N－モノメチルフェニル－N’－モノメチルフェニル－p－フェニレンジアミン

のラットにおける

２８日間反復投与経口毒性試験報告書

株式会社化合物安全性研究所

陳 述 書

表　　題：N-ﾓﾉﾒﾁﾙﾌｪﾆﾙ-N'-ﾓﾉﾒﾁﾙﾌｪﾆﾙ-p-ﾌｪﾆﾚﾝｼﾞｱﾐﾝ のラットにおける28日間反復投与経口毒性試験性試験

試験番号：ＳＲ－９１２７

1．本試験は「新規化学物質に係る試験及び指定化学物質に係る有害性の調査の項目等を定める命令第４条に規定する試験施設に関する基準」（昭和59年３月31日環保業第39号、薬発第 229号、59基局第 85号通達）並びに「OECD優良試験所指針Ｃ（81）30 最終別添２」に従い、試験方法は「新規化学物質に係る試験の方法について」（昭和59年７月13日環保業第５号、薬発第 16号、59基局第 392号）、「新規化学物質に係る試験の方法についての一部改正について」（昭和 61年12月５日 61基局第 1014号）及び OECDテストガイドラインに準拠して実施したものであります。

2．本試験は、試験計画書に従って実施し、その目的を達成し、試験の信頼性に悪影響を及ぼした事態は認められませんでした。

株式会社化合物安全性研究所

試験責任者　[redacted]　1992 年 8 月 21 日

運営管理者　[redacted]　1992 年 8 月 21 日

陳　述　書
（査察終了確認書）

所　長
[redacted]

試験の表題　N-モノメチルフェニル-N'-モノメチルフェニル-P-フェニレンジアミンのラットにおける28日間反復投与経口毒性試験

（試験番号　ＳＲ－９１２７　）

本試験は、「新規化学物質に係る試験及び指定化学物質に係る有害性の調査の項目等を定める命令第４条に規定する試験施設に関する基準」（昭和59年 3月31日環保業第39号、薬発第 229号、59基局第85号通達）、「OECD優良試験所指針Ｃ(81)30最終別添 2」、「新規化学物質に係る試験の方法について」（昭和59年 7月13日環保業第 5号、薬発第16号、59基局第 392号）、「新規化学物質に係る試験の方法についての一部改正について」（昭和61年12月5日61基局第1014号）及びOECDテストガイドラインに従い実施され化合物安全性研究所ＱＡＵにより査察された。

査　察　日	査　　察　　項　　目	＊試験責任者、運営管理者への報告日
'91年 7月25日	試験計画書	'91年11月27日
'91年 7月31日	試験計画書変更確認書	
'91年 8月 7日	試験計画書変更確認書	
'91年10月 1日	試験計画書変更確認書	
'91年11月19日	試験計画書変更確認書	
'91年11月20日	動物受入（動物、飼育環境条件）	
'91年11月26日	群分け（検疫・馴化記録、標識、動物番号、飼育環境条件）	
'91年11月26日	検疫（眼底検査）	
'91年11月26日	試験計画書変更確認書	
'91年11月27日	被験物質受入記録	
'91年11月27日	投与（被験物質の調製、測定、観察、飼育環境条件）	
'91年12月18日	試験計画書変更確認書	'92年 1月27日
'91年12月20日	試験計画書変更確認書	
'91年12月25日	剖検（投与期間終了時：採血、器官重量測定、病理組織学的検査；器官・組織固定）	
'91年12月27日	尿検査（投与期間最終週）	
'92年 1月 7日	測定（回復期間：観察、飼育環境条件）	
'92年 1月17日	血液学的検査	
'92年 1月17日	血液化学的検査記録	
'92年 2月21日	病理組織学的検査記録	'92年 4月 2日
'92年 3月26日	動物飼育管理記録	

＊：査察報告書による。

査察日	査察項目	*試験責任者、運営管理者への報告日
'92年 3月27日	生データ	'92年 4月 2日
'92年 3月31日	報告書草案	
'92年 8月21日	最終報告書	'92年 8月21日

*：査察報告書による。

運営管理者への報告及び承認日

'91年 7月25日　QAU査察計画書
'91年11月27日　査察報告書
'92年 1月27日　査察報告書
'92年 4月 2日　査察報告書
'92年 8月21日　陳述書、査察報告書

本試験は試験計画書に従って実施され、また本報告書には当該試験に使用した方法及び手順が正確に記載されており、試験成績には当該試験の実施過程において得られた生データを正確に反映していることを確認した。

株式会社化合物安全性研究所
QAU責任者
[redacted] 1992年 8月 21日

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28日間反復投与経口毒性試験

試験番号　ＳＲ－９１２７

試験施設　株式会社化合物安全性研究所
札幌市北区北30条西11丁目２番20号

試験期間
試験開始日：１９９１年　７月２５日
動物受入日：１９９１年１１月２０日
投与開始日：１９９１年１１月２７日（雄）
１９９１年１１月２８日（雌）
投与終了日：１９９１年１２月２４日（雄）
１９９１年１２月２５日（雌）
投与終了時解剖日：１９９１年１２月２５日（雄）
１９９１年１２月２６日（雌）
回復試験終了日：１９９２年　１月　７日（雄）
１９９２年　１月　８日（雌）
回復試験終了時解剖日：１９９２年　１月　８日（雄）
１９９２年　１月　９日（雌）
報告書草案作成日：１９９２年　４月　２日
最終報告書作成日：１９９２年　８月２１日
試験終了日：１９９２年　８月２１日

運営管理者　[redacted]

試験責任者

試験に従事した研究者

動物管理責任者：　[redacted]
臨床検査責任者：
病理検査責任者：
副試験責任者：

要　約

N-ﾓﾉﾒﾁﾙﾌｪﾆﾙ-N'-ﾓﾉﾒﾁﾙﾌｪﾆﾙ-p-ﾌｪﾆﾚﾝｼﾞｱﾐﾝ（既存化学物質 No. 3-0146）の4、20及び100mg/kg/dayを Crj:CD（SD）系雌雄ラットに 28日間経口反復投与し、その毒性及び投与後 14日間休薬した際の回復性を検討し、以下の知見が得られた。

1．肝臓に対する影響として、血中のアルカリフォスファターゼの増加、アルブミンの減少及び A/G比の低下が 100mg/kg 群の雌で、活性化部分トロンボプラスチン時間の延長が 20mg/kg以上の群の雄及び 100mg/kg群の雌で、肝臓の体重重量比の上昇が 100mg/kg群の雌雄で認められた。また、血中の乳酸脱水素酵素の減少が 100mg/kg 群の雌で認められた。

2．甲状腺に対する影響として、重量の増加及び体重重量比の上昇が 100mg/kg 群の雌で認められた。

3．副腎に対する影響として、重量の増加及び体重重量比の上昇が 100mg/kg 群の雌で、束状帯内層を主とするコレステリン様物質の沈着及び皮質細胞の単細胞壊死が 100 mg/kg 群の雄1例で認められた。また、血中のカルシウムの減少が 20mg/kg以上の群の雄で、カリウムの減少が 100mg/kg群の雌で認められた。

4．腎臓に対する影響として、体重重量比の上昇が 100mg/kg群の雌雄で認められた。

5．その他に、血色素量の減少が 100mg/kg群の雌で認められた。

6．上述の変化はその多くが14日間の休薬により消失し、回復傾向はあるものと考えられた。しかし、回復期間終了時には、100mg/kg群の雌で血中の総蛋白、アルブミン、アルカリフォスファターゼ、カリウム及びカルシウムが投与期間終了時と同様の変動を示し、100mg/kg群の雄1例で副腎束状帯内層を主とする皮質細胞の単細胞壊死が認められた。

7．以上のことから、本試験における既存化学物質 No.3-0146投与による無影響量は雄で4mg/kg/day、雌で 20mg/kg/dayと考えられた。

緒　言

N-ﾓﾉﾒﾁﾙﾌｪﾆﾙ-N'-ﾓﾉﾒﾁﾙﾌｪﾆﾙ-p-ﾌｪﾆﾚﾝｼﾞｱﾐﾝ（既存化学物質 No. 3-0146）をラットに28日間経口反復投与し、その毒性及び投与後14日間休薬した際の回復性を検討したので、その成績を報告する。

なお、本試験は「新規化学物質に係る試験及び指定化学物質に係る有害性の調査の項目等を定める命令第４条に規定する試験施設に関する基準」（昭和59年３月31日環保業第39号、薬発第 229号、59基局第 85号通達）並びに「OECD優良試験所指針Ｃ（81）30 最終別添２」に従い、試験方法は「新規化学物質に係る試験の方法について」（昭和59年７月13日環保業第５号、薬発第 16号、59基局第 392号）、「新規化学物質に係る試験の方法についての一部改正について」（昭和 61年12月５日 61基局第 1014号）及び OECDテストガイドラインに準拠した。

材料及び方法

１．被験物質

被験物質は、厚生省生活衛生局より提供された N-ﾓﾉﾒﾁﾙﾌｪﾆﾙ-N'-ﾓﾉﾒﾁﾙﾌｪﾆﾙ-p-ﾌｪﾆﾚﾝｼﾞｱﾐﾝ（以下、既存化学物質 No. 3-0146と称す。Lot 番号：AR-8，純度：75％以上）である。被験物質は、水に溶けず、アセトン、ベンゼンに良く溶ける、黒褐色粒状の物質であり、密閉容器に入れ、冷所（２～８℃）遮光下で保存した。なお、被験物質の品質は 1993年８月まで保証されている。

被験物質の高濃度懸濁液の調製は週１回以上の頻度で次の通り行った。乳鉢にて粉砕し、300μm メッシュのふるい（飯田製作所）にかけた被験物質を精秤し、１w/v％となるように 0.5％カルボキシメチルセルロースナトリウム溶液（以下、0.5％ CMC-Na溶液。日本薬局方CMC-Na：Lot No. OX13，丸石製薬株式会社、局方精製水：Lot No. 108067，110039 及び 111021，ヤクハン製薬株式会社）で懸濁した。また、中間及び低濃度の懸濁液は、１％懸濁液を 0.04 及び 0.2w/v％となるように、0.5％CMC-Na溶液で用時希釈して調製した。なお、既存化学物質 No.3-0146の調製液について、１％懸濁液が７日間安定であること、0.04、0.2 及び１％懸濁液が規定の濃度であり均一であることが精工

化学株式会社により確認されている（分析結果書、平成３年11月16日及び12月２日付）。

２．試験動物

生後４週齢の Crj:CD (SD) 系の SPF ラットを、1991年11月20日に（雄：48匹，体重範囲 64～77g、雌：48匹，体重範囲 71～84g）、日本チャールス・リバー株式会社より受け入れ、雄６日間雌７日間の馴化飼育を行った。馴化期間中、一般状態観察を１日１回、体重測定を２回、眼底検査を１回実施し、異常がなく、順調に発育を示した動物を試験に用いた。

３．飼育環境条件

動物の飼育は、温度 23±３℃、湿度 55±10%、換気回数 10～15回／時間及び照明時間 12時間（午前８時から午後８時まで点灯）に設定されたバリアシステムの飼育室（142号室）において、ブラケット式金属製金網床ケージ（260W×380D×180H,mm）を用いて行った。ケージ当たりの収容匹数は、群分け前は５匹以内、群分け後は１匹とした。ケージの交換は２週に１回の頻度で行った。

飼育室内の清掃は１日１回以上、床の清拭消毒は１日１回の頻度で行った。なお、消毒には塩素系消毒薬（ヤクラックス，ヤクハン製薬株式会社）及びヨウ素系消毒薬（ダイヤザン，旭硝子株式会社）を１週間単位で交互に使用した。

飼料は固型飼料（CRF-1、オリエンタル酵母工業株式会社）を金属製給餌器を用いて、飲料水は水道水（札幌市水道水）を自動給水装置を用いて、それぞれ自由に摂取させた。給餌器の交換は２週に１回の頻度で、自動給水装置の水抜きは週１回、給水器の交換は２日に１回の頻度で実施した。

飼料の分析及び検査は財団法人日本食品分析センターで実施（分析試験成績書：第 44100152-001及び 44110115-001号）し、各混入物質について当社 SOPの許容範囲内であることを確認した。飲料水の水質検査は株式会社福田水文センターで実施（水質検査結果書：第 03529号）し、当社 SOPの水質基準の範囲内であることを確認した。

４．試験群の設定、群分け及び個体識別

試験群は、本試験の用量設定試験（14日間反復投与試験）の結果を参考に設定した。すなわち、最低用量である 100mg/kg 群の雄あるいは雌で、体重の増加抑制、血液凝固時間、プロトロンビン時間あるいは活性化部分トロンボプラスチン時間の延長、GOT の減少傾向、総コレステロールあるいはトリグリセリドの増加傾向、総蛋白及びアルブミンの減少、肝臓の体重重量比の上昇、副腎束状帯表層部にコレステリン様物質の沈着及

び単細胞壊死が認められ、既存化学物質 No.3-0146投与による影響が認められた。これらのことから、本試験の高用量は雌雄動物に対して確実に影響が現れると推測される100mg/kg/day、中間及び低用量は 100mg/kg 群における変動及び投与期間の延長を考慮して 20 及び４mg/kg/day（公比５）、さらに 0.5%CMC-Na溶液を投与する対照を設け、計４群とした（Table 1）。

動物数は、対照群で雌雄各14匹、４及び 20mg/kg群で雌雄各７匹、100mg/kg群で雌雄各14匹とした。群分けは、馴化飼育の最終日（投与開始２日前）に各群の体重が均一になるように体重別層化無作為抽出法により行った。

動物の識別は、群分け時にイヤーパンチを用いて、群識別を右耳に、ケージ内個体識別を左耳に行った。ケージには性別毎に色分けしたカードに試験番号、試験群及び動物番号を明記して標示した。

５．投与経路及び投与方法

投与経路は、被験物質が人体に経口的に暴露される可能性があることから、経口投与とした。投与は、胃ゾンデを用いて強制的に胃内に行い、１日１回連続 28回行った。投与容量は、体重１kg当たり10mlとして投与日に最も近い日に測定した体重に基づいて算出した。

投与は５週齢から開始し、投与開始時の平均体重（体重範囲）は雄で 132.5g（123～142g）、雌で 129.7g（118～145g）であった。投与時刻は午前10時から午後１時の間とした。

６．観察、測定及び検査項目

(1)一般状態観察

投与期間中、全例について１日１回以上の頻度で、視診及び触診により行動、外観などを観察した。

(2)体重測定

全例について、投与開始前日、投与１日目（投与前）、投与２、７、14、21及び28日目（投与終了日）、回復性試験開始日（回復１日目）、２、７及び14日目及び剖検日に、電子天秤（ザルトリウス 1401BMP7-2 及び 1407MP8-1、カールツァイス株式会社）を用いて測定した。なお、投与開始前日の体重は投与容量算出のために測定した。また、体重増加量［（投与28日目体重－投与１日目体重）及び（回復14日目体重－回復１日目体重）］、及びそれぞれの体重増加率［（体重増加量／投与１日目体重）×

100 及び（体重増加量／回復１日目体重）×100］を算出した。

(3)摂餌量測定

全例について投与１日目（投与前）、投与２、７、14、21及び28日目、回復性試験開始日、２、７及び14日目に、電子天秤（ザルトリウス 1401BMP7-2及び 1407MP8-1、カールツァイス株式会社）を用いて測定した。一定量をケージ毎にセットし、翌日に残量を測定し、１匹当たりの１日分の摂餌量を算出した。

(4)飲水量測定

全例について投与１日目（投与前）、投与２、７、14、21及び28日目、回復性試験開始日、２、７及び 14日目に、電子天秤（ザルトリウス 1401BMP7-2及び 1407MP8-1、カールツァイス株式会社）を用いて測定した。一定量をケージ毎にセットし、翌日に残量を測定し、１匹当たりの１日分の飲水量を算出した。

(5)尿検査

投与期間の最終週（投与23～24日目）及び回復期間最終週（回復11～12日目）に全例についてラット用代謝ケージ（夏目製作所）に収容して非絶食下で採尿を行った。約３時間の蓄尿の一部を用いて①～⑧の項目を検査し、21時間蓄尿を用いて⑨～⑬の項目の検査を行った。

①ｐＨ	試験紙法（マルティスティックス：マイルス・三共）
②蛋白（Pro）	試験紙法（マルティスティックス：マイルス・三共）
③糖　（Glu）	試験紙法（マルティスティックス：マイルス・三共）
④ケトン体（Ket）	試験紙法（マルティスティックス：マイルス・三共）
⑤ウロビリノーゲン（Uro）	試験紙法（マルティスティックス：マイルス・三共）
⑥ビリルビン（Bil）	試験紙法（マルティスティックス：マイルス・三共）
⑦潜血反応（Occult blood）	試験紙法（マルティスティックス：マイルス・三共）
⑧沈渣（Sediment）	鏡検
⑨比重（Grav）	屈折計法（アタゴ製ユリコン）
⑩尿量（U-Vol）	容量測定
⑪ナトリウム（U-Na）	炎光法（コーニング 480型炎光光度計）
⑫カリウム（U-K）	炎光法（コーニング 480型炎光光度計）
⑬クロール（U-Cl）	電量滴定法（平沼 Cl-6M型クロライドカウンター）

(6)血液学的検査

投与期間及び回復期間終了の翌日に全例について、約 16時間絶食した後、エーテル麻酔下で大腿静脈より採血し、EDTA·2K で処理した血液を用いて、①～⑨、⑬の項目について検査を行った。さらに、⑩の項目は無処理血液を用いて、⑪、⑫項目については腹部大動脈より採血し、クエン酸ナトリウムで処理した後、3000rpmで 10分間遠心分離して得られた血漿を用いて検査を行った。

①赤血球数（RBC）	電気抵抗法（コールター原理） （コールターカウンター T660型）
②ヘマトクリット値（Ht）	RBC，MCV値より算出 （コールターカウンター T660型）
③血色素量（Hb）	シアンメトヘモグロビン法（国際法） （コールターカウンター T660型）
④平均赤血球容積（MCV）	電気抵抗法（コールター原理） （コールターカウンター T660型）
⑤平均赤血球ヘモグロビン量（MCH）	RBC，Hb値より算出 （コールターカウンター T660型）
⑥平均赤血球ヘモグロビン濃度（MCHC）	Ht，Hb値より算出 （コールターカウンター T660型）
⑦網赤血球率（Ret）	Brecher法
⑧血小板数（Plat）	電気抵抗法（コールター原理） （コールターカウンター T660型）
⑨白血球数（WBC）	電気抵抗法（コールター原理） （コールターカウンター T660型）
⑩凝固時間（CT）	流体粘度変化による空気圧測定法 （グライナー社製マイクロコアグロメーター）
⑪プロトロンビン時間（PT）	トロンボプラスチン法 （AMELUNG KC-10A バクスターKK）
⑫活性化部分トロンボプラスチン時間（APTT）	エラジン酸法 （AMELUNG KC-10A バクスターKK）

⑬白血球型別百分率（Hemogram of WBC）　メイ・ギムザ染色標本鏡検

(7)血液化学的検査

投与期間及び回復期間終了の翌日に全例について、血液学的検査のための採血後、腹部大動脈より採血し 3000rpm で 10分間の遠心分離して、得られた血清を用いて次の検査を行った。

①ＧＯＴ	IFCC法（日立 7150形自動分析装置）
②ＧＰＴ	IFCC法（日立 7150形自動分析装置）
③アルカリフォスファターゼ（AlP）	ベッセイ・ローリー法 （日立 7150形自動分析装置）
④乳酸脱水素酵素（LDH）	ロブレスキー・ラ・デュー法 （日立7150形自動分析装置）
⑤γ－ＧＴＰ	包接Ｌ-γ-グルタミル-ｐ-ニトロアニリド 基質法（日立 7150形自動分析装置）
⑥血糖（Glu）	ヘキソキナーゼ法 （日立 7150形自動分析装置）
⑦総コレステロール（T-Cho）	酵素法（日立 7150形自動分析装置）
⑧トリグリセリド（TG）	遊離グリセロール消去法 （日立 7150形自動分析装置）
⑨総ビリルビン（T-Bil）	アゾビリルビン法（日立7150形自動分析装置）
⑩尿素窒素（BUN）	ウレアーゼ・インドフェノール法 （日立 7150形自動分析装置）
⑪クレアチニン（Crea）	ヤッフェ法（日立 7150形自動分析装置）
⑫ナトリウム（Na）	炎光法（コーニング 480型炎光光度計）
⑬カリウム（K）	炎光法（コーニング 480型炎光光度計）
⑭クロール（Cl）	電量滴定法 （平沼 CL-6M型クロライドカウンター）
⑮カルシウム（Ca）	OCPC法（日立 7150形自動分析装置）
⑯無機リン（P）	フィスケ・サバロー法 （日立 7150形自動分析装置）
⑰総蛋白（TP）	ビウレット法（日立 7150形自動分析装置）

⑱アルブミン（Alb）　　BCG法（日立 7150形自動分析装置）

⑲A／G比（A/G）　　TP，Alb値より算出する。

⑳蛋白分画　　セルロースアセテート膜電気泳動法

㉑リン脂質（PL）　　酵素法（日立7150形自動分析装置）

(8)剖検及び器官重量測定

投与期間及び回復期間終了の翌日に、全例について体外表を観察し、エーテル麻酔下で採血後、放血致死させ、全身の器官及び組織を肉眼的に観察した。また、摘出器官のうち脳、下垂体、甲状腺＊、肺、心臓、肝臓、腎臓＊、脾臓、副腎＊、精巣＊、卵巣＊、胸腺、精嚢、前立腺、精巣上体＊及び子宮の重量を電子天秤（FX-300、エー・アンド・デイ株式会社，ザルトリウス 1601AMP8-1、カールツァイス株式会社，PT320、メトラー社)を用いて測定した。なお、＊印の器官は左右別に測定した。さらに、器官体重重量比［（器官重量／動物体重）× 100］を算出した。

(9)病理組織学的検査

投与期間及び回復期間終了の翌日に、全例について肝臓、腎臓、脾臓、心臓、肺、脳、下垂体、副腎、甲状腺、上皮小体、胸腺、腸間膜リンパ節、膵臓、舌、下顎リンパ節、顎下腺、舌下腺、耳下腺、乳腺、皮膚、眼球、ハーダー腺、胸骨及び大腿骨（骨髄を含む）、脊髄（頸部）、骨格筋（外側広筋）、胸部大動脈、喉頭、気管、気管支、食道、胃（前胃・腺胃）、十二指腸、空腸、回腸、盲腸、結腸、直腸、膀胱、精巣、精巣上体、精嚢、前立腺、卵巣、子宮、膣、坐骨神経及び異常所見部位を10%中性緩衝ホルマリン液で固定し、保存した。なお、眼球及びハーダー腺はデビットソン液で固定した。全例の全摘出器官・組織についてパラフィン包埋後薄切し、ヘマトキシリン・エオジン染色標本を作製し、病理組織学的検査を行った。

7．統計処理

体重、摂餌量、飲水量、尿検査の定量的項目、血液学的検査及び血液化学的検査の各項目、器官重量、器官体重重量比は、Bartlettの検定法によって分散を検定した。その結果、等分散（$p>0.05$）を示した項目については一元配置分散分析法によって解析し、有意な場合（$p<0.10$）、Dunnettの検定法により対照群と既存化学物質 No. 3-0146投与群との比較を行った。一方、不等分散（$p<0.05$）を示した項目及び尿検査の定性的項目については Kruskal-Wallis 法により解析し、有意な場合（$p<0.10$）、Mann-WhitneyのU-検定法により対照群と既存化学物質 No. 3-0146投与群との比較を行った。

一般状態観察、剖検及び病理組織学的検査結果について、Fisherの正確確率検定法により対照群と既存化学物質 No. 3-0146 投与群との比較を行った。

なお、対照群との検定については、危険率５％以下を統計学的に有意とした。

成　　績

1．一般状態観察

一般状態観察の成績を Table ２～３、INDIVIDUAL DATA 1-1-1～1-4-2、Appendix 1-1 に示した。

(1)投与期間

雄では、頸部あるいは背部に痂皮が投与 15ないし 18日目以降に対照群の２例、20 mg/kg群の１例及び 100mg/kg群の２例に認められた。なお、出現頻度は対照群と比較して有意な差は認められなかった。

雌では、症状は認められなかった。

(2)回復期間

雄では、頸部あるいは背部に痂皮が回復期間中に対照群及び 100mg/kg群の各１例に認められた。なお、いずれも投与期間中に上記症状がみられた例であった。また、出現頻度は対照群と比較して有意な差は認められなかった。

雌では、症状は認められなかった。

2．体重推移

体重推移を Figure１～２、Table ４～５、INDIVIDUAL DATA 2-1-1～2-4-2に示した。

(1)投与期間

雌雄ともに、対照群と比較して有意な差は認められなかった。

(2)回復期間

雄では、対照群と比較して有意な差は認められなかった。

雌では、対照群と比較して 100mg/kg 群で回復７日目に体重の減少が認められたが、回復期間中の体重増加量及び増加率には有意な差は認められなかった。

3．摂餌量

摂餌量の変化を Figure ３～４、Table ６～７、INDIVIDUAL DATA 3-1-1～3-4-2に示した。

(1)投与期間

雌雄ともに、対照群と比較して有意な差は認められなかった。

(2)回復期間

雌雄ともに、対照群と比較して有意な差は認められなかった。

4．飲水量

飲水量の変化を Figure 5～6、Table 8～9、INDIVIDUAL DATA 4-1-1～4-4-2に示した。

(1)投与期間

雌雄ともに、対照群と比較して有意な差は認められなかった。

(2)回復期間

雌雄ともに、対照群と比較して有意な差は認められなかった。

5．尿検査

尿検査の成績を Table 10～13、INDIVIDUAL DATA 5-1-1～5-4-4に示した。

(1)投与 23日目検査

雌雄ともに、対照群と比較して有意な差は認められなかった。

(2)回復 11日目検査

雄では、対照群と比較して 100mg/kg群でカリウムの減少が認められたが、背景データ（Appendix 2-1）の範囲内の変動であった。

雌では、対照群と比較して有意な差は認められなかった。

6．血液学的検査

血液学的検査の成績を Table 14～17、INDIVIDUAL DATA 6-1-1～6-4-4に示した。

(1)投与期間終了時検査

雄では、対照群と比較して 20mg/kg以上の群で活性化部分トロンボプラスチン時間の延長が認められた。

雌では、対照群と比較して 100mg/kg 群で血色素量及び白血球数の減少、活性化部分トロンボプラスチン時間の延長が認められた。

(2)回復期間終了時検査

雄では、対照群と比較して血小板数の増加が認められたが、背景データ（Appendix 2-2）の範囲内の変動であった。

雌では、対照群と比較して有意な差は認められなかった。

7．血液化学的検査

血液化学的検査の成績を Table 18～21、INDIVIDUAL DATA 7-1-1～7-4-4に示した。

(1)投与期間終了時検査

雄では、対照群と比較して 20mg/kg群でカルシウムの減少が、100mg/kg群でアルカリフォスファターゼの増加、カルシウムの減少が認められた。また、有意な差は認められなかったが、100mg/kg群で GOT及び乳酸脱水素酵素の減少傾向がみられた。

雌では、対照群と比較して 100mg/kg群でアルブミンの減少、A/G比及びアルブミン分画の低下、α_1-グロブリン分画の上昇、乳酸脱水素酵素の減少、カリウムの減少が認められた。また、有意な差は認められなかったが、100mg/kg群で GOTの減少傾向及びアルカリフォスファターゼの増加傾向がみられた。

(2)回復期間終了時検査

雄では、対照群と比較して有意な差は認められなかった。

雌では、対照群と比較して 100mg/kg 群で総蛋白及びアルブミンの減少、アルカリフォスファターゼの増加、カリウム及びカルシウムの減少が認められた。

8．器官重量

器官重量及び器官体重重量比の成績を Table 22～25、INDIVIDUAL DATA 8-1-1～8-4-6に示した。

(1)投与期間終了時解剖例

雄では、対照群と比較して 100mg/kg 群で肝臓及び腎臓（左右）の体重重量比の上昇が認められた。また、有意な差は認められなかったが、100mg/kg群で副腎重量の増加傾向がみられた。

雌では、対照群と比較して 100mg/kg 群で甲状腺（右）重量の増加及び体重重量比の上昇、肝臓及び腎臓（右）の体重重量比の上昇、副腎（左右）重量の増加及び体重重量比の上昇が認められた。また、有意な差は認められなかったが、100mg/kg群で甲状腺（左）及び腎臓（左）重量の増加傾向がみられた。

(2)回復期間終了時解剖例

雌雄ともに、対照群と比較して有意な差は認められなかった。

9．剖検

剖検の成績を Table 26～27、INDIVIDUAL DATA 9-1-1～9-4-2、Appendix 1-2 に示した。

(1)投与期間終了時解剖例

雄では、精巣（左）の小型が対照群の１例に、甲状腺（右）及び上皮小体（右）の無形成、甲状腺（左）の大型が 20mg/kg群の雄１例に、頸部あるいは背部に痂皮が対照群、20及び 100mg/kg 群の各１例に認められた。なお、出現頻度はいずれの所見も対照群と比較して有意な差は認められなかった。

雌では、異常は認められなかった。

(2)回復期間終了時解剖例

雄では、頸部あるいは背部に痂皮が対照群及び 100mg/kg 群の各１例に認められた。なお、出現頻度は対照群と比較して有意な差は認められなかった。

雌では、異常は認められなかった。

10．病理組織学的検査

病理組織学的検査の成績を Table 28～29、INDIVIDUAL DATA 10-1-1～10-4-2、Appendix 1-2に示した。

(1)投与期間終了時解剖例

腎臓：尿細管上皮の硝子滴沈着及び好酸体沈着、停留嚢胞、尿円柱、間質におけるリンパ球を主とする限局性の細胞浸潤が対照群及び既存化学物質 No.3-0146投与群の雄１～２例に認められた。

肺：血管壁における石灰沈着が対照群及び 100mg/kg群の雄各１例、20mg/kg群の雌１例に認められた。

下垂体：線毛上皮嚢胞は対照群及び 100mg/kg群の雄各１例、４mg/kg群の雌１例に認められた。

甲状腺（右）：無形成が 20mg/kg群の雄１例に、胚性甲状腺の遺残が 100mg/kg 群の雌１例に認められた。

上皮小体（右）：無形成が、甲状腺（右）の無形成のみられた 20mg/kg群の雄１例に認められた。

副腎：束状帯内層を主とするコレステリン様物質の沈着及び皮質細胞の単細胞壊死（Photo. H-1～H-2）が 100mg/kg群の雄１例に認められた。

膀胱：漿膜におけるリンパ球を主とする細胞浸潤が 100mg/kg群の雄１例に認められた。

前立腺：前立腺炎が 100mg/kg群の雄２例に認められた。

卵巣（左）：卵胞嚢胞が 20mg/kg群の雌１例に認められた。

皮膚：剖検における頸部あるいは背部の痂皮に対応して次の所見が認められた。対照群の雄１例に潰瘍、表皮の肥厚及び真皮の線維化が、20mg/kg 群の雄１例に潰瘍、表皮の肥厚、真皮の線維化及び皮下織における膿瘍、100mg/kg群の雄１例に潰瘍、真皮の肥厚、真皮の線維化、真皮における膿瘍、痂皮形成、皮下織におけるリンパ球を主とする細胞浸潤及び皮下織の水腫が認められた。

その他に肝臓を含め異常は認められなかった。なお、剖検における甲状腺（左）の大型及び精巣（左）の小型に対応する所見は認められなかった。また、出現頻度はいずれの所見も対照群と比較して有意な差は認められなかった。

(2)回復期間終了時解剖例

腎臓：尿細管上皮の硝子滴沈着及び好酸体沈着が 100mg/kg群の雄２例に認められた。

肺：血管壁におけるカルシウム沈着が 100mg/kg群の雄１例に認められた。

副腎：束状帯内層を主とする皮質細胞の単細胞壊死（Photo. H-3～H-4）が 100mg/kg群の雄１例に認められた。

前立腺：前立腺炎が対照群の雄３例及び 100mg/kg群の雄１例に認められた。

卵巣（左）：黄体嚢胞が 100mg/kg群の雌１例に認められた。

皮膚：剖検における頸部あるいは背部の痂皮に対応して次の所見が認められた。対照群の雄１例に潰瘍、表皮の肥厚、真皮の線維化、真皮における膿瘍及び痂皮形成が、100mg/kg群の雄１例に表皮の肥厚、真皮の線維化、痂皮形成、真皮表層の水腫及び表皮の水腫が認められた。

その他に肝臓を含め異常は認められなかった。なお、出現頻度はいずれの所見も対照群と比較して有意な差は認められなかった。

考　察

既存化学物質 No.3-0146の4、20及び 100mg/kg/dayを Crj:CD (SD) 系雌雄ラットに28日間経口反復投与し、その毒性及び投与後14日間休薬した際の回復性を検討した。

肝臓に対する影響として、血中のアルカリフォスファターゼの増加、アルブミンの減少及び A/G比の低下が 100mg/kg群の雌で、活性化部分トロンボプラスチン時間の延長が 20 mg/kg 以上の群の雄及び 100mg/kg群の雌で、肝臓の体重重量比の上昇が 100mg/kg群の雌雄で認められた。これらの変化は、病理組織学的な異常を伴うものではなかったが、14日間反復投与試験と同様であり、既存化学物質 No.3-0146の肝臓・胆道系に対する影響が示唆された[1]。さらに、100mg/kg群の雌では血中の乳酸脱水素酵素の減少が認められ、前述した肝臓に対する影響に伴って肝機能低下を示しているものと考えられた。以上のように肝臓に影響を及ぼす要因としては、被験物質の化学構造及びその代謝過程にあるものと考えられた。既存化学物質 No.3-0146は、第2アミンと芳香環を有する分子量 290の物質である。よってその代謝過程は、水酸化、グルクロン酸抱合を経て大部分は胆汁中に排泄されるものと予想される[2]。その後、腸管から再吸収され、腸肝循環する可能性があり[1]、既存化学物質 No.3-0146の未変化体ないし代謝産物が肝臓や胆道系に影響を及ぼすことが推察された。

甲状腺に対する影響として、重量の増加及び体重重量比の上昇が 100mg/kg 群の雌で認められた。甲状腺ホルモンの貯蔵、代謝及び胆汁排泄（腸肝循環を含む）に関して肝臓が重要な働きをする[1]ことから、既存化学物質 No.3-0146の肝臓に対する影響との関連が考えられた。

副腎に対する影響として、重量の増加及び体重重量比の上昇が 100mg/kg 群の雌で、束状帯内層を主とするコレステリン様物質の沈着及び皮質細胞の単細胞壊死が同群の雄1例で認められた。このことから、既存化学物質 No.3-0146投与による副腎機能の亢進が窺われるが、本所見について 300あるいは 1000mg/kgを14日間投与した場合と比較すると本試験では内層に限局しており、その程度は軽いものであった。また、血中のカルシウムの減少が 20mg/kg以上の群の雄で、カリウムの減少が 100mg/kg 群の雌で認められ、副腎を介した糖質あるいは鉱質コルチコイド作用の亢進[3]に基づく変化と考えられた。

腎臓に対する影響として、体重重量比の上昇が 100mg/kg 群の雌雄で認められた。しかしながら、血液及び病理変化はみられなかったことから二次的な影響と考えられた。

その他に、投与期間終了時に 100mg/kg 群の雌で血色素量の減少が認められた。同様な変化は 14日間投与試験においても認められており、既存化学物質 No.3-0146 投与による影響と考えられた。

上述の変化はその多くが14日間の休薬により消失し、回復傾向はあるものと考えられた。しかし、100mg/kg群の雌で血中の総蛋白、アルブミン、アルカリフォスファターゼ、カリウム及びカルシウムが投与期間終了時と同様の変動を示し、100mg/kg群の雄１例で副腎束状帯に内層を主としてに単細胞の壊死が残存していることから、肝臓及び副腎に対する影響は完全には回復されないものと考えられた。

20及び 100mg/kg 群でみられた頸部あるいは背部の痂皮については、対照群で認められた皮膚所見と比較して程度及び観察例数に差がないことから、既存化学物質 No.3-0146投与との関連性はないものと考えられた。また、100mg/kg群における白血球数の減少については、背景データ（Appendix 2-3）の範囲内の変動であり、1000mg/kg 投与では認められないことから、既存化学物質 No.3-0146投与との関連性はないものと考えられた。

以上のことから、本試験の既存化学物質 No.3-0146投与による無影響量は雄で４mg/kg/day、雌で 20mg/kg/dayと考えられた。

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

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認められなかった。

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3．[redacted](1983)．生理学，p536～543．株式会社文光堂．第17版第13刷．

資料の保管

下記の資料を試験終了後10年間、株式会社化合物安全性研究所　資料保管室及び検体保管室に保管し、その後の保管については試験委託者との協議により決定する。

1．試験計画書、試験計画書変更確認書
2．試験関連文書
3．生データ
4．報告書関係
5．標本
6．写真ネガ
7．被験物質サンプル

試験責任者・副試験責任者　承認

試験責任者：[redacted]　1992年8月21日

副試験責任者：[redacted]　1992年8月21日

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Figure 2. Body weight changes of female rats dosed orally with Substance No.3-0146 for 28 days followed by the 14-day recovery period

Figure 3. Food consumption of male rats dosed orally with Substance No.3-0146 for 28 days followed by the 14-day recovery period

Figure 4. Food consumption of female rats dosed orally with Substance No.3-0146 for 28 days followed by the 14-day recovery period

Figure 5. Water consumption of male rats dosed orally with Substance No.3-0146 for 28 days followed by the 14-day recovery period

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Table 18. Biochemical findings in male rats killed at the end of the administration period of the 28-day repeated dose oral toxicity study of Substance No.3-0146

Table 19. Biochemical findings in female rats killed at the end of the administration period of the 28-day repeated dose oral toxicity study of Substance No.3-0146

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Table 21. Biochemical findings in female rats killed at the end of the 14-day recovery period after the 28-day oral administration of Substance No.3-0146

Table 22. Absolute and relative organ weights in male rats killed at the end of the administration period of the 28-day repeated dose oral toxicity study of Substance No.3-0146

Table 23. Absolute and relative organ weights in female rats killed at the end of the administration period of the 28-day repeated dose oral toxicity study of Substance No.3-0146

Table 24. Absolute and relative organ weight in male rats killed at the end of the 14-day recovery period after the 28-day oral administration of Substance No.3-0146

Table 25. Absolute and relative organ weight in female rats killed at the end of the 14-day recovery period after the 28-day oral administration of Substance No.3-0146

Table 26. Gross findings in rats killed at the end of the administration period of the 28-day repeated dose oral toxicity study of Substance No.3-0146

Table 27. Gross findings in rats killed at the end of the 14-day recovery period after the 28-day oral administration of Substance No.3-0146

Table 28. Histopathological findings in rats killed at the end of the administration period of the 28-day repeated dose oral toxicity study of Substance No.3-0146

Table 29. Histopathological findings in rats killed at the end of the 14-day recovery period after the 28-day oral administration of Substance No.3-0146

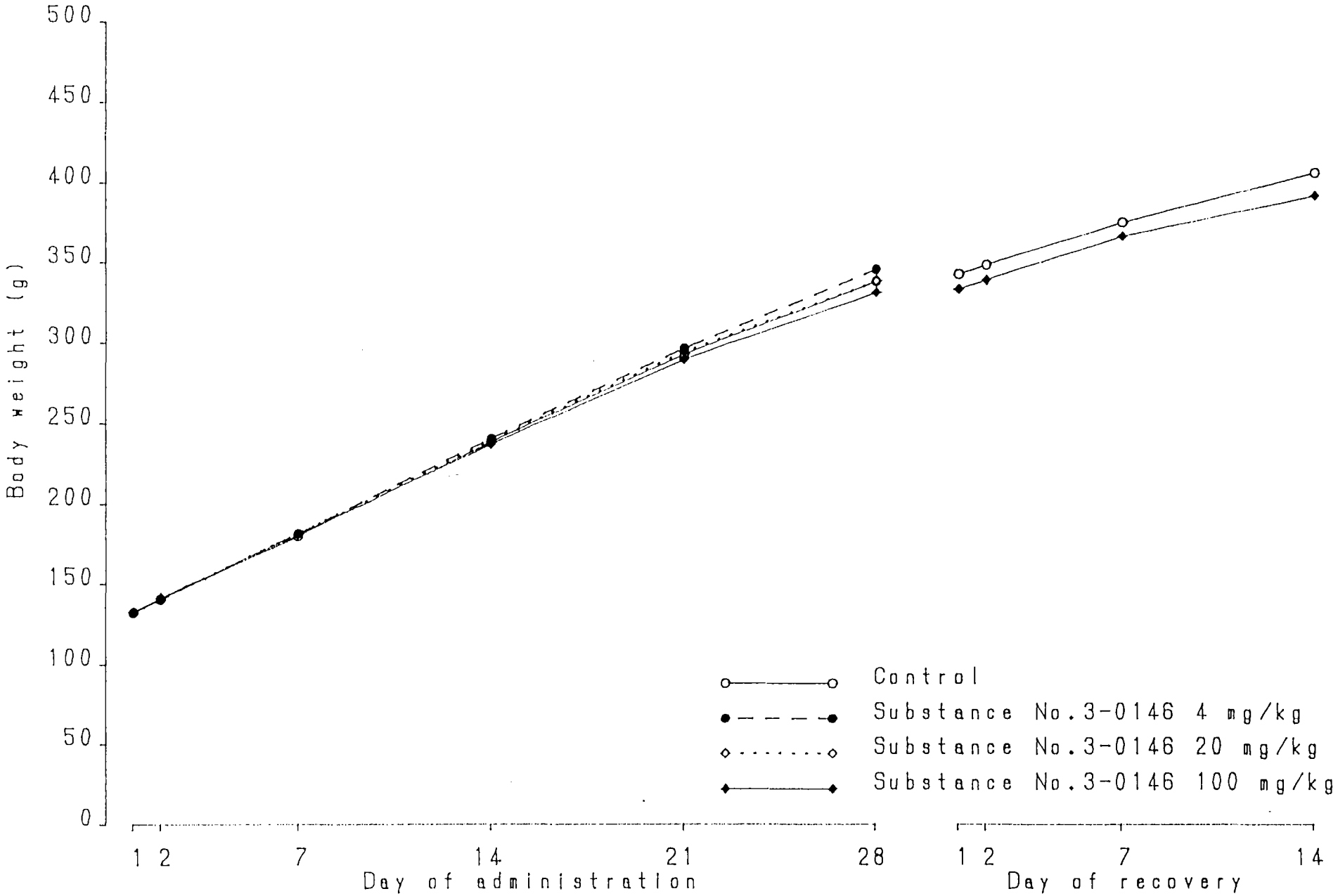

Figure 1. Body weight changes of male rats dosed orally with Substance No.3-0146 for 28 days followed by the 14-day recovery period

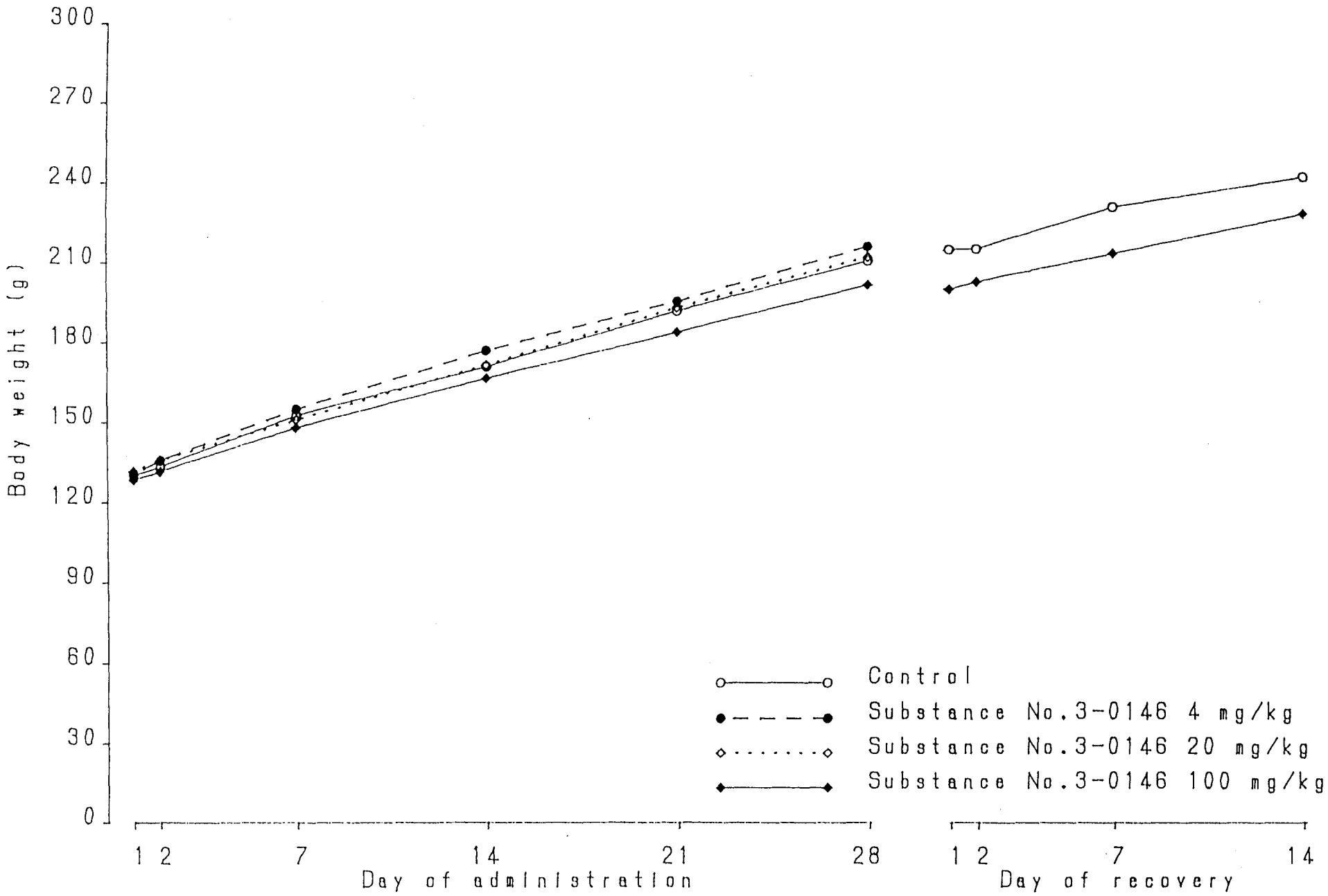

Figure 2. Body weight changes of female rats dosed orally with Substance No.3-0146 for 28 days followed by the 14-day recovery period

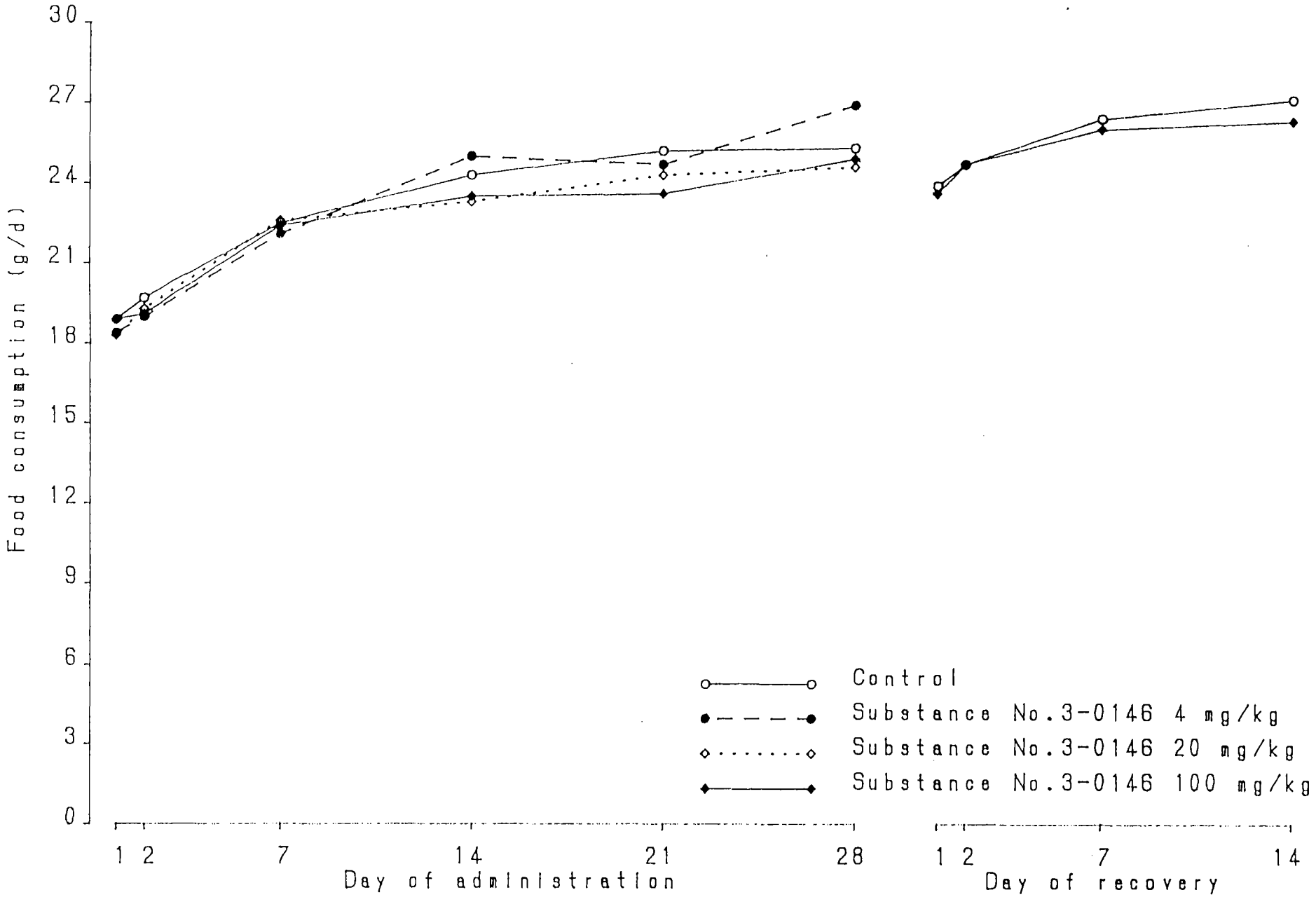

Figure 3. Food consumption of male rats dosed orally with Substance No.3-0146 for 28 days followed by the 14-day recovery period

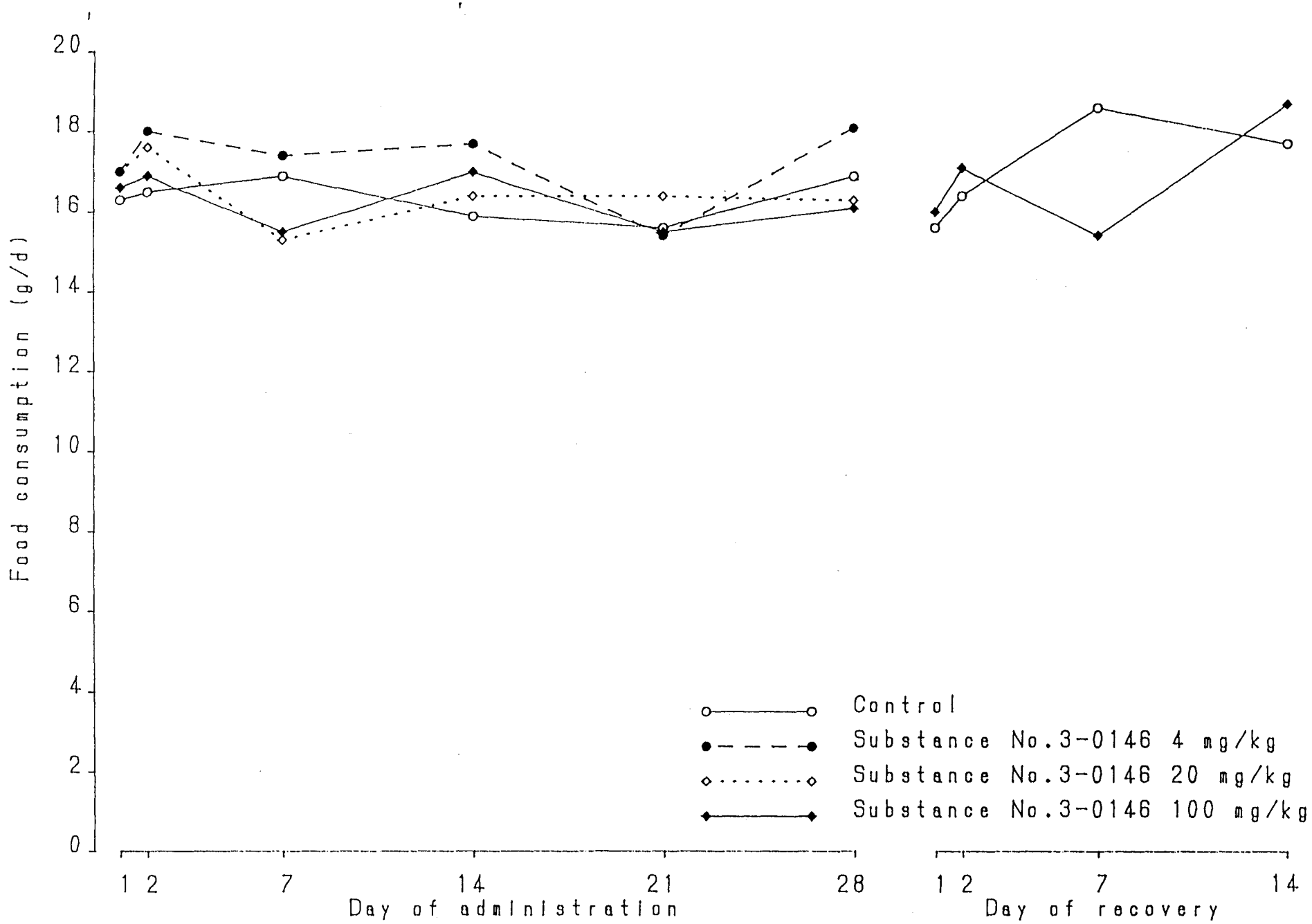

Figure 4. Food consumption of female rats dosed orally with Substance No.3-0146 for 28 days followed by the 14-day recovery period

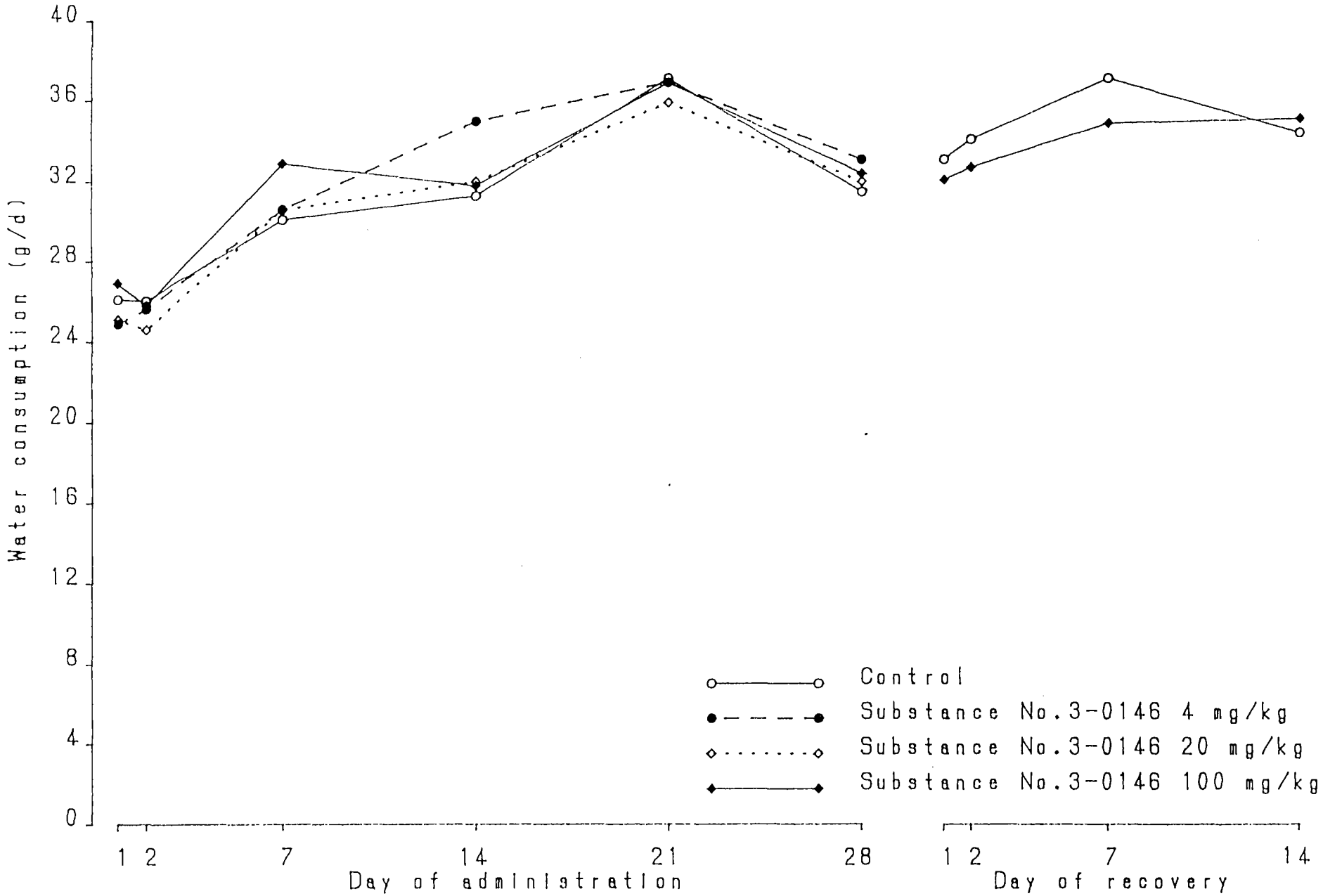

Figure 5. Water consumption of male rats dosed orally with Substance No.3-0146 for 28 days followed by the 14-day recovery period

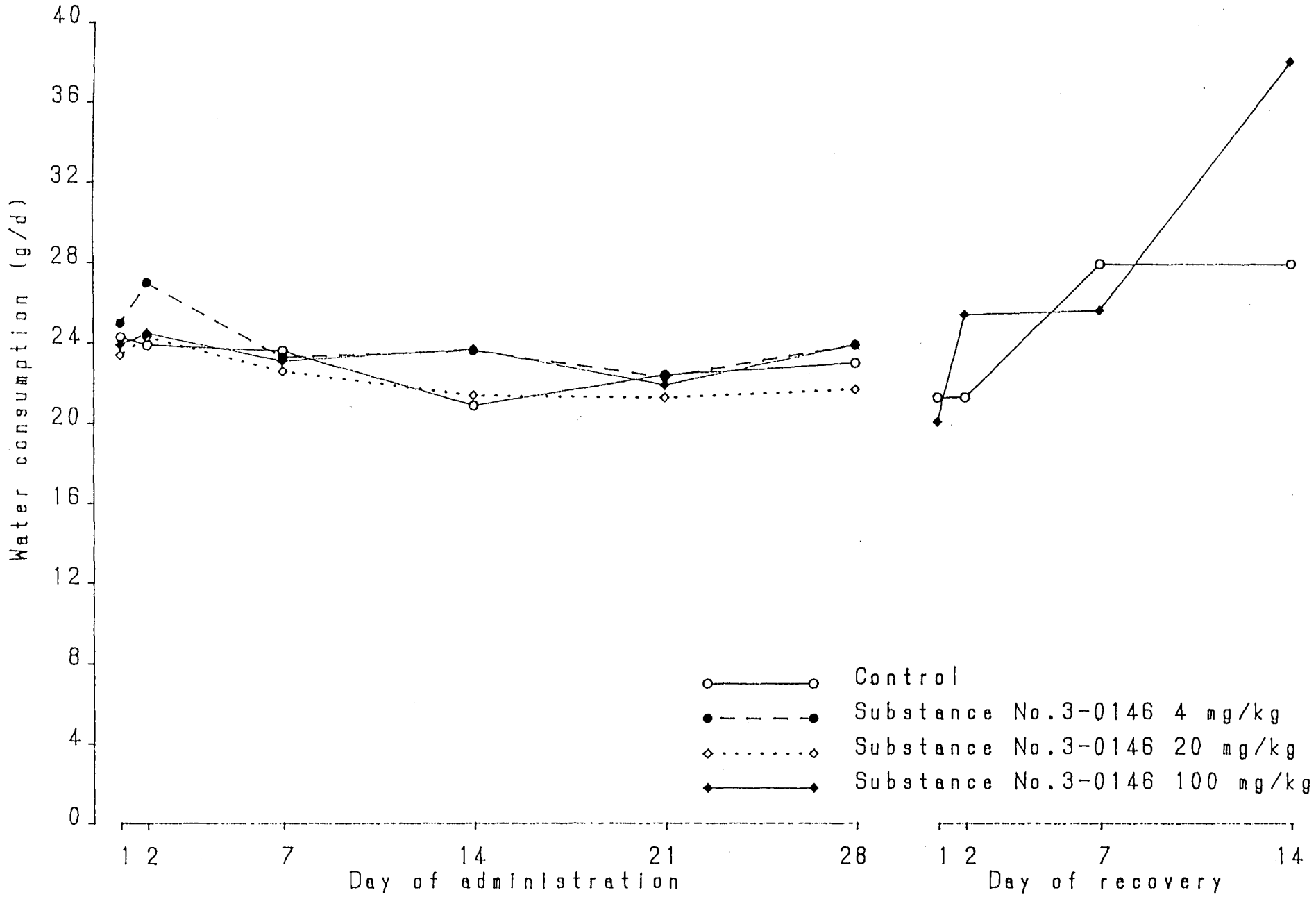

Figure 6. Water consumption of female rats dosed orally with Substance No.3-0146 for 28 days followed by the 14-day recovery period

Table 1. Experimental design for the 28-day repeated dose oral toxicity study of Substance No.3-0146 and the 14-day recovery study in rats

Group	Concentration of Substance No.3-0146 (w/v %)	Volume (ml/kg)	No. of animals[a]					
			Total		Administration		Recovery	
			Male	Female	Male	Female	Male	Female
Control[b]	0	10	14	14	7[c]	7	7[c]	7
Substance No.3-0146[d] 4 mg/kg	0.04	10	7	7	7	7	0	0
Substance No.3-0146 20 mg/kg	0.2	10	7	7	7	7	0	0
Substance No.3-0146 100 mg/kg	1	10	14	14	7	7	7	7

a: Crj:CD(SD) rats were dosed orally for 28 days from the age of 5 weeks.
b: Control was 0.5% carboxymethylcellulose sodium in distilled water.
c: Killed at the end of the administration or recovery period.
d: Substance No.3-0146 was suspended in control solution.

Table 2. General appearance of rats during the administration period of the 28-day repeated dose oral toxicity study of Substance No.3-0146

	Male				Female			
		Substance No.3-0146 (mg/kg)				Substance No.3-0146 (mg/kg)		
Group	Control	4	20	100	Control	4	20	100
No. of animals examined	14	7	7	14	14	7	7	14
Scab/Disseminated scabs of cervical or dorsal region	2[a]	0	1	2	0	0	0	0

a: Values are no. of animals with findings.

Table 3. General appearance of rats during the 14-day recovery period after the 28-day oral administration of Substance No.3-0146

	Male		Female	
Group	Control	Substance No.3-0146 100 mg/kg	Control	Substance No.3-0146 100 mg/kg
No. of animals examined	7	7	7	7
Scab/Disseminated scabs of cervical or dorsal region	1[a]	1	0	0

a: Values are no. of animals with findings.

Table 4. Body weight changes of male rats dosed orally with Substance No.3-0146 for 28 days followed by the 14-day recovery period

Group	No. of animals	Day of administration 1	2	7	14	21	28	Body weight gain Day 1-28	% a
Control	14	b 132.0	140.7	179.8	238.4	292.9	338.1	206.071	156.420
		5.3	5.2	6.6	12.0	17.4	19.9	19.998	17.229
Substance No.3-0146 4 mg/kg	7	132.6	140.6	181.9	240.4	296.6	345.4	212.857	160.510
		4.7	6.3	9.4	13.6	17.5	23.5	20.924	14.199
Substance No.3-0146 20 mg/kg	7	132.6	141.3	181.6	238.7	294.1	338.3	205.714	155.394
		4.2	5.1	7.4	10.5	16.1	15.6	16.173	14.362
Substance No.3-0146 100 mg/kg	14	132.9	141.5	181.3	236.9	289.4	331.1	198.286	149.242
		5.9	6.1	9.2	13.3	17.2	22.2	18.681	12.261

(continued)

Table 4. (continued)

Group	No. of animals	Day of recovery 1	2	7	14	Body weight gain Day 1-14	%
Control	7	342.7	348.6	375.0	405.7	63.000	18.239
		29.5	32.1	39.0	43.7	16.703	3.600
Substance No.3-0146 100 mg/kg	7	333.1	338.9	366.1	391.6	58.429	17.447
		12.4	14.0	20.4	24.7	12.869	3.257

a: (Body weight gain / body weight on day 1) x 100.
b: Values are means and S.D. thereunder, and expressed in gram.

Table 5. Body weight changes of female rats dosed orally with Substance No.3-0146 for 28 days followed by the 14-day recovery period

Group	No. of animals	Day of administration 1	2	7	14	21	28	Body weight gain Day 1-28	% a
Control	14	b 129.8	133.3	152.7	171.1	191.9	210.6	80.786	62.166
		6.8	7.2	10.2	16.5	19.0	19.8	16.273	11.740
Substance No.3-0146 4 mg/kg	7	130.4	135.6	155.0	177.0	195.4	216.0	85.571	65.366
		6.9	7.7	9.3	14.6	19.5	21.6	16.257	10.521
Substance No.3-0146 20 mg/kg	7	131.4	135.9	151.1	171.7	193.1	212.1	80.714	61.437
		4.5	5.6	5.1	12.4	13.2	17.3	16.173	12.258
Substance No.3-0146 100 mg/kg	14	128.3	131.4	148.1	166.7	183.9	201.7	73.429	57.297
		5.2	5.0	7.1	8.5	8.7	11.5	9.725	8.013

(continued)

Table 5. (continued)

Group	No. of animals	Day of recovery 1	2	7	14	Body weight gain Day 1-14	%
Control	7	214.9	215.1	230.6	241.9	27.000	12.566
		13.5	16.5	15.9	17.3	8.446	3.883
Substance No.3-0146 100 mg/kg	7	199.9	202.7	213.3*	228.1	28.286	14.096
		13.5	13.4	13.5	17.8	5.851	2.440

a: (Body weight gain / body weight on day 1) x 100.
b: Values are means and S.D. thereunder, and expressed in gram.
*: Differs from control, $p<0.05$.

Table 6. Food consumption of male rats dosed orally with Substance No.3-0146 for 28 days followed by the 14-day recovery period

Group	No. of animals	Day of administration 1	2	7	14	21	28
Control	14	18.9[a] 1.4	19.7 1.3	22.5 1.5	24.3 1.8	25.2 3.7	25.3 2.8
Substance No.3-0146 4 mg/kg	7	18.4 0.5	19.0 1.9	22.1 2.4	25.0 2.7	24.7 2.5	26.9 4.1
Substance No.3-0146 20 mg/kg	7	18.3 1.0	19.3 1.4	22.6 1.6	23.3 2.1	24.3 2.9	24.6 1.9
Substance No.3-0146 100 mg/kg	14	18.9 1.4	19.1 2.0	22.4 2.3	23.5 2.0	23.6 2.2	24.9 2.8

(continued)

Table 6. (continued)

Group	No. of animals	Day of recovery 1	2	7	14
Control	7	23.9 3.2	24.7 3.0	26.4 3.8	27.1 3.5
Substance No.3-0146 100 mg/kg	7	23.6 1.7	24.7 1.8	26.0 2.8	26.3 3.0

a: Values are means and S.D. thereunder, and expressed in gram/day.

Table 7. Food consumption of female rats dosed orally with Substance No.3-0146 for 28 days followed by the 14-day recovery period

Group	No. of animals	Day of administration 1	2	7	14	21	28
Control	14	16.3[a] 2.0	16.5 1.9	16.9 2.0	15.9 2.7	15.6 2.5	16.9 1.8
Substance No.3-0146 4 mg/kg	7	17.0 2.4	18.0 1.7	17.4 1.6	17.7 1.6	15.4 2.9	18.1 2.2
Substance No.3-0146 20 mg/kg	7	17.0 1.6	17.6 1.5	15.3 1.3	16.4 2.8	16.4 2.1	16.3 3.6
Substance No.3-0146 100 mg/kg	14	16.6 1.4	16.9 1.4	(13)[b] 15.5 1.5	17.0 1.2	15.5 2.4	16.1 2.2

(continued)

Table 7. (continued)

Group	No. of animals	Day of recovery 1	2	7	14
Control	7	15.6	16.4	18.6	17.7
		2.2	4.8	4.3	3.9
Substance No.3-0146 100 mg/kg	7	16.0	17.1	15.4	18.7
		3.1	2.4	3.2	4.0

a: Values are means and S.D. thereunder, and expressed in gram/day.
b: Values in parentheses are no. of animals examined.

Table 8. Water consumption of male rats dosed orally with Substance No.3-0146 for 28 days followed by the 14-day recovery period

Group	No. of animals	Day of administration 1	2	7	14	21	28
Control	14	26.1[a] 2.3	26.0 2.1	30.1 2.3	31.3 3.5	37.1 5.7	31.5 4.7
Substance No.3-0146 4 mg/kg	7	24.9 2.5	25.6 2.2	30.6 4.8	35.0 5.9	36.9 5.8	33.1 6.2
Substance No.3-0146 20 mg/kg	7	25.1 1.2	24.6 1.0	30.6 2.4	32.0 3.2	35.9 3.4	32.0 4.6
Substance No.3-0146 100 mg/kg	14	26.9 2.5	25.8 3.0	32.9 8.4	31.8 4.3	36.9 4.6	32.4 4.9

(continued)

Table 8. (continued)

Group	No. of animals	Day of recovery 1	2	7	14
Control	7	33.1	34.1	37.1	34.4
		9.8	6.5	10.0	9.3
Substance No.3-0146 100 mg/kg	7	32.1	32.7	34.9	35.1
		3.2	3.4	3.4	3.8

a: Values are means and S.D. thereunder, and expressed in gram/day.

Table 9. Water consumption of female rats dosed orally with Substance No.3-0146 for 28 days followed by the 14-day recovery period

Group	No. of animals	Day of administration 1	2	7	14	21	28
Control	14	24.3[a] 5.6	23.9 4.2	23.6 3.5	20.9 6.1	22.4 5.3	23.0 2.9
Substance No.3-0146 4 mg/kg	7	25.0 3.8	27.0 4.7	23.3 4.9	23.6 2.0	22.3 5.1	23.9 4.7
Substance No.3-0146 20 mg/kg	7	23.4 4.3	24.3 4.5	22.6 3.7	21.4 5.3	21.3 4.2	21.7 6.2
Substance No.3-0146 100 mg/kg	14	23.9 3.3	24.5 4.0	23.1 4.3	23.7 5.0	21.9 4.4	23.9 5.4

(continued)

Table 9. (continued)

Group	No. of animals	Day of recovery 1	2	7	14
Control	7	21.3	21.3	27.9	27.9
		4.3	8.1	5.8	10.6
Substance No.3-0146 100 mg/kg	7	20.1	25.4	25.6	38.0
		3.3	7.7	10.9	20.7

a: Values are means and S.D. thereunder, and expressed in gram/day.

Table 10. Urinary findings in male rats on day 23 of administration of the 28-day repeated dose oral toxicity study of Substance No.3-0146

Group	No. of animals	pH				Pro				Glu	Ket		Uro	Bil	Occult blood		
		6.5	7.5	8.0	8.5	-	±	+	++	-	-	±	0.1 EU/dl	-	-	±	+
Control	14	0[a]	3	4	7	2	8	3	1	14	12	2	14	14	14	0	0
Substance No.3-0146 4 mg/kg	7	0	0	3	4	0	4	3	0	7	7	0	7	7	7	0	0
Substance No.3-0146 20 mg/kg	7	0	1	1	5	0	4	3	0	7	7	0	7	7	7	0	0
Substance No.3-0146 100 mg/kg	14	1	1	2	10	0	8	5	1	14	14	0	14	14	12	1	1

Group	No. of animals	Urinary sediments							Specific gravirity			
		RBC	WBC	Epithelial cell				Others				
				Squamous		Round	Small round		1.021-1.030	1.031-1.040	1.041-1.050	1.050<
		-	-	-	±	-	-	-				
Control	14	14	14	14	0	14	14	14	1	5	5	3
Substance No.3-0146 4 mg/kg	7	7	7	6	1	7	7	7	1	2	4	0
Substance No.3-0146 20 mg/kg	7	7	7	7	0	7	7	7	1	2	3	1
Substance No.3-0146 100 mg/kg	14	14	14	13	1	14	14	14	2	3	9	0

(continued)

Table 10. (continued)

Group	No. of animals	U-Vol ml/21hr	U-Na mEq/21hr	U-K mEq/21hr	U-Cl mEq/21hr
		b			
Control	14	14.75	1.3352	3.2707	1.9842
		3.58	0.2883	0.4753	0.3835
Substance No.3-0146 4 mg/kg	7	16.07	1.3574	3.2310	1.9239
		4.47	0.4353	0.7373	0.6401
Substance No.3-0146 20 mg/kg	7	16.29	1.4273	3.2554	1.9981
		5.95	0.4412	0.7116	0.7116
Substance No.3-0146 100 mg/kg	14	15.71	1.2596	3.0983	1.8231
		3.89	0.4742	0.6599	0.6280

a: Values are no. of animals with findings.
b: Values are means and S.D. thereunder.

Table 11. Urinary findings in female rats on day 23 of administration of the 28-day repeated dose oral toxicity study of Substance No.3-0146

Group	No. of animals	pH					Pro				Glu	Ket	Uro	Bil	Occult blood	
		6.5	7.0	7.5	8.0	8.5	-	±	+	++	-	-	0.1 EU/dl	-	-	±
Control	14	0[a]	1	1	3	9	2	10	2	0	14	14	14	14	14	0
Substance No.3-0146 4 mg/kg	7	0	1	0	2	4	1	4	2	0	7	7	7	7	7	0
Substance No.3-0146 20 mg/kg	7	2	0	1	3	1	2	2	2	1	7	7	7	7	7	0
Substance No.3-0146 100 mg/kg	14	3	0	3	2	6	3	3	6	2	14	14	14	14	12	2

Group	No. of animals	Urinary sediments							Specific gravirity			
		RBC	WBC	Epithelial cell: Squamous		Epithelial cell: Round	Epithelial cell: Small round	Epithelial cell: Others	1.011-1.020	1.031-1.040	1.041-1.050	1.050<
		-	-	-	±	-	-	-				
Control	14	14	14	13	1	14	14	14	0	4	8	2
Substance No.3-0146 4 mg/kg	7	7	7	7	0	7	7	7	0	2	5	0
Substance No.3-0146 20 mg/kg	7	7	7	6	1	7	7	7	0	1	4	2
Substance No.3-0146 100 mg/kg	14	14	14	13	1	14	14	14	2	6	4	2

(continued)

Table 11. (continued)

Group	No. of animals	U-Vol ml/21hr	U-Na mEq/21hr	U-K mEq/21hr	U-Cl mEq/21hr
		b			
Control	14	10.18	1.0357	2.2481	1.4516
		3.89	0.3987	0.6410	0.4855
Substance No.3-0146 4 mg/kg	7	12.14	1.1986	2.4124	1.6340
		3.90	0.1535	0.3337	0.1878
Substance No.3-0146 20 mg/kg	7	9.86	1.1560	2.2726	1.5374
		4.59	0.1604	0.4533	0.2572
Substance No.3-0146 100 mg/kg	14	10.89	0.8969	2.0031	1.2014
		4.05	0.3044	0.5757	0.4328

a: Values are no. of animals with findings.
b: Values are means and S.D. thereunder.

Table 12. Urinary findings in male rats on day 11 of recovery after the 28-day oral administration of Substance No.3-0146

Group	No. of animals	pH				Pro		Glu	Ket	Uro	Bil	Occult blood	
		7.0	7.5	8.0	8.5	±	+	-	-	0.1 EU/dl	-	-	+
Control	7	1[a]	1	3	2	2	5	7	7	7	7	7	0
Substance No.3-0146 100 mg/kg	7	0	4	1	2	3	4	7	7	7	7	6	1

Group	No. of animals	Urinary sediments							Specific gravirity			
		RBC	WBC	Epithelial cell								
				Squamous		Round	Small round	Others				
		-	-	-	±	-	-	-	1.021-1.030	1.031-1.040	1.041-1.050	1.050<
Control	7	7	7	6	1	7	7	7	0	1	3	3
Substance No.3-0146 100 mg/kg	7	7	7	6	1	7	7	7	2	2	2	1

(continued)

Table 12. (continued)

Group	No. of animals	U-Vol ml/21hr	U-Na mEq/21hr	U-K mEq/21hr	U-Cl mEq/21hr
		b			
Control	7	14.57	1.5774	3.7283	2.3079
		4.46	0.2681	0.5048	0.2692
Substance No.3-0146 100 mg/kg	7	15.21	1.1290	2.8381*	1.5587
		2.64	0.6603	0.8212	0.9036

a: Values are no. of animals with findings.
b: Values are means and S.D. thereunder.
*: Differs from control, $p<0.05$.

Table 13. Urinary findings in female rats on day 11 of recovery after the 28-day oral administration of Substance No.3-0146

Group	No. of animals	pH				Pro				Glu	Ket	Uro	Bil	Occult blood
		7.0	7.5	8.0	8.5	-	±	+	++	-	-	0.1 EU/dl	-	-
Control	7	0[a]	1	2	4	1	3	2	1	7	7	7	7	7
Substance No.3-0146 100 mg/kg	7	1	2	2	2	0	4	3	0	7	7	7	7	7

Group	No. of animals	Urinary sediments							Specific gravirity			
		RBC	WBC	Epithelial cell				Others				
				Squamous		Round	Small round		1.021-1.030	1.031-1.040	1.041-1.050	1.050<
		-	-	-	±	-	-	-				
Control	7	7	7	7	0	7	7	7	1	2	3	1
Substance No.3-0146 100 mg/kg	7	7	7	6	1	7	7	7	1	2	4	0

(continued)

Table 13. (continued)

Group	No. of animals	U-Vol ml/21hr	U-Na mEq/21hr	U-K mEq/21hr	U-Cl mEq/21hr
		b			
Control	7	14.00	1.1394	2.4747	1.5943
		7.90	0.4556	0.7948	0.5908
Substance No.3-0146 100 mg/kg	7	12.93	1.2094	2.4193	1.6220
		2.01	0.3506	0.5930	0.5165

a: Values are no. of animals with findings.
b: Values are means and S.D. thereunder.

Table 14. Hematological findings in male rats killed at the end of the administration period of the 28-day repeated dose oral toxicity study of Substance No.3-0146

Group	No. of animals	RBC $10^6/\mu l$	Ht. %	Hb. g/dl	MCV fl	MCH pg	MCHC %	WBC $10^3/\mu l$	Plat $10^3/\mu l$
Control	7	7.407[a]	45.67	14.81	61.66	19.96	32.39	16.20	1166.4
		0.217	1.46	0.54	0.86	0.42	0.60	5.70	58.3
Substance No.3-0146 4 mg/kg	7	7.243	44.54	14.44	61.51	19.90	32.39	11.56	1116.0
		0.127	0.82	0.25	0.96	0.39	0.17	3.36	92.4
Substance No.3-0146 20 mg/kg	7	7.181	44.23	14.56	61.59	20.21	32.84	13.11	1189.6
		0.334	1.87	0.80	0.92	0.39	0.58	3.43	96.0
Substance No.3-0146 100 mg/kg	7	7.193	44.33	14.69	61.63	20.36	33.07	12.01	1144.6
		0.260	2.05	0.68	2.06	0.42	0.66	2.66	92.3

(continued)

Table 14. (continued)

Group	No. of animals	Ret %.	CT sec.	PT sec.	APTT sec.	Hemogram of WBC: Neutro. Stab. %	Neutro. Seg. %	Eos. %	Bas. %	Mono. %	Lymp. %	Others %
Control	7	20.0	183.9	12.54	25.40	0.0	10.7	0.7	0.0	0.0	88.6	0.0
		4.2	54.8	0.40	1.52	0.0	2.9	0.8	0.0	0.0	2.7	0.0
Substance No.3-0146 4 mg/kg	7	21.1	182.3	13.13	26.47	0.1	8.7	0.6	0.0	0.0	90.6	0.0
		3.2	50.7	0.61	3.00	0.4	3.5	0.8	0.0	0.0	4.0	0.0
Substance No.3-0146 20 mg/kg	7	21.3	178.7	13.19	28.56*	0.3	10.0	0.3	0.0	0.0	89.4	0.0
		4.8	45.0	0.62	2.43	0.5	5.2	0.5	0.0	0.0	5.3	0.0
Substance No.3-0146 100 mg/kg	7	19.0	229.6	13.09	30.49**	0.1	10.4	0.1	0.0	0.0	89.3	0.0
		2.2	53.4	0.48	2.22	0.4	3.4	0.4	0.0	0.0	3.5	0.0

a: Values are means and S.D. thereunder.
*: Differs from control, $p<0.05$.
**: Differs from control, $p<0.01$.

Table 15. Hematological findings in female rats killed at the end of the administration period of the 28-day repeated dose oral toxicity study of Substance No.3-0146

Group	No. of animals	RBC $10^6/\mu l$	Ht. %	Hb. g/dl	MCV fl	MCH pg	MCHC %	WBC $10^3/\mu l$	Plat $10^3/\mu l$
Control	7	7.560[a]	46.16	15.66	61.06	20.67	33.87	12.64	1115.6
		0.194	1.74	0.37	1.82	0.47	0.55	2.94	54.1
Substance No.3-0146 4 mg/kg	7	7.637	45.61	15.49	59.80	20.27	33.90	9.83	1156.0
		0.378	1.02	0.26	1.84	0.95	0.79	3.06	64.4
Substance No.3-0146 20 mg/kg	7	7.603	45.57	15.41	59.97	20.26	33.81	10.06	1193.4
		0.318	1.42	0.32	1.81	0.71	0.76	3.68	156.8
Substance No.3-0146 100 mg/kg	7	7.540	44.63	15.10*	59.21	20.00	33.80	8.51*	1176.9
		0.333	1.28	0.36	1.65	0.64	0.48	2.03	64.6

(continued)

Table 15. (continued)

Group	No. of animals	Ret %.	CT sec.	PT sec.	APTT sec.	Hemogram of WBC: Neutro. Stab. %	Neutro. Seg. %	Eos. %	Bas. %	Mono. %	Lymp. %	Others %
Control	7	13.1	226.3	13.49	22.61	0.3	8.7	0.4	0.0	0.0	90.6	0.0
		1.5	75.4	0.38	1.10	0.5	2.1	0.8	0.0	0.0	2.1	0.0
Substance No.3-0146 4 mg/kg	7	12.3	166.4	13.67	22.93	0.1	10.1	0.4	0.0	0.0	89.3	0.0
		2.4	69.6	0.67	1.08	0.4	2.7	0.8	0.0	0.0	2.4	0.0
Substance No.3-0146 20 mg/kg	7	12.1	211.3	13.60	23.47	0.3	9.3	0.6	0.0	0.0	89.9	0.0
		2.9	38.1	0.47	2.41	0.5	3.7	0.8	0.0	0.0	3.3	0.0
Substance No.3-0146 100 mg/kg	7	13.4	231.7	12.76	26.26**	0.3	10.4	0.3	0.0	0.0	89.0	0.0
		1.9	48.9	0.66	1.57	0.8	3.0	0.5	0.0	0.0	3.4	0.0

a: Values are means and S.D. thereunder.
*: Differs from control, $p<0.05$.
**: Differs from control, $p<0.01$.

Table 16. Hematological findings in male rats killed at the end of the 14-day recovery period after the 28-day oral administration of Substance No.3-0146

Group	No. of animals	RBC $10^6/\mu l$	Ht. %	Hb. g/dl	MCV fl	MCH pg	MCHC %	WBC $10^3/\mu l$	Plat $10^3/\mu l$
Control	7	7.976[a]	47.23	14.94	59.33	18.73	31.61	16.21	1108.4
		0.218	1.06	0.22	1.80	0.48	0.38	3.68	103.0
Substance No.3-0146 100 mg/kg	7	8.164	48.06	15.09	58.86	18.44	31.36	16.11	1215.0*
		0.333	1.81	0.59	0.76	0.30	0.56	5.58	74.1

(continued)

Table 16. (continued)

Group	No. of animals	Ret %.	CT sec.	PT sec.	APTT sec.	Hemogram of WBC: Neutro. Stab. %	Neutro. Seg. %	Eos. %	Bas. %	Mono. %	Lymp. %	Others %
Control	7	15.1	250.0	14.16	28.96	0.0	10.6	0.1	0.0	0.0	89.3	0.0
		2.7	24.9	0.51	2.04	0.0	6.9	0.4	0.0	0.0	6.7	0.0
Substance No.3-0146 100 mg/kg	7	13.6	225.4	13.70	27.87	0.1	8.6	0.4	0.0	0.0	90.9	0.0
		2.1	51.3	0.59	3.54	0.4	3.1	0.8	0.0	0.0	3.3	0.0

a: Values are means and S.D. thereunder.
*: Differs from control, $p<0.05$.

Table 17. Hematological findings in female rats killed at the end of the 14-day recovery period after the 28-day oral administration of Substance No.3-0146

Group	No. of animals	RBC $10^6/\mu l$	Ht. %	Hb. g/dl	MCV fl	MCH pg	MCHC %	WBC $10^3/\mu l$	Plat $10^3/\mu l$
Control	7	7.959[a]	46.23	15.29	58.11	19.17	33.01	10.29	1150.9
		0.340	1.78	0.62	1.64	0.71	0.66	2.50	93.8
Substance No.3-0146 100 mg/kg	7	8.093	46.66	15.31	57.66	18.89	32.77	9.50	1101.7
		0.206	0.78	0.44	0.93	0.69	0.79	2.41	115.3

(continued)

Table 17. (continued)

Group	No. of animals	Ret %.	CT sec.	PT sec.	APTT sec.	Hemogram of WBC: Neutro. Stab. %	Neutro. Seg. %	Eos. %	Bas. %	Mono. %	Lymp. %	Others %
			(6)b									
Control	7	11.9	216.3	13.90	22.96	0.1	10.7	1.0	0.0	0.0	88.1	0.0
		2.8	25.7	0.18	2.28	0.4	3.1	0.6	0.0	0.0	3.2	0.0
Substance No.3-0146 100 mg/kg	7	13.3	233.4	13.91	23.31	0.1	11.0	0.6	0.0	0.0	88.3	0.0
		3.1	67.9	0.42	0.96	0.4	2.9	0.8	0.0	0.0	3.0	0.0

a: Values are means and S.D. thereunder.
b: Values in parentheses are no. of animals examined.

Table 18. Biochemical findings in male rats killed at the end of the administration period of the 28-day repeated dose oral toxicity study of Substance No.3-0146

Group	No. of animals	TP g/dl	Alb g/dl	A/G	Protein fractions (%) Alb	Globulin α_1	Globulin α_2	Globulin β	Globulin γ	GOT IU/l	GPT IU/l	ALP IU/l	LDH IU/l	γ-GTP IU/l	T-Bil mg/dl
Control	7	5.64[a]	2.37	0.721	51.04	19.73	6.07	16.06	7.10	113.7	32.4	401.3	2136.3	0.66	0.10
		0.11	0.13	0.069	3.10	1.72	0.80	1.63	0.83	30.3	4.9	73.8	1357.9	0.21	0.00
Substance No.3-0146 4 mg/kg	7	5.56	2.31	0.707	51.03	19.61	5.59	16.21	7.56	107.6	29.6	455.7	1975.9	0.80	0.10
		0.16	0.09	0.026	1.27	0.90	0.56	0.84	0.75	14.9	1.6	35.6	795.6	0.31	0.00
Substance No.3-0146 20 mg/kg	7	5.66	2.31	0.690	50.06	20.06	5.30	16.47	8.11	107.0	28.1	454.1	1936.4	0.70	0.10
		0.21	0.13	0.074	4.40	1.25	0.65	2.01	3.08	17.1	3.8	73.1	733.2	0.17	0.00
Substance No.3-0146 100 mg/kg	7	5.56	2.30	0.704	49.89	19.74	5.99	16.93	7.46	100.7	28.0	513.6*	1640.9	0.79	0.10
		0.13	0.15	0.077	4.21	1.59	1.59	2.41	1.09	13.7	3.4	113.9	546.4	0.44	0.00

(continued)

Table 18. (continued)

Group	No. of animals	Glu mg/dl	T-Cho mg/dl	TG mg/dl	PL mg/dl	BUN mg/dl	Crea mg/dl	Na mEq/l	K mEq/l	Cl mEq/l	Ca mg/dl	P mg/dl
Control	7	128.9	76.3	52.9	130.0	16.09	0.49	144.71	4.570	105.3	9.63	8.84
		16.4	16.2	21.6	19.6	1.40	0.07	1.78	0.307	1.5	0.08	0.63
Substance No.3-0146 4 mg/kg	7	122.6	71.4	57.0	123.1	16.86	0.46	145.00	4.497	106.0	9.46	9.11
		14.2	13.9	25.0	18.9	2.27	0.05	1.71	0.188	2.0	0.21	0.70
Substance No.3-0146 20 mg/kg	7	124.1	71.3	67.1	121.3	15.44	0.47	145.29	4.591	105.3	9.40*	9.21
		18.9	15.0	19.1	14.2	1.41	0.08	1.58	0.251	0.8	0.12	0.57
Substance No.3-0146 100 mg/kg	7	134.1	71.3	70.9	119.6	15.06	0.46	144.29	4.494	105.0	9.40*	9.07
		13.2	8.7	37.2	13.9	2.03	0.08	2.34	0.254	1.0	0.10	0.50

a: Values are means and S.D. thereunder.
*: Differs from control, $p<0.05$.

Table 19. Biochemical findings in female rats killed at the end of the administration period of the 28-day repeated dose oral toxicity study of Substance No.3-0146

Group	No. of animals	TP g/dl	Alb g/dl	A/G	Protein fractions (%) Alb	Globulin α_1	Globulin α_2	Globulin β	Globulin γ	GOT IU/l	GPT IU/l	ALP IU/l	LDH IU/l	γ-GTP IU/l	T-Bil mg/dl
Control	7	5.79[a]	2.60	0.814	54.50	17.04	6.36	16.24	5.86	121.3	23.9	284.4	2643.0	1.06	0.10
		0.18	0.08	0.058	1.45	1.71	0.55	0.78	0.81	16.6	2.2	50.7	746.8	0.43	0.00
Substance No.3-0146 4 mg/kg	7	5.80	2.59	0.803	53.90	18.31	5.97	16.09	5.73	118.3	22.6	311.7	2632.1	0.97	0.10
		0.20	0.16	0.074	1.29	1.07	0.89	0.58	1.29	21.8	3.0	72.8	884.0	0.55	0.00
Substance No.3-0146 20 mg/kg	7	5.90	2.60	0.784	54.06	18.54	6.16	15.70	5.54	101.1	23.0	306.9	1923.7	0.74	0.10
		0.14	0.08	0.053	1.53	1.88	1.08	1.13	0.58	16.4	3.3	96.9	724.7	0.38	0.00
Substance No.3-0146 100 mg/kg	7	5.84	2.44*	0.716*	51.43**	19.51*	6.79	16.49	5.79	98.1	24.6	342.6	1376.6**	1.10	0.10
		0.22	0.05	0.043	1.28	1.15	0.90	0.61	1.06	15.8	2.2	86.9	425.1	0.43	0.00

(continued)

Table 19. (continued)

Group	No. of animals	Glu mg/dl	T-Cho mg/dl	TG mg/dl	PL mg/dl	BUN mg/dl	Crea mg/dl	Na mEq/l	K mEq/l	Cl mEq/l	Ca mg/dl	P mg/dl
Control	7	107.9	71.7	19.6	139.0	20.64	0.59	143.36	4.280	108.0	9.40	7.71
		14.1	11.4	6.8	17.1	1.29	0.04	1.03	0.093	1.8	0.28	0.51
Substance No.3-0146 4 mg/kg	7	110.3	70.1	26.7	132.9	20.70	0.60	143.07	4.250	106.9	9.40	7.46
		10.7	11.9	10.6	19.4	2.20	0.08	2.05	0.143	1.1	0.29	0.47
Substance No.3-0146 20 mg/kg	7	103.9	68.7	23.0	131.4	22.14	0.60	142.57	4.356	107.6	9.54	7.81
		8.1	17.3	10.0	28.5	3.13	0.06	1.67	0.221	1.6	0.18	0.77
Substance No.3-0146 100 mg/kg	7	126.0	65.4	26.0	127.7	18.47	0.60	143.29	3.883**	106.7	9.36	7.49
		24.1	12.4	16.3	25.1	1.85	0.06	1.58	0.134	1.6	0.14	0.74

a: Values are means and S.D. thereunder.
*: Differs from control, $p<0.05$.
**: Differs from control, $p<0.01$.

Table 20. Biochemical findings in male rats killed at the end of the 14-day recovery period after the 28-day oral administration of Substance No.3-0146

Group	No. of animals	TP g/dl	Alb g/dl	A/G	Protein fractions (%) Alb	Globulin α_1	Globulin α_2	Globulin β	Globulin γ	GOT IU/l	GPT IU/l	ALP IU/l	LDH IU/l	γ-GTP IU/l	T-Bil mg/dl
Control	7	5.84[a]	2.47	0.730	49.07	21.99	6.21	15.43	7.30	107.6	30.1	294.6	2174.9	1.54	0.10
		0.17	0.08	0.051	1.68	0.73	0.53	1.00	1.34	15.0	4.8	46.4	953.5	0.29	0.00
Substance No.3-0146 100 mg/kg	7	5.84	2.43	0.707	48.16	20.31	6.90	15.99	8.64	103.4	28.1	336.0	2033.6	1.39	0.10
		0.18	0.10	0.038	1.48	2.22	0.67	0.90	2.32	19.5	2.5	39.2	665.2	0.47	0.00

(continued)

Table 20. (continued)

Group	No. of animals	Glu mg/dl	T-Cho mg/dl	TG mg/dl	PL mg/dl	BUN mg/dl	Crea mg/dl	Na mEq/l	K mEq/l	Cl mEq/l	Ca mg/dl	P mg/dl
Control	7	144.6	57.9	45.3	106.6	19.17	0.53	143.43	4.391	105.6	9.31	8.41
		17.2	8.7	19.6	12.8	2.36	0.05	0.98	0.115	1.7	0.18	0.76
Substance No.3-0146 100 mg/kg	7	141.3	57.6	39.1	105.6	17.47	0.51	143.93	4.549	105.6	9.40	8.43
		15.3	9.6	11.0	12.2	1.14	0.04	0.67	0.203	1.4	0.20	0.51

a: Values are means and S.D. thereunder.

Table 21. Biochemical findings in female rats killed at the end of the 14-day recovery period after the 28-day oral administration of Substance No.3-0146

Group	No. of animals	TP g/dl	Alb g/dl	A/G	Protein fractions (%) Alb	Globulin α_1	Globulin α_2	Globulin β	Globulin γ	GOT IU/l	GPT IU/l	ALP IU/l	LDH IU/l	γ-GTP IU/l	T-Bil mg/dl
Control	7	6.20[a]	2.86	0.849	56.44	17.79	4.89	15.01	5.87	123.0	28.6	178.3	2991.6	1.79	0.10
		0.15	0.10	0.046	1.08	1.68	0.67	0.58	1.07	32.9	5.9	35.2	1303.8	0.30	0.00
Substance No.3-0146 100 mg/kg	7	5.87**	2.70*	0.849	56.69	17.20	5.06	14.89	6.17	118.6	27.9	250.1**	2751.1	1.81	0.10
		0.18	0.13	0.059	1.83	1.81	0.66	0.93	0.73	24.2	4.1	39.7	920.4	0.54	0.00

(continued)

Table 21. (continued)

Group	No. of animals	Glu mg/dl	T-Cho mg/dl	TG mg/dl	PL mg/dl	BUN mg/dl	Crea mg/dl	Na mEq/l	K mEq/l	Cl mEq/l	Ca mg/dl	P mg/dl
Control	7	116.9	59.4	18.1	124.9	21.09	0.59	143.43	4.323	107.0	9.59	6.91
		21.8	14.1	10.2	23.6	2.79	0.07	0.73	0.073	1.2	0.22	0.82
Substance No.3-0146 100 mg/kg	7	133.7	47.7	17.7	107.4	20.29	0.60	143.21	4.030*	107.0	9.33*	6.34
		20.4	3.8	12.5	8.3	1.67	0.06	0.86	0.408	2.0	0.17	0.95

a: Values are means and S.D. thereunder.
*: Differs from control, $p<0.05$.
**: Differs from control, $p<0.01$.

Table 22. Absolute and relative organ weights in male rats killed at the end of the administration period of the 28-day repeated dose oral toxicity study of Substance No.3-0146

Group	No. of animals	Body weight g	Brain		Pituitary gland		Thyroid				Thymus		Heart	
							Right		Left					
			g	%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	g	%
Control	7	314.1[a]	2.040	0.650	10.16	3.236	8.40	2.680	7.49	2.380	804.3	255.786	1.127	0.357
		5.6	0.061	0.012	0.99	0.326	3.36	1.082	2.64	0.841	121.0	35.840	0.051	0.017
Substance No.3-0146 4 mg/kg	7	317.6	2.089	0.660	10.73	3.384	8.63	2.716	8.74	2.771	820.0	259.043	1.169	0.367
		18.9	0.060	0.054	0.53	0.184	2.01	0.596	1.63	0.611	141.7	47.070	0.060	0.020
							(6)[b]	(6)	(6)	(6)				
Substance No.3-0146 20 mg/kg	7	312.6	2.099	0.674	10.73	3.431	9.03	2.870	8.80	2.805	832.9	266.190	1.184	0.380
		16.1	0.086	0.037	0.64	0.115	1.92	0.533	1.08	0.298	168.7	52.061	0.045	0.029
Substance No.3-0146 100 mg/kg	7	310.4	2.091	0.677	10.69	3.430	9.11	2.919	7.81	2.513	805.9	259.259	1.173	0.377
		27.0	0.031	0.053	1.48	0.219	2.71	0.813	2.21	0.656	145.1	37.020	0.149	0.021

(continued)

Table 22. (continued-1)

Group	No. of animals	Lung		Liver		Spleen		Kidney				Adrenal			
								Right		Left		Right		Left	
		g	%	g	%	g	%	g	%	g	%	mg	10^{-3}%	mg	10^{-3}%
Control	7	1.206	0.384	9.710	3.087	0.684	0.219	1.207	0.384	1.223	0.389	23.1	7.361	25.0	7.953
		0.090	0.030	0.760	0.215	0.047	0.017	0.115	0.034	0.092	0.025	3.1	0.953	4.0	1.254
Substance No.3-0146 4 mg/kg	7	1.243	0.393	9.763	3.067	0.683	0.214	1.281	0.404	1.267	0.400	21.7	6.847	24.3	7.649
		0.063	0.021	1.023	0.152	0.106	0.026	0.106	0.024	0.096	0.024	2.0	0.613	2.4	0.644
Substance No.3-0146 20 mg/kg	7	1.283	0.411	9.893	3.164	0.697	0.226	1.269	0.404	1.257	0.403	22.0	7.036	24.9	7.957
		0.077	0.037	0.551	0.112	0.090	0.038	0.105	0.031	0.093	0.024	3.5	1.019	3.6	1.123
Substance No.3-0146 100 mg/kg	7	1.229	0.397	10.301	3.313*	0.671	0.214	1.366	0.440**	1.364	0.440**	24.7	7.934	27.1	8.719
		0.085	0.014	1.148	0.109	0.149	0.041	0.156	0.022	0.173	0.024	3.8	0.650	4.7	1.019

(continued)

Table 22. (continued-2)

Group	No. of animals	Testis Right g	Testis Right %	Testis Left g	Testis Left %	Epididymis Right g	Epididymis Right %	Epididymis Left g	Epididymis Left %	Prostate mg	Prostate 10^{-3}%	Seminal vesicle g	Seminal vesicle %
Control	7	1.440	0.459	1.319	0.421	0.303	0.097	0.291	0.094	401.4	127.526	0.756	0.239
		0.084	0.026	0.190	0.065	0.032	0.011	0.034	0.013	97.1	29.892	0.144	0.045
Substance No.3-0146 4 mg/kg	7	1.361	0.431	1.319	0.414	0.296	0.091	0.290	0.091	425.9	134.163	0.886	0.280
		0.079	0.038	0.052	0.030	0.031	0.012	0.030	0.012	48.5	13.597	0.142	0.047
Substance No.3-0146 20 mg/kg	7	1.349	0.433	1.324	0.424	0.299	0.097	0.280	0.090	371.0	118.013	0.723	0.231
		0.095	0.040	0.088	0.042	0.022	0.013	0.015	0.010	80.6	20.084	0.136	0.033
Substance No.3-0146 100 mg/kg	7	1.420	0.460	1.404	0.454	0.333	0.107	0.314	0.101	414.6	134.500	0.881	0.287
		0.030	0.047	0.067	0.048	0.031	0.011	0.039	0.016	33.3	16.146	0.113	0.054

a: Values are means and S.D. thereunder.
b: Values in parentheses are no. of animals examined.
*: Differs from control, $p<0.05$.
**: Differs from control, $p<0.01$.

Table 23. Absolute and relative organ weights in female rats killed at the end of the administration period of the 28-day repeated dose oral toxicity study of Substance No.3-0146

Group	No. of animals	Body weight	Brain		Pituitary gland		Thyroid				Thymus		Heart	
							Right		Left					
		g	g	%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	g	%
Control	7	193.3[a]	1.864	0.979	12.11	6.340	6.29	3.271	6.46	3.357	472.0	243.026	0.783	0.404
		26.9	0.065	0.123	1.45	0.919	0.97	0.459	1.80	0.940	107.7	32.522	0.101	0.019
Substance No.3-0146 4 mg/kg	7	200.9	1.843	0.924	12.14	6.049	7.09	3.530	7.40	3.680	556.0	275.879	0.830	0.414
		21.8	0.067	0.080	1.51	0.498	1.20	0.518	1.87	0.889	118.3	41.980	0.058	0.022
Substance No.3-0146 20 mg/kg	7	197.4	1.906	0.969	12.10	6.173	7.04	3.569	7.06	3.569	520.3	265.226	0.806	0.410
		14.6	0.042	0.068	1.70	1.148	1.11	0.497	1.60	0.733	92.0	53.732	0.049	0.025
Substance No.3-0146 100 mg/kg	7	188.1	1.931	1.031	12.74	6.781	8.89**	4.719**	8.19	4.334	464.1	246.474	0.806	0.430
		10.8	0.056	0.055	1.61	0.835	1.33	0.604	1.37	0.560	77.3	35.891	0.035	0.029

(continued)

Table 23. (continued-1)

Group	No. of animals	Lung		Liver		Spleen		Kidney				Adrenal			
								Right		Left		Right		Left	
		g	%	g	%	g	%	g	%	g	%	mg	10^{-3}%	mg	10^{-3}%
Control	7	0.957	0.499	5.766	2.979	0.450	0.233	0.776	0.403	0.770	0.399	25.7	13.404	27.3	14.223
		0.095	0.038	0.917	0.109	0.096	0.034	0.123	0.035	0.139	0.036	3.5	1.803	5.5	2.903
Substance No.3-0146 4 mg/kg	7	0.964	0.483	5.936	2.961	0.414	0.204	0.804	0.401	0.783	0.389	30.3	15.129	32.1	15.950
		0.082	0.044	0.593	0.208	0.069	0.014	0.093	0.027	0.112	0.034	3.3	1.313	6.0	1.711
Substance No.3-0146 20 mg/kg	7	0.941	0.477	5.830	2.951	0.436	0.220	0.786	0.401	0.787	0.400	29.9	15.220	31.9	16.193
		0.065	0.032	0.582	0.191	0.071	0.029	0.071	0.034	0.071	0.031	4.8	2.839	4.2	2.233
Substance No.3-0146 100 mg/kg	7	0.931	0.496	6.389	3.400**	0.431	0.229	0.860	0.459*	0.839	0.444	33.7**	18.011**	36.9**	19.669**
		0.066	0.026	0.524	0.279	0.095	0.039	0.104	0.034	0.112	0.037	2.6	2.262	2.0	1.893

(continued)

Table 23. (continued-2)

Group	No. of animals	Ovary Right mg	Ovary Right 10^{-3}%	Ovary Left mg	Ovary Left 10^{-3}%	Uterus g	Uterus %
Control	7	44.6	22.919	43.3	22.543	0.503	0.266
		11.6	4.234	4.6	1.998	0.150	0.085
Substance No.3-0146 4 mg/kg	7	46.7	23.373	38.6	19.179	0.471	0.237
		6.8	3.468	7.6	2.717	0.125	0.072
Substance No.3-0146 20 mg/kg	7	41.0	20.809	40.0	20.341	0.431	0.219
		5.0	2.509	4.3	2.501	0.109	0.045
Substance No.3-0146 100 mg/kg	7	45.6	24.323	46.4	24.767	0.440	0.233
		5.3	3.423	6.2	3.771	0.075	0.042

a: Values are means and S.D. thereunder.
*: Differs from control, $p<0.05$.
**: Differs from control, $p<0.01$.

Table 24. Absolute and relative organ weights in male rats killed at the end of the 14-day recovery period after the 28-day oral administration toxicity study of Substance No.3-0146

Group	No. of animals	Body weight	Brain		Pituitary gland		Thyroid				Thymus		Heart	
							Right		Left					
		g	g	%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	g	%
Control	7	377.9[a]	2.064	0.553	11.90	3.163	9.44	2.514	9.51	2.527	578.7	154.446	1.263	0.336
		41.7	0.050	0.055	1.30	0.323	1.24	0.375	2.39	0.649	78.7	25.635	0.083	0.029
Substance No.3-0146 100 mg/kg	7	364.1	2.074	0.571	12.74	3.507	9.41	2.580	9.19	2.529	668.9	183.107	1.311	0.361
		24.4	0.072	0.050	1.33	0.353	1.39	0.293	1.11	0.301	160.2	39.440	0.144	0.038

(continued)

Table 24. (continued-1)

Group	No. of animals	Lung		Liver		Spleen		Kidney				Adrenal			
								Right		Left		Right		Left	
		g	%	g	%	g	%	g	%	g	%	mg	10^{-3}%	mg	10^{-3}%
Control	7	1.303	0.347	11.041	2.909	0.723	0.191	1.371	0.364	1.357	0.359	24.9	6.613	25.7	6.884
		0.056	0.026	1.847	0.163	0.082	0.023	0.123	0.024	0.129	0.021	3.2	0.828	4.5	1.367
Substance No.3-0146 100 mg/kg	7	1.289	0.356	10.550	2.899	0.717	0.197	1.429	0.394	1.397	0.384	23.6	6.520	26.0	7.194
		0.066	0.018	0.947	0.200	0.073	0.021	0.095	0.040	0.126	0.043	4.1	1.395	4.2	1.477

(continued)

Table 24. (continued-2)

Group	No. of animals	Testis Right g	Testis Right %	Testis Left g	Testis Left %	Epididymis Right g	Epididymis Right %	Epididymis Left g	Epididymis Left %	Prostate mg	Prostate 10^{-3}%	Seminal vesicle g	Seminal vesicle %
Control	7	1.509	0.404	1.497	0.400	0.447	0.119	0.440	0.117	500.9	133.841	1.157	0.309
		0.059	0.046	0.046	0.045	0.028	0.016	0.027	0.014	79.5	25.751	0.166	0.056
Substance No.3-0146 100 mg/kg	7	1.506	0.414	1.477	0.407	0.434	0.119	0.430	0.119	535.9	147.150	1.073	0.296
		0.088	0.027	0.085	0.021	0.030	0.012	0.025	0.012	89.1	23.148	0.148	0.035

a: Values are means and S.D. thereunder.

Table 25. Absolute and relative organ weights in female rats killed at the end of the 14-day recovery period after the 28-day oral administration toxicity study of Substance No.3-0146

Group	No. of animals	Body weight	Brain		Pituitary gland		Thyroid				Thymus		Heart	
							Right		Left					
		g	g	%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	g	%
Control	7	223.7[a]	1.930	0.866	13.84	6.221	5.50	2.450	6.14	2.734	473.3	211.574	0.859	0.384
		14.3	0.056	0.055	1.62	0.899	1.77	0.766	1.55	0.601	93.1	40.754	0.078	0.015
Substance No.3-0146 100 mg/kg	7	209.6	1.887	0.901	12.81	6.114	6.13	2.943	5.60	2.663	417.7	198.231	0.817	0.391
		15.0	0.082	0.049	1.53	0.649	1.20	0.633	0.84	0.281	100.2	40.614	0.052	0.013

(continued)

Table 25. (continued-1)

Group	No. of animals	Lung		Liver		Spleen		Kidney				Adrenal			
								Right		Left		Right		Left	
		g	%	g	%	g	%	g	%	g	%	mg	10^{-3}%	mg	10^{-3}%
Control	7	1.007	0.451	6.304	2.817	0.441	0.196	0.856	0.381	0.853	0.380	30.3	13.584	32.3	14.504
		0.045	0.032	0.525	0.120	0.083	0.029	0.093	0.028	0.094	0.030	1.8	1.202	3.4	1.980
Substance No.3-0146 100 mg/kg	7	0.970	0.463	5.786	2.760	0.424	0.200	0.810	0.384	0.784	0.374	31.7	15.043	34.3	16.271
		0.107	0.040	0.594	0.170	0.090	0.041	0.106	0.026	0.093	0.024	6.6	2.438	6.9	2.521

(continued)

Table 25. (continued-2)

Group	No. of animals	Ovary Right mg	Ovary Right 10^{-3}%	Ovary Left mg	Ovary Left 10^{-3}%	Uterus g	Uterus %
Control	7	46.6	20.804	43.6	19.511	0.440	0.196
		5.6	2.021	7.2	3.111	0.196	0.083
Substance No.3-0146 100 mg/kg	7	42.9	20.413	41.4	19.774	0.477	0.227
		7.6	3.075	5.4	2.243	0.196	0.084

a: Values are means and S.D. thereunder.

Table 26. Gross findings in rats killed at the end of the administration period of the 28-day repeated dose oral toxicity study of Substance No.3-0146

	Male				Female			
		Substance No.3-0146 (mg/kg)				Substance No.3-0146 (mg/kg)		
Group	Control	4	20	100	Control	4	20	100
No. of animals examined	7	7	7	7	7	7	7	7
	a							
Thyroid (right) : Aplasia	0	0	1	0	0	0	0	0
Thyroid (left) : Large size	0	0	1	0	0	0	0	0
Parathyroid (right) : Aplasia	0	0	1	0	0	0	0	0
Testis (left) : Small size	1	0	0	0	-	-	-	-
Skin of cervical or dorsal region : Scab/Scabs	1	0	1	1	0	0	0	0

a: Values are no. of animals with findings.

Table 27. Gross findings in rats killed at the end of the 14-day recovery period after the 28-day oral administration of Substance No.3-0146

	Male		Female	
Group	Control	Substance No.3-0146 100 mg/kg	Control	Substance No.3-0146 100 mg/kg
No. of animals examined	7	7	7	7
Skin of cervical or dorsal region : Scabs	1[a]	1	0	0

a: Values are no. of animals with findings.

Table 28. Histopathological findings in rats killed at the end of the administration period of the 28-day repeated dose oral toxicity study of Substance No.3-0146

Group	Grade[a]	Male				Female			
			Substance No.3-0146 (mg/kg)				Substance No.3-0146 (mg/kg)		
		Control	4	20	100	Control	4	20	100
No. of animals examined		7	7	7	7	7	7	7	7
		[b]							
Kidney (right/left) : Hyaline droplet deposition in tubular epithelium	+	2	1	0	0	0	0	0	0
Eosinophilic body deposition in tubular epithelium	+	2	1	0	0	0	0	0	0
Retention cyst	+	0	0	0	1	0	0	0	0
Urinary cast	+	0	0	0	1	0	0	0	0
Focal interstitial infiltration of cells, mainly lymphocytes	+	0	1	1	1	0	0	0	0
Lung : Calcium deposition in blood-vessel wall	+	1	0	0	1	0	0	1	0
Pituitary gland : Ciliated epithelial cyst	+	1	0	0	1	0	1	0	0
Thyroid (right) : Persistent embryonic thyroid	+	0	0	0	0	0	0	0	1
Aplasia	*	0	0	1	0	0	0	0	0
Parathyroid (right) : Aplasia	*	0	0	1	0	0	0	0	0
Adrenals : Deposition of cholesterin-like substance, mainly in inner layer of zona fasciculata	+	0	0	0	1	0	0	0	0
Single cell necrosis of cortical cells, mainly in inner layer of zona fasciculata	+	0	0	0	1	0	0	0	0
Urinary bladder : Infiltration of cells, mainly lymphocytes in serosa	+	0	0	0	1	0	0	0	0
Prostate : Prostatitis	+	0	0	0	2	-	-	-	-
Ovary (left) : Follicular cyst	+	-	-	-	-	0	0	1	0

(continued)

Table 28. (continued)

Group	Grade	Male				Female			
			Substance No.3-0146 (mg/kg)				Substance No.3-0146 (mg/kg)		
		Control	4	20	100	Control	4	20	100
No. of animals examined		7	7	7	7	7	7	7	7
Skin of cervical or dorsal region : Ulcer	+	0(1) c	# d	0(1)	1(1)	#	#	#	#
	++	1(1)	#	1(1)	1(1)	#	#	#	#
	+++	0(1)	#	0(1)	1(1)	#	#	#	#
Thickening of epidermis	+	1(1)	#	1(1)	1(1)	#	#	#	#
Fibrosis in dermis	+	1(1)	#	1(1)	1(1)	#	#	#	#
Abscess	+	0(1)	#	1(1)	1(1)	#	#	#	#
Scab formation	+	0(1)	#	0(1)	1(1)	#	#	#	#
Infiltration of cells, mainly lymphocytes in subcutaneous tissue	+	0(1)	#	0(1)	1(1)	#	#	#	#
Subcutaneous edema	+	0(1)	#	0(1)	1(1)	#	#	#	#

There were no abnormal findings in the liver, spleen, heart, cerebrum, cerebellum, sciatic nerve, spinal cord, eyeballs, Harder's glands, thymus, mesenteric lymph node, left thyroid, left parathyroid, aorta, pancreas, submandibular glands, sublingual glands, parotid glands, submandibular lymph nodes, larynx, trachea, bronchus, tongue, esophagus, fore stomach, glandular stomach, duodenum, jejunum, ileum, cecum, colon, rectum, femur, sternum, mammary gland, skin (abdominal region), skeletal muscle, testes, epididymides, seminal vesicles, right ovary, uterus or vagina.

a: + = slight, ++ = moderate and +++ = severe changes, and * = detected.
b: Values are no. of animals with findings.
c: Values in parentheses are no. of animals examined.
d: # = not examined.

Table 29. Histopathological findings in rats killed at the end of the 14-day recovery period after the 28-day oral administration of Substance No.3-0146

Group	Grade[a]	Male: Control	Male: Substance No.3-0146 100 mg/kg	Female: Control	Female: Substance No.3-0146 100 mg/kg
No. of animals examined		7	7	7	7
		b			
Kidneys : Hyaline droplet deposition in tubular epithelium	+	0	2	0	0
Eosinophilic body deposition in tubular epithelium	+	0	2	0	0
Lung : Calcium deposition in blood-vessel wall	+	0	1	0	0
Adrenals : Single cell necrosis of cortical cells mainly in inner layer of zona fasciculata	+	0	1	0	0
Prostate : Prostatitis	+	3	1	-	-
Ovary (left) : Lutein cyst	+	-	-	0	1
Skin of cervical or dorsal region : Ulcer	+	1(1) c	0(1)	# d	#
Thickening of epidermis	+	1(1)	0(1)	#	#
	++	0(1)	1(1)	#	#
Fibrosis in dermis	+	1(1)	1(1)	#	#
Abscess	+	1(1)	0(1)	#	#
Scab formation	+	1(1)	1(1)	#	#
Edema in superficial zone of dermis	+	0(1)	1(1)	#	#
Epidermal edema	+	0(1)	1(1)	#	#

There were no abnormal findings in the liver, spleen, heart, cerebrum, cerebellum, sciatic nerve, spinal cord, eyeballs, Harder's glands, pituitary gland, thymus, mesenteric lymph node, thyroids, parathyroids, aorta, pancreas, submandibular glands, sublingual glands, parotid glands, submandibular lymph nodes, bronchus, larynx, trachea, tongue, esophagus, fore stomach, glandular stomach, duodenum, jejunum, ileum, cecum, colon, rectum, femur, sternum, mammary gland, skin (abdominal region), skeletal muscle, urinary bladder, testes, epididymides, seminal vesicles, right ovary, uterus or vagina.

a: + = slight and ++ = moderate changes.
b: Values are no. of animals with findings.
c: Values in parentheses are no. of animals examined.
d: # = not examined.

Photographs

Photo. H-1 Control Male No. 101 Killed at the end of adm. H.E. x200
Adrenal : Normal

Photo. H-2 Substance No.3-0146 100 mg/kg Male No. 407 Killed at the end of adm. H.E. x200
Adrenal : Deposition of cholesterin-like substance and single cell necrosis of cortical cells, mainly in inner layer of zona fasciculata (slight change)

Photo. H-3 Control Male No. 108 Killed at the end of recovery H.E. x200
Adrenal : Normal

Photo. H-4 Substance No.3-0146 100 mg/kg Male No. 414 Killed at the end of recovery H.E. x200
Adrenal : Single cell necrosis of cortical cells, mainly in inner layer of zona fasciculata (slight change)

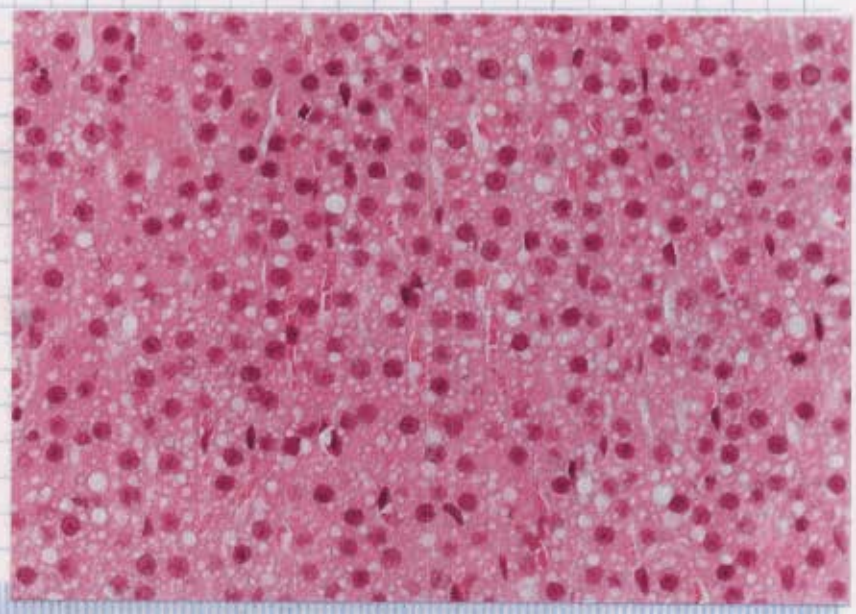

Photo. H-1

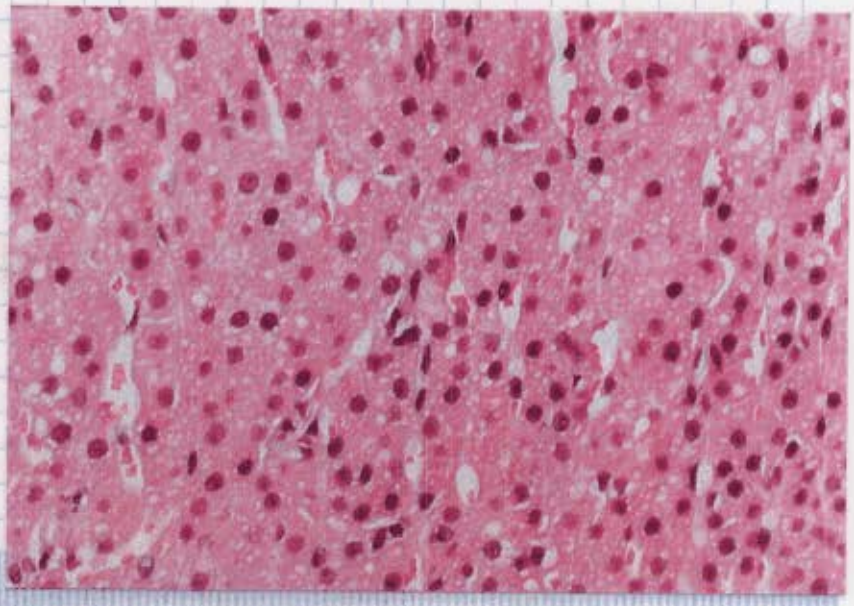

Photo. H-2

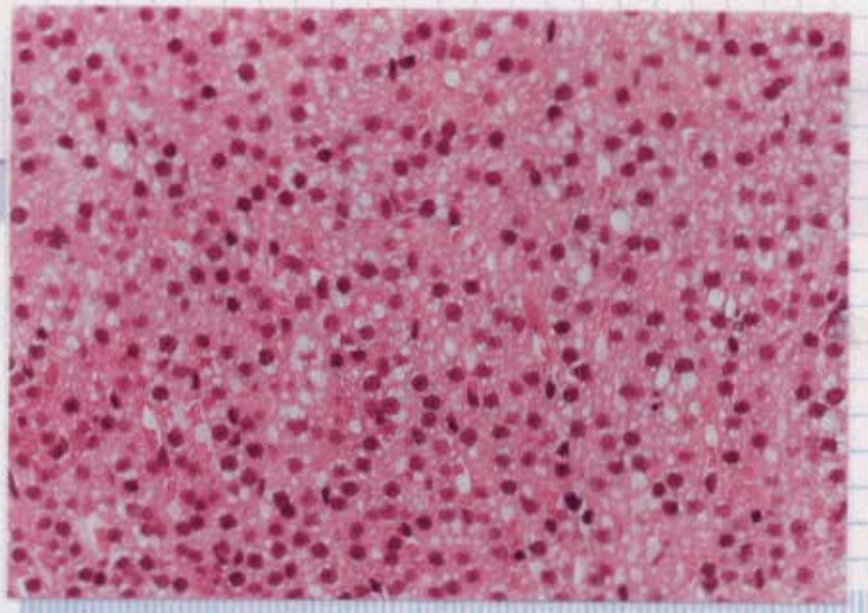

Photo. H-3

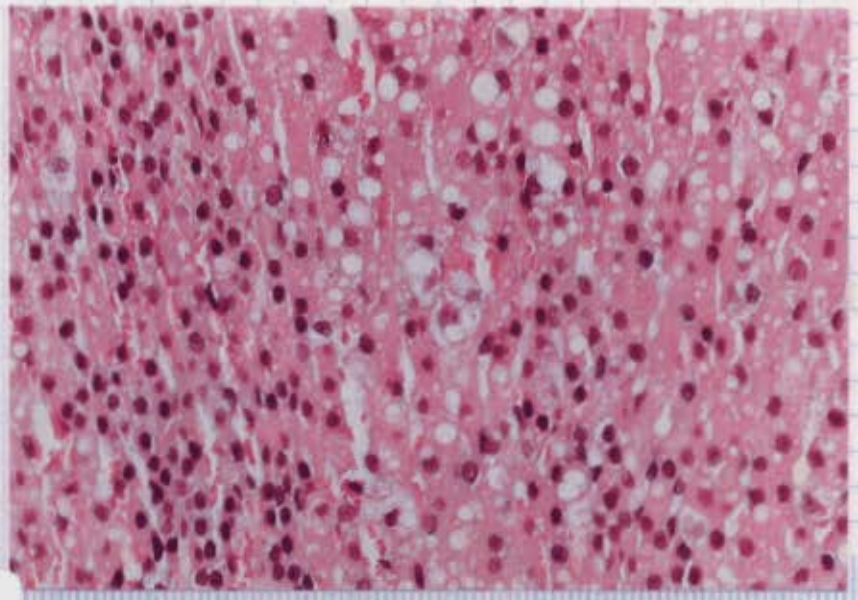

Photo. H-4

Individual data

Symbols and process of statistical analyses in individual data

INDIVIDUAL DATA	1-1-1 ~ 1-4-2	----------	General appearance
	2-1-1 ~ 2-4-2	----------	Body weights
	3-1-1 ~ 3-4-2	----------	Food consumption
	4-1-1 ~ 4-4-2	----------	Water consumption
	5-1-1 ~ 5-4-4	----------	Urinary findings
	6-1-1 ~ 6-4-4	----------	Hematological findings
	7-1-1 ~ 7-4-4	----------	Biochemical findings
	8-1-1 ~ 8-4-6	----------	Absolute and relative organ weights
	9-1-1 ~ 9-4-2	----------	Gross findings
	10-1-1 ~ 10-4-2	----------	Histopathological findings

Symbols and process of statistical analyses in INDIVIDUAL DATA

M/C : Values for Bartlett's test for homogeneity of variance,
p<0.05 ----------> Kruskal-Wallis test
p>0.05 ----------> One way analysis of variance

F : Values for one way analysis of variance,
p<0.1 ----------> Dunnett's procedure

H : Values for Kruskal-Wallis test,
p<0.1 ----------> Mann-Whitney test

† : Significant difference, p<0.1

* : Significant difference, p<0.05

** : Significant difference, p<0.01

---

t' : Values for Dunnett's procedure

U : Values for Mann-Whitney test

* : Significant difference from control, p<0.05

** : Significant difference from control, p<0.01

INDIVIDUAL DATA 1-1-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Administration
General appearance ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal No.	Observation day	Signs
101	a) 1-28	Normal
	b) Autopsy day	Normal
102	1-17	Normal
	18-28	Scab of cervical region (left 12 x 9 --> 14 x 10 --> 9 x 8, mm)
	Autopsy day	Scab of cervical region (left 9 x 8, mm)
103	1-28	Normal
	Autopsy day	Normal
104	1-28	Normal
	Autopsy day	Normal
105	1-28	Normal
	Autopsy day	Normal
106	1-28	Normal
	Autopsy day	Normal
107	1-28	Normal
	Autopsy day	Normal
108	1-28	Normal
109	1-28	Normal

(continued)

INDIVIDUAL DATA 1-1-1 (continued)

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Administration
General appearance ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal No.	Observation day	Signs
110	1-28	Normal
111	1-28	Normal
112	1-28	Normal
113	1-17	Normal
	18-28	Scab of cervical region (left 14 x 13 --> 14 x 10 --> 15 x 14 --> 20 x 15, mm)
114	1-28	Normal

a): Day of administration.
b): Not dosed.

INDIVIDUAL DATA 1-1-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Administration
General appearance ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 4 mg/kg

Animal No.	Observation day	Signs
201	a) 1-28	Normal
	b) Autopsy day	Normal
202	1-28	Normal
	Autopsy day	Normal
203	1-28	Normal
	Autopsy day	Normal
204	1-28	Normal
	Autopsy day	Normal
205	1-28	Normal
	Autopsy day	Normal
206	1-28	Normal
	Autopsy day	Normal
207	1-28	Normal
	Autopsy day	Normal

a): Day of administration.
b): Not dosed.

INDIVIDUAL DATA 1-1-3

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Administration
General appearance ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 20 mg/kg

Animal No.	Observation day	Signs
301	a) 1-28	Normal
	b) Autopsy day	Normal
302	1-28	Normal
	Autopsy day	Normal
303	1-28	Normal
	Autopsy day	Normal
304	1-28	Normal
	Autopsy day	Normal
305	1-14	Normal
	15-17	Scabs of cervical region (right 18 x 16, mm, left 15 x 10, mm)
	18-28	Scab of cervical region (38 x 15 --> 42 x 19 --> 41 x 21, mm)
	Autopsy day	Scab of cervical region (41 x 21, mm)
306	1-28	Normal
	Autopsy day	Normal
307	1-28	Normal
	Autopsy day	Normal

a): Day of administration.
b): Not dosed.

INDIVIDUAL DATA 1-1-4

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Administration
General appearance ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Observation day	Signs
401	a) 1-28	Normal
	b) Autopsy day	Normal
402	1-28	Normal
	Autopsy day	Normal
403	1-28	Normal
	Autopsy day	Normal
404	1-28	Normal
	Autopsy day	Normal
405	1-28	Normal
	Autopsy day	Normal
406	1-28	Normal
	Autopsy day	Normal
407	1-17	Normal
	18-27	Scab of cervical region (22 x 5 --> 14 x 11 --> 16 x 14, mm)
	28	Scabs of cervical region (right 19 x 16, mm, left 5 x 5, mm) and dorsal region, 9 x 6, mm)
	Autopsy day	Scabs of cervical region (right 19 x 16, mm, left 5 x 5, mm) and dorsal region, 9 x 6, mm)
408	1-28	Normal

(continued)

INDIVIDUAL DATA 1-1-4 (continued)

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Administration
General appearance ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Observation day	Signs
409	1-28	Normal
410	1-28	Normal
411	1-28	Normal
412	1-28	Normal
413	1-28	Normal
414	1-14	Normal
	15-22	Scabs of cervical region (right 21 x 10 --> 18 x 14 --> 15 x 7, mm, left 19 x 9 --> 16 x 12 --> 15 x 13, mm)
	23-27	Scabs of cervical region (right 14 x 7, mm, left 14 x 10, mm) and dorsal region (left 12 x 9, mm)
	28	Scabs of cervical region (right 16 x 11, mm, left 11 x 8, mm) and disseminated scabs of dorsal region

a): Day of administration.
b): Not dosed.

INDIVIDUAL DATA 1-2-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Administration
General appearance ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

Animal No.	Observation day	Signs
151	a) 1-28	Normal
	b) Autopsy day	Normal
152	1-28	Normal
	Autopsy day	Normal
153	1-28	Normal
	Autopsy day	Normal
154	1-28	Normal
	Autopsy day	Normal
155	1-28	Normal
	Autopsy day	Normal
156	1-28	Normal
	Autopsy day	Normal
157	1-28	Normal
	Autopsy day	Normal
158	1-28	Normal
159	1-28	Normal

(continued)

INDIVIDUAL DATA 1-2-1 (continued)

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Administration
General appearance ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

Animal No.	Observation day	Signs
160	1-28	Normal
161	1-28	Normal
162	1-28	Normal
163	1-28	Normal
164	1-28	Normal

a): Day of administration.
b): Not dosed.

INDIVIDUAL DATA 1-2-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Administration
General appearance ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 4 mg/kg

Animal No.	Observation day	Signs
251	1-28 a)	Normal
	Autopsy day b)	Normal
252	1-28	Normal
	Autopsy day	Normal
253	1-28	Normal
	Autopsy day	Normal
254	1-28	Normal
	Autopsy day	Normal
255	1-28	Normal
	Autopsy day	Normal
256	1-28	Normal
	Autopsy day	Normal
257	1-28	Normal
	Autopsy day	Normal

a): Day of administration.
b): Not dosed.

INDIVIDUAL DATA 1-2-3

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Administration
General appearance ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 20 mg/kg

Animal No.	Observation day	Signs
351	a) 1-28	Normal
	b) Autopsy day	Normal
352	1-28	Normal
	Autopsy day	Normal
353	1-28	Normal
	Autopsy day	Normal
354	1-28	Normal
	Autopsy day	Normal
355	1-28	Normal
	Autopsy day	Normal
356	1-28	Normal
	Autopsy day	Normal
357	1-28	Normal
	Autopsy day	Normal

a): Day of administration.
b): Not dosed.

INDIVIDUAL DATA 1-2-4

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Administration
General appearance ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Observation day	Signs
451	a) 1-28	Normal
	b) Autopsy day	Normal
452	1-28	Normal
	Autopsy day	Normal
453	1-28	Normal
	Autopsy day	Normal
454	1-28	Normal
	Autopsy day	Normal
455	1-28	Normal
	Autopsy day	Normal
456	1-28	Normal
	Autopsy day	Normal
457	1-28	Normal
	Autopsy day	Normal
458	1-28	Normal
459	1-28	Normal

(continued)

INDIVIDUAL DATA 1-2-4 (continued)

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Administration
General appearance ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Observation day	Signs
460	1-28	Normal
461	1-28	Normal
462	1-28	Normal
463	1-28	Normal
464	1-28	Normal

a): Day of administration.
b): Not dosed.

INDIVIDUAL DATA 1-3-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Recovery
General appearance ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal No.	Observation day a)	Signs
108	1-14	Normal
	Autopsy day	Normal
109	1-14	Normal
	Autopsy day	Normal
110	1-14	Normal
	Autopsy day	Normal
111	1-14	Normal
	Autopsy day	Normal
112	1-14	Normal
	Autopsy day	Normal
113	1-14	Scab of cervical region (left 20 x 15 --> 14 x 8 --> 13 x 11 --> 14 x 13, mm)
	Autopsy day	Scab of cervical region (left 14 x 13, mm)
114	1-14	Normal
	Autopsy day	Normal

a): Day of recovery.

INDIVIDUAL DATA 1-3-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Recovery
General appearance ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Observation day a)	Signs
408	1-14	Normal
	Autopsy day	Normal
409	1-14	Normal
	Autopsy day	Normal
410	1-14	Normal
	Autopsy day	Normal
411	1-14	Normal
	Autopsy day	Normal
412	1-14	Normal
	Autopsy day	Normal
413	1-14	Normal
	Autopsy day	Normal
414	1-4	Scabs of cervical region (right 16 x 11, mm, left 11 x 8, mm), and disseminated scabs of dorsal region
	5-7	Scabs of cervical region (right 5 x 3, mm, left 5 x 5, mm), dorsal region (right 15 x 8, mm), and disseminated scabs of left dorsal region
	8-9	Scabs of cervical region (left 5 x 2, mm ; dorsal region, right 12 x 3, mm), and disseminated scabs of right cervical and left dorsal region
	10-12	Scabs of cervical region (left 10 x 5, mm) and dorsal region (right 18 x 7, mm)
	13-14	Scab of right dorsal region (18 x 7 --> 15 x 6, mm)
	Autopsy day	Scab of right dorsal region (15 x 6, mm)

a): Day of recovery.

INDIVIDUAL DATA 1-4-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Recovery
General appearance ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

Animal No.	Observation day a)	Signs
158	1-14	Normal
	Autopsy day	Normal
159	1-14	Normal
	Autopsy day	Normal
160	1-14	Normal
	Autopsy day	Normal
161	1-14	Normal
	Autopsy day	Normal
162	1-14	Normal
	Autopsy day	Normal
163	1-14	Normal
	Autopsy day	Normal
164	1-14	Normal
	Autopsy day	Normal

a): Day of recovery.

INDIVIDUAL DATA 1-4-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Recovery
General appearance ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Observation day a)	Signs
458	1-14	Normal
	Autopsy day	Normal
459	1-14	Normal
	Autopsy day	Normal
460	1-14	Normal
	Autopsy day	Normal
461	1-14	Normal
	Autopsy day	Normal
462	1-14	Normal
	Autopsy day	Normal
463	1-14	Normal
	Autopsy day	Normal
464	1-14	Normal
	Autopsy day	Normal

a): Day of recovery.

INDIVIDUAL DATA 2-1-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Body weights (g) ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal No.	Day of administration 1	2	7	14	21	28	Body weight gain Day 1-28	%
101	125	134	175	241	299	347	222.00	177.60
102	127	136	177	237	297	340	213.00	167.72
103	131	138	180	237	291	342	211.00	161.07
104	133	142	186	251	305	343	210.00	157.89
105	132	141	176	233	286	328	196.00	148.48
106	133	143	174	226	276	331	198.00	148.87
107	140	149	190	247	295	345	205.00	146.43
108	125	132	164	209	259	304	179.00	143.20
109	125	136	178	233	275	318	193.00	154.40
110	130	138	184	256	330	386	256.00	196.92
111	134	144	182	247	312	364	230.00	171.64
112	135	144	179	231	281	325	190.00	140.74
113	137	146	186	248	300	330	193.00	140.88
114	141	147	186	242	294	330	189.00	134.04
N	14	14	14	14	14	14	14	14
MEAN	132.0	140.7	179.8	238.4	292.9	338.1	206.071	156.420
S.D.	5.3	5.2	6.6	12.0	17.4	19.9	19.998	17.229
S.E.	1.4	1.4	1.8	3.2	4.7	5.3	5.345	4.605
M/C	1.0485	0.6136	1.6550	0.5249	0.0582	1.1139	0.4499	1.4377
F	0.0638	0.0664	0.1453	0.1328	0.3116	0.7792	0.9768	1.0688

INDIVIDUAL DATA 2-1-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Body weights (g) ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 4 mg/kg

Animal	Day of administration						Body weight gain	
No.	1	2	7	14	21	28	Day 1-28	%
201	126	132	170	224	284	336	210.00	166.67
202	129	136	182	245	305	354	225.00	174.42
203	130	136	171	224	267	301	171.00	131.54
204	133	143	190	255	309	353	220.00	165.41
205	134	141	177	233	290	341	207.00	154.48
206	136	146	191	246	302	356	220.00	161.76
207	140	150	192	256	319	377	237.00	169.29
N	7	7	7	7	7	7	7	7
MEAN	132.6	140.6	181.9	240.4	296.6	345.4	212.857	160.510
S.D.	4.7	6.3	9.4	13.6	17.5	23.5	20.924	14.199
S.E.	1.8	2.4	3.6	5.1	6.6	8.9	7.908	5.367

INDIVIDUAL DATA 2-1-3

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Body weights (g) ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 20 mg/kg

Animal	Day of administration						Body weight gain	
No.	1	2	7	14	21	28	Day 1-28	%
301	128	137	181	246	313	356	228.00	178.13
302	130	138	177	234	288	336	206.00	158.46
303	131	139	178	238	294	341	210.00	160.31
304	129	136	171	227	292	333	204.00	158.14
305	134	143	184	228	266	311	177.00	132.09
306	137	148	186	241	293	334	197.00	143.80
307	139	148	194	257	313	357	218.00	156.83
N	7	7	7	7	7	7	7	7
MEAN	132.6	141.3	181.6	238.7	294.1	338.3	205.714	155.394
S.D.	4.2	5.1	7.4	10.5	16.1	15.6	16.173	14.362
S.E.	1.6	1.9	2.8	4.0	6.1	5.9	6.113	5.428

INDIVIDUAL DATA 2-1-4

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Body weights (g) ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Day of administration 1	2	7	14	21	28	Body weight gain Day 1-28	%
401	127	136	171	221	270	305	178.00	140.16
402	123	133	168	218	262	294	171.00	139.02
403	131	142	182	231	272	310	179.00	136.64
404	135	143	186	242	294	339	204.00	151.11
405	135	144	187	247	301	353	218.00	161.48
406	140	150	194	263	322	373	233.00	166.43
407	142	151	197	258	315	361	219.00	154.23
408	127	135	174	233	297	342	215.00	169.29
409	129	136	176	231	285	334	205.00	158.91
410	126	133	168	222	277	320	194.00	153.97
411	133	142	178	229	277	317	184.00	138.35
412	134	142	182	236	299	338	204.00	152.24
413	137	146	188	240	284	317	180.00	131.39
414	141	148	187	245	296	333	192.00	136.17
N	14	14	14	14	14	14	14	14
MEAN	132.9	141.5	181.3	236.9	289.4	331.1	198.286	149.242
S.D.	5.9	6.1	9.2	13.3	17.2	22.2	18.681	12.261
S.E.	1.6	1.6	2.5	3.6	4.6	5.9	4.993	3.277

INDIVIDUAL DATA 2-2-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Body weights (g) ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

Animal No.	Day of administration 1	2	7	14	21	28	Body weight gain Day 1-28	%
151	118	124	135	144	152	169	51.00	43.22
152	123	128	144	161	178	194	71.00	57.72
153	129	131	150	172	188	203	74.00	57.36
154	127	134	161	182	203	226	99.00	77.95
155	136	143	170	208	233	252	116.00	85.29
156	132	131	157	176	202	219	87.00	65.91
157	135	133	151	163	180	200	65.00	48.15
158	123	125	140	151	181	207	84.00	68.29
159	127	133	152	178	198	221	94.00	74.02
160	130	137	158	180	203	215	85.00	65.38
161	131	134	151	165	187	210	79.00	60.31
162	126	130	146	163	186	198	72.00	57.14
163	135	131	152	162	183	201	66.00	48.89
164	145	152	171	191	212	233	88.00	60.69
N	14	14	14	14	14	14	14	14
MEAN	129.8	133.3	152.7	171.1	191.9	210.6	80.786	62.166
S.D.	6.8	7.2	10.2	16.5	19.0	19.8	16.273	11.740
S.E.	1.8	1.9	2.7	4.4	5.1	5.3	4.349	3.138
M/C	1.9302	2.1938	3.9059	5.2604	7.9331*	4.3187	3.7324	2.1573
F	0.4986	1.0655	1.2403	0.9722		1.3172	1.2971	1.0444
H					3.4824			

INDIVIDUAL DATA 2-2-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Body weights (g) ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 4 mg/kg

Animal No.	Day of administration 1	2	7	14	21	28	Body weight gain Day 1-28	%
251	120	124	141	153	164	180	60.00	50.00
252	125	129	151	173	191	210	85.00	68.00
253	130	135	159	187	217	235	105.00	80.77
254	136	140	150	181	194	221	85.00	62.50
255	131	137	161	168	183	205	74.00	56.49
256	130	136	153	178	198	214	84.00	64.62
257	141	148	170	199	221	247	106.00	75.18
N	7	7	7	7	7	7	7	7
MEAN	130.4	135.6	155.0	177.0	195.4	216.0	85.571	65.366
S.D.	6.9	7.7	9.3	14.6	19.5	21.6	16.257	10.521
S.E.	2.6	2.9	3.5	5.5	7.4	8.2	6.145	3.977

INDIVIDUAL DATA 2-2-3

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Body weights (g) ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 20 mg/kg

Animal No.	Day of administration 1	2	7	14	21	28	Body weight gain Day 1-28	%
351	125	129	150	177	198	217	92.00	73.60
352	130	135	150	173	186	196	66.00	50.77
353	131	137	152	166	182	201	70.00	53.44
354	129	131	151	173	198	227	98.00	75.97
355	131	133	142	149	177	194	63.00	48.09
356	135	141	154	174	194	209	74.00	54.81
357	139	145	159	190	217	241	102.00	73.38
N	7	7	7	7	7	7	7	7
MEAN	131.4	135.9	151.1	171.7	193.1	212.1	80.714	61.437
S.D.	4.5	5.6	5.1	12.4	13.2	17.3	16.173	12.258
S.E.	1.7	2.1	1.9	4.7	5.0	6.5	6.113	4.633

INDIVIDUAL DATA 2-2-4

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Body weights (g) ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Day of administration 1	2	7	14	21	28	Body weight gain Day 1-28	%
451	126	123	144	172	188	206	80.00	63.49
452	118	127	149	165	184	206	88.00	74.58
453	129	134	155	175	189	209	80.00	62.02
454	132	137	154	177	189	203	71.00	53.79
455	126	132	150	165	171	188	62.00	49.21
456	131	136	151	170	183	200	69.00	52.67
457	138	139	159	178	202	223	85.00	61.59
458	121	122	128	144	165	172	51.00	42.15
459	125	128	146	168	181	208	83.00	66.40
460	129	131	148	166	187	204	75.00	58.14
461	128	133	148	167	185	198	70.00	54.69
462	134	133	149	165	189	208	74.00	55.22
463	132	135	149	161	182	200	68.00	51.52
464	127	130	144	161	180	199	72.00	56.69
N	14	14	14	14	14	14	14	14
MEAN	128.3	131.4	148.1	166.7	183.9	201.7	73.429	57.297
S.D.	5.2	5.0	7.1	8.5	8.7	11.5	9.725	8.013
S.E.	1.4	1.3	1.9	2.3	2.3	3.1	2.599	2.142

INDIVIDUAL DATA 2-3-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Body weights (g) ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal No.	Day of recovery 1	2	7	14	Body weight gain Day 1-14	%
108	311	311	335	369	58.00	18.65
109	322	327	351	375	53.00	16.46
110	394	405	446	489	95.00	24.11
111	372	378	410	439	67.00	18.01
112	330	335	358	397	67.00	20.30
113	336	343	368	396	60.00	17.86
114	334	341	357	375	41.00	12.28
N	7	7	7	7	7	7
MEAN	342.7	348.6	375.0	405.7	63.000	18.239
S.D.	29.5	32.1	39.0	43.7	16.703	3.600
S.E.	11.1	12.1	14.7	16.5	6.313	1.361
M/C	3.7367	3.4503	2.1692	1.7004	0.3724	0.0554
F	0.6285	0.5373	0.2840	0.5555	0.3290	0.1860

INDIVIDUAL DATA 2-3-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Body weights (g) ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

Animal	Day of recovery				Body weight gain	
No.	1	2	7	14	Day 1-14	%
408	350	358	394	428	78.00	22.29
409	334	346	371	391	57.00	17.07
410	327	330	354	380	53.00	16.21
411	318	324	342	361	43.00	13.52
412	344	350	379	404	60.00	17.44
413	319	321	342	365	46.00	14.42
414	340	343	381	412	72.00	21.18
N	7	7	7	7	7	7
MEAN	333.1	338.9	366.1	391.6	58.429	17.447
S.D.	12.4	14.0	20.4	24.7	12.869	3.257
S.E.	4.7	5.3	7.7	9.4	4.864	1.231

INDIVIDUAL DATA 2-4-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Body weights (g) ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

Animal No.	Day of recovery 1	2	7	14	Body weight gain Day 1-14	%
158	210	212	224	251	41.00	19.52
159	223	222	237	241	18.00	8.07
160	223	229	246	256	33.00	14.80
161	210	208	224	230	20.00	9.52
162	199	195	212	225	26.00	13.07
163	202	199	216	222	20.00	9.90
164	237	241	255	268	31.00	13.08
N	7	7	7	7	7	7
MEAN	214.9	215.1	230.6	241.9	27.000	12.566
S.D.	13.5	16.5	15.9	17.3	8.446	3.883
S.E.	5.1	6.2	6.0	6.5	3.192	1.468
M/C	0.0002	0.2433	0.1561	0.0057	0.7299	1.1551
F	4.3196†	2.3955	4.8172*	2.1398	0.1096	0.7792

INDIVIDUAL DATA 2-4-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Body weights (g) ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal	Day of recovery				Body weight gain	
No.	1	2	7	14	Day 1-14	%
458	172	175	186	192	20.00	11.63
459	207	215	228	241	34.00	16.43
460	208	207	220	241	33.00	15.87
461	203	209	221	237	34.00	16.75
462	213	212	216	237	24.00	11.27
463	195	200	210	218	23.00	11.79
464	201	201	212	231	30.00	14.93
N	7	7	7	7	7	7
MEAN	199.9	202.7	213.3	228.1	28.286	14.096
S.D.	13.5	13.4	13.5	17.8	5.851	2.440
S.E.	5.1	5.1	5.1	6.7	2.212	0.922
t'	2.0784		2.1948*			

INDIVIDUAL DATA 3-1-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Food consumption (g) ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal No.	Day of administration 1	2	7	14	21	28
101	19	19	21	24	22	24
102	19	21	22	27	32	30
103	18	19	23	27	28	27
104	18	19	23	24	24	23
105	17	20	22	23	22	22
106	17	19	20	21	22	29
107	20	21	24	24	24	26
108	19	18	20	23	25	24
109	17	18	23	24	18	23
110	19	19	23	26	29	29
111	20	22	25	25	27	27
112	21	21	24	24	27	26
113	21	21	23	26	29	22
114	20	19	22	22	24	22
N	14	14	14	14	14	14
MEAN	18.9	19.7	22.5	24.3	25.2	25.3
S.D.	1.4	1.3	1.5	1.8	3.7	2.8
S.E.	0.4	0.3	0.4	0.5	1.0	0.8
M/C	6.5680	2.8668	3.6252	1.5472	3.4515	3.4710
F	0.6696	0.4060	0.0707	1.1606	0.6975	0.8725

INDIVIDUAL DATA 3-1-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Food consumption (g) ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 4 mg/kg

Animal No.	Day of administration 1	2	7	14	21	28
201	18	15	20	23	25	26
202	19	19	24	27	27	29
203	18	19	19	22	20	19
204	18	20	25	28	26	29
205	19	19	20	22	25	25
206	18	20	24	25	23	28
207	19	21	23	28	27	32
N	7	7	7	7	7	7
MEAN	18.4	19.0	22.1	25.0	24.7	26.9
S.D.	0.5	1.9	2.4	2.7	2.5	4.1
S.E.	0.2	0.7	0.9	1.0	0.9	1.6

INDIVIDUAL DATA 3-1-3

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Food consumption (g) ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 20 mg/kg

Animal No.	Day of administration 1	2	7	14	21	28
301	17	18	24	25	28	24
302	18	19	20	22	24	24
303	19	18	22	25	25	27
304	17	19	21	22	26	27
305	19	19	24	20	21	23
306	19	22	23	23	20	22
307	19	20	24	26	26	25
N	7	7	7	7	7	7
MEAN	18.3	19.3	22.6	23.3	24.3	24.6
S.D.	1.0	1.4	1.6	2.1	2.9	1.9
S.E.	0.4	0.5	0.6	0.8	1.1	0.7

INDIVIDUAL DATA 3-1-4

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Food consumption (g) ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Day of administration 1	2	7	14	21	28
401	20	19	20	21	20	19
402	17	19	20	23	20	22
403	18	19	24	23	22	22
404	20	20	27	25	24	25
405	19	19	22	25	25	26
406	21	23	25	28	28	29
407	20	21	24	24	25	27
408	17	16	20	21	25	27
409	18	17	23	24	24	27
410	17	17	19	21	22	23
411	19	18	20	21	22	23
412	18	18	22	24	25	26
413	21	20	23	24	24	25
414	20	22	24	25	25	28
N	14	14	14	14	14	14
MEAN	18.9	19.1	22.4	23.5	23.6	24.9
S.D.	1.4	2.0	2.3	2.0	2.2	2.8
S.E.	0.4	0.5	0.6	0.5	0.6	0.7

INDIVIDUAL DATA 3-2-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Food consumption (g) ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

Animal No.	Day of administration 1	2	7	14	21	28
151	12	15	14	13	10	14
152	13	14	17	17	15	18
153	17	17	16	17	17	15
154	17	17	20	17	16	19
155	17	19	17	20	17	18
156	15	15	18	14	17	17
157	16	15	17	15	13	16
158	17	16	13	13	19	18
159	17	17	19	19	15	19
160	19	20	20	20	20	19
161	18	17	17	15	15	18
162	15	16	17	12	15	15
163	16	14	16	13	14	15
164	19	19	16	18	16	15
N	14	14	14	14	14	14
MEAN	16.3	16.5	16.9	15.9	15.6	16.9
S.D.	2.0	1.9	2.0	2.7	2.5	1.8
S.E.	0.5	0.5	0.5	0.7	0.7	0.5
M/C	2.8835	0.9570	1.8217	9.5767*	0.6176	4.5280
F	0.3532	1.5377	3.6709*		0.2637	1.3121
H				2.4950		

INDIVIDUAL DATA 3-2-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Food consumption (g) ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 4 mg/kg

Animal No.	Day of administration 1	2	7	14	21	28
251	14	16	17	17	16	16
252	20	17	16	16	16	17
253	16	17	18	19	17	17
254	20	19	16	19	16	19
255	16	17	20	16	9	16
256	15	21	19	20	17	21
257	18	19	16	17	17	21
N	7	7	7	7	7	7
MEAN	17.0	18.0	17.4	17.7	15.4	18.1
S.D.	2.4	1.7	1.6	1.6	2.9	2.2
S.E.	0.9	0.7	0.6	0.6	1.1	0.8
t'			0.6464			

INDIVIDUAL DATA 3-2-3

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Food consumption (g) ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 20 mg/kg

Animal No.	Day of administration 1	2	7	14	21	28
351	15	16	16	18	16	19
352	16	17	14	17	15	11
353	17	18	16	16	15	16
354	16	17	16	16	16	19
355	17	16	14	11	16	15
356	18	19	14	17	16	13
357	20	20	17	20	21	21
N	7	7	7	7	7	7
MEAN	17.0	17.6	15.3	16.4	16.4	16.3
S.D.	1.6	1.5	1.3	2.8	2.1	3.6
S.E.	0.6	0.6	0.5	1.0	0.8	1.4
t'			2.1240			

INDIVIDUAL DATA 3-2-4

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Food consumption (g) ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Day of administration 1	2	7	14	21	28
451	16	15	16	16	17	18
452	15	19	(29)	17	10	18
453	15	17	18	17	14	18
454	18	17	16	18	16	13
455	17	15	14	15	13	15
456	15	18	16	19	14	18
457	19	19	18	17	19	18
458	16	17	13	16	16	11
459	17	15	14	18	14	16
460	15	18	14	15	15	17
461	16	18	16	17	18	14
462	18	15	16	17	18	16
463	18	17	15	18	15	16
464	18	17	15	18	18	17
N	14	14	13	14	14	14
MEAN	16.6	16.9	15.5	17.0	15.5	16.1
S.D.	1.4	1.4	1.5	1.2	2.4	2.2
S.E.	0.4	0.4	0.4	0.3	0.7	0.6
t'			2.2795			

( ): Excluded from statistical analysis.

INDIVIDUAL DATA 3-3-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Food consumption (g) ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal No.	Day of recovery 1	2	7	14
108	21	21	24	23
109	21	22	24	25
110	27	28	32	32
111	28	28	30	28
112	25	26	24	30
113	25	26	29	29
114	20	22	22	23
N	7	7	7	7
MEAN	23.9	24.7	26.4	27.1
S.D.	3.2	3.0	3.8	3.5
S.E.	1.2	1.1	1.4	1.3
M/C	1.9873	1.3603	0.5671	0.1246
F	0.0436	0.0000	0.0577	0.2368

INDIVIDUAL DATA 3-3-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Food consumption (g) ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Day of recovery 1	2	7	14
408	25	25	26	30
409	23	28	26	24
410	24	24	27	25
411	21	23	22	23
412	24	26	26	26
413	22	23	24	25
414	26	24	31	31
N	7	7	7	7
MEAN	23.6	24.7	26.0	26.3
S.D.	1.7	1.8	2.8	3.0
S.E.	0.6	0.7	1.0	1.1

INDIVIDUAL DATA 3-4-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Food consumption (g) ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

Animal No.	Day of recovery 1	2	7	14
158	17	17	20	23
159	16	17	19	17
160	18	25	27	23
161	18	14	18	15
162	14	11	14	14
163	13	12	17	14
164	13	19	15	18
N	7	7	7	7
MEAN	15.6	16.4	18.6	17.7
S.D.	2.2	4.8	4.3	3.9
S.E.	0.8	1.8	1.6	1.5
M/C	0.5470	2.3827	0.4522	0.0025
F	0.0900	0.1256	2.4200	0.2248

INDIVIDUAL DATA 3-4-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Food consumption (g) ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Day of recovery 1	2	7	14
458	11	15	17	11
459	18	19	18	20
460	18	19	15	20
461	18	20	20	24
462	19	18	11	20
463	13	14	15	17
464	15	15	12	19
N	7	7	7	7
MEAN	16.0	17.1	15.4	18.7
S.D.	3.1	2.4	3.2	4.0
S.E.	1.2	0.9	1.2	1.5

INDIVIDUAL DATA 4-1-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Water consumption (g) ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal No.	Day of administration 1	2	7	14	21	28
101	25	27	30	32	34	29
102	26	29	32	34	42	38
103	27	26	31	32	36	29
104	23	25	30	32	36	31
105	25	24	27	26	28	24
106	24	25	28	28	36	30
107	30	29	31	35	38	35
108	26	24	33	36	38	36
109	25	25	30	29	32	27
110	25	25	31	33	40	37
111	26	27	30	29	41	33
112	26	24	27	28	34	31
113	32	30	35	37	52	37
114	26	24	27	27	33	24
N	14	14	14	14	14	14
MEAN	26.1	26.0	30.1	31.3	37.1	31.5
S.D.	2.3	2.1	2.3	3.5	5.7	4.7
S.E.	0.6	0.6	0.6	0.9	1.5	1.3
M/C	3.4265	7.6676	22.1194**	3.1941	2.1317	0.7585
F	1.5971	0.6052		1.3110	0.1038	0.1854
H			0.5899			

INDIVIDUAL DATA 4-1-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Water consumption (g) ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 4 mg/kg

Animal No.	Day of administration 1	2	7	14	21	28
201	22	22	27	31	37	30
202	27	27	34	40	44	39
203	22	23	24	28	27	23
204	26	27	35	41	38	36
205	26	26	26	29	32	28
206	28	28	36	42	42	38
207	23	26	32	34	38	38
N	7	7	7	7	7	7
MEAN	24.9	25.6	30.6	35.0	36.9	33.1
S.D.	2.5	2.2	4.8	5.9	5.8	6.2
S.E.	0.9	0.8	1.8	2.2	2.2	2.3

INDIVIDUAL DATA 4-1-3

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Water consumption (g) ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 20 mg/kg

Animal No.	Day of administration 1	2	7	14	21	28
301	24	25	31	32	40	29
302	24	23	27	28	33	31
303	26	25	31	36	40	41
304	24	24	28	29	35	33
305	25	25	31	30	33	32
306	26	26	34	33	32	26
307	27	24	32	36	38	32
N	7	7	7	7	7	7
MEAN	25.1	24.6	30.6	32.0	35.9	32.0
S.D.	1.2	1.0	2.4	3.2	3.4	4.6
S.E.	0.5	0.4	0.9	1.2	1.3	1.7

INDIVIDUAL DATA 4-1-4

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Water consumption (g) ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Day of administration 1	2	7	14	21	28
401	27	25	30	27	30	24
402	24	26	27	26	30	27
403	27	28	32	34	38	33
404	30	27	39	40	44	38
405	26	25	28	30	34	29
406	32	33	36	39	43	38
407	26	23	28	29	34	28
408	26	23	25	28	32	26
409	24	23	58	32	42	35
410	23	22	26	31	37	36
411	26	23	28	28	35	32
412	27	29	37	34	41	40
413	30	28	33	35	39	34
414	28	26	33	32	37	34
N	14	14	14	14	14	14
MEAN	26.9	25.8	32.9	31.8	36.9	32.4
S.D.	2.5	3.0	8.4	4.3	4.6	4.9
S.E.	0.7	0.8	2.2	1.1	1.2	1.3

INDIVIDUAL DATA 4-2-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Water consumption (g) ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

Animal No.	Day of administration 1	2	7	14	21	28
151	27	23	19	20	13	22
152	18	24	23	18	22	24
153	27	24	22	24	24	19
154	21	24	24	26	19	25
155	27	29	32	34	29	21
156	22	20	26	16	27	25
157	22	17	22	19	18	23
158	23	21	18	13	14	24
159	19	26	25	25	22	29
160	24	28	26	28	29	20
161	25	23	25	17	27	26
162	18	23	20	13	20	18
163	27	19	24	16	21	23
164	40	33	25	23	28	23
N	14	14	14	14	14	14
MEAN	24.3	23.9	23.6	20.9	22.4	23.0
S.D.	5.6	4.2	3.5	6.1	5.3	2.9
S.E.	1.5	1.1	0.9	1.6	1.4	0.8
M/C	3.6216	0.2247	1.1330	6.7832	0.6427	5.7462
F	0.1638	0.9008	0.1161	0.9366	0.0903	0.3754

INDIVIDUAL DATA 4-2-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Water consumption (g) ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 4 mg/kg

Animal No.	Day of administration 1	2	7	14	21	28
251	21	25	25	22	22	20
252	20	20	21	20	18	20
253	23	25	24	24	21	20
254	30	31	18	26	16	25
255	26	34	33	24	30	32
256	26	25	20	25	28	28
257	29	29	22	24	21	22
N	7	7	7	7	7	7
MEAN	25.0	27.0	23.3	23.6	22.3	23.9
S.D.	3.8	4.7	4.9	2.0	5.1	4.7
S.E.	1.4	1.8	1.8	0.8	1.9	1.8

INDIVIDUAL DATA 4-2-3

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Water consumption (g) ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 20 mg/kg

Animal No.	Day of administration 1	2	7	14	21	28
351	19	23	22	23	20	23
352	22	23	28	21	19	11
353	27	26	24	21	21	27
354	18	19	20	18	17	25
355	22	20	17	13	20	19
356	27	27	21	24	22	18
357	29	32	26	30	30	29
N	7	7	7	7	7	7
MEAN	23.4	24.3	22.6	21.4	21.3	21.7
S.D.	4.3	4.5	3.7	5.3	4.2	6.2
S.E.	1.6	1.7	1.4	2.0	1.6	2.3

INDIVIDUAL DATA 4-2-4

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Water consumption (g) ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Day of administration 1	2	7	14	21	28
451	23	20	20	25	20	26
452	19	27	26	30	18	32
453	23	27	30	28	17	26
454	24	24	24	26	24	20
455	26	28	28	27	20	27
456	33	33	31	34	25	33
457	25	21	24	20	22	22
458	24	25	17	20	25	13
459	22	21	19	22	13	20
460	22	23	19	19	22	23
461	24	28	23	26	29	20
462	26	18	20	18	22	22
463	24	26	22	19	29	29
464	20	22	20	18	20	21
N	14	14	14	14	14	14
MEAN	23.9	24.5	23.1	23.7	21.9	23.9
S.D.	3.3	4.0	4.3	5.0	4.4	5.4
S.E.	0.9	1.1	1.2	1.3	1.2	1.4

INDIVIDUAL DATA 4-3-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Water consumption (g) ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal No.	Day of recovery 1	2	7	14
108	34	34	44	37
109	25	30	29	27
110	35	40	41	40
111	36	36	37	34
112	27	30	27	28
113	52	44	54	51
114	23	25	28	24
N	7	7	7	7
MEAN	33.1	34.1	37.1	34.4
S.D.	9.8	6.5	10.0	9.3
S.E.	3.7	2.5	3.8	3.5
M/C	5.7295*	2.1681	5.3818*	3.9271*
F		0.2660		
H	0.0041		0.0371	0.2004

INDIVIDUAL DATA 4-3-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Water consumption (g) ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Day of recovery 1	2	7	14
408	26	27	33	32
409	35	36	32	31
410	32	35	35	35
411	31	29	32	32
412	33	33	35	39
413	32	34	35	36
414	36	35	42	41
N	7	7	7	7
MEAN	32.1	32.7	34.9	35.1
S.D.	3.2	3.4	3.4	3.8
S.E.	1.2	1.3	1.3	1.4

INDIVIDUAL DATA 4-4-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Water consumption (g) ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

Animal No.	Day of recovery 1	2	7	14
158	19	20	22	40
159	25	23	32	41
160	27	34	34	32
161	24	18	29	18
162	15	12	19	17
163	18	13	26	17
164	21	29	33	30
N	7	7	7	7
MEAN	21.3	21.3	27.9	27.9
S.D.	4.3	8.1	5.8	10.6
S.E.	1.6	3.1	2.2	4.0
M/C	0.3328	0.0142	2.1397	2.3081
F	0.3112	0.9674	0.2394	1.3324

INDIVIDUAL DATA 4-4-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
Water consumption (g) ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Day of recovery 1	2	7	14
458	16	19	26	16
459	19	25	25	26
460	23	23	18	35
461	24	41	27	38
462	23	24	14	25
463	20	28	48	79
464	16	18	21	47
N	7	7	7	7
MEAN	20.1	25.4	25.6	38.0
S.D.	3.3	7.7	10.9	20.7
S.E.	1.3	2.9	4.1	7.8

INDIVIDUAL DATA 5-1-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Day 23 of adm.
Urinary findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal No.	pH	Pro	Glu	Ket	Uro EU/dl	Bil	Occult blood	Urinary sediments RBC	WBC	Epithelial cell Squamous	Round	Small round	Others	Grav
101	8.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.047
102	7.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.043
103	8.0	+	−	−	0.1	−	−	−	−	−	−	−	−	1.051[a)]
104	7.5	+	−	−	0.1	−	−	−	−	−	−	−	−	1.046
105	8.5	−	−	−	0.1	−	−	−	−	−	−	−	−	1.036
106	7.5	−	−	−	0.1	−	−	−	−	−	−	−	−	1.051[a)]
107	8.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.038
108	8.0	±	−	−	0.1	−	−	−	−	−	−	−	−	1.038
109	8.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.025
110	8.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.037
111	8.0	++	−	±	0.1	−	−	−	−	−	−	−	−	1.044
112	8.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.041
113	8.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.040
114	8.0	+	−	±	0.1	−	−	−	−	−	−	−	−	1.051[a)]
N	14	14	14	14	14	14	14	14	14	14	14	14	14	14
H	1.3558	1.4863	0.0000	4.1000	0.0000	0.0000	4.0976	0.0000	0.0000	2.5625	0.0000	0.0000	0.0000	0.9819

a): Over the maximum value of scale.

INDIVIDUAL DATA 5-1-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Day 23 of adm.
Urinary findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 4 mg/kg

								Urinary sediments						
										Epithelial cell				
Animal No.	pH	Pro	Glu	Ket	Uro EU/dl	Bil	Occult blood	RBC	WBC	Squamous	Round	Small round	Others	Grav
201	8.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.041
202	8.0	+	−	−	0.1	−	−	−	−	−	−	−	−	1.047
203	8.5	+	−	−	0.1	−	−	−	−	−	−	−	−	1.035
204	8.0	±	−	−	0.1	−	−	−	−	−	−	−	−	1.023
205	8.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.045
206	8.5	+	−	−	0.1	−	−	−	−	±	−	−	−	1.043
207	8.0	±	−	−	0.1	−	−	−	−	−	−	−	−	1.039
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7

INDIVIDUAL DATA 5-1-3

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Day 23 of adm.
Urinary findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 20 mg/kg

Animal No.	pH	Pro	Glu	Ket	Uro EU/dl	Bil	Occult blood	Urinary sediments RBC	WBC	Epithelial cell Squamous	Round	Small round	Others	Grav
301	8.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.033
302	8.5	+	−	−	0.1	−	−	−	−	−	−	−	−	1.048
303	7.5	+	−	−	0.1	−	−	−	−	−	−	−	−	1.034
304	8.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.023
305	8.5	+	−	−	0.1	−	−	−	−	−	−	−	−	1.051[a)]
306	8.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.044
307	8.0	±	−	−	0.1	−	−	−	−	−	−	−	−	1.045
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7

a): Over the maximum value of scale.

INDIVIDUAL DATA 5-1-4

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Day 23 of adm.
Urinary findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

								Urinary sediments						
										Epithelial cell				
Animal No.	pH	Pro	Glu	Ket	Uro EU/dl	Bil	Occult blood	RBC	WBC	Squamous	Round	Small round	Others	Grav
401	8.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.045
402	8.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.043
403	7.5	+	−	−	0.1	−	−	−	−	−	−	−	−	1.046
404	8.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.041
405	8.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.050
406	6.5	±	−	−	0.1	−	−	−	−	±	−	−	−	1.045
407	8.0	++	−	−	0.1	−	±	−	−	−	−	−	−	1.044
408	8.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.023
409	8.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.032
410	8.0	+	−	−	0.1	−	−	−	−	−	−	−	−	1.040
411	8.5	+	−	−	0.1	−	−	−	−	−	−	−	−	1.043
412	8.5	+	−	−	0.1	−	−	−	−	−	−	−	−	1.031
413	8.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.038
414	8.5	+	−	−	0.1	−	+	−	−	−	−	−	−	1.024
N	14	14	14	14	14	14	14	14	14	14	14	14	14	14

INDIVIDUAL DATA 5-1-5

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Day 23 of adm.
Urinary findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal No.	U-Vol ml/21hr	U-Na mEq/21hr	U-K mEq/21hr	U-Cl mEq/21hr
101	12.0	1.344	3.492	2.028
102	15.0	1.440	3.360	2.055
103	10.0	1.380	3.300	2.150
104	14.0	1.708	3.570	2.128
105	15.0	0.960	2.655	1.470
106	11.0	1.441	3.212	2.211
107	19.0	1.672	4.009	2.337
108	15.0	1.170	2.910	1.905
109	22.0	0.704	2.112	0.946
110	19.5	1.482	3.627	2.145
111	14.0	1.288	3.570	2.016
112	15.0	1.140	3.270	2.025
113	15.5	1.225	3.069	1.845
114	9.5	1.739	3.634	2.518
N	14	14	14	14
MEAN	14.75	1.3352	3.2707	1.9842
S.D.	3.58	0.2883	0.4753	0.3835
S.E.	0.96	0.0770	0.1270	0.1025
M/C	2.4972	3.1429	2.1919	4.0970
F	0.2738	0.2834	0.2061	0.2342

INDIVIDUAL DATA 5-1-6

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Day 23 of adm.
Urinary findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 4 mg/kg

Animal No.	U-Vol ml/21hr	U-Na mEq/21hr	U-K mEq/21hr	U-Cl mEq/21hr
201	16.0	1.808	3.520	2.432
202	13.0	1.183	3.627	2.158
203	12.0	0.696	2.316	1.020
204	24.5	0.907	2.058	1.005
205	13.5	1.674	3.537	2.147
206	14.0	1.498	3.542	2.170
207	19.5	1.736	4.017	2.535
N	7	7	7	7
MEAN	16.07	1.3574	3.2310	1.9239
S.D.	4.47	0.4353	0.7373	0.6401
S.E.	1.69	0.1645	0.2787	0.2419

INDIVIDUAL DATA 5-1-7

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Day 23 of adm.
Urinary findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 20 mg/kg

Animal No.	U-Vol ml/21hr	U-Na mEq/21hr	U-K mEq/21hr	U-Cl mEq/21hr
301	18.0	1.206	2.880	1.530
302	11.0	1.309	3.278	2.112
303	24.5	1.985	4.067	2.720
304	23.0	0.805	2.208	0.690
305	8.5	1.186	2.754	2.006
306	13.5	1.485	3.416	2.201
307	15.5	2.015	4.185	2.728
N	7	7	7	7
MEAN	16.29	1.4273	3.2554	1.9981
S.D.	5.95	0.4412	0.7116	0.7116
S.E.	2.25	0.1668	0.2690	0.2690

INDIVIDUAL DATA 5-1-8

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Day 23 of adm.
Urinary findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

Animal No.	U-Vol ml/21hr	U-Na mEq/21hr	U-K mEq/21hr	U-Cl mEq/21hr
401	11.5	1.035	3.278	1.990
402	13.5	1.323	3.267	2.133
403	13.5	1.539	3.686	2.214
404	15.0	1.440	3.360	2.160
405	12.0	1.530	3.564	2.316
406	14.5	1.653	3.959	2.393
407	10.5	0.462	2.352	0.893
408	23.5	0.588	1.857	0.776
409	21.5	1.204	3.053	1.785
410	15.5	1.147	3.038	1.705
411	13.5	1.809	3.510	2.268
412	20.0	1.600	3.100	2.040
413	17.5	1.855	3.570	2.328
414	18.0	0.450	1.782	0.522
N	14	14	14	14
MEAN	15.71	1.2596	3.0983	1.8231
S.D.	3.89	0.4742	0.6599	0.6280
S.E.	1.04	0.1267	0.1764	0.1679

INDIVIDUAL DATA 5-2-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Day 23 of adm.
Urinary findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

								Urinary sediments						
										Epithelial cell				
Animal No.	pH	Pro	Glu	Ket	Uro EU/dl	Bil	Occult blood	RBC	WBC	Squamous	Round	Small round	Others	Grav
151	8.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.035
152	7.5	+	−	−	0.1	−	−	−	−	−	−	−	−	1.047
153	8.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.050
154	8.0	±	−	−	0.1	−	−	−	−	−	−	−	−	1.043
155	8.0	±	−	−	0.1	−	−	−	−	−	−	−	−	1.036
156	8.5	±	−	−	0.1	−	−	−	−	±	−	−	−	1.034
157	8.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.044
158	7.0	±	−	−	0.1	−	−	−	−	−	−	−	−	1.046
159	8.0	±	−	−	0.1	−	−	−	−	−	−	−	−	1.051[a)]
160	8.5	−	−	−	0.1	−	−	−	−	−	−	−	−	1.031
161	8.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.045
162	8.5	+	−	−	0.1	−	−	−	−	−	−	−	−	1.051[a)]
163	8.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.045
164	8.5	−	−	−	0.1	−	−	−	−	−	−	−	−	1.041
N	14	14	14	14	14	14	14	14	14	14	14	14	14	14
H	5.6738	2.4808	0.0000	0.0000	0.0000	0.0000	4.1000	0.0000	0.0000	1.0513	0.0000	0.0000	0.0000	3.1244

a): Over the maximum value of scale.

INDIVIDUAL DATA 5-2-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Day 23 of adm.
Urinary findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 4 mg/kg

								Urinary sediments						
										Epithelial cell				
Animal No.	pH	Pro	Glu	Ket	Uro EU/dl	Bil	Occult blood	RBC	WBC	Squamous	Round	Small round	Others	Grav
251	8.0	−	−	−	0.1	−	−	−	−	−	−	−	−	1.030
252	8.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.050
253	8.5	+	−	−	0.1	−	−	−	−	−	−	−	−	1.041
254	8.0	±	−	−	0.1	−	−	−	−	−	−	−	−	1.050
255	8.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.030
256	8.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.040
257	7.0	+	−	−	0.1	−	−	−	−	−	−	−	−	1.046
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7

INDIVIDUAL DATA 5-2-3

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Day 23 of adm.
Urinary findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 20 mg/kg

								Urinary sediments						
										Epithelial cell				
Animal No.	pH	Pro	Glu	Ket	Uro EU/dl	Bil	Occult blood	RBC	WBC	Squamous	Round	Small round	Others	Grav
351	6.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.041
352	8.0	+	−	−	0.1	−	−	−	−	−	−	−	−	1.051[a)]
353	8.0	−	−	−	0.1	−	−	−	−	±	−	−	−	1.032
354	7.5	+	−	−	0.1	−	−	−	−	−	−	−	−	1.049
355	6.5	++	−	−	0.1	−	−	−	−	−	−	−	−	1.051[a)]
356	8.0	±	−	−	0.1	−	−	−	−	−	−	−	−	1.049
357	8.5	−	−	−	0.1	−	−	−	−	−	−	−	−	1.043
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7

a): Over the maximum value of scale.

INDIVIDUAL DATA 5-2-4

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Day 23 of adm.
Urinary findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal No.	pH	Pro	Glu	Ket	Uro EU/dl	Bil	Occult blood	Urinary sediments RBC	WBC	Epithelial cell Squamous	Round	Small round	Others	Grav
451	8.5	+	−	−	0.1	−	±	−	−	−	−	−	−	1.035
452	8.5	−	−	−	0.1	−	−	−	−	−	−	−	−	1.017
453	7.5	+	−	−	0.1	−	−	−	−	−	−	−	−	1.042
454	8.5	±	−	−	0.1	−	±	−	−	−	−	−	−	1.051[a)]
455	7.5	+	−	−	0.1	−	−	−	−	−	−	−	−	1.036
456	8.5	−	−	−	0.1	−	−	−	−	−	−	−	−	1.033
457	7.5	+	−	−	0.1	−	−	−	−	−	−	−	−	1.051[a)]
458	6.5	+	−	−	0.1	−	−	−	−	−	−	−	−	1.020
459	8.5	−	−	−	0.1	−	−	−	−	−	−	−	−	1.040
460	8.5	±	−	−	0.1	−	−	−	−	±	−	−	−	1.048
461	8.0	±	−	−	0.1	−	−	−	−	−	−	−	−	1.040
462	6.5	++	−	−	0.1	−	−	−	−	−	−	−	−	1.042
463	8.0	+	−	−	0.1	−	−	−	−	−	−	−	−	1.048
464	6.5	++	−	−	0.1	−	−	−	−	−	−	−	−	1.032
N	14	14	14	14	14	14	14	14	14	14	14	14	14	14

a): Over the maximum value of scale.

INDIVIDUAL DATA 5-2-5

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Day 23 of adm.
Urinary findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

Animal No.	U-Vol ml/21hr	U-Na mEq/21hr	U-K mEq/21hr	U-Cl mEq/21hr
151	19.0	1.634	2.926	2.128
152	7.5	0.675	1.763	1.043
153	7.0	0.924	1.869	1.302
154	12.5	1.650	2.850	2.100
155	13.0	1.430	2.522	1.573
156	14.0	0.700	1.932	1.022
157	10.5	1.103	2.594	1.722
158	9.0	0.954	2.547	1.503
159	8.0	1.140	2.424	1.432
160	5.0	0.200	0.610	0.355
161	11.5	1.162	2.783	1.886
162	4.0	0.642	1.590	0.956
163	11.0	1.089	2.816	1.705
164	10.5	1.197	2.247	1.596
N	14	14	14	14
MEAN	10.18	1.0357	2.2481	1.4516
S.D.	3.89	0.3987	0.6410	0.4855
S.E.	1.04	0.1066	0.1713	0.1298
M/C	0.2473	8.9229*	3.1699	7.0963
F	0.4817		1.0174	2.2776†
H		7.0580†		

INDIVIDUAL DATA 5-2-6

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Day 23 of adm.
Urinary findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 4 mg/kg

Animal No.	U-Vol ml/21hr	U-Na mEq/21hr	U-K mEq/21hr	U-Cl mEq/21hr
251	17.5	1.243	2.433	1.680
252	9.0	1.224	2.610	1.746
253	9.0	1.062	1.854	1.377
254	10.5	1.376	2.940	1.922
255	18.0	1.368	2.448	1.674
256	11.0	0.957	2.222	1.419
257	10.0	1.160	2.380	1.620
N	7	7	7	7
MEAN	12.14	1.1986	2.4124	1.6340
S.D.	3.90	0.1535	0.3337	0.1878
S.E.	1.47	0.0580	0.1261	0.0710
t'				0.9826
U		33.0000		

INDIVIDUAL DATA 5-2-7

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Day 23 of adm.
Urinary findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 20 mg/kg

Animal No.	U-Vol ml/21hr	U-Na mEq/21hr	U-K mEq/21hr	U-Cl mEq/21hr
351	11.5	1.334	2.381	1.817
352	6.0	0.984	1.746	1.194
353	18.0	1.332	2.700	1.656
354	9.5	1.302	2.575	1.815
355	4.0	1.020	1.554	1.208
356	8.0	1.016	2.288	1.512
357	12.0	1.104	2.664	1.560
N	7	7	7	7
MEAN	9.86	1.1560	2.2726	1.5374
S.D.	4.59	0.1604	0.4533	0.2572
S.E.	1.73	0.0606	0.1713	0.0972
t'				0.4622
U		39.0000		

INDIVIDUAL DATA 5-2-8

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Day 23 of adm.
Urinary findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal No.	U-Vol ml/21hr	U-Na mEq/21hr	U-K mEq/21hr	U-Cl mEq/21hr
451	15.5	1.101	2.697	1.612
452	18.5	0.370	1.314	0.426
453	11.0	1.221	2.475	1.606
454	7.0	1.218	2.310	1.519
455	11.0	0.968	2.002	1.287
456	12.0	0.624	1.872	0.876
457	8.5	0.935	2.525	1.581
458	17.0	0.799	1.649	0.935
459	11.0	0.935	2.244	1.265
460	7.0	0.903	1.785	1.225
461	11.5	1.150	2.415	1.484
462	11.5	1.277	2.657	1.725
463	5.0	0.755	1.270	0.840
464	6.0	0.300	0.828	0.438
N	14	14	14	14
MEAN	10.89	0.8969	2.0031	1.2014
S.D.	4.05	0.3044	0.5757	0.4328
S.E.	1.08	0.0813	0.1539	0.1157
t'				1.6517
U		80.0000		

INDIVIDUAL DATA 5-3-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Day 11 of recovery
Urinary findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal No.	pH	Pro	Glu	Ket	Uro EU/dl	Bil	Occult blood	Urinary sediments RBC	WBC	Epithelial cell Squamous	Round	Small round	Others	Grav
108	7.0	+	−	−	0.1	−	−	−	−	−	−	−	−	1.043
109	8.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.051[a)]
110	8.0	+	−	−	0.1	−	−	−	−	±	−	−	−	1.046
111	7.5	+	−	−	0.1	−	−	−	−	−	−	−	−	1.050
112	8.5	+	−	−	0.1	−	−	−	−	−	−	−	−	1.051[a)]
113	8.0	±	−	−	0.1	−	−	−	−	−	−	−	−	1.037
114	8.0	+	−	−	0.1	−	−	−	−	−	−	−	−	1.051[a)]
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7
H	0.1611	0.2889	0.0000	0.0000	0.0000	0.0000	1.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	2.0245

a): Over the maximum value of scale.

INDIVIDUAL DATA 5-3-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Day 11 of recovery
Urinary findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

								Urinary sediments						
										Epithelial cell				
Animal No.	pH	Pro	Glu	Ket	Uro EU/dl	Bil	Occult blood	RBC	WBC	Squamous	Round	Small round	Others	Grav
408	8.0	±	−	−	0.1	−	−	−	−	−	−	−	−	1.026
409	8.5	+	−	−	0.1	−	−	−	−	−	−	−	−	1.048
410	7.5	+	−	−	0.1	−	−	−	−	−	−	−	−	1.051[a)]
411	7.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.030
412	8.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.040
413	7.5	+	−	−	0.1	−	−	−	−	±	−	−	−	1.049
414	7.5	+	−	−	0.1	−	+	−	−	−	−	−	−	1.040
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7

a): Over the maximum value of scale.

INDIVIDUAL DATA 5-3-3

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Day 11 of recovery
Urinary findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal No.	U-Vol ml/21hr	U-Na mEq/21hr	U-K mEq/21hr	U-Cl mEq/21hr
108	14.0	1.260	2.912	1.820
109	10.0	1.575	3.240	2.170
110	18.0	1.890	4.392	2.646
111	15.0	1.965	4.110	2.475
112	12.0	1.314	3.780	2.424
113	22.5	1.463	3.915	2.205
114	10.5	1.575	3.749	2.415
N	7	7	7	7
MEAN	14.57	1.5774	3.7283	2.3079
S.D.	4.46	0.2681	0.5048	0.2692
S.E.	1.68	0.1013	0.1908	0.1018
M/C	1.4477	3.9967*	1.2625	6.6773**
F	0.1077		5.9695*	
H		1.8040		2.9821[1]

INDIVIDUAL DATA 5-3-4

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Day 11 of recovery
Urinary findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

Animal No.	U-Vol ml/21hr	U-Na mEq/21hr	U-K mEq/21hr	U-Cl mEq/21hr
408	20.0	0.480	1.880	0.740
409	15.5	2.155	3.813	2.868
410	11.5	1.397	3.467	2.151
411	15.5	0.341	1.628	0.388
412	15.5	0.853	2.682	1.225
413	13.0	1.716	3.328	2.314
414	15.5	0.961	3.069	1.225
N	7	7	7	7
MEAN	15.21	1.1290	2.8381	1.5587
S.D.	2.64	0.6603	0.8212	0.9036
S.E.	1.00	0.2496	0.3104	0.3415
t'			2.4432*	
U				11.0000

INDIVIDUAL DATA 5-4-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Day 11 of recovery
Urinary findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

								Urinary sediments						
										Epithelial cell				
Animal No.	pH	Pro	Glu	Ket	Uro EU/dl	Bil	Occult blood	RBC	WBC	Squamous	Round	Small round	Others	Grav
158	8.5	+	−	−	0.1	−	−	−	−	−	−	−	−	1.040
159	8.0	−	−	−	0.1	−	−	−	−	−	−	−	−	1.045
160	7.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.041
161	8.5	+	−	−	0.1	−	−	−	−	−	−	−	−	1.037
162	8.5	++	−	−	0.1	−	−	−	−	−	−	−	−	1.051[a)]
163	8.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.045
164	8.0	±	−	−	0.1	−	−	−	−	−	−	−	−	1.027
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7
H	1.6513	0.0049	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	1.0000	0.0000	0.0000	0.0000	0.0372

a): Over the maximum value of scale.

INDIVIDUAL DATA 5-4-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Day 11 of recovery
Urinary findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

								Urinary sediments						
										Epithelial cell				
Animal No.	pH	Pro	Glu	Ket	Uro EU/dl	Bil	Occult blood	RBC	WBC	Squamous	Round	Small round	Others	Grav
458	8.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.045
459	8.5	+	−	−	0.1	−	−	−	−	−	−	−	−	1.043
460	7.5	+	−	−	0.1	−	−	−	−	±	−	−	−	1.046
461	7.5	±	−	−	0.1	−	−	−	−	−	−	−	−	1.036
462	7.0	+	−	−	0.1	−	−	−	−	−	−	−	−	1.041
463	8.0	±	−	−	0.1	−	−	−	−	−	−	−	−	1.040
464	8.0	±	−	−	0.1	−	−	−	−	−	−	−	−	1.029
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7

INDIVIDUAL DATA 5-4-3

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Day 11 of recovery
Urinary findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

Animal No.	U-Vol ml/21hr	U-Na mEq/21hr	U-K mEq/21hr	U-Cl mEq/21hr
158	9.0	0.450	1.377	0.684
159	7.5	0.773	1.673	1.035
160	13.5	1.269	2.619	1.593
161	19.5	1.560	3.198	2.223
162	7.0	0.896	2.093	1.442
163	12.5	1.288	2.825	1.950
164	29.0	1.740	3.538	2.233
N	7	7	7	7
MEAN	14.00	1.1394	2.4747	1.5943
S.D.	7.90	0.4556	0.7948	0.5908
S.E.	2.98	0.1722	0.3004	0.2233
M/C	8.1775**	0.3753	0.4686	0.0999
F		0.1038	0.0219	0.0087
H	0.2624			

INDIVIDUAL DATA 5-4-4

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : Day 11 of recovery
Urinary findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal No.	U-Vol ml/21hr	U-Na mEq/21hr	U-K mEq/21hr	U-Cl mEq/21hr
458	12.0	1.308	2.796	1.968
459	14.5	1.581	2.813	2.059
460	9.5	1.007	2.195	1.549
461	15.0	1.320	2.565	1.605
462	14.5	1.479	2.828	1.958
463	13.5	1.242	2.565	1.674
464	11.5	0.529	1.173	0.541
N	7	7	7	7
MEAN	12.93	1.2094	2.4193	1.6220
S.D.	2.01	0.3506	0.5930	0.5165
S.E.	0.76	0.1325	0.2241	0.1952

INDIVIDUAL DATA 6-1-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Hematological findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal No.	RBC $10^6/\mu l$	Ht. %	Hb. g/dl	MCV fl	MCH pg	MCHC %	WBC $10^3/\mu l$	Plat $10^3/\mu l$
101	7.47	45.7	14.9	61.2	19.9	32.6	16.6	1195
102	7.63	46.6	15.4	61.1	20.1	33.0	27.7	1051
103	7.26	45.3	14.4	62.4	19.8	31.7	18.2	1190
104	7.23	44.8	14.4	61.9	19.9	32.1	10.8	1182
105	7.55	45.8	14.5	60.6	19.2	31.6	11.5	1128
106	7.08	43.4	14.4	61.3	20.3	33.1	14.6	1198
107	7.63	48.1	15.7	63.1	20.5	32.6	14.0	1221
N	7	7	7	7	7	7	7	7
MEAN	7.407	45.67	14.81	61.66	19.96	32.39	16.20	1166.4
S.D.	0.217	1.46	0.54	0.86	0.42	0.60	5.70	58.3
S.E.	0.082	0.55	0.20	0.33	0.16	0.23	2.16	22.0
M/C	4.8232	4.5582	6.6077	6.6953	0.0625	8.7412*	3.8013	1.5956
F	1.2526	1.1763	0.4946	0.0161	1.9797		1.9542	0.9289
H						7.4507†		

INDIVIDUAL DATA 6-1-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Hematological findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 4 mg/kg

Animal No.	RBC $10^6/\mu l$	Ht. %	Hb. g/dl	MCV fl	MCH pg	MCHC %	WBC $10^3/\mu l$	Plat $10^3/\mu l$
201	7.17	44.5	14.5	62.1	20.2	32.5	17.3	1273
202	7.17	45.5	14.8	63.4	20.6	32.5	13.7	995
203	7.39	44.7	14.4	60.5	19.4	32.2	11.0	1156
204	7.19	44.0	14.3	61.2	19.8	32.5	12.2	1115
205	7.07	43.1	14.0	61.0	19.8	32.4	8.7	1117
206	7.30	44.6	14.5	61.1	19.8	32.5	7.0	1017
207	7.41	45.4	14.6	61.3	19.7	32.1	11.0	1139
N	7	7	7	7	7	7	7	7
MEAN	7.243	44.54	14.44	61.51	19.90	32.39	11.56	1116.0
S.D.	0.127	0.82	0.25	0.96	0.39	0.17	3.36	92.4
S.E.	0.048	0.31	0.09	0.36	0.15	0.06	1.27	34.9
U						20.5000		

INDIVIDUAL DATA 6-1-3

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Hematological findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 20 mg/kg

Animal No.	RBC $10^6/\mu l$	Ht. %	Hb. g/dl	MCV fl	MCH pg	MCHC %	WBC $10^3/\mu l$	Plat $10^3/\mu l$
301	7.58	46.2	15.7	60.9	20.7	33.9	14.7	1202
302	6.84	41.3	13.5	60.4	19.7	32.6	11.9	1080
303	7.22	45.1	14.8	62.4	20.4	32.8	18.1	1358
304	7.20	44.6	14.7	62.0	20.4	32.9	11.0	1154
305	6.70	42.1	13.5	62.8	20.1	32.0	16.3	1271
306	7.58	46.0	15.0	60.7	19.7	32.6	8.1	1132
307	7.15	44.3	14.7	61.9	20.5	33.1	11.7	1130
N	7	7	7	7	7	7	7	7
MEAN	7.181	44.23	14.56	61.59	20.21	32.84	13.11	1189.6
S.D.	0.334	1.87	0.80	0.92	0.39	0.58	3.43	96.0
S.E.	0.126	0.71	0.30	0.35	0.15	0.22	1.30	36.3
U						15.5000		

INDIVIDUAL DATA 6-1-4

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Hematological findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

Animal No.	RBC $10^6/\mu l$	Ht. %	Hb. g/dl	MCV fl	MCH pg	MCHC %	WBC $10^3/\mu l$	Plat $10^3/\mu l$
401	7.17	42.4	14.3	59.1	19.9	33.7	11.8	1112
402	7.28	45.1	14.7	61.9	20.1	32.5	14.4	993
403	7.48	44.4	15.2	59.4	20.3	34.2	10.2	1148
404	7.16	45.0	14.8	62.9	20.6	32.8	10.4	1164
405	7.47	46.7	15.5	62.5	20.7	33.1	15.3	1132
406	7.07	45.9	14.9	64.9	21.0	32.4	8.0	1156
407	6.72	40.8	13.4	60.7	19.9	32.8	14.0	1307
N	7	7	7	7	7	7	7	7
MEAN	7.193	44.33	14.69	61.63	20.36	33.07	12.01	1144.6
S.D.	0.260	2.05	0.68	2.06	0.42	0.66	2.66	92.3
S.E.	0.098	0.78	0.26	0.78	0.16	0.25	1.01	34.9
U						12.5000		

INDIVIDUAL DATA 6-1-5

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Hematological findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

					Hemogram of WBC						
					Neutro.						
Animal No.	Ret %.	CT sec.	PT sec.	APTT sec.	Stab. %	Seg. %	Eos. %	Bas. %	Mono. %	Lymp. %	Others %
101	19	184	12.1	26.0	0	11	0	0	0	89	0
102	20	241	12.9	22.7	0	10	1	0	0	89	0
103	26	176	12.2	27.7	0	11	0	0	0	89	0
104	20	151	12.1	26.1	0	10	1	0	0	89	0
105	24	216	13.0	24.9	0	16	0	0	0	84	0
106	18	235	12.6	25.1	0	11	2	0	0	87	0
107	13	84	12.9	25.3	0	6	1	0	0	93	0
N	7	7	7	7	7	7	7	7	7	7	7
MEAN	20.0	183.9	12.54	25.40	0.0	10.7	0.7	0.0	0.0	88.6	0.0
S.D.	4.2	54.8	0.40	1.52	0.0	2.9	0.8	0.0	0.0	2.7	0.0
S.E.	1.6	20.7	0.15	0.57	0.0	1.1	0.3	0.0	0.0	1.0	0.0
M/C	3.4074	0.2460	1.3629	2.4981	∞**	2.2325	3.8316	0.0000	0.0000	2.5208	0.0000
F	0.5709	1.5512	2.1419	6.4432**		0.3637	1.2121	0.0000	0.0000	0.3010	0.0000
H					2.2500						

INDIVIDUAL DATA 6-1-6

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Hematological findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 4 mg/kg

					Hemogram of WBC						
					Neutro.						
Animal No.	Ret %.	CT sec.	PT sec.	APTT sec.	Stab. %	Seg. %	Eos. %	Bas. %	Mono. %	Lymp. %	Others %
201	24	182	12.8	21.6	0	7	0	0	0	93	0
202	23	207	13.9	28.9	0	8	1	0	0	91	0
203	19	179	14.0	27.7	0	5	1	0	0	94	0
204	19	221	12.9	29.4	1	8	0	0	0	91	0
205	25	131	12.3	23.8	0	16	2	0	0	82	0
206	22	251	12.9	25.1	0	10	0	0	0	90	0
207	16	105	13.1	28.8	0	7	0	0	0	93	0
N	7	7	7	7	7	7	7	7	7	7	7
MEAN	21.1	182.3	13.13	26.47	0.1	8.7	0.6	0.0	0.0	90.6	0.0
S.D.	3.2	50.7	0.61	3.00	0.4	3.5	0.8	0.0	0.0	4.0	0.0
S.E.	1.2	19.2	0.23	1.14	0.1	1.3	0.3	0.0	0.0	1.5	0.0
t'				0.8518							

INDIVIDUAL DATA 6-1-7

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Hematological findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 20 mg/kg

					Hemogram of WBC						
					Neutro.						
Animal No.	Ret %,	CT sec.	PT sec.	APTT sec.	Stab. %	Seg. %	Eos. %	Bas. %	Mono. %	Lymp. %	Others %
301	20	137	12.7	28.2	0	5	0	0	0	95	0
302	24	223	13.7	29.2	0	7	1	0	0	92	0
303	17	117	12.6	29.2	0	5	0	0	0	95	0
304	25	219	12.8	28.6	1	7	1	0	0	91	0
305	29	155	12.7	23.7	1	18	0	0	0	81	0
306	18	172	13.7	29.2	0	14	0	0	0	86	0
307	16	228	14.1	31.8	0	14	0	0	0	86	0
N	7	7	7	7	7	7	7	7	7	7	7
MEAN	21.3	178.7	13.19	28.56	0.3	10.0	0.3	0.0	0.0	89.4	0.0
S.D.	4.8	45.0	0.62	2.43	0.5	5.2	0.5	0.0	0.0	5.3	0.0
S.E.	1.8	17.0	0.24	0.92	0.2	2.0	0.2	0.0	0.0	2.0	0.0
t'				2.5100*							

INDIVIDUAL DATA 6-1-8

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Hematological findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

					Hemogram of WBC						
					Neutro.						
Animal No.	Ret %.	CT sec.	PT sec.	APTT sec.	Stab. %	Seg. %	Eos. %	Bas. %	Mono. %	Lymp. %	Others %
401	19	253	13.6	31.5	0	8	0	0	0	92	0
402	15	158	13.8	28.6	0	10	0	0	0	90	0
403	19	224	12.6	29.6	0	7	0	0	0	93	0
404	21	238	13.2	32.0	0	8	0	0	0	92	0
405	18	317	12.5	27.2	1	11	0	0	0	88	0
406	22	171	12.9	30.7	0	12	1	0	0	87	0
407	19	246	13.0	33.8	0	17	0	0	0	83	0
N	7	7	7	7	7	7	7	7	7	7	7
MEAN	19.0	229.6	13.09	30.49	0.1	10.4	0.1	0.0	0.0	89.3	0.0
S.D.	2.2	53.4	0.48	2.22	0.4	3.4	0.4	0.0	0.0	3.5	0.0
S.E.	0.8	20.2	0.18	0.84	0.1	1.3	0.1	0.0	0.0	1.3	0.0
t'				4.0432**							

INDIVIDUAL DATA 6-2-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Hematological findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

Animal No.	RBC $10^6/\mu l$	Ht. %	Hb. g/dl	MCV fl	MCH pg	MCHC %	WBC $10^3/\mu l$	Plat $10^3/\mu l$
151	7.81	45.2	15.5	57.9	19.8	34.2	10.8	1050
152	7.35	44.0	15.1	59.8	20.5	34.3	18.1	1177
153	7.67	46.9	15.8	61.2	20.5	33.6	9.2	1091
154	7.40	44.8	15.5	60.6	20.9	34.5	12.0	1119
155	7.40	46.2	15.8	62.4	21.3	34.1	14.8	1172
156	7.50	46.7	15.6	62.2	20.8	33.4	12.3	1049
157	7.79	49.3	16.3	63.3	20.9	33.0	11.3	1151
N	7	7	7	7	7	7	7	7
MEAN	7.560	46.16	15.66	61.06	20.67	33.87	12.64	1115.6
S.D.	0.194	1.74	0.37	1.82	0.47	0.55	2.94	54.1
S.E.	0.073	0.66	0.14	0.69	0.18	0.21	1.11	20.4
M/C	2.4064	1.6042	0.7549	0.0790	2.7668	1.9276	1.8951	9.2235*
F	0.1352	1.4577	3.4885*	1.3043	1.0546	0.0361	2.3409†	
H								3.5129

INDIVIDUAL DATA 6-2-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Hematological findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 4 mg/kg

Animal No.	RBC $10^6/\mu l$	Ht. %	Hb. g/dl	MCV fl	MCH pg	MCHC %	WBC $10^3/\mu l$	Plat $10^3/\mu l$
251	7.40	45.6	15.5	61.6	20.9	33.9	15.3	1172
252	7.36	44.2	15.1	60.0	20.5	34.1	10.1	1227
253	7.36	44.9	15.9	61.0	21.6	35.4	12.2	1221
254	7.29	44.8	15.3	61.5	20.9	34.1	6.6	1157
255	8.26	46.6	15.7	56.4	19.0	33.6	9.3	1175
256	7.95	46.9	15.5	59.0	19.4	33.0	8.1	1080
257	7.84	46.3	15.4	59.1	19.6	33.2	7.2	1060
N	7	7	7	7	7	7	7	7
MEAN	7.637	45.61	15.49	59.80	20.27	33.90	9.83	1156.0
S.D.	0.378	1.02	0.26	1.84	0.95	0.79	3.06	64.4
S.E.	0.143	0.39	0.10	0.70	0.36	0.30	1.16	24.3
t'			0.9717				1.7625	

INDIVIDUAL DATA 6-2-3

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Hematological findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 20 mg/kg

Animal No.	RBC $10^6/\mu l$	Ht. %	Hb. g/dl	MCV fl	MCH pg	MCHC %	WBC $10^3/\mu l$	Plat $10^3/\mu l$
351	7.32	44.4	15.1	60.6	20.6	34.0	10.9	1485
352	8.13	46.6	15.9	57.3	19.5	34.1	12.7	1202
353	7.77	45.1	15.2	58.0	19.5	33.7	6.0	1003
354	7.18	43.4	15.2	60.5	21.1	35.0	6.6	1189
355	7.63	45.5	15.2	59.6	19.9	33.4	11.7	1242
356	7.45	46.4	15.8	62.3	21.2	34.0	15.7	1194
357	7.74	47.6	15.5	61.5	20.0	32.5	6.8	1039
N	7	7	7	7	7	7	7	7
MEAN	7.603	45.57	15.41	59.97	20.26	33.81	10.06	1193.4
S.D.	0.318	1.42	0.32	1.81	0.71	0.76	3.68	156.8
S.E.	0.120	0.54	0.12	0.68	0.27	0.29	1.39	59.3
t'			1.3766				1.6193	

INDIVIDUAL DATA 6-2-4

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Hematological findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal No.	RBC $10^6/\mu l$	Ht. %	Hb. g/dl	MCV fl	MCH pg	MCHC %	WBC $10^3/\mu l$	Plat $10^3/\mu l$
451	7.86	46.5	15.6	59.1	19.8	33.5	6.7	1213
452	7.11	43.2	14.9	60.7	20.9	34.4	9.6	1290
453	7.13	44.3	14.8	62.2	20.7	33.4	8.3	1154
454	7.93	46.0	15.4	58.0	19.4	33.4	5.2	1186
455	7.61	44.7	15.4	58.7	20.2	34.4	10.5	1174
456	7.73	44.6	14.9	57.7	19.2	33.4	10.8	1138
457	7.41	43.1	14.7	58.1	19.8	34.1	8.5	1083
N	7	7	7	7	7	7	7	7
MEAN	7.540	44.63	15.10	59.21	20.00	33.80	8.51	1176.9
S.D.	0.333	1.28	0.36	1.65	0.64	0.48	2.03	64.6
S.E.	0.126	0.48	0.13	0.63	0.24	0.18	0.77	24.4
t'			3.1581*				2.5855*	

INDIVIDUAL DATA 6-2-5

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Hematological findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

					Hemogram of WBC						
					Neutro.						
Animal No.	Ret %	CT sec.	PT sec.	APTT sec.	Stab. %	Seg. %	Eos. %	Bas. %	Mono. %	Lymp. %	Others %
151	16	193	13.1	23.3	0	9	0	0	0	91	0
152	13	374	13.9	22.4	0	10	0	0	0	90	0
153	12	286	13.4	22.5	0	12	1	0	0	87	0
154	14	180	13.8	23.7	0	9	0	0	0	91	0
155	13	179	12.9	22.3	1	6	0	0	0	93	0
156	12	184	13.5	23.6	0	9	2	0	0	89	0
157	12	188	13.8	20.5	1	6	0	0	0	93	0
N	7	7	7	7	7	7	7	7	7	7	7
MEAN	13.1	226.3	13.49	22.61	0.3	8.7	0.4	0.0	0.0	90.6	0.0
S.D.	1.5	75.4	0.38	1.10	0.5	2.1	0.8	0.0	0.0	2.1	0.0
S.E.	0.6	28.5	0.14	0.42	0.2	0.8	0.3	0.0	0.0	0.8	0.0
M/C	2.7839	3.1223	2.3535	5.1402	2.9619	1.6579	1.6118	0.0000	0.0000	1.8261	0.0000
F	0.5649	1.7089	4.0185*	7.2852**	0.1200	0.5014	0.1818	0.0000	0.0000	0.4084	0.0000

INDIVIDUAL DATA 6-2-6

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Hematological findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 4 mg/kg

					Hemogram of WBC						
					Neutro.						
Animal No.	Ret %.	CT sec.	PT sec.	APTT sec.	Stab. %	Seg. %	Eos. %	Bas. %	Mono. %	Lymp. %	Others %
251	11	210	13.6	21.9	0	13	0	0	0	87	0
252	13	289	12.8	21.4	1	11	1	0	0	87	0
253	11	170	13.1	22.7	0	11	0	0	0	89	0
254	17	164	13.4	23.1	0	11	0	0	0	89	0
255	10	101	14.0	22.9	0	12	0	0	0	88	0
256	13	79	14.8	24.2	0	5	2	0	0	93	0
257	11	152	14.0	24.3	0	8	0	0	0	92	0
N	7	7	7	7	7	7	7	7	7	7	7
MEAN	12.3	166.4	13.67	22.93	0.1	10.1	0.4	0.0	0.0	89.3	0.0
S.D.	2.4	69.6	0.67	1.08	0.4	2.7	0.8	0.0	0.0	2.4	0.0
S.E.	0.9	26.3	0.25	0.41	0.1	1.0	0.3	0.0	0.0	0.9	0.0
t'			0.6249	0.3604							

INDIVIDUAL DATA 6-2-7

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Hematological findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 20 mg/kg

					Hemogram of WBC						
					Neutro.						
Animal No.	Ret %.	CT sec.	PT sec.	APTT sec.	Stab. %	Seg. %	Eos. %	Bas. %	Mono. %	Lymp. %	Others %
351	13	150	13.4	22.5	1	7	0	0	0	92	0
352	10	209	14.1	26.0	1	4	1	0	0	94	0
353	15	228	13.6	24.1	0	15	0	0	0	85	0
354	16	273	14.0	27.2	0	9	0	0	0	91	0
355	13	229	12.7	21.5	0	11	0	0	0	89	0
356	10	197	13.8	22.4	0	7	1	0	0	92	0
357	8	193	13.6	20.6	0	12	2	0	0	86	0
N	7	7	7	7	7	7	7	7	7	7	7
MEAN	12.1	211.3	13.60	23.47	0.3	9.3	0.6	0.0	0.0	89.9	0.0
S.D.	2.9	38.1	0.47	2.41	0.5	3.7	0.8	0.0	0.0	3.3	0.0
S.E.	1.1	14.4	0.18	0.91	0.2	1.4	0.3	0.0	0.0	1.3	0.0
t'			0.3845	0.9829							

INDIVIDUAL DATA 6-2-8

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Hematological findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

					Hemogram of WBC						
					Neutro.						
Animal No.	Ret %.	CT sec.	PT sec.	APTT sec.	Stab. %	Seg. %	Eos. %	Bas. %	Mono. %	Lymp. %	Others %
451	11	271	14.1	26.5	0	7	1	0	0	92	0
452	17	215	12.4	26.2	0	15	0	0	0	85	0
453	14	293	12.4	25.9	0	11	0	0	0	89	0
454	13	237	12.3	24.4	2	13	1	0	0	84	0
455	13	196	12.7	27.5	0	7	0	0	0	93	0
456	12	150	12.3	24.5	0	11	0	0	0	89	0
457	14	260	13.1	28.8	0	9	0	0	0	91	0
N	7	7	7	7	7	7	7	7	7	7	7
MEAN	13.4	231.7	12.76	26.26	0.3	10.4	0.3	0.0	0.0	89.0	0.0
S.D.	1.9	48.9	0.66	1.57	0.8	3.0	0.5	0.0	0.0	3.4	0.0
S.E.	0.7	18.5	0.25	0.59	0.3	1.1	0.2	0.0	0.0	1.3	0.0
t'			2.4514	4.1775**							

INDIVIDUAL DATA 6-3-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Hematological findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal No.	RBC $10^6/\mu l$	Ht. %	Hb. g/dl	MCV fl	MCH pg	MCHC %	WBC $10^3/\mu l$	Plat $10^3/\mu l$
108	8.07	48.1	15.2	59.6	18.8	31.6	18.9	1083
109	7.92	46.3	14.9	58.4	18.8	32.1	18.9	980
110	7.62	47.0	14.9	61.7	19.5	31.7	19.9	1117
111	7.94	47.7	14.8	60.1	18.6	31.0	10.9	980
112	8.21	45.9	14.7	55.9	17.9	32.0	12.6	1178
113	7.83	46.7	14.8	59.6	18.9	31.6	18.6	1164
114	8.24	48.9	15.3	60.0	18.6	31.3	13.7	1257
N	7	7	7	7	7	7	7	7
MEAN	7.976	47.23	14.94	59.33	18.73	31.61	16.21	1108.4
S.D.	0.218	1.06	0.22	1.80	0.48	0.38	3.68	103.0
S.E.	0.082	0.40	0.08	0.68	0.18	0.14	1.39	38.9
M/C	0.9582	1.5127	4.6353*	3.6983	1.0582	0.8245	0.9351	0.5920
F	1.5715	1.0942		0.4078	1.7937	1.0041	0.0016	4.9356*
H			0.4994					

INDIVIDUAL DATA 6-3-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Hematological findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

Animal No.	RBC $10^6/\mu l$	Ht. %	Hb. g/dl	MCV fl	MCH pg	MCHC %	WBC $10^3/\mu l$	Plat $10^3/\mu l$
408	7.89	46.6	14.5	59.1	18.3	31.1	24.2	1152
409	8.08	47.8	14.9	59.1	18.4	31.1	21.5	1201
410	7.73	45.3	14.3	58.6	18.4	31.5	13.6	1368
411	8.59	50.8	15.5	59.1	18.0	30.5	18.5	1210
412	8.14	47.9	15.0	58.8	18.4	31.3	13.3	1238
413	8.62	49.5	16.0	57.4	18.6	32.3	7.9	1154
414	8.10	48.5	15.4	59.9	19.0	31.7	13.8	1182
N	7	7	7	7	7	7	7	7
MEAN	8.164	48.06	15.09	58.86	18.44	31.36	16.11	1215.0
S.D.	0.333	1.81	0.59	0.76	0.30	0.56	5.58	74.1
S.E.	0.126	0.68	0.22	0.29	0.12	0.21	2.11	28.0
t'								2.2216*

INDIVIDUAL DATA 6-3-3

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Hematological findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

					Hemogram of WBC						
					Neutro.						
Animal No.	Ret %.	CT sec.	PT sec.	APTT sec.	Stab. %	Seg. %	Eos. %	Bas. %	Mono. %	Lymp. %	Others %
108	18	287	14.1	28.7	0	8	0	0	0	92	0
109	17	239	13.7	29.8	0	4	1	0	0	95	0
110	15	257	13.9	25.9	0	6	0	0	0	94	0
111	11	267	13.9	28.2	0	12	0	0	0	88	0
112	14	207	15.1	30.5	0	9	0	0	0	91	0
113	18	248	13.8	27.5	0	25	0	0	0	75	0
114	13	245	14.6	32.1	0	10	0	0	0	90	0
N	7	7	7	7	7	7	7	7	7	7	7
MEAN	15.1	250.0	14.16	28.96	0.0	10.6	0.1	0.0	0.0	89.3	0.0
S.D.	2.7	24.9	0.51	2.04	0.0	6.9	0.4	0.0	0.0	6.7	0.0
S.E.	1.0	9.4	0.19	0.77	0.0	2.6	0.1	0.0	0.0	2.5	0.0
M/C	0.2611	2.6845	0.1157	1.5890	∞**	3.1930	2.7433	0.0000	0.0000	2.6238	0.0000
F	1.4696	1.3008	2.4132	0.4941		0.4921	0.7500	0.0000	0.0000	0.3084	0.0000
H					1.0000						

INDIVIDUAL DATA 6-3-4

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Hematological findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

					Hemogram of WBC						
					Neutro.						
Animal No.	Ret %.	CT sec.	PT sec.	APTT sec.	Stab. %	Seg. %	Eos. %	Bas. %	Mono. %	Lymp. %	Others %
408	17	241	13.5	28.2	0	5	0	0	0	95	0
409	13	292	13.0	24.9	1	6	0	0	0	93	0
410	13	250	13.9	25.3	0	9	0	0	0	91	0
411	12	156	13.4	28.2	0	12	2	0	0	86	0
412	16	241	14.6	35.0	0	6	1	0	0	93	0
413	11	244	14.3	28.5	0	9	0	0	0	91	0
414	13	154	13.2	25.0	0	13	0	0	0	87	0
N	7	7	7	7	7	7	7	7	7	7	7
MEAN	13.6	225.4	13.70	27.87	0.1	8.6	0.4	0.0	0.0	90.9	0.0
S.D.	2.1	51.3	0.59	3.54	0.4	3.1	0.8	0.0	0.0	3.3	0.0
S.E.	0.8	19.4	0.22	1.34	0.1	1.2	0.3	0.0	0.0	1.2	0.0

INDIVIDUAL DATA 6-4-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Hematological findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

Animal No.	RBC $10^6/\mu l$	Ht. %	Hb. g/dl	MCV fl	MCH pg	MCHC %	WBC $10^3/\mu l$	Plat $10^3/\mu l$
158	7.92	43.8	14.4	55.3	18.1	32.8	10.4	1299
159	7.41	44.8	14.6	60.5	19.7	32.5	13.3	1096
160	8.43	48.8	15.7	57.9	18.6	32.1	7.4	1244
161	8.26	47.4	15.5	57.4	18.7	32.7	7.0	1027
162	7.91	45.6	15.4	57.6	19.4	33.7	9.7	1094
163	7.71	45.5	15.2	59.0	19.7	33.4	13.2	1165
164	8.07	47.7	16.2	59.1	20.0	33.9	11.0	1131
N	7	7	7	7	7	7	7	7
MEAN	7.959	46.23	15.29	58.11	19.17	33.01	10.29	1150.9
S.D.	0.340	1.78	0.62	1.64	0.71	0.66	2.50	93.8
S.E.	0.128	0.67	0.24	0.62	0.27	0.25	0.95	35.5
M/C	1.3291	3.3601	0.6777	1.6879	0.0025	0.1728	0.0078	0.2350
F	0.7999	0.3397	0.0099	0.4100	0.5848	0.3857	0.3580	0.7648

INDIVIDUAL DATA 6-4-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Hematological findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal No.	RBC $10^6/\mu l$	Ht. %	Hb. g/dl	MCV fl	MCH pg	MCHC %	WBC $10^3/\mu l$	Plat $10^3/\mu l$
458	8.25	47.1	15.0	57.1	18.1	31.8	11.7	941
459	8.25	47.6	16.1	57.7	19.5	33.8	11.3	1157
460	7.76	45.5	15.0	58.6	19.3	32.9	11.3	1168
461	8.05	46.0	15.3	57.2	19.0	33.2	6.6	1224
462	8.30	46.6	14.8	56.1	17.8	31.7	7.8	1061
463	7.88	46.3	15.5	58.7	19.6	33.4	11.3	1201
464	8.16	47.5	15.5	58.2	18.9	32.6	6.5	960
N	7	7	7	7	7	7	7	7
MEAN	8.093	46.66	15.31	57.66	18.89	32.77	9.50	1101.7
S.D.	0.206	0.78	0.44	0.93	0.69	0.79	2.41	115.3
S.E.	0.078	0.30	0.17	0.35	0.26	0.30	0.91	43.6

INDIVIDUAL DATA 6-4-3

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Hematological findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

					Hemogram of WBC						
					Neutro.						
Animal No.	Ret %.	CT sec.	PT sec.	APTT sec.	Stab. %	Seg. %	Eos. %	Bas. %	Mono. %	Lymp. %	Others %
158	16	#	13.6	19.2	0	9	1	0	0	90	0
159	11	252	14.1	23.6	0	7	0	0	0	93	0
160	12	199	13.8	20.9	0	13	1	0	0	86	0
161	11	218	14.0	23.5	0	16	1	0	0	83	0
162	8	241	14.1	25.3	0	12	1	0	0	87	0
163	10	186	13.8	22.7	1	9	1	0	0	89	0
164	15	202	13.9	25.5	0	9	2	0	0	89	0
N	7	6	7	7	7	7	7	7	7	7	7
MEAN	11.9	216.3	13.90	22.96	0.1	10.7	1.0	0.0	0.0	88.1	0.0
S.D.	2.8	25.7	0.18	2.28	0.4	3.1	0.6	0.0	0.0	3.2	0.0
S.E.	1.1	10.5	0.07	0.86	0.1	1.2	0.2	0.0	0.0	1.2	0.0
M/C	0.0780	3.9219*	3.4323	3.6841	0.0000	0.0265	0.5223	0.0000	0.0000	0.0234	0.0000
F	0.8065		0.0069	0.1463	0.0000	0.0319	1.3500	0.0000	0.0000	0.0075	0.0000
H		0.0205									

#: Blank value.

INDIVIDUAL DATA 6-4-4

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Hematological findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

					Hemogram of WBC						
					Neutro.						
Animal No.	Ret %.	CT sec.	PT sec.	APTT sec.	Stab. %	Seg. %	Eos. %	Bas. %	Mono. %	Lymp. %	Others %
458	12	263	13.4	22.2	1	13	0	0	0	86	0
459	12	214	14.5	23.3	0	8	0	0	0	92	0
460	15	164	13.8	23.9	0	12	0	0	0	88	0
461	14	306	13.8	24.8	0	12	1	0	0	87	0
462	9	332	13.5	23.9	0	12	2	0	0	86	0
463	12	191	14.4	22.2	0	6	1	0	0	93	0
464	19	164	14.0	22.9	0	14	0	0	0	86	0
N	7	7	7	7	7	7	7	7	7	7	7
MEAN	13.3	233.4	13.91	23.31	0.1	11.0	0.6	0.0	0.0	88.3	0.0
S.D.	3.1	67.9	0.42	0.96	0.4	2.9	0.8	0.0	0.0	3.0	0.0
S.E.	1.2	25.7	0.16	0.36	0.1	1.1	0.3	0.0	0.0	1.1	0.0

INDIVIDUAL DATA 7-1-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Biochemical findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal No.	TP g/dl	Alb g/dl	A/G	Protein fractions (%) Alb	Globulin α_1	Globulin α_2	Globulin β	Globulin γ	GOT IU/l	GPT IU/l	ALP IU/l	LDH IU/l	γ-GTP IU/l	T-Bil mg/dl
101	5.6	2.2	0.64	45.7	21.9	6.4	18.4	7.6	179	35	546	5078	1.0	0.1
102	5.8	2.4	0.70	50.0	17.7	7.6	17.8	6.9	113	41	374	1227	0.7	0.1
103	5.6	2.2	0.64	50.2	22.2	5.8	14.8	7.0	105	27	349	2333	0.5	0.1
104	5.8	2.4	0.70	53.6	19.4	6.1	15.1	5.8	105	32	367	1865	0.9	0.1
105	5.6	2.5	0.80	51.3	19.3	5.8	15.6	8.0	108	34	457	1573	0.5	0.1
106	5.6	2.5	0.80	50.9	19.4	5.0	16.7	8.0	83	31	368	1138	0.5	0.1
107	5.5	2.4	0.77	55.6	18.2	5.8	14.0	6.4	103	27	348	1740	0.5	0.1
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	5.64	2.37	0.721	51.04	19.73	6.07	16.06	7.10	113.7	32.4	401.3	2136.3	0.66	0.10
S.D.	0.11	0.13	0.069	3.10	1.72	0.80	1.63	0.83	30.3	4.9	73.8	1357.9	0.21	0.00
S.E.	0.04	0.05	0.026	1.17	0.65	0.30	0.61	0.31	11.4	1.8	27.9	513.2	0.08	0.00
M/C	2.4517	1.5463	6.0840	7.7680	2.5525	8.1114*	5.5915	16.3070**	4.9244	5.8836	6.5456	5.1679	5.6365	0.0000
F	0.8301	0.4307	0.2750	0.2219	0.1292		0.3079		0.4882	2.2289	2.3537[1]	0.3608	0.3608	0.0000
H						3.2344		0.8160						

INDIVIDUAL DATA 7-1-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Biochemical findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 4 mg/kg

Animal No.	TP g/dl	Alb g/dl	A/G	Protein fractions (%) Alb	Globulin α_1	Globulin α_2	Globulin β	Globulin γ	GOT IU/l	GPT IU/l	ALP IU/l	LDH IU/l	γ-GTP IU/l	T-Bil mg/dl
201	5.6	2.3	0.69	49.0	20.2	6.1	16.7	8.0	127	31	417	3271	0.5	0.1
202	5.5	2.3	0.71	51.0	18.7	5.1	17.5	7.7	95	31	504	1699	0.5	0.1
203	5.5	2.3	0.71	52.9	18.9	6.2	15.4	6.6	96	27	442	1540	0.8	0.1
204	5.9	2.5	0.73	51.2	21.2	4.9	15.2	7.5	125	31	505	2831	1.1	0.1
205	5.5	2.3	0.71	50.9	19.3	5.8	15.6	8.4	106	28	449	1825	1.2	0.1
206	5.4	2.3	0.74	50.1	19.0	6.0	16.7	8.2	90	29	423	964	0.5	0.1
207	5.5	2.2	0.66	52.1	20.0	5.0	16.4	6.5	114	30	450	1701	1.0	0.1
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	5.56	2.31	0.707	51.03	19.61	5.59	16.21	7.56	107.6	29.6	455.7	1975.9	0.80	0.10
S.D.	0.16	0.09	0.026	1.27	0.90	0.56	0.84	0.75	14.9	1.6	35.6	795.6	0.31	0.00
S.E.	0.06	0.03	0.010	0.48	0.34	0.21	0.32	0.28	5.6	0.6	13.4	300.7	0.12	0.00
t'											1.2873			

INDIVIDUAL DATA 7-1-3

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Biochemical findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 20 mg/kg

Animal No.	TP g/dl	Alb g/dl	A/G	Protein fractions (%) Alb	Globulin α_1	Globulin α_2	Globulin β	Globulin γ	GOT IU/l	GPT IU/l	ALP IU/l	LDH IU/l	γ-GTP IU/l	T-Bil mg/dl
301	5.3	2.2	0.70	49.6	20.6	6.3	16.2	7.3	120	21	436	2699	0.5	0.1
302	5.5	2.3	0.71	52.4	21.2	5.5	15.4	5.5	136	30	373	3117	0.6	0.1
303	5.7	2.3	0.67	48.6	19.0	5.3	17.9	9.2	95	28	392	1295	0.8	0.1
304	5.6	2.5	0.80	55.2	19.0	4.9	14.6	6.3	116	27	592	2157	0.6	0.1
305	5.9	2.1	0.55	41.3	18.3	5.6	20.2	14.6	94	31	481	1517	0.8	0.1
306	5.8	2.4	0.70	51.7	21.1	4.2	16.4	6.6	96	33	480	1329	1.0	0.1
307	5.8	2.4	0.70	51.6	21.2	5.3	14.6	7.3	92	27	425	1441	0.6	0.1
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	5.66	2.31	0.690	50.06	20.06	5.30	16.47	8.11	107.0	28.1	454.1	1936.4	0.70	0.10
S.D.	0.21	0.13	0.074	4.40	1.25	0.65	2.01	3.08	17.1	3.8	73.1	733.2	0.17	0.00
S.E.	0.08	0.05	0.028	1.66	0.47	0.24	0.76	1.16	6.5	1.5	27.6	277.1	0.07	0.00
t'											1.2501			

INDIVIDUAL DATA 7-1-4

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Biochemical findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

Animal No.	TP g/dl	Alb g/dl	A/G	Protein fractions (%) Alb	Globulin α_1	Globulin α_2	Globulin β	Globulin γ	GOT IU/l	GPT IU/l	ALP IU/l	LDH IU/l	γ-GTP IU/l	T-Bil mg/dl
401	5.5	2.3	0.71	49.4	18.0	8.9	16.5	7.2	90	25	484	1525	0.5	0.1
402	5.6	2.3	0.69	53.0	19.0	5.4	16.0	6.6	110	30	684	2128	0.5	0.1
403	5.4	2.3	0.74	50.8	19.1	4.9	16.5	8.7	87	29	519	1255	0.5	0.1
404	5.6	2.3	0.69	51.6	21.1	5.2	15.2	6.9	96	26	540	1448	1.6	0.1
405	5.8	2.4	0.70	48.1	21.4	5.4	15.8	9.3	123	24	480	2594	1.2	0.1
406	5.5	2.5	0.83	54.6	18.0	4.6	16.2	6.6	110	28	309	1558	0.5	0.1
407	5.5	2.0	0.57	41.7	21.6	7.5	22.3	6.9	89	34	579	978	0.7	0.1
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	5.56	2.30	0.704	49.89	19.74	5.99	16.93	7.46	100.7	28.0	513.6	1640.9	0.79	0.10
S.D.	0.13	0.15	0.077	4.21	1.59	1.59	2.41	1.09	13.7	3.4	113.9	546.4	0.44	0.00
S.E.	0.05	0.06	0.029	1.59	0.60	0.60	0.91	0.41	5.2	1.3	43.1	206.5	0.17	0.00
t'											2.6557*			

INDIVIDUAL DATA 7-1-5

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Biochemical findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal No.	Glu mg/dl	T-Cho mg/dl	TG mg/dl	PL mg/dl	BUN mg/dl	Crea mg/dl	Na mEq/l	K mEq/l	Cl mEq/l	Ca mg/dl	P mg/dl
101	159	96	89	156	14.7	0.4	144.5	4.92	104	9.6	9.6
102	118	75	26	131	18.1	0.5	144.0	4.43	103	9.7	8.7
103	118	81	39	132	15.1	0.5	143.0	4.61	105	9.7	9.4
104	137	91	59	145	14.7	0.4	144.0	4.65	105	9.6	8.4
105	121	46	49	93	17.8	0.6	145.0	4.90	107	9.5	9.3
106	112	74	70	129	16.0	0.5	148.5	4.03	106	9.6	7.8
107	137	71	38	124	16.2	0.5	144.0	4.45	107	9.7	8.7
N	7	7	7	7	7	7	7	7	7	7	7
MEAN	128.9	76.3	52.9	130.0	16.09	0.49	144.71	4.570	105.3	9.63	8.84
S.D.	16.4	16.2	21.6	19.6	1.40	0.07	1.78	0.307	1.5	0.08	0.63
S.E.	6.2	6.1	8.1	7.4	0.53	0.03	0.67	0.116	0.6	0.03	0.24
M/C	0.8534	2.2268	3.0711	1.1317	2.0215	0.9252	1.0726	1.2990	5.8567	6.5221	0.7017
F	0.7587	0.2272	0.7036	0.5157	1.3162	0.2683	0.3627	0.2708	0.6524	4.5563*	0.4706

INDIVIDUAL DATA 7-1-6

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Biochemical findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 4 mg/kg

Animal No.	Glu mg/dl	T-Cho mg/dl	TG mg/dl	PL mg/dl	BUN mg/dl	Crea mg/dl	Na mEq/l	K mEq/l	Cl mEq/l	Ca mg/dl	P mg/dl
201	132	83	97	147	14.8	0.5	148.0	4.80	104	9.4	10.0
202	146	54	43	105	15.5	0.5	146.0	4.25	109	9.1	8.9
203	123	64	41	110	16.5	0.4	145.0	4.49	107	9.5	8.8
204	104	85	37	137	19.4	0.5	144.5	4.50	104	9.8	10.1
205	127	89	86	145	16.3	0.5	142.5	4.53	105	9.4	8.5
206	109	65	36	110	14.9	0.4	145.0	4.29	108	9.5	8.3
207	117	60	59	108	20.6	0.4	144.0	4.62	105	9.5	9.2
N	7	7	7	7	7	7	7	7	7	7	7
MEAN	122.6	71.4	57.0	123.1	16.86	0.46	145.00	4.497	106.0	9.46	9.11
S.D.	14.2	13.9	25.0	18.9	2.27	0.05	1.71	0.188	2.0	0.21	0.70
S.E.	5.4	5.3	9.4	7.1	0.86	0.02	0.65	0.071	0.8	0.08	0.26
t'										2.3920	

INDIVIDUAL DATA 7-1-7

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Biochemical findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 20 mg/kg

Animal No.	Glu mg/dl	T-Cho mg/dl	TG mg/dl	PL mg/dl	BUN mg/dl	Crea mg/dl	Na mEq/l	K mEq/l	Cl mEq/l	Ca mg/dl	P mg/dl
301	157	49	103	107	13.9	0.4	145.5	4.69	104	9.4	9.1
302	129	59	60	101	17.2	0.6	145.0	4.95	105	9.4	10.4
303	129	92	56	134	14.4	0.4	145.0	4.73	105	9.5	9.0
304	111	79	61	136	15.1	0.5	147.5	4.63	106	9.5	9.4
305	119	63	83	118	14.2	0.5	147.0	4.61	106	9.3	9.1
306	128	74	48	118	17.3	0.5	143.0	4.21	106	9.2	8.7
307	96	83	59	135	16.0	0.4	144.0	4.32	105	9.5	8.8
N	7	7	7	7	7	7	7	7	7	7	7
MEAN	124.1	71.3	67.1	121.3	15.44	0.47	145.29	4.591	105.3	9.40	9.21
S.D.	18.9	15.0	19.1	14.2	1.41	0.08	1.58	0.251	0.8	0.12	0.57
S.E.	7.1	5.7	7.2	5.4	0.53	0.03	0.60	0.095	0.3	0.04	0.22
t'										3.1894*	

INDIVIDUAL DATA 7-1-8

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Biochemical findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Glu mg/dl	T-Cho mg/dl	TG mg/dl	PL mg/dl	BUN mg/dl	Crea mg/dl	Na mEq/l	K mEq/l	Cl mEq/l	Ca mg/dl	P mg/dl
401	157	70	64	127	15.3	0.4	146.0	4.89	105	9.5	9.8
402	122	59	46	99	16.6	0.5	140.0	4.14	105	9.5	8.8
403	134	73	110	132	15.6	0.4	143.5	4.56	104	9.3	8.4
404	137	68	41	115	15.2	0.5	143.0	4.56	105	9.3	9.1
405	140	72	45	119	14.4	0.4	147.0	4.66	105	9.4	8.6
406	133	69	54	107	11.0	0.4	145.0	4.25	104	9.5	9.4
407	116	88	136	138	17.3	0.6	145.5	4.40	107	9.3	9.4
N	7	7	7	7	7	7	7	7	7	7	7
MEAN	134.1	71.3	70.9	119.6	15.06	0.46	144.29	4.494	105.0	9.40	9.07
S.D.	13.2	8.7	37.2	13.9	2.03	0.08	2.34	0.254	1.0	0.10	0.50
S.E.	5.0	3.3	14.0	5.2	0.77	0.03	0.89	0.096	0.4	0.04	0.19
t'										3.1894*	

INDIVIDUAL DATA 7-2-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Biochemical findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

Animal No.	TP g/dl	Alb g/dl	A/G	Protein fractions (%) Alb	Globulin α_1	Globulin α_2	Globulin β	Globulin γ	GOT IU/l	GPT IU/l	ALP IU/l	LDH IU/l	γ-GTP IU/l	T-Bil mg/dl
151	5.6	2.5	0.80	56.9	16.3	5.6	15.6	5.6	134	20	231	3393	0.7	0.1
152	5.8	2.5	0.75	54.4	16.1	7.1	15.1	7.3	112	26	217	2509	0.5	0.1
153	5.9	2.7	0.84	54.6	16.1	6.7	16.0	6.6	121	26	287	2477	0.8	0.1
154	5.8	2.6	0.81	54.6	17.7	6.1	16.2	5.4	114	25	280	2693	1.6	0.1
155	6.1	2.6	0.74	52.0	20.2	6.1	16.4	5.3	149	24	349	3649	1.6	0.1
156	5.7	2.7	0.90	54.0	17.9	6.0	17.1	5.0	122	24	281	2433	1.0	0.1
157	5.6	2.6	0.86	55.0	15.0	6.9	17.3	5.8	97	22	346	1347	1.2	0.1
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	5.79	2.60	0.814	54.50	17.04	6.36	16.24	5.86	121.3	23.9	284.4	2643.0	1.06	0.10
S.D.	0.18	0.08	0.058	1.45	1.71	0.55	0.78	0.81	16.6	2.2	50.7	746.8	0.43	0.00
S.E.	0.07	0.03	0.022	0.55	0.65	0.21	0.30	0.31	6.3	0.8	19.1	282.3	0.16	0.00
M/C	1.1991	7.0191	1.7698	0.2656	2.5755	2.4626	3.3793	3.7172	0.8022	1.4321	2.3992	2.8152	0.8502	0.0000
F	0.5236	4.0000*	4.0495*	6.9565**	3.2264*	1.1089	1.1726	0.1343	3.0445*	0.7500	0.6470	5.1334**	0.8609	0.0000

INDIVIDUAL DATA 7-2-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Biochemical findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 4 mg/kg

Animal No.	TP g/dl	Alb g/dl	A/G	Protein fractions (%) Alb	Globulin α_1	Globulin α_2	Globulin β	Globulin γ	GOT IU/l	GPT IU/l	ALP IU/l	LDH IU/l	γ-GTP IU/l	T-Bil mg/dl
251	5.7	2.5	0.78	52.9	18.8	6.8	16.1	5.4	139	20	242	3730	0.5	0.1
252	5.8	2.8	0.93	55.0	16.2	5.2	15.0	8.6	138	24	387	3686	1.2	0.1
253	5.8	2.7	0.87	53.9	18.5	5.7	16.3	5.6	97	28	210	1888	0.5	0.1
254	5.7	2.4	0.72	52.4	18.8	7.0	16.4	5.4	81	19	285	1289	0.6	0.1
255	6.0	2.7	0.81	52.8	18.5	6.9	16.8	5.0	118	22	303	2704	1.7	0.1
256	5.5	2.4	0.77	55.9	17.8	5.1	16.3	4.9	124	21	405	2576	1.7	0.1
257	6.1	2.6	0.74	54.4	19.6	5.1	15.7	5.2	131	24	350	2552	0.6	0.1
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	5.80	2.59	0.803	53.90	18.31	5.97	16.09	5.73	118.3	22.6	311.7	2632.1	0.97	0.10
S.D.	0.20	0.16	0.074	1.29	1.07	0.89	0.58	1.29	21.8	3.0	72.8	884.0	0.55	0.00
S.E.	0.08	0.06	0.028	0.49	0.41	0.34	0.22	0.49	8.2	1.2	27.5	334.1	0.21	0.00
t'		0.2641	0.3684	0.8077	1.5879				0.3148			0.0284		

INDIVIDUAL DATA 7-2-3

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Biochemical findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 20 mg/kg

Animal No.	TP g/dl	Alb g/dl	A/G	Protein fractions (%) Alb	Globulin α_1	Globulin α_2	Globulin β	Globulin γ	GOT IU/l	GPT IU/l	ALP IU/l	LDH IU/l	γ-GTP IU/l	T-Bil mg/dl
351	5.7	2.6	0.83	56.5	14.4	8.0	15.8	5.3	81	27	216	1512	0.5	0.1
352	5.8	2.7	0.87	55.6	19.2	4.8	13.8	6.6	93	21	403	1533	0.5	0.1
353	6.0	2.6	0.76	54.3	19.9	5.9	14.7	5.2	113	25	318	2623	1.0	0.1
354	5.9	2.5	0.73	52.8	18.7	6.9	16.0	5.6	102	21	274	1811	0.5	0.1
355	5.8	2.5	0.75	53.1	19.6	6.4	15.8	5.1	128	19	272	2976	0.7	0.1
356	6.1	2.6	0.74	52.3	18.6	6.0	17.1	6.0	85	27	200	846	0.5	0.1
357	6.0	2.7	0.81	53.8	19.4	5.1	16.7	5.0	106	21	465	2165	1.5	0.1
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	5.90	2.60	0.784	54.06	18.54	6.16	15.70	5.54	101.1	23.0	306.9	1923.7	0.74	0.10
S.D.	0.14	0.08	0.053	1.53	1.88	1.08	1.13	0.58	16.4	3.3	96.9	724.7	0.38	0.00
S.E.	0.05	0.03	0.020	0.58	0.71	0.41	0.43	0.22	6.2	1.2	36.6	273.9	0.14	0.00
t'			0.9669	0.5962	1.8734				2.1137			1.8820		

INDIVIDUAL DATA 7-2-4

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Biochemical findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal No.	TP g/dl	Alb g/dl	A/G	Protein fractions (%) Alb	Globulin α_1	Globulin α_2	Globulin β	Globulin γ	GOT IU/l	GPT IU/l	ALP IU/l	LDH IU/l	γ -GTP IU/l	T-Bil mg/dl
451	5.8	2.4	0.70	51.9	19.4	6.7	15.7	6.3	94	25	357	1408	0.7	0.1
452	5.5	2.4	0.77	51.2	19.5	6.1	16.0	7.2	71	23	311	562	1.4	0.1
453	6.2	2.5	0.67	50.4	19.2	6.9	17.0	6.5	98	25	213	1530	1.2	0.1
454	5.9	2.4	0.68	51.7	19.4	8.4	16.1	4.4	110	28	494	1840	1.0	0.1
455	5.7	2.5	0.78	50.0	21.8	6.8	16.8	4.6	112	21	323	1461	0.5	0.1
456	6.0	2.5	0.71	53.9	17.9	5.5	16.4	6.3	87	24	394	1125	1.8	0.1
457	5.8	2.4	0.70	50.9	19.4	7.1	17.4	5.2	115	26	306	1710	1.1	0.1
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	5.84	2.44	0.716	51.43	19.51	6.79	16.49	5.79	98.1	24.6	342.6	1376.6	1.10	0.10
S.D.	0.22	0.05	0.043	1.28	1.15	0.90	0.61	1.06	15.8	2.2	86.9	425.1	0.43	0.00
S.E.	0.08	0.02	0.016	0.48	0.44	0.34	0.23	0.40	6.0	0.8	32.8	160.7	0.16	0.00
t'		2.9055*	3.1771*	4.1347**	3.0867*				2.4285			3.3136**		

INDIVIDUAL DATA 7-2-5

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Biochemical findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

Animal No.	Glu mg/dl	T-Cho mg/dl	TG mg/dl	PL mg/dl	BUN mg/dl	Crea mg/dl	Na mEq/l	K mEq/l	Cl mEq/l	Ca mg/dl	P mg/dl
151	100	62	16	125	22.1	0.6	145.0	4.21	108	8.9	7.8
152	119	57	11	109	18.7	0.5	144.0	4.28	111	9.7	6.9
153	102	81	26	151	21.7	0.6	144.0	4.25	109	9.6	7.3
154	134	63	29	138	20.2	0.6	142.5	4.23	106	9.3	7.5
155	105	72	24	140	21.9	0.6	143.0	4.48	106	9.6	8.1
156	92	80	17	153	19.6	0.6	142.0	4.22	109	9.2	8.0
157	103	87	14	157	20.3	0.6	143.0	4.29	107	9.5	8.4
N	7	7	7	7	7	7	7	7	7	7	7
MEAN	107.9	71.7	19.6	139.0	20.64	0.59	143.36	4.280	108.0	9.40	7.71
S.D.	14.1	11.4	6.8	17.1	1.29	0.04	1.03	0.093	1.8	0.28	0.51
S.E.	5.3	4.3	2.6	6.5	0.49	0.01	0.39	0.035	0.7	0.11	0.19
M/C	7.5443	1.3712	4.2897	1.7806	4.3764	3.1490	2.4933	4.2316	1.5977	3.9502	2.0806
F	2.7547†	0.2764	0.5675	0.2925	3.2554*	0.0968	0.3345	13.0107**	1.0640	0.8413	0.5219

INDIVIDUAL DATA 7-2-6

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Biochemical findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 4 mg/kg

Animal No.	Glu mg/dl	T-Cho mg/dl	TG mg/dl	PL mg/dl	BUN mg/dl	Crea mg/dl	Na mEq/l	K mEq/l	Cl mEq/l	Ca mg/dl	P mg/dl
251	123	75	25	144	19.8	0.6	144.0	4.32	108	9.1	6.8
252	121	81	28	145	19.6	0.5	145.0	4.20	107	9.6	7.2
253	113	78	37	145	21.9	0.6	140.5	4.42	105	9.7	7.5
254	107	83	21	153	21.4	0.5	146.0	4.29	108	9.6	7.8
255	113	57	43	124	17.2	0.6	142.0	4.11	107	9.4	7.0
256	103	54	11	98	20.7	0.7	141.0	4.03	106	8.9	7.9
257	92	63	22	121	24.3	0.7	143.0	4.38	107	9.5	8.0
N	7	7	7	7	7	7	7	7	7	7	7
MEAN	110.3	70.1	26.7	132.9	20.70	0.60	143.07	4.250	106.9	9.40	7.46
S.D.	10.7	11.9	10.6	19.4	2.20	0.08	2.05	0.143	1.1	0.29	0.47
S.E.	4.1	4.5	4.0	7.3	0.83	0.03	0.77	0.054	0.4	0.11	0.18
t'	0.2938				0.0482			0.3628			

INDIVIDUAL DATA 7-2-7

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Biochemical findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 20 mg/kg

Animal No.	Glu mg/dl	T-Cho mg/dl	TG mg/dl	PL mg/dl	BUN mg/dl	Crea mg/dl	Na mEq/l	K mEq/l	Cl mEq/l	Ca mg/dl	P mg/dl
351	107	65	15	123	21.7	0.6	141.0	4.35	107	9.7	8.1
352	97	56	17	105	24.9	0.6	142.0	4.08	108	9.6	6.6
353	114	59	29	122	16.8	0.6	145.0	4.47	110	9.4	7.5
354	103	67	25	126	19.2	0.5	140.5	4.26	105	9.4	7.7
355	97	106	25	193	23.6	0.6	144.5	4.69	107	9.8	9.2
356	95	71	10	133	23.6	0.6	142.5	4.12	109	9.6	7.8
357	114	57	40	118	25.2	0.7	142.5	4.52	107	9.3	7.8
N	7	7	7	7	7	7	7	7	7	7	7
MEAN	103.9	68.7	23.0	131.4	22.14	0.60	142.57	4.356	107.6	9.54	7.81
S.D.	8.1	17.3	10.0	28.5	3.13	0.06	1.67	0.221	1.6	0.18	0.77
S.E.	3.0	6.6	3.8	10.8	1.18	0.02	0.63	0.083	0.6	0.07	0.29
t'	0.4838				1.2642			0.9155			

INDIVIDUAL DATA 7-2-8

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Biochemical findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Glu mg/dl	T-Cho mg/dl	TG mg/dl	PL mg/dl	BUN mg/dl	Crea mg/dl	Na mEq/l	K mEq/l	Cl mEq/l	Ca mg/dl	P mg/dl
451	108	42	9	84	17.4	0.5	146.0	4.08	110	9.5	7.7
452	133	62	30	123	20.3	0.6	141.5	3.95	105	9.2	6.7
453	151	74	20	143	18.5	0.6	144.0	3.71	107	9.3	6.5
454	105	79	60	155	20.5	0.6	144.0	3.87	106	9.6	7.0
455	142	70	24	138	19.7	0.7	142.0	3.84	106	9.3	8.3
456	151	72	18	145	15.4	0.6	142.0	3.74	107	9.3	8.1
457	92	59	21	106	17.5	0.6	143.5	3.99	106	9.3	8.1
N	7	7	7	7	7	7	7	7	7	7	7
MEAN	126.0	65.4	26.0	127.7	18.47	0.60	143.29	3.883	106.7	9.36	7.49
S.D.	24.1	12.4	16.3	25.1	1.85	0.06	1.58	0.134	1.6	0.14	0.74
S.E.	9.1	4.7	6.2	9.5	0.70	0.02	0.60	0.051	0.6	0.05	0.28
t'	2.1946				1.8302			4.8022**			

INDIVIDUAL DATA 7-3-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Biochemical findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal No.	TP g/dl	Alb g/dl	A/G	Protein fractions (%) Alb	Globulin α_1	Globulin α_2	Globulin β	Globulin γ	GOT IU/l	GPT IU/l	ALP IU/l	LDH IU/l	γ-GTP IU/l	T-Bil mg/dl
108	5.9	2.5	0.73	48.6	22.6	5.9	15.3	7.6	129	26	268	3870	1.3	0.1
109	5.6	2.4	0.75	47.9	22.9	6.4	14.7	8.1	97	33	359	1868	1.6	0.1
110	5.9	2.4	0.68	48.3	22.5	5.2	17.6	6.4	119	28	351	2630	1.8	0.1
111	6.0	2.5	0.71	51.4	21.7	6.4	14.8	5.7	121	37	305	2489	1.6	0.1
112	5.6	2.5	0.80	51.5	21.5	6.2	15.0	5.8	100	23	243	1791	1.8	0.1
113	6.0	2.4	0.66	47.3	21.9	6.8	15.6	8.4	91	31	249	808	1.0	0.1
114	5.9	2.6	0.78	48.5	20.8	6.6	15.0	9.1	96	33	287	1768	1.7	0.1
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	5.84	2.47	0.730	49.07	21.99	6.21	15.43	7.30	107.6	30.1	294.6	2174.9	1.54	0.10
S.D.	0.17	0.08	0.051	1.68	0.73	0.53	1.00	1.34	15.0	4.8	46.4	953.5	0.29	0.00
S.E.	0.06	0.03	0.019	0.64	0.28	0.20	0.38	0.51	5.7	1.8	17.6	360.4	0.11	0.00
M/C	0.0158	0.2899	0.4947	0.0907	5.7605*	0.3118	0.0657	1.5862	0.3845	2.0636	0.1608	0.7031	1.1528	0.0000
F	0.0000	0.8710	0.9089	1.1660		4.4796†	1.1936	1.7565	0.1982	0.9561	3.2557†	0.1034	0.5681	0.0000
H					1.4800									

INDIVIDUAL DATA 7-3-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Biochemical findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

Animal No.	TP g/dl	Alb g/dl	A/G	Protein fractions (%) Alb	Globulin α_1	Globulin α_2	Globulin β	Globulin γ	GOT IU/l	GPT IU/l	ALP IU/l	LDH IU/l	γ-GTP IU/l	T-Bil mg/dl
408	5.6	2.3	0.69	49.8	19.3	7.5	16.9	6.5	115	25	363	2506	1.8	0.1
409	6.1	2.5	0.69	47.2	20.1	7.2	16.4	9.1	78	28	308	1371	1.3	0.1
410	5.7	2.3	0.67	48.5	22.9	6.1	16.6	5.9	103	30	389	1740	1.8	0.1
411	5.9	2.5	0.73	50.2	21.7	6.0	14.6	7.5	105	25	319	2304	0.5	0.1
412	6.0	2.5	0.71	46.7	22.8	6.6	15.7	8.2	84	28	377	1326	1.1	0.1
413	5.7	2.5	0.78	48.3	17.8	7.7	15.0	11.2	137	32	295	3168	1.6	0.1
414	5.9	2.4	0.68	46.4	17.6	7.2	16.7	12.1	102	29	301	1820	1.6	0.1
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	5.84	2.43	0.707	48.16	20.31	6.90	15.99	8.64	103.4	28.1	336.0	2033.6	1.39	0.10
S.D.	0.18	0.10	0.038	1.48	2.22	0.67	0.90	2.32	19.5	2.5	39.2	665.2	0.47	0.00
S.E.	0.07	0.04	0.014	0.56	0.84	0.25	0.34	0.88	7.4	1.0	14.8	251.4	0.18	0.00
t'						2.1165					1.8043			

INDIVIDUAL DATA 7-3-3

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Biochemical findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal No.	Glu mg/dl	T-Cho mg/dl	TG mg/dl	PL mg/dl	BUN mg/dl	Crea mg/dl	Na mEq/l	K mEq/l	Cl mEq/l	Ca mg/dl	P mg/dl
108	132	65	38	119	20.7	0.5	142.5	4.63	105	9.3	9.2
109	126	53	28	91	17.7	0.5	144.5	4.36	108	9.0	7.8
110	162	63	84	113	22.7	0.5	143.5	4.40	103	9.4	9.7
111	173	43	44	86	17.8	0.6	142.5	4.42	104	9.5	8.4
112	142	56	43	109	18.2	0.5	143.0	4.33	106	9.2	8.1
113	132	69	26	115	21.1	0.6	143.0	4.30	106	9.5	8.1
114	145	56	54	113	16.0	0.5	145.0	4.30	107	9.3	7.6
N	7	7	7	7	7	7	7	7	7	7	7
MEAN	144.6	57.9	45.3	106.6	19.17	0.53	143.43	4.391	105.6	9.31	8.41
S.D.	17.2	8.7	19.6	12.8	2.36	0.05	0.98	0.115	1.7	0.18	0.76
S.E.	6.5	3.3	7.4	4.8	0.89	0.02	0.37	0.043	0.6	0.07	0.29
M/C	0.0779	0.0519	1.7349	0.0100	2.7295	0.3574	0.7503	1.7117	0.2351	0.0803	0.8936
F	0.1424	0.0034	0.5220	0.0223	2.9370	0.3750	1.2458	3.1681	0.0000	0.7200	0.0017

INDIVIDUAL DATA 7-3-4

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Biochemical findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Glu mg/dl	T-Cho mg/dl	TG mg/dl	PL mg/dl	BUN mg/dl	Crea mg/dl	Na mEq/l	K mEq/l	Cl mEq/l	Ca mg/dl	P mg/dl
408	140	48	37	93	16.1	0.5	143.0	4.21	104	9.0	8.9
409	161	76	37	130	18.1	0.5	143.5	4.57	106	9.5	8.7
410	114	58	39	106	17.4	0.5	145.0	4.51	108	9.4	8.2
411	139	59	39	108	19.3	0.6	143.5	4.46	106	9.5	7.4
412	156	61	26	104	18.1	0.5	144.0	4.63	106	9.5	8.5
413	144	52	62	104	17.1	0.5	144.0	4.89	104	9.6	8.5
414	135	49	34	94	16.2	0.5	144.5	4.57	105	9.3	8.8
N	7	7	7	7	7	7	7	7	7	7	7
MEAN	141.3	57.6	39.1	105.6	17.47	0.51	143.93	4.549	105.6	9.40	8.43
S.D.	15.3	9.6	11.0	12.2	1.14	0.04	0.67	0.203	1.4	0.20	0.51
S.E.	5.8	3.6	4.2	4.6	0.43	0.01	0.25	0.077	0.5	0.08	0.19

INDIVIDUAL DATA 7-4-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Biochemical findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

Animal No.	TP g/dl	Alb g/dl	A/G	Protein fractions (%) Alb	Globulin α_1	Globulin α_2	Globulin β	Globulin γ	GOT IU/l	GPT IU/l	ALP IU/l	LDH IU/l	γ-GTP IU/l	T-Bil mg/dl
158	6.1	2.9	0.90	57.3	15.6	4.9	15.9	6.3	171	34	225	4940	1.6	0.1
159	6.1	2.8	0.84	57.7	15.6	4.6	15.0	7.1	100	27	160	1851	1.5	0.1
160	6.2	2.9	0.87	56.8	19.5	4.4	14.2	5.1	100	22	179	2325	1.5	0.1
161	6.1	2.9	0.90	57.0	17.3	5.4	14.4	5.9	93	27	146	1770	1.8	0.1
162	6.1	2.7	0.79	55.0	18.6	4.7	15.1	6.6	149	34	157	4138	2.2	0.1
163	6.5	3.0	0.85	56.3	18.3	4.1	15.1	6.2	152	35	151	3920	2.2	0.1
164	6.3	2.8	0.79	55.0	19.6	6.1	15.4	3.9	96	21	230	1997	1.7	0.1
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	6.20	2.86	0.849	56.44	17.79	4.89	15.01	5.87	123.0	28.6	178.3	2991.6	1.79	0.10
S.D.	0.15	0.10	0.046	1.08	1.68	0.67	0.58	1.07	32.9	5.9	35.2	1303.8	0.30	0.00
S.E.	0.06	0.04	0.017	0.41	0.64	0.25	0.22	0.40	12.4	2.2	13.3	492.8	0.11	0.00
M/C	0.1480	0.4281	0.3537	1.4914	0.0313	0.0016	1.2085	0.7765	0.5132	0.7275	0.0812	0.6585	1.7318	0.0000
F	13.5641**	6.6000*	0.0000	0.0918	0.3932	0.2318	0.0973	0.3777	0.0821	0.0704	12.8305**	0.1589	0.0151	0.0000

INDIVIDUAL DATA 7-4-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Biochemical findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal No.	TP g/dl	Alb g/dl	A/G	Protein fractions (%) Alb	Globulin α_1	Globulin α_2	Globulin β	Globulin γ	GOT IU/l	GPT IU/l	ALP IU/l	LDH IU/l	γ-GTP IU/l	T-Bil mg/dl
458	5.8	2.7	0.87	56.7	17.0	4.6	14.9	6.8	156	28	256	4214	1.5	0.1
459	5.6	2.7	0.93	57.3	14.6	4.5	16.1	7.5	99	33	194	2034	2.2	0.1
460	5.9	2.7	0.84	55.6	17.6	5.8	15.0	6.0	114	24	322	2145	2.3	0.1
461	6.1	2.8	0.84	55.3	20.5	4.9	13.6	5.7	82	25	247	1614	1.0	0.1
462	6.1	2.9	0.90	58.7	16.6	4.3	14.8	5.6	130	25	251	3180	1.3	0.1
463	5.8	2.6	0.81	59.1	16.2	5.3	13.9	5.5	134	34	219	3495	2.3	0.1
464	5.8	2.5	0.75	54.1	17.9	6.0	15.9	6.1	115	26	262	2576	2.1	0.1
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	5.87	2.70	0.849	56.69	17.20	5.06	14.89	6.17	118.6	27.9	250.1	2751.1	1.81	0.10
S.D.	0.18	0.13	0.059	1.83	1.81	0.66	0.93	0.73	24.2	4.1	39.7	920.4	0.54	0.00
S.E.	0.07	0.05	0.022	0.69	0.68	0.25	0.35	0.28	9.2	1.5	15.0	347.9	0.20	0.00
t'	3.6829**	2.5690*									3.5820**			

INDIVIDUAL DATA 7-4-3

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Biochemical findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

Animal No.	Glu mg/dl	T-Cho mg/dl	TG mg/dl	PL mg/dl	BUN mg/dl	Crea mg/dl	Na mEq/l	K mEq/l	Cl mEq/l	Ca mg/dl	P mg/dl
158	155	69	34	140	19.1	0.6	143.5	4.23	107	9.3	7.6
159	109	45	8	98	19.2	0.7	144.0	4.25	109	9.9	8.4
160	138	86	29	168	18.4	0.5	144.0	4.28	107	9.5	5.9
161	112	51	11	116	21.4	0.6	143.5	4.37	106	9.4	6.6
162	94	55	21	123	26.7	0.6	143.0	4.41	106	9.7	6.5
163	110	60	9	125	21.8	0.6	144.0	4.32	108	9.8	6.7
164	100	50	15	104	21.0	0.5	142.0	4.40	106	9.5	6.7
N	7	7	7	7	7	7	7	7	7	7	7
MEAN	116.9	59.4	18.1	124.9	21.09	0.59	143.43	4.323	107.0	9.59	6.91
S.D.	21.8	14.1	10.2	23.6	2.79	0.07	0.73	0.073	1.2	0.22	0.82
S.E.	8.2	5.3	3.9	8.9	1.06	0.03	0.28	0.027	0.4	0.08	0.31
M/C	0.0244	7.5504**	0.2192	5.2105*	1.4203	0.1752	0.1416	11.7957**	1.5933	0.3484	0.1190
F	2.2399		0.0050		0.4233	0.1765	0.2523		0.0000	6.0000*	1.4397
H		3.4708†		3.2070†				5.0110*			

INDIVIDUAL DATA 7-4-4

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Biochemical findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Glu mg/dl	T-Cho mg/dl	TG mg/dl	PL mg/dl	BUN mg/dl	Crea mg/dl	Na mEq/l	K mEq/l	Cl mEq/l	Ca mg/dl	P mg/dl
458	119	52	14	111	21.5	0.6	143.0	3.75	106	9.3	7.3
459	124	51	21	116	22.2	0.5	142.0	3.92	107	9.2	6.6
460	164	48	11	105	20.4	0.7	144.0	3.85	106	9.2	5.1
461	155	43	17	112	17.4	0.6	144.5	3.75	110	9.5	5.0
462	144	46	44	115	21.4	0.6	143.0	3.97	104	9.5	6.8
463	115	43	8	96	20.2	0.6	142.5	4.92	109	9.5	7.3
464	115	51	9	97	18.9	0.6	143.5	4.05	107	9.1	6.3
N	7	7	7	7	7	7	7	7	7	7	7
MEAN	133.7	47.7	17.7	107.4	20.29	0.60	143.21	4.030	107.0	9.33	6.34
S.D.	20.4	3.8	12.5	8.3	1.67	0.06	0.86	0.408	2.0	0.17	0.95
S.E.	7.7	1.4	4.7	3.1	0.63	0.02	0.32	0.154	0.8	0.06	0.36
t'										2.4495*	
U		10.0000		10.5000				7.0000*			

INDIVIDUAL DATA 8-1-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PRIOD : End of adm.
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal No.	Body weight g	Brain g	Brain %	Pituitary gland mg	Pituitary gland 10^{-3}%	Thyroid Right mg	Thyroid Right 10^{-3}%	Thyroid Left mg	Thyroid Left 10^{-3}%	Thymus mg	Thymus 10^{-3}%	Heart g	Heart %
101	323	2.16	0.67	9.9	3.07	3.9	1.21	5.7	1.76	1034	320.12	1.17	0.36
102	311	1.99	0.64	8.9	2.86	6.6	2.12	7.4	2.38	867	278.78	1.07	0.34
103	311	2.04	0.66	11.4	3.67	14.3	4.60	10.7	3.44	693	222.83	1.21	0.39
104	320	2.04	0.64	9.6	3.00	10.9	3.41	10.1	3.16	755	235.94	1.15	0.36
105	310	2.03	0.65	9.4	3.03	8.8	2.84	8.1	2.61	684	220.65	1.10	0.35
106	308	1.97	0.64	10.4	3.38	7.0	2.27	2.9	0.94	828	268.83	1.10	0.36
107	316	2.05	0.65	11.5	3.64	7.3	2.31	7.5	2.37	769	243.35	1.09	0.34
N	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	314.1	2.040	0.650	10.16	3.236	8.40	2.680	7.49	2.380	804.3	255.786	1.127	0.357
S.D.	5.6	0.061	0.012	0.99	0.326	3.36	1.082	2.64	0.841	121.0	35.840	0.051	0.017
S.E.	2.1	0.023	0.004	0.38	0.123	1.27	0.409	1.00	0.318	45.7	13.546	0.019	0.006
M/C	10.5289*	5.0031	11.0633*	7.0699	5.8548	2.2477	3.2649	4.0384	4.5146	0.6182	1.1179	11.7374**	1.9042
F		1.2846		0.5670	1.1870	0.1158	0.1461	0.7305	0.6828	0.0598	0.0708		1.5083
H	0.9244		1.4702									2.7919	

INDIVIDUAL DATA 8-1-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PRIOD : End of adm.
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 4 mg/kg

Animal No.	Body weight	Brain		Pituitary gland		Thyroid				Thymus		Heart	
						Right		Left					
	g	g	%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	g	%
201	312	1.99	0.64	11.3	3.62	8.3	2.66	6.7	2.15	1012	324.36	1.10	0.35
202	323	2.14	0.66	11.2	3.47	10.1	3.13	10.6	3.28	741	229.41	1.14	0.35
203	281	2.15	0.77	9.9	3.52	7.9	2.81	10.5	3.74	754	268.33	1.12	0.40
204	323	2.14	0.66	10.6	3.28	10.6	3.28	9.6	2.97	1005	311.15	1.17	0.36
205	321	2.09	0.65	10.2	3.18	4.7	1.46	6.7	2.09	849	264.49	1.15	0.36
206	319	2.07	0.65	11.1	3.48	8.7	2.73	8.9	2.79	645	202.19	1.26	0.39
207	344	2.04	0.59	10.8	3.14	10.1	2.94	8.2	2.38	734	213.37	1.24	0.36
N	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	317.6	2.089	0.660	10.73	3.384	8.63	2.716	8.74	2.771	820.0	259.043	1.169	0.367
S.D.	18.9	0.060	0.054	0.53	0.184	2.01	0.596	1.63	0.611	141.7	47.070	0.060	0.020
S.E.	7.1	0.023	0.020	0.20	0.069	0.76	0.225	0.62	0.231	53.6	17.791	0.023	0.007

INDIVIDUAL DATA 8-1-3

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PRIOD : End of adm.
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 20 mg/kg

Animal No.	Body weight	Brain		Pituitary gland		Thyroid Right		Thyroid Left		Thymus		Heart	
	g	g	%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	g	%
301	330	2.17	0.66	11.4	3.45	8.7	2.64	7.5	2.27	828	250.91	1.23	0.37
302	307	2.12	0.69	11.1	3.62	11.0	3.58	8.6	2.80	731	238.11	1.21	0.39
303	313	1.97	0.63	11.0	3.51	7.5	2.40	8.9	2.84	1014	323.96	1.14	0.36
304	306	2.22	0.73	10.4	3.40	(#)[a]	#	(16.0)[a]	#	1075	351.31	1.12	0.37
305	285	2.02	0.71	9.7	3.40	6.6	2.32	8.0	2.81	619	217.19	1.24	0.44
306	314	2.07	0.66	10.2	3.25	8.9	2.83	9.2	2.93	687	218.79	1.18	0.38
307	333	2.12	0.64	11.3	3.39	11.5	3.45	10.6	3.18	876	263.06	1.17	0.35
N	7	7	7	7	7	6	6	6	6	7	7	7	7
MEAN	312.6	2.099	0.674	10.73	3.431	9.03	2.870	8.80	2.805	832.9	266.190	1.184	0.380
S.D.	16.1	0.086	0.037	0.64	0.115	1.92	0.533	1.08	0.298	168.7	52.061	0.045	0.029
S.E.	6.1	0.032	0.014	0.24	0.043	0.78	0.217	0.44	0.122	63.8	19.677	0.017	0.011

a): With abnormal findings.
( ): Excluded from statistical analysis.
#: Blank value.

INDIVIDUAL DATA 8-1-4

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PRIOD : End of adm.
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Body weight	Brain		Pituitary gland		Thyroid				Thymus		Heart	
						Right		Left					
	g	g	%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	g	%
401	285	2.03	0.71	8.8	3.09	5.2	1.82	6.5	2.28	676	237.19	0.99	0.35
402	278	2.08	0.75	9.6	3.45	10.2	3.67	9.1	3.27	730	262.59	1.06	0.38
403	289	2.11	0.73	9.1	3.15	5.6	1.94	6.6	2.28	699	241.87	1.04	0.36
404	313	2.08	0.66	11.3	3.61	12.4	3.96	4.0	1.28	858	274.12	1.23	0.39
405	325	2.11	0.65	11.6	3.57	9.5	2.92	9.5	2.92	1061	326.46	1.18	0.36
406	347	2.11	0.61	12.3	3.54	9.8	2.82	10.3	2.97	919	264.84	1.34	0.39
407	336	2.12	0.63	12.1	3.60	11.1	3.30	8.7	2.59	698	207.74	1.37	0.41
N	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	310.4	2.091	0.677	10.69	3.430	9.11	2.919	7.81	2.513	805.9	259.259	1.173	0.377
S.D.	27.0	0.031	0.053	1.48	0.219	2.71	0.813	2.21	0.656	145.1	37.020	0.149	0.021
S.E.	10.2	0.012	0.020	0.56	0.083	1.03	0.307	0.83	0.248	54.8	13.992	0.056	0.008

INDIVIDUAL DATA 8-1-5

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PRIOD : End of adm.
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal No.	Lung		Liver		Spleen		Kidney				Adrenal			
							Right		Left		Right		Left	
	g	%	g	%	g	%	g	%	g	%	mg	10^{-3}%	mg	10^{-3}%
101	1.19	0.37	11.03	3.41	0.64	0.20	1.28	0.40	1.31	0.41	23	7.12	24	7.43
102	1.03	0.33	9.15	2.94	0.78	0.25	1.02	0.33	1.08	0.35	27	8.68	29	9.32
103	1.30	0.42	10.12	3.25	0.65	0.21	1.32	0.42	1.29	0.41	21	6.75	26	8.36
104	1.21	0.38	9.87	3.08	0.67	0.21	1.33	0.42	1.30	0.41	26	8.13	25	7.81
105	1.18	0.38	8.91	2.87	0.70	0.23	1.10	0.35	1.13	0.36	22	7.10	23	7.42
106	1.24	0.40	9.91	3.22	0.69	0.22	1.19	0.39	1.18	0.38	18	5.84	18	5.84
107	1.29	0.41	8.98	2.84	0.66	0.21	1.21	0.38	1.27	0.40	25	7.91	30	9.49
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	1.206	0.384	9.710	3.087	0.684	0.219	1.207	0.384	1.223	0.389	23.1	7.361	25.0	7.953
S.D.	0.090	0.030	0.760	0.215	0.047	0.017	0.115	0.034	0.092	0.025	3.1	0.953	4.0	1.254
S.E.	0.034	0.011	0.287	0.081	0.018	0.006	0.044	0.013	0.035	0.010	1.2	0.360	1.5	0.474
M/C	0.7844	5.4715	3.2740	3.6057	6.4884	4.7359	1.2781	1.3010	3.7006	0.0264	2.3519	2.2042	2.3148	2.4386
F	1.1613	1.2313	0.6185	3.7110*	0.0707	0.1986	1.9851	4.6790*	1.8322	5.7901**	1.3004	2.3171	0.7776	1.3603

INDIVIDUAL DATA 8-1-6

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PRIOD : End of adm.
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 4 mg/kg

Animal	Lung		Liver		Spleen		Kidney				Adrenal			
							Right		Left		Right		Left	
No.	g	%	g	%	g	%	g	%	g	%	mg	10^{-3}%	mg	10^{-3}%
201	1.18	0.38	9.40	3.01	0.71	0.23	1.17	0.38	1.16	0.37	23	7.37	27	8.65
202	1.17	0.36	10.08	3.12	0.76	0.24	1.29	0.40	1.33	0.41	22	6.81	25	7.74
203	1.21	0.43	8.03	2.86	0.46	0.16	1.19	0.42	1.20	0.43	19	6.76	20	7.12
204	1.28	0.40	10.27	3.18	0.72	0.22	1.28	0.40	1.27	0.39	25	7.74	27	8.36
205	1.27	0.40	9.90	3.08	0.68	0.21	1.20	0.37	1.18	0.37	21	6.54	23	7.17
206	1.24	0.39	9.30	2.92	0.67	0.21	1.39	0.44	1.30	0.41	22	6.90	24	7.52
207	1.35	0.39	11.36	3.30	0.78	0.23	1.45	0.42	1.43	0.42	20	5.81	24	6.98
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	1.243	0.393	9.763	3.067	0.683	0.214	1.281	0.404	1.267	0.400	21.7	6.847	24.3	7.649
S.D.	0.063	0.021	1.023	0.152	0.106	0.026	0.106	0.024	0.096	0.024	2.0	0.613	2.4	0.644
S.E.	0.024	0.008	0.387	0.057	0.040	0.010	0.040	0.009	0.036	0.009	0.7	0.232	0.9	0.243
t'				0.2443				1.3190		0.8720				

INDIVIDUAL DATA 8-1-7

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PRIOD : End of adm.
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 20 mg/kg

Animal	Lung		Liver		Spleen		Kidney				Adrenal			
							Right		Left		Right		Left	
No.	g	%	g	%	g	%	g	%	g	%	mg	10^{-3}%	mg	10^{-3}%
301	1.28	0.39	10.37	3.14	0.65	0.20	1.39	0.42	1.30	0.39	25	7.58	28	8.48
302	1.36	0.44	10.17	3.31	0.68	0.22	1.12	0.36	1.09	0.36	19	6.19	22	7.17
303	1.36	0.43	10.16	3.25	0.79	0.25	1.33	0.42	1.31	0.42	19	6.07	21	6.71
304	1.29	0.42	9.31	3.04	0.67	0.22	1.23	0.40	1.25	0.41	18	5.88	21	6.86
305	1.28	0.45	8.92	3.13	0.85	0.30	1.27	0.45	1.23	0.43	22	7.72	26	9.12
306	1.28	0.41	10.25	3.26	0.59	0.19	1.16	0.37	1.23	0.39	27	8.60	30	9.55
307	1.13	0.34	10.07	3.02	0.65	0.20	1.38	0.41	1.39	0.42	24	7.21	26	7.81
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	1.283	0.411	9.893	3.164	0.697	0.226	1.269	0.404	1.257	0.403	22.0	7.036	24.9	7.957
S.D.	0.077	0.037	0.551	0.112	0.090	0.038	0.105	0.031	0.093	0.024	3.5	1.019	3.6	1.123
S.E.	0.029	0.014	0.208	0.042	0.034	0.014	0.040	0.012	0.035	0.009	1.3	0.385	1.4	0.424
t'				0.9424				1.3190		1.0900				

#: Blank value.
( ): Excluded from statistical analysis.

INDIVIDUAL DATA 8-1-8

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PRIOD : End of adm.
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Lung		Liver		Spleen		Kidney				Adrenal			
							Right		Left		Right		Left	
	g	%	g	%	g	%	g	%	g	%	mg	10^{-3}%	mg	10^{-3}%
401	1.16	0.41	8.97	3.15	0.44	0.15	1.13	0.40	1.12	0.39	22	7.72	23	8.07
402	1.11	0.40	8.91	3.21	0.73	0.26	1.24	0.45	1.22	0.44	22	7.91	26	9.35
403	1.22	0.42	9.79	3.39	0.57	0.20	1.30	0.45	1.23	0.43	22	7.61	25	8.65
404	1.18	0.38	10.28	3.28	0.64	0.20	1.44	0.46	1.43	0.46	22	7.03	22	7.03
405	1.28	0.39	10.87	3.34	0.64	0.20	1.42	0.44	1.45	0.45	25	7.69	27	8.31
406	1.35	0.39	11.64	3.35	0.78	0.22	1.61	0.46	1.56	0.45	30	8.65	34	9.80
407	1.30	0.39	11.65	3.47	0.90	0.27	1.42	0.42	1.54	0.46	30	8.93	33	9.82
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	1.229	0.397	10.301	3.313	0.671	0.214	1.366	0.440	1.364	0.440	24.7	7.934	27.1	8.719
S.D.	0.085	0.014	1.148	0.109	0.149	0.041	0.156	0.022	0.173	0.024	3.8	0.650	4.7	1.019
S.E.	0.032	0.005	0.434	0.041	0.056	0.015	0.059	0.008	0.065	0.009	1.4	0.246	1.8	0.385
t'				2.7575*				3.6742**		3.9240**				

INDIVIDUAL DATA 8-1-9

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PRIOD : End of adm.
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal	Testis				Epididymis				Prostate		Seminal vesicle	
	Right		Left		Right		Left					
No.	g	%	g	%	g	%	g	%	mg	10^{-3}%	g	%
101	1.57	0.49	0.91	0.28	0.32	0.10	0.23	0.07	478	147.99	0.90	0.28
102	1.29	0.41	1.27	0.41	0.27	0.09	0.27	0.09	320	102.89	0.57	0.18
103	1.46	0.47	1.46	0.47	0.28	0.09	0.29	0.09	459	147.59	0.91	0.29
104	1.45	0.45	1.43	0.45	0.32	0.10	0.34	0.11	460	143.75	0.84	0.26
105	1.42	0.46	1.37	0.44	0.33	0.11	0.30	0.10	456	147.10	0.77	0.25
106	1.48	0.48	1.41	0.46	0.26	0.08	0.30	0.10	217	70.45	0.56	0.18
107	1.41	0.45	1.38	0.44	0.34	0.11	0.31	0.10	420	132.91	0.74	0.23
N	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	1.440	0.459	1.319	0.421	0.303	0.097	0.291	0.094	401.4	127.526	0.756	0.239
S.D.	0.084	0.026	0.190	0.065	0.032	0.011	0.034	0.013	97.1	29.892	0.144	0.045
S.E.	0.032	0.010	0.072	0.025	0.012	0.004	0.013	0.005	36.7	11.298	0.055	0.017
M/C	6.4778	1.8985	11.4809**	3.2108	0.9732	0.1262	4.5426	1.1654	6.9557	4.0901	0.4005	1.3097
F	2.3771†	1.1519		0.9414	2.3843†	2.1638	1.5304	1.1014	0.8102	0.9587	2.7522†	2.7149†
H			6.4159†									

INDIVIDUAL DATA 8-1-10

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PRIOD : End of adm.
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 4 mg/kg

Animal	Testis				Epididymis				Prostate		Seminal vesicle	
	Right		Left		Right		Left					
No.	g	%	g	%	g	%	g	%	mg	10^{-3}%	g	%
201	1.27	0.41	1.26	0.40	0.25	0.08	0.25	0.08	399	127.88	0.75	0.24
202	1.35	0.42	1.33	0.41	0.33	0.10	0.33	0.10	522	161.61	0.93	0.29
203	1.42	0.51	1.36	0.48	0.32	0.11	0.30	0.11	368	130.96	0.90	0.32
204	1.28	0.40	1.29	0.40	0.26	0.08	0.25	0.08	432	133.75	0.91	0.28
205	1.46	0.45	1.36	0.42	0.30	0.09	0.31	0.10	439	136.76	0.65	0.20
206	1.31	0.41	1.25	0.39	0.32	0.10	0.30	0.09	418	131.03	1.07	0.34
207	1.44	0.42	1.38	0.40	0,29	0.08	0.29	0.08	403	117.15	0.99	0.29
N	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	1.361	0.431	1.319	0.414	0.296	0.091	0.290	0.091	425.9	134.163	0.886	0.280
S.D.	0.079	0.038	0.052	0.030	0.031	0.012	0.030	0.012	48.5	13.597	0.142	0.047
S.E.	0.030	0.014	0.020	0.012	0.012	0.005	0.011	0.005	18.3	5.139	0.054	0.018
t'	1.9303				0.4545						1.8070	1.7029
U			13.5000									

INDIVIDUAL DATA 8-1-11

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PRIOD : End of adm.
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 20 mg/kg

Animal	Testis				Epididymis				Prostate		Seminal vesicle	
	Right		Left		Right		Left					
No.	g	%	g	%	g	%	g	%	mg	10^{-3}%	g	%
301	1.45	0.44	1.40	0.42	0.31	0.09	0.29	0.09	413	125.15	0.87	0.26
302	1.28	0.42	1.28	0.42	0.31	0.10	0.29	0.09	341	111.07	0.71	0.23
303	1.38	0.44	1.36	0.43	0.30	0.10	0.28	0.09	350	111.82	0.65	0.21
304	1.30	0.42	1.25	0.41	0.27	0.09	0.26	0.08	333	108.82	0.76	0.25
305	1.41	0.49	1.39	0.49	0.33	0.12	0.30	0.11	294	103.16	0.56	0.20
306	1.43	0.46	1.41	0.45	0.30	0.10	0.28	0.09	331	105.41	0.59	0.19
307	1.19	0.36	1.18	0.35	0.27	0.08	0.26	0.08	535	160.66	0.92	0.28
N	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	1.349	0.433	1.324	0.424	0.299	0.097	0.280	0.090	371.0	118.013	0.723	0.231
S.D.	0.095	0.040	0.088	0.042	0.022	0.013	0.015	0.010	80.6	20.084	0.136	0.033
S.E.	0.036	0.015	0.033	0.016	0.008	0.005	0.006	0.004	30.5	7.591	0.052	0.013
t'	2.2462				0.2727						0.4567	0.2936
U			18.5000									

#: Blank value.
( ): Excluded from statistical analysis.

INDIVIDUAL DATA 8-1-12

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PRIOD : End of adm.
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

Animal	Testis				Epididymis				Prostate		Seminal vesicle	
	Right		Left		Right		Left					
No.	g	%	g	%	g	%	g	%	mg	10^{-3}%	g	%
401	1.40	0.49	1.38	0.48	0.30	0.11	0.29	0.10	412	144.56	1.12	0.39
402	1.46	0.53	1.43	0.51	0.37	0.13	0.37	0.13	426	153.24	0.86	0.31
403	1.42	0.49	1.41	0.49	0.29	0.10	0.29	0.10	415	143.60	0.89	0.31
404	1.42	0.45	1.37	0.44	0.32	0.10	0.29	0.09	412	131.63	0.76	0.24
405	1.45	0.45	1.52	0.47	0.34	0.10	0.36	0.11	383	117.85	0.87	0.27
406	1.37	0.39	1.30	0.37	0.34	0.10	0.27	0.08	376	108.36	0.83	0.24
407	1.42	0.42	1.42	0.42	0.37	0.11	0.33	0.10	478	142.26	0.84	0.25
N	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	1.420	0.460	1.404	0.454	0.333	0.107	0.314	0.101	414.6	134.500	0.881	0.287
S.D.	0.030	0.047	0.067	0.048	0.031	0.011	0.039	0.016	33.3	16.146	0.113	0.054
S.E.	0.011	0.018	0.025	0.018	0.012	0.004	0.015	0.006	12.6	6.103	0.043	0.021
t'	0.4914				1.9091						1.7474	1.9965
U			19.0000									

INDIVIDUAL DATA 8-2-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PRIOD : End of adm.
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

Animal No.	Body weight g	Brain g	Brain %	Pituitary gland mg	Pituitary gland 10^{-3}%	Thyroid Right mg	Thyroid Right 10^{-3}%	Thyroid Left mg	Thyroid Left 10^{-3}%	Thymus mg	Thymus 10^{-3}%	Heart g	Heart %
151	155	1.81	1.17	11.6	7.48	5.1	3.29	4.7	3.03	378	243.87	0.62	0.40
152	178	1.95	1.10	12.6	7.08	7.1	3.99	8.9	5.00	449	252.25	0.77	0.43
153	188	1.85	0.98	10.9	5.80	5.2	2.77	4.0	2.13	364	193.62	0.72	0.38
154	208	1.92	0.92	15.0	7.21	7.7	3.70	6.6	3.17	590	283.65	0.83	0.40
155	241	1.92	0.80	12.1	5.02	6.8	2.82	7.9	3.28	647	268.46	0.95	0.39
156	199	1.81	0.91	12.0	6.03	5.9	2.96	5.5	2.76	409	205.53	0.80	0.40
157	184	1.79	0.97	10.6	5.76	6.2	3.37	7.6	4.13	467	253.80	0.79	0.43
N	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	193.3	1.864	0.979	12.11	6.340	6.29	3.271	6.46	3.357	472.0	243.026	0.783	0.404
S.D.	26.9	0.065	0.123	1.45	0.919	0.97	0.459	1.80	0.940	107.7	32.522	0.101	0.019
S.E.	10.2	0.024	0.047	0.55	0.347	0.37	0.173	0.68	0.355	40.7	12.292	0.038	0.007
M/C	5.1300	1.3187	4.1875	0.1692	3.5763	0.5790	0.4601	0.6177	1.6788	1.1238	1.6808	6.8066	1.0425
F	0.5506	3.2691*	1.8562	0.2774	0.9237	6.3129**	10.6659**	1.3058	1.9690	1.3005	0.9719	0.6028	1.4652

INDIVIDUAL DATA 8-2-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PRIOD : End of adm.
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 4 mg/kg

Animal No.	Body weight	Brain		Pituitary gland		Thyroid				Thymus		Heart	
						Right		Left					
	g	g	%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	g	%
251	165	1.73	1.05	9.0	5.45	4.7	2.85	4.4	2.67	408	247.27	0.74	0.45
252	195	1.80	0.92	13.2	6.77	7.8	4.00	10.6	5.44	557	285.64	0.79	0.41
253	222	1.84	0.83	12.3	5.54	8.3	3.74	7.8	3.51	457	205.86	0.84	0.38
254	206	1.83	0.89	12.6	6.12	7.3	3.54	6.3	3.06	662	321.36	0.85	0.41
255	189	1.88	0.99	12.5	6.61	7.6	4.02	7.2	3.81	490	259.26	0.82	0.43
256	198	1.88	0.95	11.8	5.96	7.5	3.79	7.8	3.94	571	288.38	0.84	0.42
257	231	1.94	0.84	13.6	5.89	6.4	2.77	7.7	3.33	747	323.38	0.93	0.40
N	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	200.9	1.843	0.924	12.14	6.049	7.09	3.530	7.40	3.680	556.0	275.879	0.830	0.414
S.D.	21.8	0.067	0.080	1.51	0.498	1.20	0.518	1.87	0.889	118.3	41.980	0.058	0.022
S.E.	8.2	0.025	0.030	0.57	0.188	0.45	0.196	0.71	0.336	44.7	15.867	0.022	0.008
t'		0.6860				1.2881	0.9264						

INDIVIDUAL DATA 8-2-3

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PRIOD : End of adm.
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 20 mg/kg

Animal No.	Body weight	Brain		Pituitary gland		Thyroid Right		Thyroid Left		Thymus		Heart	
	g	g	%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	g	%
351	199	1.91	0.96	9.6	4.82	6.8	3.42	5.6	2.81	391	196.48	0.78	0.39
352	187	1.84	0.98	11.6	6.20	5.9	3.16	5.7	3.05	674	360.43	0.76	0.41
353	188	1.95	1.04	11.4	6.06	6.9	3.67	9.0	4.79	527	280.32	0.83	0.44
354	211	1.96	0.93	12.9	6.11	9.0	4.27	8.0	3.79	589	279.15	0.90	0.43
355	179	1.88	1.05	15.2	8.49	7.4	4.13	6.4	3.58	472	263.69	0.77	0.43
356	197	1.92	0.97	12.2	6.19	5.7	2.89	5.6	2.84	526	267.01	0.78	0.40
357	221	1.88	0.85	11.8	5.34	7.6	3.44	9.1	4.12	463	209.50	0.82	0.37
N	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	197.4	1.906	0.969	12.10	6.173	7.04	3.569	7.06	3.569	520.3	265.226	0.806	0.410
S.D.	14.6	0.042	0.068	1.70	1.148	1.11	0.497	1.60	0.733	92.0	53.732	0.049	0.025
S.E.	5.5	0.016	0.026	0.64	0.434	0.42	0.188	0.60	0.277	34.8	20.309	0.018	0.010
t'		1.3262				1.2191	1.0645						

INDIVIDUAL DATA 8-2-4

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PRIOD : End of adm.
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Body weight	Brain		Pituitary gland		Thyroid				Thymus		Heart	
						Right		Left					
	g	g	%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	g	%
451	187	1.98	1.06	12.3	6.58	8.0	4.28	8.1	4.33	425	227.27	0.74	0.40
452	190	1.93	1.02	12.9	6.79	9.8	5.16	7.7	4.05	467	245.79	0.86	0.45
453	192	1.99	1.04	15.1	7.86	9.4	4.90	10.1	5.26	407	211.98	0.81	0.42
454	192	1.86	0.97	10.1	5.26	8.3	4.32	8.6	4.48	405	210.94	0.81	0.42
455	170	1.85	1.09	11.6	6.82	9.0	5.29	6.9	4.06	405	238.24	0.81	0.48
456	181	1.97	1.09	13.7	7.57	6.8	3.76	6.3	3.48	541	298.90	0.80	0.44
457	205	1.94	0.95	13.5	6.59	10.9	5.32	9.6	4.68	599	292.20	0.81	0.40
N	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	188.1	1.931	1.031	12.74	6.781	8.89	4.719	8.19	4.334	464.1	246.474	0.806	0.430
S.D.	10.8	0.056	0.055	1.61	0.835	1.33	0.604	1.37	0.560	77.3	35.891	0.035	0.029
S.E.	4.1	0.021	0.021	0.61	0.315	0.50	0.228	0.52	0.212	29.2	13.565	0.013	0.011
t'		2.1494				4.1862**	5.1845**						

INDIVIDUAL DATA 8-2-5

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PRIOD : End of adm.
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

Animal	Lung		Liver		Spleen		Kidney				Adrenal			
							Right		Left		Right		Left	
No.	g	%	g	%	g	%	g	%	g	%	mg	10^{-3}%	mg	10^{-3}%
151	0.79	0.51	4.43	2.86	0.32	0.21	0.56	0.36	0.54	0.35	26	16.77	30	19.35
152	1.00	0.56	5.07	2.85	0.52	0.29	0.74	0.42	0.70	0.39	22	12.36	24	13.48
153	0.94	0.50	5.84	3.11	0.40	0.21	0.69	0.37	0.69	0.37	21	11.17	18	9.57
154	0.99	0.48	6.24	3.00	0.40	0.19	0.92	0.44	0.92	0.44	30	14.42	31	14.90
155	1.06	0.44	7.25	3.01	0.62	0.26	0.88	0.37	0.93	0.39	30	12.45	35	14.52
156	1.04	0.52	6.18	3.11	0.45	0.23	0.83	0.42	0.79	0.40	26	13.07	26	13.07
157	0.88	0.48	5.35	2.91	0.44	0.24	0.81	0.44	0.82	0.45	25	13.59	27	14.67
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	0.957	0.499	5.766	2.979	0.450	0.233	0.776	0.403	0.770	0.399	25.7	13.404	27.3	14.223
S.D.	0.095	0.038	0.917	0.109	0.096	0.034	0.123	0.035	0.139	0.036	3.5	1.803	5.5	2.903
S.E.	0.036	0.014	0.347	0.041	0.036	0.013	0.047	0.013	0.052	0.014	1.3	0.681	2.1	1.097
M/C	1.1476	1.6055	2.3144	4.4336	1.0882	5.2725	1.6627	0.4021	2.3561	0.1859	2.0874	3.4031	6.4309	1.8731
F	0.2536	0.5762	1.2262	7.8902**	0.2155	1.1939	0.9963	5.2712**	0.5169	3.6236*	5.6892**	5.6065**	4.8816**	7.3178**

INDIVIDUAL DATA 8-2-6

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PRIOD : End of adm.
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 4 mg/kg

Animal No.	Lung		Liver		Spleen		Kidney				Adrenal			
							Right		Left		Right		Left	
	g	%	g	%	g	%	g	%	g	%	mg	10^{-3}%	mg	10^{-3}%
251	0.90	0.55	5.32	3.22	0.32	0.19	0.68	0.41	0.63	0.38	26	15.76	26	15.76
252	0.95	0.49	5.89	3.02	0.37	0.19	0.86	0.44	0.82	0.42	28	14.36	31	15.90
253	0.98	0.44	6.58	2.96	0.51	0.23	0.80	0.36	0.78	0.35	30	13.51	32	14.41
254	0.86	0.42	6.60	3.20	0.44	0.21	0.85	0.41	0.90	0.44	29	14.08	31	15.05
255	0.99	0.52	5.48	2.90	0.37	0.20	0.69	0.37	0.66	0.35	33	17.46	31	16.40
256	0.95	0.48	5.27	2.66	0.40	0.20	0.81	0.41	0.76	0.38	30	15.15	29	14.65
257	1.12	0.48	6.41	2.77	0.49	0.21	0.94	0.41	0.93	0.40	36	15.58	45	19.48
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	0.964	0.483	5.936	2.961	0.414	0.204	0.804	0.401	0.783	0.389	30.3	15.129	32.1	15.950
S.D.	0.082	0.044	0.593	0.208	0.069	0.014	0.093	0.027	0.112	0.034	3.3	1.313	6.0	1.711
S.E.	0.031	0.017	0.224	0.078	0.026	0.005	0.035	0.010	0.042	0.013	1.2	0.496	2.3	0.647
t'				0.1559				0.0818		0.5425	2.3527	1.5144	1.9410	1.4478

INDIVIDUAL DATA 8-2-7

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PRIOD : End of adm.
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 20 mg/kg

Animal	Lung		Liver		Spleen		Kidney				Adrenal			
							Right		Left		Right		Left	
No.	g	%	g	%	g	%	g	%	g	%	mg	10^{-3}%	mg	10^{-3}%
351	1.04	0.52	5.83	2.93	0.41	0.21	0.77	0.39	0.83	0.42	29	14.57	32	16.08
352	0.86	0.46	4.86	2.60	0.41	0.22	0.73	0.39	0.73	0.39	31	16.58	33	17.65
353	0.93	0.49	5.78	3.07	0.38	0.20	0.73	0.39	0.78	0.41	27	14.36	28	14.89
354	1.02	0.48	6.69	3.17	0.53	0.25	0.94	0.45	0.92	0.44	37	17.54	40	18.96
355	0.90	0.50	5.57	3.11	0.36	0.20	0.78	0.44	0.75	0.42	35	19.55	33	18.44
356	0.92	0.47	5.73	2.91	0.54	0.27	0.78	0.40	0.71	0.36	24	12.18	28	14.21
357	0.92	0.42	6.35	2.87	0.42	0.19	0.77	0.35	0.79	0.36	26	11.76	29	13.12
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	0.941	0.477	5.830	2.951	0.436	0.220	0.786	0.401	0.787	0.400	29.9	15.220	31.9	16.193
S.D.	0.065	0.032	0.582	0.191	0.071	0.029	0.071	0.034	0.071	0.031	4.8	2.839	4.2	2.233
S.E.	0.025	0.012	0.220	0.072	0.027	0.011	0.027	0.013	0.027	0.012	1.8	1.073	1.6	0.844
t'				0.2469				0.0818		0.0775	2.1321	1.5947	1.8268	1.6513

INDIVIDUAL DATA 8-2-8

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PRIOD : End of adm.
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Lung		Liver		Spleen		Kidney				Adrenal			
							Right		Left		Right		Left	
	g	%	g	%	g	%	g	%	g	%	mg	10^{-3}%	mg	10^{-3}%
451	0.89	0.48	5.71	3.05	0.42	0.22	0.87	0.47	0.86	0.46	32	17.11	34	18.18
452	0.94	0.49	6.26	3.29	0.43	0.23	0.86	0.45	0.83	0.44	32	16.84	35	18.42
453	0.98	0.51	7.28	3.79	0.44	0.23	0.90	0.47	0.89	0.46	32	16.67	38	19.79
454	0.92	0.48	6.00	3.13	0.36	0.19	0.78	0.41	0.78	0.41	31	16.15	36	18.75
455	0.92	0.54	6.15	3.62	0.34	0.20	0.74	0.44	0.73	0.43	38	22.35	39	22.94
456	0.83	0.46	6.56	3.62	0.40	0.22	0.81	0.45	0.73	0.40	36	19.89	39	21.55
457	1.04	0.51	6.76	3.30	0.63	0.31	1.06	0.52	1.05	0.51	35	17.07	37	18.05
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	0.931	0.496	6.389	3.400	0.431	0.229	0.860	0.459	0.839	0.444	33.7	18.011	36.9	19.669
S.D.	0.066	0.026	0.524	0.279	0.095	0.039	0.104	0.034	0.112	0.037	2.6	2.262	2.0	1.893
S.E.	0.025	0.010	0.198	0.105	0.036	0.015	0.039	0.013	0.042	0.014	1.0	0.855	0.7	0.715
t'				3.8329**				3.1914*		2.4799	4.1172**	4.0465**	3.8249**	4.5648**

INDIVIDUAL DATA 8-2-9

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PRIOD : End of adm.
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

Animal No.	Ovary Right mg	Ovary Right 10^{-3}%	Ovary Left mg	Ovary Left 10^{-3}%	Uterus g	Uterus %
151	36	23.23	39	25.16	0.44	0.28
152	40	22.47	44	24.72	0.56	0.31
153	35	18.62	39	20.74	0.33	0.18
154	58	27.88	48	23.08	0.50	0.24
155	56	23.24	49	20.33	0.34	0.14
156	56	28.14	46	23.12	0.75	0.38
157	31	16.85	38	20.65	0.60	0.33
N	7	7	7	7	7	7
MEAN	44.6	22.919	43.3	22.543	0.503	0.266
S.D.	11.6	4.234	4.6	1.998	0.150	0.085
S.E.	4.4	1.600	1.7	0.755	0.057	0.032
M/C	5.5923	1.4724	2.3932	2.4003	2.5522	3.8484
F	0.7295	1.2869	2.5490†	5.3689**	0.5342	0.6781

INDIVIDUAL DATA 8-2-10

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PRIOD : End of adm.
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 4 mg/kg

Animal No.	Ovary Right mg	Ovary Right 10^{-3}%	Ovary Left mg	Ovary Left 10^{-3}%	Uterus g	Uterus %
251	42	25.45	37	22.42	0.44	0.27
252	36	18.46	34	17.44	0.47	0.24
253	51	22.97	45	20.27	0.41	0.18
254	48	23.30	33	16.02	0.60	0.29
255	56	29.63	34	17.99	0.67	0.35
256	43	21.72	34	17.17	0.30	0.15
257	51	22.08	53	22.94	0.41	0.18
N	7	7	7	7	7	7
MEAN	46.7	23.373	38.6	19.179	0.471	0.237
S.D.	6.8	3.468	7.6	2.717	0.125	0.072
S.E.	2.6	1.311	2.9	1.027	0.047	0.027
t'			1.5155	2.2305		

INDIVIDUAL DATA 8-2-11

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PRIOD : End of adm.
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 20 mg/kg

Animal No.	Ovary Right mg	Ovary Right 10^{-3}%	Ovary Left mg	Ovary Left 10^{-3}%	Uterus g	Uterus %
351	43	21.61	32	16.08	0.41	0.21
352	42	22.46	40	21.39	0.33	0.18
353	33	17.55	39	20.74	0.46	0.24
354	48	22.75	43	20.38	0.66	0.31
355	43	24.02	40	22.35	0.38	0.21
356	36	18.27	46	23.35	0.37	0.19
357	42	19.00	40	18.10	0.41	0.19
N	7	7	7	7	7	7
MEAN	41.0	20.809	40.0	20.341	0.431	0.219
S.D.	5.0	2.509	4.3	2.501	0.109	0.045
S.E.	1.9	0.949	1.6	0.945	0.041	0.017
t'			1.0562	1.4596		

INDIVIDUAL DATA 8-2-12

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PRIOD : End of adm.
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Ovary Right mg	Ovary Right 10^{-3}%	Ovary Left mg	Ovary Left 10^{-3}%	Uterus g	Uterus %
451	38	20.32	41	21.93	0.36	0.19
452	45	23.68	36	18.95	0.50	0.26
453	54	28.13	50	26.04	0.42	0.22
454	48	25.00	48	25.00	0.33	0.17
455	49	28.82	47	27.65	0.44	0.26
456	44	24.31	55	30.39	0.53	0.29
457	41	20.00	48	23.41	0.50	0.24
N	7	7	7	7	7	7
MEAN	45.6	24.323	46.4	24.767	0.440	0.233
S.D.	5.3	3.423	6.2	3.771	0.075	0.042
S.E.	2.0	1.294	2.3	1.425	0.029	0.016
t'			1.0103	1.4747		

INDIVIDUAL DATA 8-3-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal No.	Body weight	Brain		Pituitary gland		Thyroid				Thymus		Heart	
						Right		Left					
	g	g	%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	g	%
108	345	1.99	0.58	9.3	2.70	11.3	3.28	12.6	3.65	627	181.74	1.14	0.33
109	349	2.14	0.61	12.6	3.61	9.2	2.64	9.5	2.72	487	139.54	1.27	0.36
110	460	2.07	0.45	13.4	2.91	11.0	2.39	11.9	2.59	599	130.22	1.32	0.29
111	406	2.06	0.51	11.9	2.93	9.1	2.24	8.4	2.07	555	136.70	1.34	0.33
112	370	2.11	0.57	12.6	3.41	8.7	2.35	10.4	2.81	520	140.54	1.16	0.31
113	365	2.03	0.56	12.0	3.29	7.9	2.16	8.2	2.25	722	197.81	1.34	0.37
114	350	2.05	0.59	11.5	3.29	8.9	2.54	5.6	1.60	541	154.57	1.27	0.36
N	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	377.9	2.064	0.553	11.90	3.163	9.44	2.514	9.51	2.527	578.7	154.446	1.263	0.336
S.D.	41.7	0.050	0.055	1.30	0.323	1.24	0.375	2.39	0.649	78.7	25.635	0.083	0.029
S.E.	15.8	0.019	0.021	0.49	0.122	0.47	0.142	0.90	0.245	29.7	9.689	0.031	0.011
M/C	1.5280	0.7422	0.0471	0.0020	0.0430	0.0727	0.3382	2.9652	2.9997	2.5949	0.9978	1.6351	0.3682
F	0.5633	0.0918	0.4359	1.4402	3.6283	0.0016	0.1333	0.1087	0.0000	1.7855	2.5988	0.5982	2.0041

INDIVIDUAL DATA 8-3-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Body weight	Brain		Pituitary gland		Thyroid Right		Thyroid Left		Thymus		Heart	
	g	g	%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	g	%
408	401	2.02	0.50	12.3	3.07	11.7	2.92	8.3	2.07	750	187.03	1.33	0.33
409	368	1.99	0.54	11.3	3.07	9.9	2.69	10.5	2.85	969	263.32	1.27	0.35
410	354	2.09	0.59	12.2	3.45	7.2	2.03	9.4	2.66	472	133.33	1.41	0.40
411	336	2.17	0.65	12.7	3.78	8.8	2.62	8.6	2.56	592	176.19	1.05	0.31
412	376	2.04	0.54	15.1	4.02	8.9	2.37	8.4	2.23	646	171.81	1.28	0.34
413	334	2.04	0.61	11.7	3.50	9.2	2.75	8.2	2.46	561	167.96	1.32	0.40
414	380	2.17	0.57	13.9	3.66	10.2	2.68	10.9	2.87	692	182.11	1.52	0.40
N	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	364.1	2.074	0.571	12.74	3.507	9.41	2.580	9.19	2.529	668.9	183.107	1.311	0.361
S.D.	24.4	0.072	0.050	1.33	0.353	1.39	0.293	1.11	0.301	160.2	39.440	0.144	0.038
S.E.	9.2	0.027	0.019	0.50	0.133	0.53	0.111	0.42	0.114	60.6	14.907	0.054	0.014
t'					1.9048								

INDIVIDUAL DATA 8-3-3

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal No.	Lung		Liver		Spleen		Kidney Right		Kidney Left		Adrenal Right		Adrenal Left	
	g	%	g	%	g	%	g	%	g	%	mg	10^{-3}%	mg	10^{-3}%
108	1.26	0.37	10.15	2.94	0.63	0.18	1.21	0.35	1.19	0.34	21	6.09	22	6.38
109	1.33	0.38	9.56	2.74	0.61	0.17	1.43	0.41	1.32	0.38	22	6.30	23	6.59
110	1.41	0.31	14.82	3.22	0.73	0.16	1.60	0.35	1.61	0.35	24	5.22	20	4.35
111	1.31	0.32	11.92	2.94	0.79	0.19	1.40	0.34	1.36	0.33	30	7.39	31	7.64
112	1.30	0.35	10.93	2.95	0.81	0.22	1.32	0.36	1.40	0.38	25	6.76	26	7.03
113	1.25	0.34	10.11	2.77	0.80	0.22	1.32	0.36	1.29	0.35	28	7.67	32	8.77
114	1.26	0.36	9.80	2.80	0.69	0.20	1.32	0.38	1.33	0.38	24	6.86	26	7.43
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	1.303	0.347	11.041	2.909	0.723	0.191	1.371	0.364	1.357	0.359	24.9	6.613	25.7	6.884
S.D.	0.056	0.026	1.847	0.163	0.082	0.023	0.123	0.024	0.129	0.021	3.2	0.828	4.5	1.367
S.E.	0.021	0.010	0.698	0.062	0.031	0.009	0.046	0.009	0.049	0.008	1.2	0.313	1.7	0.517
M/C	0.1576	0.6523	2.3028	0.2222	0.0870	0.0451	0.3627	1.4991	0.0049	2.6031	0.3613	1.4412	0.0190	0.0334
F	0.1904	0.5217	0.3925	0.0105	0.0190	0.2275	0.9486	2.8761	0.3448	2.0041	0.4271	0.0229	0.0149	0.1661

INDIVIDUAL DATA 8-3-4

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

Animal	Lung		Liver		Spleen		Kidney				Adrenal			
							Right		Left		Right		Left	
No.	g	%	g	%	g	%	g	%	g	%	mg	10^{-3}%	mg	10^{-3}%
408	1.34	0.33	11.55	2.88	0.68	0.17	1.40	0.35	1.39	0.35	26	6.48	29	7.23
409	1.35	0.37	11.89	3.23	0.64	0.17	1.41	0.38	1.34	0.36	22	5.98	21	5.71
410	1.30	0.37	10.03	2.83	0.69	0.19	1.24	0.35	1.18	0.33	18	5.08	22	6.21
411	1.23	0.37	9.06	2.70	0.69	0.21	1.44	0.43	1.39	0.41	27	8.04	31	9.23
412	1.36	0.36	10.64	2.83	0.81	0.22	1.49	0.40	1.40	0.37	24	6.38	24	6.38
413	1.19	0.36	10.38	3.11	0.68	0.20	1.52	0.46	1.50	0.45	29	8.68	31	9.28
414	1.25	0.33	10.30	2.71	0.83	0.22	1.50	0.39	1.58	0.42	19	5.00	24	6.32
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	1.289	0.356	10.550	2.899	0.717	0.197	1.429	0.394	1.397	0.384	23.6	6.520	26.0	7.194
S.D.	0.066	0.018	0.947	0.200	0.073	0.021	0.095	0.040	0.126	0.043	4.1	1.395	4.2	1.477
S.E.	0.025	0.007	0.358	0.075	0.027	0.008	0.036	0.015	0.047	0.016	1.6	0.527	1.6	0.558

INDIVIDUAL DATA 8-3-5

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal	Testis				Epididymis				Prostate		Seminal vesicle	
	Right		Left		Right		Left					
No.	g	%	g	%	g	%	g	%	mg	10^{-3}%	g	%
108	1.50	0.43	1.50	0.43	0.42	0.12	0.41	0.12	555	160.87	1.03	0.30
109	1.49	0.43	1.49	0.43	0.43	0.12	0.42	0.12	472	135.24	1.15	0.33
110	1.42	0.31	1.42	0.31	0.42	0.09	0.42	0.09	534	116.09	1.15	0.25
111	1.55	0.38	1.52	0.37	0.45	0.11	0.45	0.11	441	108.62	1.03	0.25
112	1.61	0.44	1.51	0.41	0.45	0.12	0.44	0.12	400	108.11	1.07	0.29
113	1.50	0.41	1.57	0.43	0.50	0.14	0.49	0.13	636	174.25	1.51	0.41
114	1.49	0.43	1.47	0.42	0.46	0.13	0.45	0.13	468	133.71	1.16	0.33
N	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	1.509	0.404	1.497	0.400	0.447	0.119	0.440	0.117	500.9	133.841	1.157	0.309
S.D.	0.059	0.046	0.046	0.045	0.028	0.016	0.027	0.014	79.5	25.751	0.166	0.056
S.E.	0.022	0.017	0.017	0.017	0.011	0.006	0.010	0.005	30.1	9.733	0.063	0.021
M/C	0.9063	1.5207	1.9291	3.1043	0.0214	0.3664	0.0297	0.0897	0.0706	0.0628	0.0702	1.1313
F	0.0051	0.2450	0.3017	0.1453	0.6864	0.0000	0.5122	0.0423	0.6014	1.0341	1.0084	0.2685

INDIVIDUAL DATA 8-3-6

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

Animal	Testis				Epididymis				Prostate		Seminal vesicle	
	Right		Left		Right		Left					
No.	g	%	g	%	g	%	g	%	mg	10^{-3}%	g	%
408	1.53	0.38	1.55	0.39	0.40	0.10	0.40	0.10	652	162.59	1.24	0.31
409	1.41	0.38	1.41	0.38	0.41	0.11	0.42	0.11	450	122.28	1.03	0.28
410	1.41	0.40	1.37	0.39	0.42	0.12	0.44	0.12	511	144.35	1.12	0.32
411	1.48	0.44	1.44	0.43	0.45	0.13	0.42	0.13	634	188.69	0.77	0.23
412	1.62	0.43	1.59	0.42	0.43	0.11	0.42	0.11	533	141.76	1.11	0.30
413	1.47	0.44	1.43	0.43	0.44	0.13	0.43	0.13	410	122.75	1.15	0.34
414	1.62	0.43	1.55	0.41	0.49	0.13	0.48	0.13	561	147.63	1.09	0.29
N	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	1.506	0.414	1.477	0.407	0.434	0.119	0.430	0.119	535.9	147.150	1.073	0.296
S.D.	0.088	0.027	0.085	0.021	0.030	0.012	0.025	0.012	89.1	23.148	0.148	0.035
S.E.	0.033	0.010	0.032	0.008	0.011	0.005	0.010	0.005	33.7	8.749	0.056	0.013

INDIVIDUAL DATA 8-4-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

Animal No.	Body weight	Brain		Pituitary gland		Thyroid Right		Thyroid Left		Thymus		Heart	
	g	g	%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	g	%
158	227	1.92	0.85	15.5	6.83	4.3	1.89	4.7	2.07	557	245.37	0.90	0.40
159	218	1.92	0.88	15.0	6.88	5.3	2.43	4.9	2.25	320	146.79	0.81	0.37
160	234	1.84	0.79	14.4	6.15	5.4	2.31	8.5	3.63	512	218.80	0.91	0.39
161	213	1.96	0.92	14.0	6.57	7.1	3.33	4.6	2.16	576	270.42	0.83	0.39
162	212	1.97	0.93	12.0	5.66	6.4	3.02	5.8	2.74	461	217.45	0.77	0.36
163	212	1.89	0.89	14.8	6.98	2.4	1.13	6.9	3.25	382	180.19	0.80	0.38
164	250	2.01	0.80	11.2	4.48	7.6	3.04	7.6	3.04	505	202.00	0.99	0.40
N	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	223.7	1.930	0.866	13.84	6.221	5.50	2.450	6.14	2.734	473.3	211.574	0.859	0.384
S.D.	14.3	0.056	0.055	1.62	0.899	1.77	0.766	1.55	0.601	93.1	40.754	0.078	0.015
S.E.	5.4	0.021	0.021	0.61	0.340	0.67	0.290	0.59	0.227	35.2	15.404	0.029	0.006
M/C	0.0136	0.8084	0.0627	0.0174	0.5788	0.8125	0.2021	1.9764	2.9261	0.0300	0.0001	0.8728	0.0754
F	3.2472'	1.2956	1.6304	1.4928	0.0653	0.6018	1.7218	0.6663	0.0811	1.1546	0.3765	1.3802	0.8721

INDIVIDUAL DATA 8-4-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Body weight	Brain		Pituitary gland		Thyroid Right		Thyroid Left		Thymus		Heart	
	g	g	%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	g	%
458	181	1.74	0.96	10.0	5.52	6.3	3.48	4.0	2.21	270	149.17	0.71	0.39
459	223	1.92	0.86	13.1	5.87	4.2	1.88	5.7	2.56	556	249.33	0.83	0.37
460	219	1.91	0.87	14.5	6.62	7.3	3.33	5.5	2.51	452	206.39	0.83	0.38
461	215	1.93	0.90	12.3	5.72	5.1	2.37	5.7	2.65	385	179.07	0.85	0.40
462	217	1.98	0.91	12.5	5.76	6.0	2.76	6.7	3.09	492	226.73	0.87	0.40
463	197	1.92	0.97	14.5	7.36	6.3	3.20	5.4	2.74	453	229.95	0.80	0.41
464	215	1.81	0.84	12.8	5.95	7.7	3.58	6.2	2.88	316	146.98	0.83	0.39
N	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	209.6	1.887	0.901	12.81	6.114	6.13	2.943	5.60	2.663	417.7	198.231	0.817	0.391
S.D.	15.0	0.082	0.049	1.53	0.649	1.20	0.633	0.84	0.281	100.2	40.614	0.052	0.013
S.E.	5.7	0.031	0.019	0.58	0.245	0.45	0.239	0.32	0.106	37.9	15.350	0.020	0.005
t'	1.8020												

INDIVIDUAL DATA 8-4-3

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

Animal	Lung		Liver		Spleen		Kidney				Adrenal			
							Right		Left		Right		Left	
No.	g	%	g	%	g	%	g	%	g	%	mg	10^{-3}%	mg	10^{-3}%
158	0.91	0.40	6.93	3.05	0.48	0.21	0.82	0.36	0.87	0.38	28	12.33	26	11.45
159	1.00	0.46	5.88	2.70	0.47	0.22	0.75	0.34	0.79	0.36	30	13.76	35	16.06
160	1.03	0.44	6.53	2.79	0.37	0.16	1.00	0.43	1.03	0.44	29	12.39	31	13.25
161	1.02	0.48	6.10	2.86	0.39	0.18	0.82	0.38	0.80	0.38	29	13.62	31	14.55
162	1.02	0.48	5.70	2.69	0.41	0.19	0.83	0.39	0.82	0.39	33	15.57	34	16.04
163	1.02	0.48	5.97	2.82	0.37	0.17	0.80	0.38	0.75	0.35	31	14.62	36	16.98
164	1.05	0.42	7.02	2.81	0.60	0.24	0.97	0.39	0.91	0.36	32	12.80	33	13.20
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	1.007	0.451	6.304	2.817	0.441	0.196	0.856	0.381	0.853	0.380	30.3	13.584	32.3	14.504
S.D.	0.045	0.032	0.525	0.120	0.083	0.029	0.093	0.028	0.094	0.030	1.8	1.202	3.4	1.980
S.E.	0.017	0.012	0.198	0.045	0.031	0.011	0.035	0.011	0.036	0.011	0.7	0.454	1.3	0.748
M/C	3.6432	0.2638	0.0848	0.6536	0.0403	0.6630	0.0952	0.0187	0.0012	0.3044	7.5129**	2.5681	2.6387	0.3207
F	0.7176	0.3422	2.9947	0.5268	0.1368	0.0515	0.7427	0.0387	1.8788	0.1564		2.0159	0.4788	2.1275
H											0.4136			

INDIVIDUAL DATA 8-4-4

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal	Lung		Liver		Spleen		Kidney				Adrenal			
							Right		Left		Right		Left	
No.	g	%	g	%	g	%	g	%	g	%	mg	10^{-3}%	mg	10^{-3}%
458	0.82	0.45	5.02	2.77	0.28	0.15	0.65	0.36	0.64	0.35	23	12.71	25	13.81
459	1.00	0.45	5.78	2.59	0.47	0.21	0.88	0.39	0.85	0.38	29	13.00	31	13.90
460	1.15	0.53	6.67	3.05	0.52	0.24	0.93	0.42	0.88	0.40	39	17.81	42	19.18
461	1.02	0.47	6.01	2.80	0.33	0.15	0.80	0.37	0.79	0.37	33	15.35	35	16.28
462	0.97	0.45	6.24	2.88	0.40	0.18	0.92	0.42	0.88	0.41	39	17.97	42	19.35
463	0.96	0.49	5.09	2.58	0.49	0.25	0.72	0.37	0.70	0.36	24	12.18	27	13.71
464	0.87	0.40	5.69	2.65	0.48	0.22	0.77	0.36	0.75	0.35	35	16.28	38	17.67
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	0.970	0.463	5.786	2.760	0.424	0.200	0.810	0.384	0.784	0.374	31.7	15.043	34.3	16.271
S.D.	0.107	0.040	0.594	0.170	0.090	0.041	0.106	0.026	0.093	0.024	6.6	2.438	6.9	2.521
S.E.	0.040	0.015	0.225	0.064	0.034	0.015	0.040	0.010	0.035	0.009	2.5	0.921	2.6	0.953

INDIVIDUAL DATA 8-4-5

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

Animal No.	Ovary Right mg	Ovary Right 10^{-3}%	Ovary Left mg	Ovary Left 10^{-3}%	Uterus g	Uterus %
158	55	24.23	39	17.18	0.41	0.18
159	46	21.10	43	19.72	0.35	0.16
160	45	19.23	33	14.10	0.88	0.38
161	47	22.07	43	20.19	0.34	0.16
162	38	17.92	50	23.58	0.37	0.17
163	43	20.28	42	19.81	0.40	0.19
164	52	20.80	55	22.00	0.33	0.13
N	7	7	7	7	7	7
MEAN	46.6	20.804	43.6	19.511	0.440	0.196
S.D.	5.6	2.021	7.2	3.111	0.196	0.083
S.E.	2.1	0.764	2.7	1.176	0.074	0.032
M/C	0.4966	0.9496	0.4291	0.5822	0.0001	0.0003
F	1.0799	0.0792	0.3989	0.0329	0.1258	0.4932

INDIVIDUAL DATA 8-4-6

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Absolute and relative organ weights ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Ovary Right mg	Ovary Right 10^{-3}%	Ovary Left mg	Ovary Left 10^{-3}%	Uterus g	Uterus %
458	32	17.68	34	18.78	0.29	0.16
459	43	19.28	45	20.18	0.37	0.17
460	39	17.81	43	19.63	0.52	0.24
461	38	17.67	34	15.81	0.87	0.40
462	51	23.50	42	19.35	0.43	0.20
463	43	21.83	44	22.34	0.33	0.17
464	54	25.12	48	22.33	0.53	0.25
N	7	7	7	7	7	7
MEAN	42.9	20.413	41.4	19.774	0.477	0.227
S.D.	7.6	3.075	5.4	2.243	0.196	0.084
S.E.	2.9	1.162	2.0	0.848	0.074	0.032

INDIVIDUAL DATA 9-1-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Gross findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal No.	Findings
101	Testis (left) : Small size
102	Skin of cervical region : Scab (left 9 x 8, mm)
103	Normal
104	Normal
105	Normal
106	Normal
107	Normal

INDIVIDUAL DATA 9-1-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Gross findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 4 mg/kg

Animal No.	Findings
201	Normal
202	Normal
203	Normal
204	Normal
205	Normal
206	Normal
207	Normal

INDIVIDUAL DATA 9-1-3

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Gross findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 20 mg/kg

Animal No.	Findings
301	Normal
302	Normal
303	Normal
304	Thyroid (right) : Aplasia Thyroid (left) : Large size Parathyroid (right) : Aplasia
305	Skin of cervical region : Scab (41 x 21, mm)
306	Normal
307	Normal

INDIVIDUAL DATA 9-1-4

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Gross findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Findings
401	Normal
402	Normal
403	Normal
404	Normal
405	Normal
406	Normal
407	Skin of cervical region : Scab (right 19 x 16, mm, left 5 x 5, mm) Skin of dorsal region : Scab (9 x 6, mm)

INDIVIDUAL DATA 9-2-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Gross findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

Animal No.	Findings
151	Normal
152	Normal
153	Normal
154	Normal
155	Normal
156	Normal
157	Normal

INDIVIDUAL DATA 9-2-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Gross findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 4 mg/kg

Animal No.	Findings
251	Normal
252	Normal
253	Normal
254	Normal
255	Normal
256	Normal
257	Normal

INDIVIDUAL DATA 9-2-3

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Gross findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 20 mg/kg

Animal No.	Findings
351	Normal
352	Normal
353	Normal
354	Normal
355	Normal
356	Normal
357	Normal

INDIVIDUAL DATA 9-2-4

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Gross findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Findings
451	Normal
452	Normal
453	Normal
454	Normal
455	Normal
456	Normal
457	Normal

INDIVIDUAL DATA 9-3-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Gross findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal No.	Findings
108	Normal
109	Normal
110	Normal
111	Normal
112	Normal
113	Skin of cervical region : Scab (right 14 x 13, mm)
114	Normal

INDIVIDUAL DATA 9-3-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Gross findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Findings
408	Normal
409	Normal
410	Normal
411	Normal
412	Normal
413	Normal
414	Skin of dorsal region : Scab (right 15 x 6, mm)

INDIVIDUAL DATA 9-4-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Gross findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

Animal No.	Findings
158	Normal
159	Normal
160	Normal
161	Normal
162	Normal
163	Normal
164	Normal

INDIVIDUAL DATA 9-4-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Gross findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal No.	Findings
458	Normal
459	Normal
460	Normal
461	Normal
462	Normal
463	Normal
464	Normal

INDIVIDUAL DATA 10-1-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal No.	101	102	103	104	105	106	107
Organ : Findings							
	a)						
Liver : Abnormal findings	-	-	-	-	-	-	-
Kidney (right) : Hyaline droplet deposition in tubular epithelium	-	-	-	+	+	-	-
Eosinophilic body deposition in tubular epithelium	-	-	-	+	+	-	-
Kidney (left) : Hyaline droplet deposition in tubular epithelium	-	-	-	+	+	-	-
Eosinophilic body deposition in tubular epithelium	-	-	-	+	+	-	-
Spleen : Abnormal findings	-	-	-	-	-	-	-
Heart : Abnormal findings	-	-	-	-	-	-	-
Lung : Calcium deposition in blood-vessel wall	-	+	-	-	-	-	-
Cerebrum : Abnormal findings	-	-	-	-	-	-	-
Cerebellum : Abnormal findings	-	-	-	-	-	-	-
Sciatic nerve : Abnormal findings	-	-	-	-	-	-	-
Spinal cord : Abnormal findings	-	-	-	-	-	-	-
Eyeball (right) : Abnormal findings	-	-	-	-	-	-	-
Eyeball (left) : Abnormal findings	-	-	-	-	-	-	-
Harder's gland (right) : Abnormal findings	-	-	-	-	-	-	-
Harder's gland (left) : Abnormal findings	-	-	-	-	-	-	-
Pituitary gland : Ciliated epithelial cyst	-	-	-	+	-	-	-
Thymus : Abnormal findings	-	-	-	-	-	-	-
Mesenteric lymph node : Abnormal findings	-	-	-	-	-	-	-
Thyroid (right) : Abnormal findings	-	-	-	-	-	-	-
Thyroid (left) : Abnormal findings	-	-	-	-	-	-	-
Parathyroid (right) : Abnormal findings	-	-	-	-	-	# b)	# b)
Parathyroid (left) : Abnormal findings	-	-	-	-	-	-	-
Aorta : Abnormal findings	-	-	-	-	-	-	-
Pancreas : Abnormal findings	-	-	-	-	-	-	-

(continued)

INDIVIDUAL DATA 10-1-1 (continued-1)

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal No.	101	102	103	104	105	106	107
Organ : Findings							
Adrenal (right) : Abnormal findings	-	-	-	-	-	-	-
Adrenal (left) : Abnormal findings	-	-	-	-	-	-	-
Submandibular gland (right) : Abnormal findings	-	-	-	-	-	-	-
Submandibular gland (left) : Abnormal findings	-	-	-	-	-	-	-
Sublingual gland (right) : Abnormal findings	-	-	-	-	-	-	-
Sublingual gland (left) : Abnormal findings	-	-	-	-	-	-	-
Parotid gland (right) : Abnormal findings	-	-	-	-	-	-	-
Parotid gland (left) : Abnormal findings	-	-	-	-	-	-	-
Submandibular lymph node (right) : Abnormal findings	-	-	-	-	-	-	-
Submandibular lymph node (left) : Abnormal findings	-	-	-	-	-	-	-
Bronchus : Abnormal findings	-	-	-	-	-	-	-
Larynx : Abnormal findings	-	-	-	-	-	-	-
Trachea : Abnormal findings	-	-	-	-	-	-	-
Tongue : Abnormal findings	-	-	-	-	-	-	-
Esophagus : Abnormal findings	-	-	-	-	-	-	-
Fore stomach : Abnormal findings	-	-	-	-	-	-	-
Glandular stomach : Abnormal findings	-	-	-	-	-	-	-
Duodenum : Abnormal findings	-	-	-	-	-	-	-
Jejunum : Abnormal findings	-	-	-	-	-	-	-
Ileum : Abnormal findings	-	-	-	-	-	-	-
Cecum : Abnormal findings	-	-	-	-	-	-	-
Colon : Abnormal findings	-	-	-	-	-	-	-
Rectum : Abnormal findings	-	-	-	-	-	-	-
Femur : Abnormal findings	-	-	-	-	-	-	-
Sternum : Abnormal findings	-	-	-	-	-	-	-
Skin of abdominal region : Abnormal findings	-	-	-	-	-	-	-

(continued)

INDIVIDUAL DATA 10-1-1 (continued-2)

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal No.	101	102	103	104	105	106	107
Organ : Findings							
Mammary gland : Abnormal findings	-	-	-	-	-	-	-
Skeletal muscle : Abnormal findings	-	-	-	-	-	-	-
Urinary bladder : Abnormal findings	-	-	-	-	-	-	-
Testis (right) : Abnormal findings	-	-	-	-	-	-	-
Testis (left) : Abnormal findings	-	-	-	-	-	-	-
Epididymis (right) : Abnormal findings	-	-	-	-	-	-	-
Epididymis (left) : Abnormal findings	-	-	-	-	-	-	-
Prostate : Abnormal findings	-	-	-	-	-	-	-
Seminal vesicle (right) : Abnormal findings	-	-	-	-	-	-	-
Seminal vesicle (left) : Abnormal findings	-	-	-	-	-	-	-
Skin of left cervical region : Ulcer	#	++	#	#	#	#	#
Thickening of epidermis	#	+	#	#	#	#	#
Fibrosis in dermis	#	+	#	#	#	#	#

a): - = normal, + = slight and ++ = moderate changes and # = not examined.
b): Because of an operation error.

INDIVIDUAL DATA 10-1-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 4 mg/kg

Animal No.	201	202	203	204	205	206	207
Organ : Findings							
	a)						
Liver : Abnormal findings	-	-	-	-	-	-	-
Kidney (right) : Hyaline droplet deposition in tubular epithelium	+	-	-	-	-	-	-
Eosinophilic body deposition in tubular epithelium	+	-	-	-	-	-	-
Kidney (left) : Hyaline droplet deposition in tubular epithelium	+	-	-	-	-	-	-
Eosinophilic body deposition in tubular epithelium	+	-	-	-	-	-	-
Focal interstitial infiltration of cells, mainly lymphocytes	-	-	-	-	-	-	+
Spleen : Abnormal findings	-	-	-	-	-	-	-
Heart : Abnormal findings	-	-	-	-	-	-	-
Lung : Abnormal findings	-	-	-	-	-	-	-
Cerebrum : Abnormal findings	-	-	-	-	-	-	-
Cerebellum : Abnormal findings	-	-	-	-	-	-	-
Sciatic nerve : Abnormal findings	-	-	-	-	-	-	-
Spinal cord : Abnormal findings	-	-	-	-	-	-	-
Eyeball (right) : Abnormal findings	-	-	-	-	-	-	-
Eyeball (left) : Abnormal findings	-	-	-	-	-	-	-
Harder's gland (right) : Abnormal findings	-	-	-	-	-	-	-
Harder's gland (left) : Abnormal findings	-	-	-	-	-	-	-
Pituitary gland : Abnormal findings	-	-	-	-	-	-	-
Thymus : Abnormal findings	-	-	-	-	-	-	-
Mesenteric lymph node : Abnormal findings	-	-	-	-	-	-	-
Thyroid (right) : Abnormal findings	-	-	-	-	-	-	-
Thyroid (left) : Abnormal findings	-	-	-	-	-	-	-
Parathyroid (right) : Abnormal findings	-	-	-	-	-	-	-
Parathyroid (left) : Abnormal findings	-	-	-	-	-	-	-
Aorta : Abnormal findings	-	-	-	-	-	-	-

(continued)

INDIVIDUAL DATA 10-1-2 (continued-1)

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 4 mg/kg

Animal No.	201	202	203	204	205	206	207
Organ : Findings							
Pancreas : Abnormal findings	-	-	-	-	-	-	-
Adrenal (right) : Abnormal findings	-	-	-	-	-	-	-
Adrenal (left) : Abnormal findings	-	-	-	-	-	-	-
Submandibular gland (right) : Abnormal findings	-	-	-	-	-	-	-
Submandibular gland (left) : Abnormal findings	-	-	-	-	-	-	-
Sublingual gland (right) : Abnormal findings	-	-	-	-	-	-	-
Sublingual gland (left) : Abnormal findings	-	-	-	-	-	-	-
Parotid gland (right) : Abnormal findings	-	-	-	-	-	-	-
Parotid gland (left) : Abnormal findings	-	-	-	-	-	-	-
Submandibular lymph node (right) : Abnormal findings	-	-	-	-	-	-	-
Submandibular lymph node (left) : Abnormal findings	-	-	-	-	-	-	-
Bronchus : Abnormal findings	-	-	-	-	-	-	-
Larynx : Abnormal findings	-	-	-	-	-	-	-
Trachea : Abnormal findings	-	-	-	-	-	-	-
Tongue : Abnormal findings	-	-	-	-	-	-	-
Esophagus : Abnormal findings	-	-	-	-	-	-	-
Fore stomach : Abnormal findings	-	-	-	-	-	-	-
Glandular stomach : Abnormal findings	-	-	-	-	-	-	-
Duodenum : Abnormal findings	-	-	-	-	-	-	-
Jejunum : Abnormal findings	-	-	-	-	-	-	-
Ileum : Abnormal findings	-	-	-	-	-	-	-
Cecum : Abnormal findings	-	-	-	-	-	-	-
Colon : Abnormal findings	-	-	-	-	-	-	-
Rectum : Abnormal findings	-	-	-	-	-	-	-
Femur : Abnormal findings	-	-	-	-	-	-	-

(continued)

INDIVIDUAL DATA 10-1-2 (continued-2)

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 4 mg/kg

Animal No.	201	202	203	204	205	206	207
Organ : Findings							
Sternum : Abnormal findings	-	-	-	-	-	-	-
Skin of abdominal region : Abnormal findings	-	-	-	-	-	-	-
Mammary gland : Abnormal findings	-	-	-	-	-	-	-
Skeletal muscle : Abnormal findings	-	-	-	-	-	-	-
Urinary bladder : Abnormal findings	-	-	-	-	-	-	-
Testis (right) : Abnormal findings	-	-	-	-	-	-	-
Testis (left) : Abnormal findings	-	-	-	-	-	-	-
Epididymis (right) : Abnormal findings	-	-	-	-	-	-	-
Epididymis (left) : Abnormal findings	-	-	-	-	-	-	-
Prostate : Abnormal findings	-	-	-	-	-	-	-
Seminal vesicle (right) : Abnormal findings	-	-	-	-	-	-	-
Seminal vesicle (left) : Abnormal findings	-	-	-	-	-	-	-

a): - = normal and + = slight change.

INDIVIDUAL DATA 10-1-3

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 20 mg/kg

Animal No.	301	302	303	304	305	306	307
Organ : Findings							
	a)						
Liver : Abnormal findings	-	-	-	-	-	-	-
Kidney (right) : Abnormal findings	-	-	-	-	-	-	-
Kidney (left) : Focal interstitial infiltration of cells, mainly lymphocytes	-	-	-	-	-	+	-
Spleen : Abnormal findings	-	-	-	-	-	-	-
Heart : Abnormal findings	-	-	-	-	-	-	-
Lung : Abnormal findings	-	-	-	-	-	-	-
Cerebrum : Abnormal findings	-	-	-	-	-	-	-
Cerebellum : Abnormal findings	-	-	-	-	-	-	-
Sciatic nerve : Abnormal findings	-	-	-	-	-	-	-
Spinal cord : Abnormal findings	-	-	-	-	-	-	-
Eyeball (right) : Abnormal findings	-	-	-	-	-	-	-
Eyeball (left) : Abnormal findings	-	-	-	-	-	-	-
Harder's gland (right) : Abnormal findings	-	-	-	-	-	-	-
Harder's gland (left) : Abnormal findings	-	-	-	-	-	-	-
Pituitary gland : Abnormal findings	-	-	-	-	-	-	-
Thymus : Abnormal findings	-	-	-	-	-	-	-
Mesenteric lymph node : Abnormal findings	-	-	-	-	-	-	-
Thyroid (right) : Aplasia	-	-	-	*	-	-	-
Thyroid (left) : Abnormal findings	-	-	-	-	-	-	-
Parathyroid (right) : Aplasia	-	-	-	*	# b)	-	-
Parathyroid (left) : Abnormal findings	-	-	-	-	-	-	-
Aorta : Abnormal findings	-	-	-	-	-	-	-
Pancreas : Abnormal findings	-	-	-	-	-	-	-
Adrenal (right) : Abnormal findings	-	-	-	-	-	-	-
Adrenal (left) : Abnormal findings	-	-	-	-	-	-	-

(continued)

INDIVIDUAL DATA 10-1-3 (continued-1)

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 20 mg/kg

Animal No.	301	302	303	304	305	306	307
Organ : Findings							
Submandibular gland (right) : Abnormal findings	-	-	-	-	-	-	-
Submandibular gland (left) : Abnormal findings	-	-	-	-	-	-	-
Sublingual gland (right) : Abnormal findings	-	-	-	-	-	-	-
Sublingual gland (left) : Abnormal findings	-	-	-	-	-	-	-
Parotid gland (right) : Abnormal findings	-	-	-	-	-	-	-
Parotid gland (left) : Abnormal findings	-	-	-	-	-	-	-
Submandibular lymph node (right) : Abnormal findings	-	-	-	-	-	-	-
Submandibular lymph node (left) : Abnormal findings	-	-	-	-	-	-	-
Bronchus : Abnormal findings	-	-	-	-	-	-	-
Larynx : Abnormal findings	-	-	-	-	-	-	-
Trachea : Abnormal findings	-	-	-	-	-	-	-
Tongue : Abnormal findings	-	-	-	-	-	-	-
Esophagus : Abnormal findings	-	-	-	-	-	-	-
Fore stomach : Abnormal findings	-	-	-	-	-	-	-
Glandular stomach : Abnormal findings	-	-	-	-	-	-	-
Duodenum : Abnormal findings	-	-	-	-	-	-	-
Jejunum : Abnormal findings	-	-	-	-	-	-	-
Ileum : Abnormal findings	-	-	-	-	-	-	-
Cecum : Abnormal findings	-	-	-	-	-	-	-
Colon : Abnormal findings	-	-	-	-	-	-	-
Rectum : Abnormal findings	-	-	-	-	-	-	-
Femur : Abnormal findings	-	-	-	-	-	-	-
Sternum : Abnormal findings	-	-	-	-	-	-	-
Skin of abdominal region : Abnormal findings	-	-	-	-	-	-	-

(continued)

INDIVIDUAL DATA 10-1-3 (continued-2)

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 20 mg/kg

Animal No.	301	302	303	304	305	306	307
Organ : Findings							
Mammary gland : Abnormal findings	-	-	-	-	-	-	-
Skeletal muscle : Abnormal findings	-	-	-	-	-	-	-
Urinary bladder : Abnormal findings	-	-	-	-	-	-	-
Testis (right) : Abnormal findings	-	-	-	-	-	-	-
Testis (left) : Abnormal findings	-	-	-	-	-	-	-
Epididymis (right) : Abnormal findings	-	-	-	-	-	-	-
Epididymis (left) : Abnormal findings	-	-	-	-	-	-	-
Prostate : Abnormal findings	-	-	-	-	-	-	-
Seminal vesicle (right) : Abnormal findings	-	-	-	-	-	-	-
Seminal vesicle (left) : Abnormal findings	-	-	-	-	-	-	-
Skin of cervical region : Ulcer	#	#	#	#	++	#	#
Thickening of epidermis	#	#	#	#	+	#	#
Fibrosis in dermis	#	#	#	#	+	#	#
Abscess in subcutaneous tissue	#	#	#	#	+	#	#

a): - = normal, + = slight and ++ = moderate changes, * = detected and # = not examined.
b): Because of an operation error.

INDIVIDUAL DATA 10-1-4

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

Animal No.	401	402	403	404	405	406	407
Organ : Findings	a)						
Liver : Abnormal findings	-	-	-	-	-	-	-
Kidney (right) : Abnormal findings	-	-	-	-	-	-	-
Kidney (left) : Retention cyst	-	-	-	-	-	-	+
Urinary cast	-	-	-	-	-	-	+
Focal interstitial infiltration of cells, mainly lymphocytes	-	-	-	-	-	-	+
Spleen : Abnormal findings	-	-	-	-	-	-	-
Heart : Abnormal findings	-	-	-	-	-	-	-
Lung : Calcium deposition in blood-vessel wall	-	+	-	-	-	-	-
Cerebrum : Abnormal findings	-	-	-	-	-	-	-
Cerebellum : Abnormal findings	-	-	-	-	-	-	-
Sciatic nerve : Abnormal findings	-	-	-	-	-	-	-
Spinal cord : Abnormal findings	-	-	-	-	-	-	-
Eyeball (right) : Abnormal findings	-	-	-	-	-	-	-
Eyeball (left) : Abnormal findings	-	-	-	-	-	-	-
Harder's gland (right) : Abnormal findings	-	-	-	-	-	-	-
Harder's gland (left) : Abnormal findings	-	-	-	-	-	-	-
Pituitary gland : Ciliated epithelial cyst	-	-	-	+	-	-	-
Thymus : Abnormal findings	-	-	-	-	-	-	-
Mesenteric lymph node : Abnormal findings	-	-	-	-	-	-	-
Thyroid (right) : Abnormal findings	-	-	-	-	-	-	-
Thyroid (left) : Abnormal findings	-	-	-	-	-	-	-
Parathyroid (right) : Abnormal findings	-	-	-	# b)	-	-	-
Parathyroid (left) : Abnormal findings	-	-	-	-	-	-	-
Aorta : Abnormal findings	-	-	-	-	-	-	-
Pancreas : Abnormal findings	-	-	-	-	-	-	-
Adrenal (right) : Deposition of cholesterin-like substance mainly in inner layer of zona fasciculata	-	-	-	-	-	-	+
Single cell necrosis of cortical cells mainly in inner layer of zona fasciculata	-	-	-	-	-	-	+

(continued)

INDIVIDUAL DATA 10-1-4 (continued-1)

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

Animal No.	401	402	403	404	405	406	407
Organ : Findings							
Adrenal (left) : Deposition of cholesterin-like substance mainly in inner layer of zona fasciculata	-	-	-	-	-	-	+
Single cell necrosis of cortical cells mainly in inner layer of zona fasciculata	-	-	-	-	-	-	+
Submandibular gland (right) : Abnormal findings	-	-	-	-	-	-	-
Submandibular gland (left) : Abnormal findings	-	-	-	-	-	-	-
Sublingual gland (right) : Abnormal findings	-	-	-	-	-	-	-
Sublingual gland (left) : Abnormal findings	-	-	-	-	-	-	-
Parotid gland (right) : Abnormal findings	-	-	-	-	-	-	-
Parotid gland (left) : Abnormal findings	-	-	-	-	-	-	-
Submandibular lymph node (right) : Abnormal findings	-	-	-	-	-	-	-
Submandibular lymph node (left) : Abnormal findings	-	-	-	-	-	-	-
Bronchus : Abnormal findings	-	-	-	-	-	-	-
Larynx : Abnormal findings	-	-	-	-	-	-	-
Trachea : Abnormal findings	-	-	-	-	-	-	-
Tongue : Abnormal findings	-	-	-	-	-	-	-
Esophagus : Abnormal findings	-	-	-	-	-	-	-
Fore stomach : Abnormal findings	-	-	-	-	-	-	-
Glandular stomach : Abnormal findings	-	-	-	-	-	-	-
Duodenum : Abnormal findings	-	-	-	-	-	-	-
Jejunum : Abnormal findings	-	-	-	-	-	-	-
Ileum : Abnormal findings	-	-	-	-	-	-	-
Cecum : Abnormal findings	-	-	-	-	-	-	-
Colon : Abnormal findings	-	-	-	-	-	-	-
Rectum : Abnormal findings	-	-	-	-	-	-	-
Femur : Abnormal findings	-	-	-	-	-	-	-
Sternum : Abnormal findings	-	-	-	-	-	-	-
Skin of abdominal region : Abnormal findings	-	-	-	-	-	-	-
Mammary gland : Abnormal findings	-	-	-	-	-	-	-

(continued)

INDIVIDUAL DATA 10-1-4 (continued-2)

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

Animal No.	401	402	403	404	405	406	407
Organ : Findings							
Skeletal muscle : Abnormal findings	-	-	-	-	-	-	-
Urinary bladder : Infiltration of cells, mainly lymphocytes in serosa	-	-	-	-	-	-	+
Prostate : Prostatitis	-	+	-	-	-	-	+
Testis (right) : Abnormal findings	-	-	-	-	-	-	-
Testis (left) : Abnormal findings	-	-	-	-	-	-	-
Epididymis (right) : Abnormal findings	-	-	-	-	-	-	-
Epididymis (left) : Abnormal findings	-	-	-	-	-	-	-
Prostate : Abnormal findings	-	-	-	-	-	-	-
Seminal vesicle (right) : Abnormal findings	-	-	-	-	-	-	-
Seminal vesicle (left) : Abnormal findings	-	-	-	-	-	-	-
Skin of left cervical region : Ulcer	#	#	#	#	#	#	+++
Thickening of epidermis	#	#	#	#	#	#	+
Fibrosis in dermis	#	#	#	#	#	#	+
Abscess in dermis	#	#	#	#	#	#	+
Scab formation	#	#	#	#	#	#	+
Infiltration of cells, mainly lymphocytes in subcutaneous tissue	#	#	#	#	#	#	+
Subcutaneous edema	#	#	#	#	#	#	+
Skin of dorsal region : Ulcer	#	#	#	#	#	#	+
Thickening of epidermis	#	#	#	#	#	#	+
Fibrosis in dermis	#	#	#	#	#	#	+
Scab formation	#	#	#	#	#	#	+
Skin of right cervical region : Ulcer	#	#	#	#	#	#	++
Thickening of epidermis	#	#	#	#	#	#	+
Fibrosis in dermis	#	#	#	#	#	#	+
Scab formation	#	#	#	#	#	#	+

a): - = normal, + = slight, ++ = moderate and +++ = severe changes and # = not examined.
b): Because of an operation error.

INDIVIDUAL DATA 10-2-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

Animal No.	151	152	153	154	155	156	157
Organ : Findings							
	a)						
Liver : Abnormal findings	-	-	-	-	-	-	-
Kidney (right) : Abnormal findings	-	-	-	-	-	-	-
Kidney (left) : Abnormal findings	-	-	-	-	-	-	-
Spleen : Abnormal findings	-	-	-	-	-	-	-
Heart : Abnormal findings	-	-	-	-	-	-	-
Lung : Abnormal findings	-	-	-	-	-	-	-
Cerebrum : Abnormal findings	-	-	-	-	-	-	-
Cerebellum : Abnormal findings	-	-	-	-	-	-	-
Sciatic nerve : Abnormal findings	-	-	-	-	-	-	-
Spinal cord : Abnormal findings	-	-	-	-	-	-	-
Eyeball (right) : Abnormal findings	-	-	-	-	-	-	-
Eyeball (left) : Abnormal findings	-	-	-	-	-	-	-
Harder's gland (right) : Abnormal findings	-	-	-	-	-	-	-
Harder's gland (left) : Abnormal findings	-	-	-	-	-	-	-
Pituitary gland : Abnormal findings	-	-	-	-	-	-	-
Thymus : Abnormal findings	-	-	-	-	-	-	-
Mesenteric lymph node : Abnormal findings	-	-	-	-	-	-	-
Thyroid (right) : Abnormal findings	-	-	-	-	-	-	-
Thyroid (left) : Abnormal findings	-	-	-	-	-	-	-
Parathyroid (right) : Abnormal findings	-	# b)	-	-	-	-	-
Parathyroid (left) : Abnormal findings	-	-	-	-	-	-	-
Aorta : Abnormal findings	-	-	-	-	-	-	-
Pancreas : Abnormal findings	-	-	-	-	-	-	-
Adrenal (right) : Abnormal findings	-	-	-	-	-	-	-
Adrenal (left) : Abnormal findings	-	-	-	-	-	-	-

(continued)

INDIVIDUAL DATA 10-2-1 (continued-1)

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

Animal No.	151	152	153	154	155	156	157
Organ : Findings							
Submandibular gland (right) : Abnormal findings	-	-	-	-	-	-	-
Submandibular gland (left) : Abnormal findings	-	-	-	-	-	-	-
Sublingual gland (right) : Abnormal findings	-	-	-	-	-	-	-
Sublingual gland (left) : Abnormal findings	-	-	-	-	-	-	-
Parotid gland (right) : Abnormal findings	-	-	-	-	-	-	-
Parotid gland (left) : Abnormal findings	-	-	-	-	-	-	-
Submandibular lymph node (right) : Abnormal findings	-	-	-	-	-	-	-
Submandibular lymph node (left) : Abnormal findings	-	-	-	-	-	-	-
Bronchus : Abnormal findings	-	-	-	-	-	-	-
Larynx : Abnormal findings	-	-	-	-	-	-	-
Trachea : Abnormal findings	-	-	-	-	-	-	-
Tongue : Abnormal findings	-	-	-	-	-	-	-
Esophagus : Abnormal findings	-	-	-	-	-	-	-
Fore stomach : Abnormal findings	-	-	-	-	-	-	-
Glandular stomach : Abnormal findings	-	-	-	-	-	-	-
Duodenum : Abnormal findings	-	-	-	-	-	-	-
Jejunum : Abnormal findings	-	-	-	-	-	-	-
Ileum : Abnormal findings	-	-	-	-	-	-	-
Cecum : Abnormal findings	-	-	-	-	-	-	-
Colon : Abnormal findings	-	-	-	-	-	-	-
Rectum : Abnormal findings	-	-	-	-	-	-	-
Femur : Abnormal findings	-	-	-	-	-	-	-
Sternum : Abnormal findings	-	-	-	-	-	-	-
Skin of abdominal region : Abnormal findings	-	-	-	-	-	-	-
Mammary gland : Abnormal findings	-	-	-	-	-	-	-

(continued)

INDIVIDUAL DATA 10-2-1 (continued-2)

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

Animal No.	151	152	153	154	155	156	157
Organ : Findings							
Skeletal muscle : Abnormal findings	-	-	-	-	-	-	-
Urinary bladder : Abnormal findings	-	-	-	-	-	-	-
Ovary (right) : Abnormal findings	-	-	-	-	-	-	-
Ovary (left) : Abnormal findings	-	-	-	-	-	-	-
Uterus : Abnormal findings	-	-	-	-	-	-	-
Vagina : Abnormal findings	-	-	-	-	-	-	-

a): - = normal and # = not examined.
b): Because of an operation error.

INDIVIDUAL DATA 10-2-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 4 mg/kg

Animal No.	251	252	253	254	255	256	257
Organ : Findings							
	a)						
Liver : Abnormal findings	-	-	-	-	-	-	-
Kidney (right) : Abnormal findings	-	-	-	-	-	-	-
Kidney (left) : Abnormal findings	-	-	-	-	-	-	-
Spleen : Abnormal findings	-	-	-	-	-	-	-
Heart : Abnormal findings	-	-	-	-	-	-	-
Lung : Abnormal findings	-	-	-	-	-	-	-
Cerebrum : Abnormal findings	-	-	-	-	-	-	-
Cerebellum : Abnormal findings	-	-	-	-	-	-	-
Sciatic nerve : Abnormal findings	-	-	-	-	-	-	-
Spinal cord : Abnormal findings	-	-	-	-	-	-	-
Eyeball (right) : Abnormal findings	-	-	-	-	-	-	-
Eyeball (left) : Abnormal findings	-	-	-	-	-	-	-
Harder's gland (right) : Abnormal findings	-	-	-	-	-	-	-
Harder's gland (left) : Abnormal findings	-	-	-	-	-	-	-
Pituitary gland : Ciliated epithelial cyst	-	+	-	-	-	-	-
Thymus : Abnormal findings	-	-	-	-	-	-	-
Mesenteric lymph node : Abnormal findings	-	-	-	-	-	-	-
Thyroid (right) : Abnormal findings	-	-	-	-	-	-	-
Thyroid (left) : Abnormal findings	-	-	-	-	-	-	-
Parathyroid (right) : Abnormal findings	-	-	-	-	# b)	-	-
Parathyroid (left) : Abnormal findings	-	-	-	-	-	-	-
Aorta : Abnormal findings	-	-	-	-	-	-	-
Pancreas : Abnormal findings	-	-	-	-	-	-	-
Adrenal (right) : Abnormal findings	-	-	-	-	-	-	-
Adrenal (left) : Abnormal findings	-	-	-	-	-	-	-

(continued)

INDIVIDUAL DATA 10-2-2 (continued-1)

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 4 mg/kg

Animal No.	251	252	253	254	255	256	257
Organ : Findings							
Submandibular gland (right) : Abnormal findings	-	-	-	-	-	-	-
Submandibular gland (left) : Abnormal findings	-	-	-	-	-	-	-
Sublingual gland (right) : Abnormal findings	-	-	-	-	-	-	-
Sublingual gland (left) : Abnormal findings	-	-	-	-	-	-	-
Parotid gland (right) : Abnormal findings	-	-	-	-	-	-	-
Parotid gland (left) : Abnormal findings	-	-	-	-	-	-	-
Submandibular lymph node (right) : Abnormal findings	-	-	-	-	-	-	-
Submandibular lymph node (left) : Abnormal findings	-	-	-	-	-	-	-
Bronchus : Abnormal findings	-	-	-	-	-	-	-
Larynx : Abnormal findings	-	-	-	-	-	-	-
Trachea : Abnormal findings	-	-	-	-	-	-	-
Tongue : Abnormal findings	-	-	-	-	-	-	-
Esophagus : Abnormal findings	-	-	-	-	-	-	-
Fore stomach : Abnormal findings	-	-	-	-	-	-	-
Glandular stomach : Abnormal findings	-	-	-	-	-	-	-
Duodenum : Abnormal findings	-	-	-	-	-	-	-
Jejunum : Abnormal findings	-	-	-	-	-	-	-
Ileum : Abnormal findings	-	-	-	-	-	-	-
Cecum : Abnormal findings	-	-	-	-	-	-	-
Colon : Abnormal findings	-	-	-	-	-	-	-
Rectum : Abnormal findings	-	-	-	-	-	-	-
Femur : Abnormal findings	-	-	-	-	-	-	-
Sternum : Abnormal findings	-	-	-	-	-	-	-
Skin of abdominal region : Abnormal findings	-	-	-	-	-	-	-
Mammary gland : Abnormal findings	-	-	-	-	-	-	-

(continued)

INDIVIDUAL DATA 10-2-2 (continued-2)

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 4 mg/kg

Animal No.	251	252	253	254	255	256	257
Organ : Findings							
Skeletal muscle : Abnormal findings	-	-	-	-	-	-	-
Urinary bladder : Abnormal findings	-	-	-	-	-	-	-
Ovary (right) : Abnormal findings	-	-	-	-	-	-	-
Ovary (left) : Abnormal findings	-	-	-	-	-	-	-
Uterus : Abnormal findings	-	-	-	-	-	-	-
Vagina : Abnormal findings	-	-	-	-	-	-	-

a): - = normal, + = slight change and # = not examined.
b): Because of an operation error.

INDIVIDUAL DATA 10-2-3

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 20 mg/kg

Animal No.	351	352	353	354	355	356	357
Organ : Findings							
	a)						
Liver : Abnormal findings	-	-	-	-	-	-	-
Kidney (right) : Abnormal findings	-	-	-	-	-	-	-
Kidney (left) : Abnormal findings	-	-	-	-	-	-	-
Spleen : Abnormal findings	-	-	-	-	-	-	-
Heart : Abnormal findings	-	-	-	-	-	-	-
Lung : Calcium deposition in blood-vessel wall	-	-	+	-	-	-	-
Cerebrum : Abnormal findings	-	-	-	-	-	-	-
Cerebellum : Abnormal findings	-	-	-	-	-	-	-
Sciatic nerve : Abnormal findings	-	-	-	-	-	-	-
Spinal cord : Abnormal findings	-	-	-	-	-	-	-
Eyeball (right) : Abnormal findings	-	-	-	-	-	-	-
Eyeball (left) : Abnormal findings	-	-	-	-	-	-	-
Harder's gland (right) : Abnormal findings	-	-	-	-	-	-	-
Harder's gland (left) : Abnormal findings	-	-	-	-	-	-	-
Pituitary gland : Ciliated epithelial cyst	-	+	-	-	-	-	-
Thymus : Abnormal findings	-	-	-	-	-	-	-
Mesenteric lymph node : Abnormal findings	-	-	-	-	-	-	-
Thyroid (right) : Abnormal findings	-	-	-	-	-	-	-
Thyroid (left) : Abnormal findings	-	-	-	-	-	-	-
Parathyroid (right) : Abnormal findings	-	-	# b)	-	-	-	# b)
Parathyroid (left) : Abnormal findings	-	-	-	-	-	# b)	-
Aorta : Abnormal findings	-	-	-	-	-	-	-
Pancreas : Abnormal findings	-	-	-	-	-	-	-
Adrenal (right) : Abnormal findings	-	-	-	-	-	-	-
Adrenal (left) : Abnormal findings	-	-	-	-	-	-	-

(continued)

INDIVIDUAL DATA 10-2-3 (continued-1)

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 20 mg/kg

Animal No.	351	352	353	354	355	356	357
Organ : Findings							
Submandibular gland (right) : Abnormal findings	-	-	-	-	-	-	-
Submandibular gland (left) : Abnormal findings	-	-	-	-	-	-	-
Sublingual gland (right) : Abnormal findings	-	-	-	-	-	-	-
Sublingual gland (left) : Abnormal findings	-	-	-	-	-	-	-
Parotid gland (right) : Abnormal findings	-	-	-	-	-	-	-
Parotid gland (left) : Abnormal findings	-	-	-	-	-	-	-
Submandibular lymph node (right) : Abnormal findings	-	-	-	-	-	-	-
Submandibular lymph node (left) : Abnormal findings	-	-	-	-	-	-	-
Bronchus : Abnormal findings	-	-	-	-	-	-	-
Larynx : Abnormal findings	-	-	-	-	-	-	-
Trachea : Abnormal findings	-	-	-	-	-	-	-
Tongue : Abnormal findings	-	-	-	-	-	-	-
Esophagus : Abnormal findings	-	-	-	-	-	-	-
Fore stomach : Abnormal findings	-	-	-	-	-	-	-
Glandular stomach : Abnormal findings	-	-	-	-	-	-	-
Duodenum : Abnormal findings	-	-	-	-	-	-	-
Jejunum : Abnormal findings	-	-	-	-	-	-	-
Ileum : Abnormal findings	-	-	-	-	-	-	-
Cecum : Abnormal findings	-	-	-	-	-	-	-
Colon : Abnormal findings	-	-	-	-	-	-	-
Rectum : Abnormal findings	-	-	-	-	-	-	-
Femur : Abnormal findings	-	-	-	-	-	-	-
Sternum : Abnormal findings	-	-	-	-	-	-	-
Skin of abdominal region : Abnormal findings	-	-	-	-	-	-	-
Mammary gland : Abnormal findings	-	-	-	-	-	-	-

(continued)

INDIVIDUAL DATA 10-2-3 (continued-2)

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 20 mg/kg

Animal No.	351	352	353	354	355	356	357
Organ : Findings							
Skeletal muscle : Abnormal findings	-	-	-	-	-	-	-
Urinary bladder : Abnormal findings	-	-	-	-	-	-	-
Ovary (right) : Abnormal findings	-	-	-	-	-	-	-
Ovary (left) : Follicular cyst	-	-	-	-	-	+	-
Uterus : Abnormal findings	-	-	-	-	-	-	-
Vagina : Abnormal findings	-	-	-	-	-	-	-

a): - = normal, + = slight change and # = not examined.
b): Because of an operation error.

INDIVIDUAL DATA 10-2-4

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal No.	451	452	453	454	455	456	457
Organ : Findings							
	a)						
Liver : Abnormal findings	-	-	-	-	-	-	-
Kidney (right) : Abnormal findings	-	-	-	-	-	-	-
Kidney (left) : Abnormal findings	-	-	-	-	-	-	-
Spleen : Abnormal findings	-	-	-	-	-	-	-
Heart : Abnormal findings	-	-	-	-	-	-	-
Lung : Abnormal findings	-	-	-	-	-	-	-
Cerebrum : Abnormal findings	-	-	-	-	-	-	-
Cerebellum : Abnormal findings	-	-	-	-	-	-	-
Sciatic nerve : Abnormal findings	-	-	-	-	-	-	-
Spinal cord : Abnormal findings	-	-	-	-	-	-	-
Eyeball (right) : Abnormal findings	-	-	-	-	-	-	-
Eyeball (left) : Abnormal findings	-	-	-	-	-	-	-
Harder's gland (right) : Abnormal findings	-	-	-	-	-	-	-
Harder's gland (left) : Abnormal findings	-	-	-	-	-	-	-
Pituitary gland : Ciliated epithelial cyst	-	+	-	-	-	-	-
Thymus : Abnormal findings	-	-	-	-	-	-	-
Mesenteric lymph node : Abnormal findings	-	-	-	-	-	-	-
Thyroid (right) : Persistent embryonic thyroid	-	-	-	-	-	-	+
Thyroid (left) : Abnormal findings	-	-	-	-	-	-	-
Parathyroid (right) : Abnormal findings	-	-	-	-	-	-	-
Parathyroid (left) : Abnormal findings	-	-	-	-	-	-	-
Aorta : Abnormal findings	-	-	-	-	-	-	-
Pancreas : Abnormal findings	-	-	-	-	-	-	-
Adrenal (right) : Abnormal findings	-	-	-	-	-	-	-
Adrenal (left) : Abnormal findings	-	-	-	-	-	-	-

(continued)

INDIVIDUAL DATA 10-2-4 (continued-1)

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal No.	451	452	453	454	455	456	457
Organ : Findings							
Submandibular gland (right) : Abnormal findings	-	-	-	-	-	-	-
Submandibular gland (left) : Abnormal findings	-	-	-	-	-	-	-
Sublingual gland (right) : Abnormal findings	-	-	-	-	-	-	-
Sublingual gland (left) : Abnormal findings	-	-	-	-	-	-	-
Parotid gland(right) : Abnormal findings	-	-	-	-	-	-	-
Parotid gland (left) : Abnormal findings	-	-	-	-	-	-	-
Submandibular lymph node (right) : Abnormal findings	-	-	-	-	-	-	-
Submandibular lymph node (left) : Abnormal findings	-	-	-	-	-	-	-
Bronchus : Abnormal findings	-	-	-	-	-	-	-
Larynx : Abnormal findings	-	-	-	-	-	-	-
Trachea : Abnormal findings	-	-	-	-	-	-	-
Tongue : Abnormal findings	-	-	-	-	-	-	-
Esophagus : Abnormal findings	-	-	-	-	-	-	-
Fore stomach : Abnormal findings	-	-	-	-	-	-	-
Glandular stomach : Abnormal findings	-	-	-	-	-	-	-
Duodenum : Abnormal findings	-	-	-	-	-	-	-
Jejunum : Abnormal findings	-	-	-	-	-	-	-
Ileum : Abnormal findings	-	-	-	-	-	-	-
Cecum : Abnormal findings	-	-	-	-	-	-	-
Colon : Abnormal findings	-	-	-	-	-	-	-
Rectum : Abnormal findings	-	-	-	-	-	-	-
Femur : Abnormal findings	-	-	-	-	-	-	-
Sternum : Abnormal findings	-	-	-	-	-	-	-
Skin of abdominal region : Abnormal findings	-	-	-	-	-	-	-
Mammary gland : Abnormal findings	-	-	-	-	-	-	-

(continued)

INDIVIDUAL DATA 10-2-4 (continued-2)

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of adm.
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal No.	451	452	453	454	455	456	457
Organ : Findings							
Skeletal muscle : Abnormal findings	-	-	-	-	-	-	-
Urinary bladder : Abnormal findings	-	-	-	-	-	-	-
Ovary (right) : Abnormal findings	-	-	-	-	-	-	-
Ovary (left) : Abnormal findings	-	-	-	-	-	-	-
Uterus : Abnormal findings	-	-	-	-	-	-	-
Vagina : Abnormal findings	-	-	-	-	-	-	-

a): - = normal and + = slight change.

INDIVIDUAL DATA 10-3-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal No.	108	109	110	111	112	113	114
Organ : Findings							
	a)						
Liver : Abnormal findings	-	-	-	-	-	-	-
Kidney (right) : Abnormal findings	-	-	-	-	-	-	-
Kidney (left) : Abnormal findings	-	-	-	-	-	-	-
Spleen : Abnormal findings	-	-	-	-	-	-	-
Heart : Abnormal findings	-	-	-	-	-	-	-
Lung : Abnormal findings	-	-	-	-	-	-	-
Cerebrum : Abnormal findings	-	-	-	-	-	-	-
Cerebellum : Abnormal findings	-	-	-	-	-	-	-
Sciatic nerve : Abnormal findings	-	-	-	-	-	-	-
Spinal cord : Abnormal findings	-	-	-	-	-	-	-
Eyeball (right) : Abnormal findings	-	-	-	-	-	-	-
Eyeball (left) : Abnormal findings	-	-	-	-	-	-	-
Harder's gland (right) : Abnormal findings	-	-	-	-	-	-	-
Harder's gland (left) : Abnormal findings	-	-	-	-	-	-	-
Pituitary gland : Abnormal findings	-	-	-	-	-	-	-
Thymus : Abnormal findings	-	-	-	-	-	-	-
Mesenteric lymph node : Abnormal findings	-	-	-	-	-	-	-
Thyroid (right) : Abnormal findings	-	-	-	-	-	-	-
Thyroid (left) : Abnormal findings	-	-	-	-	-	-	-
Parathyroid (right) : Abnormal findings	-	-	-	-	-	-	-
Parathyroid (left) : Abnormal findings	-	-	-	# b)	-	-	-
Aorta : Abnormal findings	-	-	-	-	-	-	-
Pancreas : Abnormal findings	-	-	-	-	-	-	-
Adrenal (right) : Abnormal findings	-	-	-	-	-	-	-
Adrenal (left) : Abnormal findings	-	-	-	-	-	-	-

(continued)

INDIVIDUAL DATA 10-3-1 (continued-1)

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal No.	108	109	110	111	112	113	114
Organ : Findings							
Submandibular gland (right) : Abnormal findings	-	-	-	-	-	-	-
Submandibular gland (left) : Abnormal findings	-	-	-	-	-	-	-
Sublingual gland (right) : Abnormal findings	-	-	-	-	-	-	-
Sublingual gland (left) : Abnormal findings	-	-	-	-	-	-	-
Parotid gland (right) : Abnormal findings	-	-	-	-	-	-	-
Parotid gland (left) : Abnormal findings	-	-	-	-	-	-	-
Submandibular lymph node (right) : Abnormal findings	-	-	-	-	-	-	-
Submandibular lymph node (left) : Abnormal findings	-	-	-	-	-	-	-
Bronchus : Abnormal findings	-	-	-	-	-	-	-
Larynx : Abnormal findings	-	-	-	-	-	-	-
Trachea : Abnormal findings	-	-	-	-	-	-	-
Tongue : Abnormal findings	-	-	-	-	-	-	-
Esophagus : Abnormal findings	-	-	-	-	-	-	-
Fore stomach : Abnormal findings	-	-	-	-	-	-	-
Glandular stomach : Abnormal findings	-	-	-	-	-	-	-
Duodenum : Abnormal findings	-	-	-	-	-	-	-
Jejunum : Abnormal findings	-	-	-	-	-	-	-
Ileum : Abnormal findings	-	-	-	-	-	-	-
Cecum : Abnormal findings	-	-	-	-	-	-	-
Colon : Abnormal findings	-	-	-	-	-	-	-
Rectum : Abnormal findings	-	-	-	-	-	-	-
Femur : Abnormal findings	-	-	-	-	-	-	-
Sternum : Abnormal findings	-	-	-	-	-	-	-
Skin of abdominal region : Abnormal findings	-	-	-	-	-	-	-
Mammary gland : Abnormal findings	-	-	-	-	-	-	-

(continued)

INDIVIDUAL DATA 10-3-1 (continued-2)

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Control

Animal No.	108	109	110	111	112	113	114
Organ : Findings							
Skeletal muscle : Abnormal findings	-	-	-	-	-	-	-
Urinary bladder : Abnormal findings	-	-	-	-	-	-	-
Testis (right) : Abnormal findings	-	-	-	-	-	-	-
Testis (left) : Abnormal findings	-	-	-	-	-	-	-
Epididymis (right) : Abnormal findings	-	-	-	-	-	-	-
Epididymis (left) : Abnormal findings	-	-	-	-	-	-	-
Prostate : Prostatitis	+	-	-	+	-	-	+
Seminal vesicle (right) : Abnormal findings	-	-	-	-	-	-	-
Seminal vesicle (left) : Abnormal findings	-	-	-	-	-	-	-
Skin of right cervical region : Ulcer	#	#	#	#	#	+	#
Thickening of epidermis	#	#	#	#	#	+	#
Fibrosis in dermis	#	#	#	#	#	+	#
Abscess in dermis	#	#	#	#	#	+	#
Scab formation	#	#	#	#	#	+	#

a): - = normal, + = slight change and # = not examined.
b): Because of an operation error.

INDIVIDUAL DATA 10-3-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

Animal No.	408	409	410	411	412	413	414
Organ : Findings							
	a)						
Liver : Abnormal findings	-	-	-	-	-	-	-
Kidney (right) : Hyaline droplet deposition in tubular epithelium	-	-	-	+	-	+	-
Eosinophilic body deposition in tubular epithelium	-	-	-	+	-	+	-
Kidney (left) : Hyaline droplet deposition in tubular epithelium	-	-	-	+	-	+	-
Eosinophilic body deposition in tubular epithelium	-	-	-	+	-	+	-
Spleen : Abnormal findings	-	-	-	-	-	-	-
Heart : Abnormal findings	-	-	-	-	-	-	-
Lung : Calcium deposition in blood-vessel wall	-	-	-	-	-	-	+
Cerebrum : Abnormal findings	-	-	-	-	-	-	-
Cerebellum : Abnormal findings	-	-	-	-	-	-	-
Sciatic nerve : Abnormal findings	-	-	-	-	-	-	-
Spinal cord : Abnormal findings	-	-	-	-	-	-	-
Eyeball (right) : Abnormal findings	-	-	-	-	-	-	-
Eyeball (left) : Abnormal findings	-	-	-	-	-	-	-
Harder's gland (right) : Abnormal findings	-	-	-	-	-	-	-
Harder's gland (left) : Abnormal findings	-	-	-	-	-	-	-
Pituitary gland : Abnormal findings	-	-	-	-	-	-	-
Thymus : Abnormal findings	-	-	-	-	-	-	-
Mesenteric lymph node : Abnormal findings	-	-	-	-	-	-	-
Thyroid (right) : Abnormal findings	-	-	-	-	-	-	-
Thyroid (left) : Abnormal findings	-	-	-	-	-	-	-
Parathyroid (right) : Abnormal findings	‡ b)	-	-	-	-	-	-
Parathyroid (left) : Abnormal findings	-	-	-	‡ b)	-	-	-
Aorta : Abnormal findings	-	-	-	-	-	-	-
Pancreas : Abnormal findings	-	-	-	-	-	-	-

(continued)

INDIVIDUAL DATA 10-3-2 (continued-1)

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

Animal No.	408	409	410	411	412	413	414
Organ : Findings							
Adrenal (right) : Single cell necrosis of cortical cells mainly in inner layer of zona fasciculata	-	-	-	-	-	-	+
Adrenal (left) : Single cell necrosis of cortical cells mainly in inner layer of zona fasciculata	-	-	-	-	-	-	+
Submandibular gland (right) : Abnormal findings	-	-	-	-	-	-	-
Submandibular gland (left) : Abnormal findings	-	-	-	-	-	-	-
Sublingual gland (right) : Abnormal findings	-	-	-	-	-	-	-
Sublingual gland (left) : Abnormal findings	-	-	-	-	-	-	-
Parotid gland (right) : Abnormal findings	-	-	-	-	-	-	-
Parotid gland (left) : Abnormal findings	-	-	-	-	-	-	-
Submandibular lymph node (right) : Abnormal findings	-	-	-	-	-	-	-
Submandibular lymph node (left) : Abnormal findings	-	-	-	-	-	-	-
Bronchus : Abnormal findings	-	-	-	-	-	-	-
Larynx : Abnormal findings	-	-	-	-	-	-	-
Trachea : Abnormal findings	-	-	-	-	-	-	-
Tongue : Abnormal findings	-	-	-	-	-	-	-
Esophagus : Abnormal findings	-	-	-	-	-	-	-
Fore stomach : Abnormal findings	-	-	-	-	-	-	-
Glandular stomach : Abnormal findings	-	-	-	-	-	-	-
Duodenum : Abnormal findings	-	-	-	-	-	-	-
Jejunum : Abnormal findings	-	-	-	-	-	-	-
Ileum : Abnormal findings	-	-	-	-	-	-	-
Cecum : Abnormal findings	-	-	-	-	-	-	-
Colon : Abnormal findings	-	-	-	-	-	-	-
Rectum : Abnormal findings	-	-	-	-	-	-	-
Femur : Abnormal findings	-	-	-	-	-	-	-
Sternum : Abnormal findings	-	-	-	-	-	-	-

(continued)

INDIVIDUAL DATA 10-3-2 (continued-2)

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Male GROUP : Substance No.3-0146 100 mg/kg

Animal No.	408	409	410	411	412	413	414
Organ : Findings							
Skin of abdominal region : Abnormal findings	-	-	-	-	-	-	-
Mammary gland : Abnormal findings	-	-	-	-	-	-	-
Skeletal muscle : Abnormal findings	-	-	-	-	-	-	-
Urinary bladder : Abnormal findings	-	-	-	-	-	-	-
Testis (right) : Abnormal findings	-	-	-	-	-	-	-
Testis (left) : Abnormal findings	-	-	-	-	-	-	-
Epididymis (right) : Abnormal findings	-	-	-	-	-	-	-
Epididymis (left) : Abnormal findings	-	-	-	-	-	-	-
Prostate : Prostatitis	-	-	-	-	-	-	+
Seminal vesicle (right) : Abnormal findings	-	-	-	-	-	-	-
Seminal vesicle (left) : Abnormal findings	-	-	-	-	-	-	-
Skin of right dorsal region : Thickening of epidermis	#	#	#	#	#	#	++
Fibrosis in dermis	#	#	#	#	#	#	+
Scab formation	#	#	#	#	#	#	+
Edema in superficial zone of dermis	#	#	#	#	#	#	+
Epidermal edema	#	#	#	#	#	#	+

a): - = normal, + = slight and ++ = moderate changes and # = not examined.
b): Because of an operation error.

INDIVIDUAL DATA 10-4-1

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

Animal No.	151	152	153	154	155	156	157
Organ : Findings							
	a)						
Liver : Abnormal findings	-	-	-	-	-	-	-
Kidney (right) : Abnormal findings	-	-	-	-	-	-	-
Kidney (left) : Abnormal findings	-	-	-	-	-	-	-
Spleen : Abnormal findings	-	-	-	-	-	-	-
Heart : Abnormal findings	-	-	-	-	-	-	-
Lung : Abnormal findings	-	-	-	-	-	-	-
Cerebrum : Abnormal findings	-	-	-	-	-	-	-
Cerebellum : Abnormal findings	-	-	-	-	-	-	-
Sciatic nerve : Abnormal findings	-	-	-	-	-	-	-
Spinal cord : Abnormal findings	-	-	-	-	-	-	-
Eyeball (right) : Abnormal findings	-	-	-	-	-	-	-
Eyeball (left) : Abnormal findings	-	-	-	-	-	-	-
Harder's gland (right) : Abnormal findings	-	-	-	-	-	-	-
Harder's gland (left) : Abnormal findings	-	-	-	-	-	-	-
Pituitary gland : Abnormal findings	-	-	-	-	-	-	-
Thymus : Abnormal findings	-	-	-	-	-	-	-
Mesenteric lymph node : Abnormal findings	-	-	-	-	-	-	-
Thyroid (right) : Abnormal findings	-	-	-	-	-	-	-
Thyroid (left) : Abnormal findings	-	-	-	-	-	-	-
Parathyroid (right) : Abnormal findings	-	-	-	-	-	-	-
Parathyroid (left) : Abnormal findings	-	-	-	-	-	-	-
Aorta : Abnormal findings	-	-	-	-	-	-	-
Pancreas : Abnormal findings	-	-	-	-	-	-	-
Adrenal (right) : Abnormal findings	-	-	-	-	-	-	-
Adrenal (left) : Abnormal findings	-	-	-	-	-	-	-

(continued)

INDIVIDUAL DATA 10-4-1 (continued-1)

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

Animal No.	151	152	153	154	155	156	157
Organ : Findings							
Submandibular gland (right) : Abnormal findings	-	-	-	-	-	-	-
Submandibular gland (left) : Abnormal findings	-	-	-	-	-	-	-
Sublingual gland (right) : Abnormal findings	-	-	-	-	-	-	-
Sublingual gland (left) : Abnormal findings	-	-	-	-	-	-	-
Parotid gland (right) : Abnormal findings	-	-	-	-	-	-	-
Parotid gland (left) : Abnormal findings	-	-	-	-	-	-	-
Submandibular lymph node (right) : Abnormal findings	-	-	-	-	-	-	-
Submandibular lymph node (left) : Abnormal findings	-	-	-	-	-	-	-
Bronchus : Abnormal findings	-	-	-	-	-	-	-
Larynx : Abnormal findings	-	-	-	-	-	-	-
Trachea : Abnormal findings	-	-	-	-	-	-	-
Tongue : Abnormal findings	-	-	-	-	-	-	-
Esophagus : Abnormal findings	-	-	-	-	-	-	-
Fore stomach : Abnormal findings	-	-	-	-	-	-	-
Glandular stomach : Abnormal findings	-	-	-	-	-	-	-
Duodenum : Abnormal findings	-	-	-	-	-	-	-
Jejunum : Abnormal findings	-	-	-	-	-	-	-
Ileum : Abnormal findings	-	-	-	-	-	-	-
Cecum : Abnormal findings	-	-	-	-	-	-	-
Colon : Abnormal findings	-	-	-	-	-	-	-
Rectum : Abnormal findings	-	-	-	-	-	-	-
Femur : Abnormal findings	-	-	-	-	-	-	-
Sternum : Abnormal findings	-	-	-	-	-	-	-
Skin of abdominal region : Abnormal findings	-	-	-	-	-	-	-
Mammary gland : Abnormal findings	-	-	-	-	-	-	-

(continued)

INDIVIDUAL DATA 10-4-1 (continued-2)

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Control

Animal No.	151	152	153	154	155	156	157
Organ : Findings							
Skeletal muscle : Abnormal findings	-	-	-	-	-	-	-
Urinary bladder : Abnormal findings	-	-	-	-	-	-	-
Ovary (right) : Abnormal findings	-	-	-	-	-	-	-
Ovary (left) : Abnormal findings	-	-	-	-	-	-	-
Uterus : Abnormal findings	-	-	-	-	-	-	-
Vagina : Abnormal findings	-	-	-	-	-	-	-

a): - = normal and + = slight change.

INDIVIDUAL DATA 10-4-2

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal No.	151	152	153	154	155	156	157
Organ : Findings							
	a)						
Liver : Abnormal findings	-	-	-	-	-	-	-
Kidney (right) : Abnormal findings	-	-	-	-	-	-	-
Kidney (left) : Abnormal findings	-	-	-	-	-	-	-
Spleen : Abnormal findings	-	-	-	-	-	-	-
Heart : Abnormal findings	-	-	-	-	-	-	-
Lung : Abnormal findings	-	-	-	-	-	-	-
Cerebrum : Abnormal findings	-	-	-	-	-	-	-
Cerebellum : Abnormal findings	-	-	-	-	-	-	-
Sciatic nerve : Abnormal findings	-	-	-	-	-	-	-
Spinal cord : Abnormal findings	-	-	-	-	-	-	-
Eyeball (right) : Abnormal findings	-	-	-	-	-	-	-
Eyeball (left) : Abnormal findings	-	-	-	-	-	-	-
Harder's gland (right) : Abnormal findings	-	-	-	-	-	-	-
Harder's gland (left) : Abnormal findings	-	-	-	-	-	-	-
Pituitary gland : Abnormal findings	-	-	-	-	-	-	-
Thymus : Abnormal findings	-	-	-	-	-	-	-
Mesenteric lymph node : Abnormal findings	-	-	-	-	-	-	-
Thyroid (right) : Abnormal findings	-	-	-	-	-	-	-
Thyroid (left) : Abnormal findings	-	-	-	-	-	-	-
Parathyroid (right) : Abnormal findings	-	-	-	-	-	-	-
Parathyroid (left) : Abnormal findings	-	-	-	-	-	-	-
Aorta : Abnormal findings	-	-	-	-	-	-	-
Pancreas : Abnormal findings	-	-	-	-	-	-	-
Adrenal (right) : Abnormal findings	-	-	-	-	-	-	-
Adrenal (left) : Abnormal findings	-	-	-	-	-	-	-

(continued)

INDIVIDUAL DATA 10-4-2 (continued-1)

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal No.	151	152	153	154	155	156	157
Organ : Findings							
Submandibular gland (right) : Abnormal findings	-	-	-	-	-	-	-
Submandibular gland (left) : Abnormal findings	-	-	-	-	-	-	-
Sublingual gland (right) : Abnormal findings	-	-	-	-	-	-	-
Sublingual gland (left) : Abnormal findings	-	-	-	-	-	-	-
Parotid gland (right) : Abnormal findings	-	-	-	-	-	-	-
Parotid gland (left) : Abnormal findings	-	-	-	-	-	-	-
Submandibular lymph node (right) : Abnormal findings	-	-	-	-	-	-	-
Submandibular lymph node (left) : Abnormal findings	-	-	-	-	-	-	-
Bronchus : Abnormal findings	-	-	-	-	-	-	-
Larynx : Abnormal findings	-	-	-	-	-	-	-
Trachea : Abnormal findings	-	-	-	-	-	-	-
Tongue : Abnormal findings	-	-	-	-	-	-	-
Esophagus : Abnormal findings	-	-	-	-	-	-	-
Fore stomach : Abnormal findings	-	-	-	-	-	-	-
Glandular stomach : Abnormal findings	-	-	-	-	-	-	-
Duodenum : Abnormal findings	-	-	-	-	-	-	-
Jejunum : Abnormal findings	-	-	-	-	-	-	-
Ileum : Abnormal findings	-	-	-	-	-	-	-
Cecum : Abnormal findings	-	-	-	-	-	-	-
Colon : Abnormal findings	-	-	-	-	-	-	-
Rectum : Abnormal findings	-	-	-	-	-	-	-
Femur : Abnormal findings	-	-	-	-	-	-	-
Sternum : Abnormal findings	-	-	-	-	-	-	-
Skin of abdominal region : Abnormal findings	-	-	-	-	-	-	-
Mammary gland : Abnormal findings	-	-	-	-	-	-	-

(continued)

INDIVIDUAL DATA 10-4-2 (continued-2)

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.) PERIOD : End of recovery
Histopathological findings ANIMAL : Rat,Crj:CD(SD) SEX : Female GROUP : Substance No.3-0146 100 mg/kg

Animal No.	151	152	153	154	155	156	157
Organ : Findings							
Skeletal muscle : Abnormal findings	-	-	-	-	-	-	-
Urinary bladder : Abnormal findings	-	-	-	-	-	-	-
Ovary (right) : Abnormal findings	-	-	-	-	-	-	-
Ovary (left) : Lutein cyst	+	-	-	-	-	-	-
Uterus : Abnormal findings	-	-	-	-	-	-	-
Vagina : Abnormal findings	-	-	-	-	-	-	-

a): - = normal and + = slight change.

Appendix

Appendix 1-1 ～ 1-2　一般状態観察、剖検及び病理組織学的検査結果（出現頻度）の統計処理
－ Fisher の正確確率検定法

Appendix 2-1 ～ 2-3　尿検査及び血液学的検査の背景データ

Appendix 1-1

一般状態観察結果（出現頻度）の統計処理 ― Fisher の正確確率検定法

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
ANIMAL : Rat,Crj:CD(SD) SEX : GROUP : Control

Animal No.	P	Q	R	S	T	U	V
1	+	+	+	-	-	+	-
2	+	+	+	-	-	-	-
3	-	-	-	-	-	-	-
4	-	-	-	-	-	-	-
5	-	-	-	-	-	-	-
6	-	-	-	-	-	-	-
7	-	-	-	-	-	-	-
8	-	-	-	-	-	#	#
9	-	-	-	-	-	#	#
10	-	-	-	-	-	#	#
11	-	-	-	-	-	#	#
12	-	-	-	-	-	#	#
13	-	-	-	-	-	#	#
14	-	-	-	-	-	#	#
N	14	14	14	14	14	7	7
TOTAL	2	2	2	0	0	1	0
%	14.3	14.3	14.3	0.0	0.0	14.3	0.0
X^2							

#: Blank value.

Appendix 1-2

剖検及び病理組織学的検査結果（出現頻度）の統計処理 － Fisher の正確確率検定法

STUDY NO. SR-9127 TITLE : Substance No.3-0146 Repeated dose toxicity 28d (p.o.)
ANIMAL : Rat,Crj:CD(SD) SEX : GROUP : Control

Animal No.	A	B	C	D	E	F	G	H
1	-	-	+	+	+	+	-	+
2	-	-	-	-	+	+	-	+
3	-	-	-	-	-	-	-	+
4	-	-	-	-	-	-	-	-
5	-	-	-	-	-	-	-	-
6	-	-	-	-	-	-	-	-
7	-	-	-	-	-	-	-	-
N	7	7	7	7	7	7	7	7
TOTAL	0	0	1	1	2	2	0	3
%	0.0	0.0	14.3	14.3	28.6	28.6	0.0	42.9
X^2								

Appendix 2-1

STUDY No. SR-9127

尿検査の背景データ，Rat, Crj:CD(SD)系（Male）　　1988年10月～　1989年12月

週齢	投　与	U-Vol	U-Grav	U-Na	U-K	U-Cl	U-Ca	U-IP	U-NAG	U-GGT
8823 7 w	生食 5 ml	11.67 4.24	1.0442 0.0141	1.35 0.58	2.69 0.76	1.83 0.74	1.64 0.93		178.45 50.45	430.3 233.1
8823 7 w	生食 5 ml	10.97 1.72	1.0493 0.0049	2.10 0.41	3.09 0.51	2.69 0.53	2.64 0.87		161.73 35.42	710.8 649.9
8823 7 w	生食 5 ml	12.43 1.38	1.0423 0.0026	1.59 0.36	3.07 0.33	2.19 0.31	2.63 1.09		169.22 30.75	175.2 119.2
8823 7 w	生食 5 ml	11.52 2.98	1.0478 0.0059	1.96 0.19	3.39 0.15	2.38 0.22	1.86 1.18		134.82 37.36	170.0 85.5
8823 7 w	生食 5 ml	12.20 2.20	1.0500 0.0032	1.93 0.23	3.95 0.42	2.70 0.36	2.82 0.97		168.48 37.81	203.3 148.4
8882 7 w	1% MC 1 ml	14.33 2.08	1.0403 0.0032	1.67 0.21	3.10 0.17	2.16 0.02				
8823 8 w	生食 5 ml	14.62 2.69	1.0453 0.0070	2.36 0.25	3.65 0.51	2.88 0.42	2.28 0.86		262.28 48.64	473.5 462.0
8823 10 w	生食 5 ml	17.58 5.30	1.0433 0.0069	2.33 0.48	3.80 0.39	2.93 0.41	1.77 0.91		342.53 109.57	761.5 643.8
8926 10 w	H_2O 10 ml	16.88 3.32	1.0316 0.0065	0.63 0.40	1.20 0.34	0.42 0.30				
8803 10 w	H_2O 2 ml	16.96 5.46	1.0387 0.0098	0.54 0.24	1.88 0.63	1.23 0.54				
8830 17 w	H_2O 10 ml	16.13 3.32	1.0402 0.0080	1.12 0.70	2.65 0.94	1.23 0.95				
8910 17 w	5% ｺﾞﾑ 5 ml	17.40 7.59	1.0390 0.0112	0.93 0.60	2.63 0.78	1.26 0.83	1.38 0.51	15.37 6.73		
8859 19 w	生食 10 ml	13.29 3.48	1.0398 0.0088	1.55 0.75	2.17 0.77	1.63 0.86	0.45 0.13	16.78 4.28		
8803 19 w	H_2O 2 ml	17.24 4.92	1.0392 0.0090	1.19 0.52	2.83 0.77	1.54 0.74				
8910 22 w	5%ｺﾞﾑ 5 ml	17.11 7.52	1.0372 0.0108	0.67 0.63	2.46 1.02	0.95 0.96	1.53 1.09	14.86 6.90		
8859 31 w	生食 10 ml	13.24 3.64	1.0430 0.0091	1.54 0.64	2.24 0.65	1.64 0.74	1.35 0.76	15.15 7.18		
8803 32 w	H_2O 2 ml	13.11 5.05	1.0415 0.0080	0.78 0.44	2.18 0.79	0.90 0.71				
8803 36 w	H_2O 2 ml	16.72 8.34	1.0390 0.0126	0.81 0.55	2.40 0.75	0.97 0.76				

GGT: γ-GTP

5%ｺﾞﾑ: 5%ｱﾗﾋﾞｱｺﾞﾑ溶液

1%MC: 1%ﾒﾁﾙｾﾙﾛｰｽ溶液

Appendix 2-3

STUDY No. SR-9127

1988年10月～ 1989年12月

血液学的検査の背景データ，Rat, Crj:CD(SD)系 (Female)

週齢	投 与	PT	APTT	RBC	HT	Hb	WBC	Plat	Ret	St	Seg	Eos	Mono	Lymp
8916 6 w	生食 10 ml			6.840 0.298	44.44 1.52	14.80 0.45	7.90 1.37	1264.2 108.3		0.4 0.5	9.2 3.2	1.0 0.7	0.2 0.4	89.2 3.7
8882 8 w	1% MC 1 ml			7.340 0.400	45.44 1.85	15.06 0.53	8.93 3.62	1034.4 75.0		0.71 0.64	9.00 2.35	0.36 0.38	0.0 0.0	89.93 2.75
8926 10 w	H_2O 10 ml			7.456 0.342	45.06 1.67	15.15 0.50	10.37 3.84	1146.3 102.6		0.4 0.5	9.5 3.1	0.9 0.8	0.2 0.4	89.0 3.4
8830 17 w	H_2O 10 ml	11.18 0.52	25.28 3.13	8.656 0.367	47.72 2.26	16.00 0.80	7.74 2.44	975.3 107.3	17.0 3.2	0.96 0.66	10.42 2.68	0.83 0.81	0.04 0.14	87.5 3.37
8910 18 w	5%ｺﾞﾑ 5 ml	10.56 0.30	20.45 2.09	7.866 0.379	45.14 1.95	15.24 0.59	6.65 1.95	1153.5 127.2	13.4 2.8	0.5 0.5	15.8 6.2	1.3 1.3	0.2 0.4	82.2 6.6
8890 19 w	0.5%CM 10 ml	10.46 0.24	21.43 2.71	8.157 0.509	44.90 2.54	14.87 0.70	6.33 1.83	908.8 101.0		1.2 1.0	11.9 5.2	1.0 1.1	0.1 0.3	85.8 6.0
8910 22 w	5%ｺﾞﾑ 5 ml	10.72 0.41	18.92 1.38	7.950 0.395	44.65 1.78	14.65 0.62	7.58 2.40	1174.3 97.4	16.8 1.0	0.5 0.5	13.5 4.0	1.0 0.9	0.0 0.0	85.0 4.1
8890 24 w	0.5%CM 10 ml	10.69 0.35	20.38 1.84	8.474 0.277	46.27 1.49	14.99 0.34	5.21 1.40	960.6 114.2		0.8 0.8	19.6 7.2	1.3 0.7	0.1 0.3	78.2 7.9
8859 31 w	生食 10 ml	10.62 0.32	20.07 1.92	7.670 0.346	43.50 1.44	14.65 0.60	6.78 1.72	1156.5 128.4	15.5 3.6	0.5 0.7	17.6 6.6	1.5 1.1	0.1 0.3	80.3 7.1
8803 32 w	H_2O 2 ml	11.17 0.39	18.70 1.96	7.693 0.435	42.11 2.01	14.31 0.62	5.78 2.33	948.0 131.0	20.3 4.4	1.25 0.79	15.38 5.76	1.23 0.90	0.03 0.11	82.13 6.32
8803 36 w	H_2O 2 ml	10.57 0.51	19.98 3.22	8.270 0.535	45.69 2.54	15.31 0.62	6.50 2.37	982.3 73.4	14.1 1.9	1.15 0.53	19.00 7.27	1.20 0.79	0.00 0.00	78.65 7.30
8891 57 w	0.5%CM 10 ml			8.062 0.325	46.96 1.60	14.71 0.53	6.14 1.20	1040.6 101.3		0.7 0.9	23.6 11.8	1.1 0.9	0.0 0.0	74.5 12.6

5% ｺﾞﾑ : 5% ｱﾗﾋﾞｱｱﾋﾞﾑ溶液
1% MC : 1% ﾒﾁﾙｾﾙﾛｰｽ溶液