

最 終 報 告 書

ピグメントエロー-14 のラットを用いた
2 週間回復性観察を含む 28 日間反復経口投与毒性試験



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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。



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2 週間回復性観察を含む 28 日間反復経口投与毒性試験

B-4650

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陳 述 書

試 験 番 号 ： B-4650

試 験 表 題 ： ピグメントエロー-14 のラットを用いた 2 週間回復性観察を含む 28 日間反復
経口投与毒性試験

本試験は以下に示す基準に準拠して実施したものであります。

- ・ “OECD Principles of Good Laboratory Practice” (as revised 1997)



信頼性保証陳述書

試験番号 : B-4650

試験表題 : ピグメントエロー-14 のラットを用いた 2 週間回復性観察を含む
28 日間反復経口投与毒性試験

本試験は以下に示す基準に準拠して実施されたことを保証致します。

- ・ “OECD Principles of Good Laboratory Practice” (as revised in 1997)

2001 年 5 月 30 日

調査日及び報告日

調 査 の 対 象	調 査 日	試験責任者及び運営管理者への報告日
試験計画書	2000 年 11 月 20 日	2000 年 11 月 21 日
試験計画書情報入力	2000 年 11 月 22 日	2000 年 11 月 24 日
作業予定表	2000 年 11 月 22 日	2000 年 11 月 24 日
動物入荷	2000 年 11 月 22 日	2000 年 11 月 24 日
被験物質調製指示シート	2000 年 11 月 24 日	2000 年 11 月 24 日
被験液の濃度・均一性確認	2000 年 11 月 24 日	2000 年 11 月 27 日
検疫 (馴化) ・群構成・飼育管理	2000 年 11 月 27 日	2000 年 11 月 28 日
体重・摂餌量測定・投与・症状観察・飼育管理	2000 年 11 月 29 日	2000 年 11 月 30 日
被験物質 (調製・保存)	2000 年 12 月 1 日	2000 年 12 月 4 日
詳細な一般状態の観察・飼育管理	2000 年 12 月 5 日	2000 年 12 月 5 日
尿検査	2000 年 12 月 22 日	2000 年 12 月 25 日
尿検査	2000 年 12 月 23 日	2000 年 12 月 25 日
摂水量測定・飼育管理	2000 年 12 月 23 日	2000 年 12 月 25 日
機能検査・握力測定・自発運動量測定	2000 年 12 月 26 日	2000 年 12 月 27 日
採血・剖検	2000 年 12 月 27 日	2000 年 12 月 28 日

調 査 の 対 象	調 査 日	試験責任者及び運営管理者への報告日
血液学検査・血液化学検査	2000 年 12 月 27 日	2000 年 12 月 28 日
体重・摂餌量測定・飼育管理	2000 年 12 月 29 日	2001 年 1 月 5 日
病理組織学検査	2001 年 1 月 18 日	2001 年 1 月 19 日
病理組織学検査	2001 年 1 月 22 日	2001 年 1 月 22 日
病理組織学検査	2001 年 1 月 24 日	2001 年 1 月 24 日
中間報告書・図・表・付表	2001 年 3 月 7 日	2001 年 3 月 7 日
最終報告書草案	2001 年 3 月 30 日	2001 年 3 月 30 日
生データ・図・表・付表	2001 年 5 月 24 日	2001 年 5 月 24 日
再調査	2001 年 5 月 29 日	2001 年 5 月 30 日
最終報告書	2001 年 5 月 30 日	2001 年 5 月 30 日

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試験実施概要

1. 試験計画書

試験番号 : B-4650

試験表題 : ピグメントエロー-14 のラットを用いた 2 週間回復性観察を含む 28 日間
反復経口投与毒性試験2. 試験目的 : 被験物質をラットに 28 日間反復経口投与し、その影響を明らかにすると
ともに、その後 2 週間の回復期間を設けて障害の可逆性を調べた。3. 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
〒151-0066 東京都渋谷区西原 2-49-104. 試験受託者 : 株式会社ボゾリサーチセンター
〒156-0042 東京都世田谷区羽根木 1-3-11
[REDACTED]5. 試験実施施設 : 株式会社ボゾリサーチセンター 御殿場研究所
〒412-0039 静岡県御殿場市かまど 1284

6. 被験物質

供給者 : [REDACTED]

被験物質名 : ピグメントエロー-14
(別名 : ベンジジンエロー)

受領日 : 2000 年 9 月 14 日

保存場所 : 御殿場研究所 被験物質保存室及び第 2 研究棟被験物質調製室

7. 試験日程

試験開始日 : 2000 年 11 月 20 日

動物入荷日 : 2000 年 11 月 22 日

実験開始日（投与開始日）

： 2000 年 11 月 29 日 （雄・雌）
 投与終了日 ： 2000 年 12 月 26 日 （雄・雌）
 投与終了剖検日 ： 2000 年 12 月 27 日 （雄・雌）
 回復終了剖検日 ： 2001 年 1 月 10 日 （雄・雌）

実験終了日（病理学検査終了日）

： 2001 年 2 月 23 日
 試験終了日 ： 2001 年 5 月 30 日

8. 試験責任者 ： 株式会社ボゾリサーチセンター 第2研究部

9. 試験担当者

試験主担当者 :
 臨床検査責任者 :
 病理検査責任者 :
 化学分析責任者 :
 統計解析責任者 :

10. 試験成績の信頼性に影響を及ぼしたと思われる環境要因

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

11. 資料保存

試験計画書（原本）、記録文書、生データ、報告書類（最終報告書の原本を含む）及び標本は株式会社ボゾリサーチセンター 御殿場研究所の資料保存施設に保存する。なお、その期間は最終報告書提出後 10 年間とする。期間終了後の保存については、経済産業省 製品評価技術センターと株式会社ボゾリサーチセンター間で協議し、その処置を決定する。ただし、長期保存に耐えられない生体試料（尿、血漿、血清）については、最終報告書提出後 1 年を経過した時点で廃棄する。

12. 試験責任者の署名又は記名・なつ印

 201 年 5 月 30 日



試験従事者一覧

検疫・馴化

群分け :

被験液の調製 :

投与、一般状態観察、体重・摂餌量測定

詳細な一般状態の観察、機能検査、握力・自発運動量測定

尿検査（摂水量測定を含む）

採血、血液学・血液化学検査

剖検（器官重量測定を含む）

被験液の分析

病理組織学検査

統計解析

要 約

ピグメントエロー-14 の反復投与による変化とその回復性を 7 週齢の Sprague-Dawley 系 SPF ラット [Crj:CD(SD)IGS] を用いて検討した。投与量は 0 (媒体: オリーブ油)、100、300 及び 1000mg/kg/日とし、28 日間強制経口投与した。1 群の動物数は、対照群及び 1000mg/kg 投与群で雌雄各 10 匹、100 及び 300mg/kg 投与群で雌雄各 5 匹とし、このうち対照群と 1000mg/kg 投与群の雌雄各 5 匹については、28 日間の投与後 2 週間の回復期間を設けた。

1. 一般状態

投与期間及び回復期間を通じて、死亡はみられなかった。

被験物質の排泄による黄色調便が、投与 2 日以降全用量群の雌雄全例にみられた。

2. 詳細な一般状態、機能検査、握力及び自発運動量

黄色調便が詳細な一般状態の観察で 1000mg/kg 投与群の雄 1 例にみられた。

3. 体重及び摂餌量

被験物質投与の影響はみられなかった。

4. 尿 (摂水量を含む)、血液及び血液化学検査

被験物質投与の影響はみられなかった。

5. 器官重量、剖検及び病理組織学検査

被験物質投与の影響はみられなかった。

6. 回復試験

黄色調便が投与期間に引き続き 1000mg/kg 回復群の雌雄全例にみられたが、回復 3 日に消失した。

以上の如く、全用量群の雌雄で被験物質の糞中排泄による黄色調便がみられたのみで、毒性的に意義のある変化は認められなかった。したがって、ピグメントエロー-14 の本試験条件下でのラットにおける無影響量は雌雄とも 1000mg/kg/日と推定された。

結 言

経済産業省 製品評価技術センターの依頼により、ピグメントエロー-14 の安全性評価の一環として、ラットを用いた経口投与による 28 日間反復投与毒性試験及び 2 週間回復性試験を実施したので、その成績を報告する。なお、本試験は以下の基準及びガイドラインなどに準拠し、実施した。

- ・ “OECD Principles of Good Laboratory Practice” (as revised 1997)
- ・ “OECD Guideline for Testing of Chemicals 407, Repeated Dose 28-day Oral Toxicity Study in Rodents (1995)”
- ・ 「実験動物の飼養及び保管等に関する基準」
(総理府告示第 6 号、昭和 55 年 3 月 27 日)
- ・ 「動物実験に関する指針」
(財) 日本実験動物学会、昭和 62 年 5 月 22 日)

試験材料及び方法

1. 被験物質及び媒体

1) 被験物質

被験物質は

被 験 物 質 名 : ピグメントエロー-14

(別名: ベンジジンエロー)

ロ ッ ト 番 号

性 状 : やまぶき色粉末

安 定 性 : 冷暗所で安定

保 存 方 法 : 冷暗所 (冷蔵庫内)

保 存 場 所 : 御殿場研究所 被験物質保存室及び第2研究棟被験物質調製室

なお、被験物質約 5g を保存試料として御殿場研究所被験物質保存室に保存し、動物試験終了後の残余の被験物質はすべて試験委託者に返却した。

2) 媒体

名 称 : オリーブ油

規 格 : 日局

ロ ッ ト 番 号 : 0711、0922

メ ー カ ー : 丸石製薬株式会社

保 存 方 法 : 室温

保 存 場 所 : 第2研究棟被験物質調製室

媒体の選択理由 : 被験液の調製法を検討するための予備調製をメノウ乳鉢を用いて行った結果、被験物質は 0.5%メチルセルロース水溶液では馴染まず、これに Tween 80 を加えても改善はみられなかった。一方、オリーブ油では肉眼的に均一な混和液となり、胃ゾンデの使用も問題はなかったことから適当と判断した。

2. 被験液

1) 調製方法

各濃度ごとに被験物質を秤量し、メノウ乳鉢を用いてオリーブ油と混合して、10、30 及び 100mg/mL 液を調製した。

2) 調製頻度

7日に1回以上の頻度で調製した。

3) 保存方法

褐色ガラス瓶に入れて冷蔵（1～8℃）保存した。

4) 安定性

1及び200mg/mL濃度の被験液は、冷蔵（1～8℃）8日間の後室温4時間まで安定（許容範囲：初期値に対して10%以内の減少）であることを株式会社ボゾリサーチセンター 御殿場研究所にて吸光光度法（測定波長422nm）で確認した。

5) 濃度・均一性確認

投与第1週及び投与第4週の投与に用いる各濃度の被験液について株式会社ボゾリサーチセンター 御殿場研究所で吸光光度法（測定波長422nm）により分析した結果、濃度は表示値に対して99.7～103.7%であり、いずれも許容範囲（表示値±10%）内であった。また、変動係数は1.0～3.2%であり、均一性についても許容範囲（CV10%以内）内であった。

3. 試験動物種及び系統の選択理由

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

4. 試験動物

Sprague-Dawley系SPFラット〔Crj:CD(SD)IGS、日本チャールス・リバー株式会社、厚木飼育センター〕の雌雄各42匹^注を6週齢で入手し、当所で7日間検疫・馴化飼育した後、体重増加が順調で一般状態に異常を認めない健康な雌雄各30匹を選び7週齢で試験に供した。投与開始日の体重範囲は、雄で228～256g、雌で171～195gであり、各動物の体重は雌雄ともに平均値±20%（雄：191～287g、雌：148～222g）以内であった。群分け後の余剰動物は、投与7日にエーテル深麻酔で安楽死させた。

^注：注文匹数は雌雄各40匹であったが、実際には雌雄各42匹が納入された。

5. 飼育条件

動物は、温度20～24℃、相対湿度39～60%、換気回数1時間10～15回、照明1日12時間（07：00～19：00）の動物飼育室（飼育室番号：602号室）で、ブラケット式金属製網ケージ（W190×D350×H170mm：リードエンジニアリング株式会社）に1匹ずつ収容し、固

形飼料 CRF-1（放射線滅菌：オリエンタル酵母工業株式会社）及び飲料水（御殿場市営水道水：自動給水装置使用）を自由に摂取させて飼育した。

6. 飼料及び飲料水中の混入物質

飼料及び飲料水中の混入物質の分析に関する報告書を下記の施設から入手し、試験成績に影響のないことを確認して当該報告書を生データ中に保存した。

供試飼料ロットについての分析報告書（財団法人日本食品分析センター）

水道法に準拠する水質の分析報告書（財団法人静岡県生活科学検査センター、年4回）

7. 動物の識別

動物は入荷時に小動物用耳標をつけて個体識別を行った。飼育ケージには、入荷時から群分け前までの間は試験番号、性別及び耳標番号を明記したケージラベルを表示した。群分け後は、群分け前まで使用したケージラベルの裏に投与量ごとに色分けしたラベルをつけ、試験番号、投与経路、投与量、性、動物番号、耳標番号及び剖検予定日を明記し、表示した。ただし、詳細な一般状態の観察、機能検査、握力測定及び自発運動量測定中は、観察者に対して投与の情報を制限（ブラインド）するためケージラベルを裏返して、試験番号、性別及び耳標番号のみを表示した。

8. 群分け

4. 試験動物に示した手順で選択した個体を群分け当日（投与開始の2日前）の体重により層別化し、各群の平均体重ができるだけ均等となるように各群を構成した。個体の割付けはコンピュータを用いたブロック配置法及び無作為抽出法の組合せ（ブロック配置法で必要な群を構成し、試験群及び群内の個体番号を無作為に割当て）により行った。

9. 投与経路、投与期間、投与回数及び回復期間とそれらの選択理由

毒性試験法ガイドラインに準じ、投与経路は経口投与を選択し、投与期間は28日間とした。投与回数は、反復投与試験で一般的に行われている1日1回（7回/週）とした。回復期間は障害の可逆性を検討するのに適当と考えられる2週間（14日間）とし、この間投与を行わなかった。

10. 投与方法

投与容量は 10mL/kg 体重とし、胃ゾンデを用いて強制経口投与した（08：10～12：08 の間）。
 対照群には媒体（オリブ油）を同様に投与した。個体ごとの投与液量は最新の体重を基準に算出した。

11. 投与量及び群構成

投与量は 100、300 及び 1000mg/kg の 3 用量とし、対照群を加えて 4 群とした。1 群当たりの動物を主群では雌雄各 5 匹、回復群では対照群及び高用量群で雌雄各 5 匹とした。群構成を表 1. に示した。

表 1. 群構成表

試験群	投与量 (mg/kg)	濃 度 (mg/mL)	投与容量 (mL/kg)	性	主 群		回 復 群	
					動物数	動物番号	動物数	動物番号
対照群	0	0	10	雄	5	1001～1005	5	1006～1010
				雌	5	1101～1105	5	1106～1110
低用量群	100	10	10	雄	5	2001～2005	—	—
				雌	5	2101～2105	—	—
中用量群	300	30	10	雄	5	3001～3005	—	—
				雌	5	3101～3105	—	—
高用量群	1000	100	10	雄	5	4001～4005	5	4006～4010
				雌	5	4101～4105	5	4106～4110

12. 投与量の設定根拠

先に実施したピグメントエロー-14 のラットを用いた 14 日間反復経口投与毒性予備試験（試験番号：U-2096、投与量：0、40、200 及び 1000mg/kg）¹⁾の結果を基に設定した。すなわち、1000mg/kg 投与群の雄で赤血球数、ヘモグロビン量及びヘマトクリット値に軽度な増加がみられたのみで、明かな毒性変化は認められなかった。このことから、本試験における投与量は毒性試験法ガイドラインの上限である 1000mg/kg を高用量とし、以下公比約 3 で 300 及び 100mg/kg を設定した。

13. 観察及び検査の方法

1) 一般状態の観察

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

なお、試験日は投与開始日を投与1日、投与1～7日を投与第1週、回復開始日（投与期間終了の翌日）を回復1日、回復1～7日を回復第1週として起算し、表示した。

2) 詳細な一般状態の観察

全動物について、投与開始前（投与開始5日前）に1回、投与期間中（投与7、14、21及び28日）及び回復期間（回復7及び14日）は毎週1回、以下の検査を行った。なお、投与期間中の観察は投与2時間後から開始し、観察者に対しては投与量などの情報を制限（ブラインド）し、動物をランダムに配置した状態で行った。

(1) ホームケージ内観察（スコアについては添付資料1参照）

姿勢、痙攣、異常行動

(2) 手に持った観察（スコアについては添付資料2参照）

ホームケージからの取り出し易さ、ハンドリングに対する反応（ハンドリング時の発声を含む）、被毛・皮膚の状態（被毛の汚れ、粗毛、外傷、皮膚の色など）、眼球（眼球突出、眼瞼の開き具合）、眼・鼻の分泌物、可視粘膜、自律神経機能（流涙、立毛、瞳孔径、呼吸）

(3) オープンフィールド内観察（スコアについては添付資料3参照）

観察は箱型オープンフィールド（W73×D42×H20cm）を用い、個体ごとに1分間行った。

覚醒状態、歩行、姿勢、振戦、痙攣、立ち上がり回数、排泄物（排糞数、排尿）、常同行動（身繕い、旋回など）、異常行動（自咬、後方突進など）

3) 機能検査

全動物について、投与第4週（投与28日）及び回復終了週（回復14日）に詳細な一般状態の観察に引き続いて以下の検査をブラインドで行った（スコアについては添付資料4参照）。なお、空中正向反射は約30cmの高さから動物を仰向けの状態で3回落下させたときの着地の状態の点数を合計して評価した。着地開脚幅は、約30cmの高さから2回落下させ、それぞれ両後肢間の距離を平均した値で評価した。

聴覚反応、接近反応、接触反応、痛覚反応、瞳孔反射、空中正向反射、着地開脚幅

4) 握力測定

機能検査に引き続き、全動物の前肢及び後肢の握力（CPU ゲージ MODEL-9502A、アイコーエンジニアリング株式会社）の測定をブラインドで行った。握力は前・後肢とも 2 回測定し、平均した値で評価した。

5) 自発運動量測定

上記握力測定に引き続き、全動物の自発運動量（実験動物用自発運動センサー NS-AS01、株式会社ニューロサイエンス）の測定をブラインドで行った。測定は 1 時間とし、10 分間隔及び 60 分間の運動量を集計して評価した。

6) 体重測定

投与期間中は投与 1、4 及び 7 日の 3 回、その後は 3～4 日ごとに週 2 回、測定当日の投与前（07：46～09：20 の間）に測定した。回復期間中は回復 1、3 及び 7 日、以降は 3～4 日ごとに週 2 回（08：07～09：44 の間）測定した。また、相対器官重量算出のため、剖検日にも絶食後の体重を測定した。

7) 摂餌量測定

投与開始日の投与前に 1 回、前日からの 1 日量を、その後は 3 ないし 4 日間の累積摂取量を当日の投与前（08：24～10：43 の間）に測定し、1 匹 1 日量を算出した。回復第 1 週は、回復 1～3 日及び回復 3～7 日までの 2 ないし 4 日間を、その後は 3～4 日ごとに 3 ないし 4 日間の累積摂取量を測定（08：18～09：52 の間）して、1 匹 1 日量を算出した。

8) 摂水量測定

尿検査時に、尿検査対象動物について前日からの 1 日当たりの摂水量を吸水瓶を用いて測定した。

9) 尿検査

投与第4週（投与24～25日）及び回復終了週（回復10～11日）に検査を行った。

投与期間中は検査当日の投与後に主群及び回復群の全動物を、回復期間中は回復群の全動物を、それぞれ採尿器をセットしたケージに収容し、絶食・自由摂水下で4時間尿を、次いで自由摂食・自由摂水下でその後の20時間尿を採取し、表2.に記載した項目及び方法により検査した。

表2. 尿検査の項目、測定法及び使用機器など

1) 4時間尿についての検査		2) 20時間尿についての検査	
検査項目	測定方法	検査項目	測定方法
pH	URIFLET 7A 試験紙 ^{a)} (アークレイ㈱)	尿量	容量測定
たん白質		浸透圧	氷点降下法 ^{b)} (単位: mOsm/kg)
ケトン体			
グルコース			
潜血			
ビリルビン			
ウロビリノーゲン			
色調	肉眼観察		
沈渣	鏡検法		
尿量	容量測定		
使用測定機器			
^{a)} : mini AUTION ANALYZER MA-4210 (アークレイ㈱)			
^{b)} : 全自動浸透圧測定装置 オートアンドスタット OM-6030 (アークレイ㈱)			

10) 血液学検査

投与期間及び回復期間終了の翌日の計画剖検時に、前日から一夜（約 16～19 時間）絶食させた全動物についてエーテル麻酔下に開腹し、腹大動脈から EDTA-2K 加採血瓶（SB-41：シスメックス株式会社）に血液を採取した。得られた血液について表 3.-1) に記載した項目及び方法により検査した。また、3.8%クエン酸ナトリウム溶液加試験管（血液 9 容に対し 1 容の割合）に採取した血液を遠心分離（約 1,600×g、10 分間）し、得られた血漿について表 3.-2) に記載した項目及び方法により検査した。

表 3. 血液学検査の項目、測定法及び使用機器など

1) EDTA-2K 加血液についての検査		
測定項目	測定方法	単 位
赤血球数 (RBC)	電気抵抗変化検出法 ^{c)}	10 ⁴ /μL
ヘモグロビン量 (Hb)	シアンメトヘモグロビン法 ^{c)}	g/dL
ヘマトクリット値 (Ht)	赤血球数及び平均赤血球容積から算出	%
平均赤血球容積 (MCV)	電気抵抗変化検出法 ^{c)}	fL
平均赤血球血色素量 (MCH)	赤血球数及びヘモグロビン量から算出	pg
平均赤血球血色素濃度 (MCHC)	ヘモグロビン量及びヘマトクリット値から算出	%
網赤血球率	Brecher 法	%
血小板数	電気抵抗変化検出法 ^{c)}	10 ⁴ /μL
白血球数	電気抵抗変化検出法 ^{c)}	10 ³ /μL
白血球百分率	May-Giemsa 染色による鏡検法	%
2) クエン酸ナトリウム加血液から分離した血漿についての検査		
検査項目	測定方法	単 位
プロトロンビン時間 (PT)	クロット法 ^{d)}	s
活性化部分トロンボ プラスチン時間 (APTT)	クロット法 ^{d)}	s
フィブリノーゲン量	トロンボプラスチン法 ^{d)}	mg/dL
使用測定機器		
^{c)} : コールター全自動 8 項目血球アナライザー T890 (ベックマン・コールター(株))		
^{d)} : 血液凝固自動測定装置 ACL 100 (Instrumentation Laboratory)		

11) 血液化学検査

血液学検査用試料と同時に採取した血液を凝固促進剤入り試験管（ベノジェクトⅡ-オートセップ：テルモ株式会社）に取り、遠心分離（約 1,600×g、10 分間）し、得られた血清について表 4.-1) に記載の項目及び方法により検査した。また、ヘパリン加試験管（血液 1mL 当たり約 20 単位のヘパリン）に採取した血液を遠心分離（約 1,600×g、10 分間）し、得られた血漿について表 4.-2) に記載の項目及び方法により検査した。

表 4. 血液化学検査の項目、測定法及び使用機器など

1) 分離した血清についての検査		
検査項目	測定方法	単 位
AIP	Bessey-Lowry 法 ^{e)}	IU/L
総コレステロール (T. cho)	CEH-COD-POD 法 ^{e)}	mg/dL
トリグリセライド (TG)	GK-GPO-POD 法 ^{e)}	mg/dL
リン脂質 (PL)	PLD-ChOD-POD 法 ^{e)}	mg/dL
総ビリルビン (T. bilirubin)	アゾビリルビン法 ^{e)}	mg/dL
グルコース	Hexokinase-G6PD 法 ^{e)}	mg/dL
尿素窒素 (BUN)	Urease-GLDH 法 ^{e)}	mg/dL
クレアチニン	Jaffé 法 ^{e)}	mg/dL
ナトリウム (Na)	イオン選択電極法 ^{e)}	mmol/L
カリウム (K)	イオン選択電極法 ^{e)}	mmol/L
塩素 (Cl)	イオン選択電極法 ^{e)}	mmol/L
カルシウム (Ca)	OCPC 法 ^{e)}	mg/dL
無機リン (P)	モリブデン酸法 ^{e)}	mg/dL
総たん白質 (TP)	Biuret 法 ^{e)}	g/dL
アルブミン	BCG 法 ^{e)}	g/dL
A/G 比	総たん白質及びアルブミンから算出	
2) ヘパリン加血液から分離した血漿についての検査		
検査項目	測定方法	単 位
GOT (ASAT)	UV-rate 法 ^{e)}	IU/L
GPT (ALAT)	UV-rate 法 ^{e)}	IU/L
LDH	UV-rate 法 ^{e)}	IU/L
γ-GTP	γ-グルタミル-3-カルボキシ-4-ニトロアニリド法 ^{e)}	IU/L
使用測定機器		
^{e)} : 全自動分析装置 Monarch (Instrumentation Laboratory)		

12) 病理学検査

(1) 剖検

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

(2) 器官重量測定

すべての計画剖検動物について、表 5. に示す器官の重量（絶対重量）を測定するとともに絶対重量と剖検時の体重から体重 100g 当たりの重量（相対重量）を算出した。両側性の器官については左右別々に測定したが、その合計値で評価した。

(3) 病理組織学検査

すべての動物について、表 5. に示す保存対象器官／組織をリン酸緩衝 10%ホルマリン液に固定・保存した。ただし、眼球、ハーダー腺、視神経はリン酸緩衝液で調製した 3% グルタルアルデヒド・2.5%ホルマリン液で固定、精巣及び精巣上体はブアン液で固定した後、リン酸緩衝 10%ホルマリン液で保存した。その後、表 5. に示すパラフィン包埋対象器官／組織をパラフィン包埋し、主群の対照群と高用量群の全動物並びにその他の群の動物で肉眼的に異常がみられた部位について切片とし、ヘマトキシリン・エオジン染色標本を作製して鏡検した。

表 5. 病理学検査対象器官/組織

組 織	保存	病理組織 包埋	病理組織		秤量
			H・E	特染	
大脳	○	○	○		○ (脳として)
小脳	○	○	○		
橋	○	○	○		
脊髄 (胸部)	○	○	○		
坐骨神経	○	○	○		
眼球	○	○	○		
視神経	○				
ハーダー腺	○				
下垂体	○	○	○		
甲状腺 (上皮小体を含む)	○	○	○		
副腎	○	○	○		○
胸腺	○	○	○		○
脾臓	○	○	○		○
頸下リンパ節	○	○	○		
腸間膜リンパ節	○	○	○		
心臓	○	○	○		○
胸大動脈	○				
気管	○	○	○		
肺 (気管支を含む)	○	○	○		○
舌	○				
食道	○				
胃	○	○	○		
十二指腸	○	○	○		
空腸	○	○	○		
回腸 (パイエル板を含む)	○	○	○		

組 織	保存	病理組織 包埋	病理組織		秤量
			H・E	特染	
盲腸	○	○	○		
結腸	○	○	○		
直腸	○	○	○		
顎下腺	○				
舌下腺	○				
肝臓	○	○	○		○
脾臓	○				
腎臓	○	○	○		○
膀胱	○	○	○		
精巣/卵巣	○/○	○/○	○/○		○/○
精巣上体/子宮	○/○	○/○	○/○		○/○
前立腺/陰	○/○	○/○	○/○		
精囊	○				
乳腺	○				
胸骨 (骨髄を含む)	○	○	○		
大腿骨 (骨髄を含む)	○	○	○		
大腿部骨格筋	○	○	○		
皮膚 (鼠径部)	○				
肉眼的異常部位	○	○	○		
喉頭	○				

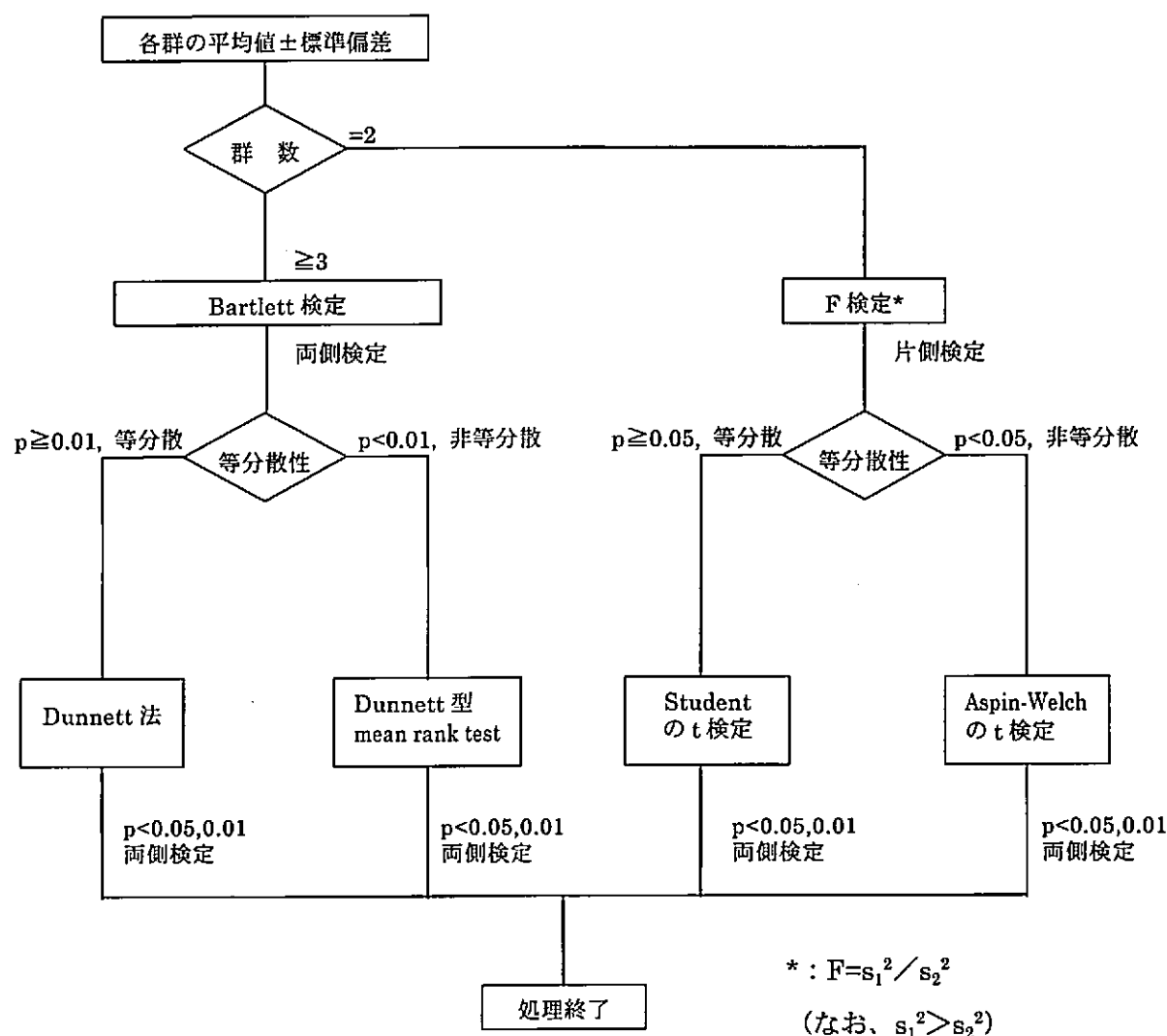
他に個体識別部 (耳標を装着した耳介) を摘出し保存した。

各項目該当ある場合は○で示した。

14. 統計解析

- 1) 計量データ（体重、摂餌量、摂水量、尿、詳細な一般状態及び機能検査の定量的項目、握力、自発運動量、血液学検査、血液化学検査及び器官重量）

下記の模式図に示す方法に従って検定した^{2, 3)}。



- 2) 詳細な一般状態の観察及び機能検査のスコア化したデータ
 χ^2 検定法又はMann-WhitneyのU検定等を用いた（有意水準0.05及び0.01、両側）²⁾。
- 3) 尿の定性的データ
 累積 χ^2 検定法を用いた（有意水準0.05及び0.01、両側）⁴⁾。

試験結果

1. 一般状態

成績を Table 1-1～1-3 に示した。

1) 投与期間

いずれの動物にも死亡は認められなかった。

全用量群で、黄色調便が投与 2 日より投与期間終了日まで雌雄全例にみられたのみで、他に異常は観察されなかった。

2) 回復期間

いずれの動物にも死亡は認められなかった。

1000mg/kg 回復群で、投与期間から引き続いて黄色調便が雌雄全例にみられたが、回復 3 日には消失し、その後異常は観察されなかった。

2. 詳細な一般状態

成績を Table 2-1～2-21 に示した。

観察はホームケージ内、手に持って及びオープンフィールド内でそれぞれ行い、投与開始前に 1 回、投与期間及び回復期間中は毎週 1 回実施した（スコアの基準は添付資料 1～3 参照）。

1) 投与期間

(1) ホームケージ内観察

いずれの動物にも異常はみられなかった。

(2) 手に持った観察

いずれの動物にも異常はみられなかった。

(3) オープンフィールド内観察

投与第 1、2 及び 3 週に一般状態でも観察された黄色調便が 1000mg/kg 投与群の雄各 1 例にみられたのみで、特記すべき変化はなかった。

2) 回復期間

(1) ホームケージ内観察

いずれの動物にも異常はみられなかった。

(2) 手に持った観察

いずれの動物にも異常はみられなかった。

(3) オープンフィールド内観察

いずれの動物にも異常はみられなかった。

3. 機能検査

成績を Table 2-22 及び 2-23 に示した。

検査は投与第 4 週及び回復第 2 週に実施した（スコアの基準は添付資料 4 参照）。

1) 投与第 4 週

いずれの動物にも異常はみられなかった。

2) 回復第 2 週

いずれの動物にも異常はみられなかった。

4. 握力

成績を Table 2-24 及び 2-25 に示した。

測定は投与第 4 週及び回復第 2 週に前肢及び後肢について実施した。

1) 投与第 4 週

雌雄とも各用量群と対照群との間に有意な差はみられなかった。

2) 回復第 2 週

雌雄とも 1000mg/kg 回復群と対照群との間に有意な差はみられなかった。

5. 自発運動量

成績を Fig. 1-1～1-4 及び Table 2-26、2-27 に示した。

測定は投与第 4 週及び回復第 2 週に実施し、10 分ごとの値と 60 分間合計の値で集計した。

1) 投与第 4 週

雌雄とも各用量群と対照群との間に有意な差はみられなかった。

2) 回復第 2 週

1000mg/kg 回復群の雄で 30～40 分と 60 分間累積における自発運動量の有意な増加がみられたが、投与第 4 週にはみられない変化であった。

6. 体重

成績を Fig. 2 及び Table 3-1、3-2 に示した。

1) 投与期間

各用量群の体重は、雌雄とも対照群と同様に推移した。

2) 回復期間

1000mg/kg 回復群の体重は対照群と同様に推移したが、雌で回復期間を通じた増加量に有意な高値がみられた。

7. 摂餌量

成績を Fig. 3 及び Table 4-1、4-2 に示した。

1) 投与期間

各用量群の摂餌量は、雌雄とも対照群と同様に推移した。

2) 回復期間

1000mg/kg 回復群の摂餌量は、雌雄とも対照群と同様に推移した。

8. 尿検査（摂水量を含む）

成績を Table 5-1～5-8 に示した。

1) 投与第4週

1000mg/kg 投与群では、尿たん白質の有意な増加が雌にみられた。

その他、100 及び 300mg/kg 投与群の雄で尿たん白質及び尿ケトン体の有意な減少がみられ、300mg/kg 投与群の雄では更に摂水量及び尿量の有意な増加（それぞれ 35 及び 115% 増）と尿浸透圧の有意な減少（32%減）がみられたが、いずれも用量に応じた変化ではなかった。

2) 回復終了週

1000mg/kg 回復群の雄で、尿量の有意な増加（68%増）がみられた。しかし、これは投与第4週にはみられない変化であった。

9. 血液学検査

成績を Table 6-1～6-4 に示した。

1) 投与期間終了時

1000mg/kg 投与群で、単球比率の有意な増加（300%増）が雌にみられた。

なお、300mg/kg 投与群の雄でプロトロンビン時間の有意な延長（10%増）がみられたが、用量に応じた変化ではなかった。

2) 回復期間終了時

1000mg/kg 回復群の雄で、白血球数の有意な増加（31%増）及び桿状核好中球比率の有意な減少（77%減）がみられた。しかし、これらは投与期間終了時にはみられない変化であった。

10. 血液化学検査

成績を Table 7-1～7-4 に示した。

1) 投与期間終了時

100 及び 1000mg/kg 投与群の雄で、GOT（ASAT）活性の有意な減少（それぞれ 25 及び 23%減）がみられた。

2) 回復期間終了時

1000mg/kg 回復群の雄で、総ビリルビン、尿素窒素及びクレアチニンの有意な増加（それぞれ 10、8 及び 7%増）がみられた。しかし、これらは投与期間終了時にはみられない変化であった。

11. 器官重量

成績を Table 8-1～8-8 に示した。

1) 投与期間終了時

雌雄とも各用量群と対照群との間に有意な重量差を示す器官はみられなかった。

2) 回復期間終了時

雌雄とも 1000mg/kg 回復群と対照群との間に有意な重量差を示す器官はみられなかった。

12. 剖検所見

成績を Table 9-1 及び 9-2 に示した。

1) 投与期間終了時

以下の所見がみられたが、出現状況からいずれも偶発所見と考えられた。

甲状腺 : 片側の小型と逆側の大型が 300mg/kg 投与群の雄 1/5 例にみられた。

肺 : 暗赤色巣が 100 及び 1000mg/kg 投与群の雄各 1/5 例にみられた。

精巣、精巣上部、前立腺

： 小型が 100mg/kg 投与群の 1/5 例にみられた。

2) 回復期間終了時

以下の所見がみられたが、出現状況からいずれも偶発所見と考えられた。

胃： 腺胃の暗赤色巣が対照群及び 1000mg/kg 回復群の雄各 2/5 例にみられた。

小腸（回腸）

： 憩室が 1000mg/kg 回復群の雄 1/5 例にみられた。

精巣上部： 黄白色巣（片側性）が対照群の 1/5 例にみられた。

13. 病理組織学検査

成績を Table 10-1～10-4 に示した。

1) 投与期間終了時

対照群及び高用量群について検査し、以下の所見がみられたがその出現状況からいずれも偶発所見と考えられた。

肝 臓： 軽微な微小肉芽腫が対照群の雄 1/5 例と 1000mg/kg 投与群の雄 2/5 例にみられた。

盲腸、直腸

： 軽微な粘膜内細胞浸潤が 1000mg/kg 投与群の雌 1/5 例にみられた。

腎 臓： のう胞が対照群の雌 1/5 例にみられた。

前立腺： 軽微ないし軽度なリンパ球性細胞浸潤が対照群の雄 1/5 例と 1000mg/kg 投与群の雄 2/5 例にみられた。

その他の群の肉眼的異常部位について検査し、以下の所見がみられた。

甲状腺（上皮小体を含む）

： 300mg/kg 投与群の雄 1/5 例で肉眼観察された片側の大型と逆側の小型は、組織学的には異常はみられなかった。

肺： 100mg/kg 投与群の雄 1/5 例で肉眼観察された暗赤色巣は、組織学的には軽微な限局性出血であり軽微な炎症性細胞浸潤を伴っていた。なお、肉眼的な暗赤色巣が観察された 1000mg/kg 投与群の雄 1/5 例では、組織学的な異常は認められなかった。

精巣、精巣上部、前立腺

： 100mg/kg 投与群の雄 1/5 例で肉眼観察された小型は、組織学的には精

巢で中等度の精細管の萎縮、精巢上体で中等度の精子の減少であったが、前立腺に組織学的な異常はみられなかった。

2) 回復期間終了時

肉眼的異常部位について検査し、以下の所見がみられたがその出現状況からいずれも偶発所見と考えられた。

胃 : 対照群及び1000mg/kg投与群の雄各2/5例で肉眼的に観察された腺胃の暗赤色巣は、組織学的には軽微ないし軽度なびらんであった。

小腸（回腸）

: 1000mg/kg投与群の雄1/5例で肉眼的に観察された憩室は、組織学的にも憩室であった。

精巢上体 : 対照群の1/5例で肉眼的に観察された黄白色巣は、組織学的には軽度な精子肉芽腫であった。

考 察

ピグメントエロー-14 の反復投与による変化とその回復性を 7 週齢の Sprague-Dawley 系 SPF ラット〔Crj:CD(SD)IGS〕を用いて検討した。投与量は 0（媒体：オリブ油）、100、300 及び 1000mg/kg/日とし、28 日間強制経口投与した。1 群の動物数は、対照群及び 1000mg/kg 投与群で雌雄各 10 匹、100 及び 300mg/kg 投与群で雌雄各 5 匹とし、このうち対照群と 1000mg/kg 投与群の雌雄各 5 匹については、28 日間の投与後 2 週間の回復期間を設けた。

投与期間及び回復期間を通じて死亡動物はみられなかった。また、機能検査、握力、自発運動量、体重、摂餌量及び器官重量に変化はみられなかった。

一般状態では、黄色調便が各用量群の雌雄全例にみられた。この変化は投与 2 日から回復 2 日まで観察され、やまぶき色の被験物質が糞中に排出されたことによるものと推測された。

詳細な一般状態では、黄色調便が投与期間中の検査で 1000mg/kg 投与群の雄 1 例にみられたのみで、他に異常は認められなかった。

尿検査では、1000mg/kg 投与群の雌で尿たん白質の有意な増加がみられた。しかし、対照群の陽性範囲を越えたのはわずか 1 例のみであり、尿潜血などの変化や腎臓の組織学的変化も認められなかったことから、特記すべき変化ではなかった。

血液学検査では、1000mg/kg 投与群の雌で単球比率の有意な増加がみられた。この変化は、軽度で好中球比率の変化もなく、また、肝臓や脾臓などの網内系細胞に組織学的変化もなかったことから、毒性を示唆する変化とは考え難かった。

血液化学検査では、100 及び 1000mg/kg 投与群の雌で GOT (ASAT) 活性の有意な減少がみられたが、用量との関連性がないことから偶発性の変化と考えられた。

病理学検査では、1000mg/kg 投与群の組織学的検査において肝臓の微小肉芽腫及び前立腺のリンパ球性細胞浸潤が雄各 2 例に、盲腸と直腸の粘膜内細胞浸潤が雌 1 例にみられた。肝臓と前立腺の病変は対照群の動物でもみられ、盲腸と直腸についてもこの種のラットで偶発的にみられる病変であった。このことから、これらの病変に被験物質投与との関連性はないと考えられた。

回復試験では、上述した黄色調便のほかに被験物質投与によると考えられる変化はみられなかった。

以上の如く、各用量群の雌雄で被験物質の糞中排泄による黄色調便がみられたのみで、毒性

学的に意義のある変化は認められなかった。したがって、ピグメントエロー-14 の本試験条件下でのラットにおける無影響量は雌雄とも 1000mg/kg/日と推定された。

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詳細な一般状態の観察におけるスコア (1)

－ Home cage observation －

1 Posture (N, F, H)

N Normal

F Flattened

H Hunched

2 Convulsion (0-3)

0 None

1 Minor

2 Moderate

3 Severe

3 Abnormal behavior (0-3)

0 None

1 Minor

2 Moderate

3 Severe

詳細な一般状態の観察におけるスコア (2)

- In the hand observation -

- | | | | |
|---|----------------------------|----|------------------------------|
| 1 | Removal from cage (1-5) | 9 | Pupil size (1-4) |
| 1 | Atypically docile | 1 | Miosis |
| 2 | Easy | 2 | Normal |
| 3 | Some resistance/avoidance | 3 | Half opened pupil |
| 4 | Difficult | 4 | Mydriasis |
| 5 | Very difficult | | |
| 2 | Fur condition (0-3) | 10 | Lacrimation (0/1) |
| 0 | Normal | 0 | Normal |
| 1 | Slight | 1 | Present |
| 2 | Moderate | | |
| 3 | Marked | 11 | Salivation (0-3) |
| 3 | Skin (0-3) | 0 | None |
| 0 | Normal | 1 | Slight |
| 1 | Slight | 2 | Moderate |
| 2 | Moderate | 3 | Marked |
| 3 | Marked | 12 | Secretions-Eye, Nose (0/1) |
| 4 | Piloerection (0/1) | 0 | Absent |
| 0 | Absent | 1 | Present |
| 1 | Present | 13 | Vocalization (0-3) |
| 5 | Mucosal membranes (0-3) | 0 | None |
| 0 | Normal | 1 | Soft |
| 1 | Slight | 2 | Moderate |
| 2 | Moderate | 3 | Loud/aggressive |
| 3 | Marked | 14 | Reactivity to handling (1-5) |
| 6 | Abnormal respiration (0-3) | 1 | Atypical docile |
| 0 | Absent | 2 | Easy |
| 1 | Slight | 3 | Slightly awkward |
| 2 | Moderate | 4 | Difficult |
| 3 | Marked | 5 | Very difficult |
| 7 | Palpebral closure (0-3) | | |
| 0 | Normal | | |
| 1 | Slightly closed | | |
| 2 | Half closed | | |
| 3 | Completely closed | | |
| 8 | Exophthalmos (0/1) | | |
| 0 | Absent | | |
| 1 | Present | | |

詳細な一般状態の観察におけるスコア (3)

- Open field observation -

- | | |
|--|---|
| <p>1 Posture (N, F, H)
N Normal
F Flattened
H Hunched</p> <p>2 Gait (U, 0-3)
U No/minimal location
0 Normal
1 Slight
2 Moderate
3 Marked</p> <p>3 Arousal (1-5)
1 Unconscious/semi-conscious
2 Reduced awareness
3 Normal
4 Increased alertness
5 Markedly alert</p> <p>4 Tremor (0-3)
0 None
1 Slight
2 Moderate
3 Marked</p> <p>5 Convulsion (0-3)
0 None
1 Minor
2 Moderate
3 Severe</p> <p>6 Abnormal behavior (0-3)
0 None
1 Minor
2 Moderate
3 Severe</p> <p>7 Grooming (0-2)
0 None
1 Occasional bouts (up to four)
2 Numerous bouts (more than four)</p> | <p>8 Urination (0-3)
0 None
1 Small amount
2 Moderate amount
3 Large/excessive amount</p> |
|--|---|

機能検査におけるスコア
— Manipulative test —

- 1 Approach response (1-3)
 - 1 No reaction/ignores
 - 2 Normal
 - 3 Abnormally fearful/aggressive reaction
- 2 Touch response (1-3)
 - 1 No reaction/ignores
 - 2 Normal
 - 3 Abnormally fearful/aggressive reaction
- 3 Auditory response (1-4)
 - 1 None
 - 2 Weak
 - 3 Normal
 - 4 Exaggerate
- 4 Tail pinch response (1-4)
 - 1 None
 - 2 Weak
 - 3 Normal
 - 4 Exaggerate
- 5 Pupillary reflex (P, F, L, R)
 - P Pass, both
 - F Failed, neither
 - L Left pupil responds
 - R Right pupil responds
- 6 Aerial righting reflex
 - 0 Normal
 - 1 Land on side
 - 2 Land on back

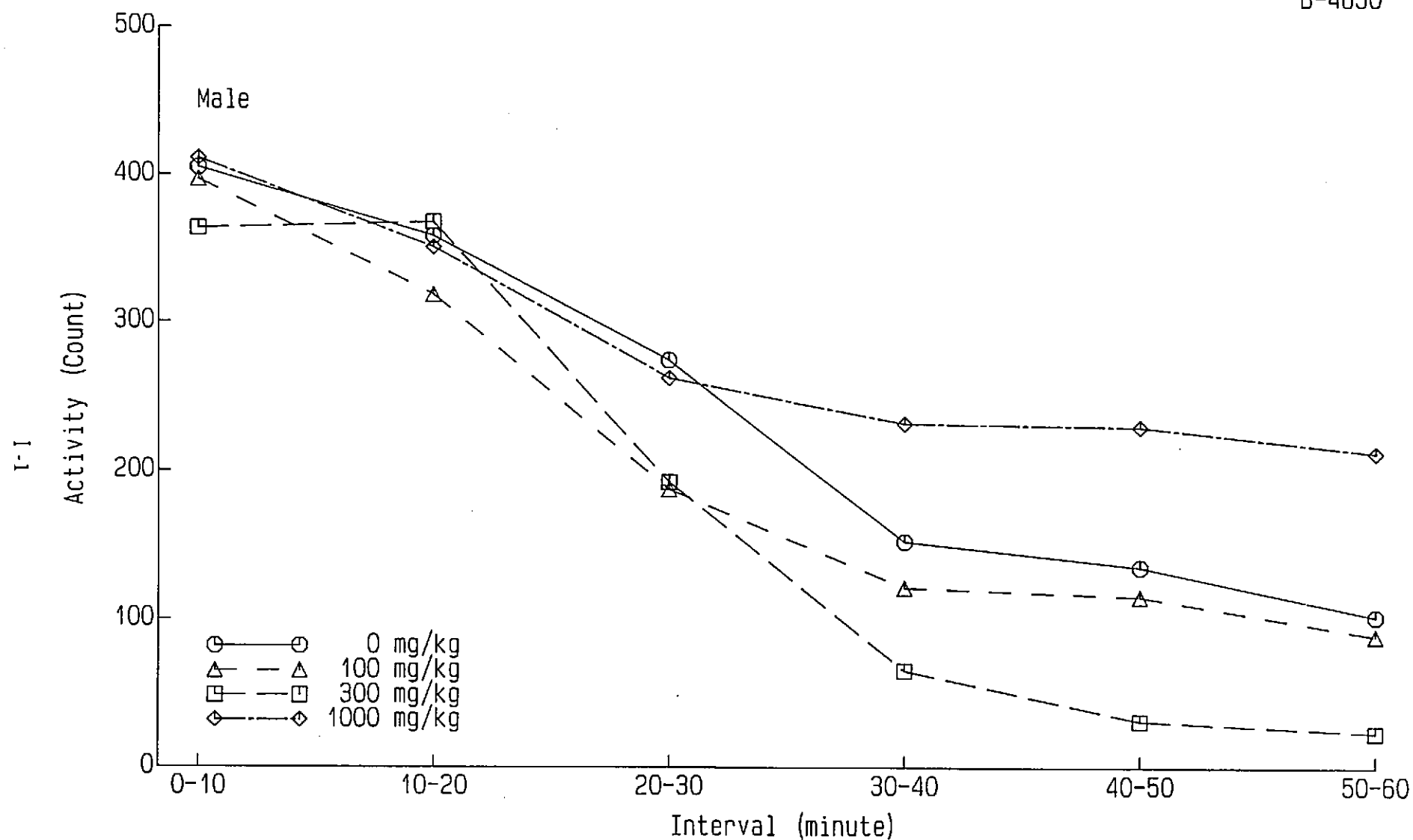


Fig.1-1 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

—— Motor Activity (4 weeks) ——

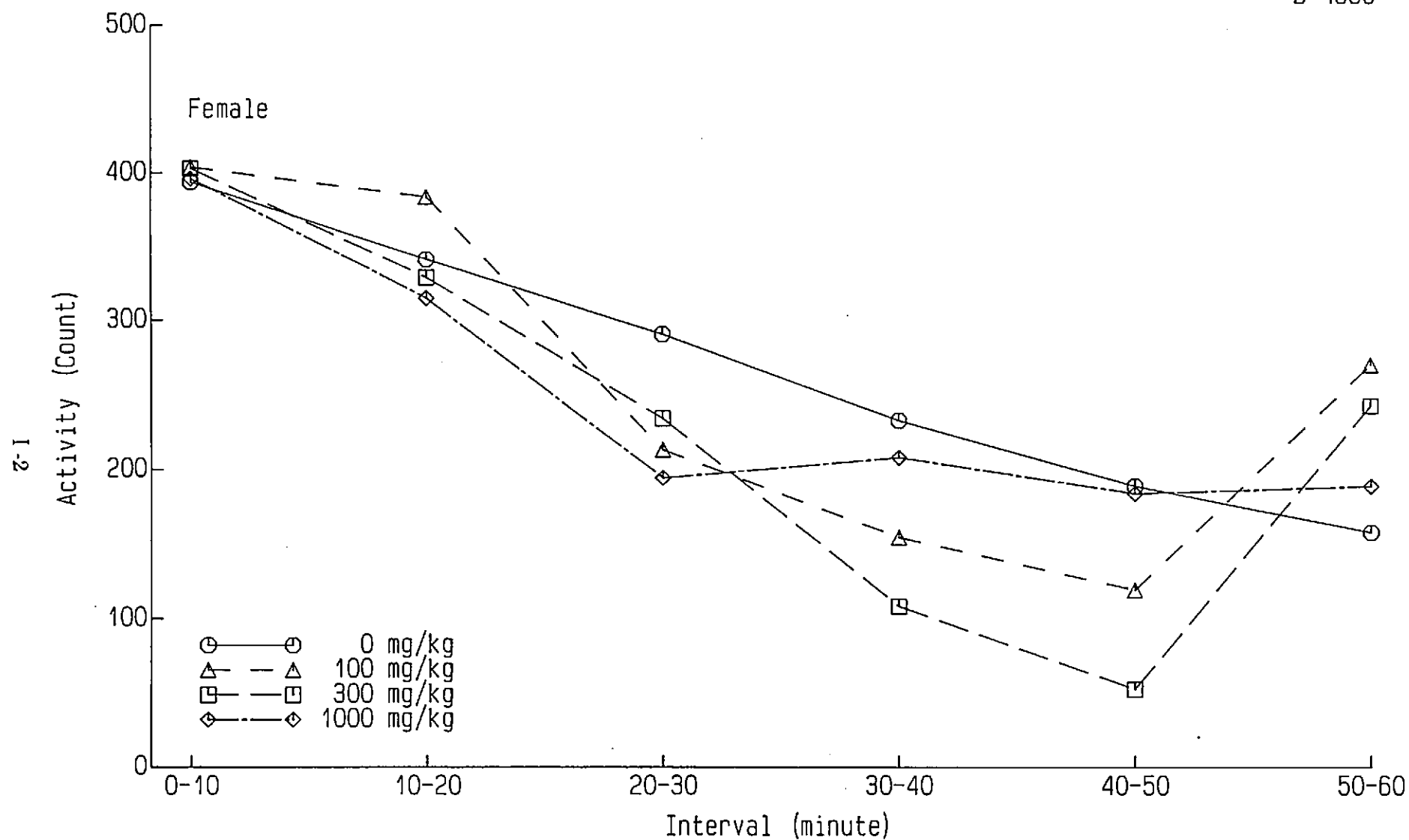


Fig.1-2 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

—— Motor Activity (4 weeks) ——

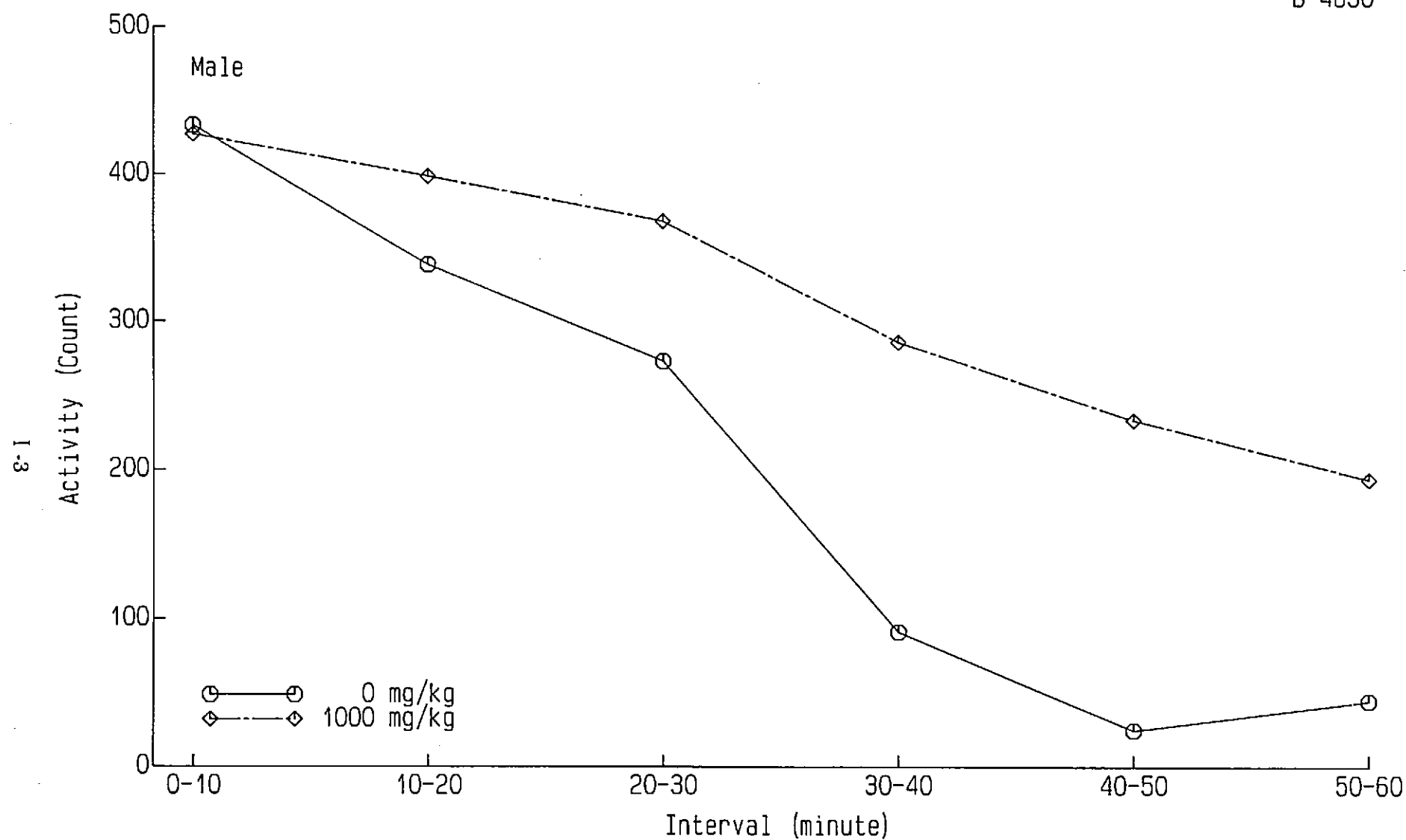


Fig.1-3 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

—— Motor Activity (Recovery 2 weeks) ——

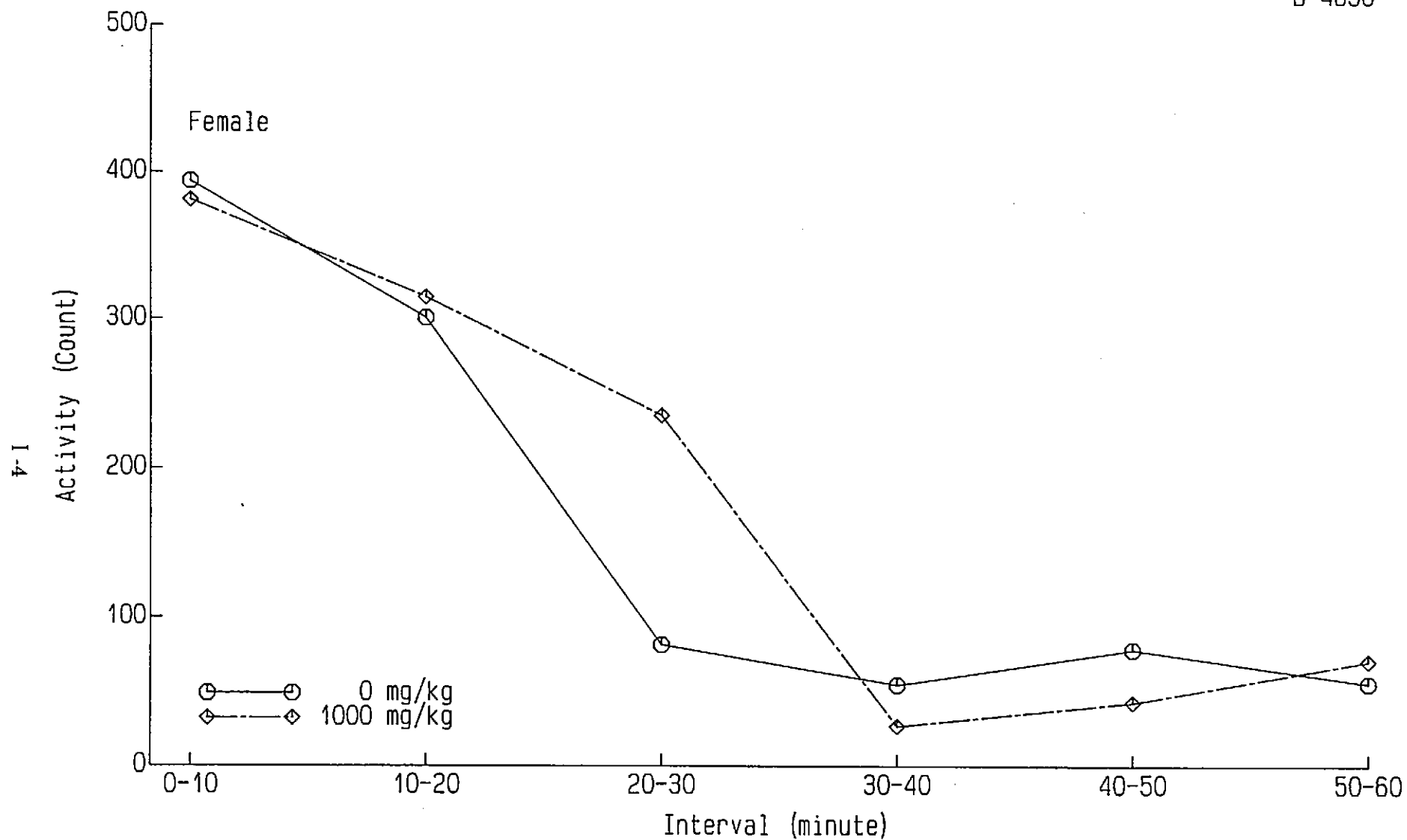


Fig.1-4 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

— Motor Activity (Recovery 2 weeks) —

B-4650

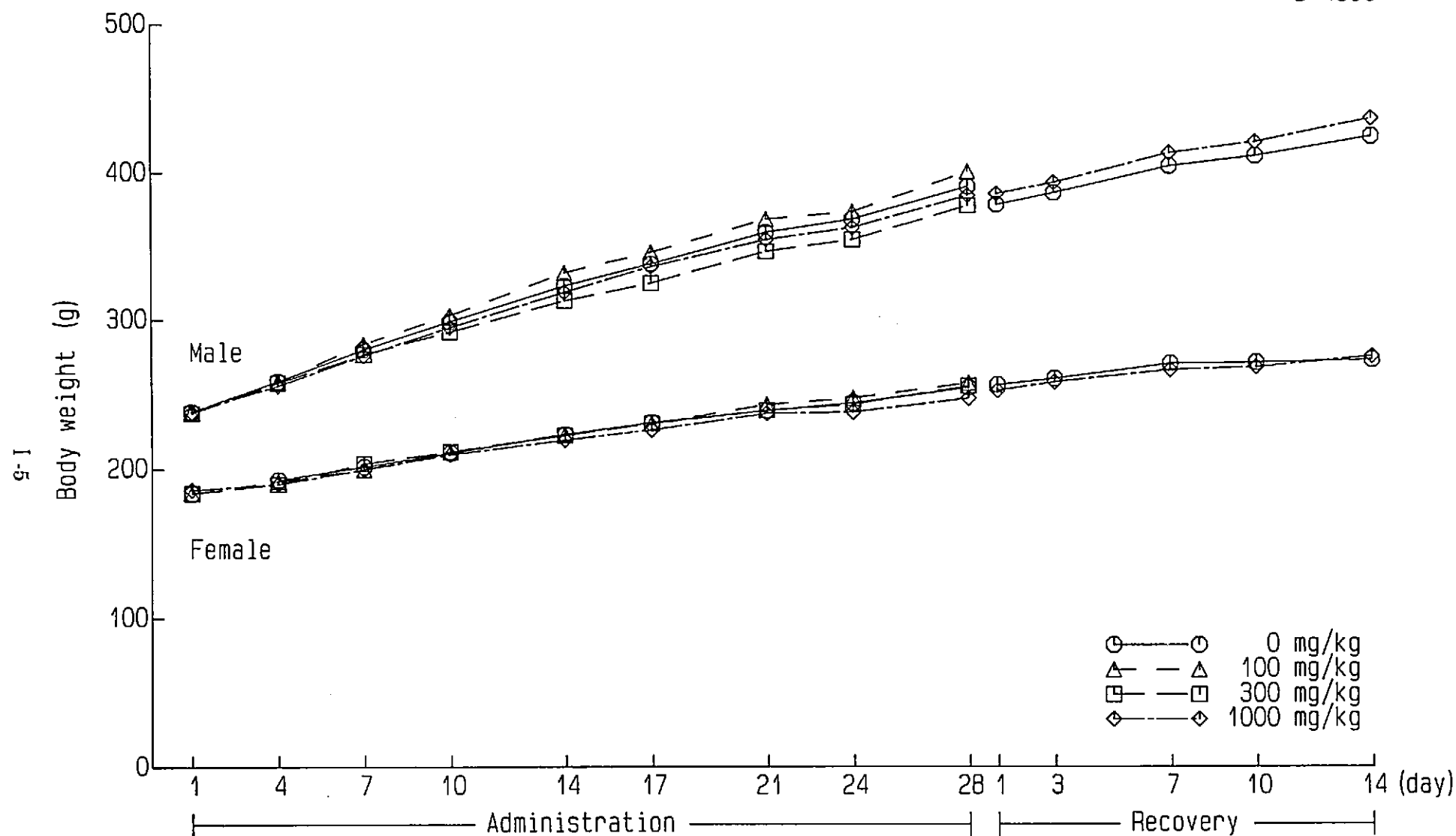


Fig.2 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

—— Body weight ——

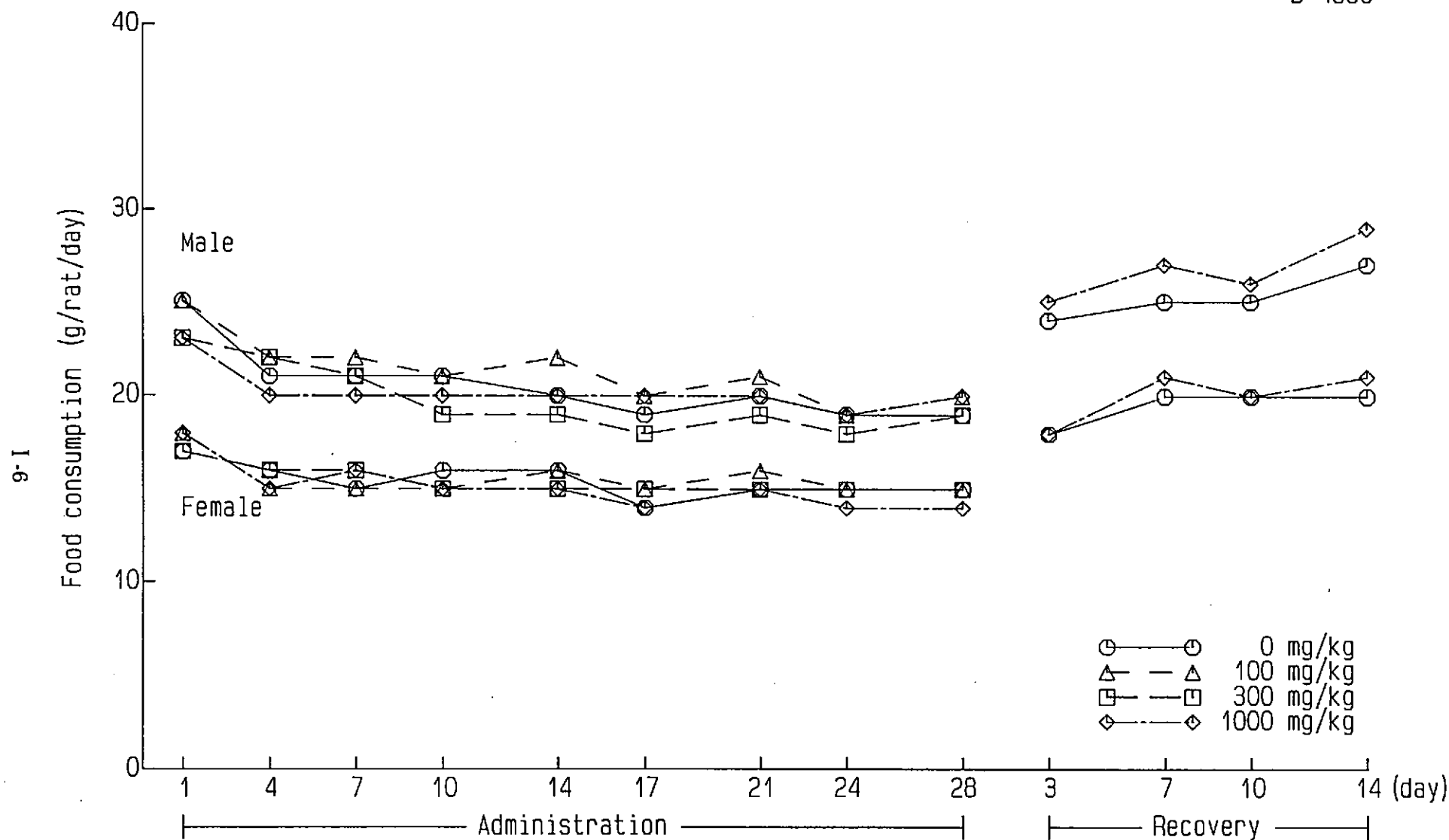


Fig.3 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

—— Food consumption ——

Table 1-1 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Clinical signs (Administration period)

Sex	Dose mg/kg	Findings	Day of administration													
			1	2	3	4	5	6	7	8	9	10	11	12	13	14
Male	0	No. of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10
		No abnormality	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	100	No. of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5
		No abnormality	5	0	0	0	0	0	0	0	0	0	0	0	0	0
		Feces, yellowish	0	5	5	5	5	5	5	5	5	5	5	5	5	5
	300	No. of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5
		No abnormality	5	0	0	0	0	0	0	0	0	0	0	0	0	0
		Feces, yellowish	0	5	5	5	5	5	5	5	5	5	5	5	5	5
	1000	No. of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10
		No abnormality	10	0	0	0	0	0	0	0	0	0	0	0	0	0
		Feces, yellowish	0	10	10	10	10	10	10	10	10	10	10	10	10	10
Female	0	No. of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10
		No abnormality	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	100	No. of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5
		No abnormality	5	0	0	0	0	0	0	0	0	0	0	0	0	0
		Feces, yellowish	0	5	5	5	5	5	5	5	5	5	5	5	5	5
	300	No. of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5
		No abnormality	5	0	0	0	0	0	0	0	0	0	0	0	0	0
		Feces, yellowish	0	5	5	5	5	5	5	5	5	5	5	5	5	5
	1000	No. of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10
		No abnormality	10	0	0	0	0	0	0	0	0	0	0	0	0	0
		Feces, yellowish	0	10	10	10	10	10	10	10	10	10	10	10	10	10

Table 1-2 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Clinical signs (Administration period)

Sex	Dose mg/kg	Findings	Day of administration													
			15	16	17	18	19	20	21	22	23	24	25	26	27	28
Male	0	No. of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10
		No abnormality	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	100	No. of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5
		No abnormality	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Feces, yellowish	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	300	No. of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5
		No abnormality	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Feces, yellowish	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	1000	No. of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10
		No abnormality	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Feces, yellowish	10	10	10	10	10	10	10	10	10	10	10	10	10	10
Female	0	No. of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10
		No abnormality	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	100	No. of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5
		No abnormality	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Feces, yellowish	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	300	No. of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5
		No abnormality	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Feces, yellowish	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	1000	No. of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10
		No abnormality	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Feces, yellowish	10	10	10	10	10	10	10	10	10	10	10	10	10	10

Table 1-3

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
 Clinical signs (Recovery period)

Sex	Dose mg/kg	Findings	Day of recovery													
			1	2	3	4	5	6	7	8	9	10	11	12	13	14
Male	0	No. of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5
		No abnormality	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	1000	No. of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5
		No abnormality	0	0	5	5	5	5	5	5	5	5	5	5	5	5
		Feces, yellowish	5	5	0	0	0	0	0	0	0	0	0	0	0	0
Female	0	No. of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5
		No abnormality	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	1000	No. of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5
		No abnormality	0	0	5	5	5	5	5	5	5	5	5	5	5	5
		Feces, yellowish	5	5	0	0	0	0	0	0	0	0	0	0	0	0

Table 2-1 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Home cage observations (Pre administration)

Sex		Male				Female			
Dose (mg/kg)		0	100	300	1000	0	100	300	1000
Parameter	No. of animals	10	5	5	10	10	5	5	10
Posture (N,F,H)									
N : Normal		10	5	5	10	10	5	5	10
Convulsion (0-3)									
0 : None		10	5	5	10	10	5	5	10
Abnormal behavior (0-3)									
0 : None		10	5	5	10	10	5	5	10

No significant difference in any treated groups from control group.

Table 2-2 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
 Home cage observations (1 week)

Sex		Male				Female			
Dose (mg/kg)		0	100	300	1000	0	100	300	1000
Parameter	No. of animals	10	5	5	10	10	5	5	10
Posture (N,F,H)									
N : Normal		10	5	5	10	10	5	5	10
Convulsion (0-3)									
0 : None		10	5	5	10	10	5	5	10
Abnormal behavior (0-3)									
0 : None		10	5	5	10	10	5	5	10

No significant difference in any treated groups from control group.

Table 2-3 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Home cage observations (2 weeks)

Sex		Male				Female			
Dose (mg/kg)		0	100	300	1000	0	100	300	1000
Parameter	No. of animals	10	5	5	10	10	5	5	10
Posture (N,F,H)									
N : Normal		10	5	5	10	10	5	5	10
Convulsion (0-3)									
0 : None		10	5	5	10	10	5	5	10
Abnormal behavior (0-3)									
0 : None		10	5	5	10	10	5	5	10

No significant difference in any treated groups from control group.

Table 2-4 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Home cage observations (3 weeks)

Sex		Male				Female			
Dose (mg/kg)		0	100	300	1000	0	100	300	1000
Parameter	No. of animals	10	5	5	10	10	5	5	10
Posture (N,F,H)									
N : Normal		10	5	5	10	10	5	5	10
Convulsion (0-3)									
0 : None		10	5	5	10	10	5	5	10
Abnormal behavior (0-3)									
0 : None		10	5	5	10	10	5	5	10

No significant difference in any treated groups from control group.

Table 2-5 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Home cage observations (4 weeks)

Parameter	Sex	Male				Female			
		Dose (mg/kg)				Dose (mg/kg)			
	No. of animals	0	100	300	1000	0	100	300	1000
		10	5	5	10	10	5	5	10
Posture (N,F,H)									
N : Normal		10	5	5	10	10	5	5	10
Convulsion (0-3)									
0 : None		10	5	5	10	10	5	5	10
Abnormal behavior (0-3)									
0 : None		10	5	5	10	10	5	5	10

No significant difference in any treated groups from control group.

Table 2-6 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Home cage observations (Recovery 1 week)

Parameter	Sex	Male		Female	
	Dose (mg/kg)	0	1000	0	1000
	No. of animals	5	5	5	5
Posture (N,F,H)					
N : Normal		5	5	5	5
Convulsion (0-3)					
0 : None		5	5	5	5
Abnormal behavior (0-3)					
0 : None		5	5	5	5

No significant difference between treated group and control group.

Table 2-7 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Home cage observations (Recovery 2 weeks)

Parameter	Sex	Male		Female	
	Dose (mg/kg)	0	1000	0	1000
	No. of animals	5	5	5	5
Posture (N,F,H)					
N : Normal		5	5	5	5
Convulsion (0-3)					
0 : None		5	5	5	5
Abnormal behavior (0-3)					
0 : None		5	5	5	5

No significant difference between treated group and control group.

Table 2-8 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
In the hand observations (Pre administration)

Parameter	Sex	Male				Female			
	Dose (mg/kg)	0	100	300	1000	0	100	300	1000
	No. of animals	10	5	5	10	10	5	5	10
Removal from cage (1-5)									
2 : Easy		9	4	5	9	10	4	4	6
3 : Some resistance/avoidance		1	1	0	1	0	1	1	4
Vocalization (0-3)									
0 : None		10	4	5	10	10	5	5	9
1 : Soft		0	1	0	0	0	0	0	1
Reactivity to handling (1-5)									
2 : Easy		9	4	5	9	10	4	4	7
3 : Slightly awkward		1	1	0	1	0	1	1	3
Fur condition (0-3)									
0 : Normal		10	5	5	10	10	5	5	10
Skin (0-3)									
0 : Normal		10	5	5	10	10	5	5	10
Piloerection(0/1)									
0 : Absent		10	5	5	10	10	5	5	10
Mucosal membranes (0-3)									
0 : Normal		10	5	5	10	10	5	5	10
Secretions-Eye, Nose (0/1)									
0 : Absent		10	5	5	10	10	5	5	10
Palpebral closure (0-3)									
0 : Normal		10	5	5	10	10	5	5	10
Exophthalmos (0/1)									
0 : Absent		10	5	5	10	10	5	5	10
Pupil size (1-4)									
2 : Normal		10	5	5	10	10	5	5	10
Lacrimation (0/1)									
0 : Normal		10	5	5	10	10	5	5	10
Salivation (0-3)									
0 : None		10	5	5	10	10	5	5	10
Abnormal respiration (0-3)									
0 : Absent		10	5	5	10	10	5	5	10

No significant difference in any treated groups from control group.

Table 2-9 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
In the hand observations (1 week)

Parameter	Sex	Male				Female			
	Dose (mg/kg)	0	100	300	1000	0	100	300	1000
	No. of animals	10	5	5	10	10	5	5	10
Removal from cage (1-5)									
2 : Easy		10	5	5	10	10	5	5	10
Vocalization (0-3)									
0 : None		10	4	5	8	9	4	5	10
1 : Soft		0	1	0	2	1	1	0	0
Reactivity to handling (1-5)									
2 : Easy		10	5	5	10	10	5	5	10
Fur condition (0-3)									
0 : Normal		10	5	5	10	10	5	5	10
Skin (0-3)									
0 : Normal		10	5	5	10	10	5	5	10
Piloerection(0/1)									
0 : Absent		10	5	5	10	10	5	5	10
Mucosal membranes (0-3)									
0 : Normal		10	5	5	10	10	5	5	10
Secretions-Eye, Nose (0/1)									
0 : Absent		10	5	5	10	10	5	5	10
Palpebral closure (0-3)									
0 : Normal		10	5	5	10	10	5	5	10
Exophthalmos (0/1)									
0 : Absent		10	5	5	10	10	5	5	10
Pupil size (1-4)									
2 : Normal		10	5	5	10	10	5	5	10
Lacrimation (0/1)									
0 : Normal		10	5	5	10	10	5	5	10
Salivation (0-3)									
0 : None		10	5	5	10	10	5	5	10
Abnormal respiration (0-3)									
0 : Absent		10	5	5	10	10	5	5	10

No significant difference in any treated groups from control group.

Table 2-10 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
In the hand observations (2 weeks)

Parameter	Sex	Male				Female			
	Dose (mg/kg)	0	100	300	1000	0	100	300	1000
	No. of animals	10	5	5	10	10	5	5	10
Removal from cage (1-5)									
2 : Easy		10	4	5	10	10	5	5	10
3 : Some resistance/avoidance		0	1	0	0	0	0	0	0
Vocalization (0-3)									
0 : None		10	4	5	10	10	5	5	9
1 : Soft		0	1	0	0	0	0	0	1
Reactivity to handling (1-5)									
2 : Easy		10	4	5	10	10	5	5	10
3 : Slightly awkward		0	1	0	0	0	0	0	0
Fur condition (0-3)									
0 : Normal		10	5	5	10	10	5	5	10
Skin (0-3)									
0 : Normal		10	5	5	10	10	5	5	10
Piloerection(0/1)									
0 : Absent		10	5	5	10	10	5	5	10
Mucosal membranes (0-3)									
0 : Normal		10	5	5	10	10	5	5	10
Secretions-Eye, Nose (0/1)									
0 : Absent		10	5	5	10	10	5	5	10
Palpebral closure (0-3)									
0 : Normal		10	5	5	10	10	5	5	10
Exophthalmos (0/1)									
0 : Absent		10	5	5	10	10	5	5	10
Pupil size (1-4)									
2 : Normal		10	5	5	10	10	5	5	10
Lacrimation (0/1)									
0 : Normal		10	5	5	10	10	5	5	10
Salivation (0-3)									
0 : None		10	5	5	10	10	5	5	10
Abnormal respiration (0-3)									
0 : Absent		10	5	5	10	10	5	5	10

No significant difference in any treated groups from control group.

Table 2-11 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
In the hand observations (3 weeks)

Parameter	Sex	Male				Female			
	Dose (mg/kg)	0	100	300	1000	0	100	300	1000
	No. of animals	10	5	5	10	10	5	5	10
Removal from cage (1-5) 2 : Easy		10	5	5	10	10	5	5	10
Vocalization (0-3) 0 : None 1 : Soft		10 0	4 1	5 0	8 2	10 0	5 0	5 0	10 0
Reactivity to handling (1-5) 2 : Easy		10	5	5	10	10	5	5	10
Fur condition (0-3) 0 : Normal		10	5	5	10	10	5	5	10
Skin (0-3) 0 : Normal		10	5	5	10	10	5	5	10
Piloerection(0/1) 0 : Absent		10	5	5	10	10	5	5	10
Mucosal membranes (0-3) 0 : Normal		10	5	5	10	10	5	5	10
Secretions-Eye, Nose (0/1) 0 : Absent		10	5	5	10	10	5	5	10
Palpebral closure (0-3) 0 : Normal		10	5	5	10	10	5	5	10
Exophthalmos (0/1) 0 : Absent		10	5	5	10	10	5	5	10
Pupil size (1-4) 2 : Normal		10	5	5	10	10	5	5	10
Lacrimation (0/1) 0 : Normal		10	5	5	10	10	5	5	10
Salivation (0-3) 0 : None		10	5	5	10	10	5	5	10
Abnormal respiration (0-3) 0 : Absent		10	5	5	10	10	5	5	10

No significant difference in any treated groups from control group.

Table 2-12 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
in the hand observations (4 weeks)

Parameter	Sex Dose (mg/kg) No. of animals	Male				Female			
		0	100	300	1000	0	100	300	1000
		10	5	5	10	10	5	5	10
Removal from cage (1-5) 2 : Easy		10	5	5	10	10	5	5	10
Vocalization (0-3) 0 : None		10	5	5	10	10	5	5	10
Reactivity to handling (1-5) 2 : Easy		10	5	5	10	10	5	5	10
Fur condition (0-3) 0 : Normal		10	5	5	10	10	5	5	10
Skin (0-3) 0 : Normal		10	5	5	10	10	5	5	10
Piloerection(0/1) 0 : Absent		10	5	5	10	10	5	5	10
Mucosal membranes (0-3) 0 : Normal		10	5	5	10	10	5	5	10
Secretions-Eye, Nose (0/1) 0 : Absent		10	5	5	10	10	5	5	10
Palpebral closure (0-3) 0 : Normal		10	5	5	10	10	5	5	10
Exophthalmos (0/1) 0 : Absent		10	5	5	10	10	5	5	10
Pupil size (1-4) 2 : Normal		10	5	5	10	10	5	5	10
Lacrimation (0/1) 0 : Normal		10	5	5	10	10	5	5	10
Salivation (0-3) 0 : None		10	5	5	10	10	5	5	10
Abnormal respiration (0-3) 0 : Absent		10	5	5	10	10	5	5	10

No significant difference in any treated groups from control group.

Table 2-13 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
In the hand observations (Recovery 1 week)

Parameter	Sex	Male		Female	
	Dose (mg/kg)	0	1000	0	1000
	No. of animals	5	5	5	5
Removal from cage (1-5)					
2 : Easy		5	5	5	5
Vocalization (0-3)					
0 : None		5	5	5	5
Reactivity to handling (1-5)					
2 : Easy		5	5	5	5
Fur condition (0-3)					
0 : Normal		5	5	5	5
Skin (0-3)					
0 : Normal		5	5	5	5
Piloerection(0/1)					
0 : Absent		5	5	5	5
Mucosal membranes (0-3)					
0 : Normal		5	5	5	5
Secretions-Eye, Nose (0/1)					
0 : Absent		5	5	5	5
Palpebral closure (0-3)					
0 : Normal		5	5	5	5
Exophthalmos (0/1)					
0 : Absent		5	5	5	5
Pupil size (1-4)					
2 : Normal		5	5	5	5
Lacrimation (0/1)					
0 : Normal		5	5	5	5
Salivation (0-3)					
0 : None		5	5	5	5
Abnormal respiration (0-3)					
0 : Absent		5	5	5	5

No significant difference between treated group and control group.

Table 2-14 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
In the hand observations (Recovery 2 weeks)

Parameter	Sex	Male		Female	
	Dose (mg/kg)	0	1000	0	1000
	No. of animals	5	5	5	5
Removal from cage (1-5)					
2 : Easy		5	5	5	5
Vocalization (0-3)					
0 : None		5	5	5	5
Reactivity to handling (1-5)					
2 : Easy		5	5	5	5
Fur condition (0-3)					
0 : Normal		5	5	5	5
Skin (0-3)					
0 : Normal		5	5	5	5
Piloerection(0/1)					
0 : Absent		5	5	5	5
Mucosal membranes (0-3)					
0 : Normal		5	5	5	5
Secretions-Eye, Nose (0/1)					
0 : Absent		5	5	5	5
Palpebral closure (0-3)					
0 : Normal		5	5	5	5
Exophthalmos (0/1)					
0 : Absent		5	5	5	5
Pupil size (1-4)					
2 : Normal		5	5	5	5
Lacrimation (0/1)					
0 : Normal		5	5	5	5
Salivation (0-3)					
0 : None		5	5	5	5
Abnormal respiration (0-3)					
0 : Absent		5	5	5	5

No significant difference between treated group and control group.

Table 2-15 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Open field observation (Pre administration)

Sex	Dose (mg/kg)	Male				Female			
		0	100	300	1000	0	100	300	1000
Parameter	No. of animals	10	5	5	10	10	5	5	10
Posture (N,F,H)									
N : Normal		10	5	5	10	10	5	5	10
Gait (U,0-3)									
0 : Normal		10	5	5	10	10	5	5	10
Arousal (1-5)									
3 : Normal		10	5	5	10	10	5	5	10
Tremor (0-3)									
0 : None		10	5	5	10	10	5	5	10
Convulsion (0-3)									
0 : None		10	5	5	10	10	5	5	10
Abnormal behavior (0-3)									
0 : None		10	5	5	10	10	5	5	10
Grooming (0-2)									
0 : None		10	5	5	10	10	5	5	10
Rearing		4+ 2	4+ 1	4+ 2	4+ 2	4+ 2	6+ 2	5+ 1	3+ 2
Urination (0-3)									
0 : None		9	5	5	10	10	5	5	10
1 : Small amount		1	0	0	0	0	0	0	0
Defecation count		0+ 0	0+ 0	0+ 0	0+ 0	0+ 0	0+ 0	0+ 0	0+ 0

No significant difference in any treated groups from control group.

Table 2-16 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Open field observation (1 week)

Sex	Dose (mg/kg)	Male				Female			
		0	100	300	1000	0	100	300	1000
Parameter	No. of animals	10	5	5	10	10	5	5	10
Posture (N,F,H)									
N : Normal		10	5	5	10	10	5	5	10
Gait(U,0-3)									
U : No/minimal location		2	2	0	2	0	0	0	0
0 : Normal		8	3	5	8	10	5	5	10
Arousal (1-5)									
3 : Normal		10	5	5	10	10	5	5	10
Tremor (0-3)									
0 : None		10	5	5	10	10	5	5	10
Convulsion (0-3)									
0 : None		10	5	5	10	10	5	5	10
Abnormal behavior(0-3)									
0 : None		10	5	5	10	10	5	5	10
Grooming (0-2)									
0 : None		10	5	4	10	10	5	5	10
1 : Occasional bouts (up to four)		0	0	1	0	0	0	0	0
Rearing		2± 2	1± 1	1± 1	1± 1	4± 2	5± 2	4± 3	2± 2
Urination (0-3)									
0 : None		10	4	4	8	10	5	5	10
1 : Small amount		0	1	1	2	0	0	0	0
Defecation count		0± 0	0± 0	0± 1	1± 1a)	0± 0	0± 0	0± 0	0± 0

No significant difference in any treated groups from control group.

a): 2/10 males had defecation and, yellowish feces were observed 1 out of the 2 males.

Table 2-17 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Open field observation (2 weeks)

Sex	Dose (mg/kg)	Male				Female			
		0	100	300	1000	0	100	300	1000
Parameter	No. of animals	10	5	5	10	10	5	5	10
Posture (N,F,H)									
N : Normal		10	5	5	10	10	5	5	10
Gait (L,0-3)									
L : No/minimal location		1	2	1	1	0	0	0	0
0 : Normal		9	3	4	9	10	5	5	10
Arousal (1-5)									
3 : Normal		10	5	5	10	10	5	5	10
Tremor (0-3)									
0 : None		10	5	5	10	10	5	5	10
Convulsion (0-3)									
0 : None		10	5	5	10	10	5	5	10
Abnormal behavior(0-3)									
0 : None		10	5	5	10	10	5	5	10
Grooming (0-2)									
0 : None		10	5	5	10	10	5	5	10
Rearing		1± 1	1± 2	2± 2	2± 2	4± 3	4± 1	4± 3	3± 2
Urination (0-3)									
0 : None		10	5	3	10	10	5	5	10
1 : Small amount		0	0	1	0	0	0	0	0
2 : Moderate amount		0	0	1	0	0	0	0	0
Defecation count		1± 1	0± 1	1± 1	0± 1a)	0± 0	0± 0	0± 0	0± 0

No significant difference in any treated groups from control group.

a): 1/10 males had defecation and, yellowish feces were observed.

Table 2-18 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Open field observation (3 weeks)

Sex		Male				Female			
Dose (mg/kg)		0	100	300	1000	0	100	300	1000
Parameter	No. of animals	10	5	5	10	10	5	5	10
Posture (N,F,H)									
N : Normal		10	5	5	10	10	5	5	10
Gait (U,0-3)									
U : No/minimal location		0	2	0	0	0	0	0	0
0 : Normal		10	3	5	10	10	5	5	10
Arousal (1-5)									
3 : Normal		10	5	5	10	10	5	5	10
Tremor (0-3)									
0 : None		10	5	5	10	10	5	5	10
Convulsion (0-3)									
0 : None		10	5	5	10	10	5	5	10
Abnormal behavior(0-3)									
0 : None		10	5	5	10	10	5	5	10
Grooming (0-2)									
0 : None		10	5	5	10	10	5	5	10
Rearing		2± 1	1± 2	3± 4	2± 2	5± 3	5± 3	5± 2	5± 3
Urination (0-3)									
0 : None		10	5	5	10	10	5	5	10
Defecation count		0± 0	1± 1	0± 1	0± 1a)	0± 0	0± 0	0± 0	0± 0

No significant difference in any treated groups from control group.
a): 1/10 males had defecation and, yellowish feces were observed.

Table 2-19

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Open field observation (4 weeks)

Parameter	Sex	Male				Female			
	Dose (mg/kg)	0	100	300	1000	0	100	300	1000
	No. of animals	10	5	5	10	10	5	5	10
Posture (N,F,H)									
N : Normal		10	5	5	10	10	5	5	10
Gait(U,0-3)									
U : No/minimal location		0	0	0	3	0	0	0	0
0 : Normal		10	5	5	7	10	5	5	10
Arousal (1-5)									
3 : Normal		10	5	5	10	10	5	5	10
Tremor (0-3)									
0 : None		10	5	5	10	10	5	5	10
Convulsion (0-3)									
0 : None		10	5	5	10	10	5	5	10
Abnormal behavior(0-3)									
0 : None		10	5	5	10	10	5	5	10
Grooming (0-2)									
0 : None		10	5	5	10	10	5	5	10
Rearing		3± 2	1± 1	2± 2	2± 2	5± 3	5± 2	4± 2	4± 3
Urination (0-3)									
0 : None		10	5	5	10	10	5	5	10
Defecation count		0± 0	0± 1	0± 0	0± 0	0± 0	0± 0	0± 0	0± 0

No significant difference in any treated groups from control group.

Table 2-20 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Open field observation (Recovery 1 week)

Parameter	Sex	Male		Female	
	Dose (mg/kg)	0	1000	0	1000
	No. of animals	5	5	5	5
Posture (N,F,H)					
N : Normal		5	5	5	5
Gait(U,0-3)					
0 : Normal		5	5	5	5
Arousal (1-5)					
3 : Normal		5	5	5	5
Tremor (0-3)					
0 : None		5	5	5	5
Convulsion (0-3)					
0 : None		5	5	5	5
Abnormal behavior(0-3)					
0 : None		5	5	5	5
Grooming (0-2)					
0 : None		5	5	5	5
Rearing		2± 2	2± 2	5± 3	6± 2
Urination (0-3)					
0 : None		5	5	5	5
Defecation count		0± 0	0± 0	0± 0	0± 0

No significant difference between treated group and control group.

Table 2-21

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Open field observation (Recovery 2 weeks)

Parameter	Sex Dose (mg/kg) No. of animals	Male		Female	
		0	1000	0	1000
		5	5	5	5
Posture (N,F,H)					
N : Normal		5	5	5	5
Gait (U,0-3)					
U : No/minimal location		0	1	0	0
0 : Normal		5	4	5	5
Arousal (1-5)					
3 : Normal		5	5	5	5
Tremor (0-3)					
0 : None		5	5	5	5
Convulsion (0-3)					
0 : None		5	5	5	5
Abnormal behavior (0-3)					
0 : None		5	5	5	5
Grooming (0-2)					
0 : None		5	5	5	5
Rearing		3 \pm 1	2 \pm 1	4 \pm 3	4 \pm 1
Urination (0-3)					
0 : None		5	5	5	5
Defecation count		0 \pm 0	0 \pm 0	0 \pm 0	0 \pm 0

No significant difference between treated group and control group.

Table 2-22 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Manipulative test (4 weeks)

Parameter	Sex Dose (mg/kg) No. of animals	Male				Female			
		0	100	300	1000	0	100	300	1000
		10	5	5	10	10	5	5	10
Approach response (1-3) 2 : Normal		10	5	5	10	10	5	5	10
Touch response (1-3) 2 : Normal		10	5	5	10	10	5	5	10
Auditory response (1-4) 3 : Normal		10	5	5	10	10	5	5	10
Tail pinch response (1-4) 3 : Normal		10	5	5	10	10	5	5	10
Pupillary reflex(P,F,L,R) P : Pass. both		10	5	5	10	10	5	5	10
Aerial righting reflex		0± 0	0± 0	0± 0	0± 0	0± 0	0± 0	0± 0	0± 0
Landing foot splay		81±23	84±27	66±20	73±19	57±19	72±11	61±15	57±24

No significant difference in any treated groups from control group.

Table 2-23 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Manipulative test (Recovery 2 weeks)

Parameter	Sex Dose (mg/kg) No. of animals	Male		Female	
		0	1000	0	1000
		5	5	5	5
Approach response (1-3)					
2 : Normal		5	5	5	5
Touch response (1-3)					
2 : Normal		5	5	5	5
Auditory response (1-4)					
3 : Normal		5	5	5	5
Tail pinch response (1-4)					
3 : Normal		5	5	5	5
Pupillary reflex(P,F,L,R)					
P : Pass, both		5	5	5	5
Aerial righting reflex		0± 0	0± 0	0± 0	0± 0
Landing foot splay		65± 6	58±17	59±13	42±11

No significant difference between treated group and control group.

Table 2-24 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Grip strength (4 week)

Sex	Dose mg/kg		Fore limb g	Hind limb g
Male	0	No.	10	10
		Mean	1040	546
		S.D.	149	119
	100	No.	5	5
		Mean	1028	519
		S.D.	195	60
	300	No.	5	5
		Mean	1041	512
		S.D.	165	33
	1000	No.	10	10
		Mean	992	525
		S.D.	161	109
Female	0	No.	10	10
		Mean	896	453
		S.D.	140	107
	100	No.	5	5
		Mean	953	496
		S.D.	168	120
	300	No.	5	5
		Mean	911	433
		S.D.	136	74
	1000	No.	10	10
		Mean	933	547
		S.D.	148	107

No significant difference from control group in any treated groups

Table 2-25 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Grip strength (Recovery 2 week)

Sex	Dose mg/kg		Fore limb g	Hind limb g
Male	0	No.	5	5
		Mean	1124	535
		S.D.	127	22
	1000	No.	5	5
		Mean	1104	517
		S.D.	115	64
Female	0	No.	5	5
		Mean	1024	489
		S.D.	112	60
	1000	No.	5	5
		Mean	1095	504
		S.D.	43	75

No significant difference between treated group and control group.

Table 2-26

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Motor activity (4 weeks)

Sex	Dose mg/kg		Interval (minutes)						
			0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
Male	0	No.	10	10	10	10	10	10	10
		Mean	405	359	275	153	136	103	1431
		S.D.	52	84	164	153	130	93	388
	100	No.	5	5	5	5	5	5	5
		Mean	397	319	188	122	116	90	1233
		S.D.	9	46	141	137	130	133	237
	300	No.	5	5	5	5	5	5	5
		Mean	364	368	193	66	32	24	1047
		S.D.	46	86	170	58	28	17	290
	1000	No.	10	10	10	10	10	10	10
		Mean	411	351	263	233	231	214	1702
		S.D.	51	70	149	152	179	157	584
Female	0	No.	10	10	10	10	10	10	10
		Mean	394	341	291	234	190	159	1609
		S.D.	50	80	159	139	147	127	474
	100	No.	5	5	5	5	5	5	5
		Mean	404	384	214	155	120	271	1547
		S.D.	21	62	102	160	142	69	210
	300	No.	5	5	5	5	5	5	5
		Mean	403	329	235	109	53	244	1373
		S.D.	32	94	157	132	49	138	548
	1000	No.	10	10	10	10	10	10	10
		Mean	396	315	195	209	185	190	1489
		S.D.	27	109	162	127	130	134	515

No significant difference in any treated groups from control group.

Table 2-27 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Motor activity (Recovery 2 weeks)

Sex	Dose mg/kg		Interval (minutes)						Total(0-60)
			0-10	10-20	20-30	30-40	40-50	50-60	
Male	0	No.	5	5	5	5	5	5	5
		Mean	433	339	274	92	25	45	1207
		S.D.	37	183	146	110	25	49	409
	1000	No.	5	5	5	5	5	5	5
		Mean	427	399	369	287*	235	195	1912*
		S.D.	35	43	42	117	183	174	524
Female	0	No.	5	5	5	5	5	5	5
		Mean	394	301	82	55	79	56	968
		S.D.	46	94	111	61	105	104	204
	1000	No.	5	5	5	5	5	5	5
		Mean	381	315	236	27	43	71	1073
		S.D.	57	108	153	41	42	87	365

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

Table 3-1 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Body weight (Administration period)

Sex	Dose mg/kg		Day of administration								Gain 1-28	
			1	4	7	10	14	17	21	24		28
Male	0	No.	10	10	10	10	10	10	10	10	10	10
		Mean	239	259	280	299	323	338	360	369	391	152
		S.D.	8	11	13	14	16	19	23	26	31	30
	100	No.	5	5	5	5	5	5	5	5	5	5
		Mean	239	259	284	303	332	346	369	374	401	163
		S.D.	5	7	9	11	11	14	16	18	19	19
	300	No.	5	5	5	5	5	5	5	5	5	5
		Mean	238	258	277	292	313	325	347	355	378	140
		S.D.	7	7	7	10	9	12	12	15	12	12
	1000	No.	10	10	10	10	10	10	10	10	10	10
		Mean	239	256	276	295	319	336	355	363	385	146
		S.D.	5	8	12	14	16	17	19	20	22	20
Female	0	No.	10	10	10	10	10	10	10	10	10	10
		Mean	184	193	202	211	224	232	240	245	255	71
		S.D.	7	8	9	8	10	13	13	12	13	10
	100	No.	5	5	5	5	5	5	5	5	5	5
		Mean	184	192	200	212	224	231	244	248	258	74
		S.D.	7	8	3	7	8	8	6	9	8	8
	300	No.	5	5	5	5	5	5	5	5	5	5
		Mean	184	190	204	212	223	231	240	244	256	72
		S.D.	6	11	9	15	14	14	13	13	11	8
	1000	No.	10	10	10	10	10	10	10	10	10	10
		Mean	186	190	200	210	220	227	238	239	248	63
		S.D.	6	6	5	9	9	9	11	11	12	9

Unit : g

No significant difference in any treated groups from control group.

Table 3-2 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Body weight (Recovery period)

Sex	Dose mg/kg		Day of recovery					Gain 1-14
			1	3	7	10	14	
Male	0	No.	5	5	5	5	5	5
		Mean	379	387	405	412	425	46
		S.D.	40	41	43	43	47	8
	1000	No.	5	5	5	5	5	5
		Mean	386	394	414	421	437	51
		S.D.	21	22	25	27	31	11
Female	0	No.	5	5	5	5	5	5
		Mean	257	261	271	272	274	18
		S.D.	14	16	17	14	13	3
	1000	No.	5	5	5	5	5	5
		Mean	253	259	267	269	276	24*
		S.D.	14	12	13	17	16	4

Unit : g

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

Table 4-1 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Food consumption (Administration period)

Sex	Dose mg/kg		Day of administration								
			1	4	7	10	14	17	21	24	28
Male	0	No.	10	10	10	10	10	10	10	10	10
		Mean	25	21	21	21	20	19	20	19	19
		S.D.	2	2	2	2	2	2	3	2	2
	100	No.	5	5	5	5	5	5	5	5	5
		Mean	25	22	22	21	22	20	21	19	20
		S.D.	2	1	2	2	3	2	3	3	3
	300	No.	5	5	5	5	5	5	5	5	5
		Mean	23	22	21	19	19	18	19	18	19
		S.D.	2	2	1	2	2	3	2	1	2
	1000	No.	10	10	10	10	10	10	10	10	10
		Mean	23	20	20	20	20	20	20	19	20
		S.D.	0	1	2	2	2	1	1	1	1
Female	0	No.	10	10	10	10	10	10	10	10	10
		Mean	17	16	15	16	16	14	15	15	15
		S.D.	3	1	1	1	1	1	2	2	1
	100	No.	5	5	5	5	5	5	5	5	5
		Mean	18	15	15	15	16	15	16	15	15
		S.D.	3	2	1	2	2	2	1	2	1
	300	No.	5	5	5	5	5	5	5	5	5
		Mean	17	16	16	15	15	15	15	15	15
		S.D.	3	2	1	2	2	2	1	1	1
	1000	No.	10	10	10	10	10	10	10	10	10
		Mean	18	15	16	15	15	14	15	14	14
		S.D.	2	1	2	2	1	2	2	2	2

Unit : g/rat/day

No significant difference in any treated groups from control group.

Table 4-2 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Food consumption (Recovery period)

Sex	Dose mg/kg		Day of recovery			
			3	7	10	14
Male	0	No.	5	5	5	5
		Mean	24	25	25	27
		S.D.	2	3	3	3
	1000	No.	5	5	5	5
		Mean	25	27	26	29
		S.D.	2	1	2	2
Female	0	No.	5	5	5	5
		Mean	18	20	20	20
		S.D.	3	1	2	1
	1000	No.	5	5	5	5
		Mean	18	21	20	21
		S.D.	2	2	2	3

Unit : g/rat/day

No significant difference between treated group and control group.

Table 5-1 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Urinalysis (4 weeks)

Sex	Dose mg/kg	No.	pH									1) Protein					2) Ketone body					3) Glucose							
			5.0	5.5	6.0	6.5	7.0	7.5	8.0	8.5	9.0	-	+	++	+++	++++	-	+	++	+++	++++	-	+	++	+++	++++			
Male	0	10	0	0	0	0	0	0	2	5	3	0	1	7	2	0	0	3	4	3	0	0	0	10	0	0	0	0	0
	100	5	0	0	0	0	0	0	2	3	0	0	5	0	0	0	0	5	0	0	0	0	0*	5	0	0	0	0	0
	300	5	0	0	0	0	0	0	1	3	1	2	1	2	0	0	0*	5	0	0	0	0	0*	5	0	0	0	0	0
	1000	10	0	0	0	0	0	0	1	8	1	0	4	6	0	0	0	7	2	1	0	0	0	10	0	0	0	0	0
Female	0	10	0	0	0	0	4	1	4	1	0	5	3	2	0	0	0	9	0	1	0	0	0	10	0	0	0	0	0
	100	5	0	0	0	0	0	0	4	1	0	1	2	2	0	0	0	5	0	0	0	0	0	5	0	0	0	0	0
	300	5	0	0	0	1	0	1	1	2	0	1	1	3	0	0	0	3	0	2	0	0	0	5	0	0	0	0	0
	1000	10	0	0	1	0	1	1	2	5	0	0	5	4	1	0	0*	7	2	1	0	0	0	9	1	0	0	0	0
1) - : 0 - 5 mg/dL			+- : 10 - 20 mg/dL			+ : 30 - 70 mg/dL			++ : 100 - 200 mg/dL			+++ : 250 - 400 mg/dL			++++ : >400 mg/dL														
2) - : 0 mg/dL			+- : 5 mg/dL			+ : 10 - 20 mg/dL			++ : 30 - 45 mg/dL			+++ : 60 - 80 mg/dL			++++ : >80 mg/dL														
3) - : 0 - 10 mg/dL			+- : 30 - 50 mg/dL			+ : 70 - 100 mg/dL			++ : 150 - 200 mg/dL			+++ : 300 - 500 mg/dL			++++ : ≥1000 mg/dL														
* : p<0.05 ; ** : p<0.01 (Significant difference from control group)																													

Table 5-2 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Urinalysis (4 weeks)

Sex	Dose mg/kg	No.	4) Occult blood					5) Bilirubin					6) Urobilinogen					7) Color		
			-	+-	+	++	+++	-	+-	+	++	+++	++++	+-	+	++	+++	LY	Y	DY
Male	0	10	10	0	0	0	0	10	0	0	0	0	0	9	1	0	0	0	10	0
	100	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	0	5	0
	300	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	0	5	0
	1000	10	10	0	0	0	0	10	0	0	0	0	0	8	2	0	0	0	10	0
Female	0	10	10	0	0	0	0	10	0	0	0	0	0	9	1	0	0	0	10	0
	100	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	0	5	0
	300	5	5	0	0	0	0	5	0	0	0	0	0	3	2	0	0	0	5	0
	1000	10	9	1	0	0	0	10	0	0	0	0	0	9	0	1	0	0	10	0
4)			-	+-	+	++	+++	+	+-	+	++	+++	++++	+-	+	++	+++	++++		
5)			-	+-	+	++	+++	+	+-	+	++	+++	++++	+-	+	++	+++	++++		
6)			-	+-	+	++	+++	+	+-	+	++	+++	++++	+-	+	++	+++	++++		
7)			LY	Y	DY			LY	Y	DY				LY	Y	DY				

4) - : 0 mg/dL +- : 0.03 mg/dL + : 0.06 - 0.1 mg/dL ++ : 0.2 - 0.5 mg/dL +++ : ≥1.0 mg/dL
 5) - : 0 mg/dL +- : 0.2 mg/dL + : 0.5 - 1.0 mg/dL ++ : 2.0 - 4.0 mg/dL +++ : 6.0 - 10.0 mg/dL ++++ : >10.0 mg/dL
 6) +- : 0.2 - 1.0 mg/dL + : 2.0 - 3.0 mg/dL ++ : 4.0 - 6.0 mg/dL +++ : 8.0 - 12.0 mg/dL ++++ : >12.0 mg/dL
 7) LY : Light yellow Y : Yellow DY : Dark yellow
 No significant difference in any treated groups from control group.

Table 5-3 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Urinalysis (4 weeks)

			URINE SEDIMENT																																		
Sex	Dose mg/kg	No.	RBC					WBC					SEC					SREC					Cast			CRYSTALLIZATION											
																										PS					CO						
			-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	-	+-	+	++	+++	-	+-	+	++	+++		
Male	0	10	10	0	0	0	0	10	0	0	0	0	0	0	10	0	0	0	0	0	10	0	0	10	0	0	9	1	0	0	0	0	10	0	0	0	0
	100	5	5	0	0	0	0	5	0	0	0	0	0	0	5	0	0	0	0	0	5	0	0	5	0	0	5	0	0	0	0	0	5	0	0	0	0
	300	5	5	0	0	0	0	5	0	0	0	0	0	0	5	0	0	0	0	0	5	0	0	5	0	0	5	0	0	0	0	0	5	0	0	0	0
	1000	10	10	0	0	0	0	10	0	0	0	0	0	0	10	0	0	0	0	0	10	0	0	10	0	0	10	0	0	0	0	0	10	0	0	0	0
Female	0	10	10	0	0	0	0	10	0	0	0	0	0	0	10	0	0	0	0	0	10	0	0	10	0	0	10	0	0	0	0	0	10	0	0	0	0
	100	5	5	0	0	0	0	5	0	0	0	0	0	0	5	0	0	0	0	0	5	0	0	4	1	0	0	0	0	0	5	0	0	0	0		
	300	5	5	0	0	0	0	5	0	0	0	0	0	0	5	0	0	0	0	0	5	0	0	4	1	0	0	0	0	5	0	0	0	0			
	1000	10	10	0	0	0	0	10	0	0	0	0	0	0	10	0	0	0	0	0	10	0	0	7	3	0	0	0	0	10	0	0	0	0			

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

No significant difference in any treated groups from control group.

Table 5-4 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Water intake and urinalysis (4 weeks)

Sex	Dose mg/kg	No.		Water intake mL/24h	Urine volume mL/24h	Osmolality mOsm/kg
Male	0	10	Mean	37	6.0	1756
			S.D.	7	3.1	445
	100	5	Mean	38	9.8	1545
			S.D.	5	3.4	426
	300	5	Mean	50*	12.9*	1201*
			S.D.	11	7.7	480
	1000	10	Mean	43	7.3	1795
			S.D.	9	2.2	289
Female	0	10	Mean	36	5.5	1563
			S.D.	5	2.2	462
	100	5	Mean	30	6.3	1804
			S.D.	5	4.3	726
	300	5	Mean	38	7.4	1534
			S.D.	12	5.7	513
	1000	10	Mean	41	5.5	1624
			S.D.	20	2.4	418

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

Table 5-5 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Urinalysis (Recovery)

Sex	Dose mg/kg	No.	pH									1) Protein					2) Ketone body					3) Glucose							
			5.0	5.5	6.0	6.5	7.0	7.5	8.0	8.5	9.0	-	+-	+	++	+++	++++	-	+-	+	++	+++	++++	-	+-	+	++	+++	++++
Male	0	5	0	0	0	0	0	0	0	3	2	0	0	2	2	1	0	2	2	1	0	0	0	5	0	0	0	0	0
	1000	5	0	0	0	0	0	0	0	1	2	2	0	1	2	1	1	0	3	2	0	0	0	0	5	0	0	0	0
Female	0	5	0	0	0	0	1	0	1	3	0	1	1	3	0	0	0	4	1	0	0	0	0	5	0	0	0	0	0
	1000	5	0	0	0	0	0	0	0	4	1	0	1	3	1	0	0	0	4	1	0	0	0	0	4	1	0	0	0
1) - : 0 - 5 mg/dL			+- : 10 - 20 mg/dL			+ : 30 - 70 mg/dL			++ : 100 - 200 mg/dL			+++ : 250 - 400 mg/dL			++++ : >400 mg/dL														
2) - : 0 mg/dL			+- : 5 mg/dL			+ : 10 - 20 mg/dL			++ : 30 - 45 mg/dL			+++ : 60 - 80 mg/dL			++++ : >80 mg/dL														
3) - : 0 - 10 mg/dL			+- : 30 - 50 mg/dL			+ : 70 - 100 mg/dL			++ : 150 - 200 mg/dL			+++ : 300 - 500 mg/dL			++++ : ≥1000 mg/dL														
No significant difference between treated group and control group.																													

Table 5-6 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Urinalysis (Recovery)

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

4) - : 0 mg/dL +- : 0.03 mg/dL + : 0.06 - 0.1 mg/dL ++ : 0.2 - 0.5 mg/dL +++ : ≥1.0 mg/dL
 5) - : 0 mg/dL +- : 0.2 mg/dL + : 0.5 - 1.0 mg/dL ++ : 2.0 - 4.0 mg/dL +++ : 6.0 - 10.0 mg/dL ++++ : >10.0 mg/dL
 6) +- : 0.2 - 1.0 mg/dL + : 2.0 - 3.0 mg/dL ++ : 4.0 - 6.0 mg/dL +++ : 8.0 - 12.0 mg/dL ++++ : >12.0 mg/dL
 7) LY : Light yellow Y : Yellow DY : Dark yellow
 No significant difference between treated group and control group.

Table 5-7 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Urinalysis (Recovery)

Sex	Dose mg/kg	No.	URINE SEDIMENT															CRYSTALLIZATION																		
			RBC					WBC					SEC					SREC					Cast			PS					CO					
			-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	-	+-	+	-	+-	+	-	+-	+							
Male	0	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	2	3	0	0	0	5	0	0	0	0
	1000	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	3	2	0	0	0	5	0	0	0	0
Female	0	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	4	1	0	0	0	5	0	0	0	0
	1000	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	5	0	0	0	0	5	0	0	0	0
SEC : Squamous Epithelial Cell			-					: Negative																												
SREC : Small Round Epithelial Cell			+-					: Slight																												
PS : Phosphate Salts			+					: Mild																												
CO : Calcium Oxalate			++					: Moderate																												
			+++					: Severe																												

No significant difference between treated group and control group.

Table 5-8 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Water intake and urinalysis (Recovery)

Sex	Dose mg/kg	No.		Water intake mL/24h	Urine volume mL/24h	Osmolality mOsm/kg
Male	0	5	Mean	40	6.9	2444
			S.D.	9	1.6	238
	1000	5	Mean	44	11.6*	1887
			S.D.	11	3.6	532
Female	0	5	Mean	51	7.6	1975
			S.D.	28	3.5	643
	1000	5	Mean	37	10.1	1583
			S.D.	7	3.9	430

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

Table G-1 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Hematology (4 weeks)

Sex	Dose mg/kg	No.		RBC ×10 ⁶ /μL	Hb g/dL	Ht %	MCV fL	MCH pg	MCHC %	Reticu- locyte %	Plate- let ×10 ³ /μL	PT s	APTT s	Fibri- nogen mg/dL
Male	0	5	Mean	772	15.3	45	58.0	19.8	34.2	2.2	96.0	11.6	15.7	245
			S.D.	19	0.5	1	1.4	0.6	0.3	0.5	4.8	0.5	0.8	9
	100	5	Mean	768	15.5	45	58.8	20.2	34.3	2.0	96.2	12.2	16.2	257
			S.D.	12	0.3	1	1.5	0.5	0.3	0.4	10.7	0.4	2.3	26
	300	5	Mean	792	15.7	46	57.7	19.8	34.3	2.2	103.7	12.8*	18.6	259
			S.D.	46	0.5	1	1.6	0.6	0.2	0.4	12.3	1.1	1.8	19
	1000	5	Mean	775	15.4	45	57.6	19.8	34.3	2.1	96.9	12.4	16.6	264
			S.D.	46	0.9	3	1.8	0.9	0.7	0.7	10.0	0.7	2.4	8
Female	0	5	Mean	753	15.4	44	57.8	20.5	35.5	1.8	105.7	11.7	16.7	216
			S.D.	28	0.7	2	1.3	0.5	0.8	0.4	12.5	0.5	2.2	21
	100	5	Mean	742	15.1	42	56.8	20.4	35.9	1.8	105.6	11.7	17.2	199
			S.D.	52	0.5	2	1.2	0.9	1.0	0.5	7.3	0.4	1.7	9
	300	5	Mean	732	15.4	43	58.7	21.1	35.8	2.3	100.7	11.5	15.7	220
			S.D.	49	0.6	2	2.1	1.0	0.8	0.5	11.4	0.5	1.5	22
	1000	5	Mean	742	15.2	43	57.9	20.5	35.3	1.8	97.9	11.5	16.3	209
			S.D.	35	0.9	3	1.9	0.7	0.6	0.3	10.9	0.6	1.0	24

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

Table G-2 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Hematology (4 weeks)

Sex	Dose mg/kg	No.		WBC	Differential leukocyte counts (%)						
				$\times 10^3/\mu\text{L}$	Lymph.	Stab	Seg.	Eosino.	Baso.	Mono.	Others
Male	0	5	Mean	96	86.2	0.9	11.6	0.8	0.0	0.5	0.0
			S.D.	26	6.5	0.7	4.9	1.0	0.0	0.0	0.0
	100	5	Mean	92	89.7	0.4	9.1	0.4	0.0	0.4	0.0
			S.D.	26	4.9	0.4	5.3	0.2	0.0	0.4	0.0
	300	5	Mean	104	87.3	0.8	11.1	0.3	0.0	0.5	0.0
			S.D.	17	2.5	0.3	2.5	0.4	0.0	0.6	0.0
	1000	5	Mean	129	89.4	1.0	9.2	0.2	0.0	0.2	0.0
			S.D.	46	4.6	1.2	4.3	0.4	0.0	0.3	0.0
Female	0	5	Mean	75	86.3	1.0	11.7	0.8	0.0	0.2	0.0
			S.D.	30	5.6	0.8	5.3	0.6	0.0	0.3	0.0
	100	5	Mean	65	87.8	0.8	10.1	1.0	0.0	0.3	0.0
			S.D.	15	1.4	1.0	1.6	1.2	0.0	0.4	0.0
	300	5	Mean	84	85.1	1.0	13.0	0.5	0.0	0.4	0.0
			S.D.	18	3.2	1.1	2.8	0.5	0.0	0.4	0.0
	1000	5	Mean	77	88.4	0.2	10.1	0.5	0.0	0.8*	0.0
			S.D.	16	2.0	0.3	1.8	0.6	0.0	0.3	0.0

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

Table 6-3

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
 Hematology (Recovery)

Sex	Dose mg/kg	No.		RBC ×10 ⁶ /μL	Hb g/dL	Ht %	MCV fL	MCH pg	MCHC %	Reticu- loocyte %	Plate- let ×10 ³ /μL	PT s	APTT s	Fibri- nogen mg/dL
Male	0	5	Mean	810	15.3	46	56.5	18.9	33.5	1.8	95.0	13.8	19.9	247
			S.D.	29	0.5	1	1.0	0.6	0.5	0.5	7.2	0.9	0.9	28
	1000	5	Mean	786	15.2	45	57.3	19.3	33.7	1.7	106.1	13.0	18.4	260
			S.D.	20	0.7	2	1.6	0.7	0.4	0.2	13.5	0.7	2.4	26
Female	0	5	Mean	791	15.5	46	57.9	19.6	33.8	1.6	100.8	11.4	14.7	209
			S.D.	31	0.8	2	1.7	0.7	0.4	0.3	7.8	0.3	1.5	22
	1000	5	Mean	798	15.5	46	57.8	19.5	33.7	1.8	104.0	11.5	15.6	200
			S.D.	27	0.4	2	1.5	0.5	0.3	0.4	6.4	0.5	0.6	10

No significant difference between treated group and control group.

Table 6-4 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Hematology (Recovery)

Sex	Dose mg/kg	No.		WBC	Differential leukocyte counts (%)						
				$\times 10^9/\mu\text{L}$	Lymph.	Stab	Seg.	Eosino.	Baso.	Mono.	Others
Male	0	5	Mean	74	83.1	1.3	14.7	0.6	0.0	0.3	0.0
			S.D.	13	7.3	0.8	6.8	0.4	0.0	0.3	0.0
	1000	5	Mean	97*	83.3	0.3*	15.7	0.6	0.0	0.1	0.0
			S.D.	16	3.5	0.4	3.8	0.4	0.0	0.2	0.0
	0	5	Mean	71	86.8	0.9	10.6	1.4	0.0	0.3	0.0
			S.D.	14	6.1	0.7	6.1	0.7	0.0	0.3	0.0
Female	1000	5	Mean	87	93.4	0.6	4.8	1.1	0.0	0.1	0.0
			S.D.	23	4.3	0.4	3.4	1.0	0.0	0.2	0.0

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

Table 7-1 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Blood chemistry (4 weeks)

Sex	Dose mg/kg	No.		GOT (ASAT) IU/L	GPT (ALAT) IU/L	LDH IU/L	ALP IU/L	γ -GTP IU/L	TP g/dL	Albumin g/dL	A/G	T.cho mg/dL	TG mg/dL	PL mg/dL
Male	0	5	Mean	49	29	52	328	1.6	5.8	3.7	1.87	55	49	96
			S.D.	9	3	38	63	0.2	0.3	0.1	0.22	5	11	11
	100	5	Mean	49	28	45	326	1.6	6.0	3.8	1.75	46	48	87
			S.D.	8	2	26	85	0.3	0.4	0.2	0.30	7	13	12
	300	5	Mean	47	29	45	366	1.5	5.7	3.8	1.91	56	67	99
			S.D.	6	3	16	56	0.2	0.2	0.1	0.15	11	36	11
	1000	5	Mean	52	30	53	403	1.8	5.7	3.8	1.91	58	52	98
			S.D.	7	2	32	53	0.2	0.2	0.1	0.11	10	21	10
Female	0	5	Mean	65	29	31	201	2.1	6.2	3.9	1.71	50	23	87
			S.D.	14	10	17	35	0.2	0.2	0.0	0.18	11	2	18
	100	5	Mean	49*	26	27	189	1.9	6.0	3.9	1.88	58	30	104
			S.D.	5	1	7	43	0.2	0.5	0.1	0.20	3	8	12
	300	5	Mean	54	29	26	174	1.9	6.2	3.9	1.73	59	25	105
			S.D.	5	6	6	46	0.3	0.2	0.0	0.11	8	4	6
	1000	5	Mean	50*	26	24	190	1.9	6.2	4.0	1.74	62	30	111
			S.D.	6	1	3	20	0.4	0.3	0.3	0.10	10	11	20

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

Table 7-2 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Blood chemistry (4 weeks)

Sex	Dose mg/kg	No.		T.bili- rubin mg/dL	Glucose mg/dL	BUN mg/dL	Crea- tinine mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL
Male	0	5	Mean	0.11	151	8	0.56	143	4.7	110	9.7	8.6
			S.D.	0.01	24	0	0.02	1	0.2	1	0.2	0.1
	100	5	Mean	0.11	153	8	0.57	144	4.6	110	9.7	8.6
			S.D.	0.01	11	1	0.04	1	0.2	2	0.3	0.4
	300	5	Mean	0.12	140	8	0.53	143	4.7	108	9.5	8.3
			S.D.	0.01	12	1	0.04	1	0.3	1	0.2	0.6
	1000	5	Mean	0.11	145	9	0.55	143	4.8	110	9.6	8.6
			S.D.	0.01	18	1	0.06	1	0.2	2	0.3	0.6
Female	0	5	Mean	0.09	146	10	0.60	142	4.8	111	9.4	6.8
			S.D.	0.02	16	1	0.05	2	0.0	2	0.1	0.6
	100	5	Mean	0.10	160	12	0.62	141	4.7	111	9.5	6.9
			S.D.	0.01	15	2	0.07	1	0.5	0	0.2	0.6
	300	5	Mean	0.10	143	10	0.57	142	5.0	111	9.4	6.9
			S.D.	0.01	11	1	0.04	1	0.1	1	0.3	0.6
	1000	5	Mean	0.09	140	12	0.59	141	4.8	110	9.5	6.9
			S.D.	0.02	8	2	0.04	1	0.2	1	0.2	0.6

No significant difference in any treated groups from control group.

Table 7-3 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Blood chemistry (Recovery)

Sex	Dose mg/kg	No.		GOT (ASAT) IU/L	GPT (ALAT) IU/L	LDH IU/L	ALP IU/L	γ -GTP IU/L	TP g/dL	Albumin g/dL	A/G	T.cho mg/dL	TG mg/dL	PL mg/dL
Male	0	5	Mean	66	32	27	252	1.8	5.9	3.7	1.69	61	32	95
			S.D.	5	3	6	23	0.2	0.2	0.1	0.16	7	9	6
	1000	5	Mean	63	33	34	245	1.9	6.1	3.7	1.56	72	33	106
			S.D.	8	3	5	47	0.2	0.2	0.1	0.09	16	9	13
Female	0	5	Mean	53	24	20	115	1.8	6.3	4.0	1.73	79	29	123
			S.D.	3	5	4	19	0.6	0.3	0.1	0.23	8	5	9
	1000	5	Mean	55	27	22	118	1.9	6.6	4.1	1.66	82	32	137
			S.D.	3	6	5	22	0.3	0.4	0.2	0.12	16	9	27

No significant difference between treated group and control group.

Table 7-4

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
 Blood chemistry (Recovery)

Sex	Dose mg/kg	No.		T.bili- rubin mg/dL	Glucose mg/dL	BUN mg/dL	Crea- tinine mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL
Male	0	5	Mean	0.10	122	12	0.56	142	4.6	109	9.5	8.0
			S.D.	0.01	15	1	0.02	2	0.2	2	0.1	0.4
	1000	5	Mean	0.11*	133	13*	0.60**	142	4.6	108	9.5	8.3
			S.D.	0.00	10	1	0.01	1	0.2	2	0.3	0.4
Female	0	5	Mean	0.10	128	14	0.59	140	4.9	110	9.8	7.9
			S.D.	0.02	10	2	0.04	1	0.4	1	0.2	0.7
	1000	5	Mean	0.11	131	13	0.59	140	5.0	111	9.8	7.6
			S.D.	0.03	11	1	0.02	1	0.4	1	0.3	0.7

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

Table 8-1 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Absolute and relative organ weight (4 weeks)
Male

	Dose mg/kg		Body weight	Brain	Thymus	Heart	Lung	Liver	Spleen	Kidney (R+L)
			g	g(g/100g BW)	mg(mg/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)
Absolute	0	No.	5	5	5	5	5	5	5	5
		Mean	382	2.05	404	1.23	1.34	11.75	0.64	2.66
		S.D.	10	0.19	77	0.07	0.07	0.76	0.07	0.08
	100	No.	5	5	5	5	5	5	5	5
		Mean	377	1.99	454	1.18	1.28	12.06	0.68	2.57
		S.D.	18	0.06	149	0.10	0.11	1.50	0.05	0.24
	300	No.	5	5	5	5	5	5	5	5
		Mean	357	1.99	381	1.17	1.25	11.02	0.66	2.62
		S.D.	15	0.02	89	0.05	0.04	1.48	0.09	0.30
	1000	No.	5	5	5	5	5	5	5	5
		Mean	361	2.00	459	1.21	1.29	10.92	0.67	2.67
		S.D.	24	0.09	174	0.03	0.07	1.53	0.09	0.10
Relative	0	No.		5	5	5	5	5	5	5
		Mean		0.54	106	0.32	0.35	3.08	0.17	0.70
		S.D.		0.05	22	0.01	0.02	0.16	0.02	0.02
	100	No.		5	5	5	5	5	5	5
		Mean		0.53	122	0.31	0.34	3.19	0.18	0.68
		S.D.		0.01	47	0.02	0.02	0.26	0.02	0.04
	300	No.		5	5	5	5	5	5	5
		Mean		0.56	107	0.33	0.35	3.08	0.19	0.73
		S.D.		0.02	23	0.01	0.01	0.33	0.03	0.06
	1000	No.		5	5	5	5	5	5	5
		Mean		0.56	126	0.34	0.36	3.01	0.18	0.74
		S.D.		0.06	43	0.02	0.02	0.25	0.02	0.07

No significant difference in any treated groups from control group.

Table 8-2 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
 Absolute and relative organ weight (4 weeks)
 Male

Dose mg/kg		Adrenal (R+L) mg(mg/100g BW)	Testis (R+L) g(g/100g BW)	Epididymis (R+L) mg(mg/100g BW)
Absolute	0	No.	5	5
		Mean	55	2.98
		S.D.	9	0.15
	100	No.	5	5
		Mean	56	2.46
		S.D.	5	1.03
	300	No.	5	5
		Mean	49	2.91
		S.D.	8	0.37
	1000	No.	5	5
		Mean	52	3.12
		S.D.	10	0.19
Relative	0	No.	5	5
		Mean	14	0.78
		S.D.	2	0.04
	100	No.	5	5
		Mean	15	0.65
		S.D.	1	0.26
	300	No.	5	5
		Mean	14	0.82
		S.D.	2	0.11
	1000	No.	5	5
		Mean	14	0.87
		S.D.	3	0.10

No significant difference in any treated groups from control group.

Table 8-3 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Absolute and relative organ weight (4 weeks)
Female

	Dose mg/kg		Body weight	Brain	Thymus	Heart	Lung	Liver	Spleen	Kidney (R+L)
			g	g(g/100g BW)	mg(mg/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)
Absolute	0	No.	5	5	5	5	5	5	5	5
		Mean	241	1.91	403	0.84	1.05	6.98	0.49	1.67
		S.D.	11	0.11	129	0.06	0.07	0.40	0.06	0.12
	100	No.	5	5	5	5	5	5	5	5
		Mean	245	1.88	412	0.84	1.03	7.11	0.46	1.76
		S.D.	9	0.07	49	0.03	0.04	0.50	0.03	0.12
	300	No.	5	5	5	5	5	5	5	5
		Mean	242	1.86	412	0.81	1.01	7.17	0.50	1.76
		S.D.	15	0.08	49	0.03	0.07	0.79	0.05	0.10
	1000	No.	5	5	5	5	5	5	5	5
		Mean	234	1.87	404	0.77	1.04	6.79	0.52	1.69
		S.D.	9	0.12	58	0.04	0.06	0.63	0.05	0.12
Relative	0	No.		5	5	5	5	5	5	5
		Mean		0.79	166	0.35	0.43	2.90	0.20	0.69
		S.D.		0.05	44	0.02	0.02	0.12	0.01	0.04
	100	No.		5	5	5	5	5	5	5
		Mean		0.77	168	0.34	0.42	2.91	0.19	0.72
		S.D.		0.03	16	0.02	0.02	0.25	0.02	0.05
	300	No.		5	5	5	5	5	5	5
		Mean		0.77	170	0.34	0.42	2.96	0.21	0.73
		S.D.		0.05	18	0.03	0.03	0.27	0.02	0.04
	1000	No.		5	5	5	5	5	5	5
		Mean		0.80	173	0.33	0.45	2.90	0.22	0.73
		S.D.		0.04	28	0.01	0.02	0.20	0.01	0.06

No significant difference in any treated groups from control group.

Table 8-4 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
 Absolute and relative organ weight (4 weeks)
 Female

Dose mg/kg		Adrenal (R+L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	0	No.	5	5
		Mean	69	466
		S.D.	4	112
	100	No.	5	5
		Mean	64	530
		S.D.	6	90
	300	No.	5	5
		Mean	67	462
		S.D.	6	94
	1000	No.	5	5
		Mean	63	492
		S.D.	4	137
Relative	0	No.	5	5
		Mean	29	193
		S.D.	1	39
	100	No.	5	5
		Mean	26	216
		S.D.	2	35
	300	No.	5	5
		Mean	28	193
		S.D.	4	46
	1000	No.	5	5
		Mean	27	212
		S.D.	2	68

No significant difference in any treated groups from control group.

Table 8-5 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Absolute and relative organ weight (Recovery)
Male

	Dose mg/kg		Body weight	Brain	Thymus	Heart	Lung	Liver	Spleen	Kidney (R+L)
			g	g(g/100g BW)	mg(mg/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)
Absolute	0	No.	5	5	5	5	5	5	5	5
		Mean	395	2.01	325	1.19	1.28	10.14	0.61	2.87
		S.D.	43	0.09	82	0.06	0.12	1.41	0.04	0.34
	1000	No.	5	5	5	5	5	5	5	5
		Mean	405	2.05	359	1.24	1.26	10.73	0.66	2.85
		S.D.	28	0.11	66	0.08	0.08	0.91	0.07	0.15
Relative	0	No.		5	5	5	5	5	5	5
		Mean		0.52	82	0.30	0.33	2.56	0.16	0.73
		S.D.		0.06	13	0.03	0.02	0.09	0.02	0.06
	1000	No.		5	5	5	5	5	5	5
		Mean		0.51	89	0.31	0.31	2.65	0.16	0.70
		S.D.		0.03	20	0.01	0.02	0.08	0.02	0.06

No significant difference between treated group and control group.

Table 8-6 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
 Absolute and relative organ weight (Recovery)
 Male

			Adrenal (R+L) mg(mg/100g BW)	Testis (R+L) g(g/100g BW)	Epididymis (R+L) mg(mg/100g BW)
Absolute	0	No.	5	5	5
		Mean	56	3.12	1018
		S.D.	13	0.27	79
	1000	No.	5	5	5
		Mean	56	3.15	1054
		S.D.	11	0.32	136
Relative	0	No.	5	5	5
		Mean	14	0.80	261
		S.D.	2	0.14	40
	1000	No.	5	5	5
		Mean	14	0.77	259
		S.D.	3	0.05	18

No significant difference between treated group and control group.

Table 8-7

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
 Absolute and relative organ weight (Recovery)
 Female

	Dose mg/kg		Body weight	Brain	Thymus	Heart	Lung	Liver	Spleen	Kidney (R+L)
			g	g(g/100g BW)	mg(mg/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)
Absolute	0	No.	5	5	5	5	5	5	5	5
		Mean	258	1.92	371	0.86	1.08	6.90	0.49	1.84
		S.D.	15	0.06	58	0.08	0.02	0.42	0.09	0.12
	1000	No.	5	5	5	5	5	5	5	5
		Mean	255	1.86	343	0.82	1.07	6.85	0.56	1.84
		S.D.	16	0.10	65	0.06	0.10	0.82	0.06	0.09
Relative	0	No.		5	5	5	5	5	5	5
		Mean		0.75	144	0.33	0.42	2.67	0.19	0.71
		S.D.		0.05	27	0.02	0.02	0.11	0.04	0.03
	1000	No.		5	5	5	5	5	5	5
		Mean		0.73	135	0.32	0.42	2.68	0.22	0.72
		S.D.		0.06	22	0.01	0.02	0.18	0.02	0.03

No significant difference between treated group and control group.

Table 8-8 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
 Absolute and relative organ weight (Recovery)
 Female

			Adrenal (R+L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	0	No.	5	5	5
		Mean	72	82.6	432
		S.D.	10	7.6	91
	1000	No.	5	5	5
		Mean	69	76.5	483
		S.D.	9	10.5	93
Relative	0	No.	5	5	5
		Mean	28	32.1	168
		S.D.	5	4.0	38
	1000	No.	5	5	5
		Mean	27	29.9	189
		S.D.	3	2.4	30

No significant difference between treated group and control group.

Table 9-1 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Gross pathological findings (4 weeks)

Sex	Organs Findings	Dose (mg/kg) No. of animals	0 5	100 5	300 5	1000 5
Male	Thyroid					
	Large or small (unilateral)		0	0	1	0
	Lung					
	Focus, dark red		0	1	0	1
	Testis					
	Small (bilateral)		0	1	0	0
	Epididymis					
	Small (bilateral)		0	1	0	0
	Prostate					
	Small		0	1	0	0

No lesions were found in females.

Table 9-2 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Gross pathological findings (Recovery)

Sex	Organs Findings	Dose (mg/kg) No. of animals	0	1000
			5	5
Male	Stomach			
	Focus, dark red, glandular stomach		2	2
	Small intestine			
	Diverticulum		0	1
	Epididymis			
	Focus, yellowish white (unilateral)		1	0

No lesions were found in females.

Table 10-1

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Histopathological findings (4 weeks)

Male

Organs	Dose (mg/kg) No. of animals Grade	0						1000					
		0	1	2	3	4	P TE	0	1	2	3	4	P TE
Liver													
-microgranuloma		4	1				5	3	2				5
Prostate													
-cell infiltration, lymphocytic		4	1				5	3	1	1			5
0 : No remarkable changes 1 : Slight 2 : Mild 3 : Moderate 4 : Severe P : Present TE : Total Examined													

Table 10-2 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
 Histopathological findings (4 weeks)
 Female

Organs -findings	Dose (mg/kg) No. of animals Grade	0							1000						
		0	1	2	3	4	P	TE	0	1	2	3	4	P	TE
Cecum															
-cell infiltration, mucosa		5						5	4	1				5	
Rectum															
-cell infiltration, mucosa		5						5	4	1				5	
Kidney															
-cyst		4					1	5	5					5	
0 : No remarkable changes 1 : Slight 2 : Mild 3 : Moderate 4 : Severe P : Present TE : Total Examined															

Table 10-3 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
 Histopathological findings in gross lesion (4 weeks)

Sex	Dose mg/kg	Animal number	Organs	Gross pathological findings	Histopathological findings
Male	100	2003	Lung (Bronchus)	-Focus, dark red	-Hemorrhage, focal (+-) -Cell infiltration, inflammatory (+-)
		2004	Testis	-Small (bilateral)	-Atrophy, seminiferous tubule (++)
			Epididymis	-Small (bilateral)	-Decrease, sperm (++)
			Prostate	-Small	-No remarkable changes
	300	3001	Thyroid (Parathyroid)	-Large or small (unilateral)	-No remarkable changes

+- : Slight ++ : Moderate

Table 10-4 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Histopathological findings in gross lesion (Recovery)

Sex	Dose mg/kg	Animal number	Organs	Gross pathological findings	Histopathological findings
Male	0	1006	Stomach	-Focus, dark red, glandular stomach	-Erosion, glandular stomach (+)
		1007	Epididymis	-Focus, yellowish white (unilateral)	-Granuloma, spermatic (+)
		1008	Stomach	-Focus, dark red, glandular stomach	-Erosion, glandular stomach (+-)
	1000	4006	Stomach	-Focus, dark red, glandular stomach	-Erosion, glandular stomach (+)
		4007	Stomach Ileum (Peyer's patch)	-Focus, dark red, glandular stomach -Diverticulum	-Erosion, glandular stomach (+) -Diverticulum (P)
+- : Slight + : Mild P : Present					

Appendix 1

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual clinical signs (Administration period)

Dose (mg/kg) : 0

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

- : No abnormality

Appendix 2

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual clinical signs (Administration period)

Dose (mg/kg) : 0

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

- : No abnormality

Appendix 3

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual clinical signs (Administration period)

Dose (mg/kg) : 100

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

- : No abnormality
A : Feces, yellowish

Appendix 4 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
 Individual clinical signs (Administration period)
 Dose (mg/kg) : 100

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

A : Feces, yellowish

Appendix 5

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual clinical signs (Administration period)

Dose (mg/kg) : 300

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

- : No abnormality
A : Feces, yellowish

Appendix 6

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual clinical signs (Administration period)

Dose (mg/kg) : 300

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

A : Feces, yellowish

Appendix 7 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
 Individual clinical signs (Administration period)
 Dose (mg/kg) : 1000

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

- : No abnormality
 A : Feces, yellowish

Appendix 8

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual clinical signs (Administration period)

Dose (mg/kg) : 1000

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

A : Feces, yellowish

Appendix 9

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual clinical signs (Recovery period)

Dose (mg/kg) : 0

Sex	Animal number	Day of recovery													
		1	2	3	4	5	6	7	8	9	10	11	12	13	14
Male	1006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1010	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Female	1106	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1107	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1108	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1109	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	1110	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- : No abnormality

Appendix 10

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual clinical signs (Recovery period)

Dose (mg/kg) : 1000

Sex	Animal number	Day of recovery													
		1	2	3	4	5	6	7	8	9	10	11	12	13	14
Male	4006	A	A	-	-	-	-	-	-	-	-	-	-	-	-
	4007	A	A	-	-	-	-	-	-	-	-	-	-	-	-
	4008	A	A	-	-	-	-	-	-	-	-	-	-	-	-
	4009	A	A	-	-	-	-	-	-	-	-	-	-	-	-
	4010	A	A	-	-	-	-	-	-	-	-	-	-	-	-
Female	4106	A	A	-	-	-	-	-	-	-	-	-	-	-	-
	4107	A	A	-	-	-	-	-	-	-	-	-	-	-	-
	4108	A	A	-	-	-	-	-	-	-	-	-	-	-	-
	4109	A	A	-	-	-	-	-	-	-	-	-	-	-	-
	4110	A	A	-	-	-	-	-	-	-	-	-	-	-	-

- : No abnormality
A : Feces, yellowish

Appendix 11 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
 Individual home cage observation (Pre administration)
 Dose (mg/kg) : 0

Parameter	Male										Female									
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix 12 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
 Individual home cage observation (Pre administration)
 Dose (mg/kg) : 100

Parameter	Male					Female				
	2	2	2	2	2	2	2	2	2	2
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	1	2	3	4	5
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior (0-3)	0	0	0	0	0	0	0	0	0	0

Appendix 13

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual home cage observation (Pre administration)

Dose (mg/kg) : 300

Parameter	Male					Female				
	3	3	3	3	3	3	3	3	3	3
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	1	2	3	4	5
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior (0-3)	0	0	0	0	0	0	0	0	0	0

Appendix 14

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual home cage observation (Pre administration)

Dose (mg/kg) : 1000

Parameter	Male										Female									
	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix 15 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Individual home cage observation (1 week)
Dose (mg/kg) : 0

Parameter	Male										Female									
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix 16 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
 Individual home cage observation (1 week)
 Dose (mg/kg) : 100

Parameter	Male					Female				
	2	2	2	2	2	2	2	2	2	2
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	1	2	3	4	5
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior (0-3)	0	0	0	0	0	0	0	0	0	0

Appendix 17 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
 Individual home cage observation (1 week)
 Dose (mg/kg) : 300

Parameter	Male					Female				
	3	3	3	3	3	3	3	3	3	3
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	1	2	3	4	5
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior (0-3)	0	0	0	0	0	0	0	0	0	0

Appendix 18

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual home cage observation (1 week)

Dose (mg/kg) : 1000

Parameter	Male										Female									
	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix 19

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual home cage observation (2 weeks)

Dose (mg/kg) : 0

Parameter	Male										Female									
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix 20

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual home cage observation (2 weeks)

Dose (mg/kg) : 100

Parameter	Male					Female				
	2	2	2	2	2	2	2	2	2	2
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	1	2	3	4	5
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior (0-3)	0	0	0	0	0	0	0	0	0	0

Appendix 21 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Individual home cage observation (2 weeks)
Dose (mg/kg) : 300

Parameter	Male					Female				
	3	3	3	3	3	3	3	3	3	3
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	1	2	3	4	5
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior (0-3)	0	0	0	0	0	0	0	0	0	0

Appendix 22

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual home cage observation (2 weeks)

Dose (mg/kg) : 1000

Parameter	Male										Female									
	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix 23 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Individual home cage observation (3 weeks)
Dose (mg/kg) : 0

Parameter	Male										Female									
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix 24

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual home cage observation (3 weeks)

Dose (mg/kg) : 100

Parameter	Male					Female				
	2	2	2	2	2	2	2	2	2	2
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	1	2	3	4	5
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior (0-3)	0	0	0	0	0	0	0	0	0	0

Appendix 25

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual home cage observation (3 weeks)

Dose (mg/kg) : 300

Parameter	Male					Female				
	3	3	3	3	3	3	3	3	3	3
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	1	2	3	4	5
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior (0-3)	0	0	0	0	0	0	0	0	0	0

Appendix 26

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual home cage observation (3 weeks)

Dose (mg/kg) : 1000

Parameter	Male										Female									
	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix 27 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
 Individual home cage observation (4 weeks)
 Dose (mg/kg) : 0

Parameter	Male										Female									
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix 28

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual home cage observation (4 weeks)

Dose (mg/kg) : 100

Parameter	Male					Female				
	2	2	2	2	2	2	2	2	2	2
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	1	2	3	4	5
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior (0-3)	0	0	0	0	0	0	0	0	0	0

Appendix 29

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual home cage observation (4 weeks)

Dose (mg/kg) : 300

Parameter	Male					Female				
	3	3	3	3	3	3	3	3	3	3
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	1	2	3	4	5
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior (0-3)	0	0	0	0	0	0	0	0	0	0

Appendix 30

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual home cage observation (4 weeks)

Dose (mg/kg) : 1000

Parameter	Male										Female									
	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix 31 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Individual home cage observation (Recovery 1 week)
Dose (mg/kg) : 0

Parameter	Male					Female				
	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	1	0	0	0	0	1
	6	7	8	9	0	6	7	8	9	0
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior (0-3)	0	0	0	0	0	0	0	0	0	0

Appendix 32

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual home cage observation (Recovery 1 week)

Dose (mg/kg) : 1000

Parameter	Male					Female				
	4	4	4	4	4	4	4	4	4	4
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	1	0	0	0	0	1
	6	7	8	9	0	6	7	8	9	0
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior (0-3)	0	0	0	0	0	0	0	0	0	0

Appendix 33

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual home cage observation (Recovery 2 weeks)

Dose (mg/kg) : 0

Parameter	Male					Female				
	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	1	0	0	0	0	1
	6	7	8	9	0	6	7	8	9	0
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior (0-3)	0	0	0	0	0	0	0	0	0	0

Appendix 34

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual home cage observation (Recovery 2 weeks)

Dose (mg/kg) : 1000

Parameter	Male					Female				
	4	4	4	4	4	4	4	4	4	4
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	1	0	0	0	0	1
	6	7	8	9	0	6	7	8	9	0
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior (0-3)	0	0	0	0	0	0	0	0	0	0

Appendix 35 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
 Individual in the hand observation (Pre administration)
 Dose (mg/kg) : 0

Parameter	Male										Female									
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
Removal from cage (1-5)	2	2	2	2	2	2	3	2	2	2	2	2	2	2	2	2	2	2	2	2
Vocalization (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling (1-5)	2	2	2	2	2	2	3	2	2	2	2	2	2	2	2	2	2	2	2	2
Fur condition (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Skin (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection(0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose (0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos (0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size (1-4)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Lacrimation (0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Salivation (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix 36

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual in the hand observation (Pre administration)

Dose (mg/kg) : 100

Parameter	Male					Female				
	2 0 0 1	2 0 0 2	2 0 0 3	2 0 0 4	2 0 0 5	2 1 0 1	2 1 0 2	2 1 0 3	2 1 0 4	2 1 0 5
Removal from cage (1-5)	2	2	2	2	3	2	2	2	2	3
Vocalization (0-3)	0	0	0	0	1	0	0	0	0	0
Reactivity to handling (1-5)	2	2	2	2	3	2	2	2	2	3
Fur condition (0-3)	0	0	0	0	0	0	0	0	0	0
Skin (0-3)	0	0	0	0	0	0	0	0	0	0
Piloerection(0/1)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes (0-3)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose (0/1)	0	0	0	0	0	0	0	0	0	0
Palpebral closure (0-3)	0	0	0	0	0	0	0	0	0	0
Exophthalmos (0/1)	0	0	0	0	0	0	0	0	0	0
Pupil size (1-4)	2	2	2	2	2	2	2	2	2	2
Lacrimation (0/1)	0	0	0	0	0	0	0	0	0	0
Salivation (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration (0-3)	0	0	0	0	0	0	0	0	0	0

Appendix 37

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual in the hand observation (Pre administration)

Dose (mg/kg) : 300

Parameter	Male					Female				
	3	3	3	3	3	3	3	3	3	3
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	1	2	3	4	5
Removal from cage (1-5)	2	2	2	2	2	2	2	2	2	3
Vocalization (0-3)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling (1-5)	2	2	2	2	2	2	2	2	2	3
Fur condition (0-3)	0	0	0	0	0	0	0	0	0	0
Skin (0-3)	0	0	0	0	0	0	0	0	0	0
Piloerection(0/1)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes (0-3)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose (0/1)	0	0	0	0	0	0	0	0	0	0
Palpebral closure (0-3)	0	0	0	0	0	0	0	0	0	0
Exophthalmos (0/1)	0	0	0	0	0	0	0	0	0	0
Pupil size (1-4)	2	2	2	2	2	2	2	2	2	2
Lacrimation (0/1)	0	0	0	0	0	0	0	0	0	0
Salivation (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration (0-3)	0	0	0	0	0	0	0	0	0	0

Appendix 38

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual in the hand observation (Pre administration)

Dose (mg/kg) : 1000

Parameter	Male										Female									
	4 0 0 1	4 0 0 2	4 0 0 3	4 0 0 4	4 0 0 5	4 0 0 6	4 0 0 7	4 0 0 8	4 0 0 9	4 0 0 0	4 1 0 1	4 1 0 2	4 1 0 3	4 1 0 4	4 1 0 5	4 1 0 6	4 1 0 7	4 1 0 8	4 1 0 9	4 1 0 0
Removal from cage (1-5)	2	2	2	2	2	2	2	3	2	2	2	3	2	2	2	3	3	3	2	2
Vocalization (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Reactivity to handling (1-5)	2	2	2	2	2	2	2	3	2	2	2	3	2	2	2	3	2	3	2	2
Fur condition (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Skin (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection(0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose (0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos (0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size (1-4)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Lacrimation (0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Salivation (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix 39

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual in the hand observation (1 week)

Dose (mg/kg) : 0

Parameter	Male										Female									
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
Removal from cage (1-5)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Vocalization (0-3)	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0
Reactivity to handling (1-5)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Fur condition (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Skin (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection(0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose (0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos (0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size (1-4)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Lacrimation (0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Salivation (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix 40

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual in the hand observation (1 week)

Dose (mg/kg) : 100

Parameter	Male					Female				
	2	2	2	2	2	2	2	2	2	2
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	1	2	3	4	5
Removal from cage (1-5)	2	2	2	2	2	2	2	2	2	2
Vocalization (0-3)	0	0	0	0	1	1	0	0	0	0
Reactivity to handling (1-5)	2	2	2	2	2	2	2	2	2	2
Fur condition (0-3)	0	0	0	0	0	0	0	0	0	0
Skin (0-3)	0	0	0	0	0	0	0	0	0	0
Piloerection(0/1)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes (0-3)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose (0/1)	0	0	0	0	0	0	0	0	0	0
Palpebral closure (0-3)	0	0	0	0	0	0	0	0	0	0
Exophthalmos (0/1)	0	0	0	0	0	0	0	0	0	0
Pupil size (1-4)	2	2	2	2	2	2	2	2	2	2
Lacrimation (0/1)	0	0	0	0	0	0	0	0	0	0
Salivation (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration (0-3)	0	0	0	0	0	0	0	0	0	0

Appendix 41

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual in the hand observation (1 week)

Dose (mg/kg) : 300

Parameter	Male					Female				
	3	3	3	3	3	3	3	3	3	3
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	1	2	3	4	5
Removal from cage (1-5)	2	2	2	2	2	2	2	2	2	2
Vocalization (0-3)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling (1-5)	2	2	2	2	2	2	2	2	2	2
Fur condition (0-3)	0	0	0	0	0	0	0	0	0	0
Skin (0-3)	0	0	0	0	0	0	0	0	0	0
Piloerection(0/1)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes (0-3)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose (0/1)	0	0	0	0	0	0	0	0	0	0
Palpebral closure (0-3)	0	0	0	0	0	0	0	0	0	0
Exophthalmos (0/1)	0	0	0	0	0	0	0	0	0	0
Pupil size (1-4)	2	2	2	2	2	2	2	2	2	2
Lacrimation (0/1)	0	0	0	0	0	0	0	0	0	0
Salivation (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration (0-3)	0	0	0	0	0	0	0	0	0	0

Appendix 42

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual in the hand observation (1 week)

Dose (mg/kg) : 1000

Parameter	Male										Female									
	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
Removal from cage (1-5)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Vocalization (0-3)	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling (1-5)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Fur condition (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Skin (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection(0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose (0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos (0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size (1-4)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Lacrimation (0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Salivation (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix 43

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual in the hand observation (2 weeks)

Dose (mg/kg) : 0

Parameter	Male										Female									
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
Removal from cage (1-5)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Vocalization (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling (1-5)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Fur condition (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Skin (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection(0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose (0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos (0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size (1-4)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Lacrimation (0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Salivation (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix 44

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual in the hand observation (2 weeks)

Dose (mg/kg) : 100

Parameter	Male					Female				
	2	2	2	2	2	2	2	2	2	2
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	1	2	3	4	5
Removal from cage (1-5)	2	2	2	2	3	2	2	2	2	2
Vocalization (0-3)	0	0	0	0	1	0	0	0	0	0
Reactivity to handling (1-5)	2	2	2	2	3	2	2	2	2	2
Fur condition (0-3)	0	0	0	0	0	0	0	0	0	0
Skin (0-3)	0	0	0	0	0	0	0	0	0	0
Piloerection(0/1)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes (0-3)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose (0/1)	0	0	0	0	0	0	0	0	0	0
Palpebral closure (0-3)	0	0	0	0	0	0	0	0	0	0
Exophthalmos (0/1)	0	0	0	0	0	0	0	0	0	0
Pupil size (1-4)	2	2	2	2	2	2	2	2	2	2
Lacrimation (0/1)	0	0	0	0	0	0	0	0	0	0
Salivation (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration (0-3)	0	0	0	0	0	0	0	0	0	0

Appendix 45

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual in the hand observation (2 weeks)

Dose (mg/kg) : 300

Parameter	Male					Female				
	3	3	3	3	3	3	3	3	3	3
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	1	2	3	4	5
Removal from cage (1-5)	2	2	2	2	2	2	2	2	2	2
Vocalization (0-3)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling (1-5)	2	2	2	2	2	2	2	2	2	2
Fur condition (0-3)	0	0	0	0	0	0	0	0	0	0
Skin (0-3)	0	0	0	0	0	0	0	0	0	0
Piloerection(0/1)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes (0-3)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose (0/1)	0	0	0	0	0	0	0	0	0	0
Palpebral closure (0-3)	0	0	0	0	0	0	0	0	0	0
Exophthalmos (0/1)	0	0	0	0	0	0	0	0	0	0
Pupil size (1-4)	2	2	2	2	2	2	2	2	2	2
Lacrimation (0/1)	0	0	0	0	0	0	0	0	0	0
Salivation (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration (0-3)	0	0	0	0	0	0	0	0	0	0

Appendix 46

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual in the hand observation (2 weeks)

Dose (mg/kg) : 1000

Parameter	Male										Female									
	4 0 0 1	4 0 0 2	4 0 0 3	4 0 0 4	4 0 0 5	4 0 0 6	4 0 0 7	4 0 0 8	4 0 0 9	4 0 1 0	4 1 0 1	4 1 0 2	4 1 0 3	4 1 0 4	4 1 0 5	4 1 0 6	4 1 0 7	4 1 0 8	4 1 0 9	4 1 1 0
Removal from cage (1-5)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Vocalization (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
Reactivity to handling (1-5)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Fur condition (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Skin (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection(0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose (0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos (0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size (1-4)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Lacrimation (0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Salivation (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix 47

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual in the hand observation (3 weeks)

Dose (mg/kg) : 0

Parameter	Male										Female									
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
Removal from cage (1-5)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Vocalization (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling (1-5)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Fur condition (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Skin (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection(0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose (0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos (0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size (1-4)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Lacrimation (0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Salivation (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix 48

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual in the hand observation (3 weeks)

Dose (mg/kg) : 100

Parameter	Male					Female				
	2	2	2	2	2	2	2	2	2	2
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	1	2	3	4	5
Removal from cage (1-5)	2	2	2	2	2	2	2	2	2	2
Vocalization (0-3)	0	0	0	0	1	0	0	0	0	0
Reactivity to handling (1-5)	2	2	2	2	2	2	2	2	2	2
Fur condition (0-3)	0	0	0	0	0	0	0	0	0	0
Skin (0-3)	0	0	0	0	0	0	0	0	0	0
Piloerection(0/1)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes (0-3)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose (0/1)	0	0	0	0	0	0	0	0	0	0
Palpebral closure (0-3)	0	0	0	0	0	0	0	0	0	0
Exophthalmos (0/1)	0	0	0	0	0	0	0	0	0	0
Pupil size (1-4)	2	2	2	2	2	2	2	2	2	2
Lacrimation (0/1)	0	0	0	0	0	0	0	0	0	0
Salivation (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration (0-3)	0	0	0	0	0	0	0	0	0	0

Appendix 49

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual in the hand observation (3 weeks)

Dose (mg/kg) : 300

Parameter	Male					Female				
	3	3	3	3	3	3	3	3	3	3
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	1	2	3	4	5
Removal from cage (1-5)	2	2	2	2	2	2	2	2	2	2
Vocalization (0-3)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling (1-5)	2	2	2	2	2	2	2	2	2	2
Fur condition (0-3)	0	0	0	0	0	0	0	0	0	0
Skin (0-3)	0	0	0	0	0	0	0	0	0	0
Piloerection(0/1)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes (0-3)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose (0/1)	0	0	0	0	0	0	0	0	0	0
Palpebral closure (0-3)	0	0	0	0	0	0	0	0	0	0
Exophthalmos (0/1)	0	0	0	0	0	0	0	0	0	0
Pupil size (1-4)	2	2	2	2	2	2	2	2	2	2
Lacrimation (0/1)	0	0	0	0	0	0	0	0	0	0
Salivation (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration (0-3)	0	0	0	0	0	0	0	0	0	0

Appendix 50

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual in the hand observation (3 weeks)

Dose (mg/kg) : 1000

Parameter	Male										Female									
	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
Removal from cage (1-5)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Vocalization (0-3)	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling (1-5)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Fur condition (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Skin (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection(0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose (0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos (0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size (1-4)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Lacrimation (0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Salivation (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix 51

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual in the hand observation (4 weeks)

Dose (mg/kg) : 0

Parameter	Male										Female									
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
Removal from cage (1-5)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Vocalization (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling (1-5)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Fur condition (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Skin (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection(0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose (0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos (0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size (1-4)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Lacrimation (0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Salivation (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix 52

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual in the hand observation (4 weeks)

Dose (mg/kg) : 100

Parameter	Male					Female				
	2	2	2	2	2	2	2	2	2	2
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	1	2	3	4	5
Removal from cage (1-5)	2	2	2	2	2	2	2	2	2	2
Vocalization (0-3)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling (1-5)	2	2	2	2	2	2	2	2	2	2
Fur condition (0-3)	0	0	0	0	0	0	0	0	0	0
Skin (0-3)	0	0	0	0	0	0	0	0	0	0
Piloerection(0/1)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes (0-3)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose (0/1)	0	0	0	0	0	0	0	0	0	0
Palpebral closure (0-3)	0	0	0	0	0	0	0	0	0	0
Exophthalmos (0/1)	0	0	0	0	0	0	0	0	0	0
Pupil size (1-4)	2	2	2	2	2	2	2	2	2	2
Lacrimation (0/1)	0	0	0	0	0	0	0	0	0	0
Salivation (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration (0-3)	0	0	0	0	0	0	0	0	0	0

Appendix 53

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual in the hand observation (4 weeks)

Dose (mg/kg) : 300

Parameter	Male					Female				
	3	3	3	3	3	3	3	3	3	3
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	1	2	3	4	5
Removal from cage (1-5)	2	2	2	2	2	2	2	2	2	2
Vocalization (0-3)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling (1-5)	2	2	2	2	2	2	2	2	2	2
Fur condition (0-3)	0	0	0	0	0	0	0	0	0	0
Skin (0-3)	0	0	0	0	0	0	0	0	0	0
Piloerection(0/1)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes (0-3)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose (0/1)	0	0	0	0	0	0	0	0	0	0
Palpebral closure (0-3)	0	0	0	0	0	0	0	0	0	0
Exophthalmos (0/1)	0	0	0	0	0	0	0	0	0	0
Pupil size (1-4)	2	2	2	2	2	2	2	2	2	2
Lacrimation (0/1)	0	0	0	0	0	0	0	0	0	0
Salivation (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration (0-3)	0	0	0	0	0	0	0	0	0	0

Appendix 54

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
 Individual in the hand observation (4 weeks)
 Dose (mg/kg) : 1000

Parameter	Male										Female									
	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
Removal from cage (1-5)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Vocalization (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling (1-5)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Fur condition (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Skin (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection(0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose (0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos (0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size (1-4)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Lacrimation (0/1)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Salivation (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix 55

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual in the hand observation (Recovery 1 week)

Dose (mg/kg) : 0

Parameter	Male					Female				
	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	1	0	0	0	0	1
	6	7	8	9	0	6	7	8	9	0
Removal from cage (1-5)	2	2	2	2	2	2	2	2	2	2
Vocalization (0-3)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling (1-5)	2	2	2	2	2	2	2	2	2	2
Fur condition (0-3)	0	0	0	0	0	0	0	0	0	0
Skin (0-3)	0	0	0	0	0	0	0	0	0	0
Piloerection(0/1)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes (0-3)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose (0/1)	0	0	0	0	0	0	0	0	0	0
Palpebral closure (0-3)	0	0	0	0	0	0	0	0	0	0
Exophthalmos (0/1)	0	0	0	0	0	0	0	0	0	0
Pupil size (1-4)	2	2	2	2	2	2	2	2	2	2
Lacrimation (0/1)	0	0	0	0	0	0	0	0	0	0
Salivation (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration (0-3)	0	0	0	0	0	0	0	0	0	0

Appendix 56

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
 Individual in the hand observation (Recovery 1 week)
 Dose (mg/kg) : 1000

Parameter	Male					Female				
	4	4	4	4	4	4	4	4	4	4
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	1	0	0	0	0	1
	6	7	8	9	0	6	7	8	9	0
Removal from cage (1-5)	2	2	2	2	2	2	2	2	2	2
Vocalization (0-3)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling (1-5)	2	2	2	2	2	2	2	2	2	2
Fur condition (0-3)	0	0	0	0	0	0	0	0	0	0
Skin (0-3)	0	0	0	0	0	0	0	0	0	0
Piloerection(0/1)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes (0-3)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose (0/1)	0	0	0	0	0	0	0	0	0	0
Palpebral closure (0-3)	0	0	0	0	0	0	0	0	0	0
Exophthalmos (0/1)	0	0	0	0	0	0	0	0	0	0
Pupil size (1-4)	2	2	2	2	2	2	2	2	2	2
Lacrimation (0/1)	0	0	0	0	0	0	0	0	0	0
Salivation (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration (0-3)	0	0	0	0	0	0	0	0	0	0

Appendix 57

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual in the hand observation (Recovery 2 weeks)

Dose (mg/kg) : 0

Parameter	Male					Female				
	1 0 0 6	1 0 0 7	1 0 0 8	1 0 0 9	1 0 1 0	1 1 0 6	1 1 0 7	1 1 0 8	1 1 0 9	1 1 1 0
Removal from cage (1-5)	2	2	2	2	2	2	2	2	2	2
Vocalization (0-3)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling (1-5)	2	2	2	2	2	2	2	2	2	2
Fur condition (0-3)	0	0	0	0	0	0	0	0	0	0
Skin (0-3)	0	0	0	0	0	0	0	0	0	0
Piloerection(0/1)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes (0-3)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose (0/1)	0	0	0	0	0	0	0	0	0	0
Palpebral closure (0-3)	0	0	0	0	0	0	0	0	0	0
Exophthalmos (0/1)	0	0	0	0	0	0	0	0	0	0
Pupil size (1-4)	2	2	2	2	2	2	2	2	2	2
Lacrimation (0/1)	0	0	0	0	0	0	0	0	0	0
Salivation (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration (0-3)	0	0	0	0	0	0	0	0	0	0

Appendix 58

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual in the hand observation (Recovery 2 weeks)

Dose (mg/kg) : 1000

Parameter	Male					Female				
	4	4	4	4	4	4	4	4	4	4
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	1	0	0	0	0	1
	G	7	8	9	0	G	7	8	9	0
Removal from cage (1-5)	2	2	2	2	2	2	2	2	2	2
Vocalization (0-3)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling (1-5)	2	2	2	2	2	2	2	2	2	2
Fur condition (0-3)	0	0	0	0	0	0	0	0	0	0
Skin (0-3)	0	0	0	0	0	0	0	0	0	0
Piloerection(0/1)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes (0-3)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose (0/1)	0	0	0	0	0	0	0	0	0	0
Palpebral closure (0-3)	0	0	0	0	0	0	0	0	0	0
Exophthalmos (0/1)	0	0	0	0	0	0	0	0	0	0
Pupil size (1-4)	2	2	2	2	2	2	2	2	2	2
Lacrimation (0/1)	0	0	0	0	0	0	0	0	0	0
Salivation (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration (0-3)	0	0	0	0	0	0	0	0	0	0

Appendix 59

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual open field observation (Pre administration)

Dose (mg/kg) : 0

Parameter	Male										Female									
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Gait(U,0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Arousal (1-5)	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Tremor (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior(0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Grooming (0-2)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	0	4	4	5	6	3	6	3	4	8	5	2	3	6	8	4	1	3	4	6
Urination (0-3)	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix 60

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual open field observation (Pre administration)

Dose (mg/kg) : 100

Parameter	Male					Female				
	2	2	2	2	2	2	2	2	2	2
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	1	2	3	4	5
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N
Gait(U,0-3)	0	0	0	0	0	0	0	0	0	0
Arousal (1-5)	3	3	3	3	3	3	3	3	3	3
Tremor (0-3)	0	0	0	0	0	0	0	0	0	0
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior(0-3)	0	0	0	0	0	0	0	0	0	0
Grooming (0-2)	0	0	0	0	0	0	0	0	0	0
Rearing	4	6	5	3	4	9	6	5	6	5
Urination (0-3)	0	0	0	0	0	0	0	0	0	0
Defecation count	0	0	0	0	0	0	0	0	0	0

Appendix 61

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual open field observation (Pre administration)

Dose (mg/kg) : 300

Parameter	Male					Female				
	3	3	3	3	3	3	3	3	3	3
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	1	2	3	4	5
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N
Gait(U,0-3)	0	0	0	0	0	0	0	0	0	0
Arousal (1-5)	3	3	3	3	3	3	3	3	3	3
Tremor (0-3)	0	0	0	0	0	0	0	0	0	0
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior(0-3)	0	0	0	0	0	0	0	0	0	0
Grooming (0-2)	0	0	0	0	0	0	0	0	0	0
Rearing	4	5	4	6	1	5	5	4	5	4
Urination (0-3)	0	0	0	0	0	0	0	0	0	0
Defecation count	0	0	0	0	0	0	0	0	0	0

Appendix 62

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual open field observation (Pre administration)

Dose (mg/kg) : 1000

Parameter	Male										Female									
	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
Posture (N,F,II)	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Gait(U,0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Arousal (1-5)	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Tremor (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior(0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Grooming (0-2)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	4	5	5	2	1	3	4	5	4	5	1	6	1	2	6	5	2	2	4
Urination (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Defecation count	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0

Appendix 63

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual open field observation (1 week)

Dose (mg/kg) : 0

Parameter	Male										Female									
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Gait(U,0-3)	U	0	0	0	0	0	U	0	0	0	0	0	0	0	0	0	0	0	0	0
Arousal (1-5)	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Tremor (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior(0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Grooming (0-2)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	0	2	0	4	4	5	0	0	3	1	4	5	6	4	3	1	3	3	4	8
Urination (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Defecation count	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix G4

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual open field observation (1 week)

Dose (mg/kg) : 100

Parameter	Male					Female				
	2	2	2	2	2	2	2	2	2	2
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	1	2	3	4	5
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N
Gait(U,0-3)	U	0	0	U	0	0	0	0	0	0
Arousal (1-5)	3	3	3	3	3	3	3	3	3	3
Tremor (0-3)	0	0	0	0	0	0	0	0	0	0
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior(0-3)	0	0	0	0	0	0	0	0	0	0
Grooming (0-2)	0	0	0	0	0	0	0	0	0	0
Rearing	0	2	0	0	1	7	6	3	5	3
Urination (0-3)	0	0	0	1	0	0	0	0	0	0
Defecation count	0	0	0	1	0	0	0	0	0	0

Appendix G5

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual open field observation (1 week)

Dose (mg/kg) : 300

Parameter	Male					Female				
	3	3	3	3	3	3	3	3	3	3
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	1	2	3	4	5
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N
Gait(U,0-3)	0	0	0	0	0	0	0	0	0	0
Arousal (1-5)	3	3	3	3	3	3	3	3	3	3
Tremor (0-3)	0	0	0	0	0	0	0	0	0	0
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior(0-3)	0	0	0	0	0	0	0	0	0	0
Grooming (0-2)	1	0	0	0	0	0	0	0	0	0
Rearing	1	2	0	2	0	9	5	0	3	3
Urination (0-3)	1	0	0	0	0	0	0	0	0	0
Defecation count	0	0	0	0	2	0	0	0	0	0

Appendix 66

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual open field observation (1 week)

Dose (mg/kg) : 1000

Parameter	Male										Female									
	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Gait(U,0-3)	0	U	0	0	0	U	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Arousal (1-5)	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Tremor (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior(0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Grooming (0-2)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	0	0	3	2	0	0	4	0	1	2	3	4	6	2	2	0	0	3	2	1
Urination (0-3)	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Defecation count	0	4	0	0	0	0	0	0	0	1a)	0	0	0	0	0	0	0	0	0	0

a) : Feces, yellowish

Appendix 67

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual open field observation (2 weeks)

Dose (mg/kg) : 0

Parameter	Male										Female									
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Gait(U,0-3)	0	0	0	0	0	0	U	0	0	0	0	0	0	0	0	0	0	0	0	0
Arousal (1-5)	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Tremor (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior(0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Grooming (0-2)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	0	1	1	4	0	0	0	0	2	2	6	5	4	5	3	0	0	6	3	8
Urination (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Defecation count	0	0	1	0	3	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix 68

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual open field observation (2 weeks)

Dose (mg/kg) : 100

Parameter	Male					Female				
	2	2	2	2	2	2	2	2	2	2
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	1	2	3	4	5
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N
Gait(U,0-3)	U	0	0	U	0	0	0	0	0	0
Arousal (1-5)	3	3	3	3	3	3	3	3	3	3
Tremor (0-3)	0	0	0	0	0	0	0	0	0	0
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior(0-3)	0	0	0	0	0	0	0	0	0	0
Grooming (0-2)	0	0	0	0	0	0	0	0	0	0
Rearing	4	1	1	0	0	4	5	4	4	2
Urination (0-3)	0	0	0	0	0	0	0	0	0	0
Defecation count	1	0	0	0	1	0	0	0	0	0

Appendix 69

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual open field observation (2 weeks)

Dose (mg/kg) : 300

Parameter	Male					Female				
	3	3	3	3	3	3	3	3	3	3
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	1	2	3	4	5
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N
Gait(U,0-3)	0	U	0	0	0	0	0	0	0	0
Arousal (1-5)	3	3	3	3	3	3	3	3	3	3
Tremor (0-3)	0	0	0	0	0	0	0	0	0	0
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior(0-3)	0	0	0	0	0	0	0	0	0	0
Grooming (0-2)	0	0	0	0	0	0	0	0	0	0
Rearing	3	0	2	0	4	6	6	6	0	4
Urination (0-3)	1	0	0	0	2	0	0	0	0	0
Defecation count	2	0	0	0	1	0	0	0	0	0

Appendix 70

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual open field observation (2 weeks)

Dose (mg/kg) : 1000

Parameter	Male										Female									
	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Gait(U,0-3)	0	U	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Arousal (1-5)	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Tremor (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior(0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Grooming (0-2)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	3	0	4	3	0	0	0	2	0	3	8	5	5	3	2	1	1	3	3	1
Urination (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Defecation count	0	0	0	0	0	0	0	2a)	0	0	0	0	0	0	0	0	0	0	0	0

a) : Feces, yellowish

Appendix 71

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual open field observation (3 weeks)

Dose (mg/kg) : 0

Parameter	Male										Female									
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Gait(U,0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Arousal (1-5)	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Tremor (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior(0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Grooming (0-2)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	2	4	1	4	2	3	0	1	2	0	7	7	8	6	6	0	3	6	2	9
Urination (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix 72

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual open field observation (3 weeks)

Dose (mg/kg) : 100

Parameter	Male					Female				
	2	2	2	2	2	2	2	2	2	2
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	1	2	3	4	5
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N
Gait(U,0-3)	0	U	0	0	U	0	0	0	0	0
Arousal (1-5)	3	3	3	3	3	3	3	3	3	3
Tremor (0-3)	0	0	0	0	0	0	0	0	0	0
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior(0-3)	0	0	0	0	0	0	0	0	0	0
Grooming (0-2)	0	0	0	0	0	0	0	0	0	0
Rearing	5	0	0	1	0	8	3	2	8	4
Urination (0-3)	0	0	0	0	0	0	0	0	0	0
Defecation count	0	2	0	0	2	0	0	0	0	0

Appendix 73

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual open field observation (3 weeks)

Dose (mg/kg) : 300

Parameter	Male					Female				
	3	3	3	3	3	3	3	3	3	3
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	1	2	3	4	5
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N
Gait(U,0-3)	0	0	0	0	0	0	0	0	0	0
Arousal (1-5)	3	3	3	3	3	3	3	3	3	3
Tremor (0-3)	0	0	0	0	0	0	0	0	0	0
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior(0-3)	0	0	0	0	0	0	0	0	0	0
Grooming (0-2)	0	0	0	0	0	0	0	0	0	0
Rearing	4	0	3	1	9	4	7	8	3	5
Urination (0-3)	0	0	0	0	0	0	0	0	0	0
Defecation count	0	0	0	0	2	0	0	0	0	0

Appendix 74

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual open field observation (3 weeks)

Dose (mg/kg) : 1000

Parameter	Male										Female									
	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Gait(U,0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Arousal (1-5)	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Tremor (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior(0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Grooming (0-2)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	3	3	3	4	0	0	0	3	0	4	11	4	6	4	3	6	2	4	6	1
Urination (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Defecation count	0	0	0	0	0	0	0	2a)	0	0	0	0	0	0	0	0	0	0	0	0

a) : Feces, yellowish

Appendix 75

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual open field observation (4 weeks)

Dose (mg/kg) : 0

Parameter	Male										Female									
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Gait(U,0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Arousal (1-5)	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Tremor (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior(0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Grooming (0-2)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	9	2	2	1	2	2	2	2	0	9	4	8	8	3	0	3	6	3	5
Urination (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix 76

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual open field observation (4 weeks)

Dose (mg/kg) : 100

Parameter	Male					Female				
	2	2	2	2	2	2	2	2	2	2
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	1	2	3	4	5
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N
Gait(U,0-3)	0	0	0	0	0	0	0	0	0	0
Arousal (1-5)	3	3	3	3	3	3	3	3	3	3
Tremor (0-3)	0	0	0	0	0	0	0	0	0	0
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior(0-3)	0	0	0	0	0	0	0	0	0	0
Grooming (0-2)	0	0	0	0	0	0	0	0	0	0
Rearing	2	2	0	2	0	7	6	4	8	2
Urination (0-3)	0	0	0	0	0	0	0	0	0	0
Defecation count	0	2	0	0	0	0	0	0	0	0

Appendix 77 A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
 Individual open field observation (4 weeks)
 Dose (mg/kg) : 300

Parameter	Male					Female				
	3	3	3	3	3	3	3	3	3	3
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	1	2	3	4	5
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N
Gait(U,0-3)	0	0	0	0	0	0	0	0	0	0
Arousal (1-5)	3	3	3	3	3	3	3	3	3	3
Tremor (0-3)	0	0	0	0	0	0	0	0	0	0
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior(0-3)	0	0	0	0	0	0	0	0	0	0
Grooming (0-2)	0	0	0	0	0	0	0	0	0	0
Rearing	4	1	1	2	4	6	5	6	3	2
Urination (0-3)	0	0	0	0	0	0	0	0	0	0
Defecation count	0	0	0	0	0	0	0	0	0	0

Appendix 78

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual open field observation (4 weeks)

Dose (mg/kg) : 1000

Parameter	Male										Female									
	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Gait(U,0-3)	0	U	0	0	0	U	U	0	0	0	0	0	0	0	0	0	0	0	0	0
Arousal (1-5)	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Tremor (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior(0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Grooming (0-2)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	0	5	3	0	0	0	2	0	2	8	2	5	0	6	6	1	4	2	3
Urination (0-3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Defecation count	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0

Appendix 79

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual open field observation (Recovery 1 week)

Dose (mg/kg) : 0

Parameter	Male					Female				
	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	1	0	0	0	0	1
	6	7	8	9	0	6	7	8	9	0
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N
Gait(U,0-3)	0	0	0	0	0	0	0	0	0	0
Arousal (1-5)	3	3	3	3	3	3	3	3	3	3
Tremor (0-3)	0	0	0	0	0	0	0	0	0	0
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior(0-3)	0	0	0	0	0	0	0	0	0	0
Grooming (0-2)	0	0	0	0	0	0	0	0	0	0
Rearing	0	1	3	4	4	0	4	7	8	8
Urination (0-3)	0	0	0	0	0	0	0	0	0	0
Defecation count	0	0	0	0	0	0	0	0	0	0

Appendix 80

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual open field observation (Recovery 1 week)

Dose (mg/kg) : 1000

Parameter	Male					Female				
	4	4	4	4	4	4	4	4	4	4
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	1	0	0	0	0	1
	6	7	8	9	0	6	7	8	9	0
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N
Gait(U,0-3)	0	0	0	0	0	0	0	0	0	0
Arousal (1-5)	3	3	3	3	3	3	3	3	3	3
Tremor (0-3)	0	0	0	0	0	0	0	0	0	0
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior(0-3)	0	0	0	0	0	0	0	0	0	0
Grooming (0-2)	0	0	0	0	0	0	0	0	0	0
Rearing	1	1	4	1	4	8	4	8	5	6
Urination (0-3)	0	0	0	0	0	0	0	0	0	0
Defecation count	0	0	0	0	0	0	0	0	0	0

Appendix 81

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual open field observation (Recovery 2 weeks)

Dose (mg/kg) : 0

Parameter	Male					Female				
	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	1	0	0	0	0	1
	6	7	8	9	0	6	7	8	9	0
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N
Gait(U,0-3)	0	0	0	0	0	0	0	0	0	0
Arousal (1-5)	3	3	3	3	3	3	3	3	3	3
Tremor (0-3)	0	0	0	0	0	0	0	0	0	0
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior(0-3)	0	0	0	0	0	0	0	0	0	0
Grooming (0-2)	0	0	0	0	0	0	0	0	0	0
Rearing	4	2	4	2	3	1	2	5	3	8
Urination (0-3)	0	0	0	0	0	0	0	0	0	0
Defecation count	0	0	0	0	0	0	0	0	0	0

Appendix 82

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual open field observation (Recovery 2 weeks)

Dose (mg/kg) : 1000

Parameter	Male					Female				
	4	4	4	4	4	4	4	4	4	4
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	1	0	0	0	0	1
	6	7	8	9	0	6	7	8	9	0
Posture (N,F,H)	N	N	N	N	N	N	N	N	N	N
Gait(U,0-3)	U	0	0	0	0	0	0	0	0	0
Arousal (1-5)	3	3	3	3	3	3	3	3	3	3
Tremor (0-3)	0	0	0	0	0	0	0	0	0	0
Convulsion (0-3)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior(0-3)	0	0	0	0	0	0	0	0	0	0
Grooming (0-2)	0	0	0	0	0	0	0	0	0	0
Rearing	3	1	3	1	2	6	3	5	4	4
Urination (0-3)	0	0	0	0	0	0	0	0	0	0
Defecation count	0	0	0	0	0	0	0	0	0	0

Appendix 83

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual manipulative test (4 weeks)

Dose (mg/kg) : 0

Parameter	Male										Female									
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
Approach response (1-3)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Touch response (1-3)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Auditory response (1-4)	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Tail pinch response (1-4)	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Pupillary reflex(P,F,L,R)	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
Aerial righting reflex	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Landing foot splay	88	64	83	67	67	105	114	43	108	73	59	44	81	76	26	57	81	38	65	46

Appendix 84

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual manipulative test (4 weeks)

Dose (mg/kg) : 100

Parameter	Male					Female				
	2	2	2	2	2	2	2	2	2	2
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	1	2	3	4	5
Approach response (1-3)	2	2	2	2	2	2	2	2	2	2
Touch response (1-3)	2	2	2	2	2	2	2	2	2	2
Auditory response (1-4)	3	3	3	3	3	3	3	3	3	3
Tail pinch response (1-4)	3	3	3	3	3	3	3	3	3	3
Pupillary reflex(P,F,L,R)	P	P	P	P	P	P	P	P	P	P
Aerial righting reflex	0	0	0	0	0	0	0	0	0	0
Landing foot splay	62	91	53	122	91	74	70	53	78	83

Appendix 85

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual manipulative test (4 weeks)

Dose (mg/kg) : 300

Parameter	Male					Female				
	3	3	3	3	3	3	3	3	3	3
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	0
	1	2	3	4	5	1	2	3	4	5
Approach response (1-3)	2	2	2	2	2	2	2	2	2	2
Touch response (1-3)	2	2	2	2	2	2	2	2	2	2
Auditory response (1-4)	3	3	3	3	3	3	3	3	3	3
Tail pinch response (1-4)	3	3	3	3	3	3	3	3	3	3
Pupillary reflex(P,F,L,R)	P	P	P	P	P	P	P	P	P	P
Aerial righting reflex	0	0	0	0	0	0	0	0	0	0
Landing foot splay	65	66	61	42	97	44	80	47	71	63

Appendix 86

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual manipulative test (4 weeks)

Dose (mg/kg) : 1000

Parameter	Male										Female									
	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
Approach response (1-3)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Touch response (1-3)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Auditory response (1-4)	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Tail pinch response (1-4)	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Pupillary reflex(P.F.L.R)	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
Aerial righting reflex	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Landing foot splay	61	52	81	87	67	104	77	47	60	95	96	49	91	37	47	46	55	26	81	39

Appendix 87

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual manipulative test (Recovery 2 weeks)

Dose (mg/kg) : 0

Parameter	Male					Female				
	1	1	1	1	1	1	1	1	1	1
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	1	0	0	0	0	1
	6	7	8	9	0	6	7	8	9	0
Approach response (1-3)	2	2	2	2	2	2	2	2	2	2
Touch response (1-3)	2	2	2	2	2	2	2	2	2	2
Auditory response (1-4)	3	3	3	3	3	3	3	3	3	3
Tail pinch response (1-4)	3	3	3	3	3	3	3	3	3	3
Pupillary reflex(P,F,L,R)	P	P	P	P	P	P	P	P	P	P
Aerial righting reflex	0	0	0	0	0	0	0	0	0	0
Landing foot splay	68	64	54	68	69	49	72	48	74	50

Appendix 88

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual manipulative test (Recovery 2 weeks)

Dose (mg/kg) : 1000

Parameter	Male					Female				
	4	4	4	4	4	4	4	4	4	4
	0	0	0	0	0	1	1	1	1	1
	0	0	0	0	1	0	0	0	0	1
	G	7	8	9	0	6	7	8	9	0
Approach response (1-3)	2	2	2	2	2	2	2	2	2	2
Touch response (1-3)	2	2	2	2	2	2	2	2	2	2
Auditory response (1-4)	3	3	3	3	3	3	3	3	3	3
Tail pinch response (1-4)	3	3	3	3	3	3	3	3	3	3
Pupillary reflex(P,F,L,R)	P	P	P	P	P	P	P	P	P	P
Aerial righting reflex	0	0	0	0	0	0	0	0	0	0
Landing foot splay	46	77	35	66	66	51	39	27	54	38

Appendix 89

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual grip strength (4 week)

Dose (mg/kg) : 0

Sex	Animal number	Fore limb g	Hind limb g
Male	1001	1155	358
	1002	742	534
	1003	1225	769
	1004	1127	692
	1005	1001	511
	1006	1055	578
	1007	964	527
	1008	1186	463
	1009	1070	449
	1010	877	578
Mean		1040	546
S.D.		149	119
Female	1101	1052	279
	1102	1021	350
	1103	1049	532
	1104	871	569
	1105	725	570
	1106	841	312
	1107	1064	450
	1108	777	430
	1109	860	492
	1110	704	541
Mean		896	453
S.D.		140	107

Appendix 90

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual grip strength (4 week)

Dose (mg/kg) : 100

Sex	Animal number	Fore limb g	Hind limb g
Male	2001	898	426
	2002	930	520
	2003	1205	593
	2004	838	519
	2005	1269	539
	Mean	1028	519
	S.D.	195	60
Female	2101	1142	475
	2102	892	314
	2103	1116	597
	2104	760	614
	2105	855	479
	Mean	953	496
	S.D.	168	120

Appendix 91

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual grip strength (4 week)

Dose (mg/kg) : 300

Sex	Animal number	Fore limb g	Hind limb g
Male	3001	1062	543
	3002	907	470
	3003	946	495
	3004	973	547
	3005	1318	505
	Mean	1041	512
Female	S.D.	165	33
	3101	937	404
	3102	977	322
	3103	1076	474
	3104	719	517
	3105	845	447
	Mean	911	433
	S.D.	136	74

Appendix 92

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual grip strength (4 week)

Dose (mg/kg) : 1000

Sex	Animal number	Fore limb g	Hind limb g
Male	4001	819	365
	4002	834	461
	4003	1030	747
	4004	970	545
	4005	824	460
	4006	932	449
	4007	1080	462
	4008	1354	598
	4009	1017	606
	4010	1061	552
Mean		992	525
S.D.		161	109
Female	4101	1110	569
	4102	910	518
	4103	1012	672
	4104	645	533
	4105	994	402
	4106	1000	413
	4107	857	527
	4108	1137	748
	4109	851	491
	4110	814	593
Mean		933	547
S.D.		148	107

Appendix 93

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual grip strength (Recovery 2 week)

Dose (mg/kg) : 0

Sex	Animal number	Fore limb g	Hind limb g
Male	1006	1095	558
	1007	952	551
	1008	1083	545
	1009	1282	506
	1010	1208	517
	Mean	1124	535
	S.D.	127	22
Female	1106	1060	521
	1107	1153	540
	1108	1054	532
	1109	1006	446
	1110	849	404
	Mean	1024	489
	S.D.	112	60

Appendix 94

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual grip strength (Recovery 2 week)

Dose (mg/kg) : 1000

Sex	Animal number	Fore limb g	Hind limb g
Male	4006	1056	615
	4007	1295	466
	4008	1016	547
	4009	1026	491
	4010	1128	465
	Mean	1104	517
	S.D.	115	64
Female	4106	1053	508
	4107	1053	416
	4108	1092	620
	4109	1136	506
	4110	1141	470
	Mean	1095	504
	S.D.	43	75

Appendix 95

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Individual Motor activity (4 weeks)

Dose (mg/kg) : 0

Sex	Animal number	Interval (minutes)						Total(0-60)
		0-10	10-20	20-30	30-40	40-50	50-60	
Male	1001	390	348	248	43	6	28	1063
	1002	417	387	261	23	61	11	1160
	1003	444	490	440	306	41	23	1744
	1004	432	415	398	50	14	41	1350
	1005	333	201	10	52	268	220	1084
	1006	313	335	223	54	6	148	1079
	1007	466	440	454	326	110	259	2055
	1008	370	297	270	244	248	173	1602
	1009	463	389	435	417	279	10	1993
	1010	420	287	12	16	330	118	1183
	Mean	405	359	275	153	136	103	1431
	S.D.	52	84	164	153	130	93	388
Female	1101	321	253	26	5	6	68	679
	1102	439	341	117	0	0	321	1218
	1103	457	378	444	417	248	14	1958
	1104	344	202	82	227	148	221	1224
	1105	402	294	361	263	250	281	1851
	1106	342	453	456	396	387	329	2363
	1107	375	311	379	280	233	58	1636
	1108	406	341	265	203	224	206	1645
	1109	468	444	377	283	8	0	1580
	1110	387	394	403	270	394	87	1935
	Mean	394	341	291	234	190	159	1609
	S.D.	50	80	159	139	147	127	474

Appendix 96

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Individual Motor activity (4 weeks)

Dose (mg/kg) : 100

Sex	Animal number	Interval (minutes)						Total(0-60)
		0-10	10-20	20-30	30-40	40-50	50-60	
Male	2001	403	356	140	38	28	30	995
	2002	409	287	157	32	11	60	956
	2003	395	361	396	244	40	14	1450
	2004	390	337	14	2	309	325	1377
	2005	388	256	235	296	193	21	1389
	Mean	397	319	188	122	116	90	1233
	S.D.	9	46	141	137	130	133	237
Female	2101	403	346	67	5	208	358	1387
	2102	421	492	339	106	1	216	1575
	2103	389	350	183	15	46	326	1309
	2104	378	350	209	322	327	256	1842
	2105	429	381	270	327	19	198	1624
	Mean	404	384	214	155	120	271	1547
	S.D.	21	62	102	160	142	69	210

Appendix 97

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Individual Motor activity (4 weeks)

Dose (mg/kg) : 300

Sex	Animal number	Interval (minutes)						Total(0-60)
		0-10	10-20	20-30	30-40	40-50	50-60	
Male	3001	342	410	31	17	34	52	886
	3002	421	498	397	156	11	10	1493
	3003	345	327	338	84	78	14	1186
	3004	403	328	33	18	9	21	812
	3005	309	279	164	56	27	21	856
	Mean	364	368	193	66	32	24	1047
Female	S.D.	46	86	170	58	28	17	290
	3101	407	259	149	11	5	229	1060
	3102	454	442	444	232	112	352	2036
	3103	399	231	67	27	2	12	738
	3104	385	414	354	273	89	333	1848
	3105	370	298	162	3	59	292	1184
	Mean	403	329	235	109	53	244	1373
	S.D.	32	94	157	132	49	138	548

Appendix 98

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Individual Motor activity (4 weeks)

Dose (mg/kg) : 1000

Sex	Animal number	Interval (minutes)						Total(0-60)
		0-10	10-20	20-30	30-40	40-50	50-60	
Male	4001	458	392	60	213	36	180	1339
	4002	397	251	37	32	26	6	749
	4003	409	277	298	304	334	175	1797
	4004	440	447	240	27	446	415	2015
	4005	341	297	355	305	263	301	1862
	4006	313	303	322	308	92	231	1569
	4007	431	370	363	402	243	28	1837
	4008	411	326	99	17	15	34	902
	4009	484	452	379	380	485	409	2589
	4010	425	391	473	337	369	363	2358
	Mean	411	351	263	233	231	214	1702
	S.D.	51	70	149	152	179	157	584
Female	4101	392	256	1	141	189	108	1087
	4102	413	351	57	17	8	2	848
	4103	397	353	368	362	262	316	2058
	4104	455	393	360	205	177	354	1944
	4105	414	325	195	135	271	303	1643
	4106	392	239	25	261	152	230	1299
	4107	386	385	386	271	11	112	1551
	4108	383	60	3	25	83	63	617
	4109	367	455	330	365	269	347	2133
	4110	361	329	225	304	427	61	1707
	Mean	396	315	195	209	185	190	1489
	S.D.	27	109	162	127	130	134	515

Appendix 99

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Individual Motor activity (Recovery 2 weeks)

Dose (mg/kg) : 0

Sex	Animal number	Interval (minutes)						Total(0-60)
		0-10	10-20	20-30	30-40	40-50	50-60	
Male	1006	392	427	344	288	27	26	1504
	1007	490	419	327	53	28	46	1363
	1008	442	403	345	39	0	13	1242
	1009	427	433	340	37	64	128	1429
	1010	414	11	13	41	7	10	496
	Mean	433	339	274	92	25	45	1207
	S.D.	37	183	146	110	25	49	409
Female	1106	382	317	28	4	55	3	789
	1107	406	431	264	30	8	0	1139
	1108	340	336	112	123	264	17	1192
	1109	466	236	6	0	36	241	985
	1110	378	187	1	120	31	18	735
	Mean	394	301	82	55	79	56	968
	S.D.	46	94	111	61	105	104	204

Appendix 100

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
Individual Motor activity (Recovery 2 weeks)

Dose (mg/kg) : 1000

Sex	Animal number	Interval (minutes)						Total(0-60)
		0-10	10-20	20-30	30-40	40-50	50-60	
Male	4006	450	414	369	315	417	311	2276
	4007	397	404	370	320	240	258	1989
	4008	382	326	307	82	13	10	1120
	4009	454	442	375	345	93	11	1720
	4010	453	407	425	375	412	384	2456
	Mean	427	399	369	287	235	195	1912
	S.D.	35	43	42	117	183	174	524
Female	4106	388	357	79	5	11	2	842
	4107	319	131	64	3	52	51	620
	4108	362	309	322	1	14	71	1079
	4109	473	399	329	27	113	219	1560
	4110	363	379	387	98	26	12	1265
	Mean	381	315	236	27	43	71	1073
	S.D.	57	108	153	41	42	87	365

Appendix 101

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual body weight (Administration period)

Dose (mg/kg) : 0

Sex	Animal number	Day of administration									Gain 1-28
		1	4	7	10	14	17	21	24	28	
Male	1001	239	263	286	308	337	354	376	387	412	173
	1002	256	275	289	305	326	340	361	376	394	138
	1003	235	249	273	292	321	334	361	370	393	158
	1004	237	256	280	303	334	350	365	377	406	169
	1005	244	267	296	312	335	349	380	387	413	169
	1006	239	253	273	285	303	308	326	328	340	101
	1007	231	245	258	276	295	307	321	327	343	112
	1008	241	267	286	306	325	339	353	362	380	139
	1009	239	269	297	317	346	367	399	413	442	203
	1010	228	242	264	284	311	335	355	367	388	160
	Mean	239	259	280	299	323	338	360	369	391	152
	S.D.	8	11	13	14	16	19	23	26	31	30
Female	1101	187	185	204	218	228	240	245	242	251	64
	1102	180	182	194	207	226	216	227	241	247	67
	1103	186	196	212	216	235	248	252	258	268	82
	1104	186	197	200	203	216	235	232	237	247	61
	1105	171	181	189	200	209	208	224	235	244	73
	1106	184	190	200	203	216	229	241	240	255	71
	1107	192	204	215	225	241	249	269	274	286	94
	1108	176	200	209	220	228	221	229	243	252	76
	1109	186	194	191	210	224	234	243	240	249	63
	1110	192	203	209	210	220	235	240	243	254	62
	Mean	184	193	202	211	224	232	240	245	255	71
	S.D.	7	8	9	8	10	13	13	12	13	10

Unit : g

Appendix 102

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual body weight (Administration period)

Dose (mg/kg) : 100

Sex	Animal number	Day of administration									Gain 1-28
		1	4	7	10	14	17	21	24	28	
Male	2001	242	264	288	303	327	344	364	375	397	155
	2002	245	267	293	316	335	352	370	373	400	155
	2003	235	260	286	308	345	355	384	392	419	184
	2004	234	248	270	285	315	323	344	346	373	139
	2005	237	256	283	304	336	357	381	386	418	181
	Mean	239	259	284	303	332	346	369	374	401	163
	S.D.	5	7	9	11	11	14	16	18	19	19
Female	2101	178	179	195	203	215	222	237	236	247	69
	2102	187	195	203	209	224	240	252	260	269	82
	2103	186	192	200	219	233	228	247	252	262	76
	2104	177	196	201	211	218	225	239	250	258	81
	2105	193	200	200	218	230	238	245	243	255	62
	Mean	184	192	200	212	224	231	244	248	258	74
	S.D.	7	8	3	7	8	8	6	9	8	8

Unit : g

Appendix 103

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual body weight (Administration period)

Dose (mg/kg) : 300

Sex	Animal number	Day of administration									Gain 1-28
		1	4	7	10	14	17	21	24	28	
Male	3001	241	263	278	297	317	329	344	351	371	130
	3002	241	262	281	296	315	319	345	360	379	138
	3003	245	265	285	299	321	336	356	371	392	147
	3004	229	249	273	295	316	334	360	359	386	157
	3005	232	251	266	274	298	307	328	332	362	130
	Mean	238	258	277	292	313	325	347	355	378	140
	S.D.	7	7	7	10	9	12	12	15	12	12
Female	3101	174	175	193	200	217	218	231	236	246	72
	3102	184	200	212	219	225	230	237	251	261	77
	3103	185	187	196	192	202	216	225	225	243	58
	3104	186	188	208	223	236	247	253	254	259	73
	3105	191	202	210	226	236	244	255	255	269	78
	Mean	184	190	204	212	223	231	240	244	256	72
	S.D.	6	11	9	15	14	14	13	13	11	8

Unit : g

Appendix 104

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual body weight (Administration period)

Dose (mg/kg) : 1000

Sex	Animal number	Day of administration									Gain 1-28
		1	4	7	10	14	17	21	24	28	
Male	4001	238	254	279	295	321	338	357	367	396	158
	4002	240	262	284	306	335	348	372	374	400	160
	4003	245	260	282	301	328	345	362	372	391	146
	4004	235	256	279	292	318	339	358	364	387	152
	4005	240	245	256	269	290	303	317	323	340	100
	4006	247	270	292	314	341	359	381	387	407	160
	4007	241	260	287	309	336	354	372	384	413	172
	4008	231	243	259	279	303	316	336	339	362	131
	4009	236	254	268	291	307	326	344	351	371	135
	4010	234	257	277	295	315	331	353	367	384	150
	Mean	239	256	276	295	319	336	355	363	385	146
	S.D.	5	8	12	14	16	17	19	20	22	20
Female	4101	195	197	204	205	214	224	236	237	242	47
	4102	185	195	200	217	231	238	247	248	260	75
	4103	180	186	202	214	224	224	234	238	244	64
	4104	185	186	199	211	221	225	233	233	238	53
	4105	176	185	189	193	201	210	217	222	230	54
	4106	179	182	197	199	213	219	228	229	240	61
	4107	192	197	203	208	218	235	245	254	267	75
	4108	186	188	206	216	222	231	238	232	246	60
	4109	185	191	197	214	226	231	245	246	253	68
	4110	194	195	207	223	230	236	256	253	262	68
	Mean	186	190	200	210	220	227	238	239	248	63
	S.D.	6	6	5	9	9	9	11	11	12	9

Unit : g

Appendix 105

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual body weight (Recovery period)

Dose (mg/kg) : 0

Sex	Animal number	Day of recovery					Gain 1-14
		1	3	7	10	14	
Male	1006	343	353	372	381	389	46
	1007	342	348	366	368	377	35
	1008	381	388	406	416	430	49
	1009	440	451	474	479	497	57
	1010	387	394	408	417	432	45
	Mean	379	387	405	412	425	46
	S.D.	40	41	43	43	47	8
Female	1106	247	253	266	261	266	19
	1107	281	286	298	297	298	17
	1108	249	260	266	265	271	22
	1109	251	243	252	271	269	18
	1110	255	261	274	267	268	13
	Mean	257	261	271	272	274	18
	S.D.	14	16	17	14	13	3

Unit : g

Appendix 106

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual body weight (Recovery period)

Dose (mg/kg) : 1000

Sex	Animal number	Day of recovery					Gain 1-14
		1	3	7	10	14	
Male	4006	408	415	436	448	464	56
	4007	407	419	444	452	475	68
	4008	362	370	390	394	406	44
	4009	369	377	395	403	416	47
	4010	383	388	405	408	422	39
	Mean	386	394	414	421	437	51
	S.D.	21	22	25	27	31	11
Female	4106	235	241	248	248	257	22
	4107	269	270	276	278	290	21
	4108	244	259	267	260	263	19
	4109	251	253	261	266	277	26
	4110	265	270	282	291	295	30
	Mean	253	259	267	269	276	24
	S.D.	14	12	13	17	16	4

Unit : g

Appendix 107

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual food consumption (Administration period)

Dose (mg/kg) : 0

Sex	Animal number	Day of administration								
		1	4	7	10	14	17	21	24	28
Male	1001	23	21	21	21	20	19	20	19	20
	1002	27	24	20	20	18	20	20	20	19
	1003	24	19	20	21	21	18	20	19	18
	1004	26	20	21	22	22	21	22	21	21
	1005	26	24	23	23	22	20	22	20	21
	1006	24	20	20	19	16	15	15	14	15
	1007	22	19	16	19	17	17	17	15	16
	1008	27	23	23	24	21	19	20	19	18
	1009	24	23	23	24	24	21	24	21	22
	1010	22	17	18	20	20	19	19	20	19
	Mean	25	21	21	21	20	19	20	19	19
	S.D.	2	2	2	2	2	2	3	2	2
Female	1101	18	13	16	16	15	13	13	13	13
	1102	16	15	16	15	17	14	16	15	14
	1103	20	16	16	16	18	16	16	17	15
	1104	15	17	14	15	15	14	13	12	15
	1105	13	15	14	16	16	12	16	16	15
	1106	19	15	14	15	14	15	15	14	14
	1107	20	16	17	17	18	15	17	16	16
	1108	14	18	16	16	17	13	16	18	16
	1109	19	15	15	17	16	15	16	14	14
	1110	16	15	13	14	15	15	13	12	13
	Mean	17	16	15	16	16	14	15	15	15
	S.D.	3	1	1	1	1	1	2	2	1

Unit : g/rat/day

Appendix 108

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual food consumption (Administration period)

Dose (mg/kg) : 100

Sex	Animal number	Day of administration								
		1	4	7	10	14	17	21	24	28
Male	2001	27	23	23	21	21	20	20	18	19
	2002	24	23	22	22	22	20	20	18	19
	2003	26	22	23	21	25	20	22	21	20
	2004	23	20	19	19	19	18	18	16	18
	2005	26	22	24	24	25	24	26	24	26
	Mean	25	22	22	21	22	20	21	19	20
	S.D.	2	1	2	2	3	2	3	3	3
Female	2101	17	13	15	13	14	13	14	12	14
	2102	20	16	16	16	18	18	18	16	16
	2103	20	15	16	17	17	13	16	16	14
	2104	14	17	14	14	15	15	17	16	15
	2105	19	16	14	16	15	16	16	13	15
	Mean	18	15	15	15	16	15	16	15	15
	S.D.	3	2	1	2	2	2	1	2	1

Unit : g/rat/day

Appendix 109

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual food consumption (Administration period)

Dose (mg/kg) : 300

Sex	Animal number	Day of administration								
		1	4	7	10	14	17	21	24	28
Male	3001	24	23	22	20	20	19	18	19	18
	3002	24	23	22	19	18	16	18	18	18
	3003	24	24	21	19	19	18	19	19	20
	3004	22	21	22	22	21	22	22	19	21
	3005	20	20	20	17	17	15	17	17	17
	Mean	23	22	21	19	19	18	19	18	19
S.D.	2	2	1	2	2	3	2	1	2	
Female	3101	16	14	15	14	14	12	14	15	14
	3102	13	17	15	14	14	15	16	16	16
	3103	18	14	15	13	15	15	15	15	15
	3104	17	14	17	16	16	15	15	15	15
	3105	20	19	18	19	18	16	17	14	15
	Mean	17	16	16	15	15	15	15	15	15
S.D.	3	2	1	2	2	2	1	1	1	

Unit : g/rat/day

Appendix 110

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual food consumption (Administration period)

Dose (mg/kg) : 1000

Sex	Animal number	Day of administration								
		1	4	7	10	14	17	21	24	28
Male	4001	23	20	20	18	19	19	18	19	20
	4002	23	22	23	21	21	19	21	18	20
	4003	24	21	21	21	22	21	22	20	20
	4004	24	20	20	18	19	19	19	19	19
	4005	23	17	17	17	19	18	18	16	17
	4006	23	22	23	23	23	21	22	20	21
	4007	24	20	21	20	21	21	21	21	21
	4008	23	19	19	20	22	19	21	18	19
	4009	23	20	20	20	19	19	20	17	18
	4010	23	21	20	20	19	19	21	19	21
	Mean	23	20	20	20	20	20	20	19	20
	S.D.	0	1	2	2	2	1	1	1	1
Female	4101	17	14	13	13	13	12	13	15	13
	4102	19	16	16	16	16	15	15	15	15
	4103	16	16	17	16	15	14	15	14	14
	4104	18	15	16	14	15	12	13	13	13
	4105	15	14	14	13	13	13	12	11	13
	4106	15	14	14	12	14	13	13	13	13
	4107	20	17	17	16	17	18	18	17	18
	4108	20	15	17	16	15	15	15	14	16
	4109	18	15	15	15	15	14	15	13	13
	4110	19	16	17	16	15	15	16	14	15
	Mean	18	15	16	15	15	14	15	14	14
	S.D.	2	1	2	2	1	2	2	2	2

Unit : g/rat/day

Appendix 111

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual food consumption (Recovery period)

Dose (mg/kg) : 0

Sex	Animal number	Day of recovery			
		3	7	10	14
Male	1006	22	23	23	24
	1007	21	23	22	24
	1008	25	28	27	29
	1009	28	29	28	31
	1010	24	24	23	25
	Mean	24	25	25	27
	S.D.	2	3	3	3
Female	1106	15	19	18	19
	1107	19	20	20	20
	1108	23	20	18	21
	1109	15	21	24	21
	1110	18	21	19	21
	Mean	18	20	20	20
	S.D.	3	1	2	1

Unit : g/rat/day

Appendix 112

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual food consumption (Recovery period)

Dose (mg/kg) : 1000

Sex	Animal number	Day of recovery			
		3	7	10	14
Male	4006	26	28	27	30
	4007	28	29	28	32
	4008	24	26	24	27
	4009	23	26	26	29
	4010	25	26	24	27
	Mean	25	27	26	29
	S.D.	2	1	2	2
Female	4106	15	18	18	18
	4107	19	24	23	25
	4108	21	20	17	19
	4109	17	21	21	22
	4110	19	22	21	22
	Mean	18	21	20	21
	S.D.	2	2	2	3

Unit : g/rat/day

Appendix 113

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual urinalysis (4 weeks)

Dose (mg/kg) : 0

Sex	Animal number	pH	1) Pro- tein	2) Ketone body	3) Glu- cose	4) Occult blood	5) Bili- rubin	6) Urobi- linogen	7) Color
Male	1001	9.0	+	++	-	-	-	+-	Y
	1002	8.0	+	+-	-	-	-	+-	Y
	1003	8.5	+	+	-	-	-	+	Y
	1004	9.0	+	-	-	-	-	+-	Y
	1005	9.0	+	-	-	-	-	+-	Y
	1006	8.5	+	+-	-	-	-	+-	Y
	1007	8.5	+-	-	-	-	-	+-	Y
	1008	8.5	++	+	-	-	-	+-	Y
	1009	8.5	++	+	-	-	-	+-	Y
	1010	8.0	+	+-	-	-	-	+-	Y
Female	1101	7.0	+-	-	-	-	-	+-	Y
	1102	7.5	-	-	-	-	-	+-	Y
	1103	7.0	-	-	-	-	-	+-	Y
	1104	7.0	-	-	-	-	-	+-	Y
	1105	8.0	+	-	-	-	-	+-	Y
	1106	8.0	-	-	-	-	-	+-	Y
	1107	8.0	+	+	-	-	-	+	Y
	1108	7.0	-	-	-	-	-	+-	Y
	1109	8.5	+-	-	-	-	-	+-	Y
	1110	8.0	+-	-	-	-	-	+-	Y
1)	- : 0 - 5 mg/dL	+- : 10 - 20 mg/dL	+	30 - 70 mg/dL	++ : 100 - 200 mg/dL	+++ : 250 - 400 mg/dL	++++ : >400 mg/dL		
2)	- : 0 mg/dL	+- : 5 mg/dL	+	10 - 20 mg/dL	++ : 30 - 45 mg/dL	+++ : 60 - 80 mg/dL	++++ : >80 mg/dL		
3)	- : 0 - 10 mg/dL	+- : 30 - 50 mg/dL	+	70 - 100 mg/dL	++ : 150 - 200 mg/dL	+++ : 300 - 500 mg/dL	++++ : ≥1000 mg/dL		
4)	- : 0 mg/dL	+- : 0.03 mg/dL	+	0.06 - 0.1 mg/dL	++ : 0.2 - 0.5 mg/dL	+++ : ≥1.0 mg/dL			
5)	- : 0 mg/dL	+- : 0.2 mg/dL	+	0.5 - 1.0 mg/dL	++ : 2.0 - 4.0 mg/dL	+++ : 6.0 - 10.0 mg/dL	++++ : >10.0 mg/dL		
6)	+- : 0.2 - 1.0 mg/dL	+	2.0 - 3.0 mg/dL	++ : 4.0 - 6.0 mg/dL	+++ : 8.0 - 12.0 mg/dL	++++ : >12.0 mg/dL			
7)	LY : Light yellow	Y : Yellow	DY : Dark yellow						

Appendix 114

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual urinalysis (4 weeks)

Dose (mg/kg) : 0

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

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

Appendix 115

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual water intake and urinalysis (4 weeks)

Dose (mg/kg) : 0

Sex	Animal number	Water intake mL/24h	Urine volume mL/24h	Osmolality mOsm/kg
Male	1001	54	12.4	1048
	1002	37	8.0	1250
	1003	38	4.0	2134
	1004	36	4.6	1620
	1005	41	5.4	1986
	1006	27	3.0	2322
	1007	33	8.5	1224
	1008	38	3.8	1950
	1009	32	2.4	1876
	1010	31	7.7	2152
	Mean	37	6.0	1756
	S.D.	7	3.1	445
Female	1101	43	2.8	1944
	1102	33	7.8	1288
	1103	31	3.9	1586
	1104	44	8.7	1208
	1105	31	7.3	1274
	1106	36	7.7	872
	1107	37	3.6	2474
	1108	34	4.1	1388
	1109	33	3.9	1944
	1110	34	4.8	1652
	Mean	36	5.5	1563
	S.D.	5	2.2	462

Appendix 116

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual urinalysis (4 weeks)

Dose (mg/kg) : 100

Sex	Animal number	pH	1) Pro- tein	2) Ketone body	3) Glu- cose	4) Occult blood	5) Bili- rubin	6) Urobi- linogen	7) Color
Male	2001	8.5	+-	-	-	-	-	+-	Y
	2002	8.5	+-	-	-	-	-	+-	Y
	2003	8.0	+-	-	-	-	-	+-	Y
	2004	8.5	+-	-	-	-	-	+-	Y
	2005	8.0	+-	-	-	-	-	+-	Y
Female	2101	8.0	+	-	-	-	-	+-	Y
	2102	8.0	-	-	-	-	-	+-	Y
	2103	8.0	+-	-	-	-	-	+-	Y
	2104	8.5	+-	-	-	-	-	+-	Y
	2105	8.0	+	-	-	-	-	+-	Y
1)	- : 0 - 5 mg/dL	+- : 10 - 20 mg/dL	+	30 - 70 mg/dL	++ : 100 - 200 mg/dL	+++ : 250 - 400 mg/dL	++++ : >400 mg/dL		
2)	- : 0 mg/dL	+- : 5 mg/dL	+	10 - 20 mg/dL	++ : 30 - 45 mg/dL	+++ : 60 - 80 mg/dL	++++ : >80 mg/dL		
3)	- : 0 - 10 mg/dL	+- : 30 - 50 mg/dL	+	70 - 100 mg/dL	++ : 150 - 200 mg/dL	+++ : 300 - 500 mg/dL	++++ : ≥1000 mg/dL		
4)	- : 0 mg/dL	+- : 0.03 mg/dL	+	0.06 - 0.1 mg/dL	++ : 0.2 - 0.5 mg/dL	+++ : ≥1.0 mg/dL			
5)	- : 0 mg/dL	+- : 0.2 mg/dL	+	0.5 - 1.0 mg/dL	++ : 2.0 - 4.0 mg/dL	+++ : 6.0 - 10.0 mg/dL	++++ : >10.0 mg/dL		
6)	+- : 0.2 - 1.0 mg/dL	+	2.0 - 3.0 mg/dL	++ : 4.0 - 6.0 mg/dL	+++ : 8.0 - 12.0 mg/dL	++++ : >12.0 mg/dL			
7)	LY : Light yellow	Y : Yellow		DY : Dark yellow					

Appendix 117

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual urinalysis (4 weeks)

Dose (mg/kg) : 100

Sex	Animal number	URINE SEDIMENT					CRYSTALLIZATION	
		RBC	WBC	SEC	SREC	Cast	PS	CO
Male	2001	-	-	+-	-	-	-	-
	2002	-	-	+-	-	-	-	-
	2003	-	-	+-	-	-	-	-
	2004	-	-	+-	-	-	-	-
	2005	-	-	+-	-	-	-	-
Female	2101	-	-	+-	-	-	+-	-
	2102	-	-	+-	-	-	-	-
	2103	-	-	+-	-	-	-	-
	2104	-	-	+-	-	-	-	-
	2105	-	-	+-	-	-	-	-
SEC : Squamous Epithelial Cell				-	: Negative			
SREC : Small Round Epithelial Cell				+-	: Slight			
PS : Phosphate Salts				+	: Mild			
CO : Calcium Oxalate				++	: Moderate			
				+++	: Severe			

Appendix 118

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual water intake and urinalysis (4 weeks)

Dose (mg/kg) : 100

Sex	Animal number	Water intake mL/24h	Urine volume mL/24h	Osmolality mOsm/kg
Male	2001	39	6.4	1370
	2002	44	13.6	948
	2003	35	12.6	1574
	2004	32	6.2	1740
	2005	39	10.2	2094
	Mean	38	9.8	1545
	S.D.	5	3.4	426
Female	2101	25	1.7	3082
	2102	34	11.2	1464
	2103	26	5.4	1420
	2104	30	10.3	1354
	2105	37	3.0	1698
	Mean	30	6.3	1804
	S.D.	5	4.3	726

Appendix 119

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual urinalysis (4 weeks)

Dose (mg/kg) : 300

Sex	Animal number	pH	1) Pro- tein	2) Ketone body	3) Glu- cose	4) Occult blood	5) Bili- rubin	6) Urobi- linogen	7) Color
Male	3001	8.5	+	-	-	-	-	+-	Y
	3002	8.5	+-	-	-	-	-	+-	Y
	3003	9.0	+	-	-	-	-	+-	Y
	3004	8.0	-	-	-	-	-	+-	Y
	3005	8.5	-	-	-	-	-	+-	Y
Female	3101	8.5	+-	-	-	-	-	+-	Y
	3102	7.5	+	-	-	-	-	+-	Y
	3103	8.0	-	-	-	-	-	+-	Y
	3104	6.5	+	+	-	-	-	+	Y
	3105	8.5	+	+	-	-	-	+	Y
1)	- : 0 - 5 mg/dL	+- : 10 - 20 mg/dL	+	30 - 70 mg/dL	++ : 100 - 200 mg/dL	+++ : 250 - 400 mg/dL	++++ : >400 mg/dL		
2)	- : 0 mg/dL	+- : 5 mg/dL	+	10 - 20 mg/dL	++ : 30 - 45 mg/dL	+++ : 60 - 80 mg/dL	++++ : >80 mg/dL		
3)	- : 0 - 10 mg/dL	+- : 30 - 50 mg/dL	+	70 - 100 mg/dL	++ : 150 - 200 mg/dL	+++ : 300 - 500 mg/dL	++++ : ≥1000 mg/dL		
4)	- : 0 mg/dL	+- : 0.03 mg/dL	+	0.06 - 0.1 mg/dL	++ : 0.2 - 0.5 mg/dL	+++ : ≥1.0 mg/dL			
5)	- : 0 mg/dL	+- : 0.2 mg/dL	+	0.5 - 1.0 mg/dL	++ : 2.0 - 4.0 mg/dL	+++ : 6.0 - 10.0 mg/dL	++++ : >10.0 mg/dL		
6)	+- : 0.2 - 1.0 mg/dL	+	2.0 - 3.0 mg/dL	++ : 4.0 - 6.0 mg/dL	+++ : 8.0 - 12.0 mg/dL	++++ : >12.0 mg/dL			
7)	LY : Light yellow	Y : Yellow		DY : Dark yellow					

Appendix 120

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual urinalysis (4 weeks)

Dose (mg/kg) : 300

Sex	Animal number	URINE SEDIMENT					CRYSTALLIZATION	
		RBC	WBC	SEC	SREC	Cast	PS	CO
Male	3001	-	-	+-	-	-	-	-
	3002	-	-	+-	-	-	-	-
	3003	-	-	+-	-	-	-	-
	3004	-	-	+-	-	-	-	-
	3005	-	-	+-	-	-	-	-
Female	3101	-	-	+-	-	-	-	-
	3102	-	-	+-	-	-	+-	-
	3103	-	-	+-	-	-	-	-
	3104	-	-	+-	-	-	-	-
	3105	-	-	+-	-	-	-	-
SEC : Squamous Epithelial Cell				-	: Negative			
SREC : Small Round Epithelial Cell				+-	: Slight			
PS : Phosphate Salts				+	: Mild			
CO : Calcium Oxalate				++	: Moderate			
				+++	: Severe			

Appendix 121

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual water intake and urinalysis (4 weeks)

Dose (mg/kg) : 300

Sex	Animal number	Water intake mL/24h	Urine volume mL/24h	Osmolality mOsm/kg
Male	3001	41	6.8	1816
	3002	65	24.7	476
	3003	41	5.4	1330
	3004	59	15.1	1222
	3005	43	12.7	1162
	Mean	50	12.9	1201
	S.D.	11	7.7	480
Female	3101	27	4.8	2236
	3102	31	4.9	1694
	3103	57	17.5	810
	3104	41	6.2	1488
	3105	36	3.7	1442
	Mean	38	7.4	1534
	S.D.	12	5.7	513

Appendix 122

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual urinalysis (4 weeks)

Dose (mg/kg) : 1000

Sex	Animal number	pH	1) Pro- tein	2) Ketone body	3) Glu- cose	4) Occult blood	5) Bili- rubin	6) Urobi- linogen	7) Color
Male	4001	8.5	+-	-	-	-	-	+-	Y
	4002	8.5	+-	-	-	-	-	+-	Y
	4003	9.0	+	-	-	-	-	+-	Y
	4004	8.5	+	+-	-	-	-	+-	Y
	4005	8.5	+	+-	-	-	-	+-	Y
	4006	8.5	+	-	-	-	-	+	Y
	4007	8.5	+-	-	-	-	-	+-	Y
	4008	8.5	+-	-	-	-	-	+-	Y
	4009	8.5	+	-	-	-	-	+-	Y
	4010	8.0	+	+	-	-	-	+	Y
Female	4101	8.5	+-	-	-	-	-	+-	Y
	4102	8.5	+	-	-	-	-	+-	Y
	4103	6.0	+	+-	-	-	-	+-	Y
	4104	7.0	++	+	-	-	-	++	Y
	4105	8.5	+-	-	-	-	-	+-	Y
	4106	8.5	+	+-	+-	-	-	+-	Y
	4107	8.0	+	-	-	-	-	+-	Y
	4108	7.5	+-	-	-	-	-	+-	Y
	4109	8.5	+-	-	-	-	-	+-	Y
	4110	8.0	+-	-	-	+-	-	+-	Y
1)	- : 0 - 5 mg/dL	+- : 10 - 20 mg/dL	+ : 30 - 70 mg/dL		++ : 100 - 200 mg/dL		+++ : 250 - 400 mg/dL		++++ : >400 mg/dL
2)	- : 0 mg/dL	+- : 5 mg/dL	+ : 10 - 20 mg/dL		++ : 30 - 45 mg/dL		+++ : 60 - 80 mg/dL		++++ : >80 mg/dL
3)	- : 0 - 10 mg/dL	+- : 30 - 50 mg/dL	+ : 70 - 100 mg/dL		++ : 150 - 200 mg/dL		+++ : 300 - 500 mg/dL		++++ : ≥1000 mg/dL
4)	- : 0 mg/dL	+- : 0.03 mg/dL	+ : 0.06 - 0.1 mg/dL		++ : 0.2 - 0.5 mg/dL		+++ : ≥1.0 mg/dL		
5)	- : 0 mg/dL	+- : 0.2 mg/dL	++ : 0.5 - 1.0 mg/dL		++ : 2.0 - 4.0 mg/dL		+++ : 6.0 - 10.0 mg/dL		++++ : >10.0 mg/dL
6)	+- : 0.2 - 1.0 mg/dL	+	2.0 - 3.0 mg/dL	++ : 4.0 - 8.0 mg/dL		+++ : 8.0 - 12.0 mg/dL		++++ : >12.0 mg/dL	
7)	LY : Light yellow	Y : Yellow	DY : Dark yellow						

Appendix 123

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual urinalysis (4 weeks)

Dose (mg/kg) : 1000

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

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

Appendix 124

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual water intake and urinalysis (4 weeks)

Dose (mg/kg) : 1000

Sex	Animal number	Water intake mL/24h	Urine volume mL/24h	Osmolality mOsm/kg
Male	4001	38	11.7	1154
	4002	35	7.6	2064
	4003	39	6.7	2046
	4004	45	6.6	1876
	4005	45	5.2	1754
	4006	67	4.1	1946
	4007	44	9.6	1696
	4008	37	6.1	1848
	4009	42	7.1	1502
	4010	35	7.8	2066
	Mean	43	7.3	1795
	S.D.	9	2.2	289
Female	4101	42	4.4	1788
	4102	25	5.0	1892
	4103	29	4.7	1846
	4104	30	1.7	2522
	4105	34	5.0	1208
	4106	28	2.6	1590
	4107	45	7.3	1176
	4108	52	6.7	1152
	4109	34	7.5	1498
	4110	94	9.9	1564
	Mean	41	5.5	1624
	S.D.	20	2.4	418

Appendix 125

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual urinalysis (Recovery)

Dose (mg/kg) : 0

Sex	Animal number	pH	1) Pro- tein	2) Ketone body	3) Glu- cose	4) Occult blood	5) Bili- rubin	6) Urobi- linogen	7) Color
Male	1006	8.5	+++	+	-	-	-	+	Y
	1007	9.0	+	-	-	-	-	+-	Y
	1008	8.5	+	-	-	-	-	+-	Y
	1009	8.5	++	+-	-	-	-	+	Y
	1010	9.0	++	+-	-	-	-	+-	Y
Female	1106	8.0	-	-	-	-	-	+-	Y
	1107	8.5	+	+-	-	-	-	+	Y
	1108	8.5	+-	-	-	-	-	+-	Y
	1109	8.5	+	-	-	-	-	+-	Y
	1110	7.0	+	-	-	-	-	+	Y
1)	- : 0 - 5 mg/dL	+- : 10 - 20 mg/dL	+	30 - 70 mg/dL	++ : 100 - 200 mg/dL	+++ : 250 - 400 mg/dL	++++ : >400 mg/dL		
2)	- : 0 mg/dL	+- : 5 mg/dL	+	10 - 20 mg/dL	++ : 30 - 45 mg/dL	+++ : 60 - 80 mg/dL	++++ : >80 mg/dL		
3)	- : 0 - 10 mg/dL	+- : 30 - 50 mg/dL	+	70 - 100 mg/dL	++ : 150 - 200 mg/dL	+++ : 300 - 500 mg/dL	++++ : ≥1000 mg/dL		
4)	- : 0 mg/dL	+- : 0.03 mg/dL	+	0.06 - 0.1 mg/dL	++ : 0.2 - 0.5 mg/dL	+++ : ≥1.0 mg/dL			
5)	- : 0 mg/dL	+- : 0.2 mg/dL	+	0.5 - 1.0 mg/dL	++ : 2.0 - 4.0 mg/dL	+++ : 6.0 - 10.0 mg/dL	++++ : >10.0 mg/dL		
6)	+- : 0.2 - 1.0 mg/dL	+	2.0 - 3.0 mg/dL	++ : 4.0 - 6.0 mg/dL	+++ : 8.0 - 12.0 mg/dL	++++ : >12.0 mg/dL			
7)	LY : Light yellow	Y : Yellow	DY : Dark yellow						

Appendix 126

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual urinalysis (Recovery)

Dose (mg/kg) : 0

Sex	Animal number	URINE SEDIMENT					CRYSTALLIZATION	
		RBC	WBC	SEC	SREC	Cast	PS	CO
Male	1006	-	-	+-	-	-	+-	-
	1007	-	-	+-	-	-	-	-
	1008	-	-	+-	-	-	+-	-
	1009	-	-	+-	-	-	+-	-
	1010	-	-	+-	-	-	-	-
Female	1106	-	-	+-	-	-	-	-
	1107	-	-	+-	-	-	-	-
	1108	-	-	+-	-	-	-	-
	1109	-	-	+-	-	-	-	-
	1110	-	-	+-	-	-	+-	-
SEC : Squamous Epithelial Cell		-	: Negative					
SREC : Small Round Epithelial Cell		+-	: Slight					
PS : Phosphate Salts		+	: Mild					
CO : Calcium Oxalate		++	: Moderate					
		+++	: Severe					

Appendix 127

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual water intake and urinalysis (Recovery)

Dose (mg/kg) : 0

Sex	Animal number	Water intake mL/24h	Urine volume mL/24h	Osmolality mOsm/kg
Male	1006	33	5.9	2392
	1007	39	9.7	2148
	1008	38	6.6	2356
	1009	56	6.0	2792
	1010	34	6.3	2532
	Mean	40	6.9	2444
	S.D.	9	1.6	238
Female	1106	90	10.1	1146
	1107	29	6.0	2022
	1108	44	12.3	1524
	1109	24	4.3	2590
	1110	68	5.1	2594
	Mean	51	7.6	1975
	S.D.	28	3.5	643

Appendix 128

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual urinalysis (Recovery)

Dose (mg/kg) : 1000

Sex	Animal number	pH	1) Pro- tein	2) Ketone body	3) Glu- cose	4) Occult blood	5) Bili- rubin	6) Urobi- linogen	7) Color
Male	4006	9.0	+++	+-	-	-	-	+	Y
	4007	8.5	+-	-	-	-	-	+-	Y
	4008	9.0	++	+-	-	-	-	+-	Y
	4009	8.5	+	-	-	-	-	+-	Y
	4010	8.0	+	-	-	-	-	+-	Y
Female	4106	8.0	+-	-	+-	-	-	+-	Y
	4107	8.0	-	-	-	-	-	+-	Y
	4108	8.5	+	-	-	-	-	+-	Y
	4109	8.0	+-	+-	-	-	-	+-	Y
	4110	8.0	+-	-	-	-	-	+-	Y
1)	- : 0 - 5 mg/dL	+- : 10 - 20 mg/dL	+	30 - 70 mg/dL	++ : 100 - 200 mg/dL	+++ : 250 - 400 mg/dL	++++ : >400 mg/dL		
2)	- : 0 mg/dL	+- : 5 mg/dL	+	10 - 20 mg/dL	++ : 30 - 45 mg/dL	+++ : 60 - 80 mg/dL	++++ : >80 mg/dL		
3)	- : 0 - 10 mg/dL	+- : 30 - 50 mg/dL	+	70 - 100 mg/dL	++ : 150 - 200 mg/dL	+++ : 300 - 500 mg/dL	++++ : ≥1000 mg/dL		
4)	- : 0 mg/dL	+- : 0.03 mg/dL	+	0.06 - 0.1 mg/dL	++ : 0.2 - 0.5 mg/dL	+++ : ≥1.0 mg/dL			
5)	- : 0 mg/dL	+- : 0.2 mg/dL	+	0.5 - 1.0 mg/dL	++ : 2.0 - 4.0 mg/dL	+++ : 6.0 - 10.0 mg/dL	++++ : >10.0 mg/dL		
6)	+- : 0.2 - 1.0 mg/dL	+	2.0 - 3.0 mg/dL	++ : 4.0 - 6.0 mg/dL	+++ : 8.0 - 12.0 mg/dL	++++ : >12.0 mg/dL			
7)	LY : Light yellow	Y : Yellow	DY : Dark yellow						

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Dose (mg/kg) : 1000

Sex	Animal number	URINE SEDIMENT					CRYSTALLIZATION	
		RBC	WBC	SEC	SREC	Cast	PS	CO
Male	4006	-	-	+-	-	-	-	-
	4007	-	-	+-	-	-	-	-
	4008	-	-	+-	-	-	+-	-
	4009	-	-	+-	-	-	+-	-
	4010	-	-	+-	-	-	-	-
Female	4106	-	-	+-	-	-	-	-
	4107	-	-	+-	-	-	-	-
	4108	-	-	+-	-	-	-	-
	4109	-	-	+-	-	-	-	-
	4110	-	-	+-	-	-	-	-
SEC : Squamous Epithelial Cell				-	: Negative			
SREC : Small Round Epithelial Cell				+-	: Slight			
PS : Phosphate Salts				+	: Mild			
CO : Calcium Oxalate				++	: Moderate			
				+++	: Severe			

Appendix 130

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual water intake and urinalysis (Recovery)

Dose (mg/kg) : 1000

Sex	Animal number	Water intake mL/24h	Urine volume mL/24h	Osmolality mOsm/kg
Male	4006	30	10.2	2156
	4007	53	17.0	1590
	4008	38	8.9	1986
	4009	57	13.2	1158
	4010	41	8.5	2544
	Mean	44	11.6	1887
	S.D.	11	3.6	532
Female	4106	39	12.4	1216
	4107	47	9.7	1282
	4108	36	8.5	1674
	4109	28	4.9	2284
	4110	37	15.2	1460
	Mean	37	10.1	1583
	S.D.	7	3.9	430

Appendix 131

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual hematology (4 weeks)

Dose (mg/kg) : 0

Sex	Animal number	RBC X10 ⁴ /μL	Hb g/dL	Ht %	MCV fL	MCH pg	MCHC %	Reticu- locyte %	Plate- let X10 ³ /μL	PT s	APTT s	Fibri- nogen mg/dL
Male	1001	740	14.8	44	59.0	20.1	34.0	2.9	94.5	11.1	14.6	239
	1002	778	15.8	46	59.1	20.3	34.4	1.9	94.4	12.2	16.6	248
	1003	772	15.4	45	58.0	20.0	34.5	2.4	97.5	11.2	16.0	258
	1004	786	14.8	44	55.7	18.8	33.8	1.9	90.3	12.0	15.3	244
	1005	786	15.6	46	58.1	19.8	34.1	1.7	103.2	11.6	16.1	235
	Mean	772	15.3	45	58.0	19.8	34.2	2.2	96.0	11.6	15.7	245
	S.D.	19	0.5	1	1.4	0.6	0.3	0.5	4.8	0.5	0.8	9
Female	1101	715	14.9	41	57.3	20.9	36.4	1.7	114.7	11.5	16.6	223
	1102	762	15.7	45	58.3	20.6	35.3	1.3	105.7	12.1	18.3	189
	1103	792	16.4	45	57.4	20.8	36.2	1.7	101.3	12.2	18.1	205
	1104	747	14.6	42	56.2	19.6	34.9	2.3	119.3	11.0	13.0	246
	1105	749	15.5	45	59.7	20.7	34.6	2.2	87.4	11.9	17.6	215
	Mean	753	15.4	44	57.8	20.5	35.5	1.8	105.7	11.7	16.7	216
	S.D.	28	0.7	2	1.3	0.5	0.8	0.4	12.5	0.5	2.2	21

Appendix 132

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
 Individual hematology (4 weeks)
 Dose (mg/kg) : 0

Sex	Animal number	WBC ×10 ³ /μL	Differential leukocyte counts (%)						
			Lymph.	Stab	Seg.	Eosino.	Baso.	Mono.	Others
Male	1001	81	91.5	0.5	7.5	0.0	0.0	0.5	0.0
	1002	114	88.5	0.5	9.5	1.0	0.0	0.5	0.0
	1003	117	89.0	0.5	9.5	0.5	0.0	0.5	0.0
	1004	56	75.0	2.0	20.0	2.5	0.0	0.5	0.0
	1005	110	87.0	1.0	11.5	0.0	0.0	0.5	0.0
	Mean	96	86.2	0.9	11.6	0.8	0.0	0.5	0.0
	S.D.	26	6.5	0.7	4.9	1.0	0.0	0.0	0.0
Female	1101	117	89.0	0.0	10.0	0.5	0.0	0.5	0.0
	1102	47	77.0	2.0	20.0	1.0	0.0	0.0	0.0
	1103	52	92.0	1.5	5.5	1.0	0.0	0.0	0.0
	1104	65	87.0	0.5	10.5	1.5	0.0	0.5	0.0
	1105	96	86.5	1.0	12.5	0.0	0.0	0.0	0.0
	Mean	75	86.3	1.0	11.7	0.8	0.0	0.2	0.0
	S.D.	30	5.6	0.8	5.3	0.6	0.0	0.3	0.0

Appendix 133

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual hematology (4 weeks)

Dose (mg/kg) : 100

Sex	Animal number	RBC ×10 ⁶ /μL	Hb g/dL	Ht %	MCV fL	MCH pg	MCHC %	Reticu- locyte %	Plate- let ×10 ³ /μL	PT s	APTT s	Fibri- nogen mg/dL
Male	2001	769	15.5	45	58.1	20.2	34.7	1.8	91.7	12.2	14.0	230
	2002	780	15.5	45	58.1	19.8	34.1	1.9	89.0	12.0	14.6	242
	2003	776	15.7	46	59.3	20.2	34.0	1.6	98.5	12.8	19.5	255
	2004	750	15.8	46	61.2	21.0	34.3	2.5	87.9	12.4	17.5	259
	2005	765	15.1	44	57.4	19.7	34.3	2.4	113.9	11.6	15.2	299
	Mean	768	15.5	45	58.8	20.2	34.3	2.0	96.2	12.2	16.2	257
	S.D.	12	0.3	1	1.5	0.5	0.3	0.4	10.7	0.4	2.3	26
Female	2101	659	14.2	39	58.8	21.6	36.7	1.5	96.4	11.4	18.0	194
	2102	734	15.1	42	56.6	20.6	36.3	1.7	105.2	11.8	15.2	210
	2103	751	15.3	42	55.6	20.3	36.5	1.8	111.6	12.2	17.3	207
	2104	768	15.5	44	56.9	20.2	35.6	2.6	114.0	11.3	16.1	197
	2105	797	15.3	45	56.0	19.2	34.3	1.3	101.0	12.0	19.6	189
	Mean	742	15.1	42	56.8	20.4	35.9	1.8	105.6	11.7	17.2	199
	S.D.	52	0.5	2	1.2	0.9	1.0	0.5	7.3	0.4	1.7	9

Appendix 134

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual hematology (4 weeks)

Dose (mg/kg) : 100

Sex	Animal number	WBC ×10 ³ /μL	Differential leukocyte counts (%)						
			Lymph.	Stab	Seg.	Eosino.	Baso.	Mono.	Others
Male	2001	136	92.5	1.0	5.5	0.5	0.0	0.5	0.0
	2002	88	91.0	0.5	7.5	0.5	0.0	0.5	0.0
	2003	95	92.0	0.5	7.0	0.5	0.0	0.0	0.0
	2004	71	92.0	0.0	7.0	0.0	0.0	1.0	0.0
	2005	72	81.0	0.0	18.5	0.5	0.0	0.0	0.0
	Mean	92	89.7	0.4	9.1	0.4	0.0	0.4	0.0
Female	S.D.	26	4.9	0.4	5.3	0.2	0.0	0.4	0.0
	2101	84	89.0	0.0	10.5	0.5	0.0	0.0	0.0
	2102	70	86.5	1.0	12.0	0.0	0.0	0.5	0.0
	2103	50	87.5	0.5	11.0	0.0	0.0	1.0	0.0
	2104	73	86.5	2.5	9.0	2.0	0.0	0.0	0.0
	2105	50	89.5	0.0	8.0	2.5	0.0	0.0	0.0
	Mean	65	87.8	0.8	10.1	1.0	0.0	0.3	0.0
	S.D.	15	1.4	1.0	1.6	1.2	0.0	0.4	0.0

Appendix 135

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual hematology (4 weeks)

Dose (mg/kg) : 300

Sex	Animal number	RBC ×10 ⁶ /μL	Hb g/dL	Ht %	MCV fL	MCH pg	MCHC %	Reticu- locyte %	Plate- let ×10 ³ /μL	PT s	APTT s	Fibri- nogen mg/dL
Male	3001	863	16.3	47	55.0	18.9	34.3	1.6	98.2	14.0	18.1	267
	3002	811	15.9	47	57.4	19.6	34.1	2.3	121.9	11.6	16.0	287
	3003	749	15.0	44	58.9	20.1	34.1	2.0	104.8	12.0	18.7	255
	3004	781	15.8	46	58.5	20.3	34.6	2.4	105.4	12.5	19.5	251
	3005	758	15.4	45	58.8	20.3	34.5	2.7	88.2	13.9	20.8	237
	Mean	792	15.7	46	57.7	19.8	34.3	2.2	103.7	12.8	18.6	259
	S.D.	46	0.5	1	1.6	0.6	0.2	0.4	12.3	1.1	1.8	19
Female	3101	676	15.0	41	60.3	22.2	36.8	2.6	103.2	10.8	14.1	213
	3102	694	14.7	42	59.9	21.3	35.5	2.7	105.2	11.4	17.9	207
	3103	782	15.3	43	55.2	19.6	35.5	2.5	115.9	11.6	15.4	216
	3104	726	15.6	43	58.6	21.5	36.6	1.5	92.5	11.6	16.4	259
	3105	782	16.2	47	59.6	20.7	34.8	2.3	86.7	12.1	14.9	206
	Mean	732	15.4	43	58.7	21.1	35.8	2.3	100.7	11.5	15.7	220
	S.D.	49	0.6	2	2.1	1.0	0.8	0.5	11.4	0.5	1.5	22

Appendix 136

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual hematology (4 weeks)

Dose (mg/kg) : 300

Sex	Animal number	WBC	Differential leukocyte counts (%)						
		$\times 10^3/\mu\text{L}$	Lymph.	Stab	Seg.	Eosino.	Baso.	Mono.	Others
Male	3001	124	85.0	1.0	13.5	0.0	0.0	0.5	0.0
	3002	121	87.5	0.5	10.5	0.0	0.0	1.5	0.0
	3003	93	84.5	0.5	14.0	1.0	0.0	0.0	0.0
	3004	95	89.5	1.0	9.0	0.5	0.0	0.0	0.0
	3005	87	90.0	1.0	8.5	0.0	0.0	0.5	0.0
	Mean	104	87.3	0.8	11.1	0.3	0.0	0.5	0.0
Female	S.D.	17	2.5	0.3	2.5	0.4	0.0	0.6	0.0
	3101	106	79.5	2.5	17.5	0.5	0.0	0.0	0.0
	3102	100	87.5	0.0	11.5	0.0	0.0	1.0	0.0
	3103	77	85.5	1.5	11.5	1.0	0.0	0.5	0.0
	3104	67	86.0	0.0	14.0	0.0	0.0	0.0	0.0
	3105	69	87.0	1.0	10.5	1.0	0.0	0.5	0.0
	Mean	84	85.1	1.0	13.0	0.5	0.0	0.4	0.0
	S.D.	18	3.2	1.1	2.8	0.5	0.0	0.4	0.0

Appendix 137

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual hematology (4 weeks)

Dose (mg/kg) : 1000

Sex	Animal number	RBC X10 ⁶ /μL	Hb g/dL	Ht %	MCV fL	MCH pg	MCHC %	Reticu- loocyte %	Plate- let X10 ³ /μL	PT s	APTT s	Fibri- nogen mg/dL
Male	4001	752	15.0	43	57.1	19.9	34.8	2.4	103.3	12.2	15.8	251
	4002	789	16.5	47	59.6	20.9	35.0	3.1	110.2	12.3	17.0	269
	4003	709	14.1	41	57.3	19.8	34.6	1.9	95.6	11.6	12.9	263
	4004	796	15.9	47	59.2	19.9	33.6	2.0	85.1	12.6	19.3	266
	4005	830	15.3	46	55.0	18.5	33.5	1.3	90.4	13.4	18.0	271
	Mean	775	15.4	45	57.6	19.8	34.3	2.1	96.9	12.4	16.6	264
	S.D.	46	0.9	3	1.8	0.9	0.7	0.7	10.0	0.7	2.4	8
Female	4101	722	14.6	41	56.7	20.3	35.8	1.6	101.1	12.3	16.8	192
	4102	734	15.9	44	59.9	21.6	36.0	1.7	103.5	11.5	15.5	246
	4103	709	13.9	39	55.6	19.7	35.3	1.6	110.4	11.3	17.3	218
	4104	745	15.4	45	59.7	20.7	34.7	1.6	82.5	10.7	15.0	201
	4105	799	16.0	46	57.7	20.0	34.6	2.3	91.9	11.7	17.0	187
	Mean	742	15.2	43	57.9	20.5	35.3	1.8	97.9	11.5	16.3	209
	S.D.	35	0.9	3	1.9	0.7	0.6	0.3	10.9	0.6	1.0	24

Appendix 138

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual hematology (4 weeks)

Dose (mg/kg) : 1000

Sex	Animal number	WBC ×10 ³ /μL	Differential leukocyte counts (%)						
			Lymph.	Stab	Seg.	Eosino.	Baso.	Mono.	Others
Male	4001	153	89.0	2.0	9.0	0.0	0.0	0.0	0.0
	4002	183	95.5	0.0	4.0	0.0	0.0	0.5	0.0
	4003	125	89.5	2.5	8.0	0.0	0.0	0.0	0.0
	4004	127	90.5	0.0	9.0	0.0	0.0	0.5	0.0
	4005	59	82.5	0.5	16.0	1.0	0.0	0.0	0.0
	Mean	129	89.4	1.0	9.2	0.2	0.0	0.2	0.0
Female	S.D.	46	4.6	1.2	4.3	0.4	0.0	0.3	0.0
	4101	84	91.5	0.5	7.5	0.0	0.0	0.5	0.0
	4102	88	86.0	0.0	12.5	0.5	0.0	1.0	0.0
	4103	80	87.5	0.0	10.0	1.5	0.0	1.0	0.0
	4104	49	89.0	0.0	10.5	0.0	0.0	0.5	0.0
	4105	85	88.0	0.5	10.0	0.5	0.0	1.0	0.0
	Mean	77	88.4	0.2	10.1	0.5	0.0	0.8	0.0
	S.D.	16	2.0	0.3	1.8	0.6	0.0	0.3	0.0

Appendix 139

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual hematology (Recovery)

Dose (mg/kg) : 0

Sex	Animal number	RBC ×10 ⁹ /μL	Hb g/dL	Ht %	MCV fL	MCH pg	MCHC %	Reticu- loocyte %	Plate- let ×10 ⁹ /μL	PT s	APTT s	Fibri- nogen mg/dL
Male	1006	823	15.0	46	55.3	18.2	32.9	1.7	92.9	14.3	20.3	206
	1007	823	15.2	46	55.9	18.5	33.1	1.2	102.8	15.0	20.5	235
	1008	822	15.5	46	56.3	18.8	33.4	1.5	88.4	14.0	18.4	272
	1009	823	16.0	47	56.9	19.4	34.2	2.0	102.4	13.3	20.6	273
	1010	759	14.8	44	58.0	19.5	33.7	2.4	88.5	12.6	19.5	249
	Mean	810	15.3	46	56.5	18.9	33.5	1.8	95.0	13.8	19.9	247
	S.D.	29	0.5	1	1.0	0.6	0.5	0.5	7.2	0.9	0.9	28
Female	1106	783	14.6	44	56.1	18.6	33.3	1.6	112.6	11.5	14.7	204
	1107	798	16.3	48	60.0	20.4	34.0	1.3	102.2	11.7	14.1	246
	1108	777	15.3	45	58.1	19.7	33.8	1.2	101.9	11.6	13.5	207
	1109	841	16.3	47	56.4	19.3	34.3	1.8	94.0	11.1	17.3	195
	1110	758	15.0	45	58.9	19.8	33.6	2.0	93.5	11.0	14.1	191
	Mean	791	15.5	46	57.9	19.6	33.8	1.6	100.8	11.4	14.7	209
	S.D.	31	0.8	2	1.7	0.7	0.4	0.3	7.8	0.3	1.5	22

Appendix 140

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual hematology (Recovery)

Dose (mg/kg) : 0

Sex	Animal number	WBC X10 ³ /μL	Differential leukocyte counts (%)						
			Lymph.	Stab	Seg.	Eosino.	Baso.	Mono.	Others
Male	1006	72	89.5	2.0	8.5	0.0	0.0	0.0	0.0
	1007	85	71.0	2.0	26.0	0.5	0.0	0.5	0.0
	1008	62	86.5	0.5	12.0	1.0	0.0	0.0	0.0
	1009	90	86.5	0.5	11.5	1.0	0.0	0.5	0.0
	1010	61	82.0	1.5	15.5	0.5	0.0	0.5	0.0
	Mean	74	83.1	1.3	14.7	0.6	0.0	0.3	0.0
Female	S.D.	13	7.3	0.8	6.8	0.4	0.0	0.3	0.0
	1106	88	89.5	0.5	8.0	1.5	0.0	0.5	0.0
	1107	79	76.5	0.0	21.0	2.5	0.0	0.0	0.0
	1108	53	89.0	1.5	7.5	1.5	0.0	0.5	0.0
	1109	74	92.5	1.5	5.5	0.5	0.0	0.0	0.0
	1110	61	86.5	1.0	11.0	1.0	0.0	0.5	0.0
	Mean	71	86.8	0.9	10.6	1.4	0.0	0.3	0.0
	S.D.	14	6.1	0.7	6.1	0.7	0.0	0.3	0.0

Appendix 141

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual hematology (Recovery)

Dose (mg/kg) : 1000

Sex	Animal number	RBC X10 ⁶ /μL	Hb g/dL	Ht %	MCV fL	MCH pg	MCHC %	Reticu- loocyte %	Plate- let X10 ³ /μL	PT s	APTT s	Fibri- nogen mg/dL
Male	4006	783	14.9	45	57.5	19.0	33.1	1.8	106.9	12.8	16.8	288
	4007	782	16.0	47	59.8	20.4	34.1	1.9	88.5	12.4	17.5	223
	4008	785	15.2	45	57.0	19.3	33.9	1.4	103.0	12.3	15.8	252
	4009	761	14.2	42	55.4	18.6	33.6	1.9	126.4	13.6	20.5	257
	4010	818	15.7	46	56.6	19.2	33.9	1.7	105.5	13.7	21.3	280
	Mean	786	15.2	45	57.3	19.3	33.7	1.7	106.1	13.0	18.4	260
	S.D.	20	0.7	2	1.6	0.7	0.4	0.2	13.5	0.7	2.4	26
Female	4106	791	15.2	45	57.1	19.2	33.7	2.2	109.9	12.2	15.0	189
	4107	770	15.0	44	57.5	19.5	34.0	1.4	99.5	11.1	15.4	192
	4108	817	16.1	48	59.3	19.7	33.2	1.4	96.0	11.5	15.7	199
	4109	776	15.6	46	59.4	20.1	33.8	1.9	110.5	11.0	16.6	211
	4110	834	15.7	47	55.9	18.8	33.6	1.9	104.3	11.7	15.5	208
	Mean	798	15.5	46	57.8	19.5	33.7	1.8	104.0	11.5	15.6	200
	S.D.	27	0.4	2	1.5	0.5	0.3	0.4	6.4	0.5	0.6	10

Appendix 142

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual hematology (Recovery)

Dose (mg/kg) : 1000

Sex	Animal number	WBC $\times 10^3/\mu\text{L}$	Differential leukocyte counts (%)						
			Lymph.	Stab	Seg.	Eosino.	Baso.	Mono.	Others
Male	4006	74	88.0	0.5	10.5	1.0	0.0	0.0	0.0
	4007	92	83.5	0.0	15.5	1.0	0.0	0.0	0.0
	4008	94	81.0	0.0	18.5	0.5	0.0	0.0	0.0
	4009	115	79.0	1.0	20.0	0.0	0.0	0.0	0.0
	4010	108	85.0	0.0	14.0	0.5	0.0	0.5	0.0
	Mean	97	83.3	0.3	15.7	0.6	0.0	0.1	0.0
	S.D.	16	3.5	0.4	3.8	0.4	0.0	0.2	0.0
Female	4106	71	98.5	0.5	1.0	0.0	0.0	0.0	0.0
	4107	93	97.0	0.0	2.0	1.0	0.0	0.0	0.0
	4108	61	88.0	0.5	9.5	1.5	0.0	0.5	0.0
	4109	90	91.5	1.0	5.0	2.5	0.0	0.0	0.0
	4110	121	92.0	1.0	6.5	0.5	0.0	0.0	0.0
	Mean	87	93.4	0.6	4.8	1.1	0.0	0.1	0.0
	S.D.	23	4.3	0.4	3.4	1.0	0.0	0.2	0.0

Appendix 143

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual blood chemistry (4 weeks)

Dose (mg/kg) : 0

Sex	Animal number	GOT (ASAT) IU/L	GPT (ALAT) IU/L	LDH IU/L	AlP IU/L	γ -GTP IU/L	TP g/dL	Albumin g/dL	A/G	T.cho mg/dL	TG mg/dL	PL mg/dL
Male	1001	36	29	119	259	1.3	5.8	3.7	1.76	61	67	104
	1002	54	30	27	394	1.5	5.5	3.8	2.24	56	50	109
	1003	49	25	35	370	1.8	6.0	3.8	1.73	47	43	85
	1004	61	33	43	355	1.9	6.0	3.8	1.73	57	42	99
	1005	47	28	36	263	1.7	5.5	3.6	1.89	56	42	84
	Mean	49	29	52	328	1.6	5.8	3.7	1.87	55	49	96
Female	S.D.	9	3	38	63	0.2	0.3	0.1	0.22	5	11	11
	1101	89	29	61	239	2.2	5.9	3.9	1.95	51	25	86
	1102	60	29	20	222	1.9	6.4	3.9	1.56	45	22	86
	1103	53	44	29	208	1.9	6.0	3.9	1.86	49	21	78
	1104	64	23	22	149	2.2	6.4	3.9	1.56	37	20	70
	1105	59	18	24	187	2.3	6.3	3.9	1.63	66	25	117
	Mean	65	29	31	201	2.1	6.2	3.9	1.71	50	23	87
	S.D.	14	10	17	35	0.2	0.2	0.0	0.18	11	2	18

Appendix 144

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual blood chemistry (4 weeks)

Dose (mg/kg) : 0

Sex	Animal number	T.bili- rubin mg/dL	Glucose mg/dL	BUN mg/dL	Crea- tinine mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL
Male	1001	0.12	186	8	0.56	144	4.4	110	9.9	8.6
	1002	0.11	145	8	0.58	144	4.6	110	9.8	8.6
	1003	0.10	151	8	0.58	142	4.8	109	9.5	8.5
	1004	0.11	120	8	0.56	144	4.8	110	10.0	8.8
	1005	0.10	152	9	0.52	143	4.8	109	9.5	8.5
	Mean	0.11	151	8	0.56	143	4.7	110	9.7	8.6
	S.D.	0.01	24	0	0.02	1	0.2	1	0.2	0.1
Female	1101	0.12	153	10	0.68	143	4.8	112	9.4	6.9
	1102	0.08	157	9	0.55	142	4.7	110	9.4	6.3
	1103	0.09	160	11	0.57	144	4.8	113	9.4	6.0
	1104	0.08	126	10	0.58	141	4.8	110	9.5	7.2
	1105	0.10	132	11	0.64	140	4.8	109	9.5	7.5
	Mean	0.09	146	10	0.60	142	4.8	111	9.4	6.8
	S.D.	0.02	16	1	0.05	2	0.0	2	0.1	0.6

Appendix 145

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual blood chemistry (4 weeks)

Dose (mg/kg) : 100

Sex	Animal number	GOT (ASAT) IU/L	GPT (ALAT) IU/L	LDH IU/L	AlP IU/L	γ -GTP IU/L	TP g/dL	Albumin g/dL	A/G	T.cho mg/dL	TG mg/dL	PL mg/dL
Male	2001	47	29	90	284	1.3	5.9	3.6	1.57	44	42	82
	2002	44	26	38	344	1.5	5.9	3.7	1.68	39	48	77
	2003	48	26	42	465	1.5	6.3	3.9	1.63	53	70	107
	2004	62	31	25	287	1.8	5.6	3.9	2.29	41	39	82
	2005	43	27	29	248	2.0	6.5	4.0	1.60	54	39	88
	Mean	49	28	45	326	1.6	6.0	3.8	1.75	46	48	87
Female	S.D.	8	2	26	85	0.3	0.4	0.2	0.30	7	13	12
	2101	41	25	36	178	1.8	5.6	3.8	2.11	63	38	114
	2102	53	26	25	257	2.0	5.8	3.8	1.90	58	38	117
	2103	53	26	32	195	1.8	5.7	3.8	2.00	55	25	91
	2104	48	26	26	140	1.7	6.7	4.1	1.58	58	26	105
	2105	52	27	17	173	2.3	6.2	4.0	1.82	55	22	91
	Mean	49	26	27	189	1.9	6.0	3.9	1.88	58	30	104
	S.D.	5	1	7	43	0.2	0.5	0.1	0.20	3	8	12

Appendix 146

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual blood chemistry (4 weeks)

Dose (mg/kg) : 100

Sex	Animal number	T.bili- rubin mg/dL	Glucose mg/dL	BUN mg/dL	Crea- tinine mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL
Male	2001	0.11	170	7	0.63	144	4.7	110	9.5	9.1
	2002	0.09	154	7	0.56	144	4.6	111	9.4	8.2
	2003	0.13	153	10	0.56	144	4.5	108	9.9	8.5
	2004	0.12	146	8	0.55	144	4.5	112	9.7	8.3
	2005	0.11	140	9	0.53	142	4.9	109	10.1	8.8
	Mean	0.11	153	8	0.57	144	4.6	110	9.7	8.6
Female	S.D.	0.01	11	1	0.04	1	0.2	2	0.3	0.4
	2101	0.10	184	12	0.74	142	4.4	111	9.4	7.5
	2102	0.11	154	9	0.56	142	4.2	111	9.2	6.3
	2103	0.09	145	11	0.59	140	5.4	111	9.5	6.6
	2104	0.09	157	12	0.61	141	4.7	111	9.7	7.4
	2105	0.09	158	14	0.61	142	4.8	110	9.7	6.5
	Mean	0.10	160	12	0.62	141	4.7	111	9.5	6.9
	S.D.	0.01	15	2	0.07	1	0.5	0	0.2	0.6

Appendix 147

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual blood chemistry (4 weeks)

Dose (mg/kg) : 300

Sex	Animal number	GOT (ASAT) IU/L	GPT (ALAT) IU/L	LDH IU/L	ALP IU/L	γ -GTP IU/L	TP g/dL	Albumin g/dL	A/G	T.cho mg/dL	TG mg/dL	PL mg/dL
Male	3001	42	32	59	373	1.3	5.9	3.8	1.81	43	62	87
	3002	44	25	40	309	1.6	6.0	3.8	1.73	55	129	105
	3003	47	30	32	455	1.6	5.8	3.8	1.90	69	46	111
	3004	57	29	65	365	1.2	5.5	3.7	2.06	64	59	105
	3005	47	29	30	329	1.8	5.5	3.7	2.06	48	39	86
	Mean	47	29	45	366	1.5	5.7	3.8	1.91	56	67	99
	S.D.	6	3	16	56	0.2	0.2	0.1	0.15	11	36	11
Female	3101	56	24	27	249	2.2	6.0	3.9	1.86	63	30	113
	3102	52	23	35	134	1.9	6.1	3.9	1.77	50	29	103
	3103	56	34	19	160	1.8	6.4	3.9	1.56	50	23	99
	3104	46	35	22	143	1.6	6.4	4.0	1.67	66	19	100
	3105	59	31	25	185	2.2	6.1	3.9	1.77	64	25	111
	Mean	54	29	26	174	1.9	6.2	3.9	1.73	59	25	105
	S.D.	5	6	6	46	0.3	0.2	0.0	0.11	8	4	6

Appendix 148

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual blood chemistry (4 weeks)

Dose (mg/kg) : 300

Sex	Animal number	T.bili- rubin mg/dL	Glucose mg/dL	BUN mg/dL	Crea- tinine mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL
Male	3001	0.11	155	7	0.56	142	4.2	107	9.4	7.4
	3002	0.13	145	8	0.54	141	5.0	108	9.6	8.3
	3003	0.12	123	7	0.47	143	4.8	109	9.7	8.0
	3004	0.12	144	8	0.54	143	5.0	108	9.5	8.8
	3005	0.10	135	9	0.55	144	4.7	110	9.3	8.9
	Mean	0.12	140	8	0.53	143	4.7	108	9.5	8.3
	S.D.	0.01	12	1	0.04	1	0.3	1	0.2	0.6
Female	3101	0.10	159	9	0.60	141	4.9	110	9.0	6.5
	3102	0.10	138	8	0.53	141	5.0	111	9.3	6.1
	3103	0.09	143	10	0.53	143	5.0	112	9.6	7.1
	3104	0.10	130	10	0.57	141	5.1	109	9.8	7.1
	3105	0.09	144	11	0.60	142	5.1	111	9.5	7.5
	Mean	0.10	143	10	0.57	142	5.0	111	9.4	6.9
	S.D.	0.01	11	1	0.04	1	0.1	1	0.3	0.6

Appendix 149

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual blood chemistry (4 weeks)

Dose (mg/kg) : 1000

Sex	Animal number	GOT (ASAT) IU/L	GPT (ALAT) IU/L	LDH IU/L	AlP IU/L	γ -GTP IU/L	TP g/dL	Albumin g/dL	A/G	T.cho mg/dL	TG mg/dL	PL mg/dL
Male	4001	52	29	55	398	1.5	6.0	3.8	1.73	51	60	95
	4002	47	31	42	408	1.7	5.8	3.8	1.90	47	85	97
	4003	50	27	30	477	2.0	5.7	3.8	2.00	59	40	90
	4004	47	30	107	329	1.7	5.8	3.8	1.90	72	43	116
	4005	65	32	32	403	2.1	5.4	3.6	2.00	60	32	93
	Mean	52	30	53	403	1.8	5.7	3.8	1.91	58	52	98
	S.D.	7	2	32	53	0.2	0.2	0.1	0.11	10	21	10
Female	4101	45	24	24	200	1.9	6.1	3.8	1.65	57	28	94
	4102	44	26	21	219	2.3	6.5	4.2	1.83	76	49	142
	4103	53	26	29	168	1.3	5.8	3.6	1.64	70	25	113
	4104	58	28	24	182	2.0	6.5	4.1	1.71	53	19	93
	4105	48	25	22	179	2.0	6.3	4.1	1.86	56	27	111
	Mean	50	26	24	190	1.9	6.2	4.0	1.74	62	30	111
	S.D.	6	1	3	20	0.4	0.3	0.3	0.10	10	11	20

Appendix 150

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual blood chemistry (4 weeks)

Dose (mg/kg) : 1000

Sex	Animal number	T.bili- rubin mg/dL	Glucose mg/dL	BUN mg/dL	Crea- tinine mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL
Male	4001	0.11	164	8	0.58	142	4.7	108	9.7	9.1
	4002	0.12	164	10	0.63	142	4.9	108	10.0	7.6
	4003	0.10	140	9	0.55	143	5.1	110	9.7	8.8
	4004	0.10	133	9	0.53	144	4.8	111	9.5	8.6
	4005	0.10	126	8	0.47	144	4.6	111	9.3	9.1
	Mean	0.11	145	9	0.55	143	4.8	110	9.6	8.6
	S.D.	0.01	18	1	0.06	1	0.2	2	0.3	0.6
Female	4101	0.10	147	11	0.63	143	4.7	110	9.4	5.9
	4102	0.12	132	15	0.63	142	5.1	110	9.8	7.6
	4103	0.07	150	11	0.55	140	4.7	111	9.4	7.2
	4104	0.08	132	9	0.57	141	4.8	111	9.5	6.7
	4105	0.09	141	12	0.57	140	4.6	110	9.5	7.0
	Mean	0.09	140	12	0.59	141	4.8	110	9.5	6.9
	S.D.	0.02	8	2	0.04	1	0.2	1	0.2	0.6

Appendix 151

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual blood chemistry (Recovery)

Dose (mg/kg) : 0

Sex	Animal number	GOT (ASAT) IU/L	GPT (ALAT) IU/L	LDH IU/L	ALP IU/L	γ -GTP IU/L	TP g/dL	Albumin g/dL	A/G	T.cho mg/dL	TG mg/dL	PL mg/dL
Male	1006	73	33	23	254	1.5	5.9	3.6	1.57	57	26	89
	1007	66	32	26	245	1.8	5.7	3.7	1.85	55	27	96
	1008	65	31	24	284	2.0	6.1	3.7	1.54	56	31	90
	1009	59	27	37	221	1.9	6.0	3.7	1.61	69	47	99
	1010	66	35	24	255	1.8	6.0	3.9	1.86	69	27	102
	Mean	66	32	27	252	1.8	5.9	3.7	1.69	61	32	95
	S.D.	5	3	6	23	0.2	0.2	0.1	0.16	7	9	6
Female	1106	52	26	15	116	2.0	5.9	4.0	2.11	67	28	116
	1107	51	25	21	103	1.9	6.1	3.8	1.65	87	35	133
	1108	56	29	19	111	2.4	6.7	4.0	1.48	86	31	134
	1109	55	16	19	146	0.9	6.5	4.1	1.71	81	28	117
	1110	50	26	25	97	1.6	6.5	4.1	1.71	74	21	116
	Mean	53	24	20	115	1.8	6.3	4.0	1.73	79	29	123
	S.D.	3	5	4	19	0.6	0.3	0.1	0.23	8	5	9

Appendix 152

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual blood chemistry (Recovery)

Dose (mg/kg) : 0

Sex	Animal number	T.bili- rubin mg/dL	Glucose mg/dL	BUN mg/dL	Crea- tinine mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL
Male	1006	0.10	109	10	0.52	145	4.8	111	9.3	7.8
	1007	0.10	147	12	0.56	143	4.4	110	9.6	7.8
	1008	0.11	117	11	0.57	140	4.4	107	9.5	7.8
	1009	0.09	122	12	0.56	141	4.7	109	9.5	8.1
	1010	0.09	113	13	0.58	142	4.5	110	9.5	8.7
	Mean	0.10	122	12	0.56	142	4.6	109	9.5	8.0
	S.D.	0.01	15	1	0.02	2	0.2	2	0.1	0.4
Female	1106	0.09	126	14	0.57	141	4.6	111	9.7	8.9
	1107	0.12	143	11	0.55	139	5.3	110	9.6	7.3
	1108	0.11	114	16	0.60	141	4.5	112	10.1	8.4
	1109	0.08	130	14	0.65	139	4.8	110	9.6	7.5
	1110	0.08	126	16	0.59	139	5.5	109	10.0	7.5
	Mean	0.10	128	14	0.59	140	4.9	110	9.8	7.9
	S.D.	0.02	10	2	0.04	1	0.4	1	0.2	0.7

Appendix 153

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual blood chemistry (Recovery)

Dose (mg/kg) : 1000

Sex	Animal number	GOT (ASAT) IU/L	GPT (ALAT) IU/L	LDH IU/L	ALP IU/L	γ -GTP IU/L	TP g/dL	Albumin g/dL	A/G	T.cho mg/dL	TG mg/dL	PL mg/dL
Male	4006	57	30	33	244	1.6	6.3	3.7	1.42	95	27	120
	4007	69	33	40	259	1.8	6.3	3.8	1.52	80	38	117
	4008	74	36	37	181	2.1	5.7	3.5	1.59	61	22	92
	4009	61	32	33	230	1.8	6.0	3.7	1.61	69	35	106
	4010	55	36	28	311	2.0	6.1	3.8	1.65	56	44	94
	Mean	63	33	34	245	1.9	6.1	3.7	1.56	72	33	106
	S.D.	8	3	5	47	0.2	0.2	0.1	0.09	16	9	13
Female	4106	51	31	23	110	1.8	6.4	4.0	1.67	68	18	113
	4107	54	34	30	104	1.7	7.1	4.4	1.63	93	42	165
	4108	56	29	21	110	1.7	6.7	4.1	1.58	78	31	124
	4109	58	23	20	111	2.3	6.9	4.2	1.56	104	36	166
	4110	55	19	16	157	1.8	6.0	3.9	1.86	66	32	115
	Mean	55	27	22	118	1.9	6.6	4.1	1.66	82	32	137
	S.D.	3	6	5	22	0.3	0.4	0.2	0.12	16	9	27

Appendix 154

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual blood chemistry (Recovery)

Dose (mg/kg) : 1000

Sex	Animal number	T.bili- rubin mg/dL	Glucose mg/dL	BUN mg/dL	Crea- tinine mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL
Male	4006	0.11	132	14	0.59	141	4.5	106	9.6	8.1
	4007	0.11	147	14	0.61	143	4.7	108	10.1	8.9
	4008	0.10	119	13	0.58	143	4.5	110	9.4	8.4
	4009	0.11	135	12	0.61	142	4.3	109	9.3	8.5
	4010	0.11	133	13	0.61	141	4.9	109	9.3	7.8
	Mean	0.11	133	13	0.60	142	4.6	108	9.5	8.3
	S.D.	0.00	10	1	0.01	1	0.2	2	0.3	0.4
Female	4106	0.09	119	15	0.59	140	5.4	110	9.2	8.7
	4107	0.16	134	13	0.56	138	4.9	111	10.0	7.0
	4108	0.10	120	13	0.60	141	4.7	112	9.8	7.7
	4109	0.11	139	13	0.62	139	5.6	109	9.9	7.3
	4110	0.10	144	12	0.57	141	4.6	111	9.9	7.1
	Mean	0.11	131	13	0.59	140	5.0	111	9.8	7.6
	S.D.	0.03	11	1	0.02	1	0.4	1	0.3	0.7

Appendix 155

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (4 weeks)

Sex : Male

Dose (mg/kg) : 0

	Animal number	Body weight	Brain	Thymus	Heart	Lung	Liver	Spleen
		g	g(g/100g BW)	mg(mg/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)
Absolute	1001	393	1.76	340	1.25	1.26	12.99	0.54
	1002	369	2.11	509	1.21	1.35	11.09	0.67
	1003	377	1.99	371	1.20	1.27	11.94	0.62
	1004	382	2.26	337	1.14	1.41	11.46	0.73
	1005	390	2.12	461	1.34	1.40	11.29	0.65
	Mean	382	2.05	404	1.23	1.34	11.75	0.64
	S.D.	10	0.19	77	0.07	0.07	0.76	0.07
Relative	1001		0.45	87	0.32	0.32	3.31	0.14
	1002		0.57	138	0.33	0.37	3.01	0.18
	1003		0.53	98	0.32	0.34	3.17	0.16
	1004		0.59	88	0.30	0.37	3.00	0.19
	1005		0.54	118	0.34	0.36	2.89	0.17
	Mean		0.54	106	0.32	0.35	3.08	0.17
	S.D.		0.05	22	0.01	0.02	0.16	0.02

Appendix 158

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (4 weeks)

Sex : Male

Dose (mg/kg) : 0

	Animal number	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)
Absolute	1001	1.30	1.37	2.67	26	29	55	1.51	1.44	2.95
	1002	1.27	1.37	2.64	21	23	44	1.42	1.47	2.89
	1003	1.29	1.26	2.55	24	25	49	1.46	1.39	2.85
	1004	1.32	1.36	2.68	28	32	60	1.60	1.63	3.23
	1005	1.41	1.37	2.78	31	36	67	1.49	1.47	2.96
	Mean	1.32	1.35	2.66	26	29	55	1.50	1.48	2.98
	S.D.	0.05	0.05	0.08	4	5	9	0.07	0.09	0.15
Relative	1001	0.33	0.35	0.68	7	7	14	0.38	0.37	0.75
	1002	0.34	0.37	0.72	6	6	12	0.38	0.40	0.78
	1003	0.34	0.33	0.68	6	7	13	0.39	0.37	0.76
	1004	0.35	0.36	0.70	7	8	16	0.42	0.43	0.85
	1005	0.36	0.35	0.71	8	9	17	0.38	0.38	0.76
	Mean	0.34	0.35	0.70	7	7	14	0.39	0.39	0.78
	S.D.	0.01	0.01	0.02	1	1	2	0.02	0.03	0.04

Appendix 157

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (4 weeks)

Sex : Male

Dose (mg/kg) : 0

	Animal number	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)
Absolute	1001	352	327	679
	1002	432	445	877
	1003	421	368	789
	1004	525	498	1023
	1005	465	451	916
	Mean	439	418	857
	S.D.	63	69	130
Relative	1001	90	83	173
	1002	117	121	238
	1003	112	98	209
	1004	137	130	268
	1005	119	116	235
	Mean	115	110	225
	S.D.	17	19	36

Appendix 158

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (4 weeks)

Sex : Male

Dose (mg/kg) : 100

	Animal number	Body weight	Brain	Thymus	Heart	Lung	Liver	Spleen
		g	g(g/100g BW)	mg(mg/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)
Absolute	2001	376	2.01	404	1.07	1.25	11.13	0.75
	2002	374	2.01	404	1.12	1.24	11.28	0.64
	2003	392	1.98	364	1.33	1.47	13.56	0.70
	2004	349	1.90	718	1.14	1.18	10.55	0.66
	2005	395	2.07	378	1.23	1.25	13.78	0.63
	Mean	377	1.99	454	1.18	1.28	12.06	0.68
Relative	S.D.	18	0.06	149	0.10	0.11	1.50	0.05
	2001		0.53	107	0.28	0.33	2.96	0.20
	2002		0.54	108	0.30	0.33	3.02	0.17
	2003		0.51	93	0.34	0.38	3.46	0.18
	2004		0.54	206	0.33	0.34	3.02	0.19
	2005		0.52	96	0.31	0.32	3.49	0.16
	Mean		0.53	122	0.31	0.34	3.19	0.18
	S.D.		0.01	47	0.02	0.02	0.26	0.02

Appendix 159

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (4 weeks)

Sex : Male

Dose (mg/kg) : 100

	Animal number	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)
Absolute	2001	1.13	1.16	2.29	28	32	60	1.57	1.55	3.12
	2002	1.25	1.25	2.50	24	25	49	1.49	1.44	2.93
	2003	1.40	1.42	2.82	29	31	60	1.66	1.62	3.28
	2004	1.15	1.27	2.42	25	27	52	0.38	0.38	0.76
	2005	1.38	1.43	2.81	28	31	59	1.13	1.08	2.21
	Mean	1.26	1.31	2.57	27	29	56	1.25	1.21	2.46
	S.D.	0.13	0.12	0.24	2	3	5	0.52	0.51	1.03
Relative	2001	0.30	0.31	0.61	7	9	16	0.42	0.41	0.83
	2002	0.33	0.33	0.67	6	7	13	0.40	0.39	0.78
	2003	0.36	0.36	0.72	7	8	15	0.42	0.41	0.84
	2004	0.33	0.36	0.69	7	8	15	0.11	0.11	0.22
	2005	0.35	0.36	0.71	7	8	15	0.29	0.27	0.56
	Mean	0.33	0.34	0.68	7	8	15	0.33	0.32	0.65
	S.D.	0.02	0.02	0.04	0	1	1	0.13	0.13	0.26

Appendix 160

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (4 weeks)

Sex : Male

Dose (mg/kg) : 100

	Animal number	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)
Absolute	2001	465	429	894
	2002	412	431	843
	2003	452	450	902
	2004	186	187	373
	2005	319	307	626
	Mean	367	361	728
	S.D.	116	113	228
Relative	2001	124	114	238
	2002	110	115	225
	2003	115	115	230
	2004	53	54	107
	2005	81	78	158
	Mean	97	95	192
	S.D.	29	28	57

Appendix 161

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (4 weeks)

Sex : Male

Dose (mg/kg) : 300

	Animal number	Body weight	Brain	Thymus	Heart	Lung	Liver	Spleen
		g	g(g/100g BW)	mg(mg/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)
Absolute	3001	348	2.00	313	1.11	1.20	10.50	0.68
	3002	360	1.99	381	1.14	1.21	12.76	0.54
	3003	377	2.02	375	1.25	1.29	12.37	0.65
	3004	361	1.96	529	1.16	1.29	10.10	0.78
	3005	337	1.98	309	1.19	1.25	9.35	0.64
	Mean	357	1.99	381	1.17	1.25	11.02	0.66
	S.D.	15	0.02	89	0.05	0.04	1.48	0.09
Relative	3001		0.57	90	0.32	0.34	3.02	0.20
	3002		0.55	106	0.32	0.34	3.54	0.15
	3003		0.54	99	0.33	0.34	3.28	0.17
	3004		0.54	147	0.32	0.36	2.80	0.22
	3005		0.59	92	0.35	0.37	2.77	0.19
	Mean		0.56	107	0.33	0.35	3.08	0.19
	S.D.		0.02	23	0.01	0.01	0.33	0.03

Appendix 162

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (4 weeks)

Sex : Male

Dose (mg/kg) : 300

	Animal number	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)
Absolute	3001	1.26	1.35	2.61	25	27	52	1.44	1.48	2.92
	3002	1.30	1.37	2.67	23	23	46	1.58	1.57	3.15
	3003	1.43	1.55	2.98	21	19	40	1.61	1.56	3.17
	3004	1.27	1.43	2.70	29	31	60	1.15	1.12	2.27
	3005	1.10	1.04	2.14	22	24	46	1.59	1.40	3.05
	Mean	1.27	1.35	2.62	24	25	49	1.47	1.44	2.91
	S.D.	0.12	0.19	0.30	3	4	8	0.19	0.18	0.37
Relative	3001	0.36	0.39	0.75	7	8	15	0.41	0.43	0.84
	3002	0.36	0.38	0.74	6	6	13	0.44	0.44	0.88
	3003	0.38	0.41	0.79	6	5	11	0.43	0.41	0.84
	3004	0.35	0.40	0.75	8	9	17	0.32	0.31	0.63
	3005	0.33	0.31	0.64	7	7	14	0.47	0.43	0.91
	Mean	0.36	0.38	0.73	7	7	14	0.41	0.40	0.82
	S.D.	0.02	0.04	0.06	1	2	2	0.06	0.05	0.11

Appendix 163

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (4 weeks)

Sex : Male

Dose (mg/kg) : 300

	Animal number	Epididymis (R)	Epididymis (L)	Epididymis (R+L)
		mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)
Absolute	3001	404	421	825
	3002	402	414	816
	3003	437	440	877
	3004	331	321	652
	3005	397	389	786
	Mean	394	397	791
	S.D.	39	46	84
Relative	3001	116	121	237
	3002	112	115	227
	3003	116	117	233
	3004	92	89	181
	3005	118	115	233
	Mean	111	111	222
	S.D.	11	13	23

Appendix 164

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (4 weeks)

Sex : Male

Dose (mg/kg) : 1000

	Animal number	Body weight	Brain	Thymus	Heart	Lung	Liver	Spleen
		g	g(g/100g BW)	mg(mg/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)
Absolute	4001	376	2.05	709	1.20	1.37	11.92	0.69
	4002	373	2.01	527	1.21	1.24	12.20	0.65
	4003	373	1.90	460	1.24	1.33	11.06	0.79
	4004	366	1.93	339	1.23	1.32	11.09	0.68
	4005	319	2.12	260	1.17	1.21	8.34	0.54
	Mean	361	2.00	459	1.21	1.29	10.92	0.67
Relative	S.D.	24	0.09	174	0.03	0.07	1.53	0.09
	4001		0.55	189	0.32	0.36	3.17	0.18
	4002		0.54	141	0.32	0.33	3.27	0.17
	4003		0.51	123	0.33	0.36	2.97	0.21
	4004		0.53	93	0.34	0.36	3.03	0.19
	4005		0.66	82	0.37	0.38	2.61	0.17
	Mean		0.56	126	0.34	0.36	3.01	0.18
	S.D.		0.06	43	0.02	0.02	0.25	0.02

Appendix 165

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (4 weeks)

Sex : Male

Dose (mg/kg) : 1000

	Animal number	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)
Absolute	4001	1.32	1.32	2.64	23	24	47	1.47	1.49	2.96
	4002	1.22	1.31	2.53	30	31	61	1.60	1.51	3.11
	4003	1.32	1.37	2.69	22	23	45	1.48	1.44	2.92
	4004	1.36	1.45	2.81	30	35	65	1.70	1.66	3.36
	4005	1.37	1.33	2.70	20	22	42	1.63	1.63	3.26
	Mean	1.32	1.36	2.67	25	27	52	1.58	1.55	3.12
	S.D.	0.06	0.06	0.10	5	6	10	0.10	0.09	0.19
Relative	4001	0.35	0.35	0.70	6	6	13	0.39	0.40	0.79
	4002	0.33	0.35	0.68	8	8	16	0.43	0.40	0.83
	4003	0.35	0.37	0.72	6	6	12	0.40	0.39	0.78
	4004	0.37	0.40	0.77	8	10	18	0.46	0.45	0.92
	4005	0.43	0.42	0.85	6	7	13	0.51	0.51	1.02
	Mean	0.37	0.38	0.74	7	7	14	0.44	0.43	0.87
	S.D.	0.04	0.03	0.07	1	2	3	0.05	0.05	0.10

Appendix 166

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (4 weeks)

Sex : Male

Dose (mg/kg) : 1000

	Animal number	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)
Absolute	4001	395	375	770
	4002	402	397	799
	4003	413	407	820
	4004	485	478	963
	4005	481	455	936
	Mean	435	422	858
	S.D.	44	43	86
Relative	4001	105	100	205
	4002	108	106	214
	4003	111	109	220
	4004	133	131	263
	4005	151	143	293
	Mean	122	118	239
	S.D.	20	18	38

Appendix 167

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (4 weeks)

Sex : Female

Dose (mg/kg) : 0

	Animal number	Body weight	Brain	Thymus	Heart	Lung	Liver	Spleen
		g	g(g/100g BW)	mg(mg/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)
Absolute	1101	238	1.97	394	0.84	1.13	6.67	0.53
	1102	234	2.03	321	0.75	1.00	6.84	0.47
	1103	261	1.96	628	0.91	1.09	7.57	0.56
	1104	238	1.81	326	0.88	0.97	6.64	0.42
	1105	234	1.78	347	0.81	1.04	7.20	0.47
	Mean	241	1.91	403	0.84	1.05	6.98	0.49
	S.D.	11	0.11	129	0.06	0.07	0.40	0.06
Relative	1101		0.83	166	0.35	0.47	2.80	0.22
	1102		0.87	137	0.32	0.43	2.92	0.20
	1103		0.75	241	0.35	0.42	2.90	0.21
	1104		0.76	137	0.37	0.41	2.79	0.18
	1105		0.76	148	0.35	0.44	3.08	0.20
	Mean		0.79	166	0.35	0.43	2.90	0.20
	S.D.		0.05	44	0.02	0.02	0.12	0.01

Appendix 168

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (4 weeks)

Sex : Female

Dose (mg/kg) : 0

	Animal number	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)
Absolute	1101	0.88	0.85	1.73	33	33	66	34.1	38.3	72.4
	1102	0.82	0.83	1.65	33	35	68	35.4	44.5	79.9
	1103	0.86	0.95	1.81	38	38	76	39.3	34.2	73.5
	1104	0.74	0.75	1.49	33	33	66	43.6	56.9	100.5
	1105	0.85	0.81	1.66	35	35	70	53.4	49.1	102.5
	Mean	0.83	0.84	1.67	34	35	69	41.2	44.6	85.8
	S.D.	0.05	0.07	0.12	2	2	4	7.8	8.9	14.7
Relative	1101	0.37	0.36	0.73	14	14	28	14.3	16.1	30.4
	1102	0.35	0.35	0.71	14	15	29	15.1	19.0	34.1
	1103	0.33	0.36	0.69	15	15	29	15.1	13.1	28.2
	1104	0.31	0.32	0.63	14	14	28	18.3	23.9	42.2
	1105	0.36	0.35	0.71	15	15	30	22.8	21.0	43.8
	Mean	0.34	0.35	0.69	14	15	29	17.1	18.6	35.7
	S.D.	0.02	0.02	0.04	1	1	1	3.5	4.2	7.0

Appendix 169

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (4 weeks)

Sex : Female

Dose (mg/kg) : 0

	Animal number	Uterus	
		mg(mg/100g BW)	
Absolute	1101	409	
	1102	456	
	1103	634	
	1104	333	
	1105	499	
	Mean	466	
	S.D.	112	
Relative	1101	172	
	1102	195	
	1103	243	
	1104	140	
	1105	213	
	Mean	193	
	S.D.	39	

Appendix 170

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (4 weeks)

Sex : Female

Dose (mg/kg) : 100

	Animal number	Body weight	Brain	Thymus	Heart	Lung	Liver	Spleen
		g	g(g/100g BW)	mg(mg/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)
Absolute	2101	233	1.79	412	0.80	1.05	7.19	0.47
	2102	258	1.90	491	0.84	1.02	6.84	0.41
	2103	244	1.89	415	0.87	1.04	7.13	0.49
	2104	244	1.82	375	0.87	0.96	7.86	0.45
	2105	244	1.98	367	0.81	1.06	6.52	0.46
	Mean	245	1.88	412	0.84	1.03	7.11	0.46
Relative	S.D.	9	0.07	49	0.03	0.04	0.50	0.03
	2101		0.77	177	0.34	0.45	3.09	0.20
	2102		0.74	190	0.33	0.40	2.65	0.16
	2103		0.77	170	0.36	0.43	2.92	0.20
	2104		0.75	154	0.36	0.39	3.22	0.18
	2105		0.81	150	0.33	0.43	2.67	0.19
	Mean		0.77	168	0.34	0.42	2.91	0.19
	S.D.		0.03	16	0.02	0.02	0.25	0.02

Appendix 171

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (4 weeks)

Sex : Female

Dose (mg/kg) : 100

	Animal number	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)
Absolute	2101	0.81	0.85	1.66	27	28	55	42.4	38.7	81.1
	2102	0.94	0.90	1.84	32	33	65	39.5	43.4	82.9
	2103	0.98	0.96	1.94	30	32	62	49.0	40.2	89.2
	2104	0.81	0.84	1.65	33	36	69	40.4	34.1	74.5
	2105	0.85	0.87	1.72	34	36	70	45.0	33.4	78.4
	Mean	0.88	0.88	1.76	31	33	64	43.3	38.0	81.2
	S.D.	0.08	0.05	0.12	3	3	6	3.8	4.2	5.5
Relative	2101	0.35	0.36	0.71	12	12	24	18.2	16.6	34.8
	2102	0.36	0.35	0.71	12	13	25	15.3	16.8	32.1
	2103	0.40	0.39	0.80	12	13	25	20.1	16.5	36.6
	2104	0.33	0.34	0.68	14	15	28	16.6	14.0	30.5
	2105	0.35	0.36	0.70	14	15	29	18.4	13.7	32.1
	Mean	0.36	0.36	0.72	13	14	26	17.7	15.5	33.2
	S.D.	0.03	0.02	0.05	1	1	2	1.8	1.5	2.4

Appendix 172

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (4 weeks)

Sex : Female

Dose (mg/kg) : 100

	Animal number	Uterus	
		mg	(mg/100g BW)
Absolute	2101	478	
	2102	572	
	2103	669	
	2104	452	
	2105	477	
	Mean	530	
	S.D.	90	
Relative	2101	205	
	2102	222	
	2103	274	
	2104	185	
	2105	195	
	Mean	216	
	S.D.	35	

Appendix 173

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (4 weeks)

Sex : Female

Dose (mg/kg) : 300

	Animal number	Body weight	Brain	Thymus	Heart	Lung	Liver	Spleen
		g	g(g/100g BW)	mg(mg/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)
Absolute	3101	229	1.78	399	0.83	0.91	6.87	0.49
	3102	250	1.81	470	0.80	1.05	7.24	0.56
	3103	222	1.86	372	0.84	1.03	6.59	0.50
	3104	254	1.98	458	0.82	1.08	8.50	0.52
	3105	255	1.85	362	0.76	0.98	6.64	0.43
	Mean	242	1.86	412	0.81	1.01	7.17	0.50
	S.D.	15	0.08	49	0.03	0.07	0.79	0.05
Relative	3101		0.78	174	0.36	0.40	3.00	0.21
	3102		0.72	188	0.32	0.42	2.90	0.22
	3103		0.84	168	0.38	0.46	2.97	0.23
	3104		0.78	180	0.32	0.43	3.35	0.20
	3105		0.73	142	0.30	0.38	2.60	0.17
	Mean		0.77	170	0.34	0.42	2.96	0.21
	S.D.		0.05	18	0.03	0.03	0.27	0.02

Appendix 174

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (4 weeks)

Sex : Female

Dose (mg/kg) : 300

	Animal number	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)
Absolute	3101	0.82	0.83	1.65	34	38	72	45.1	48.2	93.3
	3102	0.97	0.96	1.93	31	32	63	37.7	42.3	80.0
	3103	0.86	0.86	1.72	35	39	74	40.6	32.4	73.0
	3104	0.84	0.92	1.76	31	29	60	27.7	34.3	62.0
	3105	0.84	0.91	1.75	31	35	66	36.1	41.5	77.6
	Mean	0.87	0.90	1.76	32	35	67	37.4	39.7	77.2
	S.D.	0.06	0.05	0.10	2	4	6	6.4	6.4	11.4
Relative	3101	0.36	0.36	0.72	15	17	31	19.7	21.0	40.7
	3102	0.39	0.38	0.77	12	13	25	15.1	16.9	32.0
	3103	0.39	0.39	0.77	16	18	33	18.3	14.6	32.9
	3104	0.33	0.36	0.69	12	11	24	10.9	13.5	24.4
	3105	0.33	0.36	0.69	12	14	26	14.2	16.3	30.4
	Mean	0.36	0.37	0.73	13	15	28	15.6	16.5	32.1
	S.D.	0.03	0.01	0.04	2	3	4	3.5	2.9	5.8

Appendix 175

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (4 weeks)

Sex : Female

Dose (mg/kg) : 300

		Uterus
	Animal number	mg(mg/100g BW)
Absolute	3101	450
	3102	562
	3103	549
	3104	410
	3105	340
	Mean	462
	S.D.	94
Relative	3101	197
	3102	225
	3103	247
	3104	161
	3105	133
	Mean	193
	S.D.	46

Appendix 176

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (4 weeks)

Sex : Female

Dose (mg/kg) : 1000

	Animal number	Body weight	Brain	Thymus	Heart	Lung	Liver	Spleen
		g	g(g/100g BW)	mg(mg/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)
Absolute	4101	235	1.91	431	0.80	1.05	6.54	0.51
	4102	245	1.92	427	0.77	1.02	7.09	0.59
	4103	237	1.86	301	0.79	1.13	7.67	0.55
	4104	232	2.00	416	0.78	1.01	6.64	0.47
	4105	220	1.67	444	0.70	0.98	6.00	0.48
	Mean	234	1.87	404	0.77	1.04	6.79	0.52
Relative	S.D.	9	0.12	58	0.04	0.06	0.63	0.05
	4101		0.81	183	0.34	0.45	2.78	0.22
	4102		0.78	174	0.31	0.42	2.89	0.24
	4103		0.78	127	0.33	0.48	3.24	0.23
	4104		0.86	179	0.34	0.44	2.86	0.20
	4105		0.76	202	0.32	0.45	2.73	0.22
	Mean		0.80	173	0.33	0.45	2.90	0.22
	S.D.		0.04	28	0.01	0.02	0.20	0.01

Appendix 177

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (4 weeks)

Sex : Female

Dose (mg/kg) : 1000

	Animal number	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)
Absolute	4101	0.80	0.76	1.56	32	35	67	37.3	47.1	84.4
	4102	0.82	0.82	1.64	32	33	65	34.4	43.9	78.3
	4103	0.93	0.91	1.84	28	28	56	38.5	47.1	85.6
	4104	0.91	0.90	1.81	31	32	63	43.4	36.6	80.0
	4105	0.82	0.80	1.62	31	32	63	36.7	38.7	75.4
	Mean	0.86	0.84	1.69	31	32	63	38.1	42.7	80.7
	S.D.	0.06	0.06	0.12	2	3	4	3.3	4.8	4.2
Relative	4101	0.34	0.32	0.66	14	15	29	15.9	20.0	35.9
	4102	0.33	0.33	0.67	13	13	27	14.0	17.9	32.0
	4103	0.39	0.38	0.78	12	12	24	16.2	19.9	36.1
	4104	0.39	0.39	0.78	13	14	27	18.7	15.8	34.5
	4105	0.37	0.36	0.74	14	15	29	16.7	17.6	34.3
	Mean	0.36	0.36	0.73	13	14	27	16.3	18.2	34.6
	S.D.	0.03	0.03	0.06	1	1	2	1.7	1.8	1.6

Appendix 178

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (4 weeks)

Sex : Female

Dose (mg/kg) : 1000

	Animal number	Uterus	
		mg(mg/100g BW)	
Absolute	4101	525	
	4102	420	
	4103	409	
	4104	388	
	4105	718	
	Mean	492	
	S.D.	137	
Relative	4101	223	
	4102	171	
	4103	173	
	4104	167	
	4105	326	
	Mean	212	
	S.D.	68	

Appendix 179

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (Recovery)

Sex : Male

Dose (mg/kg) : 0

	Animal number	Body weight	Brain	Thymus	Heart	Lung	Liver	Spleen
		g	g(g/100g BW)	mg(mg/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)
Absolute	1006	364	2.08	325	1.19	1.31	8.98	0.56
	1007	353	2.04	228	1.13	1.13	8.88	0.63
	1008	400	1.87	339	1.28	1.34	10.08	0.59
	1009	463	2.07	449	1.18	1.42	12.37	0.65
	1010	393	2.01	285	1.15	1.19	10.39	0.62
	Mean	395	2.01	325	1.19	1.28	10.14	0.61
	S.D.	43	0.09	82	0.06	0.12	1.41	0.04
Relative	1006		0.57	89	0.33	0.36	2.47	0.15
	1007		0.58	65	0.32	0.32	2.52	0.18
	1008		0.47	85	0.32	0.34	2.52	0.15
	1009		0.45	97	0.25	0.31	2.67	0.14
	1010		0.51	73	0.29	0.30	2.64	0.16
	Mean		0.52	82	0.30	0.33	2.56	0.16
	S.D.		0.06	13	0.03	0.02	0.09	0.02

Appendix 180

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (Recovery)

Sex : Male

Dose (mg/kg) : 0

	Animal number	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)
Absolute	1006	1.52	1.48	3.00	22	26	48	1.73	1.74	3.47
	1007	1.17	1.17	2.34	23	24	47	1.58	1.63	3.21
	1008	1.41	1.39	2.80	31	33	64	1.57	1.55	3.12
	1009	1.55	1.71	3.26	37	37	74	1.45	1.27	2.72
	1010	1.45	1.50	2.95	22	23	45	1.54	1.53	3.07
	Mean	1.42	1.45	2.87	27	29	56	1.57	1.54	3.12
	S.D.	0.15	0.20	0.34	7	6	13	0.10	0.17	0.27
Relative	1006	0.42	0.41	0.82	6	7	13	0.48	0.48	0.95
	1007	0.33	0.33	0.66	7	7	13	0.45	0.46	0.91
	1008	0.35	0.35	0.70	8	8	16	0.39	0.39	0.78
	1009	0.33	0.37	0.70	8	8	16	0.31	0.27	0.59
	1010	0.37	0.38	0.75	6	6	11	0.39	0.39	0.78
	Mean	0.36	0.37	0.73	7	7	14	0.40	0.40	0.80
	S.D.	0.04	0.03	0.06	1	1	2	0.07	0.08	0.14

Appendix 181

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (Recovery)

Sex : Male

Dose (mg/kg) : 0

	Animal number	Epididymis (R)	Epididymis (L)	Epididymis (R+L)
		mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)
Absolute	1006	578	564	1142
	1007	496	481	977
	1008	530	516	1046
	1009	494	445	939
	1010	488	497	985
	Mean	517	501	1018
	S.D.	38	44	79
Relative	1006	159	155	314
	1007	141	136	277
	1008	133	129	262
	1009	107	96	203
	1010	124	126	251
	Mean	133	128	261
	S.D.	19	21	40

Appendix 182

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (Recovery)

Sex : Male

Dose (mg/kg) : 1000

	Animal number	Body weight	Brain	Thymus	Heart	Lung	Liver	Spleen
		g	g(g/100g BW)	mg(mg/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)
Absolute	4006	433	2.16	351	1.30	1.39	11.24	0.75
	4007	439	2.08	282	1.34	1.24	12.02	0.57
	4008	378	1.93	344	1.13	1.25	9.84	0.63
	4009	388	2.15	465	1.18	1.26	10.56	0.64
	4010	389	1.94	355	1.23	1.17	9.99	0.72
	Mean	405	2.05	359	1.24	1.26	10.73	0.66
Relative	S.D.	28	0.11	66	0.09	0.08	0.91	0.07
	4006		0.50	81	0.30	0.32	2.60	0.17
	4007		0.47	64	0.31	0.28	2.74	0.13
	4008		0.51	91	0.30	0.33	2.60	0.17
	4009		0.55	120	0.30	0.32	2.72	0.16
	4010		0.50	91	0.32	0.30	2.57	0.19
	Mean		0.51	89	0.31	0.31	2.65	0.16
	S.D.		0.03	20	0.01	0.02	0.08	0.02

Appendix 183

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (Recovery)

Sex : Male

Dose (mg/kg) : 1000

	Animal number	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)
Absolute	4006	1.45	1.41	2.86	27	27	54	1.82	1.79	3.61
	4007	1.44	1.52	2.96	29	31	60	1.66	1.63	3.29
	4008	1.50	1.52	3.02	29	29	58	1.58	1.51	3.09
	4009	1.42	1.28	2.70	33	37	70	1.42	1.39	2.81
	4010	1.34	1.35	2.69	17	22	39	1.44	1.49	2.93
	Mean	1.43	1.42	2.85	27	29	56	1.58	1.56	3.15
	S.D.	0.06	0.11	0.15	6	5	11	0.17	0.15	0.32
Relative	4006	0.33	0.33	0.66	6	6	12	0.42	0.41	0.83
	4007	0.33	0.35	0.67	7	7	14	0.38	0.37	0.75
	4008	0.40	0.40	0.80	8	8	15	0.42	0.40	0.82
	4009	0.37	0.33	0.70	9	10	18	0.37	0.36	0.72
	4010	0.34	0.35	0.69	4	6	10	0.37	0.38	0.75
	Mean	0.35	0.35	0.70	7	7	14	0.39	0.38	0.77
	S.D.	0.03	0.03	0.06	2	2	3	0.03	0.02	0.05

Appendix 184

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (Recovery)

Sex : Male

Dose (mg/kg) : 1000

	Animal number	Epididymis (R)	Epididymis (L)	Epididymis (R+L)
		mg(mg/100g BW)	mg(mg/100g BW)	mg(mg/100g BW)
Absolute	4006	625	609	1234
	4007	598	569	1167
	4008	505	476	981
	4009	490	465	955
	4010	462	473	935
	Mean	536	518	1054
	S.D.	71	66	136
Relative	4006	144	141	285
	4007	136	130	266
	4008	134	126	260
	4009	126	120	246
	4010	119	122	240
	Mean	132	128	259
	S.D.	10	8	18

Appendix 185

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (Recovery)

Sex : Female

Dose (mg/kg) : 0

	Animal number	Body weight	Brain	Thymus	Heart	Lung	Liver	Spleen
		g	g(g/100g BW)	mg(mg/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)
Absolute	1106	249	2.00	464	0.85	1.08	6.80	0.60
	1107	284	1.93	354	0.99	1.07	7.50	0.51
	1108	250	1.82	348	0.84	1.06	6.39	0.36
	1109	250	1.94	379	0.85	1.10	7.08	0.53
	1110	259	1.92	309	0.78	1.10	6.73	0.44
	Mean	258	1.92	371	0.86	1.08	6.90	0.49
	S.D.	15	0.06	58	0.08	0.02	0.42	0.09
Relative	1106		0.80	186	0.34	0.43	2.73	0.24
	1107		0.68	125	0.35	0.38	2.64	0.18
	1108		0.73	139	0.34	0.42	2.56	0.14
	1109		0.78	152	0.34	0.44	2.83	0.21
	1110		0.74	119	0.30	0.42	2.60	0.17
	Mean		0.75	144	0.33	0.42	2.67	0.19
	S.D.		0.05	27	0.02	0.02	0.11	0.04

Appendix 186

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (Recovery)

Sex : Female

Dose (mg/kg) : 0

	Animal number	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)
Absolute	1106	0.97	0.91	1.88	34	34	68	49.0	44.2	93.2
	1107	1.02	1.00	2.02	34	29	63	40.1	38.0	78.1
	1108	0.86	0.89	1.75	35	37	72	45.0	29.0	74.0
	1109	0.91	0.89	1.80	40	49	89	41.5	45.7	87.2
	1110	0.84	0.89	1.73	31	38	69	39.8	40.6	80.4
	Mean	0.92	0.92	1.84	35	37	72	43.1	39.5	82.6
	S.D.	0.08	0.05	0.12	3	7	10	3.9	6.6	7.6
Relative	1106	0.39	0.37	0.76	14	14	27	19.7	17.8	37.4
	1107	0.36	0.35	0.71	12	10	22	14.1	13.4	27.5
	1108	0.34	0.36	0.70	14	15	29	18.0	11.6	29.6
	1109	0.36	0.36	0.72	16	20	36	16.6	18.3	34.9
	1110	0.32	0.34	0.67	12	15	27	15.4	15.7	31.0
	Mean	0.35	0.36	0.71	14	15	28	16.8	15.4	32.1
	S.D.	0.03	0.01	0.03	2	4	5	2.2	2.9	4.0

Appendix 187

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (Recovery)

Sex : Female

Dose (mg/kg) : 0

	Animal number	Uterus	
		mg(mg/100g BW)	
Absolute	1106	396	
	1107	444	
	1108	397	
	1109	582	
	1110	343	
	Mean	432	
	S.D.	91	
Relative	1106	159	
	1107	158	
	1108	159	
	1109	233	
	1110	132	
	Mean	168	
	S.D.	38	

Appendix 188

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (Recovery)

Sex : Female

Dose (mg/kg) : 1000

	Animal number	Body weight	Brain	Thymus	Heart	Lung	Liver	Spleen
		g	g(g/100g BW)	mg(mg/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)	g(g/100g BW)
Absolute	4106	238	1.75	309	0.79	0.91	5.85	0.48
	4107	274	1.78	306	0.91	1.14	7.80	0.65
	4108	241	1.97	281	0.79	1.05	6.17	0.56
	4109	254	1.84	385	0.76	1.09	7.31	0.52
	4110	269	1.97	436	0.86	1.16	7.14	0.58
	Mean	255	1.86	343	0.82	1.07	6.85	0.56
Relative	S.D.	16	0.10	65	0.06	0.10	0.82	0.06
	4106		0.74	130	0.33	0.38	2.46	0.20
	4107		0.65	112	0.33	0.42	2.85	0.24
	4108		0.82	117	0.33	0.44	2.56	0.23
	4109		0.72	152	0.30	0.43	2.88	0.20
	4110		0.73	162	0.32	0.43	2.65	0.22
	Mean		0.73	135	0.32	0.42	2.68	0.22
	S.D.		0.06	22	0.01	0.02	0.18	0.02

Appendix 189

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (Recovery)

Sex : Female

Dose (mg/kg) : 1000

	Animal number	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)
Absolute	4106	0.89	0.85	1.74	28	28	56	37.7	24.2	61.9
	4107	0.99	0.95	1.94	39	43	82	47.7	39.0	86.7
	4108	0.92	0.92	1.84	36	35	71	35.0	34.9	69.9
	4109	0.88	0.87	1.75	36	36	72	43.6	35.3	78.9
	4110	0.94	0.97	1.91	30	36	66	41.6	43.7	85.3
	Mean	0.92	0.91	1.84	34	36	69	41.1	35.4	76.5
	S.D.	0.04	0.05	0.09	5	5	9	5.0	7.2	10.5
Relative	4106	0.37	0.36	0.73	12	12	24	15.8	10.2	26.0
	4107	0.36	0.35	0.71	14	16	30	17.4	14.2	31.6
	4108	0.38	0.38	0.76	15	15	29	14.5	14.5	29.0
	4109	0.35	0.34	0.69	14	14	28	17.2	13.9	31.1
	4110	0.35	0.36	0.71	11	13	25	15.5	16.2	31.7
	Mean	0.36	0.36	0.72	13	14	27	16.1	13.8	29.9
	S.D.	0.01	0.01	0.03	2	2	3	1.2	2.2	2.4

Appendix 190

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual absolute and relative organ weight (Recovery)

Sex : Female

Dose (mg/kg) : 1000

	Animal number	Uterus	
		mg(mg/100g BW)	
Absolute	4106	408	
	4107	439	
	4108	446	
	4109	478	
	4110	643	
	Mean	483	
	S.D.	93	
Relative	4106	171	
	4107	160	
	4108	185	
	4109	188	
	4110	239	
	Mean	189	
	S.D.	30	

Appendix 191

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual gross pathological findings (4 weeks)

Sex : Male

Dose (mg/kg) : 0

Organs Findings	Animal number (1001-1005)				
	1	2	3	4	5
External appearance	-	-	-	-	-
Brain	-	-	-	-	-
Spinal cord	-	-	-	-	-
Sciatic nerve	-	-	-	-	-
Pituitary	-	-	-	-	-
Salivary gland	-	-	-	-	-
Submandibular lymph node	-	-	-	-	-
Trachea	-	-	-	-	-
Thyroid	-	-	-	-	-
Large or small (unilateral)	-	-	-	-	-
Thoracic cavity	-	-	-	-	-
Thymus	-	-	-	-	-
Heart	-	-	-	-	-
Lung	-	-	-	-	-
Focus, dark red	-	-	-	-	-
Abdominal cavity	-	-	-	-	-
Liver	-	-	-	-	-
Spleen	-	-	-	-	-
Pancreas	-	-	-	-	-
Kidney	-	-	-	-	-
Adrenal	-	-	-	-	-
Esophagus	-	-	-	-	-
Stomach	-	-	-	-	-
Small intestine	-	-	-	-	-
Large intestine	-	-	-	-	-
Mesenteric lymph node	-	-	-	-	-
Bone marrow	-	-	-	-	-
Femoral muscle	-	-	-	-	-
Urinary bladder	-	-	-	-	-
Testis	-	-	-	-	-
Small (bilateral)	-	-	-	-	-
Epididymis	-	-	-	-	-
Small (bilateral)	-	-	-	-	-
Seminal vesicle	-	-	-	-	-
Prostate	-	-	-	-	-
Small	-	-	-	-	-
Other tissues or organs	-	-	-	-	-

- : No remarkable changes

Appendix 192

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual gross pathological findings (4 weeks)

Sex : Male

Dose (mg/kg) : 100

Organs Findings	Animal number (2001-2005)				
	1	2	3	4	5
External appearance	-	-	-	-	-
Brain	-	-	-	-	-
Spinal cord	-	-	-	-	-
Sciatic nerve	-	-	-	-	-
Pituitary	-	-	-	-	-
Salivary gland	-	-	-	-	-
Submandibular lymph node	-	-	-	-	-
Trachea	-	-	-	-	-
Thyroid	-	-	-	-	-
Large or small (unilateral)	-	-	-	-	-
Thoracic cavity	-	-	-	-	-
Thymus	-	-	-	-	-
Heart	-	-	-	-	-
Lung	-	-	-	-	-
Focus, dark red	-	-	+	-	-
Abdominal cavity	-	-	-	-	-
Liver	-	-	-	-	-
Spleen	-	-	-	-	-
Pancreas	-	-	-	-	-
Kidney	-	-	-	-	-
Adrenal	-	-	-	-	-
Esophagus	-	-	-	-	-
Stomach	-	-	-	-	-
Small intestine	-	-	-	-	-
Large intestine	-	-	-	-	-
Mesenteric lymph node	-	-	-	-	-
Bone marrow	-	-	-	-	-
Femoral muscle	-	-	-	-	-
Urinary bladder	-	-	-	-	-
Testis	-	-	-	-	-
Small (bilateral)	-	-	-	+	-
Epididymis	-	-	-	-	-
Small (bilateral)	-	-	-	+	-
Seminal vesicle	-	-	-	-	-
Prostate	-	-	-	-	-
Small	-	-	-	+	-
Other tissues or organs	-	-	-	-	-

- : No remarkable changes

+ : Positive for respective changes

Appendix 193

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual gross pathological findings (4 weeks)

Sex : Male

Dose (mg/kg) : 300

Organs Findings	Animal number (3001-3005)				
	1	2	3	4	5
External appearance	-	-	-	-	-
Brain	-	-	-	-	-
Spinal cord	-	-	-	-	-
Sciatic nerve	-	-	-	-	-
Pituitary	-	-	-	-	-
Salivary gland	-	-	-	-	-
Submandibular lymph node	-	-	-	-	-
Trachea	-	-	-	-	-
Thyroid	-	-	-	-	-
Large or small (unilateral)	+	-	-	-	-
Thoracic cavity	-	-	-	-	-
Thymus	-	-	-	-	-
Heart	-	-	-	-	-
Lung	-	-	-	-	-
Focus, dark red	-	-	-	-	-
Abdominal cavity	-	-	-	-	-
Liver	-	-	-	-	-
Spleen	-	-	-	-	-
Pancreas	-	-	-	-	-
Kidney	-	-	-	-	-
Adrenal	-	-	-	-	-
Esophagus	-	-	-	-	-
Stomach	-	-	-	-	-
Small intestine	-	-	-	-	-
Large intestine	-	-	-	-	-
Mesenteric lymph node	-	-	-	-	-
Bone marrow	-	-	-	-	-
Femoral muscle	-	-	-	-	-
Urinary bladder	-	-	-	-	-
Testis	-	-	-	-	-
Small (bilateral)	-	-	-	-	-
Epididymis	-	-	-	-	-
Small (bilateral)	-	-	-	-	-
Seminal vesicle	-	-	-	-	-
Prostate	-	-	-	-	-
Small	-	-	-	-	-
Other tissues or organs	-	-	-	-	-

- : No remarkable changes

+ : Positive for respective changes

Appendix 194

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual gross pathological findings (4 weeks)

Sex : Male

Dose (mg/kg) : 1000

Organs Findings	Animal number (4001-4005)				
	1	2	3	4	5
External appearance	-	-	-	-	-
Brain	-	-	-	-	-
Spinal cord	-	-	-	-	-
Sciatic nerve	-	-	-	-	-
Pituitary	-	-	-	-	-
Salivary gland	-	-	-	-	-
Submandibular lymph node	-	-	-	-	-
Trachea	-	-	-	-	-
Thyroid	-	-	-	-	-
Large or small (unilateral)	-	-	-	-	-
Thoracic cavity	-	-	-	-	-
Thymus	-	-	-	-	-
Heart	-	-	-	-	-
Lung	-	-	-	-	-
Focus, dark red	-	-	+	-	-
Abdominal cavity	-	-	-	-	-
Liver	-	-	-	-	-
Spleen	-	-	-	-	-
Pancreas	-	-	-	-	-
Kidney	-	-	-	-	-
Adrenal	-	-	-	-	-
Esophagus	-	-	-	-	-
Stomach	-	-	-	-	-
Small intestine	-	-	-	-	-
Large intestine	-	-	-	-	-
Mesenteric lymph node	-	-	-	-	-
Bone marrow	-	-	-	-	-
Femoral muscle	-	-	-	-	-
Urinary bladder	-	-	-	-	-
Testis	-	-	-	-	-
Small (bilateral)	-	-	-	-	-
Epididymis	-	-	-	-	-
Small (bilateral)	-	-	-	-	-
Seminal vesicle	-	-	-	-	-
Prostate	-	-	-	-	-
Small	-	-	-	-	-
Other tissues or organs	-	-	-	-	-

- : No remarkable changes

+ : Positive for respective changes

Appendix 195

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual gross pathological findings (4 weeks)

Sex : Female

Dose (mg/kg) : 0

Organs Findings	Animal number (1101-1105)				
	1	2	3	4	5
External appearance	-	-	-	-	-
Brain	-	-	-	-	-
Spinal cord	-	-	-	-	-
Sciatic nerve	-	-	-	-	-
Pituitary	-	-	-	-	-
Salivary gland	-	-	-	-	-
Submandibular lymph node	-	-	-	-	-
Trachea	-	-	-	-	-
Thyroid	-	-	-	-	-
Thoracic cavity	-	-	-	-	-
Thymus	-	-	-	-	-
Heart	-	-	-	-	-
Lung	-	-	-	-	-
Abdominal cavity	-	-	-	-	-
Liver	-	-	-	-	-
Spleen	-	-	-	-	-
Pancreas	-	-	-	-	-
Kidney	-	-	-	-	-
Adrenal	-	-	-	-	-
Esophagus	-	-	-	-	-
Stomach	-	-	-	-	-
Small intestine	-	-	-	-	-
Large intestine	-	-	-	-	-
Mesenteric lymph node	-	-	-	-	-
Bone marrow	-	-	-	-	-
Femoral muscle	-	-	-	-	-
Urinary bladder	-	-	-	-	-
Ovary	-	-	-	-	-
Uterus	-	-	-	-	-
Vagina	-	-	-	-	-
Other tissues or organs	-	-	-	-	-

- : No remarkable changes

Appendix 196

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual gross pathological findings (4 weeks)

Sex : Female

Dose (mg/kg) : 100

Organs Findings	Animal number (2101-2105)				
	1	2	3	4	5
External appearance	-	-	-	-	-
Brain	-	-	-	-	-
Spinal cord	-	-	-	-	-
Sciatic nerve	-	-	-	-	-
Pituitary	-	-	-	-	-
Salivary gland	-	-	-	-	-
Submandibular lymph node	-	-	-	-	-
Trachea	-	-	-	-	-
Thyroid	-	-	-	-	-
Thoracic cavity	-	-	-	-	-
Thymus	-	-	-	-	-
Heart	-	-	-	-	-
Lung	-	-	-	-	-
Abdominal cavity	-	-	-	-	-
Liver	-	-	-	-	-
Spleen	-	-	-	-	-
Pancreas	-	-	-	-	-
Kidney	-	-	-	-	-
Adrenal	-	-	-	-	-
Esophagus	-	-	-	-	-
Stomach	-	-	-	-	-
Small intestine	-	-	-	-	-
Large intestine	-	-	-	-	-
Mesenteric lymph node	-	-	-	-	-
Bone marrow	-	-	-	-	-
Femoral muscle	-	-	-	-	-
Urinary bladder	-	-	-	-	-
Ovary	-	-	-	-	-
Uterus	-	-	-	-	-
Vagina	-	-	-	-	-
Other tissues or organs	-	-	-	-	-

- : No remarkable changes

Appendix 197

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual gross pathological findings (4 weeks)

Sex : Female

Dose (mg/kg) : 300

Organs Findings	Animal number (3101-3105)				
	1	2	3	4	5
External appearance	-	-	-	-	-
Brain	-	-	-	-	-
Spinal cord	-	-	-	-	-
Sciatic nerve	-	-	-	-	-
Pituitary	-	-	-	-	-
Salivary gland	-	-	-	-	-
Submandibular lymph node	-	-	-	-	-
Trachea	-	-	-	-	-
Thyroid	-	-	-	-	-
Thoracic cavity	-	-	-	-	-
Thymus	-	-	-	-	-
Heart	-	-	-	-	-
Lung	-	-	-	-	-
Abdominal cavity	-	-	-	-	-
Liver	-	-	-	-	-
Spleen	-	-	-	-	-
Pancreas	-	-	-	-	-
Kidney	-	-	-	-	-
Adrenal	-	-	-	-	-
Esophagus	-	-	-	-	-
Stomach	-	-	-	-	-
Small intestine	-	-	-	-	-
Large intestine	-	-	-	-	-
Mesenteric lymph node	-	-	-	-	-
Bone marrow	-	-	-	-	-
Femoral muscle	-	-	-	-	-
Urinary bladder	-	-	-	-	-
Ovary	-	-	-	-	-
Uterus	-	-	-	-	-
Vagina	-	-	-	-	-
Other tissues or organs	-	-	-	-	-

- : No remarkable changes

Appendix 198

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual gross pathological findings (4 weeks)

Sex : Female

Dose (mg/kg) : 1000

Organs Findings	Animal number (4101-4105)				
	1	2	3	4	5
External appearance	-	-	-	-	-
Brain	-	-	-	-	-
Spinal cord	-	-	-	-	-
Sciatic nerve	-	-	-	-	-
Pituitary	-	-	-	-	-
Salivary gland	-	-	-	-	-
Submandibular lymph node	-	-	-	-	-
Trachea	-	-	-	-	-
Thyroid	-	-	-	-	-
Thoracic cavity	-	-	-	-	-
Thymus	-	-	-	-	-
Heart	-	-	-	-	-
Lung	-	-	-	-	-
Abdominal cavity	-	-	-	-	-
Liver	-	-	-	-	-
Spleen	-	-	-	-	-
Pancreas	-	-	-	-	-
Kidney	-	-	-	-	-
Adrenal	-	-	-	-	-
Esophagus	-	-	-	-	-
Stomach	-	-	-	-	-
Small intestine	-	-	-	-	-
Large intestine	-	-	-	-	-
Mesenteric lymph node	-	-	-	-	-
Bone marrow	-	-	-	-	-
Femoral muscle	-	-	-	-	-
Urinary bladder	-	-	-	-	-
Ovary	-	-	-	-	-
Uterus	-	-	-	-	-
Vagina	-	-	-	-	-
Other tissues or organs	-	-	-	-	-

- : No remarkable changes

Appendix 199

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual gross pathological findings (Recovery)

Sex : Male

Dose (mg/kg) : 0

Organs Findings	Animal number (1006-1010)				
	6	7	8	9	10
External appearance	-	-	-	-	-
Brain	-	-	-	-	-
Spinal cord	-	-	-	-	-
Sciatic nerve	-	-	-	-	-
Pituitary	-	-	-	-	-
Salivary gland	-	-	-	-	-
Submandibular lymph node	-	-	-	-	-
Trachea	-	-	-	-	-
Thyroid	-	-	-	-	-
Thoracic cavity	-	-	-	-	-
Thymus	-	-	-	-	-
Heart	-	-	-	-	-
Lung	-	-	-	-	-
Abdominal cavity	-	-	-	-	-
Liver	-	-	-	-	-
Spleen	-	-	-	-	-
Pancreas	-	-	-	-	-
Kidney	-	-	-	-	-
Adrenal	-	-	-	-	-
Esophagus	-	-	-	-	-
Stomach	-	-	-	-	-
Focus, dark red, glandular stomach	+	-	+	-	-
Small intestine	-	-	-	-	-
Diverticulum	-	-	-	-	-
Large intestine	-	-	-	-	-
Mesenteric lymph node	-	-	-	-	-
Bone marrow	-	-	-	-	-
Femoral muscle	-	-	-	-	-
Urinary bladder	-	-	-	-	-
Testis	-	-	-	-	-
Epididymis	-	-	-	-	-
Focus, yellowish white (unilateral)	-	+	-	-	-
Seminal vesicle	-	-	-	-	-
Prostate	-	-	-	-	-
Other tissues or organs	-	-	-	-	-

- : No remarkable changes
+ : Positive for respective changes

Appendix 200

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual gross pathological findings (Recovery)

Sex : Male

Dose (mg/kg) : 1000

Organs Findings	Animal number (4006-4010)				
	6	7	8	9	10
External appearance	-	-	-	-	-
Brain	-	-	-	-	-
Spinal cord	-	-	-	-	-
Sciatic nerve	-	-	-	-	-
Pituitary	-	-	-	-	-
Salivary gland	-	-	-	-	-
Submandibular lymph node	-	-	-	-	-
Trachea	-	-	-	-	-
Thyroid	-	-	-	-	-
Thoracic cavity	-	-	-	-	-
Thymus	-	-	-	-	-
Heart	-	-	-	-	-
Lung	-	-	-	-	-
Abdominal cavity	-	-	-	-	-
Liver	-	-	-	-	-
Spleen	-	-	-	-	-
Pancreas	-	-	-	-	-
Kidney	-	-	-	-	-
Adrenal	-	-	-	-	-
Esophagus	-	-	-	-	-
Stomach	-	-	-	-	-
Focus, dark red, glandular stomach	+	+	-	-	-
Small intestine	-	-	-	-	-
Diverticulum	-	+	-	-	-
Large intestine	-	-	-	-	-
Mesenteric lymph node	-	-	-	-	-
Bone marrow	-	-	-	-	-
Femoral muscle	-	-	-	-	-
Urinary bladder	-	-	-	-	-
Testis	-	-	-	-	-
Epididymis	-	-	-	-	-
Focus, yellowish white (unilateral)	-	-	-	-	-
Seminal vesicle	-	-	-	-	-
Prostate	-	-	-	-	-
Other tissues or organs	-	-	-	-	-

- : No remarkable changes

+ : Positive for respective changes

Appendix 201

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks
individual gross pathological findings (Recovery)

Sex : Female

Dose (mg/kg) : 0

Organs Findings	Animal number (1106-1110)				
	6	7	8	9	10
External appearance	-	-	-	-	-
Brain	-	-	-	-	-
Spinal cord	-	-	-	-	-
Sciatic nerve	-	-	-	-	-
Pituitary	-	-	-	-	-
Salivary gland	-	-	-	-	-
Submandibular lymph node	-	-	-	-	-
Trachea	-	-	-	-	-
Thyroid	-	-	-	-	-
Thoracic cavity	-	-	-	-	-
Thymus	-	-	-	-	-
Heart	-	-	-	-	-
Lung	-	-	-	-	-
Abdominal cavity	-	-	-	-	-
Liver	-	-	-	-	-
Spleen	-	-	-	-	-
Pancreas	-	-	-	-	-
Kidney	-	-	-	-	-
Adrenal	-	-	-	-	-
Esophagus	-	-	-	-	-
Stomach	-	-	-	-	-
Small intestine	-	-	-	-	-
Large intestine	-	-	-	-	-
Mesenteric lymph node	-	-	-	-	-
Bone marrow	-	-	-	-	-
Femoral muscle	-	-	-	-	-
Urinary bladder	-	-	-	-	-
Ovary	-	-	-	-	-
Uterus	-	-	-	-	-
Vagina	-	-	-	-	-
Other tissues or organs	-	-	-	-	-

- : No remarkable changes

Appendix 202

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual gross pathological findings (Recovery)

Sex : Female

Dose (mg/kg) : 1000

Organs Findings	Animal number (4106-4110)				
	6	7	8	9	10
External appearance	-	-	-	-	-
Brain	-	-	-	-	-
Spinal cord	-	-	-	-	-
Sciatic nerve	-	-	-	-	-
Pituitary	-	-	-	-	-
Salivary gland	-	-	-	-	-
Submandibular lymph node	-	-	-	-	-
Trachea	-	-	-	-	-
Thyroid	-	-	-	-	-
Thoracic cavity	-	-	-	-	-
Thymus	-	-	-	-	-
Heart	-	-	-	-	-
Lung	-	-	-	-	-
Abdominal cavity	-	-	-	-	-
Liver	-	-	-	-	-
Spleen	-	-	-	-	-
Pancreas	-	-	-	-	-
Kidney	-	-	-	-	-
Adrenal	-	-	-	-	-
Esophagus	-	-	-	-	-
Stomach	-	-	-	-	-
Small intestine	-	-	-	-	-
Large intestine	-	-	-	-	-
Mesenteric lymph node	-	-	-	-	-
Bone marrow	-	-	-	-	-
Femoral muscle	-	-	-	-	-
Urinary bladder	-	-	-	-	-
Ovary	-	-	-	-	-
Uterus	-	-	-	-	-
Vagina	-	-	-	-	-
Other tissues or organs	-	-	-	-	-

- : No remarkable changes

Appendix 203

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual histopathological findings (4 weeks)

Sex : Male

Dose (mg/kg) : 0

Organs	Animal number				
	1	1	1	1	1
-findings	0	0	0	0	0
	0	0	0	0	0
	1	2	3	4	5
Cerebrum	0	0	0	0	0
Cerebellum	0	0	0	0	0
Pons	0	0	0	0	0
Spinal cord	0	0	0	0	0
Sciatic nerve	0	0	0	0	0
Heart	0	0	0	0	0
Trachea	0	0	0	0	0
Lung (Bronchus)	0	0	0	0	0
Stomach	0	0	0	0	0
Duodenum	0	0	0	0	0
Jejunum	0	0	0	0	0
Ileum (Peyer's patch)	0	0	0	0	0
Cecum	0	0	0	0	0
Colon	0	0	0	0	0
Rectum	0	0	0	0	0
Liver					
-microgranuloma	0	0	1	0	0
Pituitary	0	0	0	0	0
Thyroid (Parathyroid)	0	0	0	0	0
Adrenal	0	0	0	0	0
Thymus	0	0	0	0	0
Spleen	0	0	0	0	0
Submandibular lymph node	0	0	0	0	0
Mesenteric lymph node	0	0	0	0	0
Kidney	0	0	0	0	0
Urinary bladder	0	0	0	0	0
Testis	0	0	0	0	0
Epididymis	0	0	0	0	0
Prostate					
-cell infiltration, lymphocytic	0	1	0	0	0
Eye	0	0	0	0	0
Sternum (Bone marrow)	0	0	0	0	0
Femur (Bone marrow)	0	0	0	0	0
Skeletal muscle	0	0	0	0	0

0 : No remarkable changes

1 : Slight

Appendix 204

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual histopathological findings (4 weeks)

Sex : Male

Dose (mg/kg) : 1000

Organs	Animal number				
	4	4	4	4	4
-findings	0	0	0	0	0
	0	0	0	0	0
	1	2	3	4	5
Cerebrum	0	0	0	0	0
Cerebellum	0	0	0	0	0
Pons	0	0	0	0	0
Spinal cord	0	0	0	0	0
Sciatic nerve	0	0	0	0	0
Heart	0	0	0	0	0
Trachea	0	0	0	0	0
Lung (Bronchus)	0	0	0	0	0
Stomach	0	0	0	0	0
Duodenum	0	0	0	0	0
Jejunum	0	0	0	0	0
Ileum (Peyer's patch)	0	0	0	0	0
Cecum	0	0	0	0	0
Colon	0	0	0	0	0
Rectum	0	0	0	0	0
Liver					
-microgranuloma	0	1	0	1	0
Pituitary	0	0	0	0	0
Thyroid (Parathyroid)	0	0	0	0	0
Adrenal	0	0	0	0	0
Thymus	0	0	0	0	0
Spleen	0	0	0	0	0
Submandibular lymph node	0	0	0	0	0
Mesenteric lymph node	0	0	0	0	0
Kidney	0	0	0	0	0
Urinary bladder	0	0	0	0	0
Testis	0	0	0	0	0
Epididymis	0	0	0	0	0
Prostate					
-cell infiltration, lymphocytic	1	0	0	2	0
Eye	0	0	0	0	0
Sternum (Bone marrow)	0	0	0	0	0
Femur (Bone marrow)	0	0	0	0	0
Skeletal muscle	0	0	0	0	0

0 : No remarkable changes

1 : Slight

2 : Mild

Appendix 205

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual histopathological findings (4 weeks)

Sex : Female

Dose (mg/kg) : 0

Organs	Animal number				
	1	1	1	1	1
-findings	1	1	1	1	1
	0	0	0	0	0
	1	2	3	4	5
Cerebrum	0	0	0	0	0
Cerebellum	0	0	0	0	0
Pons	0	0	0	0	0
Spinal cord	0	0	0	0	0
Sciatic nerve	0	0	0	0	0
Heart	0	0	0	0	0
Trachea	0	0	0	0	0
Lung (Bronchus)	0	0	0	0	0
Stomach	0	0	0	0	0
Duodenum	0	0	0	0	0
Jejunum	0	0	0	0	0
Ileum (Peyer's patch)	0	0	0	0	0
Cecum					
-cell infiltration, mucosa	0	0	0	0	0
Colon	0	0	0	0	0
Rectum					
-cell infiltration, mucosa	0	0	0	0	0
Liver	0	0	0	0	0
Pituitary	0	0	0	0	0
Thyroid (Parathyroid)	0	0	0	0	0
Adrenal	0	0	0	0	0
Thymus	0	0	0	0	0
Spleen	0	0	0	0	0
Submandibular lymph node	0	0	0	0	0
Mesenteric lymph node	0	0	0	0	0
Kidney					
-cyst	0	0	P	0	0
Urinary bladder	0	0	0	0	0
Ovary	0	0	0	0	0
Uterus	0	0	0	0	0
Vagina	0	0	0	0	0
Eye	0	0	0	0	0
Sternum (Bone marrow)	0	0	0	0	0
Femur (Bone marrow)	0	0	0	0	0
Skeletal muscle	0	0	0	0	0

0 : No remarkable changes

P : Present

Appendix 206

A 28-day oral toxicity study of Pigment Yellow-14 in rats with a recovery period of 2 weeks

Individual histopathological findings (4 weeks)

Sex : Female

Dose (mg/kg) : 1000

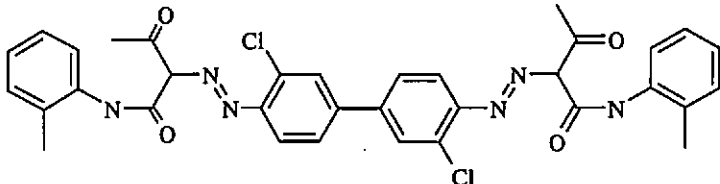
Organs	Animal number				
	4	4	4	4	4
-findings	1	1	1	1	1
	0	0	0	0	0
	1	2	3	4	5
Cerebrum	0	0	0	0	0
Cerebellum	0	0	0	0	0
Pons	0	0	0	0	0
Spinal cord	0	0	0	0	0
Sciatic nerve	0	0	0	0	0
Heart	0	0	0	0	0
Trachea	0	0	0	0	0
Lung (Bronchus)	0	0	0	0	0
Stomach	0	0	0	0	0
Duodenum	0	0	0	0	0
Jejunum	0	0	0	0	0
Ileum (Peyer's patch)	0	0	0	0	0
Cecum					
-cell infiltration, mucosa	0	1	0	0	0
Colon	0	0	0	0	0
Rectum					
-cell infiltration, mucosa	0	1	0	0	0
Liver	0	0	0	0	0
Pituitary	0	0	0	0	0
Thyroid (Parathyroid)	0	0	0	0	0
Adrenal	0	0	0	0	0
Thymus	0	0	0	0	0
Spleen	0	0	0	0	0
Submandibular lymph node	0	0	0	0	0
Mesenteric lymph node	0	0	0	0	0
Kidney					
-cyst	0	0	0	0	0
Urinary bladder	0	0	0	0	0
Ovary	0	0	0	0	0
Uterus	0	0	0	0	0
Vagina	0	0	0	0	0
Eye	0	0	0	0	0
Sternum (Bone marrow)	0	0	0	0	0
Femur (Bone marrow)	0	0	0	0	0
Skeletal muscle	0	0	0	0	0

0 : No remarkable changes

1 : Slight

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

被験物質の名称		ピグメントエロー-14					
別名		ベンジジンエロー		物理化学的性状	分子量	657.55	
構造式又は示性式（いずれも不明な場合はその製法の概要）					常温における性状	やまぶき色粉末	
<div></div> <div>C₃₄H₃₀Cl₂N₆O₄</div>					安定性	冷暗所で安定	
					融点	——	
					沸点	——	
					蒸気圧	——	
					分配係数	——	
					溶解性	——	
					極大波長	421.5nm	
					モル吸光係数	915	
試験に供した被験物質の純度	不明	不明 (乾燥減量:0.36wt%、強熱残分:11.8wt%)	Lot No.	<div></div>	溶解度	水	——
						DMSO	——
						アセトン	——
						その他	——

2. 急性毒性試験

試験 No.	試験の種類 及び期間	動物種	1群当たり の動物数	投与 経路	投与量 (mg/kg)	LD ₅₀ 値又 はNOEL (mg/kg)	実験場所
1	急性毒性試験	ラット	雄 5匹 雌 5匹	経口	0 2000	雄：LD ₅₀ 値>2000 雌：LD ₅₀ 値>2000	(株)ボゾリサーチ センター御殿場 研究所
2	投与量設定試験 (14日間)	ラット	雄 5匹 雌 5匹	経口	(mg/kg/day) 1000 200 40 0	異常なし (NOEL) 異常なし 異常なし 異常なし	(株)ボゾリサーチ センター御殿場 研究所
観察項目： 死亡率、一般状態、 体重、摂餌量、血液 学検査、血液化学検 査、器官重量、剖検							

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29日								至平成 12年12月26日			
使用動物・系統			ラット、Crj：CD（SD）IGS								1群当たり動物数			
投 与 経 路			強制経口投与（媒体：オリブ油）								雄：5匹 雌：5匹			
被験物質の 純度 不明	投 与 量	mg/kg	対照群		低用量群		中用量群		高用量群		回復群			
			0		100		300		1000		0		1000	
			♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀
死亡動物			—	—	—	—	—	—	—	—	—	—	—	—
一般状態 黄色調便			—	—	5/5 ^{a)}	5/5 ^{a)}	5/5 ^{a)}	5/5 ^{a)}	10/10 ^{a)}	10/10 ^{a)}	—	—	5/5 ^{b)}	5/5 ^{b)}
詳細な一般状態 オープンフィールド内観察 黄色調便														
					—	—	—	—	—	(1/10)			—	—
機能検査					—	—	—	—	—	—			—	—
握力 前肢					—	—	—	—	—	—			—	—
自発運動量					—	—	—	—	—	—			△	—
体重					—	—	—	—	—	—			—	—
体重増加量					—	—	—	—	—	—			—	△
摂餌量					—	—	—	—	—	—			—	—
摂水量（尿検査時）					—	—	△	—	—	—			—	—
尿検査 たん白質					▼	—	▽	—	—	△			—	—
ケトン体					▽	—	▽	—	—	—			—	—
尿量					—	—	△	—	—	—			△	—
浸透圧					—	—	▽	—	—	—			—	—
血液学検査														
プロトロンビン時間					—	—	△	—	—	—			—	—
白血球数					—	—	—	—	—	—			△	—
桿状核白血球比率					—	—	—	—	—	—			▽	—
単球比率					—	—	—	—	—	△			—	—
血液化学検査														
GOT(ASAT)					—	▽	—	—	—	▽			—	—
総ビリルビン					—	—	—	—	—	—			△	—
尿素窒素					—	—	—	—	—	—			△	—
クレアチニン					—	—	—	—	—	—			▲	—

—: 変化なし

△: 対照群に比べ有意に増加 ($p < 0.05$)

▲: 対照群に比べ有意に増加 ($p < 0.01$)

▽: 対照群に比べ有意に減少 ($p < 0.05$)

▼: 対照群に比べ有意に減少 ($p < 0.01$)

(): 統計学的な有意差はなかったが、異常を示した動物数を表す。

a): 投与2日より投与終了日まで

b): 回復2日まで

3. 28日間反復投与毒性試験

被験物質の 純度 不明	投 与 量	mg/kg	対照群		低用量群		中用量群		高用量群		回復群			
			0		100		300		1000		0		1000	
			♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀
器官重量（絶対重量）					—	—	—	—	—	—			—	—
器官重量（相対重量）					—	—	—	—	—	—			—	—
剖検所見														
甲状腺	大型（片側性）		—	—	—	—	1/5	—	—	—	—	—	—	—
	小型（片側性）		—	—	—	—	1/5	—	—	—	—	—	—	—
肺	暗赤色巣		—	—	1/5	—	—	—	1/5	—	—	—	—	—
精巣	小型（両側性）		—	/	1/5	/	—	/	—	/	—	/	—	/
精巣上体	小型（両側性）		—	/	1/5	/	—	/	—	/	—	/	—	/
	黄白色巣（片側性）		—	/	—	/	—	/	—	/	1/5	/	—	/
前立腺	小型（両側性）		—	/	1/5	/	—	/	—	/	—	/	—	/
胃	腺胃暗赤色巣		—	—	—	—	—	—	—	—	—	—	2/5	2/5
小腸（回腸）	憩室		—	—	—	—	—	—	—	—	—	—	1/5	—
組織学所見														
肝臓	微小肉芽腫	(±)	1/5	—	*	*	*	*	2/5	—	*	*	*	*
盲腸	粘膜内細胞浸潤	(±)	—	—	*	*	*	*	—	1/5	*	*	*	*
直腸	粘膜内細胞浸潤	(±)	—	—	*	*	*	*	—	1/5	*	*	*	*
腎臓	のう胞	(P)	—	1/5	*	*	*	*	—	—	*	*	*	*
前立腺	リンパ球性細胞浸潤	(±)	1/5	—	*	*	*	*	1/5	—	*	*	*	*
		(+)	—	—	*	*	*	*	1/5	—	*	*	*	*
肉眼的異常部位														
肺	限局性出血	(±)	—	—	1/1	*	*	*	—	—	*	*	*	*
	炎症性細胞浸潤	(±)	—	—	1/1	*	*	*	—	—	*	*	*	*
精巣	精細管萎縮	(++)	—	/	1/1	/	*	/	—	/	*	/	*	/
精巣上体	精子の減少	(++)	—	/	1/1	/	*	/	—	/	*	/	*	/
	精子肉芽腫	(+)	—	/	*	/	*	/	—	/	1/1	/	*	/
胃	腺胃のびらん	(±)	—	—	*	*	*	*	—	—	1/1	*	*	*
		(+)	—	—	*	*	*	*	—	—	1/1	*	2/2	*
小腸（回腸）	憩室	(P)	—	—	*	*	*	*	—	—	*	*	1/1	*
NOEL (mg/kg)			1000 mg/kg/日											
NOELの推定根拠とした変化			いずれの用量群の変化も毒性学的意義はないと判断した。											

—：変化なし

*：検査せず

(±)：軽微

(+)：軽度

(++)：中等度

(P)：有り

4. その他

反復投与毒性 試験実施施設	名 称	(株) ボゾリサーチセンター 御殿場研究所	
	所在地	静岡県御殿場市かまど 1 2 8 4	電話 0550(82)2000 Fax 0550(82)2379
試験責任者	職氏名		
試験実施年月日	平成12年11月20日より平成13年 5月30日まで		

REPEATED DOSE TOXICITY

TEST SUBSTANCE

- **Identity:** Pigment Yellow 14 (CAS No. 5468-75-7)
- **Remarks:**
 - Synonym: Benzidine Yellow
 - Source: [REDACTED] Lot No. [REDACTED] wavelength of maximum absorption at 421.5 nm, molar absorptivity 915.
 - Impurity: loss on drying 0.36 wt%, residue on ignition 11.8 wt%. Kept in a refrigerator until use.

METHOD

- **Method/guideline:** OECD TG407
- **Test type:** Repeated Dose 28-day Oral Toxicity Study
- **GLP:** Yes
- **Year:** 2001
- **Species:** Rat
- **Strain:** Crj:CD(SD)IGS
- **Route of administration:** Oral (by gavage)
- **Doses/concentration levels:** 0, 100, 300 or 1,000 mg/kg/day (in olive oil)
- **Sex:** Male & Female
- **Exposure period:** 28 days
- **Frequency of treatment:** 7 days/week
- **Control group and treatment:** Concurrent vehicle
- **Post exposure observation period:** 14 days
- **Duration of test:** 6 weeks
- **Statistical methods:** Bartlett's test and Dunnett's test or a Dunnett-type mean rank test for continuous data; Chi square test or Mann-Whitney's U-test for scored data; cumulative Chi square test for qualitative data in urinalysis.

REMARKS FIELD FOR TEST CONDITIONS

- **Test Subjects:**
 - *Age at study initiation:* 7 week old
 - *Weight at study initiation:* 228-256 g for males, 171-195 g for females
 - *No. of animals per sex per dose:* 5 per sex per dose group
- **Study Design:**
 - *Vehicle:* Olive oil
 - *Satellite groups and reasons they were added:*
 - Recovery group, in which administration was withheld for 2 weeks to examine reversibility of the changes.
 - *Clinical observations performed and frequency:*
 - General condition:* 3 times a day (but twice on Saturday, Sunday and legal holidays) during the administration period and once a day during the recovery period.
 - Functional observations:* detailed general condition, once before the first

exposure, on days 7, 14, 21 and 28 of administration and on days 7 and 14 of recovery; manipulative tests, grip strength and motor activity, on day 28 of administration and on day 14 of recovery.

Body wt.: on day 1 and twice a week thereafter during the administration period and on day 1 and twice a week thereafter during the recovery period.

Food consumption: on the same days when body wt. was determined.

Water consumption: on the same days as for urinalysis.

Urinalysis: in week 4 of administration and in the final week of recovery.

Haematology and biochemistry: on the day following the last day of the administration and on the last day of the recovery period.

– *Organs examines at necropsy:*

Organ weight: brain, adrenal, thymus, spleen, heart, lung, liver, kidney, and in addition for males, testes and epididymis and for females ovary and uterus.

Microscopic: all animals in the control and 1,000 mg/kg groups, brain, spinal cord, sciatic nerve, eyeball, pituitary, thyroid (including parathyroid), adrenal, thymus, spleen, lymph node, heart, trachea, lung, stomach, small intestine, large intestine, liver, kidney, urinary bladder, testis, epididymis, prostate, ovary, uterus, vagina, bone marrow, muscle; and macroscopical lesions in the other groups.

RESULTS

• NOAEL (NOEL)

Male: 1,000 mg/kg/day

Female: 1,000 mg/kg/day

• LOAEL (LOEL)

Not determined under the conditions tested.

REMARKS FIELD FOR RESULTS

- *Body weight*: No dose-related changes in body weight in either sex.
- *Food/water consumption*: No dose-related changes in food or water consumptions in either sex.
- *Clinical signs*: Yellowish feces was observed in all animals of all treatment groups in both sexes from day 2 of administration to day 2 of recovery.
- *Functional observations*: In the open field observation, yellowish feces was observed in 1/10 males at 1,000 mg/kg.
- *Urinalysis*: *Females*: Increase in protein at 1,000 mg/kg ($p < 0.01$).

Dose level (mg/kg/day)		0	100	300	1,000
No. of animals		10	5	5	10
Protein	degree*				
	–	5	1	1	0
	±	3	2	1	5
	+	2	2	3	4
	++	0	0	0	1

*degree: –, 0-5 mg/dL; ±, 10-20 mg/dL; +, 30-70 mg/dL; ++, 100-200 mg/dL

- **Haematology:** *Females:* Increase in monocyte proportion ($p < 0.05$) at 1,000 mg/kg.
- | Dose level (mg/kg/day) | 0 | 100 | 300 | 1,000 |
|------------------------|---------|---------|---------|---------|
| No. of animals | 10 | 5 | 5 | 10 |
| Monocyte proportion | 0.2±0.3 | 0.3±0.4 | 0.4±0.4 | 0.8±0.3 |
- **Biochem:** No dose-related changes in biochem in either sex.
- **Ophthalmologic findings:** Not examined.
- **Mortality and time to death:** None
- **Gross pathology incidence and severity:** Dark red focus in the lung in 1/5 males at 100 mg/kg and 1/5 males at 1,000 mg/kg.
- **Organ weight changes:** No dose-related changes in organ weight either sex.
- **Histopathology (incidence and severity):**
Liver: Slight microgranuloma in 1/5 males in the control group and 2/5 males at 1,000 mg/kg.
Cecum and rectum: Slight cell infiltration in mucosa in 1/5 females at 1,000 mg/kg.
Prostate: Slight or mild lymphocytic cell infiltration in 1/5 animals in the control group and 2/5 animals at 1,000 mg/kg.

CONCLUSIONS

Yellowish feces was observed in all treatment groups. In the 1,000 mg/kg group, increases of urine protein in males and monocyte proportion in females were observed. Tissue pathology revealed no test article-related change in either sex. The NOAEL was established at 1,000 mg/kg/day for both sexes.

DATA QUALITY

- **Reliabilities:** Valid without restriction

Remarks field for Data Reliability

Well conducted study, carried out by BOZO Research Center Inc. (Japan)

REFERENCES (Free Text)

Nishimura, S. Katsumata, T. *et al* (2001): A-28-day oral toxicity study of Pigment Yellow 14 in rats with a recovery period of 2 weeks.

GENERAL REMARKS

Yellowish feces was judged from its color to be due to excretion of orally ingested Pigment Yellow 14. Further, there were no related histopathological changes in the males with increased urine protein or the females with increased monocyte proportion in the 1,000 mg/kg group. Therefore, neither of these changes is thought to have any toxicological significance.