|------|------|-------|------|--------|------|
|   |          | 4w     | R:2w | 4w       | R:2w | 4w   | R:2w | 4w    | R:2w | 4w     | R:2w |
| Control   |          |        |      |          |      |      |      |       |      |        |      |
|   | 11       | 0      | 0    | 0        | 0    | 0    | 0    | 0     | 0    | 0      | 0    |
|   | 12       | 0      | 0    | 0        | 0    | 0    | 0    | 0     | 0    | 0      | 0    |
|   | 13       | 0      | 0    | 0        | 0    | 0    | 0    | 0     | 0    | 0      | 0    |
|   | 14       | 0      | 0    | 0        | 0    | 0    | 0    | 0     | 0    | 0      | 0    |
|   | 15       | 0      | 0    | 0        | 0    | 0    | 0    | 0     | 0    | 0      | 0    |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |        |      |          |      |      |      |       |      |        |      |
|   | 26       | 0      |      | 0        |      | 0    |      | 0     |      | 0      |      |
|   | 27       | 0      |      | 0        |      | 0    |      | 0     |      | 0      |      |
|   | 28       | 0      |      | 0        |      | 0    |      | 0     |      | 0      |      |
|   | 29       | 0      |      | 0        |      | 0    |      | 0     |      | 0      |      |
|   | 30       | 0      |      | 0        |      | 0    |      | 0     |      | 0      |      |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |        |      |          |      |      |      |       |      |        |      |
|   | 36       | 0      |      | 0        |      | 0    |      | 0     |      | 0      |      |
|   | 37       | 0      |      | 0        |      | 0    |      | 0     |      | 0      |      |
|   | 38       | 0      |      | 0        |      | 0    |      | 0     |      | 0      |      |
|   | 39       | 0      |      | 0        |      | 0    |      | 0     |      | 0      |      |
|   | 40       | 0      |      | 0        |      | 0    |      | 0     |      | 0      |      |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |        |      |          |      |      |      |       |      |        |      |
|   | 51       | 0      | 0    | 0        | 0    | 0    | 0    | 0     | 0    | 0      | 0    |
|   | 52       | 0      | 0    | 0        | 0    | 0    | 0    | 0     | 0    | 0      | 0    |
|   | 53       | 0      | 0    | 0        | 0    | 0    | 0    | 0     | 0    | 0      | 0    |
|   | 54       | 0      | 0    | 0        | 0    | 0    | 0    | 0     | 0    | 0      | 0    |
|   | 55       | 0      | 0    | 0        | 0    | 0    | 0    | 0     | 0    | 0      | 0    |

# Hematology

|       |                        |   |
|-------|------------------------|---|
| RBC   | ( $10^4/\text{mm}^3$ ) | Number of red blood cells                 |
| WBC   | ( $10^2/\text{mm}^3$ ) | Number of white blood cells               |
| Ht    | (%)                    | Hematocrit value                          |
| Hb    | (g/dL)                 | Hemoglobin concentration                  |
| Plat. | ( $10^4/\text{mm}^3$ ) | Number of blood platelets                 |
| MCV   | (fl)                   | Mean corpuscular volume                   |
| MCH   | (pg)                   | Mean corpuscular hemoglobin               |
| MCHC  | (%)                    | Mean corpuscular hemoglobin concentration |
| Ret.  | ( $10^{-1}\%$ )        | Number of reticulocytes                   |

|          |                        |   |
|----------|------------------------|---|
| Hemogram |                        |   |
| N-Stab   | ( $10^2/\text{mm}^3$ ) | Number of stab-form neutrophilic leukocytes |
| N-Stab   | (%)                    | Stab-form neutrophilic leukocyte ratio      |
| N-Seg.   | ( $10^2/\text{mm}^3$ ) | Number of segmented neutrophilic leukocytes |
| N-Seg.   | (%)                    | Segmented neutrophilic leukocyte ratio      |
| Eosino.  | ( $10^2/\text{mm}^3$ ) | Number of eosinophilic leukocytes           |
| Eosino.  | (%)                    | Eosinophilic leukocyte ratio                |
| Baso.    | ( $10^2/\text{mm}^3$ ) | Number of basophilic leukocytes             |
| Baso.    | (%)                    | Basophilic leukocyte ratio                  |
| Mono.    | ( $10^2/\text{mm}^3$ ) | Number of monocytes                         |
| Mono.    | (%)                    | Monocyte ratio                              |
| Lymph.   | ( $10^2/\text{mm}^3$ ) | Number of lymphocytes                       |
| Lymph.   | (%)                    | Lymphocyte ratio                            |

|                        |       |                                       |
|------------------------|-------|---------------------------------------|
| Blood coagulation test |       |                                       |
| PT                     | (Sec) | Prothrombin time                      |
| APTT                   | (Sec) | Activated partial thromboplastin time |



| Group   | Anim.No. | RBC<br>(10 <sup>4</sup> /mm <sup>3</sup> ) |       | WBC<br>(10 <sup>2</sup> /mm <sup>3</sup> ) |      | Ht<br>(%) |       | Hb<br>(g/dL) |       | Plat <sub>3</sub><br>(10 <sup>4</sup> /mm <sup>3</sup> ) |        | MCV<br>(fl) |      |
|---|----------|--|-------|--|------|-----------|-------|--------------|-------|--|--------|-------------|------|
|   |          | 4w   | R:2w  | 4w   | R:2w | 4w        | R:2w  | 4w           | R:2w  | 4w   | R:2w   | 4w          | R:2w |
| Control   |          |  |       |  |      |           |       |              |       |  |        |             |      |
|   | 1        |  | 824   |  | 75   |           | 45.2  |              | 16.1  |  | 124.6  |             | 55   |
|   | 2        |  | 855   |  | 60   |           | 46.5  |              | 16.5  |  | 117.3  |             | 54   |
|   | 3        |  | 870   |  | 69   |           | 46.9  |              | 16.5  |  | 105.2  |             | 54   |
|   | 4        |  | 827   |  | 129  |           | 43.4  |              | 15.3  |  | 132.2  |             | 52   |
|   | 5        |  | 865   |  | 93   |           | 47.6  |              | 16.8  |  | 110.2  |             | 55   |
|   | 6        | 825  |       | 180  |      | 44.6      |       | 16.2         |       | 135.1  |        | 54          |      |
|   | 7        | 757  |       | 113  |      | 47.1      |       | 17.3         |       | 141.0  |        | 62          |      |
|   | 8        | 723  |       | 97   |      | 41.9      |       | 14.9         |       | 132.3  |        | 58          |      |
|   | 9        | 783  |       | 73   |      | 44.2      |       | 15.0         |       | 131.9  |        | 56          |      |
|   | 10       | 796  |       | 66   |      | 43.5      |       | 14.9         |       | 117.8  |        | 55          |      |
|   | Mean     | 776.8                                      | 848.2 | 105.8                                      | 85.2 | 44.26     | 45.92 | 15.66        | 16.24 | 131.62   | 117.90 | 57.0        | 54.0 |
|   | +S.D.    | 38.8                                       | 21.4  | 45.5                                       | 27.3 | 1.89      | 1.66  | 1.07         | 0.58  | 8.54   | 10.84  | 3.2         | 1.2  |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |  |       |  |      |           |       |              |       |  |        |             |      |
|   | 21       | 793  |       | 53   |      | 44.2      |       | 15.7         |       | 112.2  |        | 56          |      |
|   | 22       | 756  |       | 59   |      | 42.6      |       | 15.1         |       | 116.6  |        | 56          |      |
|   | 23       | 702  |       | 35   |      | 40.5      |       | 14.2         |       | 70.1   |        | 58          |      |
|   | 24       | 811  |       | 97   |      | 47.0      |       | 15.8         |       | 118.6  |        | 58          |      |
|   | 25       | 805  |       | 76   |      | 44.9      |       | 15.2         |       | 110.7  |        | 56          |      |
|   | Mean     | 773.4                                      |       | 64.0                                       |      | 43.84     |       | 15.20        |       | 105.64   |        | 56.8        |      |
|   | +S.D.    | 45.3                                       |       | 23.6                                       |      | 2.45      |       | 0.64         |       | 20.12  |        | 1.1         |      |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |  |       |  |      |           |       |              |       |  |        |             |      |
|   | 31       | 779  |       | 92   |      | 43.0      |       | 15.6         |       | 116.7  |        | 55          |      |
|   | 32       | 765  |       | 49   |      | 42.8      |       | 14.9         |       | 130.3  |        | 56          |      |
|   | 33       | 816  |       | 79   |      | 45.3      |       | 16.4         |       | 117.5  |        | 56          |      |
|   | 34       | 781  |       | 73   |      | 45.6      |       | 15.3         |       | 124.4  |        | 58          |      |
|   | 35       | 859  |       | 71   |      | 47.3      |       | 16.3         |       | 112.6  |        | 55          |      |
|   | Mean     | 800.0                                      |       | 72.8                                       |      | 44.80     |       | 15.70        |       | 120.30   |        | 56.0        |      |
|   | +S.D.    | 38.0                                       |       | 15.6                                       |      | 1.90      |       | 0.64         |       | 7.02   |        | 1.2         |      |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |  |       |  |      |           |       |              |       |  |        |             |      |
|   | 41       |  | 875   |  | 120  |           | 45.5  |              | 16.2  |  | 134.4  |             | 52   |
|   | 42       |  | 793   |  | 88   |           | 43.1  |              | 15.7  |  | 153.3  |             | 54   |
|   | 43       |  | 816   |  | 63   |           | 45.3  |              | 15.2  |  | 107.3  |             | 56   |
|   | 44       |  | 835   |  | 76   |           | 45.2  |              | 15.8  |  | 113.3  |             | 54   |
|   | 45       |  | 798   |  | 120  |           | 42.5  |              | 15.7  |  | 125.3  |             | 53   |
|   | 46       | 819  |       | 66   |      | 45.2      |       | 16.4         |       | 155.1  |        | 55          |      |
|   | 47       | 680  |       | 110  |      | 38.3      |       | 14.6         |       | 83.4   |        | 56          |      |
|   | 48       | 774  |       | 96   |      | 43.9      |       | 15.5         |       | 129.1  |        | 57          |      |
|   | 49       | 705  |       | 55   |      | 41.2      |       | 14.4         |       | 128.4  |        | 58          |      |
|   | 50       | 785  |       | 66   |      | 43.7      |       | 15.1         |       | 123.1  |        | 56          |      |
|   | Mean     | 752.6                                      | 823.4 | 78.6                                       | 93.4 | 42.46     | 44.32 | 15.20        | 15.72 | 123.82   | 126.72 | 56.4        | 53.8 |
|   | +S.D.    | 58.0                                       | 33.2  | 23.3                                       | 25.8 | 2.74      | 1.41  | 0.80         | 0.36  | 25.80  | 18.20  | 1.1         | 1.5  |

| Group   | Anim.No. | MCH<br>(pg) |       | MCHC<br>(%) |       | Ret.<br>(10 <sup>-1</sup> %) |      | N-Stab<br>(10 <sup>2</sup> /mm <sup>3</sup> ) |      | N-Stab<br>(%) |      | N-Seg.<br>(10 <sup>2</sup> /mm <sup>3</sup> ) |      |
|---|----------|-------------|-------|-------------|-------|------------------------------|------|---|------|---------------|------|---|------|
|   |          | 4w          | R:2w  | 4w          | R:2w  | 4w                           | R:2w | 4w  | R:2w | 4w            | R:2w | 4w  | R:2w |
| Control   |          |             |       |             |       |                              |      |   |      |               |      |   |      |
|   | 1        |             | 19.5  |             | 35.6  |                              | 16   |   | 0.0  |               | 0    |   | 1.5  |
|   | 2        |             | 19.3  |             | 35.5  |                              | 23   |   | 0.0  |               | 0    |   | 1.2  |
|   | 3        |             | 19.0  |             | 35.2  |                              | 14   |   | 0.0  |               | 0    |   | 1.4  |
|   | 4        |             | 18.5  |             | 35.3  |                              | 16   |   | 0.0  |               | 0    |   | 6.5  |
|   | 5        |             | 19.4  |             | 35.3  |                              | 9    |   | 0.0  |               | 0    |   | 0.9  |
|   | 6        | 19.6        |       | 36.3        |       | 11                           |      | 0.0   |      | 0             |      | 7.2   |      |
|   | 7        | 22.9        |       | 36.7        |       | 20                           |      | 0.0   |      | 0             |      | 6.8   |      |
|   | 8        | 20.6        |       | 35.6        |       | 14                           |      | 0.0   |      | 0             |      | 7.8   |      |
|   | 9        | 19.2        |       | 33.9        |       | 18                           |      | 0.0   |      | 0             |      | 1.5   |      |
|   | 10       | 18.7        |       | 34.3        |       | 13                           |      | 0.0   |      | 0             |      | 3.3   |      |
|   | Mean     | 20.20       | 19.14 | 35.36       | 35.38 | 15.2                         | 15.6 | 0.00  | 0.00 | 0.0           | 0.0  | 5.32  | 2.30 |
|   | +S.D.    | 1.66        | 0.40  | 1.22        | 0.16  | 3.7                          | 5.0  | 0.00  | 0.00 | 0.0           | 0.0  | 2.76  | 2.36 |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |             |       |             |       |                              |      |   |      |               |      |   |      |
|   | 21       | 19.8        |       | 35.5        |       | 22                           |      | 0.0   |      | 0             |      | 2.1   |      |
|   | 22       | 20.0        |       | 35.4        |       | 16                           |      | 0.0   |      | 0             |      | 3.0   |      |
|   | 23       | 20.2        |       | 35.1        |       | 18                           |      | 0.0   |      | 0             |      | 2.1   |      |
|   | 24       | 19.5        |       | 33.6        |       | 17                           |      | 0.0   |      | 0             |      | 1.9   |      |
|   | 25       | 18.9        |       | 33.9        |       | 21                           |      | 0.0   |      | 0             |      | 2.3   |      |
|   | Mean     | 19.68       |       | 34.70       |       | 18.8                         |      | 0.00  |      | 0.0           |      | 2.28  |      |
|   | +S.D.    | 0.51        |       | 0.89        |       | 2.6                          |      | 0.00  |      | 0.0           |      | 0.43  |      |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |             |       |             |       |                              |      |   |      |               |      |   |      |
|   | 31       | 20.0        |       | 36.3        |       | 11                           |      | 0.0   |      | 0             |      | 20.2  |      |
|   | 32       | 19.5        |       | 34.8        |       | 16                           |      | 0.0   |      | 0             |      | 7.4   |      |
|   | 33       | 20.1        |       | 36.2        |       | 19                           |      | 0.0   |      | 0             |      | 6.3   |      |
|   | 34       | 19.6        |       | 33.6        |       | 15                           |      | 0.0   |      | 0             |      | 5.1   |      |
|   | 35       | 19.0        |       | 34.5        |       | 12                           |      | 0.0   |      | 0             |      | 3.6   |      |
|   | Mean     | 19.64       |       | 35.08       |       | 14.6                         |      | 0.00  |      | 0.0           |      | 8.52  |      |
|   | +S.D.    | 0.44        |       | 1.16        |       | 3.2                          |      | 0.00  |      | 0.0           |      | 6.68  |      |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |             |       |             |       |                              |      |   |      |               |      |   |      |
|   | 41       |             | 18.5  |             | 35.6  |                              | 20   |   | 0.0  |               | 0    |   | 2.4  |
|   | 42       |             | 19.8  |             | 36.4  |                              | 25   |   | 0.0  |               | 0    |   | 0.9  |
|   | 43       |             | 18.6  |             | 33.6  |                              | 13   |   | 0.0  |               | 0    |   | 2.5  |
|   | 44       |             | 18.9  |             | 35.0  |                              | 14   |   | 0.0  |               | 0    |   | 8.4  |
|   | 45       |             | 19.7  |             | 36.9  |                              | 20   |   | 0.0  |               | 0    |   | 14.4 |
|   | 46       | 20.0        |       | 36.3        |       | 16                           |      | 0.0   |      | 0             |      | 4.0   |      |
|   | 47       | 21.5        |       | 38.1        |       | 19                           |      | 0.0   |      | 0             |      | 12.1  |      |
|   | 48       | 20.0        |       | 35.3        |       | 16                           |      | 0.0   |      | 0             |      | 5.8   |      |
|   | 49       | 20.4        |       | 35.0        |       | 27                           |      | 0.0   |      | 0             |      | 6.6   |      |
|   | 50       | 19.2        |       | 34.6        |       | 12                           |      | 0.0   |      | 0             |      | 2.0   |      |
|   | Mean     | 20.22       | 19.10 | 35.86       | 35.50 | 18.0                         | 18.4 | 0.00  | 0.00 | 0.0           | 0.0  | 6.10  | 5.72 |
|   | +S.D.    | 0.84        | 0.61  | 1.40        | 1.29  | 5.6                          | 4.9  | 0.00  | 0.00 | 0.0           | 0.0  | 3.79  | 5.64 |

| Group   | Anim.No. | N-Seg.<br>(%) |      | Eosino.<br>(10 <sup>2</sup> /mm <sup>3</sup> ) |      | Eosino.<br>(%) |      | Baso.<br>(10 <sup>2</sup> /mm <sup>3</sup> ) |      | Baso.<br>(%) |      | Mono.<br>(10 <sup>2</sup> /mm <sup>3</sup> ) |      |
|---|----------|---------------|------|--|------|----------------|------|--|------|--------------|------|--|------|
|   |          | 4w            | R:2w | 4w   | R:2w | 4w             | R:2w | 4w   | R:2w | 4w           | R:2w | 4w   | R:2w |
| Control   |          |               |      |  |      |                |      |  |      |              |      |  |      |
|   | 1        |               | 2    |  | 0.0  |                | 0    |  | 0.0  |              | 0    |  | 0.8  |
|   | 2        |               | 2    |  | 0.0  |                | 0    |  | 0.0  |              | 0    |  | 3.0  |
|   | 3        |               | 2    |  | 0.0  |                | 0    |  | 0.0  |              | 0    |  | 1.4  |
|   | 4        |               | 5    |  | 0.0  |                | 0    |  | 0.0  |              | 0    |  | 0.0  |
|   | 5        |               | 1    |  | 0.9  |                | 1    |  | 0.0  |              | 0    |  | 0.9  |
|   | 6        | 4             |      | 0.0  |      | 0              |      | 0.0  |      | 0            |      | 7.2  |      |
|   | 7        | 6             |      | 0.0  |      | 0              |      | 0.0  |      | 0            |      | 1.1  |      |
|   | 8        | 8             |      | 0.0  |      | 0              |      | 0.0  |      | 0            |      | 1.0  |      |
|   | 9        | 2             |      | 0.0  |      | 0              |      | 0.0  |      | 0            |      | 2.2  |      |
|   | 10       | 5             |      | 0.0  |      | 0              |      | 0.0  |      | 0            |      | 0.0  |      |
|   | Mean     | 5.0           | 2.4  | 0.00   | 0.18 | 0.0            | 0.2  | 0.00   | 0.00 | 0.0          | 0.0  | 2.30   | 1.22 |
|   | +S.D.    | 2.2           | 1.5  | 0.00   | 0.40 | 0.0            | 0.4  | 0.00   | 0.00 | 0.0          | 0.0  | 2.85   | 1.11 |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |               |      |  |      |                |      |  |      |              |      |  |      |
|   | 21       | 4             |      | 0.0  |      | 0              |      | 0.0  |      | 0            |      | 1.1  |      |
|   | 22       | 5             |      | 0.0  |      | 0              |      | 0.0  |      | 0            |      | 0.0  |      |
|   | 23       | 6             |      | 0.0  |      | 0              |      | 0.0  |      | 0            |      | 0.7  |      |
|   | 24       | 2             |      | 0.0  |      | 0              |      | 0.0  |      | 0            |      | 0.0  |      |
|   | 25       | 3             |      | 0.0  |      | 0              |      | 0.0  |      | 0            |      | 2.3  |      |
|   | Mean     | 4.0           |      | 0.00   |      | 0.0            |      | 0.00   |      | 0.0          |      | 0.82   |      |
|   | +S.D.    | 1.6           |      | 0.00   |      | 0.0            |      | 0.00   |      | 0.0          |      | 0.95   |      |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |               |      |  |      |                |      |  |      |              |      |  |      |
|   | 31       | 22            |      | 0.9  |      | 1              |      | 0.0  |      | 0            |      | 1.8  |      |
|   | 32       | 15            |      | 0.0  |      | 0              |      | 0.0  |      | 0            |      | 1.0  |      |
|   | 33       | 8             |      | 0.0  |      | 0              |      | 0.0  |      | 0            |      | 0.0  |      |
|   | 34       | 7             |      | 0.0  |      | 0              |      | 0.0  |      | 0            |      | 0.0  |      |
|   | 35       | 5             |      | 0.0  |      | 0              |      | 0.0  |      | 0            |      | 0.0  |      |
|   | Mean     | 11.4          |      | 0.18   |      | 0.2            |      | 0.00   |      | 0.0          |      | 0.56   |      |
|   | +S.D.    | 7.0           |      | 0.40   |      | 0.4            |      | 0.00   |      | 0.0          |      | 0.82   |      |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |               |      |  |      |                |      |  |      |              |      |  |      |
|   | 41       |               | 2    |  | 0.0  |                | 0    |  | 0.0  |              | 0    |  | 0.0  |
|   | 42       |               | 1    |  | 1.8  |                | 2    |  | 0.0  |              | 0    |  | 0.9  |
|   | 43       |               | 4    |  | 0.0  |                | 0    |  | 0.0  |              | 0    |  | 0.6  |
|   | 44       |               | 11   |  | 0.0  |                | 0    |  | 0.0  |              | 0    |  | 3.0  |
|   | 45       |               | 12   |  | 2.4  |                | 2    |  | 0.0  |              | 0    |  | 1.2  |
|   | 46       | 6             |      | 0.7  |      | 1              |      | 0.0  |      | 0            |      | 0.0  |      |
|   | 47       | 11            |      | 0.0  |      | 0              |      | 0.0  |      | 0            |      | 2.2  |      |
|   | 48       | 6             |      | 0.0  |      | 0              |      | 0.0  |      | 0            |      | 1.9  |      |
|   | 49       | 12            |      | 0.0  |      | 0              |      | 0.0  |      | 0            |      | 0.6  |      |
|   | 50       | 3             |      | 0.0  |      | 0              |      | 0.0  |      | 0            |      | 0.7  |      |
|   | Mean     | 7.6           | 6.0  | 0.14   | 0.84 | 0.2            | 0.8  | 0.00   | 0.00 | 0.0          | 0.0  | 1.08   | 1.14 |
|   | +S.D.    | 3.8           | 5.1  | 0.31   | 1.17 | 0.4            | 1.1  | 0.00   | 0.00 | 0.0          | 0.0  | 0.93   | 1.13 |

| Group   | Anim.No. | Mono.<br>(%) |      | Lymph.<br>(10 <sup>2</sup> /mm <sup>3</sup> ) |       | Lymph.<br>(%) |      | PT<br>(Sec) |       | APTT<br>(Sec) |       |
|---|----------|--------------|------|---|-------|---------------|------|-------------|-------|---------------|-------|
|   |          | 4w           | R:2w | 4w  | R:2w  | 4w            | R:2w | 4w          | R:2w  | 4w            | R:2w  |
| Control   |          |              |      |   |       |               |      |             |       |               |       |
|   | 1        |              | 1    |   | 72.8  |               | 97   |             | 16.0  |               | 22.2  |
|   | 2        |              | 5    |   | 55.8  |               | 93   |             | 12.2  |               | 20.7  |
|   | 3        |              | 2    |   | 66.2  |               | 96   |             | 12.2  |               | 20.8  |
|   | 4        |              | 0    |   | 122.6 |               | 95   |             | 12.3  |               | 20.6  |
|   | 5        |              | 1    |   | 90.2  |               | 97   |             | 10.6  |               | 18.3  |
|   | 6        | 4            |      | 165.6   |       | 92            |      | 8.9         |       | 20.7          |       |
|   | 7        | 1            |      | 105.1   |       | 93            |      | 10.0        |       | 21.7          |       |
|   | 8        | 1            |      | 88.3  |       | 91            |      | 13.2        |       | 24.1          |       |
|   | 9        | 3            |      | 69.4  |       | 95            |      | 13.0        |       | 21.2          |       |
|   | 10       | 0            |      | 62.7  |       | 95            |      | 14.1        |       | 24.3          |       |
|   | Mean     | 1.8          | 1.8  | 98.22   | 81.52 | 93.2          | 95.6 | 11.84       | 12.66 | 22.40         | 20.52 |
|   | +S.D.    | 1.6          | 1.9  | 41.16   | 26.15 | 1.8           | 1.7  | 2.25        | 2.00  | 1.68          | 1.40  |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |              |      |   |       |               |      |             |       |               |       |
|   | 21       | 2            |      | 49.8  |       | 94            |      | 17.9        |       | 25.2          |       |
|   | 22       | 0            |      | 56.1  |       | 95            |      | 13.5        |       | 21.6          |       |
|   | 23       | 2            |      | 32.2  |       | 92            |      | 13.7        |       | 22.4          |       |
|   | 24       | 0            |      | 95.1  |       | 98            |      | 13.9        |       | 25.1          |       |
|   | 25       | 3            |      | 71.4  |       | 94            |      | 16.7        |       | 25.4          |       |
|   | Mean     | 1.4          |      | 60.92   |       | 94.6          |      | 15.14       |       | 23.94         |       |
|   | +S.D.    | 1.3          |      | 23.72   |       | 2.2           |      | 2.02        |       | 1.80          |       |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |              |      |   |       |               |      |             |       |               |       |
|   | 31       | 2            |      | 69.0  |       | 75            |      | 16.6        |       | 23.2          |       |
|   | 32       | 2            |      | 40.7  |       | 83            |      | 13.2        |       | 23.5          |       |
|   | 33       | 0            |      | 72.7  |       | 92            |      | 19.1        |       | 23.1          |       |
|   | 34       | 0            |      | 67.9  |       | 93            |      | 11.5        |       | 18.4          |       |
|   | 35       | 0            |      | 67.5  |       | 95            |      | 15.8        |       | 23.6          |       |
|   | Mean     | 0.8          |      | 63.56   |       | 87.6          |      | 15.24       |       | 22.36         |       |
|   | +S.D.    | 1.1          |      | 12.94   |       | 8.4           |      | 2.97        |       | 2.22          |       |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |              |      |   |       |               |      |             |       |               |       |
|   | 41       |              | 0    |   | 117.6 |               | 98   |             | 13.1  |               | 20.0  |
|   | 42       |              | 1    |   | 84.5  |               | 96   |             | 15.7  |               | 20.7  |
|   | 43       |              | 1    |   | 59.9  |               | 95   |             | 15.7  |               | 20.7  |
|   | 44       |              | 4    |   | 64.6  |               | 85   |             | 16.0  |               | 23.1  |
|   | 45       |              | 1    |   | 102.0 |               | 85   |             | 19.5  |               | 22.7  |
|   | 46       | 0            |      | 61.4  |       | 93            |      | 9.2         |       | 21.7          |       |
|   | 47       | 2            |      | 95.7  |       | 87            |      | 17.1        |       | 22.7          |       |
|   | 48       | 2            |      | 88.3  |       | 92            |      | 10.5        |       | 22.3          |       |
|   | 49       | 1            |      | 47.9  |       | 87            |      | 14.2        |       | 26.0          |       |
|   | 50       | 1            |      | 63.4  |       | 96            |      | 16.1        |       | 25.5          |       |
|   | Mean     | 1.2          | 1.4  | 71.34   | 85.72 | 91.0          | 91.8 | 13.42       | 16.00 | 23.64         | 21.44 |
|   | +S.D.    | 0.8          | 1.5  | 19.95   | 24.47 | 3.9           | 6.3  | 3.45        | 2.28  | 1.97          | 1.37  |

| Group   | Anim.No. | RBC<br>(10 <sup>4</sup> /mm <sup>3</sup> ) |       | WBC<br>(10 <sup>2</sup> /mm <sup>3</sup> ) |      | Ht<br>(%) |       | Hb<br>(g/dL) |       | Plat<br>(10 <sup>4</sup> /mm <sup>3</sup> ) |        | MCV<br>(fl) |      |
|---|----------|--|-------|--|------|-----------|-------|--------------|-------|---|--------|-------------|------|
|   |          | 4w   | R:2w  | 4w   | R:2w | 4w        | R:2w  | 4w           | R:2w  | 4w  | R:2w   | 4w          | R:2w |
| Control   |          |  |       |  |      |           |       |              |       |   |        |             |      |
|   | 11       |  | 798   |  | 45   |           | 44.2  |              | 15.6  |   | 141.2  |             | 55   |
|   | 12       |  | 791   |  | 45   |           | 43.5  |              | 16.0  |   | 97.5   |             | 55   |
|   | 13       |  | 753   |  | 41   |           | 42.7  |              | 15.0  |   | 105.7  |             | 57   |
|   | 14       |  | 756   |  | 38   |           | 42.4  |              | 15.1  |   | 118.9  |             | 56   |
|   | 15       |  | 763   |  | 39   |           | 41.5  |              | 14.5  |   | 123.0  |             | 54   |
|   | 16       | 763  |       | 40   |      | 41.8      |       | 15.0         |       | 114.9                                       |        | 55          |      |
|   | 17       | 679  |       | 37   |      | 39.2      |       | 13.9         |       | 115.3                                       |        | 58          |      |
|   | 18       | 711  |       | 42   |      | 40.3      |       | 14.2         |       | 109.6                                       |        | 57          |      |
|   | 19       | 778  |       | 56   |      | 45.4      |       | 15.7         |       | 64.3  |        | 58          |      |
|   | 20       | 808  |       | 44   |      | 44.9      |       | 15.6         |       | 110.7                                       |        | 56          |      |
|   | Mean     | 747.8                                      | 772.2 | 43.8                                       | 41.6 | 42.32     | 42.86 | 14.88        | 15.24 | 102.96                                      | 117.26 | 56.8        | 55.4 |
|   | +S.D.    | 52.1                                       | 20.8  | 7.3  | 3.3  | 2.75      | 1.04  | 0.81         | 0.58  | 21.76                                       | 16.83  | 1.3         | 1.1  |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |  |       |  |      |           |       |              |       |   |        |             |      |
|   | 26       | 798  |       | 46   |      | 44.7      |       | 15.7         |       | 137.8                                       |        | 56          |      |
|   | 27       | 779  |       | 53   |      | 43.9      |       | 15.4         |       | 113.9                                       |        | 56          |      |
|   | 28       | 735  |       | 50   |      | 41.7      |       | 14.7         |       | 117.6                                       |        | 57          |      |
|   | 29       | 778  |       | 38   |      | 45.9      |       | 16.0         |       | 117.7                                       |        | 59          |      |
|   | 30       | 750  |       | 53   |      | 42.0      |       | 14.4         |       | 137.1                                       |        | 56          |      |
|   | Mean     | 768.0                                      |       | 48.0                                       |      | 43.64     |       | 15.24        |       | 124.82                                      |        | 56.8        |      |
|   | +S.D.    | 25.2                                       |       | 6.3  |      | 1.79      |       | 0.67         |       | 11.63                                       |        | 1.3         |      |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |  |       |  |      |           |       |              |       |   |        |             |      |
|   | 36       | 779  |       | 68   |      | 43.0      |       | 15.4         |       | 108.9                                       |        | 55          |      |
|   | 37       | 723  |       | 49   |      | 46.9      |       | 14.9         |       | 119.9                                       |        | 65          |      |
|   | 38       | 793  |       | 41   |      | 44.8      |       | 15.2         |       | 97.0  |        | 56          |      |
|   | 39       | 749  |       | 65   |      | 41.4      |       | 14.6         |       | 65.5  |        | 55          |      |
|   | 40       | 846  |       | 44   |      | 46.8      |       | 16.2         |       | 102.9                                       |        | 55          |      |
|   | Mean     | 778.0                                      |       | 53.4                                       |      | 44.58     |       | 15.26        |       | 98.84                                       |        | 57.2        |      |
|   | +S.D.    | 46.7                                       |       | 12.3                                       |      | 2.40      |       | 0.61         |       | 20.47                                       |        | 4.4         |      |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |  |       |  |      |           |       |              |       |   |        |             |      |
|   | 51       |  | 783   |  | 30   |           | 44.2  |              | 15.6  |   | 125.5  |             | 56   |
|   | 52       |  | 693   |  | 25   |           | 39.4  |              | 14.0  |   | 72.7   |             | 57   |
|   | 53       |  | 777   |  | 57   |           | 41.4  |              | 14.9  |   | 71.9   |             | 53   |
|   | 54       |  | 796   |  | 34   |           | 44.4  |              | 16.2  |   | 88.2   |             | 56   |
|   | 55       |  | 771   |  | 37   |           | 41.1  |              | 14.7  |   | 95.8   |             | 53   |
|   | 56       | 766  |       | 44   |      | 42.7      |       | 15.1         |       | 126.4                                       |        | 56          |      |
|   | 57       | 743  |       | 57   |      | 43.4      |       | 15.3         |       | 63.5  |        | 58          |      |
|   | 58       | 733  |       | 91   |      | 41.5      |       | 14.6         |       | 122.5                                       |        | 57          |      |
|   | 59       | 761  |       | 44   |      | 43.7      |       | 14.9         |       | 123.2                                       |        | 57          |      |
|   | 60       | 748  |       | 64   |      | 43.3      |       | 14.7         |       | 132.5                                       |        | 58          |      |
|   | Mean     | 750.2                                      | 764.0 | 60.0                                       | 36.6 | 42.92     | 42.10 | 14.92        | 15.08 | 113.62                                      | 90.82  | 57.2        | 55.0 |
|   | +S.D.    | 13.4                                       | 40.8  | 19.4                                       | 12.3 | 0.87      | 2.15  | 0.29         | 0.85  | 28.29                                       | 21.91  | 0.8         | 1.9  |

| Group   | Anim.No. | MCH<br>(pg) |       | MCHC<br>(%) |       | Ret.<br>(10 <sup>-1</sup> %) |      | N-Stab<br>(10 <sup>2</sup> /mm <sup>3</sup> ) |      | N-Stab<br>(%) |      | N-Seg.<br>(10 <sup>2</sup> /mm <sup>3</sup> ) |      |
|---|----------|-------------|-------|-------------|-------|------------------------------|------|---|------|---------------|------|---|------|
|   |          | 4w          | R:2w  | 4w          | R:2w  | 4w                           | R:2w | 4w  | R:2w | 4w            | R:2w | 4w  | R:2w |
| Control   |          |             |       |             |       |                              |      |   |      |               |      |   |      |
|   | 11       |             | 19.5  |             | 35.3  |                              | 8    |   | 0.0  |               | 0    |   | 0.9  |
|   | 12       |             | 20.2  |             | 36.8  |                              | 4    |   | 0.0  |               | 0    |   | 0.9  |
|   | 13       |             | 19.9  |             | 35.1  |                              | 14   |   | 0.0  |               | 0    |   | 2.1  |
|   | 14       |             | 20.0  |             | 35.6  |                              | 20   |   | 0.0  |               | 0    |   | 6.5  |
|   | 15       |             | 19.0  |             | 34.9  |                              | 10   |   | 0.0  |               | 0    |   | 5.9  |
|   | 16       | 19.7        |       | 35.9        |       | 14                           |      | 0.0   |      | 0             |      | 3.2   |      |
|   | 17       | 20.5        |       | 35.5        |       | 14                           |      | 0.0   |      | 0             |      | 0.7   |      |
|   | 18       | 20.0        |       | 35.2        |       | 11                           |      | 0.0   |      | 0             |      | 2.9   |      |
|   | 19       | 20.2        |       | 34.6        |       | 9                            |      | 0.0   |      | 0             |      | 3.4   |      |
|   | 20       | 19.3        |       | 34.7        |       | 14                           |      | 0.0   |      | 0             |      | 0.4   |      |
|   | Mean     | 19.94       | 19.72 | 35.18       | 35.54 | 12.4                         | 11.2 | 0.00  | 0.00 | 0.0           | 0.0  | 2.12  | 3.26 |
|   | +S.D.    | 0.46        | 0.48  | 0.54        | 0.75  | 2.3                          | 6.1  | 0.00  | 0.00 | 0.0           | 0.0  | 1.45  | 2.74 |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |             |       |             |       |                              |      |   |      |               |      |   |      |
|   | 26       | 19.7        |       | 35.1        |       | 17                           |      | 0.0   |      | 0             |      | 0.5   |      |
|   | 27       | 19.8        |       | 35.1        |       | 13                           |      | 0.0   |      | 0             |      | 1.6   |      |
|   | 28       | 20.0        |       | 35.3        |       | 8                            |      | 0.0   |      | 0             |      | 2.0   |      |
|   | 29       | 20.6        |       | 34.9        |       | 19                           |      | 0.0   |      | 0             |      | 1.5   |      |
|   | 30       | 19.2        |       | 34.3        |       | 7                            |      | 0.0   |      | 0             |      | 3.2   |      |
|   | Mean     | 19.86       |       | 34.94       |       | 12.8                         |      | 0.00  |      | 0.0           |      | 1.76  |      |
|   | +S.D.    | 0.51        |       | 0.38        |       | 5.3                          |      | 0.00  |      | 0.0           |      | 0.98  |      |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |             |       |             |       |                              |      |   |      |               |      |   |      |
|   | 36       | 19.8        |       | 35.8        |       | 11                           |      | 0.0   |      | 0             |      | 1.4   |      |
|   | 37       | 20.6        |       | 31.8        |       | 20                           |      | 0.0   |      | 0             |      | 3.4   |      |
|   | 38       | 19.2        |       | 33.9        |       | 16                           |      | 0.0   |      | 0             |      | 3.3   |      |
|   | 39       | 19.5        |       | 35.3        |       | 9                            |      | 0.0   |      | 0             |      | 3.9   |      |
|   | 40       | 19.1        |       | 34.6        |       | 23                           |      | 0.0   |      | 0             |      | 3.1   |      |
|   | Mean     | 19.64       |       | 34.28       |       | 15.8                         |      | 0.00  |      | 0.0           |      | 3.02  |      |
|   | +S.D.    | 0.60        |       | 1.56        |       | 5.9                          |      | 0.00  |      | 0.0           |      | 0.95  |      |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |             |       |             |       |                              |      |   |      |               |      |   |      |
|   | 51       |             | 19.9  |             | 35.3  |                              | 11   |   | 0.0  |               | 0    |   | 3.9  |
|   | 52       |             | 20.2  |             | 35.5  |                              | 13   |   | 0.0  |               | 0    |   | 2.3  |
|   | 53       |             | 19.2  |             | 36.0  |                              | 19   |   | 0.0  |               | 0    |   | 5.1  |
|   | 54       |             | 20.4  |             | 36.5  |                              | 24   |   | 0.0  |               | 0    |   | 2.7  |
|   | 55       |             | 19.1  |             | 35.8  |                              | 21   |   | 0.0  |               | 0    |   | 1.9  |
|   | 56       | 19.7        |       | 35.4        |       | 22                           |      | 0.0   |      | 0             |      | 2.6   |      |
|   | 57       | 20.6        |       | 35.3        |       | 21                           |      | 0.0   |      | 0             |      | 4.6   |      |
|   | 58       | 19.9        |       | 35.2        |       | 18                           |      | 0.0   |      | 0             |      | 3.6   |      |
|   | 59       | 19.6        |       | 34.1        |       | 16                           |      | 0.0   |      | 0             |      | 0.9   |      |
|   | 60       | 19.7        |       | 33.9        |       | 11                           |      | 0.0   |      | 0             |      | 1.3   |      |
|   | Mean     | 19.90       | 19.76 | 34.78       | 35.82 | 17.6                         | 17.6 | 0.00  | 0.00 | 0.0           | 0.0  | 2.60  | 3.18 |
|   | +S.D.    | 0.41        | 0.59  | 0.72        | 0.47  | 4.4                          | 5.5  | 0.00  | 0.00 | 0.0           | 0.0  | 1.55  | 1.31 |

| Group   | Anim.No. | N-Seg.<br>(%) |      | Eosino.<br>(10 <sup>2</sup> /mm <sup>3</sup> ) |      | Eosino.<br>(%) |      | Baso.<br>(10 <sup>2</sup> /mm <sup>3</sup> ) |      | Baso.<br>(%) |      | Mono.<br>(10 <sup>2</sup> /mm <sup>3</sup> ) |      |
|---|----------|---------------|------|--|------|----------------|------|--|------|--------------|------|--|------|
|   |          | 4w            | R:2w | 4w   | R:2w | 4w             | R:2w | 4w   | R:2w | 4w           | R:2w | 4w   | R:2w |
| Control   |          |               |      |  |      |                |      |  |      |              |      |  |      |
|   | 11       |               | 2    |  | 0.0  |                | 0    |  | 0.0  |              | 0    |  | 0.5  |
|   | 12       |               | 2    |  | 0.0  |                | 0    |  | 0.0  |              | 0    |  | 2.3  |
|   | 13       |               | 5    |  | 0.8  |                | 2    |  | 0.0  |              | 0    |  | 0.0  |
|   | 14       |               | 17   |  | 0.0  |                | 0    |  | 0.0  |              | 0    |  | 0.4  |
|   | 15       |               | 15   |  | 0.4  |                | 1    |  | 0.0  |              | 0    |  | 0.4  |
|   | 16       | 8             |      | 0.4  |      | 1              |      | 0.0  |      | 0            |      | 0.4  |      |
|   | 17       | 2             |      | 0.4  |      | 1              |      | 0.0  |      | 0            |      | 0.7  |      |
|   | 18       | 7             |      | 0.8  |      | 2              |      | 0.0  |      | 0            |      | 0.0  |      |
|   | 19       | 6             |      | 0.0  |      | 0              |      | 0.0  |      | 0            |      | 0.6  |      |
|   | 20       | 1             |      | 0.4  |      | 1              |      | 0.0  |      | 0            |      | 0.0  |      |
|   | Mean     | 4.8           | 8.2  | 0.40   | 0.24 | 1.0            | 0.6  | 0.00   | 0.00 | 0.0          | 0.0  | 0.34   | 0.72 |
|   | +S.D.    | 3.1           | 7.3  | 0.28   | 0.36 | 0.7            | 0.9  | 0.00   | 0.00 | 0.0          | 0.0  | 0.33   | 0.90 |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |               |      |  |      |                |      |  |      |              |      |  |      |
|   | 26       | 1             |      | 0.0  |      | 0              |      | 0.0  |      | 0            |      | 0.5  |      |
|   | 27       | 3             |      | 0.0  |      | 0              |      | 0.0  |      | 0            |      | 1.1  |      |
|   | 28       | 4             |      | 0.0  |      | 0              |      | 0.0  |      | 0            |      | 0.5  |      |
|   | 29       | 4             |      | 0.0  |      | 0              |      | 0.0  |      | 0            |      | 0.4  |      |
|   | 30       | 6             |      | 0.5  |      | 1              |      | 0.0  |      | 0            |      | 0.5  |      |
|   | Mean     | 3.6           |      | 0.10   |      | 0.2            |      | 0.00   |      | 0.0          |      | 0.60   |      |
|   | +S.D.    | 1.8           |      | 0.22   |      | 0.4            |      | 0.00   |      | 0.0          |      | 0.28   |      |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |               |      |  |      |                |      |  |      |              |      |  |      |
|   | 36       | 2             |      | 0.7  |      | 1              |      | 0.0  |      | 0            |      | 0.0  |      |
|   | 37       | 7             |      | 0.5  |      | 1              |      | 0.0  |      | 0            |      | 1.5  |      |
|   | 38       | 8             |      | 0.0  |      | 0              |      | 0.0  |      | 0            |      | 0.0  |      |
|   | 39       | 6             |      | 0.0  |      | 0              |      | 0.0  |      | 0            |      | 0.0  |      |
|   | 40       | 7             |      | 0.4  |      | 1              |      | 0.0  |      | 0            |      | 0.4  |      |
|   | Mean     | 6.0           |      | 0.32   |      | 0.6            |      | 0.00   |      | 0.0          |      | 0.38   |      |
|   | +S.D.    | 2.3           |      | 0.31   |      | 0.5            |      | 0.00   |      | 0.0          |      | 0.65   |      |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |               |      |  |      |                |      |  |      |              |      |  |      |
|   | 51       |               | 13   |  | 0.3  |                | 1    |  | 0.0  |              | 0    |  | 0.3  |
|   | 52       |               | 9    |  | 0.3  |                | 1    |  | 0.0  |              | 0    |  | 0.8  |
|   | 53       |               | 9    |  | 0.0  |                | 0    |  | 0.0  |              | 0    |  | 0.6  |
|   | 54       |               | 8    |  | 0.0  |                | 0    |  | 0.0  |              | 0    |  | 0.3  |
|   | 55       |               | 5    |  | 0.4  |                | 1    |  | 0.0  |              | 0    |  | 0.7  |
|   | 56       | 6             |      | 0.0  |      | 0              |      | 0.0  |      | 0            |      | 1.3  |      |
|   | 57       | 8             |      | 0.6  |      | 1              |      | 0.0  |      | 0            |      | 0.6  |      |
|   | 58       | 4             |      | 0.0  |      | 0              |      | 0.0  |      | 0            |      | 0.0  |      |
|   | 59       | 2             |      | 0.4  |      | 1              |      | 0.0  |      | 0            |      | 0.9  |      |
|   | 60       | 2             |      | 0.6  |      | 1              |      | 0.0  |      | 0            |      | 0.6  |      |
|   | Mean     | 4.4           | 8.8  | 0.32   | 0.20 | 0.6            | 0.6  | 0.00   | 0.00 | 0.0          | 0.0  | 0.68   | 0.54 |
|   | +S.D.    | 2.6           | 2.9  | 0.30   | 0.19 | 0.5            | 0.5  | 0.00   | 0.00 | 0.0          | 0.0  | 0.48   | 0.23 |

| Group   | Anim.No. | Mono.<br>(%) |      | Lymph.<br>(10 <sup>2</sup> /mm <sup>3</sup> ) |       | Lymph.<br>(%) |      | PT<br>(Sec) |      | APTT<br>(Sec) |       |
|---|----------|--------------|------|---|-------|---------------|------|-------------|------|---------------|-------|
|   |          | 4w           | R:2w | 4w  | R:2w  | 4w            | R:2w | 4w          | R:2w | 4w            | R:2w  |
| Control   |          |              |      |   |       |               |      |             |      |               |       |
|   | 11       |              | 1    |   | 43.7  |               | 97   |             | 7.7  |               | 16.2  |
|   | 12       |              | 5    |   | 41.9  |               | 93   |             | 7.8  |               | 15.8  |
|   | 13       |              | 0    |   | 38.1  |               | 93   |             | 7.7  |               | 17.8  |
|   | 14       |              | 1    |   | 31.2  |               | 82   |             | 7.9  |               | 17.8  |
|   | 15       |              | 1    |   | 32.4  |               | 83   |             | 7.9  |               | 17.3  |
|   | 16       | 1            |      | 36.0  |       | 90            |      | 7.8         |      | 17.2          |       |
|   | 17       | 2            |      | 35.2  |       | 95            |      | 7.7         |      | 17.3          |       |
|   | 18       | 0            |      | 38.2  |       | 91            |      | 7.7         |      | 17.3          |       |
|   | 19       | 1            |      | 52.1  |       | 93            |      | 7.4         |      | 17.3          |       |
|   | 20       | 0            |      | 43.1  |       | 98            |      | 7.7         |      | 17.8          |       |
|   | Mean     | 0.8          | 1.6  | 40.92   | 37.46 | 93.4          | 89.6 | 7.66        | 7.80 | 17.38         | 16.98 |
|   | +S.D.    | 0.8          | 1.9  | 6.97  | 5.56  | 3.2           | 6.7  | 0.15        | 0.10 | 0.24          | 0.93  |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |              |      |   |       |               |      |             |      |               |       |
|   | 26       | 1            |      | 45.1  |       | 98            |      | 7.6         |      | 16.5          |       |
|   | 27       | 2            |      | 50.4  |       | 95            |      | 7.7         |      | 18.4          |       |
|   | 28       | 1            |      | 47.5  |       | 95            |      | 7.2         |      | 14.3          |       |
|   | 29       | 1            |      | 36.1  |       | 95            |      | 7.1         |      | 18.2          |       |
|   | 30       | 1            |      | 48.8  |       | 92            |      | 7.4         |      | 17.1          |       |
|   | Mean     | 1.2          |      | 45.58   |       | 95.0          |      | 7.40        |      | 16.90         |       |
|   | +S.D.    | 0.4          |      | 5.64  |       | 2.1           |      | 0.25        |      | 1.65          |       |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |              |      |   |       |               |      |             |      |               |       |
|   | 36       | 0            |      | 66.0  |       | 97            |      | 7.2         |      | 16.4          |       |
|   | 37       | 3            |      | 43.6  |       | 89            |      | 7.8         |      | 17.0          |       |
|   | 38       | 0            |      | 37.7  |       | 92            |      | 8.0         |      | 18.1          |       |
|   | 39       | 0            |      | 61.1  |       | 94            |      | 7.1         |      | 16.5          |       |
|   | 40       | 1            |      | 40.0  |       | 91            |      | 7.1         |      | 13.8          |       |
|   | Mean     | 0.8          |      | 49.68   |       | 92.6          |      | 7.44        |      | 16.36         |       |
|   | +S.D.    | 1.3          |      | 12.95   |       | 3.0           |      | 0.43        |      | 1.58          |       |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |              |      |   |       |               |      |             |      |               |       |
|   | 51       |              | 1    |   | 25.5  |               | 85   |             | 8.1  |               | 18.4  |
|   | 52       |              | 3    |   | 21.8  |               | 87   |             | 7.6  |               | 18.3  |
|   | 53       |              | 1    |   | 51.3  |               | 90   |             | 7.5  |               | 17.7  |
|   | 54       |              | 1    |   | 30.9  |               | 91   |             | 7.5  |               | 16.4  |
|   | 55       |              | 2    |   | 34.0  |               | 92   |             | 7.8  |               | 15.9  |
|   | 56       | 3            |      | 40.0  |       | 91            |      | 7.3         |      | 14.7          |       |
|   | 57       | 1            |      | 51.3  |       | 90            |      | 7.4         |      | 17.5          |       |
|   | 58       | 0            |      | 87.4  |       | 96            |      | 7.3         |      | 15.7          |       |
|   | 59       | 2            |      | 41.8  |       | 95            |      | 7.2         |      | 18.2          |       |
|   | 60       | 1            |      | 61.4  |       | 96            |      | 7.1         |      | 16.6          |       |
|   | Mean     | 1.4          | 1.6  | 56.38   | 32.70 | 93.6          | 89.0 | 7.26        | 7.70 | 16.54         | 17.34 |
|   | +S.D.    | 1.1          | 0.9  | 19.33   | 11.42 | 2.9           | 2.9  | 0.11        | 0.25 | 1.39          | 1.13  |



# Blood Chemistry

|         |         |                                 |
|---------|---------|---------------------------------|
| ASAT    | (IU/L)  | Aspartate aminotransferase      |
| ALAT    | (IU/L)  | Alanine aminotransferase        |
| ALP     | (IU/L)  | Alkaline phosphatase            |
| LDH     | (IU/L)  | Lactate dehydrogenase           |
| G-GTP   | (IU/L)  | Gamma - glutamyl transpeptidase |
| T.Bil.  | (mg/dL) | Total bilirubin                 |
| T.Prot. | (g/dL)  | Total protein                   |
| Albumin | (g/dL)  | Albumin                         |
| A/G     |         | Albumin / Globulin              |
| T.Chol. | (mg/dL) | Total cholesterol               |
| TGL     | (mg/dL) | Triglyceride                    |
| Glucose | (mg/dL) | Glucose                         |
| BUN     | (mg/dL) | Blood urea nitrogen             |
| Creat.  | (mg/dL) | Creatinine                      |
| ChE     | (IU/L)  | Cholinesterase                  |
| IP      | (mg/dL) | Inorganic phosphorus            |
| Ca      | (mg/dL) | Calcium                         |
| Na      | (mEq/L) | Sodium                          |
| K       | (mEq/L) | Potassium                       |
| Cl      | (mEq/L) | Chloride                        |

| Group   | Anim.No. | ASAT<br>(IU/L) |      | ALAT<br>(IU/L) |      | ALP<br>(IU/L) |       | LDH<br>(IU/L) |        | G-GTP<br>(IU/L) |      | T.Bil.<br>(mg/dL) |       |
|---|----------|----------------|------|----------------|------|---------------|-------|---------------|--------|-----------------|------|-------------------|-------|
|   |          | 4w             | R:2w | 4w             | R:2w | 4w            | R:2w  | 4w            | R:2w   | 4w              | R:2w | 4w                | R:2w  |
| Control   |          |                |      |                |      |               |       |               |        |                 |      |                   |       |
|   | 1        |                | 64   |                | 37   |               | 217   |               | 647    |                 | 0.3  |                   | 0.13  |
|   | 2        |                | 127  |                | 30   |               | 242   |               | 3843   |                 | 0.3  |                   | 0.14  |
|   | 3        |                | 86   |                | 39   |               | 309   |               | 1511   |                 | 0.4  |                   | 0.17  |
|   | 4        |                | 77   |                | 31   |               | 266   |               | 761    |                 | 0.6  |                   | 0.15  |
|   | 5        |                | 78   |                | 31   |               | 181   |               | 751    |                 | 0.2  |                   | 0.18  |
|   | 6        | 103            |      | 36             |      | 345           |       | 1753          |        | 0.7             |      | 0.10              |       |
|   | 7        | 69             |      | 27             |      | 312           |       | 636           |        | 0.9             |      | 0.12              |       |
|   | 8        | 64             |      | 29             |      | 328           |       | 575           |        | 0.8             |      | 0.10              |       |
|   | 9        | 85             |      | 27             |      | 325           |       | 804           |        | 1.1             |      | 0.11              |       |
|   | 10       | 84             |      | 31             |      | 246           |       | 646           |        | 0.1             |      | 0.08              |       |
|   | Mean     | 81.0           | 86.4 | 30.0           | 33.6 | 311.2         | 243.0 | 882.8         | 1502.6 | 0.72            | 0.36 | 0.102             | 0.154 |
|   | +S.D.    | 15.3           | 24.0 | 3.7            | 4.1  | 38.3          | 48.5  | 493.8         | 1353.2 | 0.38            | 0.15 | 0.015             | 0.021 |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |                |      |                |      |               |       |               |        |                 |      |                   |       |
|   | 21       | 71             |      | 25             |      | 401           |       | 523           |        | 0.3             |      | 0.08              |       |
|   | 22       | 92             |      | 37             |      | 251           |       | 978           |        | 0.2             |      | 0.09              |       |
|   | 23       | 78             |      | 27             |      | 287           |       | 554           |        | 0.2             |      | 0.09              |       |
|   | 24       | 83             |      | 32             |      | 359           |       | 932           |        | 0.7             |      | 0.12              |       |
|   | 25       | 79             |      | 35             |      | 350           |       | 748           |        | 0.4             |      | 0.11              |       |
|   | Mean     | 80.6           |      | 31.2           |      | 329.6         |       | 747.0         |        | 0.36            |      | 0.098             |       |
|   | +S.D.    | 7.7            |      | 5.1            |      | 59.9          |       | 209.2         |        | 0.21            |      | 0.016             |       |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |                |      |                |      |               |       |               |        |                 |      |                   |       |
|   | 31       | 78             |      | 36             |      | 276           |       | 965           |        | 0.6             |      | 0.09              |       |
|   | 32       | 81             |      | 30             |      | 271           |       | 1316          |        | 0.3             |      | 0.08              |       |
|   | 33       | 81             |      | 31             |      | 382           |       | 1111          |        | 0.4             |      | 0.08              |       |
|   | 34       | 90             |      | 29             |      | 346           |       | 1771          |        | 0.5             |      | 0.09              |       |
|   | 35       | 95             |      | 30             |      | 362           |       | 1712          |        | 0.5             |      | 0.08              |       |
|   | Mean     | 85.0           |      | 31.2           |      | 327.4         |       | 1375.0        |        | 0.46            |      | 0.084             |       |
|   | +S.D.    | 7.2            |      | 2.8            |      | 50.9          |       | 357.7         |        | 0.11            |      | 0.005             |       |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |                |      |                |      |               |       |               |        |                 |      |                   |       |
|   | 41       |                | 93   |                | 32   |               | 288   |               | 1356   |                 | 0.5  |                   | 0.16  |
|   | 42       |                | 69   |                | 28   |               | 231   |               | 496    |                 | 0.4  |                   | 0.16  |
|   | 43       |                | 83   |                | 26   |               | 363   |               | 1260   |                 | 1.1  |                   | 0.14  |
|   | 44       |                | 71   |                | 25   |               | 299   |               | 629    |                 | 0.0  |                   | 0.17  |
|   | 45       |                | 75   |                | 42   |               | 209   |               | 835    |                 | 0.3  |                   | 0.17  |
|   | 46       | 79             |      | 32             |      | 268           |       | 939           |        | 0.4             |      | 0.10              |       |
|   | 47       | 119            |      | 41             |      | 346           |       | 1446          |        | 0.9             |      | 0.09              |       |
|   | 48       | 70             |      | 28             |      | 254           |       | 740           |        | 0.2             |      | 0.11              |       |
|   | 49       | 74             |      | 27             |      | 340           |       | 378           |        | 0.9             |      | 0.08              |       |
|   | 50       | 96             |      | 32             |      | 276           |       | 1306          |        | 0.5             |      | 0.09              |       |
|   | Mean     | 87.6           | 78.2 | 32.0           | 30.6 | 296.8         | 278.0 | 961.8         | 915.2  | 0.58            | 0.46 | 0.094             | 0.160 |
|   | +S.D.    | 20.2           | 9.9  | 5.5            | 6.9  | 43.0          | 60.7  | 431.1         | 379.9  | 0.31            | 0.40 | 0.011             | 0.012 |

| Group   | Anim.No. | T.Prot.<br>(g/dL) |      | Albumin<br>(g/dL) |      | A/G   |       | T.Chol.<br>(mg/dL) |      | TGL<br>(mg/dL) |      | Glucose<br>(mg/dL) |       |
|---|----------|-------------------|------|-------------------|------|-------|-------|--------------------|------|----------------|------|--------------------|-------|
|   |          | 4w                | R:2w | 4w                | R:2w | 4w    | R:2w  | 4w                 | R:2w | 4w             | R:2w | 4w                 | R:2w  |
| Control   |          |                   |      |                   |      |       |       |                    |      |                |      |                    |       |
|   | 1        |                   | 5.7  |                   | 4.1  |       | 2.54  |                    | 58   |                | 41   |                    | 146   |
|   | 2        |                   | 5.9  |                   | 4.2  |       | 2.47  |                    | 40   |                | 29   |                    | 169   |
|   | 3        |                   | 5.6  |                   | 4.1  |       | 2.61  |                    | 41   |                | 34   |                    | 164   |
|   | 4        |                   | 5.7  |                   | 4.0  |       | 2.45  |                    | 42   |                | 60   |                    | 188   |
|   | 5        |                   | 5.6  |                   | 4.3  |       | 3.09  |                    | 55   |                | 28   |                    | 173   |
|   | 6        | 5.9               |      | 4.2               |      | 2.40  |       | 53                 |      | 22             |      | 134                |       |
|   | 7        | 5.9               |      | 4.3               |      | 2.63  |       | 52                 |      | 48             |      | 149                |       |
|   | 8        | 6.0               |      | 4.3               |      | 2.41  |       | 57                 |      | 27             |      | 155                |       |
|   | 9        | 5.4               |      | 4.0               |      | 2.95  |       | 59                 |      | 22             |      | 154                |       |
|   | 10       | 6.0               |      | 4.3               |      | 2.46  |       | 47                 |      | 48             |      | 161                |       |
|   | Mean     | 5.84              | 5.70 | 4.22              | 4.14 | 2.570 | 2.632 | 53.6               | 47.2 | 33.4           | 38.4 | 150.6              | 168.0 |
|   | +S.D.    | 0.25              | 0.12 | 0.13              | 0.11 | 0.232 | 0.264 | 4.7                | 8.6  | 13.5           | 13.1 | 10.2               | 15.2  |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |                   |      |                   |      |       |       |                    |      |                |      |                    |       |
|   | 21       | 5.7               |      | 4.1               |      | 2.61  |       | 46                 |      | 32             |      | 151                |       |
|   | 22       | 5.6               |      | 4.1               |      | 2.68  |       | 45                 |      | 30             |      | 131                |       |
|   | 23       | 5.4               |      | 4.1               |      | 3.14  |       | 36                 |      | 14             |      | 132                |       |
|   | 24       | 6.0               |      | 4.3               |      | 2.45  |       | 52                 |      | 25             |      | 163                |       |
|   | 25       | 5.7               |      | 4.1               |      | 2.65  |       | 51                 |      | 22             |      | 168                |       |
|   | Mean     | 5.68              |      | 4.14              |      | 2.706 |       | 46.0               |      | 24.6           |      | 149.0              |       |
|   | +S.D.    | 0.22              |      | 0.09              |      | 0.258 |       | 6.4                |      | 7.1            |      | 17.1               |       |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |                   |      |                   |      |       |       |                    |      |                |      |                    |       |
|   | 31       | 5.9               |      | 4.2               |      | 2.43  |       | 53                 |      | 23             |      | 141                |       |
|   | 32       | 5.4               |      | 4.1               |      | 3.17  |       | 54                 |      | 27             |      | 131                |       |
|   | 33       | 6.0               |      | 4.3               |      | 2.68  |       | 56                 |      | 28             |      | 140                |       |
|   | 34       | 5.5               |      | 4.2               |      | 3.01  |       | 54                 |      | 38             |      | 140                |       |
|   | 35       | 6.0               |      | 4.6               |      | 3.23  |       | 63                 |      | 53             |      | 126                |       |
|   | Mean     | 5.76              |      | 4.28              |      | 2.904 |       | 56.0               |      | 33.8           |      | 135.6              |       |
|   | +S.D.    | 0.29              |      | 0.19              |      | 0.340 |       | 4.1                |      | 12.1           |      | 6.7                |       |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |                   |      |                   |      |       |       |                    |      |                |      |                    |       |
|   | 41       |                   | 5.5  |                   | 3.9  |       | 2.46  |                    | 48   |                | 32   |                    | 153   |
|   | 42       |                   | 6.0  |                   | 4.1  |       | 2.13  |                    | 75   |                | 37   |                    | 163   |
|   | 43       |                   | 5.2  |                   | 3.7  |       | 2.42  |                    | 49   |                | 22   |                    | 161   |
|   | 44       |                   | 5.9  |                   | 4.1  |       | 2.22  |                    | 44   |                | 17   |                    | 156   |
|   | 45       |                   | 6.0  |                   | 4.2  |       | 2.42  |                    | 37   |                | 23   |                    | 178   |
|   | 46       | 6.0               |      | 4.3               |      | 2.54  |       | 52                 |      | 24             |      | 163                |       |
|   | 47       | 5.4               |      | 4.0               |      | 2.82  |       | 40                 |      | 22             |      | 157                |       |
|   | 48       | 6.0               |      | 4.2               |      | 2.31  |       | 57                 |      | 22             |      | 147                |       |
|   | 49       | 5.6               |      | 4.1               |      | 2.82  |       | 43                 |      | 32             |      | 121                |       |
|   | 50       | 5.7               |      | 4.0               |      | 2.35  |       | 29                 |      | 15             |      | 103                |       |
|   | Mean     | 5.74              | 5.72 | 4.12              | 4.00 | 2.568 | 2.330 | 44.2               | 50.6 | 23.0           | 26.2 | 138.2              | 162.2 |
|   | +S.D.    | 0.26              | 0.36 | 0.13              | 0.20 | 0.246 | 0.146 | 10.9               | 14.4 | 6.1            | 8.1  | 25.4               | 9.7   |

| Group   | Anim.No. | BUN<br>(mg/dL) |       | Creat.<br>(mg/dL) |       | ChE<br>(IU/L) |       | IP<br>(mg/dL) |       | Ca<br>(mg/dL) |      | Na<br>(mEq/L) |       |
|---|----------|----------------|-------|-------------------|-------|---------------|-------|---------------|-------|---------------|------|---------------|-------|
|   |          | 4w             | R:2w  | 4w                | R:2w  | 4w            | R:2w  | 4w            | R:2w  | 4w            | R:2w | 4w            | R:2w  |
| Control   |          |                |       |                   |       |               |       |               |       |               |      |               |       |
|   | 1        |                | 16.8  |                   | 0.55  |               | 380   |               | 7.07  |               | 9.7  |               | 141   |
|   | 2        |                | 19.3  |                   | 0.52  |               | 338   |               | 7.16  |               | 9.5  |               | 143   |
|   | 3        |                | 19.3  |                   | 0.49  |               | 412   |               | 7.64  |               | 9.9  |               | 141   |
|   | 4        |                | 18.0  |                   | 0.52  |               | 308   |               | 8.41  |               | 10.2 |               | 141   |
|   | 5        |                | 13.5  |                   | 0.46  |               | 401   |               | 7.33  |               | 9.8  |               | 140   |
|   | 6        | 21.7           |       | 0.62              |       | 453           |       | 9.46          |       | 10.4          |      | 141           |       |
|   | 7        | 17.8           |       | 0.61              |       | 690           |       | 9.17          |       | 10.4          |      | 140           |       |
|   | 8        | 18.7           |       | 0.46              |       | 434           |       | 8.57          |       | 10.0          |      | 144           |       |
|   | 9        | 18.8           |       | 0.46              |       | 449           |       | 8.39          |       | 10.4          |      | 145           |       |
|   | 10       | 20.4           |       | 0.42              |       | 355           |       | 9.13          |       | 10.8          |      | 144           |       |
|   | Mean     | 19.48          | 17.38 | 0.514             | 0.508 | 476.2         | 367.8 | 8.944         | 7.522 | 10.40         | 9.82 | 142.8         | 141.2 |
|   | +S.D.    | 1.55           | 2.41  | 0.094             | 0.034 | 126.0         | 43.8  | 0.447         | 0.542 | 0.28          | 0.26 | 2.2           | 1.1   |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |                |       |                   |       |               |       |               |       |               |      |               |       |
|   | 21       | 16.6           |       | 0.45              |       | 311           |       | 8.99          |       | 10.3          |      | 145           |       |
|   | 22       | 16.4           |       | 0.46              |       | 321           |       | 9.57          |       | 10.1          |      | 146           |       |
|   | 23       | 16.4           |       | 0.40              |       | 396           |       | 9.01          |       | 10.1          |      | 145           |       |
|   | 24       | 16.9           |       | 0.54              |       | 443           |       | 9.80          |       | 10.0          |      | 144           |       |
|   | 25       | 21.2           |       | 0.52              |       | 285           |       | 9.73          |       | 10.8          |      | 144           |       |
|   | Mean     | 17.50          |       | 0.474             |       | 351.2         |       | 9.420         |       | 10.26         |      | 144.8         |       |
|   | +S.D.    | 2.08           |       | 0.056             |       | 65.8          |       | 0.392         |       | 0.32          |      | 0.8           |       |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |                |       |                   |       |               |       |               |       |               |      |               |       |
|   | 31       | 21.1           |       | 0.46              |       | 418           |       | 8.83          |       | 9.4           |      | 144           |       |
|   | 32       | 18.6           |       | 0.46              |       | 338           |       | 9.50          |       | 9.9           |      | 147           |       |
|   | 33       | 19.2           |       | 0.46              |       | 402           |       | 9.13          |       | 10.5          |      | 144           |       |
|   | 34       | 20.1           |       | 0.40              |       | 357           |       | 10.15         |       | 10.0          |      | 145           |       |
|   | 35       | 17.4           |       | 0.46              |       | 557           |       | 10.34         |       | 10.9          |      | 145           |       |
|   | Mean     | 19.28          |       | 0.448             |       | 414.4         |       | 9.590         |       | 10.14         |      | 145.0         |       |
|   | +S.D.    | 1.41           |       | 0.027             |       | 86.1          |       | 0.647         |       | 0.58          |      | 1.2           |       |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |                |       |                   |       |               |       |               |       |               |      |               |       |
|   | 41       |                | 21.6  |                   | 0.64  |               | 463   |               | 8.13  |               | 9.6  |               | 144   |
|   | 42       |                | 15.3  |                   | 0.48  |               | 510   |               | 8.26  |               | 10.3 |               | 143   |
|   | 43       |                | 22.5  |                   | 0.54  |               | 385   |               | 8.59  |               | 9.8  |               | 142   |
|   | 44       |                | 14.2  |                   | 0.50  |               | 269   |               | 7.16  |               | 10.2 |               | 144   |
|   | 45       |                | 23.5  |                   | 0.63  |               | 283   |               | 8.18  |               | 10.0 |               | 143   |
|   | 46       | 25.2           |       | 0.50              |       | 385           |       | 9.61          |       | 10.2          |      | 144           |       |
|   | 47       | 15.6           |       | 0.47              |       | 370           |       | 9.40          |       | 10.3          |      | 142           |       |
|   | 48       | 17.3           |       | 0.48              |       | 433           |       | 9.47          |       | 10.8          |      | 145           |       |
|   | 49       | 15.8           |       | 0.41              |       | 410           |       | 9.64          |       | 10.8          |      | 146           |       |
|   | 50       | 19.6           |       | 0.42              |       | 435           |       | 9.97          |       | 10.8          |      | 144           |       |
|   | Mean     | 18.70          | 19.42 | 0.456             | 0.558 | 406.6         | 382.0 | 9.618         | 8.064 | 10.58         | 9.98 | 144.2         | 143.2 |
|   | +S.D.    | 3.97           | 4.33  | 0.039             | 0.074 | 28.8          | 106.7 | 0.220         | 0.536 | 0.30          | 0.29 | 1.5           | 0.8   |

| Group   | Anim.No. | K<br>(mEq/L) |      | Cl<br>(mEq/L) |       |
|---|----------|--------------|------|---------------|-------|
|   |          | 4w           | R:2w | 4w            | R:2w  |
| Control   |          |              |      |               |       |
|   | 1        |              | 3.9  |               | 102   |
|   | 2        |              | 3.8  |               | 103   |
|   | 3        |              | 4.0  |               | 103   |
|   | 4        |              | 3.8  |               | 101   |
|   | 5        |              | 3.8  |               | 101   |
|   | 6        | 4.4          |      | 102           |       |
|   | 7        | 3.8          |      | 101           |       |
|   | 8        | 3.8          |      | 103           |       |
|   | 9        | 4.0          |      | 102           |       |
|   | 10       | 3.5          |      | 99            |       |
|   | Mean     | 3.90         | 3.86 | 101.4         | 102.0 |
|   | +S.D.    | 0.33         | 0.09 | 1.5           | 1.0   |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |              |      |               |       |
|   | 21       | 3.6          |      | 105           |       |
|   | 22       | 4.0          |      | 105           |       |
|   | 23       | 3.7          |      | 105           |       |
|   | 24       | 3.9          |      | 101           |       |
|   | 25       | 4.1          |      | 103           |       |
|   | Mean     | 3.86         |      | 103.8         |       |
|   | +S.D.    | 0.21         |      | 1.8           |       |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |              |      |               |       |
|   | 31       | 4.3          |      | 104           |       |
|   | 32       | 3.8          |      | 106           |       |
|   | 33       | 4.0          |      | 104           |       |
|   | 34       | 4.0          |      | 104           |       |
|   | 35       | 4.4          |      | 102           |       |
|   | Mean     | 4.10         |      | 104.0         |       |
|   | +S.D.    | 0.24         |      | 1.4           |       |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |              |      |               |       |
|   | 41       |              | 4.1  |               | 101   |
|   | 42       |              | 3.7  |               | 101   |
|   | 43       |              | 4.0  |               | 102   |
|   | 44       |              | 3.6  |               | 101   |
|   | 45       |              | 3.7  |               | 101   |
|   | 46       | 4.3          |      | 100           |       |
|   | 47       | 3.8          |      | 103           |       |
|   | 48       | 4.1          |      | 103           |       |
|   | 49       | 3.6          |      | 105           |       |
|   | 50       | 4.3          |      | 106           |       |
|   | Mean     | 4.02         | 3.82 | 103.4         | 101.2 |
|   | +S.D.    | 0.31         | 0.22 | 2.3           | 0.4   |

| Group   | Anim.No. | ASAT<br>(IU/L) |      | ALAT<br>(IU/L) |      | ALP<br>(IU/L) |       | LDH<br>(IU/L) |        | G-GTP<br>(IU/L) |      | T.Bil.<br>(mg/dL) |       |
|---|----------|----------------|------|----------------|------|---------------|-------|---------------|--------|-----------------|------|-------------------|-------|
|   |          | 4w             | R:2w | 4w             | R:2w | 4w            | R:2w  | 4w            | R:2w   | 4w              | R:2w | 4w                | R:2w  |
| Control   |          |                |      |                |      |               |       |               |        |                 |      |                   |       |
|   | 11       |                | 67   |                | 21   |               | 129   |               | 1096   |                 | 0.2  |                   | 0.17  |
|   | 12       |                | 98   |                | 25   |               | 182   |               | 2283   |                 | 1.6  |                   | 0.18  |
|   | 13       |                | 63   |                | 24   |               | 121   |               | 925    |                 | 0.8  |                   | 0.17  |
|   | 14       |                | 73   |                | 28   |               | 195   |               | 817    |                 | 1.0  |                   | 0.15  |
|   | 15       |                | 102  |                | 27   |               | 240   |               | 2680   |                 | 1.0  |                   | 0.20  |
|   | 16       | 92             |      | 15             |      | 245           |       | 1928          |        | 0.8             |      | 0.09              |       |
|   | 17       | 67             |      | 18             |      | 287           |       | 997           |        | 0.8             |      | 0.11              |       |
|   | 18       | 85             |      | 23             |      | 164           |       | 1547          |        | 1.0             |      | 0.09              |       |
|   | 19       | 133            |      | 27             |      | 194           |       | 3067          |        | 1.0             |      | 0.10              |       |
|   | 20       | 106            |      | 21             |      | 185           |       | 2508          |        | 0.7             |      | 0.11              |       |
|   | Mean     | 96.6           | 80.6 | 20.8           | 25.0 | 215.0         | 173.4 | 2009.4        | 1560.2 | 0.86            | 0.92 | 0.100             | 0.174 |
|   | +S.D.    | 24.7           | 18.1 | 4.6            | 2.7  | 50.1          | 49.2  | 808.2         | 858.4  | 0.13            | 0.50 | 0.010             | 0.018 |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |                |      |                |      |               |       |               |        |                 |      |                   |       |
|   | 26       | 124            |      | 19             |      | 212           |       | 3317          |        | 1.0             |      | 0.11              |       |
|   | 27       | 98             |      | 23             |      | 259           |       | 1836          |        | 1.4             |      | 0.08              |       |
|   | 28       | 106            |      | 26             |      | 238           |       | 2482          |        | 1.3             |      | 0.11              |       |
|   | 29       | 87             |      | 15             |      | 217           |       | 1764          |        | 0.2             |      | 0.11              |       |
|   | 30       | 113            |      | 27             |      | 176           |       | 2730          |        | 0.6             |      | 0.10              |       |
|   | Mean     | 105.6          |      | 22.0           |      | 220.4         |       | 2425.8        |        | 0.90            |      | 0.102             |       |
|   | +S.D.    | 14.1           |      | 5.0            |      | 31.0          |       | 647.3         |        | 0.50            |      | 0.013             |       |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |                |      |                |      |               |       |               |        |                 |      |                   |       |
|   | 36       | 85             |      | 23             |      | 253           |       | 1031          |        | 0.7             |      | 0.07              |       |
|   | 37       | 102            |      | 21             |      | 270           |       | 1856          |        | 1.2             |      | 0.10              |       |
|   | 38       | 103            |      | 31             |      | 226           |       | 1804          |        | 1.2             |      | 0.08              |       |
|   | 39       | 110            |      | 26             |      | 313           |       | 1151          |        | 0.5             |      | 0.10              |       |
|   | 40       | 103            |      | 25             |      | 145           |       | 2285          |        | 1.7             |      | 0.06              |       |
|   | Mean     | 100.6          |      | 25.2           |      | 241.4         |       | 1625.4        |        | 1.06            |      | 0.082             |       |
|   | +S.D.    | 9.3            |      | 3.8            |      | 62.5          |       | 524.0         |        | 0.47            |      | 0.018             |       |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |                |      |                |      |               |       |               |        |                 |      |                   |       |
|   | 51       |                | 106  |                | 26   |               | 185   |               | 2546   |                 | 1.2  |                   | 0.15  |
|   | 52       |                | 79   |                | 20   |               | 231   |               | 1244   |                 | 0.7  |                   | 0.17  |
|   | 53       |                | 104  |                | 45   |               | 157   |               | 902    |                 | 0.4  |                   | 0.18  |
|   | 54       |                | 111  |                | 36   |               | 243   |               | 1462   |                 | 1.4  |                   | 0.20  |
|   | 55       |                | 80   |                | 24   |               | 193   |               | 524    |                 | 0.4  |                   | 0.19  |
|   | 56       | 81             |      | 19             |      | 144           |       | 1200          |        | 1.2             |      | 0.07              |       |
|   | 57       | 77             |      | 21             |      | 235           |       | 925           |        | 0.4             |      | 0.12              |       |
|   | 58       | 77             |      | 20             |      | 177           |       | 1174          |        | 1.0             |      | 0.06              |       |
|   | 59       | 68             |      | 18             |      | 213           |       | 919           |        | 0.6             |      | 0.09              |       |
|   | 60       | 103            |      | 20             |      | 177           |       | 2559          |        | 0.4             |      | 0.09              |       |
|   | Mean     | 81.2           | 96.0 | 19.6           | 30.2 | 189.2         | 201.8 | 1355.4        | 1335.6 | 0.72            | 0.82 | 0.086             | 0.178 |
|   | +S.D.    | 13.1           | 15.3 | 1.1            | 10.2 | 35.4          | 35.1  | 685.8         | 764.2  | 0.36            | 0.46 | 0.023             | 0.019 |

| Group   | Anim.No. | T.Prot.<br>(g/dL) |      | Albumin<br>(g/dL) |      | A/G   |       | T.Chol.<br>(mg/dL) |      | TGL<br>(mg/dL) |      | Glucose<br>(mg/dL) |       |
|---|----------|-------------------|------|-------------------|------|-------|-------|--------------------|------|----------------|------|--------------------|-------|
|   |          | 4w                | R:2w | 4w                | R:2w | 4w    | R:2w  | 4w                 | R:2w | 4w             | R:2w | 4w                 | R:2w  |
| Control   |          |                   |      |                   |      |       |       |                    |      |                |      |                    |       |
|   | 11       |                   | 5.9  |                   | 4.3  |       | 2.62  |                    | 44   |                | 5    |                    | 167   |
|   | 12       |                   | 5.8  |                   | 4.4  |       | 3.02  |                    | 47   |                | 9    |                    | 150   |
|   | 13       |                   | 6.7  |                   | 4.7  |       | 2.40  |                    | 74   |                | 27   |                    | 139   |
|   | 14       |                   | 5.7  |                   | 4.0  |       | 2.37  |                    | 62   |                | 8    |                    | 119   |
|   | 15       |                   | 5.7  |                   | 4.2  |       | 2.75  |                    | 60   |                | 6    |                    | 111   |
|   | 16       | 5.5               |      | 4.1               |      | 3.00  |       | 41                 |      | 8              |      | 155                |       |
|   | 17       | 5.8               |      | 4.4               |      | 3.19  |       | 54                 |      | 20             |      | 156                |       |
|   | 18       | 5.8               |      | 4.3               |      | 2.99  |       | 55                 |      | 15             |      | 157                |       |
|   | 19       | 6.0               |      | 4.4               |      | 2.68  |       | 70                 |      | 11             |      | 130                |       |
|   | 20       | 5.6               |      | 4.2               |      | 3.19  |       | 57                 |      | 12             |      | 142                |       |
|   | Mean     | 5.74              | 5.96 | 4.28              | 4.32 | 3.010 | 2.632 | 55.4               | 57.4 | 13.2           | 11.0 | 148.0              | 137.2 |
|   | +S.D.    | 0.19              | 0.42 | 0.13              | 0.26 | 0.209 | 0.268 | 10.3               | 12.2 | 4.5            | 9.1  | 11.8               | 22.8  |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |                   |      |                   |      |       |       |                    |      |                |      |                    |       |
|   | 26       | 5.6               |      | 4.2               |      | 3.06  |       | 48                 |      | 6              |      | 124                |       |
|   | 27       | 5.8               |      | 4.2               |      | 2.69  |       | 58                 |      | 9              |      | 118                |       |
|   | 28       | 6.3               |      | 4.5               |      | 2.62  |       | 64                 |      | 12             |      | 125                |       |
|   | 29       | 6.5               |      | 4.8               |      | 2.85  |       | 66                 |      | 9              |      | 127                |       |
|   | 30       | 5.6               |      | 4.2               |      | 3.05  |       | 65                 |      | 17             |      | 130                |       |
|   | Mean     | 5.96              |      | 4.38              |      | 2.854 |       | 60.2               |      | 10.6           |      | 124.8              |       |
|   | +S.D.    | 0.42              |      | 0.27              |      | 0.202 |       | 7.5                |      | 4.2            |      | 4.4                |       |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |                   |      |                   |      |       |       |                    |      |                |      |                    |       |
|   | 36       | 6.4               |      | 4.5               |      | 2.51  |       | 68                 |      | 10             |      | 144                |       |
|   | 37       | 5.0               |      | 3.8               |      | 3.28  |       | 46                 |      | 11             |      | 146                |       |
|   | 38       | 5.9               |      | 4.2               |      | 2.48  |       | 53                 |      | 12             |      | 139                |       |
|   | 39       | 5.6               |      | 4.3               |      | 3.38  |       | 70                 |      | 14             |      | 156                |       |
|   | 40       | 6.3               |      | 4.7               |      | 2.92  |       | 73                 |      | 14             |      | 153                |       |
|   | Mean     | 5.84              |      | 4.30              |      | 2.914 |       | 62.0               |      | 12.2           |      | 147.6              |       |
|   | +S.D.    | 0.57              |      | 0.34              |      | 0.419 |       | 11.8               |      | 1.8            |      | 6.9                |       |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |                   |      |                   |      |       |       |                    |      |                |      |                    |       |
|   | 51       |                   | 6.2  |                   | 4.3  |       | 2.17  |                    | 56   |                | 4    |                    | 129   |
|   | 52       |                   | 5.9  |                   | 4.3  |       | 2.63  |                    | 59   |                | 8    |                    | 143   |
|   | 53       |                   | 6.7  |                   | 4.6  |       | 2.14  |                    | 81   |                | 8    |                    | 106   |
|   | 54       |                   | 6.0  |                   | 4.3  |       | 2.52  |                    | 55   |                | 4    |                    | 130   |
|   | 55       |                   | 6.4  |                   | 4.3  |       | 2.16  |                    | 65   |                | 12   |                    | 144   |
|   | 56       | 6.3               |      | 4.8               |      | 3.01  |       | 80                 |      | 16             |      | 141                |       |
|   | 57       | 5.7               |      | 4.5               |      | 3.60  |       | 54                 |      | 15             |      | 122                |       |
|   | 58       | 6.3               |      | 4.5               |      | 2.58  |       | 72                 |      | 18             |      | 143                |       |
|   | 59       | 5.7               |      | 4.3               |      | 3.19  |       | 72                 |      | 13             |      | 147                |       |
|   | 60       | 6.0               |      | 4.4               |      | 2.91  |       | 76                 |      | 14             |      | 136                |       |
|   | Mean     | 6.00              | 6.24 | 4.50              | 4.36 | 3.058 | 2.324 | 70.8               | 63.2 | 15.2           | 7.2  | 137.8              | 130.4 |
|   | +S.D.    | 0.30              | 0.32 | 0.19              | 0.13 | 0.375 | 0.233 | 10.0               | 10.7 | 1.9            | 3.3  | 9.7                | 15.3  |

| Group   | Anim.No. | BUN<br>(mg/dL) |       | Creat.<br>(mg/dL) |       | ChE<br>(IU/L) |        | IP<br>(mg/dL) |       | Ca<br>(mg/dL) |      | Na<br>(mEq/L) |       |
|---|----------|----------------|-------|-------------------|-------|---------------|--------|---------------|-------|---------------|------|---------------|-------|
|   |          | 4w             | R:2w  | 4w                | R:2w  | 4w            | R:2w   | 4w            | R:2w  | 4w            | R:2w | 4w            | R:2w  |
| Control   |          |                |       |                   |       |               |        |               |       |               |      |               |       |
|   | 11       |                | 17.5  |                   | 0.59  |               | 2116   |               | 6.59  |               | 10.2 |               | 141   |
|   | 12       |                | 18.3  |                   | 0.55  |               | 1371   |               | 4.52  |               | 9.7  |               | 142   |
|   | 13       |                | 13.4  |                   | 0.46  |               | 2183   |               | 4.77  |               | 10.0 |               | 144   |
|   | 14       |                | 17.9  |                   | 0.57  |               | 933    |               | 6.01  |               | 9.8  |               | 144   |
|   | 15       |                | 19.8  |                   | 0.50  |               | 1156   |               | 7.59  |               | 9.8  |               | 141   |
|   | 16       | 22.5           |       | 0.46              |       | 1233          |        | 7.51          |       | 9.6           |      | 144           |       |
|   | 17       | 21.0           |       | 0.49              |       | 1364          |        | 8.59          |       | 10.1          |      | 144           |       |
|   | 18       | 22.9           |       | 0.53              |       | 1331          |        | 7.66          |       | 10.0          |      | 144           |       |
|   | 19       | 21.4           |       | 0.58              |       | 1837          |        | 7.41          |       | 10.3          |      | 143           |       |
|   | 20       | 26.9           |       | 0.57              |       | 1824          |        | 8.12          |       | 9.6           |      | 145           |       |
|   | Mean     | 22.94          | 17.38 | 0.526             | 0.534 | 1517.8        | 1551.8 | 7.858         | 5.896 | 9.92          | 9.90 | 144.0         | 142.4 |
|   | +S.D.    | 2.35           | 2.39  | 0.051             | 0.053 | 289.5         | 567.7  | 0.491         | 1.277 | 0.31          | 0.20 | 0.7           | 1.5   |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |                |       |                   |       |               |        |               |       |               |      |               |       |
|   | 26       | 21.9           |       | 0.51              |       | 2286          |        | 7.92          |       | 10.1          |      | 145           |       |
|   | 27       | 22.1           |       | 0.49              |       | 1201          |        | 8.55          |       | 9.9           |      | 145           |       |
|   | 28       | 22.2           |       | 0.50              |       | 1730          |        | 9.55          |       | 10.5          |      | 147           |       |
|   | 29       | 20.3           |       | 0.45              |       | 2212          |        | 7.54          |       | 10.6          |      | 146           |       |
|   | 30       | 18.3           |       | 0.43              |       | 1478          |        | 8.89          |       | 10.0          |      | 144           |       |
|   | Mean     | 20.96          |       | 0.476             |       | 1781.4        |        | 8.490         |       | 10.22         |      | 145.4         |       |
|   | +S.D.    | 1.68           |       | 0.034             |       | 466.8         |        | 0.793         |       | 0.31          |      | 1.1           |       |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |                |       |                   |       |               |        |               |       |               |      |               |       |
|   | 36       | 25.1           |       | 0.54              |       | 1823          |        | 8.18          |       | 10.6          |      | 145           |       |
|   | 37       | 23.3           |       | 0.52              |       | 676           |        | 8.46          |       | 10.2          |      | 146           |       |
|   | 38       | 20.0           |       | 0.50              |       | 1274          |        | 7.97          |       | 10.3          |      | 145           |       |
|   | 39       | 18.5           |       | 0.55              |       | 1778          |        | 7.17          |       | 9.8           |      | 144           |       |
|   | 40       | 25.4           |       | 0.63              |       | 1483          |        | 7.20          |       | 10.7          |      | 143           |       |
|   | Mean     | 22.46          |       | 0.548             |       | 1406.8        |        | 7.796         |       | 10.32         |      | 144.6         |       |
|   | +S.D.    | 3.08           |       | 0.050             |       | 466.0         |        | 0.584         |       | 0.36          |      | 1.1           |       |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |                |       |                   |       |               |        |               |       |               |      |               |       |
|   | 51       |                | 18.0  |                   | 0.57  |               | 1568   |               | 5.70  |               | 9.8  |               | 145   |
|   | 52       |                | 21.0  |                   | 0.58  |               | 1290   |               | 7.16  |               | 9.8  |               | 142   |
|   | 53       |                | 20.1  |                   | 0.57  |               | 1945   |               | 6.00  |               | 10.1 |               | 142   |
|   | 54       |                | 17.2  |                   | 0.54  |               | 1786   |               | 6.08  |               | 9.7  |               | 142   |
|   | 55       |                | 18.6  |                   | 0.69  |               | 1415   |               | 6.28  |               | 9.6  |               | 144   |
|   | 56       | 27.2           |       | 0.54              |       | 1505          |        | 7.66          |       | 10.1          |      | 147           |       |
|   | 57       | 25.1           |       | 0.60              |       | 1362          |        | 9.55          |       | 10.7          |      | 144           |       |
|   | 58       | 31.2           |       | 0.68              |       | 1769          |        | 9.11          |       | 10.6          |      | 141           |       |
|   | 59       | 18.5           |       | 0.45              |       | 1946          |        | 8.60          |       | 10.5          |      | 146           |       |
|   | 60       | 23.4           |       | 0.46              |       | 1085          |        | 9.64          |       | 10.4          |      | 147           |       |
|   | Mean     | 25.08          | 18.98 | 0.546             | 0.590 | 1533.4        | 1600.8 | 8.912         | 6.244 | 10.46         | 9.80 | 145.0         | 143.0 |
|   | +S.D.    | 4.69           | 1.55  | 0.097             | 0.058 | 338.0         | 266.9  | 0.813         | 0.553 | 0.23          | 0.19 | 2.5           | 1.4   |



| Group   | Anim.No. | K<br>(mEq/L) |      | Cl<br>(mEq/L) |       |
|---|----------|--------------|------|---------------|-------|
|   |          | 4w           | R:2w | 4w            | R:2w  |
| Control   |          |              |      |               |       |
|   | 11       |              | 3.8  |               | 104   |
|   | 12       |              | 4.0  |               | 104   |
|   | 13       |              | 3.5  |               | 107   |
|   | 14       |              | 3.6  |               | 107   |
|   | 15       |              | 4.1  |               | 103   |
|   | 16       | 3.8          |      | 106           |       |
|   | 17       | 3.5          |      | 104           |       |
|   | 18       | 4.0          |      | 106           |       |
|   | 19       | 3.9          |      | 106           |       |
|   | 20       | 3.9          |      | 105           |       |
|   | Mean     | 3.82         | 3.80 | 105.4         | 105.0 |
|   | +S.D.    | 0.19         | 0.25 | 0.9           | 1.9   |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |              |      |               |       |
|   | 26       | 4.1          |      | 107           |       |
|   | 27       | 3.6          |      | 108           |       |
|   | 28       | 3.6          |      | 106           |       |
|   | 29       | 3.5          |      | 107           |       |
|   | 30       | 3.9          |      | 105           |       |
|   | Mean     | 3.74         |      | 106.6         |       |
|   | +S.D.    | 0.25         |      | 1.1           |       |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |              |      |               |       |
|   | 36       | 3.9          |      | 106           |       |
|   | 37       | 3.7          |      | 109           |       |
|   | 38       | 3.7          |      | 106           |       |
|   | 39       | 3.6          |      | 107           |       |
|   | 40       | 4.1          |      | 106           |       |
|   | Mean     | 3.80         |      | 106.8         |       |
|   | +S.D.    | 0.20         |      | 1.3           |       |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |              |      |               |       |
|   | 51       |              | 3.9  |               | 108   |
|   | 52       |              | 3.4  |               | 105   |
|   | 53       |              | 3.6  |               | 105   |
|   | 54       |              | 3.7  |               | 105   |
|   | 55       |              | 3.0  |               | 105   |
|   | 56       | 3.8          |      | 108           |       |
|   | 57       | 3.9          |      | 107           |       |
|   | 58       | 3.7          |      | 105           |       |
|   | 59       | 3.7          |      | 109           |       |
|   | 60       | 4.1          |      | 110           |       |
|   | Mean     | 3.84         | 3.52 | 107.8         | 105.6 |
|   | +S.D.    | 0.17         | 0.34 | 1.9           | 1.3   |

**Gross Autopsy Findings**

**Grade**

- : No abnormal changes
- + : Slight
- ++ : Moderate
- +++ : Marked
- P : Non-graded changes

| Findings             | Group            | Control |   |   |   |    | Polyoxyethylene p-nonylphenyl ether |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
|----------------------|------------------|---------|---|---|---|----|-------------------------------------|----|----|----|----|-----|----|----|----|----|------|----|----|----|----|
|                      | Dose (mg/kg/day) |         |   |   |   |    | 20                                  |    |    |    |    | 200 |    |    |    |    | 1000 |    |    |    |    |
|                      | Animal No.       | 6       | 7 | 8 | 9 | 10 | 21                                  | 22 | 23 | 24 | 25 | 31  | 32 | 33 | 34 | 35 | 46   | 47 | 48 | 49 | 50 |
| Lung                 |                  |         |   |   |   |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Black focus, single  |                  | -       | - | - | - | P  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Black focus, several |                  | -       | - | - | - | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | P    | -  | -  | -  | -  |
| Red focus, several   |                  | P       | - | - | - | -  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Red focus, single    |                  | -       | - | - | - | -  | -                                   | -  | -  | P  | -  | -   | -  | P  | -  | -  | P    | -  | -  | -  | -  |
| Liver                |                  |         |   |   |   |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| White focus, single  |                  | -       | - | - | - | -  | -                                   | -  | P  | -  | -  | -   | -  | P  | -  | -  | -    | -  | -  | -  | -  |
| Kidney               |                  |         |   |   |   |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Cyst, single, right  |                  | -       | - | - | - | -  | -                                   | -  | -  | P  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |

| Findings            | Group            | Control |    |    |    |    | Polyoxyethylene p-nonylphenyl ether |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
|---------------------|------------------|---------|----|----|----|----|-------------------------------------|----|----|----|----|-----|----|----|----|----|------|----|----|----|----|
|                     | Dose (mg/kg/day) |         |    |    |    |    | 20                                  |    |    |    |    | 200 |    |    |    |    | 1000 |    |    |    |    |
|                     | Animal No.       | 16      | 17 | 18 | 19 | 20 | 26                                  | 27 | 28 | 29 | 30 | 36  | 37 | 38 | 39 | 40 | 56   | 57 | 58 | 59 | 60 |
| Lung                |                  |         |    |    |    |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Red focus, single   |                  | -       | -  | -  | -  | P  | -                                   | -  | -  | -  | -  | -   | -  | -  | -  | -  | -    | -  | -  | -  | -  |
| Liver               |                  |         |    |    |    |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| White focus, single |                  | P       | P  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | P  | -  | -  | P    | P  | -  | -  | -  |
| Kidney              |                  |         |    |    |    |    |                                     |    |    |    |    |     |    |    |    |    |      |    |    |    |    |
| Cyst, single, right |                  | -       | -  | -  | -  | -  | -                                   | -  | -  | -  | -  | -   | -  | P  | -  | -  | -    | -  | -  | -  | -  |

| Findings             | Group            | Control |   |   |   |   | Polyoxyethylene p-nonylphenyl ether |     |      |    |    |    |    |
|----------------------|------------------|---------|---|---|---|---|-------------------------------------|-----|------|----|----|----|----|
|                      | Dose (mg/kg/day) |         |   |   |   |   | 20                                  | 200 | 1000 |    |    |    |    |
|                      | Animal No.       | 1       | 2 | 3 | 4 | 5 |                                     |     | 41   | 42 | 43 | 44 | 45 |
| Lung                 |                  |         |   |   |   |   |                                     |     |      |    |    |    |    |
| Black focus, several |                  | -       | - | - | P | - |                                     |     | -    | -  | -  | -  | -  |
| Liver                |                  |         |   |   |   |   |                                     |     |      |    |    |    |    |
| White focus, single  |                  | -       | - | P | - | P |                                     |     | -    | -  | -  | P  | -  |
| Adrenal              |                  |         |   |   |   |   |                                     |     |      |    |    |    |    |
| Asymmetry, size      |                  | -       | - | - | - | - |                                     |     | -    | P  | -  | -  | -  |

| Findings             | Group            | Control |    |    |    |    | Polyoxyethylene p-nonylphenyl ether |     |      |    |    |    |    |
|----------------------|------------------|---------|----|----|----|----|-------------------------------------|-----|------|----|----|----|----|
|                      | Dose (mg/kg/day) |         |    |    |    |    | 20                                  | 200 | 1000 |    |    |    |    |
|                      | Animal No.       | 11      | 12 | 13 | 14 | 15 |                                     |     | 51   | 52 | 53 | 54 | 55 |
| Lung                 |                  |         |    |    |    |    |                                     |     |      |    |    |    |    |
| Black focus, several |                  | -       | -  | -  | -  | -  |                                     |     | -    | -  | -  | P  | -  |
| Liver                |                  |         |    |    |    |    |                                     |     |      |    |    |    |    |
| White focus, single  |                  | -       | -  | -  | -  | P  |                                     |     | -    | -  | P  | -  | P  |

Organ weight

|         |                    |
|---------|--------------------|
| Adre.R  | Adrenal (Right)    |
| Adre.L  | Adrenal (Left)     |
| Testi.R | Testis (Right)     |
| Testi.L | Testis (Left)      |
| Ovary.R | Ovary (Right)      |
| Ovary.L | Ovary (Left)       |
| Kid.R   | Kidney (Right)     |
| Kid.L   | Kidney (Left)      |
| Epid.R  | Epididymis (Right) |
| Epid.L  | Epididymis (Left)  |

## Appendix 10-1 Organ weight in male rats (End of drug administration)

Study No. : SBL79-02

| Group   | Anim.No. | Adre.R<br>mg | Adre.L<br>mg | Testi.R<br>mg | Testi.L<br>mg | Thymus<br>mg | Spleen<br>mg | Brain<br>mg | Heart<br>mg | Liver<br>g | Kid.R<br>mg | Kid.L<br>mg | Epid.R<br>mg |
|---|----------|--------------|--------------|---------------|---------------|--------------|--------------|-------------|-------------|------------|-------------|-------------|--------------|
| Control   |          |              |              |               |               |              |              |             |             |            |             |             |              |
|   | 6        | 18.2         | 20.1         | 1316          | 1343          | 371          | 519          | 1774        | 872         | 7.39       | 1071        | 1028        | 310          |
|   | 7        | 35.8         | 35.8         | 978           | 1354          | 583          | 958          | 2084        | 1405        | 13.04      | 1684        | 1588        | 211          |
|   | 8        | 30.6         | 31.5         | 1645          | 1645          | 643          | 681          | 2035        | 1077        | 11.59      | 1489        | 1424        | 382          |
|   | 9        | 32.8         | 32.7         | 1418          | 1388          | 552          | 579          | 1939        | 1120        | 10.60      | 1443        | 1362        | 384          |
|   | 10       | 29.2         | 27.1         | 1441          | 1449          | 623          | 624          | 1963        | 1239        | 11.31      | 1315        | 1353        | 409          |
|   | Mean     | 29.32        | 29.44        | 1359.6        | 1435.8        | 554.4        | 672.2        | 1959.0      | 1142.6      | 10.786     | 1400.4      | 1351.0      | 339.2        |
|   | +S.D.    | 6.70         | 6.08         | 244.4         | 124.0         | 108.4        | 170.5        | 118.4       | 197.6       | 2.096      | 226.9       | 203.7       | 80.6         |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |              |              |               |               |              |              |             |             |            |             |             |              |
|   | 21       | 22.6         | 23.9         | 1311          | 1299          | 443          | 696          | 1817        | 1101        | 9.38       | 1231        | 1264        | 388          |
|   | 22       | 25.7         | 24.5         | 1419          | 1415          | 626          | 634          | 2049        | 1140        | 10.52      | 1382        | 1426        | 418          |
|   | 23       | 25.7         | 28.7         | 1554          | 1490          | 427          | 707          | 1948        | 1102        | 8.68       | 1363        | 1391        | 413          |
|   | 24       | 29.7         | 31.2         | 1577          | 1543          | 552          | 673          | 1931        | 1084        | 10.18      | 1330        | 1289        | 387          |
|   | 25       | 26.1         | 32.4         | 1443          | 1469          | 438          | 550          | 1962        | 1105        | 9.45       | 1345        | 1208        | 389          |
|   | Mean     | 25.96        | 28.14        | 1460.8        | 1443.2        | 497.2        | 652.0        | 1941.4      | 1106.4      | 9.642      | 1330.2      | 1315.6      | 399.0        |
|   | +S.D.    | 2.52         | 3.84         | 108.0         | 92.7          | 88.0         | 63.5         | 83.1        | 20.5        | 0.723      | 58.8        | 90.6        | 15.2         |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |              |              |               |               |              |              |             |             |            |             |             |              |
|   | 31       | 28.6         | 30.6         | 1516          | 1519          | 399          | 674          | 1992        | 1274        | 9.92       | 1268        | 1279        | 416          |
|   | 32       | 28.3         | 33.1         | 610           | 650           | 437          | 747          | 1945        | 1110        | 10.43      | 1347        | 1339        | 310          |
|   | 33       | 26.7         | 26.8         | 1430          | 1434          | 409          | 678          | 2046        | 1195        | 11.09      | 1382        | 1394        | 411          |
|   | 34       | 25.2         | 31.6         | 1305          | 1278          | 388          | 610          | 1862        | 1083        | 8.75       | 1156        | 1129        | 375          |
|   | 35       | 29.2         | 30.2         | 1483          | 1484          | 347          | 440          | 1913        | 1003        | 7.56       | 1003        | 945         | 342          |
|   | Mean     | 27.60        | 30.46        | 1268.8        | 1273.0        | 396.0        | 629.8        | 1951.6      | 1133.0      | 9.550      | 1231.2      | 1217.2      | 370.8        |
|   | +S.D.    | 1.63         | 2.33         | 376.9         | 360.2         | 32.9         | 116.6        | 70.9        | 104.5       | 1.404      | 154.3       | 181.5       | 45.3         |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |              |              |               |               |              |              |             |             |            |             |             |              |
|   | 46       | 28.2         | 31.9         | 1626          | 1610          | 729          | 664          | 2073        | 1055        | 10.35      | 1418        | 1378        | 409          |
|   | 47       | 37.4         | 33.3         | 1253          | 1306          | 747          | 843          | 1821        | 1233        | 11.35      | 1706        | 1689        | 353          |
|   | 48       | 22.4         | 25.4         | 1491          | 1481          | 602          | 721          | 1874        | 1129        | 12.21      | 1366        | 1447        | 400          |
|   | 49       | 32.5         | 30.4         | 1197          | 1267          | 567          | 891          | 1993        | 1117        | 13.51      | 1438        | 1419        | 310          |
|   | 50       | 39.4         | 40.6         | 1370          | 1369          | 323          | 551          | 1780        | 984         | 8.53       | 1256        | 1283        | 387          |
|   | Mean     | 31.98        | 32.32        | 1387.4        | 1406.6        | 593.6        | 734.0        | 1908.2      | 1103.6      | 11.190     | 1436.8      | 1443.2      | 371.8        |
|   | +S.D.    | 6.91         | 5.51         | 174.8         | 139.6         | 170.2        | 137.0        | 122.0       | 92.5        | 1.886      | 166.2       | 150.8       | 40.6         |



| Group   | Anim.No. | Epid.L<br>mg |
|---|----------|--------------|
| Control   |          |              |
|   | 6        | 315          |
|   | 7        | 281          |
|   | 8        | 403          |
|   | 9        | 365          |
|   | 10       | 404          |
|   | Mean     | 353.6        |
|   | +S.D.    | 54.5         |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |              |
|   | 21       | 386          |
|   | 22       | 409          |
|   | 23       | 398          |
|   | 24       | 343          |
|   | 25       | 368          |
|   | Mean     | 380.8        |
|   | +S.D.    | 26.0         |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |              |
|   | 31       | 396          |
|   | 32       | 293          |
|   | 33       | 419          |
|   | 34       | 384          |
|   | 35       | 361          |
|   | Mean     | 370.6        |
|   | +S.D.    | 48.2         |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |              |
|   | 46       | 409          |
|   | 47       | 335          |
|   | 48       | 416          |
|   | 49       | 323          |
|   | 50       | 357          |
|   | Mean     | 368.0        |
|   | +S.D.    | 42.5         |

## Appendix 10-3 Organ weight in male rats (End of recovery test)

Study No. : SBL79-02

| Group   | Anim.No. | Adre.R<br>mg | Adre.L<br>mg | Testi.R<br>mg | Testi.L<br>mg | Thymus<br>mg | Spleen<br>mg | Brain<br>mg | Heart<br>mg | Liver<br>g | Kid.R<br>mg | Kid.L<br>mg | Epid.R<br>mg |
|---|----------|--------------|--------------|---------------|---------------|--------------|--------------|-------------|-------------|------------|-------------|-------------|--------------|
| Control   |          |              |              |               |               |              |              |             |             |            |             |             |              |
|   | 1        | 26.6         | 27.6         | 1340          | 1369          | 527          | 703          | 1955        | 1439        | 12.92      | 1596        | 1506        | 540          |
|   | 2        | 30.1         | 32.1         | 1458          | 1490          | 609          | 666          | 1934        | 1065        | 10.90      | 1404        | 1384        | 540          |
|   | 3        | 36.4         | 39.5         | 1404          | 1391          | 457          | 615          | 1949        | 1303        | 10.51      | 1339        | 1392        | 520          |
|   | 4        | 30.3         | 33.4         | 1367          | 1355          | 648          | 915          | 2068        | 1447        | 15.54      | 1753        | 1749        | 508          |
|   | 5        | 27.9         | 30.7         | 1576          | 1578          | 431          | 645          | 1931        | 1373        | 10.70      | 1421        | 1393        | 540          |
|   | Mean     | 30.26        | 32.66        | 1429.0        | 1436.6        | 534.4        | 708.8        | 1967.4      | 1325.4      | 12.114     | 1502.6      | 1484.8      | 529.6        |
|   | +S.D.    | 3.76         | 4.39         | 93.3          | 95.1          | 93.8         | 119.6        | 57.1        | 156.7       | 2.147      | 169.2       | 156.1       | 14.9         |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |              |              |               |               |              |              |             |             |            |             |             |              |
|   | 41       | 24.7         | 26.7         | 1290          | 1284          | 385          | 572          | 1922        | 1198        | 9.07       | 1107        | 1102        | 413          |
|   | 42       | 13.6         | 31.8         | 1741          | 1718          | 534          | 817          | 2014        | 1281        | 13.64      | 1666        | 1709        | 589          |
|   | 43       | 31.7         | 33.6         | 1508          | 1510          | 465          | 760          | 2167        | 1379        | 11.58      | 1593        | 1633        | 476          |
|   | 44       | 35.3         | 40.7         | 1580          | 1614          | 514          | 790          | 2029        | 1317        | 11.72      | 1621        | 1704        | 526          |
|   | 45       | 28.1         | 26.5         | 1506          | 1523          | 422          | 617          | 1889        | 1347        | 12.24      | 1386        | 1459        | 532          |
|   | Mean     | 26.68        | 31.86        | 1525.0        | 1529.8        | 464.0        | 711.2        | 2004.2      | 1304.4      | 11.650     | 1474.6      | 1521.4      | 507.2        |
|   | +S.D.    | 8.31         | 5.84         | 162.4         | 160.8         | 62.1         | 109.6        | 108.7       | 69.7        | 1.656      | 231.9       | 255.3       | 66.2         |

Appendix 10-4 Organ weight in male rats (End of recovery test)

Study No. : SBL79-02

| Group   | Anim.No. | Epid.L<br>mg |
|---|----------|--------------|
| Control   |          |              |
|   | 1        | 530          |
|   | 2        | 553          |
|   | 3        | 480          |
|   | 4        | 499          |
|   | 5        | 538          |
|   | Mean     | 520.0        |
|   | +S.D.    | 29.8         |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |              |
|   | 41       | 422          |
|   | 42       | 625          |
|   | 43       | 490          |
|   | 44       | 487          |
|   | 45       | 531          |
|   | Mean     | 511.0        |
|   | +S.D.    | 74.7         |

| Group   | Anim.No. | Adre.R<br>mg | Adre.L<br>mg | Ovary.R<br>mg | Ovary.L<br>mg | Thymus<br>mg | Spleen<br>mg | Brain<br>mg | Heart<br>mg | Liver<br>g | Kid.R<br>mg | Kid.L<br>mg |
|---|----------|--------------|--------------|---------------|---------------|--------------|--------------|-------------|-------------|------------|-------------|-------------|
| Control   |          |              |              |               |               |              |              |             |             |            |             |             |
|   | 16       | 35.2         | 35.7         | 54.5          | 45.1          | 608          | 608          | 1756        | 810         | 7.34       | 966         | 994         |
|   | 17       | 34.2         | 38.2         | 50.7          | 46.6          | 649          | 564          | 1845        | 979         | 8.54       | 1090        | 1076        |
|   | 18       | 24.8         | 26.4         | 48.3          | 44.5          | 399          | 415          | 1972        | 746         | 6.40       | 821         | 889         |
|   | 19       | 26.4         | 31.5         | 33.5          | 35.9          | 544          | 529          | 1872        | 761         | 6.43       | 920         | 832         |
|   | 20       | 26.8         | 29.9         | 40.4          | 42.7          | 413          | 444          | 1815        | 826         | 6.49       | 900         | 826         |
|   | Mean     | 29.48        | 32.34        | 45.48         | 42.96         | 522.6        | 512.0        | 1852.0      | 824.4       | 7.040      | 939.4       | 923.4       |
|   | +S.D.    | 4.84         | 4.68         | 8.45          | 4.19          | 112.9        | 81.0         | 79.7        | 92.6        | 0.925      | 99.2        | 108.7       |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |              |              |               |               |              |              |             |             |            |             |             |
|   | 26       | 28.7         | 29.4         | 39.7          | 44.6          | 494          | 405          | 1820        | 658         | 5.55       | 769         | 736         |
|   | 27       | 39.4         | 38.9         | 63.4          | 52.9          | 539          | 509          | 1829        | 753         | 7.11       | 1008        | 1043        |
|   | 28       | 29.7         | 32.9         | 36.9          | 35.2          | 454          | 481          | 1804        | 747         | 6.77       | 866         | 838         |
|   | 29       | 30.8         | 29.6         | 37.3          | 37.2          | 539          | 561          | 1869        | 776         | 6.60       | 930         | 892         |
|   | 30       | 35.4         | 44.9         | 49.4          | 46.6          | 565          | 431          | 1972        | 806         | 7.13       | 1018        | 1013        |
|   | Mean     | 32.80        | 35.14        | 45.34         | 43.30         | 518.2        | 477.4        | 1858.8      | 748.0       | 6.632      | 918.2       | 904.4       |
|   | +S.D.    | 4.49         | 6.67         | 11.30         | 7.20          | 44.1         | 62.0         | 67.7        | 55.4        | 0.646      | 103.9       | 126.4       |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |              |              |               |               |              |              |             |             |            |             |             |
|   | 36       | 31.6         | 40.8         | 46.5          | 36.5          | 444          | 455          | 2049        | 846         | 6.70       | 890         | 855         |
|   | 37       | 33.1         | 36.5         | 53.3          | 43.3          | 323          | 398          | 1834        | 858         | 6.27       | 955         | 945         |
|   | 38       | 35.3         | 42.2         | 48.9          | 55.9          | 478          | 517          | 1857        | 944         | 8.11       | 1117        | 1126        |
|   | 39       | 37.3         | 36.2         | 29.7          | 47.5          | 300          | 511          | 1814        | 738         | 5.77       | 757         | 705         |
|   | 40       | 37.5         | 39.3         | 35.4          | 43.4          | 390          | 404          | 1660        | 802         | 6.85       | 897         | 917         |
|   | Mean     | 34.96        | 39.00        | 42.76         | 45.32         | 387.0        | 457.0        | 1842.8      | 837.6       | 6.740      | 923.2       | 909.6       |
|   | +S.D.    | 2.59         | 2.63         | 9.84          | 7.11          | 76.2         | 56.6         | 138.8       | 75.8        | 0.874      | 130.4       | 152.5       |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |              |              |               |               |              |              |             |             |            |             |             |
|   | 56       | 31.2         | 27.8         | 31.4          | 26.1          | 569          | 440          | 1781        | 834         | 7.50       | 964         | 939         |
|   | 57       | 32.7         | 33.9         | 31.9          | 52.9          | 371          | 461          | 1854        | 817         | 6.68       | 860         | 830         |
|   | 58       | 28.6         | 32.2         | 51.2          | 46.9          | 587          | 447          | 1792        | 784         | 7.39       | 873         | 866         |
|   | 59       | 41.4         | 44.9         | 47.9          | 50.6          | 471          | 473          | 1699        | 768         | 6.75       | 801         | 811         |
|   | 60       | 32.9         | 35.9         | 37.1          | 37.6          | 615          | 401          | 1780        | 881         | 6.90       | 912         | 951         |
|   | Mean     | 33.36        | 34.94        | 39.90         | 42.82         | 522.6        | 444.4        | 1781.2      | 816.8       | 7.044      | 882.0       | 879.4       |
|   | +S.D.    | 4.81         | 6.32         | 9.16          | 11.02         | 100.6        | 27.4         | 55.2        | 44.4        | 0.377      | 60.7        | 63.2        |

## Appendix 10-6 Organ weight in female rats (End of recovery test)

Study No. : SBL79-02

| Group   | Anim.No. | Adre.R<br>mg | Adre.L<br>mg | Ovary.R<br>mg | Ovary.L<br>mg | Thymus<br>mg | Spleen<br>mg | Brain<br>mg | Heart<br>mg | Liver<br>g | Kid.R<br>mg | Kid.L<br>mg |
|---|----------|--------------|--------------|---------------|---------------|--------------|--------------|-------------|-------------|------------|-------------|-------------|
| Control   |          |              |              |               |               |              |              |             |             |            |             |             |
|   | 11       | 32.3         | 28.5         | 46.4          | 56.5          | 392          | 578          | 1850        | 874         | 6.89       | 959         | 983         |
|   | 12       | 25.4         | 26.5         | 21.9          | 36.2          | 370          | 487          | 1790        | 746         | 6.19       | 895         | 904         |
|   | 13       | 35.8         | 36.4         | 50.3          | 51.6          | 530          | 574          | 1903        | 894         | 8.55       | 1060        | 1084        |
|   | 14       | 24.4         | 30.1         | 51.2          | 44.8          | 347          | 571          | 1859        | 852         | 6.51       | 944         | 914         |
|   | 15       | 25.5         | 29.8         | 47.1          | 41.2          | 386          | 494          | 1978        | 739         | 6.14       | 984         | 977         |
|   | Mean     | 28.68        | 30.26        | 43.38         | 46.06         | 405.0        | 540.8        | 1876.0      | 821.0       | 6.856      | 968.4       | 972.4       |
|   | +S.D.    | 5.07         | 3.71         | 12.18         | 8.09          | 72.0         | 46.1         | 69.8        | 73.2        | 0.993      | 60.6        | 71.9        |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |              |              |               |               |              |              |             |             |            |             |             |
|   | 51       | 30.7         | 39.5         | 37.2          | 37.2          | 357          | 428          | 1832        | 844         | 5.80       | 894         | 877         |
|   | 52       | 32.5         | 33.1         | 35.9          | 31.6          | 387          | 357          | 1856        | 811         | 6.52       | 940         | 938         |
|   | 53       | 34.3         | 36.7         | 52.2          | 41.2          | 299          | 506          | 1883        | 771         | 6.20       | 835         | 796         |
|   | 54       | 36.2         | 36.6         | 56.4          | 47.6          | 500          | 406          | 1816        | 804         | 5.99       | 833         | 805         |
|   | 55       | 33.3         | 30.8         | 64.2          | 47.4          | 491          | 543          | 1839        | 844         | 7.32       | 965         | 895         |
|   | Mean     | 33.40        | 35.34        | 49.18         | 41.00         | 406.8        | 448.0        | 1845.2      | 814.8       | 6.366      | 893.4       | 862.2       |
|   | +S.D.    | 2.05         | 3.40         | 12.32         | 6.84          | 87.0         | 75.6         | 25.5        | 30.6        | 0.596      | 59.9        | 60.6        |

| Group   | Anim.No. | BW<br>(g) | Adre.R<br>mg/100gBW | Adre.L<br>mg/100gBW | Testi.R<br>mg/100gBW | Testi.L<br>mg/100gBW | Thymus<br>mg/100gBW | Spleen<br>mg/100gBW | Brain<br>mg/100gBW | Heart<br>mg/100gBW | Liver<br>g/100gBW | Kid.R<br>mg/100gBW | Kid.L<br>mg/100gBW | Epid.R<br>mg/100gBW |
|---|----------|-----------|---------------------|---------------------|----------------------|----------------------|---------------------|---------------------|--------------------|--------------------|-------------------|--------------------|--------------------|---------------------|
| Control   |          |           |                     |                     |                      |                      |                     |                     |                    |                    |                   |                    |                    |                     |
|   | 6        | ( 264)    | 6.9                 | 7.6                 | 498                  | 509                  | 141                 | 197                 | 672                | 330                | 2.80              | 406                | 389                | 117                 |
|   | 7        | ( 380)    | 9.4                 | 9.4                 | 257                  | 356                  | 153                 | 252                 | 548                | 370                | 3.43              | 443                | 418                | 56                  |
|   | 8        | ( 334)    | 9.2                 | 9.4                 | 493                  | 493                  | 193                 | 204                 | 609                | 322                | 3.47              | 446                | 426                | 114                 |
|   | 9        | ( 345)    | 9.5                 | 9.5                 | 411                  | 402                  | 160                 | 168                 | 562                | 325                | 3.07              | 418                | 395                | 111                 |
|   | 10       | ( 329)    | 8.9                 | 8.2                 | 438                  | 440                  | 189                 | 190                 | 597                | 377                | 3.44              | 400                | 411                | 124                 |
|   | Mean     | (330.4)   | 8.78                | 8.82                | 419.4                | 440.0                | 167.2               | 202.2               | 597.6              | 344.8              | 3.242             | 422.6              | 407.8              | 104.4               |
|   | +S.D.    | ( 42.1)   | 1.08                | 0.87                | 98.0                 | 63.4                 | 22.8                | 30.9                | 48.5               | 26.5               | 0.296             | 21.0               | 15.5               | 27.5                |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |          |           |                     |                     |                      |                      |                     |                     |                    |                    |                   |                    |                    |                     |
|   | 21       | ( 296)    | 7.6                 | 8.1                 | 443                  | 439                  | 150                 | 235                 | 614                | 372                | 3.17              | 416                | 427                | 131                 |
|   | 22       | ( 340)    | 7.6                 | 7.2                 | 417                  | 416                  | 184                 | 186                 | 603                | 335                | 3.09              | 406                | 419                | 123                 |
|   | 23       | ( 292)    | 8.8                 | 9.8                 | 532                  | 510                  | 146                 | 242                 | 667                | 377                | 2.97              | 467                | 476                | 141                 |
|   | 24       | ( 328)    | 9.1                 | 9.5                 | 481                  | 470                  | 168                 | 205                 | 589                | 330                | 3.10              | 405                | 393                | 118                 |
|   | 25       | ( 308)    | 8.5                 | 10.5                | 469                  | 477                  | 142                 | 179                 | 637                | 359                | 3.07              | 437                | 392                | 126                 |
|   | Mean     | (312.8)   | 8.32                | 9.02                | 468.4                | 462.4                | 158.0               | 209.4               | 622.0              | 354.6              | 3.080             | 426.2              | 421.4              | 127.8               |
|   | +S.D.    | ( 20.7)   | 0.69                | 1.34                | 43.3                 | 36.2                 | 17.6                | 28.3                | 30.7               | 21.3               | 0.072             | 26.2               | 34.2               | 8.8                 |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |          |           |                     |                     |                      |                      |                     |                     |                    |                    |                   |                    |                    |                     |
|   | 31       | ( 296)    | 9.7                 | 10.3                | 512                  | 513                  | 135                 | 228                 | 673                | 430                | 3.35              | 428                | 432                | 141                 |
|   | 32       | ( 338)    | 8.4                 | 9.8                 | 180                  | 192                  | 129                 | 221                 | 575                | 328                | 3.09              | 399                | 396                | 92                  |
|   | 33       | ( 328)    | 8.1                 | 8.2                 | 436                  | 437                  | 125                 | 207                 | 624                | 364                | 3.38              | 421                | 425                | 125                 |
|   | 34       | ( 278)    | 9.1                 | 11.4                | 469                  | 460                  | 140                 | 219                 | 670                | 390                | 3.15              | 416                | 406                | 135                 |
|   | 35       | ( 251)    | 11.6                | 12.0                | 591                  | 591                  | 138                 | 175                 | 762                | 400                | 3.01              | 400                | 376                | 136                 |
|   | Mean     | (298.2)   | 9.38                | 10.34               | 437.6                | 438.6                | 133.4               | 210.0               | 660.8              | 382.4              | 3.196             | 412.8              | 407.0              | 125.8               |
|   | +S.D.    | ( 35.8)   | 1.39                | 1.48                | 155.3                | 150.0                | 6.3                 | 21.0                | 69.3               | 38.5               | 0.162             | 12.9               | 22.5               | 19.8                |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |           |                     |                     |                      |                      |                     |                     |                    |                    |                   |                    |                    |                     |
|   | 46       | ( 311)    | 9.1                 | 10.3                | 523                  | 518                  | 234                 | 214                 | 667                | 339                | 3.33              | 456                | 443                | 132                 |
|   | 47       | ( 349)    | 10.7                | 9.5                 | 359                  | 374                  | 214                 | 242                 | 522                | 353                | 3.25              | 489                | 484                | 101                 |
|   | 48       | ( 344)    | 6.5                 | 7.4                 | 433                  | 431                  | 175                 | 210                 | 545                | 328                | 3.55              | 397                | 421                | 116                 |
|   | 49       | ( 362)    | 9.0                 | 8.4                 | 331                  | 350                  | 157                 | 246                 | 551                | 309                | 3.73              | 397                | 392                | 86                  |
|   | 50       | ( 269)    | 14.6                | 15.1                | 509                  | 509                  | 120                 | 205                 | 662                | 366                | 3.17              | 467                | 477                | 144                 |
|   | Mean     | (327.0)   | 9.98                | 10.14               | 431.0                | 436.4                | 180.0               | 223.4               | 589.4              | 339.0              | 3.406             | 441.2              | 443.4              | 115.8               |
|   | +S.D.    | ( 37.5)   | 2.99                | 2.98                | 86.2                 | 76.3                 | 45.3                | 19.1                | 69.4               | 22.1               | 0.230             | 42.1               | 38.5               | 23.3                |

| Group                               | Anim.No. | Epid.L<br>mg/100gBW |
|-------------------------------------|----------|---------------------|
| Control                             |          |                     |
|                                     | 6        | 119                 |
|                                     | 7        | 74                  |
|                                     | 8        | 121                 |
|                                     | 9        | 106                 |
|                                     | 10       | 123                 |
|                                     | Mean     | (330.4) 108.6       |
|                                     | +S.D.    | ( 42.1) 20.5        |
| Polyoxyethylene p-nonylphenyl ether |          |                     |
| 20 (mg/kg/day)                      |          |                     |
|                                     | 21       | 130                 |
|                                     | 22       | 120                 |
|                                     | 23       | 136                 |
|                                     | 24       | 105                 |
|                                     | 25       | 119                 |
|                                     | Mean     | (312.8) 122.0       |
|                                     | +S.D.    | ( 20.7) 11.9        |
| Polyoxyethylene p-nonylphenyl ether |          |                     |
| 200 (mg/kg/day)                     |          |                     |
|                                     | 31       | 134                 |
|                                     | 32       | 87                  |
|                                     | 33       | 128                 |
|                                     | 34       | 138                 |
|                                     | 35       | 144                 |
|                                     | Mean     | (298.2) 126.2       |
|                                     | +S.D.    | ( 35.8) 22.7        |
| Polyoxyethylene p-nonylphenyl ether |          |                     |
| 1000 (mg/kg/day)                    |          |                     |
|                                     | 46       | 132                 |
|                                     | 47       | 96                  |
|                                     | 48       | 121                 |
|                                     | 49       | 89                  |
|                                     | 50       | 133                 |
|                                     | Mean     | (327.0) 114.2       |
|                                     | +S.D.    | ( 37.5) 20.5        |

| Group   | Anim.No. | BW<br>(g) | Adre.R<br>mg/100gBW | Adre.L<br>mg/100gBW | Testi.R<br>mg/100gBW | Testi.L<br>mg/100gBW | Thymus<br>mg/100gBW | Spleen<br>mg/100gBW | Brain<br>mg/100gBW | Heart<br>mg/100gBW | Liver<br>g/100gBW | Kid.R<br>mg/100gBW | Kid.L<br>mg/100gBW | Epid.R<br>mg/100gBW |
|---|----------|-----------|---------------------|---------------------|----------------------|----------------------|---------------------|---------------------|--------------------|--------------------|-------------------|--------------------|--------------------|---------------------|
| Control   |          |           |                     |                     |                      |                      |                     |                     |                    |                    |                   |                    |                    |                     |
|   | 1        | ( 406)    | 6.6                 | 6.8                 | 330                  | 337                  | 130                 | 173                 | 482                | 354                | 3.18              | 393                | 371                | 133                 |
|   | 2        | ( 358)    | 8.4                 | 9.0                 | 407                  | 416                  | 170                 | 186                 | 540                | 297                | 3.04              | 392                | 387                | 151                 |
|   | 3        | ( 354)    | 10.3                | 11.2                | 397                  | 393                  | 129                 | 174                 | 551                | 368                | 2.97              | 378                | 393                | 147                 |
|   | 4        | ( 435)    | 7.0                 | 7.7                 | 314                  | 311                  | 149                 | 210                 | 475                | 333                | 3.57              | 403                | 402                | 117                 |
|   | 5        | ( 346)    | 8.1                 | 8.9                 | 455                  | 456                  | 125                 | 186                 | 558                | 397                | 3.09              | 411                | 403                | 156                 |
|   | Mean     | (379.8)   | 8.08                | 8.72                | 380.6                | 382.6                | 140.6               | 185.8               | 521.2              | 349.8              | 3.170             | 395.4              | 391.2              | 140.8               |
|   | +S.D.    | ( 38.8)   | 1.45                | 1.66                | 58.1                 | 58.8                 | 18.9                | 14.9                | 39.6               | 37.6               | 0.236             | 12.5               | 13.1               | 15.8                |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |          |           |                     |                     |                      |                      |                     |                     |                    |                    |                   |                    |                    |                     |
|   | 41       | ( 328)    | 7.5                 | 8.1                 | 393                  | 391                  | 117                 | 174                 | 586                | 365                | 2.77              | 338                | 336                | 126                 |
|   | 42       | ( 422)    | 3.2                 | 7.5                 | 413                  | 407                  | 127                 | 194                 | 477                | 304                | 3.23              | 395                | 405                | 140                 |
|   | 43       | ( 384)    | 8.3                 | 8.8                 | 393                  | 393                  | 121                 | 198                 | 564                | 359                | 3.02              | 415                | 425                | 124                 |
|   | 44       | ( 377)    | 9.4                 | 10.8                | 419                  | 428                  | 136                 | 210                 | 538                | 349                | 3.11              | 430                | 452                | 140                 |
|   | 45       | ( 380)    | 7.4                 | 7.0                 | 396                  | 401                  | 111                 | 162                 | 497                | 354                | 3.22              | 365                | 384                | 140                 |
|   | Mean     | (378.2)   | 7.16                | 8.44                | 402.8                | 404.0                | 122.4               | 187.6               | 532.4              | 346.2              | 3.070             | 388.6              | 400.4              | 134.0               |
|   | +S.D.    | ( 33.5)   | 2.35                | 1.48                | 12.3                 | 14.9                 | 9.6                 | 19.3                | 45.3               | 24.3               | 0.189             | 37.3               | 43.9               | 8.2                 |



Appendix 10-10 Relative organ weight in male rats (End of recovery test)

Study No. : SBL79-02

| Group   | Anim.No.      | Epid.L<br>mg/100gBW |
|---|---------------|---------------------|
| Control   |               |                     |
|   | 1             | 131                 |
|   | 2             | 154                 |
|   | 3             | 136                 |
|   | 4             | 115                 |
|   | 5             | 155                 |
|   | Mean (379.8)  | 138.2               |
|   | +S.D. ( 38.8) | 16.8                |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |               |                     |
|   | 41            | 129                 |
|   | 42            | 148                 |
|   | 43            | 128                 |
|   | 44            | 129                 |
|   | 45            | 140                 |
|   | Mean (378.2)  | 134.8               |
|   | +S.D. ( 33.5) | 8.9                 |

| Group   | Anim.No.      | BW<br>(g) | Adre.R<br>mg/100gBW | Adre.L<br>mg/100gBW | Ovary.R<br>mg/100gBW | Ovary.L<br>mg/100gBW | Thymus<br>mg/100gBW | Spleen<br>mg/100gBW | Brain<br>mg/100gBW | Heart<br>mg/100gBW | Liver<br>g/100gBW | Kid.R<br>mg/100gBW | Kid.L<br>mg/100gBW |
|---|---------------|-----------|---------------------|---------------------|----------------------|----------------------|---------------------|---------------------|--------------------|--------------------|-------------------|--------------------|--------------------|
| Control   |               |           |                     |                     |                      |                      |                     |                     |                    |                    |                   |                    |                    |
|   | 16 ( 233)     |           | 15.1                | 15.3                | 23.4                 | 19.4                 | 261                 | 261                 | 754                | 348                | 3.15              | 415                | 427                |
|   | 17 ( 249)     |           | 13.7                | 15.3                | 20.4                 | 18.7                 | 261                 | 227                 | 741                | 393                | 3.43              | 438                | 432                |
|   | 18 ( 207)     |           | 12.0                | 12.8                | 23.3                 | 21.5                 | 193                 | 200                 | 953                | 360                | 3.09              | 397                | 429                |
|   | 19 ( 202)     |           | 13.1                | 15.6                | 16.6                 | 17.8                 | 269                 | 262                 | 927                | 377                | 3.18              | 455                | 412                |
|   | 20 ( 216)     |           | 12.4                | 13.8                | 18.7                 | 19.8                 | 191                 | 206                 | 840                | 382                | 3.00              | 417                | 382                |
|   | Mean (221.4)  |           | 13.26               | 14.56               | 20.48                | 19.44                | 235.0               | 231.2               | 843.0              | 372.0              | 3.170             | 424.4              | 416.4              |
|   | +S.D. ( 19.4) |           | 1.22                | 1.21                | 2.95                 | 1.38                 | 39.4                | 29.4                | 96.8               | 17.9               | 0.161             | 22.4               | 20.7               |
| Polyoxyethylene p-nonylphenyl ether<br>20 (mg/kg/day)   |               |           |                     |                     |                      |                      |                     |                     |                    |                    |                   |                    |                    |
|   | 26 ( 190)     |           | 15.1                | 15.5                | 20.9                 | 23.5                 | 260                 | 213                 | 958                | 346                | 2.92              | 405                | 387                |
|   | 27 ( 216)     |           | 18.2                | 18.0                | 29.4                 | 24.5                 | 250                 | 236                 | 847                | 349                | 3.29              | 467                | 483                |
|   | 28 ( 211)     |           | 14.1                | 15.6                | 17.5                 | 16.7                 | 215                 | 228                 | 855                | 354                | 3.21              | 410                | 397                |
|   | 29 ( 211)     |           | 14.6                | 14.0                | 17.7                 | 17.6                 | 255                 | 266                 | 886                | 368                | 3.13              | 441                | 423                |
|   | 30 ( 224)     |           | 15.8                | 20.0                | 22.1                 | 20.8                 | 252                 | 192                 | 880                | 360                | 3.18              | 454                | 452                |
|   | Mean (210.4)  |           | 15.56               | 16.62               | 21.52                | 20.62                | 246.4               | 227.0               | 885.2              | 355.4              | 3.146             | 435.4              | 428.4              |
|   | +S.D. ( 12.6) |           | 1.60                | 2.37                | 4.84                 | 3.46                 | 18.0                | 27.5                | 43.9               | 8.8                | 0.139             | 27.1               | 39.6               |
| Polyoxyethylene p-nonylphenyl ether<br>200 (mg/kg/day)  |               |           |                     |                     |                      |                      |                     |                     |                    |                    |                   |                    |                    |
|   | 36 ( 216)     |           | 14.6                | 18.9                | 21.5                 | 16.9                 | 206                 | 211                 | 949                | 392                | 3.10              | 412                | 396                |
|   | 37 ( 198)     |           | 16.7                | 18.4                | 26.9                 | 21.9                 | 163                 | 201                 | 926                | 433                | 3.17              | 482                | 477                |
|   | 38 ( 244)     |           | 14.5                | 17.3                | 20.0                 | 22.9                 | 196                 | 212                 | 761                | 387                | 3.32              | 458                | 461                |
|   | 39 ( 183)     |           | 20.4                | 19.8                | 16.2                 | 26.0                 | 164                 | 279                 | 991                | 403                | 3.15              | 414                | 385                |
|   | 40 ( 213)     |           | 17.6                | 18.5                | 16.6                 | 20.4                 | 183                 | 190                 | 779                | 377                | 3.22              | 421                | 431                |
|   | Mean (210.8)  |           | 16.76               | 18.58               | 20.24                | 21.62                | 182.4               | 218.6               | 881.2              | 398.4              | 3.192             | 437.4              | 430.0              |
|   | +S.D. ( 22.8) |           | 2.44                | 0.90                | 4.35                 | 3.34                 | 19.1                | 34.9                | 104.3              | 21.5               | 0.083             | 31.1               | 39.8               |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |               |           |                     |                     |                      |                      |                     |                     |                    |                    |                   |                    |                    |
|   | 56 ( 235)     |           | 13.3                | 11.8                | 13.4                 | 11.1                 | 242                 | 187                 | 758                | 355                | 3.19              | 410                | 400                |
|   | 57 ( 216)     |           | 15.1                | 15.7                | 14.8                 | 24.5                 | 172                 | 213                 | 858                | 378                | 3.09              | 398                | 384                |
|   | 58 ( 224)     |           | 12.8                | 14.4                | 22.9                 | 20.9                 | 262                 | 200                 | 800                | 350                | 3.30              | 390                | 387                |
|   | 59 ( 214)     |           | 19.3                | 21.0                | 22.4                 | 23.6                 | 220                 | 221                 | 794                | 359                | 3.15              | 374                | 379                |
|   | 60 ( 208)     |           | 15.8                | 17.3                | 17.8                 | 18.1                 | 296                 | 193                 | 856                | 424                | 3.32              | 438                | 457                |
|   | Mean (219.4)  |           | 15.26               | 16.04               | 18.26                | 19.64                | 238.4               | 202.8               | 813.2              | 373.2              | 3.210             | 402.0              | 401.4              |
|   | +S.D. ( 10.4) |           | 2.58                | 3.43                | 4.31                 | 5.39                 | 46.5                | 14.0                | 43.1               | 30.3               | 0.098             | 24.0               | 32.0               |

| Group   | Anim.No.      | BW<br>(g) | Adre.R<br>mg/100gBW | Adre.L<br>mg/100gBW | Ovary.R<br>mg/100gBW | Ovary.L<br>mg/100gBW | Thymus<br>mg/100gBW | Spleen<br>mg/100gBW | Brain<br>mg/100gBW | Heart<br>mg/100gBW | Liver<br>g/100gBW | Kid.R<br>mg/100gBW | Kid.L<br>mg/100gBW |
|---|---------------|-----------|---------------------|---------------------|----------------------|----------------------|---------------------|---------------------|--------------------|--------------------|-------------------|--------------------|--------------------|
| Control   |               |           |                     |                     |                      |                      |                     |                     |                    |                    |                   |                    |                    |
|   | 11 ( 228)     |           | 14.2                | 12.5                | 20.4                 | 24.8                 | 172                 | 254                 | 811                | 383                | 3.02              | 421                | 431                |
|   | 12 ( 226)     |           | 11.2                | 11.7                | 9.7                  | 16.0                 | 164                 | 215                 | 792                | 330                | 2.74              | 396                | 400                |
|   | 13 ( 256)     |           | 14.0                | 14.2                | 19.6                 | 20.2                 | 207                 | 224                 | 743                | 349                | 3.34              | 414                | 423                |
|   | 14 ( 228)     |           | 10.7                | 13.2                | 22.5                 | 19.6                 | 152                 | 250                 | 815                | 374                | 2.86              | 414                | 401                |
|   | 15 ( 221)     |           | 11.5                | 13.5                | 21.3                 | 18.6                 | 175                 | 224                 | 895                | 334                | 2.78              | 445                | 442                |
|   | Mean (231.8)  |           | 12.32               | 13.02               | 18.70                | 19.84                | 174.0               | 233.4               | 811.2              | 354.0              | 2.948             | 418.0              | 419.4              |
|   | +S.D. ( 13.8) |           | 1.65                | 0.96                | 5.15                 | 3.20                 | 20.5                | 17.4                | 54.9               | 23.7               | 0.244             | 17.7               | 18.5               |
| Polyoxyethylene p-nonylphenyl ether<br>1000 (mg/kg/day) |               |           |                     |                     |                      |                      |                     |                     |                    |                    |                   |                    |                    |
|   | 51 ( 210)     |           | 14.6                | 18.8                | 17.7                 | 17.7                 | 170                 | 204                 | 872                | 402                | 2.76              | 426                | 418                |
|   | 52 ( 221)     |           | 14.7                | 15.0                | 16.2                 | 14.3                 | 175                 | 162                 | 840                | 367                | 2.95              | 425                | 424                |
|   | 53 ( 205)     |           | 16.7                | 17.9                | 25.5                 | 20.1                 | 146                 | 247                 | 919                | 376                | 3.02              | 407                | 388                |
|   | 54 ( 210)     |           | 17.2                | 17.4                | 26.9                 | 22.7                 | 238                 | 193                 | 865                | 383                | 2.85              | 397                | 383                |
|   | 55 ( 235)     |           | 14.2                | 13.1                | 27.3                 | 20.2                 | 209                 | 231                 | 783                | 359                | 3.11              | 411                | 381                |
|   | Mean (216.2)  |           | 15.48               | 16.44               | 22.72                | 19.00                | 187.6               | 207.4               | 855.8              | 377.4              | 2.938             | 413.2              | 398.8              |
|   | +S.D. ( 12.0) |           | 1.37                | 2.34                | 5.34                 | 3.17                 | 36.0                | 33.2                | 49.7               | 16.5               | 0.138             | 12.3               | 20.5               |

# Histopathological Findings

## Grade

- : No abnormal changes
- + : Very slight
- + : Slight
- ++ : Moderate
- +++ : Marked
- P : Non-graded change
- U : Unexamined
- N : Negative

| Findings                                 | Group            | Control |   |   |   |    | Polyoxyethylene p-nonylphenyl ether |     |      |    |    |    |    |  |
|--|------------------|---------|---|---|---|----|-------------------------------------|-----|------|----|----|----|----|--|
|  | Dose (mg/kg/day) |         |   |   |   |    | 20                                  | 200 | 1000 |    |    |    |    |  |
|  | Animal No.       | 6       | 7 | 8 | 9 | 10 |                                     |     | 46   | 47 | 48 | 49 | 50 |  |
| Heart                                    |                  |         |   |   |   |    |                                     |     |      |    |    |    |    |  |
| Myocardial degeneration, focal           |                  | -       | - | - | - | +  |                                     |     | -    | -  | -  | -  | -  |  |
| Spleen                                   |                  |         |   |   |   |    |                                     |     |      |    |    |    |    |  |
| Extramedullary hematopoiesis             |                  | -       | + | + | - | -  |                                     |     | +    | +  | +  | +  | -  |  |
| Thymus                                   |                  | -       | - | - | - | -  |                                     |     | -    | -  | -  | -  | -  |  |
| Femoral bone marrow                      |                  | -       | - | - | - | -  |                                     |     | -    | -  | -  | -  | -  |  |
| Sternal bone marrow                      |                  | -       | - | - | - | -  |                                     |     | -    | -  | -  | -  | -  |  |
| Lymph node (Mesenteric)                  |                  | -       | - | - | - | -  |                                     |     | -    | -  | -  | -  | -  |  |
| Lymph node (Submandibular)               |                  |         |   |   |   |    |                                     |     |      |    |    |    |    |  |
| Hyperplasia, plasma cell                 |                  | -       | + | - | - | -  |                                     |     | -    | -  | -  | -  | +  |  |
| Lung                                     |                  |         |   |   |   |    |                                     |     |      |    |    |    |    |  |
| Foamy cell aggregation, alveolus         |                  | -       | - | - | - | +  |                                     |     | -    | -  | +  | +  | -  |  |
| Trachea                                  |                  |         |   |   |   |    |                                     |     |      |    |    |    |    |  |
| Mononuclear cell infiltration,<br>mucosa |                  | +       | - | - | - | -  |                                     |     | -    | -  | -  | -  | -  |  |
| Bronchus/Bronchiole                      |                  | -       | - | - | - | -  |                                     |     | -    | -  | -  | -  | -  |  |
| Stomach                                  |                  | -       | - | - | - | -  |                                     |     | -    | -  | -  | -  | -  |  |
| Duodenum                                 |                  | -       | - | - | - | -  |                                     |     | -    | -  | -  | -  | -  |  |
| Jejunum                                  |                  | -       | - | - | - | -  |                                     |     | -    | -  | -  | -  | -  |  |
| Ileum                                    |                  | -       | - | - | - | -  |                                     |     | -    | -  | -  | -  | -  |  |
| Cecum                                    |                  | -       | - | - | - | -  |                                     |     | -    | -  | -  | -  | -  |  |
| Colon                                    |                  | -       | - | - | - | -  |                                     |     | -    | -  | -  | -  | -  |  |
| Rectum                                   |                  | -       | - | - | - | -  |                                     |     | -    | -  | -  | -  | -  |  |
| Liver                                    |                  |         |   |   |   |    |                                     |     |      |    |    |    |    |  |
| Mononuclear cell infiltration            |                  | +       | + | + | - | -  |                                     |     | +    | +  | +  | +  | +  |  |
| Kidney                                   |                  |         |   |   |   |    |                                     |     |      |    |    |    |    |  |
| Eosinophilic body, renal tubule          |                  | -       | + | + | - | +  |                                     |     | +    | +  | +  | -  | +  |  |
| Mineralization, renal tubule             |                  | -       | - | + | - | +  |                                     |     | -    | -  | -  | -  | -  |  |
| Basophilic change, renal tubule          |                  | -       | - | - | - | -  |                                     |     | +    | -  | -  | -  | +  |  |

| Findings                                | Group      | Control          |    |   |   |    | Polyoxyethylene p-nonylphenyl ether |     |      |    |    |    |    |  |
|---|------------|------------------|----|---|---|----|-------------------------------------|-----|------|----|----|----|----|--|
|   | Animal No. | Dose (mg/kg/day) |    |   |   |    | 20                                  | 200 | 1000 |    |    |    |    |  |
|   |            | 6                | 7  | 8 | 9 | 10 |                                     |     | 46   | 47 | 48 | 49 | 50 |  |
| Kidney                                  |            |                  |    |   |   |    |                                     |     |      |    |    |    |    |  |
| Hyaline cast, dilated tubule            |            | -                | -  | - | - | -  |                                     |     | -    | -  | +  | -  | -  |  |
| Mononuclear cell infiltration           |            | -                | -  | - | + | +  |                                     |     | -    | -  | -  | -  | -  |  |
| Urinary bladder                         |            | -                | -  | - | - | -  |                                     |     | -    | -  | -  | -  | -  |  |
| Testis                                  |            |                  |    |   |   |    |                                     |     |      |    |    |    |    |  |
| Atrophy, seminiferous tubule, bilateral |            | -                | ++ | - | - | -  |                                     |     | -    | -  | -  | -  | -  |  |
| Epididymis                              |            |                  |    |   |   |    |                                     |     |      |    |    |    |    |  |
| Absence, sperm, unilateral              |            | -                | P  | - | - | -  |                                     |     | -    | -  | -  | -  | -  |  |
| Seminal vesicle                         |            | -                | -  | - | - | -  |                                     |     | -    | -  | -  | -  | -  |  |
| Prostate                                |            | -                | -  | - | - | -  |                                     |     | -    | -  | -  | -  | -  |  |
| Pituitary                               |            | -                | -  | - | - | -  |                                     |     | -    | -  | -  | -  | -  |  |
| Adrenal                                 |            |                  |    |   |   |    |                                     |     |      |    |    |    |    |  |
| Cyst, cortex                            |            | -                | -  | - | - | -  |                                     |     | +    | -  | -  | -  | -  |  |
| Hypertrophy, cortical cell, focal       |            | -                | -  | - | + | +  |                                     |     | -    | -  | +  | +  | -  |  |
| Thyroid                                 |            |                  |    |   |   |    |                                     |     |      |    |    |    |    |  |
| Ultimobranchial body                    |            | -                | -  | P | - | P  |                                     |     | P    | P  | -  | -  | -  |  |
| Parathyroid                             |            | -                | -  | - | - | -  |                                     |     | -    | -  | -  | -  | -  |  |
| Cerebrum                                |            | -                | -  | - | - | -  |                                     |     | -    | -  | -  | -  | -  |  |
| Cerebellum                              |            | -                | -  | - | - | -  |                                     |     | -    | -  | -  | -  | -  |  |
| Sciatic nerve                           |            | -                | -  | - | - | -  |                                     |     | -    | -  | -  | -  | -  |  |
| Brain stem                              |            | -                | -  | - | - | -  |                                     |     | -    | -  | -  | -  | -  |  |
| Spinal cord (Thoracic)                  |            | -                | -  | - | - | -  |                                     |     | -    | -  | -  | -  | -  |  |
| Eyeball (Optic n.)                      |            | -                | -  | - | - | -  |                                     |     | -    | -  | -  | -  | -  |  |
| Harderian gland                         |            | -                | -  | - | - | -  |                                     |     | -    | -  | -  | -  | -  |  |
| Femur                                   |            |                  |    |   |   |    |                                     |     |      |    |    |    |    |  |
| Brown pigment, periosteum               |            | -                | -  | + | - | -  |                                     |     | +    | -  | -  | -  | +  |  |
| Sternum                                 |            | -                | -  | - | - | -  |                                     |     | -    | -  | -  | -  | -  |  |

| Findings                                   | Group            | Control    |    |    |    |    | Polyoxyethylene p-nonylphenyl ether |     |      |    |    |    |    |    |
|--|------------------|------------|----|----|----|----|-------------------------------------|-----|------|----|----|----|----|----|
|  | Dose (mg/kg/day) |            |    |    |    |    | 20                                  | 200 | 1000 |    |    |    |    |    |
|  |                  | Animal No. | 16 | 17 | 18 | 19 |                                     |     | 20   | 56 | 57 | 58 | 59 | 60 |
| Heart                                      |                  |            |    |    |    |    |                                     |     |      |    |    |    |    |    |
| Myocardial degeneration, focal             |                  | -          | -  | -  | -  | +  |                                     |     |      | -  | -  | -  | -  | -  |
| Spleen                                     |                  |            |    |    |    |    |                                     |     |      |    |    |    |    |    |
| Extramedullary hematopoiesis               |                  | -          | +  | -  | -  | -  |                                     |     |      | -  | -  | -  | -  | +  |
| Thymus                                     |                  | -          | -  | -  | -  | -  |                                     |     |      | -  | -  | -  | -  | -  |
| Femoral bone marrow                        |                  | -          | -  | -  | -  | -  |                                     |     |      | -  | -  | -  | -  | -  |
| Sternal bone marrow                        |                  | -          | -  | -  | -  | -  |                                     |     |      | -  | -  | -  | -  | -  |
| Lymph node (Mesenteric)                    |                  | -          | -  | -  | -  | -  |                                     |     |      | -  | -  | -  | -  | -  |
| Lymph node (Submandibular)                 |                  | -          | -  | -  | -  | -  |                                     |     |      | -  | -  | -  | -  | -  |
| Hyperplasia, plasma cell                   |                  | -          | -  | -  | -  | -  |                                     |     |      | -  | -  | +  | -  | -  |
| Lung                                       |                  | -          | -  | -  | -  | -  |                                     |     |      | -  | -  | -  | -  | -  |
| Trachea                                    |                  | -          | -  | -  | -  | -  |                                     |     |      | -  | -  | -  | -  | -  |
| Bronchus/Bronchiole                        |                  | -          | -  | -  | -  | -  |                                     |     |      | -  | -  | -  | -  | -  |
| Stomach                                    |                  | -          | -  | -  | -  | -  |                                     |     |      | -  | -  | -  | -  | -  |
| Duodenum                                   |                  | -          | -  | -  | -  | -  |                                     |     |      | -  | -  | -  | -  | -  |
| Jejunum                                    |                  | -          | -  | -  | -  | -  |                                     |     |      | -  | -  | -  | -  | -  |
| Ileum                                      |                  | -          | -  | -  | -  | -  |                                     |     |      | -  | -  | -  | -  | -  |
| Cecum                                      |                  | -          | -  | -  | -  | -  |                                     |     |      | -  | -  | -  | -  | -  |
| Colon                                      |                  | -          | -  | -  | -  | -  |                                     |     |      | -  | -  | -  | -  | -  |
| Rectum                                     |                  | -          | -  | -  | -  | -  |                                     |     |      | -  | -  | -  | -  | -  |
| Liver                                      |                  |            |    |    |    |    |                                     |     |      |    |    |    |    |    |
| Microvacuolization, hepatocyte, periportal |                  | +          | +  | -  | -  | +  |                                     |     |      | -  | +  | -  | -  | -  |
| Mononuclear cell infiltration              |                  | +          | +  | +  | +  | -  |                                     |     |      | +  | +  | -  | +  | +  |
| Kidney                                     |                  |            |    |    |    |    |                                     |     |      |    |    |    |    |    |
| Mineralization, renal tubule               |                  | -          | +  | -  | +  | -  |                                     |     |      | +  | +  | +  | -  | -  |
| Basophilic change, renal tubule            |                  | -          | +  | -  | +  | +  |                                     |     |      | +  | +  | +  | -  | -  |

| Findings                          | Group            | Control |    |    |    |    | Polyoxyethylene p-nonylphenyl ether |     |      |    |    |    |    |
|-----------------------------------|------------------|---------|----|----|----|----|-------------------------------------|-----|------|----|----|----|----|
|                                   | Dose (mg/kg/day) |         |    |    |    |    | 20                                  | 200 | 1000 |    |    |    |    |
|                                   | Animal No.       | 16      | 17 | 18 | 19 | 20 |                                     |     | 56   | 57 | 58 | 59 | 60 |
| Kidney                            |                  |         |    |    |    |    |                                     |     |      |    |    |    |    |
| Mononuclear cell infiltration     |                  | -       | -  | -  | -  | -  |                                     |     | -    | -  | +  | -  | +  |
| Urinary bladder                   |                  | -       | -  | -  | -  | -  |                                     |     | -    | -  | -  | -  | -  |
| Ovary                             |                  |         |    |    |    |    |                                     |     |      |    |    |    |    |
| Mononuclear cell infiltration     |                  | -       | -  | -  | -  | -  |                                     |     | -    | -  | -  | +  | -  |
| Uterus                            |                  |         |    |    |    |    |                                     |     |      |    |    |    |    |
| Dilatation, lumen                 |                  | -       | -  | -  | -  | -  |                                     |     | -    | -  | -  | -  | +  |
| Vagina                            |                  | -       | -  | -  | -  | -  |                                     |     | -    | -  | -  | -  | -  |
| Pituitary                         |                  | -       | -  | -  | -  | -  |                                     |     | -    | -  | -  | -  | -  |
| Adrenal                           |                  |         |    |    |    |    |                                     |     |      |    |    |    |    |
| Hypertrophy, cortical cell, focal |                  | -       | -  | -  | +  | +  |                                     |     | +    | -  | -  | -  | -  |
| Thyroid                           |                  |         |    |    |    |    |                                     |     |      |    |    |    |    |
| Ultimobranchial body              |                  | P       | P  | -  | P  | -  |                                     |     | -    | -  | -  | -  | -  |
| Parathyroid                       |                  | -       | -  | -  | -  | -  |                                     |     | -    | -  | -  | -  | -  |
| Cerebrum                          |                  | -       | -  | -  | -  | -  |                                     |     | -    | -  | -  | -  | -  |
| Cerebellum                        |                  | -       | -  | -  | -  | -  |                                     |     | -    | -  | -  | -  | -  |
| Sciatic nerve                     |                  | -       | -  | -  | -  | -  |                                     |     | -    | -  | -  | -  | -  |
| Brain stem                        |                  | -       | -  | -  | -  | -  |                                     |     | -    | -  | -  | -  | -  |
| Spinal cord (Thoracic)            |                  | -       | -  | -  | -  | -  |                                     |     | -    | -  | -  | -  | -  |
| Eyeball (Optic n.)                |                  | -       | -  | -  | -  | -  |                                     |     | -    | -  | -  | -  | -  |
| Harderian gland                   |                  | -       | -  | -  | -  | -  |                                     |     | -    | -  | -  | -  | -  |
| Femur                             |                  |         |    |    |    |    |                                     |     |      |    |    |    |    |
| Brown pigment, periosteum         |                  | -       | -  | -  | -  | -  |                                     |     | -    | -  | -  | +  | -  |
| Sternum                           |                  | -       | -  | -  | -  | -  |                                     |     | -    | -  | -  | -  | -  |



| Findings                                      | Group            |  | Control |   |   |   |   | Polyoxyethylene p-nonylphenyl ether |     |      |    |    |    |    |
|---|------------------|--|---------|---|---|---|---|-------------------------------------|-----|------|----|----|----|----|
|   | Dose (mg/kg/day) |  |         |   |   |   |   | 20                                  | 200 | 1000 |    |    |    |    |
|   | Animal No.       |  | 1       | 2 | 3 | 4 | 5 |                                     |     | 41   | 42 | 43 | 44 | 45 |
| Heart   |                  |  | -       | - | - | - | - |                                     |     | -    | -  | -  | -  | -  |
| Spleen  |                  |  |         |   |   |   |   |                                     |     |      |    |    |    |    |
| Extramedullary hematopoiesis                  |                  |  | -       | - | - | + | - |                                     |     | -    | +  | -  | -  | +  |
| Thymus  |                  |  | -       | - | - | - | - |                                     |     | -    | -  | -  | -  | -  |
| Femoral bone marrow                           |                  |  | -       | - | - | - | - |                                     |     | -    | -  | -  | -  | -  |
| Sternal bone marrow                           |                  |  | -       | - | - | - | - |                                     |     | -    | -  | -  | -  | -  |
| Lymph node (Mesenteric)                       |                  |  | -       | - | - | - | - |                                     |     | -    | -  | -  | -  | -  |
| Lymph node (Submandibular)                    |                  |  | -       | - | - | - | - |                                     |     | -    | -  | -  | -  | -  |
| Lung  |                  |  |         |   |   |   |   |                                     |     |      |    |    |    |    |
| Hemorrhage, focal                             |                  |  | -       | - | - | - | - |                                     |     | -    | -  | +  | -  | -  |
| Osseous metaplasia                            |                  |  | -       | - | - | - | + |                                     |     | -    | -  | -  | -  | -  |
| Foamy cell aggregation, alveolus              |                  |  | +       | - | - | + | - |                                     |     | -    | -  | -  | -  | -  |
| Mineralization, pulmonary artery              |                  |  | +       | - | - | - | - |                                     |     | -    | -  | +  | -  | -  |
| Trachea                                       |                  |  | -       | - | - | - | - |                                     |     | -    | -  | -  | -  | -  |
| Bronchus/Bronchiole                           |                  |  | -       | - | - | - | - |                                     |     | -    | -  | -  | -  | -  |
| Stomach                                       |                  |  | -       | - | - | - | - |                                     |     | -    | -  | -  | -  | -  |
| Duodenum                                      |                  |  | -       | - | - | - | - |                                     |     | -    | -  | -  | -  | -  |
| Jejunum                                       |                  |  | -       | - | - | - | - |                                     |     | -    | -  | -  | -  | -  |
| Ileum   |                  |  | -       | - | - | - | - |                                     |     | -    | -  | -  | -  | -  |
| Cecum   |                  |  | -       | - | - | - | - |                                     |     | -    | -  | -  | -  | -  |
| Colon   |                  |  | -       | - | - | - | - |                                     |     | -    | -  | -  | -  | -  |
| Rectum  |                  |  | -       | - | - | - | - |                                     |     | -    | -  | -  | -  | -  |
| Liver   |                  |  |         |   |   |   |   |                                     |     |      |    |    |    |    |
| Microvacuolization, hepatocyte,<br>periportal |                  |  | -       | - | - | + | - |                                     |     | -    | -  | -  | -  | -  |

| Findings                        | Group            | Control |   |   |   |   | Polyoxyethylene p-nonylphenyl ether |     |      |    |    |    |    |  |  |
|---------------------------------|------------------|---------|---|---|---|---|-------------------------------------|-----|------|----|----|----|----|--|--|
|                                 | Dose (mg/kg/day) |         |   |   |   |   | 20                                  | 200 | 1000 |    |    |    |    |  |  |
|                                 | Animal No.       | 1       | 2 | 3 | 4 | 5 |                                     |     | 41   | 42 | 43 | 44 | 45 |  |  |
| Liver                           |                  |         |   |   |   |   |                                     |     |      |    |    |    |    |  |  |
| Mononuclear cell infiltration   |                  | +       | + | + | + | - |                                     |     | +    | +  | -  | +  | -  |  |  |
| Necrosis, focal                 |                  | -       | - | - | - | - |                                     |     | -    | +  | -  | -  | -  |  |  |
| Kidney                          |                  |         |   |   |   |   |                                     |     |      |    |    |    |    |  |  |
| Eosinophilic body, renal tubule |                  | -       | + | + | - | + |                                     |     | +    | +  | +  | +  | +  |  |  |
| Basophilic change, renal tubule |                  | -       | - | - | + | - |                                     |     | -    | +  | -  | +  | -  |  |  |
| Urinary bladder                 |                  | -       | - | - | - | - |                                     |     | -    | -  | -  | -  | -  |  |  |
| Testis                          |                  | -       | - | - | - | - |                                     |     | -    | -  | -  | -  | -  |  |  |
| Epididymis                      |                  | -       | - | - | - | - |                                     |     | -    | -  | -  | -  | -  |  |  |
| Seminal vesicle                 |                  | -       | - | - | - | - |                                     |     | -    | -  | -  | -  | -  |  |  |
| Prostate                        |                  |         |   |   |   |   |                                     |     |      |    |    |    |    |  |  |
| Mononuclear cell infiltration   |                  | -       | - | - | - | - |                                     |     | -    | +  | -  | -  | -  |  |  |
| Pituitary                       |                  | -       | - | - | - | - |                                     |     | -    | -  | -  | -  | -  |  |  |
| Adrenal                         |                  | -       | - | - | - | - |                                     |     | -    | -  | -  | -  | -  |  |  |
| Thyroid                         |                  |         |   |   |   |   |                                     |     |      |    |    |    |    |  |  |
| Ectopic thymus                  |                  | -       | - | - | - | - |                                     |     | -    | -  | -  | -  | P  |  |  |
| Ultimobranchial body            |                  | P       | - | P | - | P |                                     |     | P    | -  | -  | -  | -  |  |  |
| Parathyroid                     |                  | -       | - | - | - | - |                                     |     | -    | -  | U  | -  | -  |  |  |
| Cerebrum                        |                  | -       | - | - | - | - |                                     |     | -    | -  | -  | -  | -  |  |  |
| Cerebellum                      |                  | -       | - | - | - | - |                                     |     | -    | -  | -  | -  | -  |  |  |
| Sciatic nerve                   |                  | -       | - | - | - | - |                                     |     | -    | -  | -  | -  | -  |  |  |
| Brain stem                      |                  | -       | - | - | - | - |                                     |     | -    | -  | -  | -  | -  |  |  |
| Spinal cord (Thoracic)          |                  | -       | - | - | - | - |                                     |     | -    | -  | -  | -  | -  |  |  |
| Eyeball (Optic n.)              |                  | -       | - | - | - | - |                                     |     | -    | -  | -  | -  | -  |  |  |
| Harderian gland                 |                  | -       | - | - | - | - |                                     |     | -    | -  | -  | -  | -  |  |  |
| Femur                           |                  |         |   |   |   |   |                                     |     |      |    |    |    |    |  |  |
| Brown pigment, periosteum       |                  | -       | + | + | + | + |                                     |     | +    | +  | +  | +  | +  |  |  |

| Findings               | Group            | Control |   |   |   |   | Polyoxyethylene p-nonylphenyl ether |     |      |    |    |    |    |
|------------------------|------------------|---------|---|---|---|---|-------------------------------------|-----|------|----|----|----|----|
|                        | Dose (mg/kg/day) |         |   |   |   |   | 20                                  | 200 | 1000 |    |    |    |    |
|                        | Animal No.       | 1       | 2 | 3 | 4 | 5 |                                     |     | 41   | 42 | 43 | 44 | 45 |
| Femur                  |                  |         |   |   |   |   |                                     |     |      |    |    |    |    |
| Hemorrhage, periosteum |                  | -       | - | + | + | - |                                     |     | +    | +  | -  | -  | -  |
| Sternum                |                  | -       | - | - | - | - |                                     |     | -    | -  | -  | -  | -  |

| Findings                         | Group      | Control          |          |          |          |          | Polyoxyethylene p-nonylphenyl ether |     |      |          |          |          |          |          |          |  |
|----------------------------------|------------|------------------|----------|----------|----------|----------|-------------------------------------|-----|------|----------|----------|----------|----------|----------|----------|--|
|                                  | Animal No. | Dose (mg/kg/day) |          |          |          |          | 20                                  | 200 | 1000 |          |          |          |          |          |          |  |
|                                  |            | 11               | 12       | 13       | 14       | 15       |                                     |     | 51   | 52       | 53       | 54       | 55       |          |          |  |
| Heart                            |            |                  |          |          |          |          |                                     |     |      |          |          |          |          |          |          |  |
| Mononuclear cell infiltration    |            | <u>+</u>         | -        | -        | -        | -        |                                     |     |      | -        | -        | -        | -        | -        | -        |  |
| Spleen                           |            |                  |          |          |          |          |                                     |     |      |          |          |          |          |          |          |  |
| Extramedullary hematopoiesis     |            | -                | <u>+</u> | <u>+</u> | <u>+</u> | -        |                                     |     |      | -        | -        | -        | -        | -        | -        |  |
| Thymus                           |            | -                | -        | -        | -        | -        |                                     |     |      | -        | -        | -        | -        | -        | -        |  |
| Femoral bone marrow              |            | -                | -        | -        | -        | -        |                                     |     |      | -        | -        | -        | -        | -        | -        |  |
| Sternal bone marrow              |            | -                | -        | -        | -        | -        |                                     |     |      | -        | -        | -        | -        | -        | -        |  |
| Lymph node (Mesenteric)          |            | -                | -        | -        | -        | -        |                                     |     |      | -        | -        | -        | -        | -        | -        |  |
| Lymph node (Submandibular)       |            | -                | -        | -        | -        | -        |                                     |     |      | -        | -        | -        | -        | -        | -        |  |
| Lung                             |            |                  |          |          |          |          |                                     |     |      |          |          |          |          |          |          |  |
| Osseous metaplasia               |            | -                | -        | -        | -        | -        |                                     |     |      | -        | -        | -        | -        | -        | <u>+</u> |  |
| Foamy cell aggregation, alveolus |            | -                | -        | -        | -        | -        |                                     |     |      | -        | <u>+</u> | -        | <u>+</u> | -        | -        |  |
| Mineralization, pulmonary artery |            | -                | -        | -        | -        | -        |                                     |     |      | -        | <u>+</u> | -        | -        | -        | -        |  |
| Inflammation, perivascular       |            | -                | -        | -        | -        | -        |                                     |     |      | -        | -        | -        | <u>+</u> | -        | -        |  |
| Trachea                          |            | -                | -        | -        | -        | -        |                                     |     |      | -        | -        | -        | -        | -        | -        |  |
| Bronchus/Bronchiole              |            | -                | -        | -        | -        | -        |                                     |     |      | -        | -        | -        | -        | -        | -        |  |
| Stomach                          |            | -                | -        | -        | -        | -        |                                     |     |      | -        | -        | -        | -        | -        | -        |  |
| Duodenum                         |            | -                | -        | -        | -        | -        |                                     |     |      | -        | -        | -        | -        | -        | -        |  |
| Jejunum                          |            | -                | -        | -        | -        | -        |                                     |     |      | -        | -        | -        | -        | -        | -        |  |
| Ileum                            |            | -                | -        | -        | -        | -        |                                     |     |      | -        | -        | -        | -        | -        | -        |  |
| Cecum                            |            | -                | -        | -        | -        | -        |                                     |     |      | -        | -        | -        | -        | -        | -        |  |
| Colon                            |            | -                | -        | -        | -        | -        |                                     |     |      | -        | -        | -        | -        | -        | -        |  |
| Rectum                           |            | -                | -        | -        | -        | -        |                                     |     |      | -        | -        | -        | -        | -        | -        |  |
| Liver                            |            |                  |          |          |          |          |                                     |     |      |          |          |          |          |          |          |  |
| Mononuclear cell infiltration    |            | <u>+</u>         | <u>+</u> | <u>+</u> | <u>+</u> | <u>+</u> |                                     |     |      | <u>+</u> | <u>+</u> | <u>+</u> | -        | <u>+</u> | <u>+</u> |  |
| Necrosis, focal                  |            | -                | -        | -        | -        | <u>+</u> |                                     |     |      | -        | -        | -        | -        | -        | -        |  |

| Findings                          | Group            | Control |    |    |    |    | Polyoxyethylene p-nonylphenyl ether |     |      |    |    |    |    |
|-----------------------------------|------------------|---------|----|----|----|----|-------------------------------------|-----|------|----|----|----|----|
|                                   | Dose (mg/kg/day) |         |    |    |    |    | 20                                  | 200 | 1000 |    |    |    |    |
|                                   | Animal No.       | 11      | 12 | 13 | 14 | 15 |                                     |     | 51   | 52 | 53 | 54 | 55 |
| Kidney                            |                  |         |    |    |    |    |                                     |     |      |    |    |    |    |
| Mineralization, renal tubule      |                  | -       | +  | -  | -  | -  |                                     |     | -    | -  | -  | -  | -  |
| Urinary bladder                   |                  | -       | -  | -  | -  | -  |                                     |     | -    | -  | -  | -  | -  |
| Ovary                             |                  | -       | -  | -  | -  | -  |                                     |     | -    | -  | -  | -  | -  |
| Uterus                            |                  | -       | -  | -  | -  | -  |                                     |     | -    | -  | -  | -  | -  |
| Vagina                            |                  | -       | -  | -  | -  | -  |                                     |     | -    | -  | -  | -  | -  |
| Pituitary                         |                  | -       | -  | -  | -  | -  |                                     |     | -    | -  | -  | -  | -  |
| Adrenal                           |                  |         |    |    |    |    |                                     |     |      |    |    |    |    |
| Hypertrophy, cortical cell, focal |                  | -       | -  | -  | -  | +  |                                     |     | -    | +  | -  | -  | -  |
| Thyroid                           |                  |         |    |    |    |    |                                     |     |      |    |    |    |    |
| Ectopic thymus                    |                  | -       | P  | -  | -  | -  |                                     |     | -    | -  | -  | -  | -  |
| Ultimobranchial body              |                  | -       | -  | -  | -  | -  |                                     |     | P    | P  | -  | -  | P  |
| Parathyroid                       |                  | U       | -  | -  | -  | -  |                                     |     | -    | -  | -  | -  | -  |
| Cerebrum                          |                  | -       | -  | -  | -  | -  |                                     |     | -    | -  | -  | -  | -  |
| Cerebellum                        |                  | -       | -  | -  | -  | -  |                                     |     | -    | -  | -  | -  | -  |
| Sciatic nerve                     |                  | -       | -  | -  | -  | -  |                                     |     | -    | -  | -  | -  | -  |
| Brain stem                        |                  | -       | -  | -  | -  | -  |                                     |     | -    | -  | -  | -  | -  |
| Spinal cord (Thoracic)            |                  | -       | -  | -  | -  | -  |                                     |     | -    | -  | -  | -  | -  |
| Eyeball (Optic n.)                |                  | -       | -  | -  | -  | -  |                                     |     | -    | -  | -  | -  | -  |
| Harderian gland                   |                  | -       | -  | -  | -  | -  |                                     |     | -    | -  | -  | -  | -  |
| Femur                             |                  |         |    |    |    |    |                                     |     |      |    |    |    |    |
| Brown pigment, periosteum         |                  | +       | +  | +  | +  | +  |                                     |     | +    | +  | -  | +  | +  |
| Sternum                           |                  | -       | -  | -  | -  | -  |                                     |     | -    | -  | -  | -  | -  |