最終報告書

表　　題：indene のラットにおける反復投与毒性･生殖発生毒性併合試験

試験番号：ＳＲ１１０８７

株式会社 化合物安全性研究所

陳 述 書

表　　題：indene のラットにおける反復投与毒性･生殖発生毒性併合試験

試験番号：ＳＲ１１０８７

１．本試験は、「新規化学物質等に係る試験を実施する試験施設に関する基準について」(平成 23 年 3 月 31 日薬食発 0331 第 8 号・平成 23･03･29 製局第 6 号・環保企発第 110331010 号厚生労働省医薬食品局長・経済産業省製造産業局長・環境省総合環境政策局長連名通知) に従い、試験方法は、「新規化学物質等に係る試験の方法について」(平成 23 年 3 月 31 日薬食発 0331 第 7 号・平成 23･03･29 製局第 5 号・環保企発第 110331009 号 厚生労働省医薬食品局長・経済産業省製造産業局長・環境省総合環境政策局長連名通知)に基づい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、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] [redacted] 2012 年 3 月 28 日

信 頼 性 保 証 書

表題：indeneのラットにおける反復投与毒性･生殖発生毒性併合試験

試験番号：ＳＲ１１０８７

本試験は、株式会社 化合物安全性研究所 ＱＡＵによって、下記のとおり査察された。

査　察　段　階	査　察　日	試験責任者への報告日	運営管理者への報告日
試験計画書	2011年9月28日	2011年9月28日	2011年9月28日
試験計画書変更書(No. 1)	2011年10月6日	2011年10月6日	2011年10月6日
試験計画書変更書(No. 2)	2011年11月8日	2011年11月8日	2011年11月8日
試験計画書変更書(No. 3)	2012年3月23日	2012年3月23日	2012年3月23日
被験物質の受入・表示・保存	2011年9月28日	2011年9月28日	2011年9月28日
投与液の調製	2011年10月7日	2011年10月7日	2011年10月7日
投与液の化学分析	2011年10月7日	2011年10月7日	2011年10月7日
被験物質のサンプリング	2011年10月14日	2011年10月14日	2011年10月14日
動物受入・検疫･馴化	2011年9月28日	2011年9月28日	2011年9月28日
群分け	2011年10月7日	2011年10月7日	2011年10月7日
投与	2011年10月11日	2011年10月11日	2011年10月11日
一般状態観察	2011年10月11日	2011年10月11日	2011年10月11日
体重測定	2011年10月11日	2011年10月11日	2011年10月11日
摂餌量測定	2011年10月11日	2011年10月11日	2011年10月11日
性周期検査	2011年10月11日	2011年10月11日	2011年10月11日
詳細な一般状態観察	2011年10月17日	2011年10月17日	2011年10月17日
生殖能検査(交配)	2011年10月24日 2011年10月25日	2011年10月25日	2011年10月25日
機能検査	2011年11月15日	2011年11月15日	2011年11月15日
尿検査	2011年11月16日 2011年11月17日	2011年11月17日	2011年11月17日
分娩および哺育状態観察	2011年11月16日	2011年11月16日	2011年11月16日
新生児の剖検	2011年11月21日	2011年11月21日	2011年11月21日
剖検・器官重量測定	2011年11月21日	2011年11月21日	2011年11月21日

SR11087

査察段階	査察日	試験責任者への報告日	運営管理者への報告日
血液学的検査	2011年11月21日 2011年11月22日	2011年11月22日	2011年11月22日
血液化学的検査	2011年11月21日 2011年11月22日 2011年12月2日	2011年12月2日	2011年12月2日
病理組織学的検査(標本作製)	2011年11月23日 2011年11月28日 2011年11月29日	2011年11月29日	2011年11月29日
病理組織学的検査(鏡検)	2011年12月20日	2011年12月20日	2011年12月20日
生データ	2012年3月19日 2012年3月21日 2012年3月22日 2012年3月23日	2012年3月23日	2012年3月23日
最終報告書(草案):図表	2012年2月23日 2012年2月24日 2012年2月25日 2012年2月27日 2012年2月28日	2012年2月28日	2012年2月28日
	2012年3月12日	2012年3月12日	2012年3月12日
最終報告書(草案):本文	2012年3月19日 2012年3月21日 2012年3月22日 2012年3月23日	2012年3月23日	2012年3月23日
	2012年3月27日	2012年3月27日	2012年3月27日
最終報告書	2012年3月28日	2012年3月28日	2012年3月28日

1. 本試験は、「新規化学物質等に係る試験を実施する試験施設に関する基準について」(平成23年3月31日 薬食発0331第8号・平成23・03・29製局第6号・環保企発第110331010号厚生労働省医薬食品局長・経済産業省製造産業局長・ 環境省総合環境政策局長連名通知)および「新規化学物質等に係る試験の方法について」(平成23年3月31日 薬食発0331第7号・平成23・03・29製局第5号・環保企発第110331009号 厚生労働省医薬食品局長・経済産業省製造産業局長・環境省総合環境政策局長連名通知に従い実施された。

2. 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およ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が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] [redacted] 2012年3月28日

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表題：indene のラットにおける反復投与毒性･生殖発生毒性併合試験

試験番号：SR11087

試験目的：indene を雌雄ラットに反復経口投与してその毒性ならびに性腺機能、交尾行動、受胎および分娩等の生殖に及ぼす毒性を検討するために行われた。

試験実施基準（GLP）および試験法ガイドライン

試験実施基準（GLP）：「新規化学物質等に係る試験を実施する試験施設に関する基準について」（平成 23 年 3 月 31 日薬食発 0331 第 8 号・平成 23･03･29 製局第 6 号・環保企発第 110331010 号厚生労働省医薬食品局長・経済産業省製造産業局長・環境省総合環境政策局長連名通知）

試験法ガイドライン：「新規化学物質等に係る試験の方法について」（平成 23 年 3 月 31 日薬食発 0331 第 7 号・平成 23･03･29 製局第 5 号・環保企発第 110331009 号 厚生労働省医薬食品局長・経済産業省製造産業局長・環境省総合環境政策局長連名通知）

動物愛護

本試験は試験施設の動物実験倫理委員会の承認を得、かつ、標準操作手順書（動物実験倫理規定）に準拠した。

法規および基準等　：「動物の愛護及び管理に関する法律」（昭和 48 年 10 月 1 日 法律第 105 号、最終改正 平成 23 年 8 月 30 日 法律第 105 号）

「実験動物の飼養及び保管並びに苦痛の軽減に関する基準」（平成 18 年 4 月 28 日 環境省告示第 88 号）

「動物実験に関する指針」（昭和 62 年 5 月 22 日承認 社団法人日本実験動物学会）

試験委託者

名称　：厚生労働省 医薬食品局

所在地　：東京都千代田区霞が関 1-2-2(〒100-8916)

連絡先　：審査管理課 化学物質安全対策室

試験施設

名称　：株式会社　化合物安全性研究所

所在地　：札幌市清田区真栄 363 番 24 (〒004-0839)

運営管理者　：[redacted]

試験責任者

氏名　：[redacted]

所属　：

試験従事者およびその業務分担

被験物質管理　：[redacted]

化学分析　：

動物管理　：

検疫・馴化　：

投与・観察・測定　：

臨床検査　：

病理検査　：

試験期間

試験開始日	: 2011 年　9 月　28 日
被験物質受入	: 2011 年　7 月　26 日
動物受入	: 2011 年　9 月　28 日
実験開始(投与開始)日	: 2011 年　10 月　11 日
交配開始	: 2011 年　10 月　24 日
新生児剖検開始	: 2011 年　11 月　20 日
母動物剖検開始	: 2011 年　11 月　21 日
雄動物の投与終了時剖検	: 2011 年　11 月　22 日
回復群の雌雄動物の剖検	: 2011 年　12 月　6 日
実験終了日	: 2012 年　1 月　31 日
試験終了日	: 2012 年　3 月　28 日

要　約

indene を、0（対照、トウモロコシ油）、4、20 および 100 mg/kg/day の用量で、1 群雌雄各 12 匹の Crl:CD(SD) ラットにおいて、雄には計 42 日間、雌に交配前 14 日間、交配期間および妊娠期間ならびに分娩後 4 日までの最長 45 日間連日経口投与し、雌雄動物の反復投与による影響、雌雄動物の生殖および新生児の発生に及ぼす影響について検討した。また、0（対照）および 100 mg/kg について、雄動物は投与 42 日後にそれぞれ 5 匹を選抜して 14 日間の回復性を検討した。雌動物は 0（対照）および 100 mg/kg を投与するサテライト群として各 10 匹を別に設定し、投与 42 日後に各群 5 匹を選抜して 14 日間の回復性を検討した。

1. 反復投与毒性

一般状態観察では、100 mg/kg 群の雌で粘液便が投与期間中単発的に認められた。

詳細な状態観察では、雌雄とも被験物質投与に関連する変化は 100 mg/kg 群まで認められなかった。

機能検査では、投与 6 週の検査で、100 mg/kg 群の雄に前肢握力に有意な低値がみられたが、回復性のある変化であった。

体重については、100 mg/kg 群の雌雄で、投与期間中体重増加抑制が認められ、体重増加量および体重増加率に有意な低値が認められた。この体重変化は休薬後の 14 日間で回復傾向が認められた。

摂餌量については、100 mg/kg 群の雄で投与初期に、主試験群の雌で交配前の投与期間に、サテライト群の雌で投与期間中に低値が散見された。

尿検査、血液化学的検査では、100 mg/kg 群まで雌雄とも被験物質投与に関連すると考えられる変化は認められなかった。

血液学的検査では、20 および 100 mg/kg 群の雄で平均赤血球ヘモグロビン濃度の有意な低値、100 mg/kg 群の雌雄で網赤血球数の有意な高値が認められ、被験物質投与に起因すると考えられた。しかしこの変化も 14 日間の回復性が確認された。このうち、20 mg/kg 群の雄で認められた平均赤血球ヘモグロビン濃度の有意な低値は、他の赤血球パラメータ、体重および摂餌量に影響がみられなかったことから、毒性変化ではないと考えられた。

剖検、器官重量および病理組織学的検査において、100 mg/kg 群まで被験物質投与に起因した変化は認められなかった。

以上の結果から、本試験条件下における indene の無影響量(NOEL) は 4 mg/kg/day、無毒性量(NOAEL) は 20mg/kg/day と考えられた。

2. 生殖発生毒性

主試験群の生殖能検査および新生児の検査では、100 mg/kg 群まで、いずれの項目にも被験物質投与に関連する変化はみられなかった。

したがって、本試験条件下における indene の反復投与による親動物の生殖に対する無影響量（NOEL）および無毒性量（NOAEL)ならびに新生児の発生に対する無影響量（NOEL）および無毒性量（NOAEL）はいずれも 100 mg/kg/day と考えられた。

緒　言

indene を、0（対照、トウモロコシ油）、4、20 および 100 mg/kg/day の用量で、1 群雌雄各 12 匹の Crl:CD(SD) ラットにおいて、雄には計 42 日間、雌に交配前 14 日間、交配期間および妊娠期間ならびに分娩後 4 日までの間連日経口投与し、雌雄動物の反復投与による影響、雌雄動物の生殖および新生児の発生に及ぼす影響について検討した。また、0（対照）および 100 mg/kg について、雄動物は投与 42 日後にそれぞれ 5 匹を選抜して 14 日間の回復性を検討した。雌動物は 0（対照）および 100 mg/kg を投与するサテライト群として各 10 匹を別に設定し、投与 42 日後に各群 5 匹を選抜して 14 日間の回復性を検討した。

材料および方法

1. 被験物質

名称　　：indene；インデン

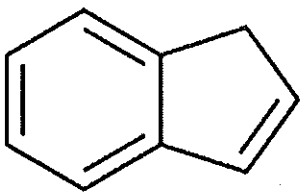
別名　　：indonaphthene；インドナフテン、1H-indene；1H-インデン

CAS No.　　：95-13-6

化審法官報公示整理番号：(4)-580

分子式　　：C_9H_8

構造式[4]　　：



分子量　　：116.15～116.17[1]

物理化学的性質　　：外観　；無色～黄褐色の液体

比重　；0.9692～0.9968(20～50℃)

融点　；-1.8～-1.6 ℃

沸点　；181.6～182.6℃

蒸気圧；13.3～80 hPa (58.5～100.8)。

引火点；58℃（密閉式）

密度　；0.99（20℃）

LogPOW；2.92

pH　　；弱酸性（飽和水溶液、25℃）

溶解性；水にほとんど溶けない（混合しない）。エタノール、クロロホルム、エーテル、アセトン、その他多くの有機溶剤に溶ける。

ロット番号　　：IG5TI

純度　　：98.9%（GC、試験成績書）[2]（Appendix 1-1）

不純物の濃度　　：不明（データなし）

製造者　　：名称　；[redacted]

所在地

入手量　　：1300 mL

安定性[3]　　：不活性ガス封入し、容器を密封し、遮光し、冷蔵保管すれば安定である。通常は極めて不安定で容易に重合する。酸素を急激に吸収する。光により除々に分解し、着色する。

投与操作終了後、使用した被験物質の純度に関する分析成績を東京化成工業株式会社から入手し、被験物質の試験期間中の安定性を確認した。（Appendix 1-2-1～1-2-3）。

保存条件　　：遮光容器に入れ、冷凍保存。

酸化されやすいため[3]、使用後は窒素ガスを封入し直ちに密栓した。遮光容器を使用し、冷凍保存した。

保存場所　　：被験物質保存室の冷凍冷蔵庫（実測範囲：-26～-30℃）

保存期間　　：2011年7月26日（受入）～2011年11月22日（最終調製日）

取扱上の注意　　：使用時は流水あるいは室温で完全に融解した。取り扱いは局所換気又は全体換気ができるドラフト内で行い、防毒マスク、手袋、保護眼鏡、長袖作業衣を着用した。

サンプリング　　：被験物質サンプルとして、約5 mLを採取し、試験施設の資料保存室に保存した。

残余被験物質の処置：関連試験も含めすべての試験操作終了後、焼却処分するために産業廃棄物として回収した。

有害性情報[3),4),5)]　　：ラット、吸入 LC_{50} 14 g/m^3、14000 mg/m^3/4H

マウス、経口、LD_{50}値は1800 mg/kg

ラット、経口、LD_{50}値は2300 mg/kg、

ラット、経口、LD_{50}＜2000 mg/kg

LD_{50}値は2000 mg/kgを上回る

2000 mg/kgで1例死亡（投与1時間後に流涙、流涎、眼瞼下

垂、異常歩行、体重減少、腹臥/横臥、呼吸数減少、体温低下、投与翌日死亡)

ラット、皮下(50v/v%濃度)、死亡、肝臓、肺、消化管に障害あり

ラット、吸入曝露(800-900 ppm、7H/6day)、肝臓、脾臓、腎臓障害あり

軽度の皮膚刺激性、強い眼刺激性、アレルギー性皮膚反応を起こすおそれあり

2. 対照物質

名称　：トウモロコシ油

ロット番号　：V0T4896

製造者　：ナカライテスク株式会社

保存条件　：室温

取扱上の注意　：特になし。

3. 投与液の調製および化学分析

調製方法　：被験物質を精秤し、所定の濃度となるように対照物質を添加後、スターラーを用いて約30分間分散(溶解)させた。最初に高用量群の濃度液(2 v/v%)を調製し、順次中用量、低用量と段階希釈して調製した。調製にはすべてガラス製器具を使用した。

投与液の安定性　：indeneの0.1 mg/mLおよび200 mg/mL濃度液は遮光下で冷蔵保存して8日間、その後室温保存で24時間安定であることが確認されている(CERTIFICATE OF ANALYSIS. 2005年8月15日, Bozo Research Center Inc.)(Appendix 2)。

調製頻度　：8日間に1回以上。

保存条件　：ガラス製の遮光容器に入れ、冷蔵保存した(1～15℃、実測範囲4.3～7.7℃)。

調製上の注意　：被験物質は完全に融解したことを確認して使用した。また、被験物質はドラフト内で取扱い、調製の際には防毒マスク、眼鏡、手袋、作業衣等を着用し、吸入、眼、皮膚および衣類等との接触を避けた。

残余投与液の処置　：残余の投与液は、焼却処分するために、産業廃棄物として回収した。

投与液の濃度確認　：被験物質の全濃度に関する投与液中の濃度を、雄の初回および最終回調製時の計2回確認した。その結果、0.08、0.4および2 v/v%の投与液は初回および最終回の調製液で、含有率はそれぞれ97.9～102.0%および94.9～97.0%であり、いずれも判定基準に適合していた(Appendix 3-1、3-2)。

濃度分析方法　　：Appendix 4 に示す。

4. 試験方法

(1) 試験系

種・系統　　：ラット、Crl:CD(SD)

微生物統御　　：SPF

生産業者　　：日本チャールス・リバー株式会社 厚木飼育センター

微生物モニタリング：動物生産業者よりデータを入手した。

動物選定理由　　：ラットはこの種の試験で通常用いられている動物種であり、繁殖成績が安定していることと当研究所における背景対照データが利用できることから、この系統を選定した。

発注動物数　　：雄 52 匹、雌 74 匹

発注動物週齢　　：雌雄とも 8 週齢

出荷体重基準　　：雄は 240～330 g、雌は 160～230 g

受入時体重範囲　　：雄は 257～294 g、雌は 182～215 g

投与開始時週齢　　：雌雄とも 10 週齢

群数　　：雄 6 群、雌 8 群(主試験群 雌雄各 4 群、サテライト群雄 2 群、雌 4 群)

各群動物数　　：主試験群 雌雄各 12 匹、サテライト群 雌雄各 5 匹

(2) 検疫および馴化

検疫方法　　：一般状態を 1 日 1 回観察し、体重を受入時(馴化 1 日)、検疫および馴化 8 日ならびに検疫および馴化期間終了日（投与開始4日前）に測定した。検疫および馴化期間中、いずれの動物にも異常はみられなかった。

性周期検査　　：雌動物について、投与開始前日まで膣垢スメア塗抹法により性周期検査を行った。検査の結果、雌 2 例に性周期の異常がみられた。

期間　　：雌雄とも、馴化 1 日(受入日)から馴化 10 日までの 9 日間。

(3) 群分け

検疫および馴化期間終了日（投与開始 4 日前）に、性周期の異常のみられた動物および体重の減少が認められた動物を除くすべての動物の体重に基づいて、層化無作為抽出法により各群の平均体重が均一になるように群分けを行った。これらの動物の体重範囲は、雄で 338～381 g、雌で 220～257 g であり、平均体重（雄、359.1 g；雌、237.4 g）の±20%以内であった。選択された動物の投与開始前 3 日から投与開始日までの一般状態の観察では、雄で 20 mg/kg 群に振り分けられた 1 例に上切歯破切および体重減少が認められたため、群分けから外れた動物で体重の近い動物と入れ替えた。また、雌で 4 mg/kg 群に振り分けられた 1 例

で、耳介に外傷が認められたため、群分けから外れた動物で体重の近い動物と入れ替えた。選抜から外れた動物は試験から除外後、標準操作手順書に従って取扱った。

(4) 動物およびケージの識別

動物　：群分け前は油性フェルトペンで尾部に印を付け、個体識別を行った。
群分け後は耳介に動物番号を入れ墨し、個体識別を行った。
新生児については、個体の識別は行わなかった。

飼育ケージ　：群分け前は性別毎に色分けしたラベルに試験番号および受入時の動物番号を明記し、各ケージの前面に標示した。
群分け後は性別毎に色分けしたラベルに試験番号、試験群および群分け後の動物番号を明記し、各ケージの前面に標示した。

(5) 動物飼育

1) 飼育環境

飼育室番号　：303 号室

温度・湿度　：22±3℃, 50±20%（実測範囲 20～24℃、42～60%）

換気回数　：10～15 回／時間

照明時間　：人工照明 12 時間（8：00～20：00）

2) 飼育器材および飼育方法

ケージの種類　：ブラケット式金属製金網床ケージ（260W×380D×180H, mm）
ただし、交尾成立雌動物については妊娠 17 日から哺育 4 日まで同ケージの金網床を小型受皿に代えて実験動物用床敷（ホワイトフレーク、日本チャールス・リバー株式会社）を使用して分娩と哺育を行わせた。

1 ケージあたりの収容動物数：
検疫および馴化期間中は 2 匹、群分け後は 1 匹、交配期間中は雌雄各 1 匹、分娩後は 1 腹を収容した。

ケージおよび給餌器の交換：
群分け時および投与 14 日に 1 回実施し、その後は 2 週に 1 回の頻度で交換した。ただし、交尾成立雌動物については妊娠 0 日および 14 日に実施した。

受皿交換　：週 2 回実施した。

自動給水装置の水抜き：週 1 回実施した。

給水器の交換　：尿検査時にのみ用いた。

小型受皿の交換　：妊娠 20 日に実施した。

室内の清掃および清拭消毒：

1日1回実施した。清拭消毒に際しては、塩素系消毒薬およびヨウ素系消毒薬を1週間単位で交互に使用した。

3) 飼料

種類・名称　：固型飼料、CRF-1

ロット番号　：110607、110908

製造業者　：オリエンタル酵母工業株式会社

給餌方法　：金属製給餌器を用いて自由に摂取させた。
ただし、剖検前日の夕刻からは全例を絶食させた。

汚染物質および微生物検査：

試験に悪影響を及ぼす恐れのある汚染物質あるいは微生物の有無を、使用した各ロットの飼料について分析した。汚染物質の分析はEurofins Analytics社（分析報告書：AR-11-JP-001269-01、AR-11-JP-002270-01）において、微生物検査は飼料製造業者（分析試験報告書：No. 11G03-084、11G03-132）がそれぞれ実施した。分析項目と許容値は株式会社 化合物安全性研究所の標準操作手順書に準拠した。分析の結果、いずれの項目にも許容値を超える値は認められなかった。

4) 飲料水

種類　：札幌市水道水

給水方法　：自動給水装置を用いて自由に摂取させた。ただし、尿検査時は給水器を用いた。

汚染物質検査　：試験に悪影響を及ぼす恐れのある汚染物質の有無を、2011年7月1日、2011年10月3日および2012年1月5日に、当該飼育室と同系統配管の最末端（301号室）から試料を採取して分析した（水質検査結果表：No. A231007、A233146、A234348）。分析は日本衛生株式会社において行い、分析データを入手した。分析項目と許容値は株式会社 化合物安全性研究所の標準操作手順書に準拠した。分析の結果、いずれの項目にも規定された許容値を超える値は認められなかった。

(6) 被験物質の投与

1) 投与量の設定

投与量　：0（対照物質のみ）、4、20および100 mg/kg/dayとした。

設定理由　：先に実施した予備試験（SR11087P）[2]（投与量0、30、100、300および1000 mg/kg/day、雌雄各4匹/群、2週間反復経口投与）の結果、

1000 mg/kg では雌 1 例が投与 6 日に死亡し、その他の動物も一般状態の悪化(排便なし、無尿、呼吸緩徐、腹臥等)、体重および摂餌量の著明な減少が認められたため、雄 1 例を投与 13 日、残り雌 3 例を投与 6 日に投与を中断して剖検した。300 mg/kg 以上の群の生存例では体重および摂餌量の低値、一般状態の異常(流涎、よろめき歩行、軟便、粘液便、橙黄色尿、赤褐色尿、被毛汚染等)が認められた。また、溶血性貧血を示唆する変化(RBC、HGB、HCT の低下、T-Bil の上昇)が認められ、剖検では脾臓の腫大、暗色調、胸腺委縮等、器官重量では脾臓重量の増加、卵巣重量の減少が認められた。100 mg/kg では用量依存的な体重増加率の低値、摂餌量減少が認められた。30 mg/kg 以上の雄でトリグリセリドの低下が認められた。以上のことから、本試験の投与期間を考慮して高用量は体重増加率および摂餌量に影響が認められた 100 mg/kg/day とした。また、30 mg/kg/day の雄でトリグセリドの低値が認められたことを考慮して公比5とし、以下 20 mg/kg/day を中用量、4 mg/kg/day を低用量に設定した。

試験群の構成　：試験群の構成と各群の動物番号は以下の通りとした。

試験群	投与量 (mg/kg)	濃度 (v/v%)	投与容量 (mL/kg)	動物数(動物番号) 雄	雌
＜主試験群＞					
対照群	0	0	5	12 (101～112)	12 (151～162)
低用量群	4	0.08	5	12 (201～212)	12 (251～262)
中用量群	20	0.4	5	12 (301～312)	12 (351～362)
高用量群	100	2	5	12 (401～412)	12 (451～462)
＜サテライト群＞					
対照群 (投与終了時剖検例)	0	0	5		5# (163～167)
(回復終了時剖検例)	0	0	5	5 (101～112)*	5# (168～172)
高用量群(投与終了時剖検例)	100	2	5		5# (463～467)
(回復終了時剖検例)	100	2	5	5 (401～412)*	5# (468～472)

対照群は他の群と同様の方法で対照物質のみを投与した。

*：主試験群から交配期間終了後に選抜した。投与 21 日の体重に基づき、各群それぞれの平均値に近似するように各群の中央値の周辺の体重を有する動物を選抜した。

#：非交配群

2) 投与

投与方法および投与経路：ディスポーザブル胃ゾンデおよびディスポーザブルシリンジを用いて強制的に胃内に経口投与した。

投与回数　：1 日 1 回、連日投与した。

投与時刻　　：9：09～11：58

投与期間　　：雄；交配14日前より42日間

雌；交配前14日間および交尾成立までの交配期間、さらに交尾成立例は妊娠期間および分娩後4日（哺育0日を分娩後0日として起算）までの期間

サテライト群については42日間

回復期間　　：投与期間終了後14日間

投与液量　　：各個体の投与液量は投与日に最も近い測定日の体重に基づいて算出した。

投与方法、投与経路、投与回数および投与期間の選定理由：

試験法ガイドラインを参考にした。

5. 観察、測定および検査項目

Ⅰ. 反復投与毒性

投与開始日を投与1日と起算し、投与42日の翌日を回復1日、交尾成立日を妊娠0日、分娩終了日を哺育0日と起算した。

1）一般状態観察

例数　　：全例

期間　　：投与1日から剖検日まで。

頻度　　：投与期間中は投与前および投与後の1日2回、回復期間中は午前および午後の1日2回、剖検日は午前中に1回観察した。

観察方法　　：個々の動物の生死、外観、行動等について観察した。異常が認められる場合は、その症状ならびに症状の持続期間を記録した。死亡動物は発見後速やかに剖検した。

2）詳細な一般状態観察

例数　　：全例

時期　　：投与開始前ならびに投与7、14、21、28、35および42日。

サテライト群の動物については、回復7および14日。

観察方法　　：あらかじめ定めたスコアリング基準を用いてスコア化した観察結果を記録した。

観察項目およびその方法：

①体位・姿勢、呼吸状態、振戦・痙攣、常同行動（回転・旋回）、異常行動（自咬）をケージ外から観察した。

②取り出し易さ、取扱い易さ、筋収縮性、立毛、被毛の状態、皮膚、

眼・眼球および粘膜の外観、瞳孔径、流涙、流涎、その他分泌物の有無について、ケージから取り出す時に観察した。

③歩行、運動協調性、環境刺激に対する反応、探索行動、排泄状態（排尿・排糞）、常同行動（身づくろい・くびふり）、異常行動（後ずさり・異常発声）、攻撃性について、オープンフィールド内で観察した。

3) 機能検査

例数　：各群の体重の平均値に近似するように選抜した雄（サテライト群を含む）およびサテライト群（回復終了時剖検例）の雌の各群5例ならびに主試験群の雌の分娩日の早いものから順に選抜した各群5例。

時期　：投与6週（投与37日）および回復2週（回復10日）。
主試験群の雌は哺育4日。

観察／測定方法　：あらかじめ定めたスコアリング基準を用いてスコア化した観察結果あるいは測定機器による測定値を記録した。
観察項目およびその方法：
①刺激に対する感覚運動反応：検査台上で以下を観察した。
視覚刺激、触覚刺激、聴覚刺激、痛覚刺激、固有受容器刺激、空中正向反射
②握力：CPUゲージ（アイコーエンジニアリング株式会社）を用いて前肢および後肢について各3回測定し、1 g単位で記録した。
③自発運動量：自発運動量測定装置（スーパーメックスおよびCompACT、室町機械株式会社）を用いて測定した。上記に引続き、10分間隔で1時間測定した。

4) 体重測定

例数　：全例

測定日　：投与1、3、5、7、10、14、21、28、35および42日の投与前、回復7および14日ならびに剖検日。
主試験群の雌は投与1、3、5、7、10、14日の投与前、妊娠0、1、3、5、7、10、14、17および20日の投与前、哺育0、1および4日の投与前ならびに分娩後5日の剖検日。
死亡例は死亡発見日に体重を測定した。

測定方法　：電子式上皿天秤（GX-2000、株式会社エー・アンド・デイ）を用いて測定し、1 g単位で記録した。

体重増加量および体重増加率：

以下の式により算出した。

〈雄およびサテライト群の雌〉

投与期間；

$$\text{体重増加量(g)} = \text{投与 42 日体重(g)} - \text{投与 1 日体重(g)}$$

$$\text{体重増加率(\%)} = \frac{\text{体重増加量(g)}}{\text{投与 1 日体重(g)}} \times 100$$

回復期間；

$$\text{体重増加量(g)} = \text{回復 14 日体重(g)} - \text{投与 42 日体重(g)}$$

$$\text{体重増加率(\%)} = \frac{\text{体重増加量(g)}}{\text{投与 42 日体重(g)}} \times 100$$

〈主試験群の雌〉

妊娠前投与期間；

$$\text{体重増加量(g)} = \text{投与 14 日体重(g)} - \text{投与 1 日体重(g)}$$

$$\text{体重増加率(\%)} = \frac{\text{体重増加量(g)}}{\text{投与 1 日体重(g)}} \times 100$$

妊娠期間；

$$\text{体重増加量(g)} = \text{妊娠 20 日体重(g)} - \text{妊娠 0 日体重(g)}$$

$$\text{体重増加率(\%)} = \frac{\text{体重増加量(g)}}{\text{妊娠 0 日体重(g)}} \times 100$$

哺育期間；

$$\text{体重増加量(g)} = \text{哺育 4 日体重(g)} - \text{哺育 0 日体重(g)}$$

$$\text{体重増加率(\%)} = \frac{\text{体重増加量(g)}}{\text{哺育 0 日体重(g)}} \times 100$$

5) 摂餌量測定

例数　：全例

測定日　：雌雄とも剖検日および交配期間を除き、体重測定と同じ日に実施した。ただし、主試験群の雌については、妊娠 0 日および哺育 0 日は給与量のみ、妊娠 20 日は残量を測定した。

測定方法　：電子式上皿天秤（GX-2000、株式会社エー・アンド・デイ）を用いて測定し、1 g 単位で記録した。投与開始前日に適当量を測定後ケージ毎に給与し、その後は測定日に残量および給与量を測定した。ただし、最終回の測定は残量のみとした。

以下の式により、摂餌量（g/rat/day）を算出した。

$$\text{摂餌量(g/rat/day)} = \frac{\text{給与量(g/rat)} - \text{残量(g/rat)}}{\text{測定日間の日数(day)}}$$

6) 尿検査

例数　　：雄は機能検査と同一の各群5例について、雌はサテライト群（回復終了時剖検例）の各群5例

時期　　：投与6週および回復2週。

採尿方法　　：非絶食下でラット用代謝ケージ（KN-646、B-1型、株式会社夏目製作所）を用いて採尿し、投与直後から約3時間の蓄尿で①～⑨を、また約21時間の蓄尿で⑩および⑪を実施した。採取した尿は検査終了後廃棄した。

検査項目および検査方法：

①尿pH	試験紙法
②蛋白(Protein)	試験紙法
③糖(Glucose)	試験紙法
④ケトン体(Ketone body)	試験紙法
⑤ウロビリノーゲン(Urobilinogen)	試験紙法
⑥ビリルビン(Bilirubin)	試験紙法
⑦潜血(Occult blood)	試験紙法
⑧色調(Color)	肉眼観察
⑨尿沈査(Urine sediment)	Sternheimer 染色法
⑩尿量(Urine Volume)	容量測定
⑪比重(Specific gravity)	屈折計法

①～⑦ マルティスティックス、シーメンスヘルスケア・ダイアグノスティクス
⑨ 顕微鏡BH-2、BH2-MDO、オリンパス光学工業株式会社
⑪ 尿比重屈折計ユリコン-S、アタゴ

7) 血液学的検査

例数　　：各群5例（主試験群の雄は機能検査に用いた動物以外から動物番号の若い順に選抜した。主試験群の雌は機能検査と同一例、サテライト群は全例。）

時期　　：剖検時［主試験群の雄およびサテライト群の雌（投与終了時剖検例）は投与42日の翌日、主試験群の雌は分娩後5日、サテライト群の雄および雌（回復終了時剖検例）は回復14日の翌日］に採血した。

採血方法　　：16～21時間の絶食下でラットをペントバルビタールナトリウム溶液（ソムノペンチル、共立製薬株式会社）の腹腔内注射により麻酔し、腹部大動脈より採血した。検査項目のうち、①～⑩および⑫についてはEDTA・2K（ベノジェクトII真空採血管、テルモ株式会社）で処理した血液約1 mLを用い、⑪については血液1 mLあたりヘパリンナトリウム（ヘパリンナトリウム注N「味の素」、1000単位/mL、味の素製薬株式会社）約20単位で処理した血液約0.1 mLを用い、⑬⑭については3.8%クエン酸ナトリウムで処理した血液約1～2 mLを3500回

転/分で10分間遠心分離して得られた血漿を用いた。得られた血液および血漿は検査終了後廃棄した。なお、白血球塗抹標本(May-Grünwald-Giemsa染色)を作製し、保存した。白血球の分布異常はみられなかったため、白血球塗抹標本の鏡検は行わなかった。なお、主試験群の雌はメトヘモグロビンとハインツ小体の検査を実施しなかった。

検査項目および検査方法：

①赤血球数(RBC)	電気抵抗検出法
②ヘマトクリット値(HCT)	電気抵抗検出法
③ヘモグロビン濃度(HGB)	SLSヘモグロビン法
④平均赤血球容積(MCV)	RBC, HCT値より算出
⑤平均赤血球ヘモグロビン量(MCH)	RBC, HGB値より算出
⑥平均赤血球ヘモグロビン濃度(MCHC)	HCT, HGB値より算出
⑦血小板数(Platelet)	電気抵抗検出法
⑧白血球数(WBC)	フローサイトメトリー法
⑨網赤血球数(Reticulocyte)	フローサイトメトリー法
⑩白血球分画 (Differential count of WBC)	フローサイトメトリー法
⑪メトヘモグロビン(Methemoglobin)	Evelyn and Malloy法
⑫ハインツ小体	ブリリアントグリーン・ ニューメチレンブルー染色法
⑬プロトロンビン時間(PT)	トロンボプラスチン法
⑭活性化部分トロンボプラスチン時間(APTT)	エラジン酸法

①～⑩ 自動血球分析装置XT-2000 iV、シスメックス
⑪ 紫外可視分光光度計 UV-160A、島津製作所
⑫ 顕微鏡 BH-2、BH2-MDO、オリンパス光学工業株式会社
⑬⑭ 血液凝固自動測定装置KC4デルタ、トリニティ・バイオテック

8) 血液化学的検査

例数　：血液学的検査と同一の各群5例

時期　：剖検時に採血した。

採血方法　：16～21時間の絶食下でラットをペントバルビタールナトリウム溶液（ソムノペンチル、共立製薬株式会社）の腹腔内注射により麻酔し、腹部大動脈より採血した。検査項目のうち、(1)および(5)については、血液1 mLあたりヘパリンナトリウム（ヘパリンナトリウム注N「味の素」、1000単位/mL、味の素製薬株式会社）約20単位で処理後、3500回転/分で10分間の遠心分離で得られた血漿を用いて検査した。他の項目については分離剤入り試験管（セパクリーン A、栄研器材株式会社）に血液を採取し、3500回転/分で10分間の遠心分離で得られた血清を用いて検査した。また、得られた血清の一部は甲状腺機能に関するホルモン(T3、T4およびTSH)測定用としてポリ

プロピレン製チューブ4本に約150μLずつ分注し、超低温フリーザー（−80℃設定）に保存した。得られた血漿および血清は検査終了後-20℃以下で凍結保存し、試験終了日に廃棄した。

検査項目および検査方法：

(1)AST	JSCC法
(2)ALT	JSCC法
(3)アルカリホスファターゼ(ALP)	JSCC法
(4)γ-GTP	L-γ-グルタミル-3-カルボキシ-4-ニトロアニリド基質法
(5)グルコース(Glucose)	ヘキソキナーゼ法
(6)総コレステロール(T-Cho)	酵素法
(7)トリグリセリド(TG)	遊離グリセロール消去法
(8)総ビリルビン(T-Bil)	酵素法
(9)総胆汁酸(TBA)	酵素サイクリング法
(10)尿素窒素(UN)	ウレアーゼ･GLDH法
(11)クレアチニン(Crea)	酵素法
(12)ナトリウム(Na)	イオン選択電極(ISE)法
(13)カリウム(K)	イオン選択電極(ISE)法
(14)クロール(Cl)	イオン選択電極(ISE)法
(15)カルシウム(Ca)	OCPC法
(16)無機リン（IP)	Fiske-Subba Row法
(17)総蛋白(TP)	ビウレット法
(18)蛋白分画(Protein fraction)	セルロースアセテート膜電気泳動法
(19)A/G比(A/G ratio)	蛋白分画より算出
(20)アルブミン(Albumin)	総蛋白と蛋白分画より算出

(1) ～(17) 自動分析装置7080形、日立ハイテクノロジーズ
(18)～(20) 自動電気泳動装置AES320、三島オリンパス

9) 剖検

例数　：全例

時期　：主試験群の雄およびサテライト群の雌（投与終了時剖検例)は投与42日の翌日、主試験群の雌は分娩後5日、サテライト群の雄および雌（回復終了時剖検例）は回復14日の翌日に剖検した。主試験群の雌1例は哺育3日に剖検した。

検査方法　：体外表を観察し、ペントバルビタールナトリウム溶液（ソムノペンチル、共立製薬株式会社）の腹腔内注射による麻酔下で採血後、放血により安楽死させ、全身の器官・組織を肉眼的に観察した。検査終了後、以下の器官・組織を10%中性緩衝ホルマリンに固定・保存した。なお、眼球およびハーダー腺はデビッドソン液で固定・保存し、精巣および精巣上体はブアン液で固定、70%エタノールに保存した。肺については固定液を注入後浸漬固定した。左右のある器官については原則として左右とも固定・保存した。

器官・組織名　：脳（大脳、小脳および脳橋）、脊髄、下垂体、胸腺、甲状腺（上皮小体を含む）、副腎、脾臓、心臓、食道、胃、肝臓、膵臓、顎下腺、十二指腸、空腸、回腸（パイエル板を含む）、盲腸、結腸、直腸、気管、肺、腎臓、膀胱、精巣、精巣上体、前立腺、精嚢（凝固腺含む）、卵巣、子宮（角部および頸部）、膣、眼球およびハーダー腺、乳腺（右腹部）、大腿骨（骨髄を含む、右）、腸間膜リンパ節、顎下リンパ節、骨格筋（腓腹筋）、坐骨神経および肉眼的異常部位（正常組織との境界部含む）。

10）器官重量測定

例数　：全例

時期　：剖検時

測定方法　：電子式上皿天秤（ER-180A、株式会社エー・アンド・デイ）を用いて以下の器官について重量を測定した。左右のある器官については、左右併せて測定した。

検査器官　：脳、下垂体、甲状腺（上皮小体含む）、心臓、肝臓、腎臓、脾臓、副腎、胸腺、精巣、精巣上体、前立腺（腹葉）、精嚢（凝固腺とともに分泌物含む）、卵巣、子宮

相対重量の算出　：以下の式から相対重量を算出した。

$$\text{相対重量}(\%) = \frac{\text{絶対重量}(g)}{\text{剖検日体重}(g)} \times 100$$

11）病理組織学的検査

例数　：剖検時に固定・保存した全例の全器官・組織について標本作製を実施し、対照群および高用量群の全例について鏡検した。雄の精巣の精子形成を精査した。腎臓および前立腺については全群の動物について検査した。その他に剖検で異常がみられた 4 mg/kg 群の精巣上体（動物番号 208）、胃、肝臓および胸腺（動物番号 255）、20 mg/kg 群の乳腺（動物番号 361）について検査した。

検査方法　：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て鏡検した。肝臓についてはさらに Oil red O 染色標本（動物番号 106、108、110、112、255、465）、腎臓については α_{2u}-グロブリン染色標本（動物番号 109、210、304、403、404）を作製し、それぞれ中性脂肪あるいは α_{2u}-グロブリンの確認を実施した。

Ⅱ．生殖発生毒性

1）性周期検査

例数　　：雌の全例

期間　　：投与開始日から主試験群は交尾成立まで、サテライト群は剖検日のみ。

方法　　：ギムザ染色による膣垢塗抹標本を作製し、光学顕微鏡下で性周期段階を観察した。

判定　　：性周期の各段階（発情前期、発情期、発情後期および発情休止期）を判定し、平均発情期間隔を算出した。平均発情期間隔が 4.0～6.0 を正常周期と判断した。

2）生殖能検査

例数　　：主試験群の雌雄の全例

時期、方法　：投与 14 日を交配開始日、交配開始日の翌日を交配 1 日とし、交配開始日の夕刻から、同試験群内の雌雄 1 対を交尾が確認されるまで 4 日間連続同居させた。

交配組み合せ　：無作為組み合せ

交尾成立の判定基準：膣内または受皿上に落下した膣栓、あるいは膣垢スメア標本中の精子確認により判定した。いずれかが認められた日を妊娠 0 日とした。

次式から群毎に交尾率を算出した。

$$\text{交尾率(Copulation index、\%)} = \frac{\text{交尾した雄/雌の数}}{\text{同居させた雄/雌の数}} \times 100$$

受胎能　　：妊娠の確認を分娩の有無および剖検時に子宮内の着床痕の計数により行った。

次式から群毎に受胎率を算出した。

$$\text{受胎率(Fertility index、\%)} = \frac{\text{受胎動物数}}{\text{交尾した雄/雌の数}} \times 100$$

3）分娩および哺育状態観察

例数　　：受胎した雌の全例

分娩観察　　：交尾が確認された雌動物は全例自然分娩させた。

分娩状態を妊娠 21 日から 25 日まで、毎日少なくとも 3 回（9：00、13：00 および 17：00）観察した。

分娩終了の確認　：9：00 に母動物が児を巣の中に集めて腹の下に抱え込んでいるのが観察された場合に分娩終了とし、その日を哺育 0 日（生後 0 日）とした。1 匹以上の生存児を出産したものを正常出産とした。

次式から群毎に出産率を算出した。

$$出産率(Gestation\ index、\%)=\frac{生児出産雌数}{妊娠雌数}\times 100$$

出産児の観察　：生後0日に正常に出産した腹毎に生存児数と死亡児数とを計数し、それらの合計を出産児数とした。

次式から腹毎に出生率を算出した。

$$出生率(Live\ birth\ index、\%)=\frac{出産時生存児数}{出産児数}\times 100$$

出産児の性比の算出：生後0および4日に個々の児動物の性を肛門と生殖突起の間の長さで判定した。死亡児も含めた生後0日の全出産児、死亡例を含めない生後0日の生存児ならびに生後4日の生存児を対象として以下を算出した。

$$生後0日の全出産児の性比(Sex\ ratio)=\frac{雄出産児数}{雄出産児数+雌出産児数}$$

$$生後0日の生存児の性比(Sex\ ratio)=\frac{雄生存児数}{雄生存児数+雌生存児数}$$

$$生後4日の生存児の性比(Sex\ ratio)=\frac{雄生存児数}{雄生存児数+雌生存児数}$$

妊娠期間の算出　：妊娠0日から哺育0日までの期間の日数を計数した。

分娩率の算出　：剖検時に各雌の子宮内の着床痕を肉眼的に計数した。

次式から腹毎に分娩率を算出した。

$$分娩率(Delivery\ index、\%)=\frac{出産児数}{着床数}\times 100$$

着床率の算出　：剖検時に各雌の卵巣の黄体数を計数した。

次式から腹毎に着床率を算出した。

$$着床率(Implantation\ index、\%)=\frac{着床数}{黄体数}\times 100$$

哺育4日の哺育率の算出：次式から群毎に算出した。

$$哺育率(Nursing\ index、\%)=\frac{哺育4日に生存児を持つ雌数}{生児出産雌数}\times 100$$

4) 新生児の一般状態観察および生存率

例数　：全例

頻度　：1回／日

期間　：生後0日から生後4日（剖検日）までとした。

観察方法　　：生存または死亡を確認し、一般状態および外表について観察した。
なお、死亡例は発見後速やかに剖検し、Whole body を 10%中性緩衝ホルマリン液で固定･保存した。

生後 4 日の新生児生存率の算出：次式により 1 腹単位で算出した。

$$\text{新生児生存率 (Viability index、\%)} = \frac{\text{生後 4 日の生存児数}}{\text{出産時生存児数}} \times 100$$

5) 新生児の体重測定

例数･時期　　：生存児全例について、生後 0、1 および 4 日に実施した。

測定方法　　：電子式上皿天秤（GX-2000、株式会社エー・アンド・デイ）を用いて雌雄別に個体別に測定し、0.1 g まで記録した。
雌雄毎に腹当たりの平均体重を求めた。

6) 新生児の剖検

時期･例数　　：生後 4 日に全例について実施した。

検査方法　　：体外表（口腔内を含む）を観察し、二酸化炭素吸入法により安楽死させ、全身の器官･組織を肉眼的に観察した。異常例については、Whole body を 10%中性緩衝ホルマリン液に固定・保存した。

5. 統計学的方法

握力、自発運動量、体重、体重増加量および増加率、摂餌量、尿量、血液学的検査、血液化学的検査、器官の絶対重量および相対重量、発情期間隔、黄体数、着床数および着床率、出産児数、出産時の生存児数および死亡児数、分娩率、出生率、性比、妊娠期間、生後 4 日の生存児数および新生児生存率の成績について平均値および標準偏差を算出し、Bartlett の検定法を行い等分散性を解析する。等分散($p > 0.05$)の場合は一元配置分散分析法で解析し、その結果、有意差がみられた場合($p \leq 0.10$)は Dunnett の検定法を用いて対照群との比較を行った。不等分散($p \leq 0.05$)の場合は Kruskal-Wallis の検定法で解析し、有意差がみられた場合($p \leq 0.10$)は Steel の検定法を用い対照群との比較を行った。なお、新生児の出生率、性比、新生児生存率および雌雄別体重については、1 腹を標本単位とした。

詳細な一般状態観察および機能検査の観察項目、尿検査の定性的項目、尿比重ならびに病理組織学的検査のうち 2 段階以上のグレードが認められた所見については、群毎の傾向を Kruskal-Wallis の検定法で解析し、有意差がみられた場合($p \leq 0.05$)は Steel の検定法を用いて対照群との比較を行った。

異常性周期の雌の出現率、交尾率、受胎率、出産率、哺育 4 日の哺育率、ならびに病理組織学的検査のうち 1 段階のグレードが認められた所見については、多試料カイ二乗検定を行い、その結果有意差が認められた場合($p \leq 0.05$)には 2 試料カイ二乗検定で対照群との比較

を行った。ただし、2試料カイ二乗検定に不適合の場合にはFisherの直接確率検定法を用いた。

対照群との比較検定については、有意水準は5%とした。

なお、死亡例の器官重量は集計から除外した。

成　績

Ⅰ. 反復投与毒性

1. 一般状態

一般状態の成績をTable 1～3、INDIVIDUAL DATA 1-1～3-4に示す。

(1) 主試験群雄

投与期間中、対照群の1例で投与23～24日に赤色尿が認められた。

被験物質投与群ではいずれの動物にも投与期間中および回復期間中に異常は認められなかった。

(2) 主試験群雌

交配前では、20 mg/kg群の1例(No. 357)で投与7～10日に上切歯の破折が認められた。

妊娠期間中では、100 mg/kg群の1例で妊娠10日に粘液便および淡緑色便が認められた。

哺育期間中では、対照群の1例(動物番号155)で分娩日に肛門・生殖器周辺の被毛汚染が認められ、哺育1日に粘液便、眼および口周囲の被毛汚染、哺育2日に体温低下が認められ、哺育3日に死亡した。その他、20 mg/kg群の1例(No. 353)に哺育1日～4日に上切歯の破折がみられたが、翌日の剖検日には消失した。他の1例(No. 361)で分娩日から鼠径部に皮下腫瘤が認められた。4および100 mg/kg群の動物には異常は認められなかった。

(3) サテライト群雌

投与期間中、100 mg/kg群の1例で投与9日および29日に粘液便が認められた。

回復期間中では、対照群および100 mg/kg群の動物には異常は認められなかった。

2. 詳細な一般状態観察

詳細な一般状態観察の成績をTable 4-1-1～6-3-2、INDIVIDUAL DATA 4-1-1～6-9-6、スコアリングの基準をINDIVIDUAL DATA 4-1-1の前に示す。

(1) 主試験群雄

投与期間中および回復期間中の観察では、いずれの項目にも各被験物質投与群と対照群の間に有意な差は認められなかった。

(2) 主試験群雌

投与期間中の観察では、いずれの項目にも各被験物質投与群と対照群の間に有意な差は認められなかった。

(3) サテライト群雌

投与期間中および回復期間中の観察では、いずれの項目にも 100 mg/kg 群と対照群との間に有意な差は認められなかった。

3. 機能検査

機能検査の成績を Table 7-1～9-2、INDIVIDUAL DATA 7-1-1～9-4-2、スコアリングの基準を INDIVIDUAL DATA 4-1-1 の前に示す。

(1) 主試験群雄

投与 6 週の検査では、100 mg/kg 群で前肢握力に対照群と比較して有意な低下が認められた。刺激に対する各感覚運動反応および自発運動量では、いずれの被験物質投与群にも対照群と比較して有意な差はみられなかった。

回復 2 週の検査では、いずれの検査項目についても、100 mg/kg 群と対照群との間に有意な差は認められなかった。

(2) 主試験群雌

哺育 4 日の検査では、4 mg/kg 群で自発運動量の 50-60 分および Total に、対照群と比較して有意な高値が認められたが、用量関連性のない変動であり、被験物質投与による変化ではないと考えられた。その他の検査項目では、いずれの被験物質投与群にも対照群と比較して有意な差は認められなかった。

(3) サテライト群雌

投与 6 週の検査では、100 mg/kg 群で自発運動量の 50-60 分に対照群と比較して有意な高値が認められた。その他の項目では 100 mg/kg 群と対照群の間に有意な差は認められなかった。

回復 2 週の検査では、いずれの項目にも 100 mg/kg 群と対照群の間に有意な差は認められなかった。

4. 体重推移

体重推移を Figure 1～3、Table 10～12、INDIVIDUAL DATA 10-1～12-2 に示す。

(1) 主試験群雄

投与期間中、100 mg/kg 群では体重の増加抑制が認められ、投与 21 および 28 日の体重に対照群と比較して有意な低値が認められ、投与期間中の体重の増加量および増加率に対照群と比較して有意な低値がみられた。

回復期間中、体重、体重の増加量および増加率に 100 mg/kg 群と対照群との間に有意な差は

認められなかった。

(2) 主試験群雌

交配前では、100 mg/kg 群で投与 3 日から体重増加抑制傾向が認められ、投与 14 日間の体重の増加量および増加率に対照群と比較して有意な低値が認められた。

妊娠期間中、100 mg/kg 群では交配前の体重増加抑制に引き続き低推移が認められ、妊娠 5 日および 20 日の体重に対照群と比較して有意な低値を示した。体重の増加量および増加率には対照群と比較して有意な差は認められなかった。

哺育期間中、体重、体重の増加量および増加率において、いずれの被験物質投与群にも対照群と比較して有意な差はみられなかった。

(3) サテライト群雌

投与期間中、100 mg/kg 群では体重増加抑制が認められ、投与 3 日および投与 7～42 日の体重に対照群と比較して有意な低値が認められ、体重の増加量および増加率も有意な低値を示した。

回復期間中、100 mg/kg 群の体重および体重増加量には対照群と比較して有意差はなく、体重増加率に有意な高値が認められた。

5. 摂餌量

摂餌量を Figure 4～6、Table 13～15、INDIVIDUAL DATA 13-1～15-2 に示す。

(1) 主試験群雄

投与期間中、100 mg/kg 群の投与 1～3 日に対照群と比較して有意な低値が認められた。4 および 20 mg/kg 群では対照群と比較して有意な差は認められなかった。

回復期間中、100 mg/kg 群では対照群と比較して有意な差は認められなかった。

(2) 主試験群雌

交配前では、100 mg/kg 群の投与 1～3 日、7～10 日に対照群と比較して有意な低値が認められた。4 および 20 mg/kg 群では対照群と比較して有意な差は認められなかった。

妊娠および哺育期間中では、いずれの被物質投与群にも対照群との間に有意な差は認められなかった。

(3) サテライト群雌

投与期間中、100 mg/kg 群の投与 1～3 日、5～7 日、10～14 日および 28～35 日に対照群と比較して有意な低値が認められた。

6. 尿検査

尿検査の成績を Table 16-1-1～17-2-2、INDIVIDUAL DATA 16-1-1～17-2-4 に示す。

(1) 主試験群雄

投与6週および回復2週の検査では、いずれの項目にも被験物質投与群と対照群の間に有意な差はみられなかった。

(2) サテライト群雌

投与6週の検査では、100 mg/kg群の尿沈査において、軽度の扁平上皮細胞の出現が5例中3例に認められ、対照群との間に有意な差が認められた。その他、100 mg/kg群で尿蛋白の程度が対照群と比較して有意に低かったが、毒性学的に意義のない変化であった。

回復2週の検査では、100 mg/kg群の尿沈査において、扁平上皮細胞の出現は5例全例に認められず、対照群では軽度の出現が5例中3例に認められた。

7. 血液学的検査

血液学的検査の成績を Table 18-1-1～20-2、INDIVIDUAL DATA 18-1-1-20-2-4 に示す。

(1) 主試験群雄

投与期間終了時(投与6週後)の検査では、20および100 mg/kg群で平均赤血球ヘモグロビン濃度に対照群と比較して有意な低値、100 mg/kg群の網赤血球数に有意な高値が認められた。その他、4 mg/kg群で活性化部分トロンボプラスチン時間に対照群と比較して有意な短縮が認められたが、用量関連性のない変動であり、被験物質投与による変化ではないと考えられた。

回復期間終了時(回復2週後)の検査では、100 mg/kg群の活性化部分トロンボプラスチン時間が対照群と比較して有意に延長した。

(2) 主試験群雌

投与期間終了時(哺育5日)の検査では、いずれの項目にも被験物質投与群と対照群を比較して有意な差は認められなかった。

(3) サテライト群雌

投与期間終了時(投与6週後)の検査では、100 mg/kg群で網赤血球数および活性化部分トロンボプラスチン時間に対照群と比較して有意な高値が認められた。

回復期間終了時(回復2週後)の検査では、いずれの項目にも100 mg/kg群と対照群を比較して有意な差は認められなかった。

8. 血液化学的検査

血液化学的検査の成績を Table 21-1-1～23-2、INDIVIDUAL DATA 21-1-1～23-2-4 に示す。

(1) 主試験群雄

投与期間終了時(投与6週後)および回復期間終了時(回復2週後)の検査には、いずれの項目においても、各被験物質投与群と対照群を比較して有意な差は認められなかった。

(2) 主試験群雌

投与期間終了時(哺育5日)の検査では、いずれの項目にも被験物質投与群と対照群と比較して有意な差は認められなかった。

(3) サテライト群雌

投与期間終了時(投与6週後)の検査では、100 mg/kg群で尿素窒素に対照群と比較して有意な低値が認められた。

回復期間終了時(回復2週後)の検査では、100 mg/kg群のA/G比の有意な高値、蛋白分画のアルブミン比の有意な高値、グロブリンα_1の有意な低値、カリウムに有意な低値が認められた。

9. 剖検所見

剖検所見をTable 24～26、INDIVIDUAL DATA 24-1-1～26-2-2に示す。

(1) 主試験群雄

投与期間終了時(投与6週後)では、片側精巣上体尾部において4 mg/kg群の1例および100 mg/kg群の2例に黄白色斑、対照群の1例に黄白色腫瘤が認められた。

回復期間終了時(回復2週後)では、いずれの群の動物にも異常は認められなかった。

(2) 主試験群雌

哺育3日に死亡した対照群の1例(動物番号155)の剖検では、前胃および腺胃粘膜に多巣性の黒色斑、脾臓および胸腺の委縮ならびに副腎肥大が認められた。

投与期間終了時(哺育5日)の剖検では、4 mg/kg群の1例(動物番号255)に前胃粘膜クレータ状の肥厚および陥凹部、胃の境界縁の肥厚、胃と脂肪組織との癒着、肝臓の黄褐色化、胸腺委縮が認められた。その他、対照群の1例に胃境界縁白色腫瘤、4 mg/kg群の1例に腺胃粘膜に黒色斑、20 mg/kg群の1例で鼠径部に緑褐色腫瘤、100 mg/kg群の1例に片側腎盂拡張が認められた。

(3) サテライト群雌

投与期間終了時(投与6週後)では、対照群の1例に腺胃粘膜に黒色斑、100 mg/kg群の1例に腺胃粘膜に隆起部が認められた。

回復期間終了時(回復2週後)ともに、いずれの群の動物にも異常は認められなかった。

10. 器官重量

器官の絶対重量および相対重量の成績をTable 27-1～29-2、INDIVIDUAL DATA 27-1-1～29-2-4に示す。

(1) 主試験群雄

投与期間終了時(投与6週後)では、いずれの被験物質投与群も対照群と比較して、有意な差は認められなかった。

回復期間終了時(回復2週後)では、100 mg/kg群において、対照群と比較して心臓の絶対重

量の有意な低値、精巣上体の相対重量の有意な高値、前立腺の絶対および相対重量の有意な低値、精嚢の絶対重量に有意な低値が認められた。

(2) 主試験群雌

投与期間終了時(哺育5日)では、いずれの器官においても各被験物質投与群と対照群との間に有意な差は認められなかった。剖検時体重において、100 mg/kg 群で対照群と比較して有意な低値が認められた。

(3) サテライト群雌

投与期間終了時(投与6週後)では、100 mg/kg 群において、対照群と比較して肝臓の相対重量の有意な高値、心臓の絶対重量の有意な低値、脳の相対重量の有意な高値が認められた。これらは剖検時体重の有意な低値に起因した変動であり、被験物質投与との関連はないものと考えられた。

回復期間終了時(回復2週後)では、100 mg/kg 群の心臓の絶対重量の有意な低値、子宮の絶対および相対重量の有意な高値が認められた。100 mg/kg 群の剖検日の性周期において、発情前期から発情期を示す動物が3例(対照群では1例)認められたことに起因する偶発変動と考えられた。

11. 病理組織学的検査

病理組織学的検査の成績を Table 30-1～32-2、INDIVIDUAL DATA 30-1-1～32-2-4 に示す。

(1) 主試験群雄

投与期間終了時(投与6週後)の検査では、全群の検査を実施した前立腺において、軽度な炎症性細胞浸潤が対照群で1例、4 mg/kg 群で9例、20 mg/kg 群で4例、100 mg/kg 群で6例、中等度の変化が20 mg/kg 群で3例に認められ、Steel の統計学的検定法では、4および100 mg/kg 群の発生頻度に対照群と比較して有意な高値が認められた。腎臓において、近位尿細管上皮の軽度な好酸性小体(α_{2u}グロブリン陽性)が対照群および20 mg/kg 群で各1例、4 mg/kg 群で2例、100 mg/kg 群で4例に認められた。その他に尿細管上皮の軽度な好塩基性化が対照群、4および100 mg/kg 群で各1例に、軽度にのう胞が20 mg/kg 群の1例に認められた。100 mg/kg 群で眼球に軽度な網膜ロゼットが2例、ハーダー腺に軽度な単核細胞浸潤が1例に認められた。その他、100 mg/kg 群で肺胞マクロファージの軽度な集簇、肺動脈の鉱質沈着、肝臓の小肉芽腫、心臓に限局性炎症が少数例に認められたが、対照群の少数例にも同程度の変化が認められた。対照群には肝臓の小葉周辺性脂肪化が2例、下垂体前葉に軽度なのう胞が1例認められた。精巣上体に肉眼的所見が認められた対照群および4 mg/kg 群の各1例、100 mg/kg 群の2例では軽度あるいは中等度の精子肉芽腫が認められたが、対照群を除きいずれも片側性の変化であった。

回復期間終了時(回復2週後)の検査では、前立腺では、軽度な炎症性細胞浸潤が対照群で2

例および100 mg/kg群で3例に認められた。腎臓では近位尿細管上皮の軽度な好酸性小体(α2uグロブリン陽性)が100 mg/kg群で1例に認められた。100 mg/kg群のみに下垂体の前葉あるいは中間葉に軽度なのう胞が各1例、眼球に網膜ロゼットならびにハーダー腺に単核細胞浸潤が各1例に認められた。その他、肺胞内に軽度な骨化生、肺動脈の軽度な鉱質沈着、肝臓の軽度小肉芽腫、心臓に限局性の軽度な炎症が100 mg/kg群の1～3例に認められたが、対照群にも同程度の変化が認められた。その他、対照群のみに肺胞マクロファージの集簇および肝臓に小葉周辺性の脂肪化が各2例、膵臓の腺房細胞の限局性の萎縮、腎臓尿細管上皮の好塩基性変化および眼球網膜の限局性の委縮が各1例に認められ、いずれも軽度な変化であった。

(2) 主試験群雌

哺育3日で死亡が認められた対照群の1例では、前胃および腺胃に軽度なびらん、腎皮質の尿細管に軽度な拡張、脾臓に中等度の濾胞委縮、軽度なヘモジデリン沈着、胸腺に中等度の委縮、副腎に重度な炎症性細胞浸潤を伴う皮質細胞の壊死が認められた。

生存例では、100 mg/kg群にのみ腎盂の軽度な拡張が1例、下垂体前葉に軽度なのう胞が1例、眼球の網様体および虹彩の軽度な好中球浸潤が1例に認められた。その他に肺胞内マクロファージ集簇、肝臓に小肉芽腫、限局性の壊死が100 mg/kg群の少数例に認められたが、対照群の少数例にも同程度の変化が認められた。対照群のみに胃境界縁に扁平上皮の軽度なのう胞が1例に認められた。肉眼所見の認められた4 mg/kg群の1例(No. 255)では、前胃に中等度の潰瘍、胃境界縁の中等度の扁平上皮過形成、中等度の肝臓小葉周辺性の脂肪化、尿細管上皮の脂肪化、中等度の胸腺委縮が認められ、他の1例(No. 259)では腺胃に軽度なびらんがみられた。また、20 mg/kg群の1例では乳腺に軽度な炎症を伴う過形成が認められた。

(3) サテライト群雌

投与期間終了時(投与6週後)の検査では、100 mg/kg群で肺胞内マクロファージ集簇およびハーダー腺に単核細胞の浸潤が1例、腺胃粘膜下に軽度な異所性導管組織あるいは肝臓小葉周辺性の軽度な脂肪化が各1例に認められた。対照群のみに腺胃びらん、肝臓の軽度な小肉芽腫、心臓に限局性の軽度な炎症、腎盂粘膜に炎症性細胞浸潤がそれぞれ1例に認められた。

回復期間終了時(回復2週後)の検査では、100 mg/kg群にのみ膵臓の腺房細胞の委縮、肝臓に小肉芽腫が各1例認められた。肺動脈に軽度な鉱質沈着が100 mg/kg群で1例および対照群で3例に認められた。その他、対照群のみに、肺胞内マクロファージ集簇、肺胞内骨化生、腎盂粘膜に炎症性細胞浸潤が各1例に認められた。

Ⅱ. 生殖発生毒性

1. 生殖能検査

生殖能検査の成績を Table 33および34、INDIVIDUAL DATA 33-1-1～34-4に示す。

性周期の異常周期を示す動物はいずれの群にも認められず、交尾率、受胎率、出産率はいず

性周期の異常周期を示す動物はいずれの群にも認められず、交尾率、受胎率、出産率はいずれの群も100%であり、平均発情期間隔、妊娠期間および哺育4日の哺育率には、被験物質投与群と対照群を比較して有意な差は認められなかった。

2. 妊娠、分娩、哺育状態および新生児生存率

妊娠、分娩、哺育状態および新生児生存率の成績を Table 34、INDIVIDUAL DATA 34-1～34-4、35-1 に示す。

黄体数、着床数、着床率、分娩率、出産児および生存児の性比、出産時の生存児数および死亡児数、出生率、生後4日の性比、生存児数および新生児生存率には、被験物質投与群と対照群の間に有意な差はみられなかった。なお、対照群の1例(動物番号155)では娩出児に乳汁(ミルクバンド)がみられず、翌日までにはすべての児が死亡した。母動物の分娩日以降の状態不良により、哺育が充分できなかったものと推察された。

3. 新生児の一般状態

新生児の一般状態の成績を Table 35、INDIVIDUAL DATA 35-1～35-4 に示す。

対照群で観察された1例の母動物を除き、すべての群で、生後0日から生後4日までの期間の死亡または不明児（母動物に食されたと推測）が少数例に認められた。その多くは胃内に乳汁がみられなかった。いずれの群の新生児にも外表異常は認められなかった。

4. 新生児の体重推移

新生児の体重推移を Figure 7、Table 36、INDIVIDUAL DATA 36-1～36-4 に示す。

4 mg/kg 群において、雌雄の生後0日、雌で生後1日の体重に対照群と比較して有意な高値がみられたが、用量関連はなく、偶発変動と考えられた。20 および 100 mg/kg 群では対照群と比較して有意な差はみられなかった。

5. 新生児の剖検

新生児の剖検の成績を Table 37、INDIVIDUAL DATA 37-1～37-2-4 に示す。

死亡児の剖検では、20 mg/kg 群の雌1例に肝臓に黄白色化および脾臓の褪色が認められ、その他の観察可能な死亡児には異常は認められなかった。生後4日の生存児の剖検では、対照群の雌1例に肝臓中間葉に黄白色斑が認められた。その他の動物には異常は認められなかった。

考　察

indene を、0（対照、トウモロコシ油）、4、20 および 100 mg/kg/day の用量で、1群雌雄各 12 匹の Crl:CD(SD) ラットにおいて、雄には計 42 日間、雌に交配前 14 日間、交配期間および妊娠期間ならびに分娩後 4 日までの最長 45 日間連日経口投与し、雌雄動物の反復投与による影響、

mg/kg について、雄動物は投与 42 日後にそれぞれ 5 匹を選抜して 14 日間の回復性を検討した。雌動物は 0 (対照)および 100 mg/kg を投与するサテライト群として各 10 匹を別に設定し、投与 42 日後に各群 5 匹を選抜して 14 日間の回復性を検討した。

1. 反復投与毒性

一般状態観察では、100 mg/kg 群の雌において、妊娠期間中に単発的に認められた粘液便および淡緑色便、同群のサテライト群雌で投与期間中に1例に単発的にみられた粘液便が認められた。この変化は 100 mg/kg のみの変化であり、被験物質投与との関連性があると考えられた。

詳細な一般状態観察では、雌雄とも被験物質投与に関連すると考えられる変化はいずれの投与群においてもみられなかった。

機能検査では、投与 6 週の検査で 100 mg/kg 群の雄で前肢握力の有意な低値が認められたが、回復 2 週の検査では同様の変化はみられず、回復性のあるものと考えられた。雌では握力に対する被験物質の影響は認められなかった。なお、同群のサテライト群の雌で 50-60 分時の自発運動量に有意な高値が認められたが、この変動値は回復 2 週の対照群のデータ値より低く、100 mg/kg 群と同程度の値であったこと、また、Total 値にはその傾向もみられていないことから、被験物質投与の影響ではないと考えられた。

体重では、100 mg/kg 群の雌雄(サテライト群の雌を含む)ともに投与初期から体重増加抑制が認められ、投与期間中低推移を示した。しかし、雄およびサテライト群の雌では回復期間中の体重、体重増加量および体重増加率に対照群との間に差はみられず、体重は回復傾向を示した。

摂餌量では、100 mg/kg 群の雄では投与初期に摂餌量の低値が認められ、同群のサテライト群の雌では投与期間中を通じて低値がみられた。

尿検査では、被験物質投与に起因する変化は認められなかった。なお、投与 6 週時の尿沈査で 100 mg/kg 群の雌に扁平上皮細胞が軽度に出現した例数に増加がみられたが、回復 2 週の尿沈査での対照群でも同程度の出現頻度が認められたことから、被験物質投与の影響ではないと考えられた。

血液学的検査では、投与期間終了時の 20 および 100 mg/kg 群の雄で平均赤血球ヘモグロビン濃度に有意な低値、100 mg/kg 群の雄およびサテライト群の雌の網赤血球数が有意な高値を示した。同群では体重および摂餌量に低値がみられていることから被験物質投与による毒性変化と考えられた。この貧血様変化は回復終了時の検査ではみられなかったことから、回復性のある変化と考えられた。20 mg/kg 群の雄でみられた平均赤血球ヘモグロビン濃度の有意な低値は、他の赤血球パラメータ、体重および摂餌量に影響が認められていないこと、当施設の背景データの範囲内であり[6]、対照群とは 2～3%程度のわずかな減少であることから、毒性変化ではないと考えられた。なお、回復期間終了時で 100 mg/kg 群の雄で活性化部分トロンボプラスチン時間に有意な延長が認められたが、投与終了時の対照群と同程度であったこと、また、当施設の背景データ[6]

延長が認められたが、投与終了時の対照群と同程度であったこと、また、当施設の背景データ[6]の範囲内にあったことから、被験物質投与の影響ではないと考えられた。

血液化学的検査では、被験物質投与に起因する変化は雌雄ともに認められなかった。なお、100 mg/kg 群のサテライト群の雌で尿素窒素に有意な低値が認められたが、当施設の背景データ[6]の範囲内であり、偶発変動と考えられた。

剖検では、100 mg/kg までの群に被験物質投与に起因する変化は雌雄ともに認められなかった。なお、100 mg/kg 群の雄 2 例に認められた精巣上体尾部の変化は片側性であり、被験物質投与に起因した変化ではないと考えられた。哺育 5 日の剖検でみられた 4 および 20 mg/kg 群の剖検所見は 100 mg/kg 群ではみられていない変化であり、被験物質投与によるものではないと考えられた。

器官重量では、100 mg/kg までの群に被験物質投与に起因する変動は雌雄ともに認められなかった。なお、雄の回復期間終了時に認められた前立腺の重量の有意な低値は投与終了時にはみられなかった変動であり、前立腺の病理組織学的検査でも後述するように被験物質投与に起因したと推測される変化は認められなかったこと、当施設の背景データ[6]の範囲内であることから偶発変動と考えられた。

病理組織学的検査では、前立腺に軽度な炎症性細胞の浸潤がすべての被験物質投与群で認められ、対照群と比較してその出現頻度が高値を示した。この所見の発生頻度は当施設の背景データ[7]でも過去 5 年間で高頻度にみられる変化(0.0～40.0%)であり、本試験ではそれを上回る発生頻度であった。しかし、対照群での発生頻度が 1 例と低く、群に偏りがあったこと、所見の程度に増強もみられないことから被験物質との関連性はないと考えられた。腎臓で認められた近位尿細管上皮の好酸性小体(α_{2u}グロブリン陽性)は 100 mg/kg 群の出現頻度がわずかに高かったが、当施設の背景データ[7]でも高頻度でみられる変化であり、統計学的にも有意差はなかったことから、被験物質投与の影響ではないと考えられた。その他、投与期間終了時および回復期間終了時の検査で 100 mg/kg 群にのみ少数例にみられた網膜ロゼットについては、発生分化異常の一つと言われる変化であり[7]、被験物質投与に起因したものではないと考えられた。その他、100 mg/kg 群の少数例にみられたハーダー腺の軽度な単核細胞浸潤、精子肉芽腫、膵臓の腺房細胞委縮については当施設の背景データでも認められる変化であり、被験物質投与に起因した変化ではないと考えられた。

以上をまとめると、indene の反復投与により 100 mg/kg 群の雄で平均赤血球ヘモグロビン濃度の低値、雌雄で網赤血球数の高値が認められ、貧血傾向が示唆された。また、100 mg/kg 群では雌雄ともに体重増加抑制および摂餌量減少が認められ、雄では前肢握力の低下がみられ、雌では単発的に粘液便が観察された。

これらの変化は被験物質投与の影響であるとともに全身状態に影響を及ぼしていることから被験物質投与による毒性と考えられた。

また、20 mg/kg群の雄で被験物質投与の影響とみられた平均赤血球ヘモグロビン濃度の低値は、他の赤血球パラメータ、体重および摂餌量に影響が認められなかったことから、毒性変化ではないと考えられた。

したがって、本試験条件下におけるindeneの無影響量（NOEL）は4 mg/kg/day、無毒性量(NOAEL)は20 mg/kg/dayと考えられた。

2. 生殖発生毒性

生殖能検査では、100 mg/kg 群まで、性周期には異常はなく、平均発情期間隔、交尾率、受胎率、着床率、出産率、分娩率、出産児数には、対照群との間に有意な差はみられなかった。

新生児の体重、一般状態および剖検では、100 mg/kg 群まで、被験物質投与に関連する変化はみられなかった。

以上をまとめると、100 mg/kg群まで、親動物の生殖能および新生児の発生に被験物質投与に関連した変化は認められなかった。

したがって、本試験条件下におけるindeneの反復投与による親動物の生殖に対する無影響量(NOEL) および無毒性量(NOAEL)ならびに新生児の発生に対する無影響量（NOEL)および無毒性量(NOAEL)はいずれも100 mg/kg/dayと考えられた。

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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要因および試験計画書に従わなかったことはなかった。

資料の保存

以下の試験関係資料を試験終了後 10 年間、株式会社 化合物安全性研究所の資料保存室に保存する。その後の保存については試験委託者との協議により決定する。

1) 試験計画書および試験計画書変更書
2) 生データその他の記録文書
3) 最終報告書
4) 標本：膣垢塗抹標本
   血液塗抹標本
   固定器官・組織
   病理組織標本(パラフィン包埋ブロックおよび光顕標本)
5) 被験物質サンプル

試験責任者の記名なつ印

試験責任者

[redacted] [redacted] 2012 年 3 月 28 日

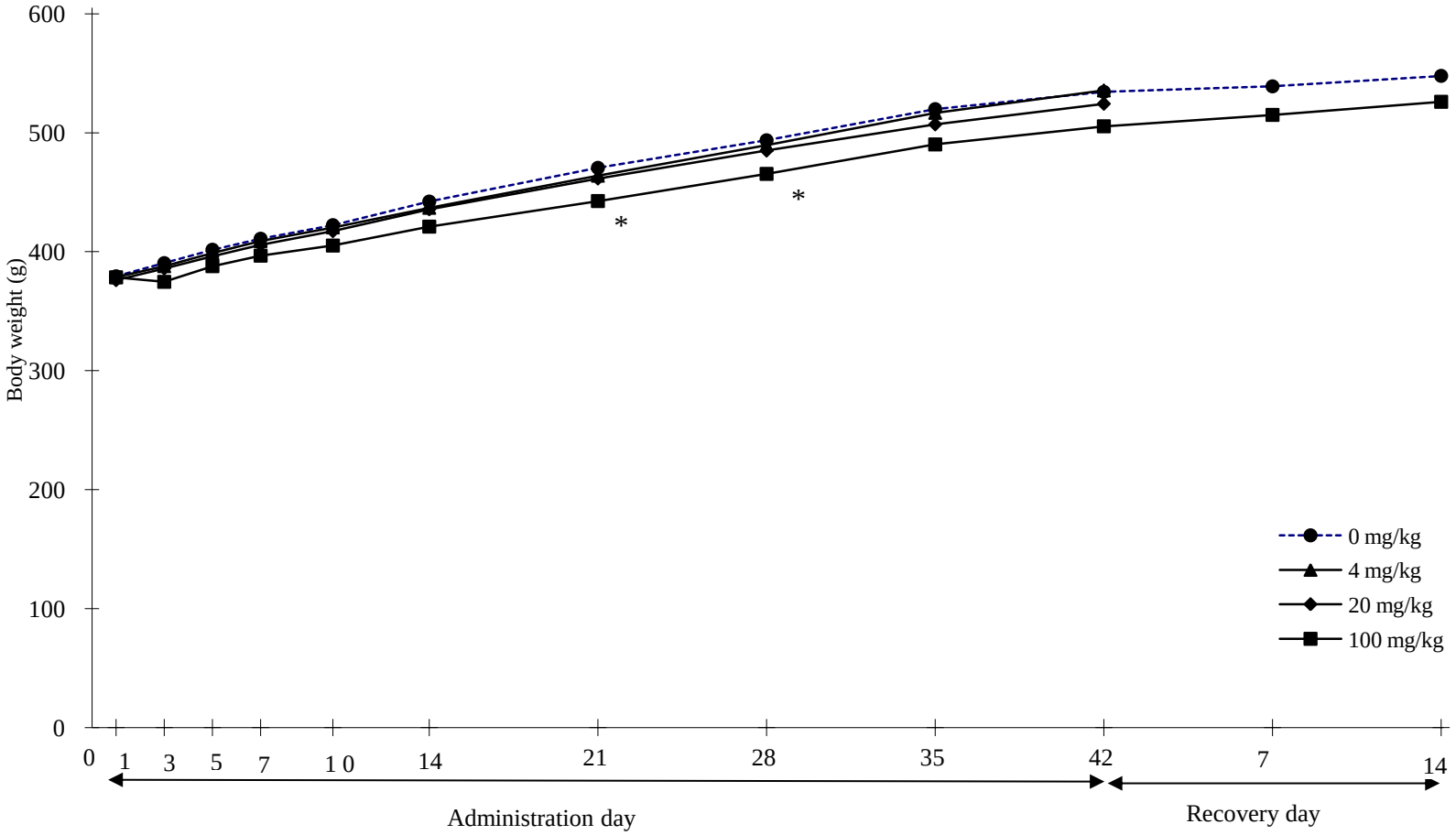


Figure 1 Body weight changes of male rats

indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

* : Significantly different from the 0 mg/kg group at $p \leqq 0.05$

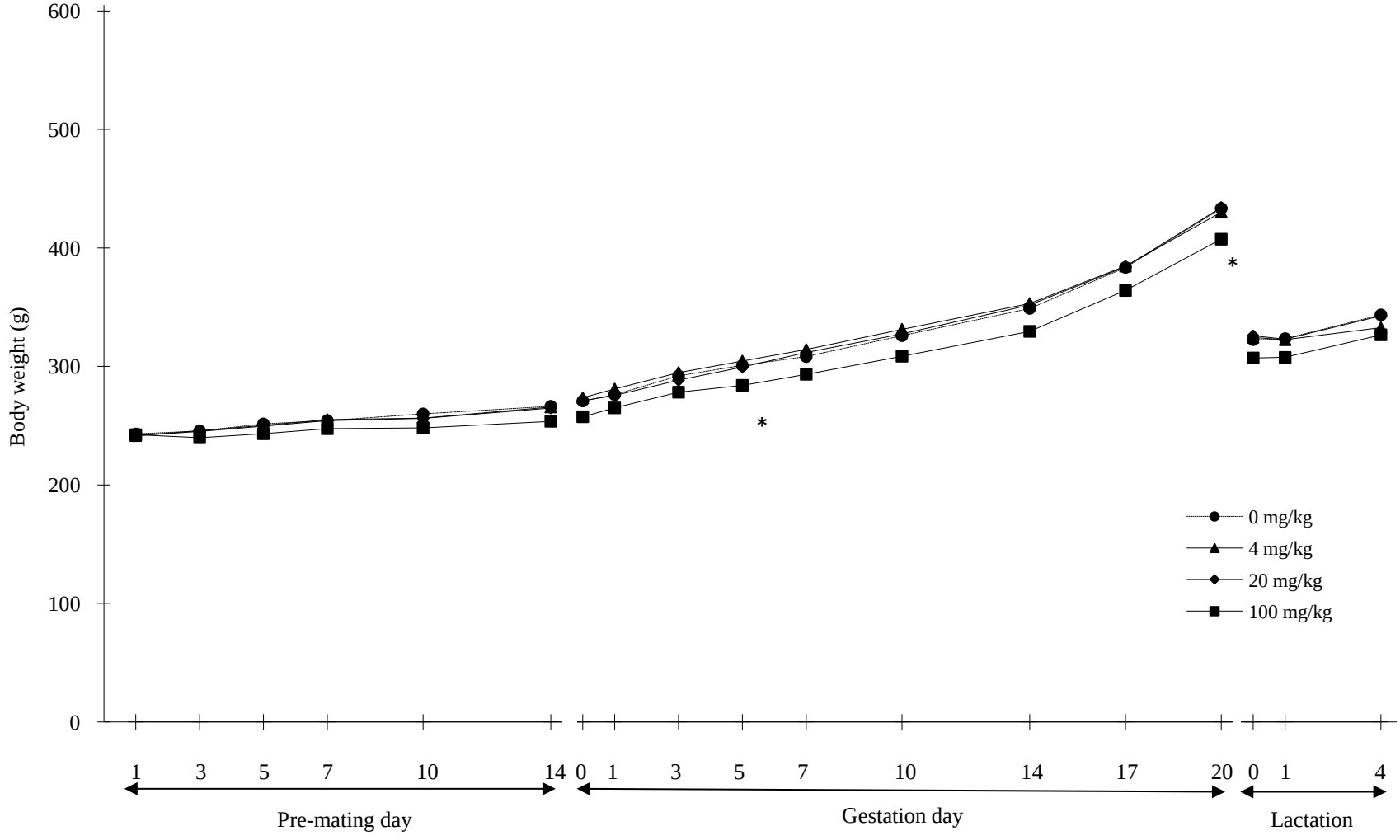


Figure 2 Body weight changes of female rats

indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

* : Significantly different from the 0 mg/kg group at $p \leqq 0.05$

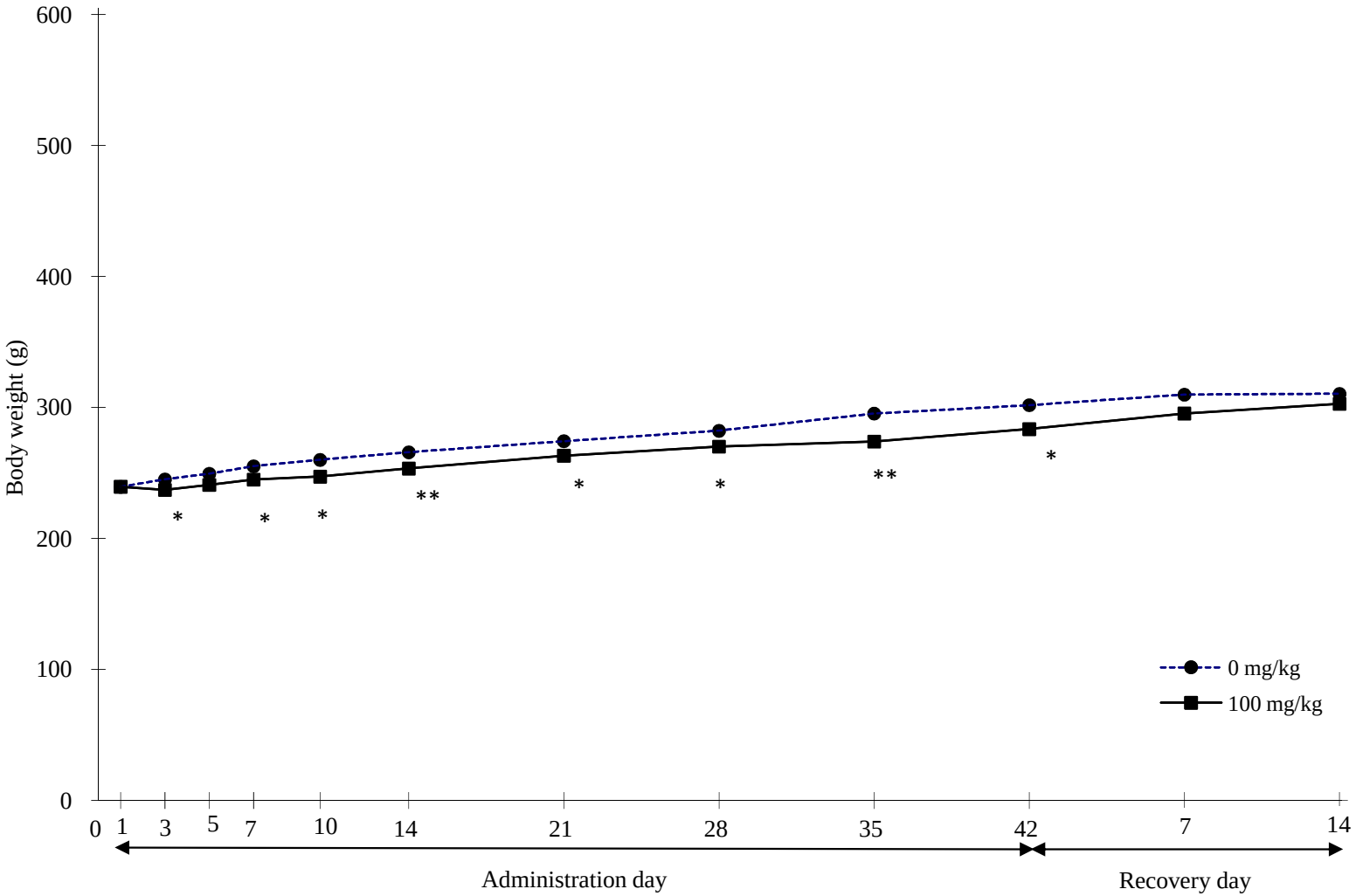


Figure 3 Body weight changes of female rats in the satellite group

indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

* : Significantly different from the 0 mg/kg group at $p \leqq 0.05$

** : Significantly different from the 0 mg/kg group at $p \leqq 0.01$

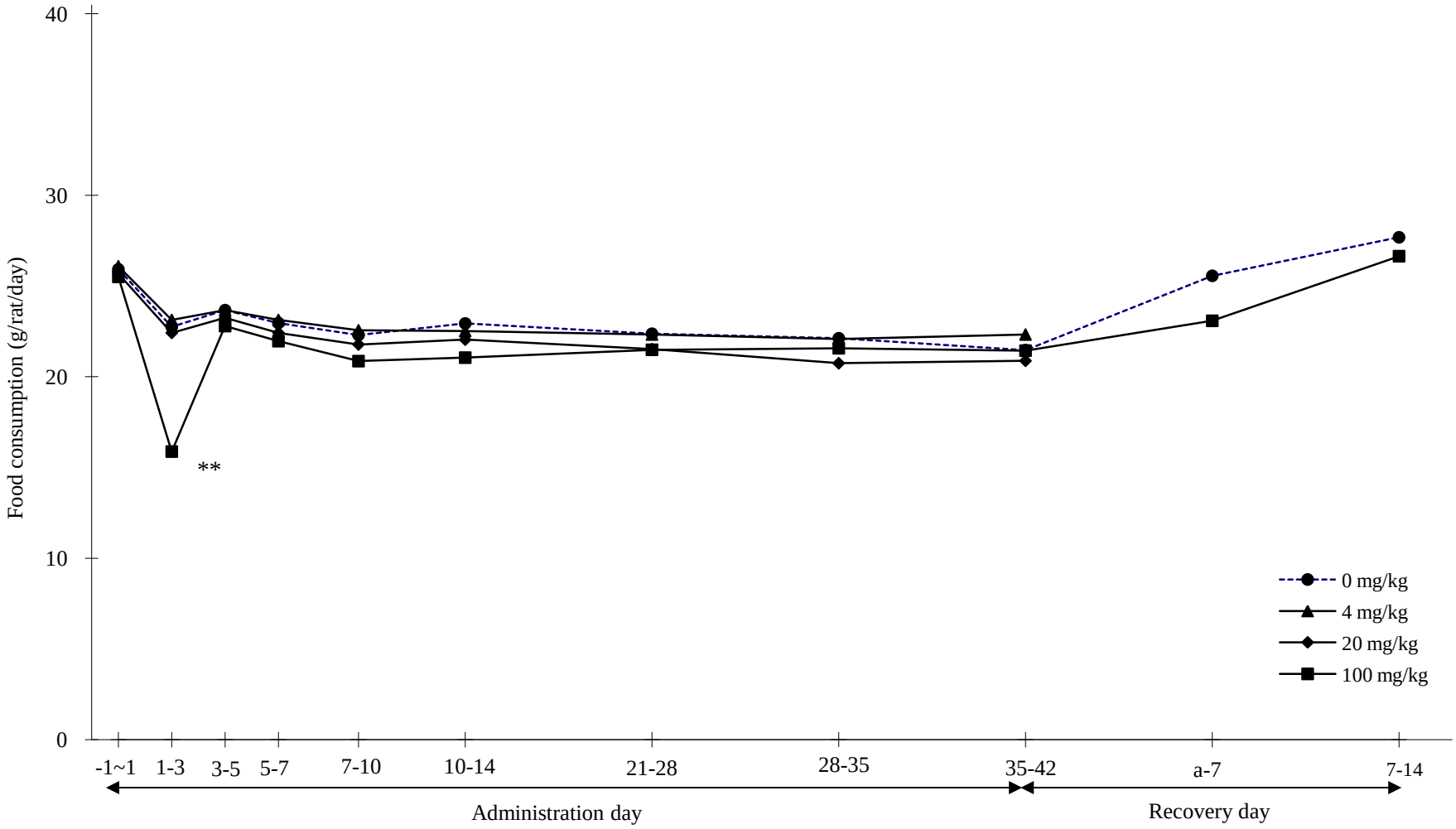


Figure 4 Food consumption of male rats

indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

** : Significantly different from the 0 mg/kg group at $p \leqq 0.01$

a: Day 42 of administration

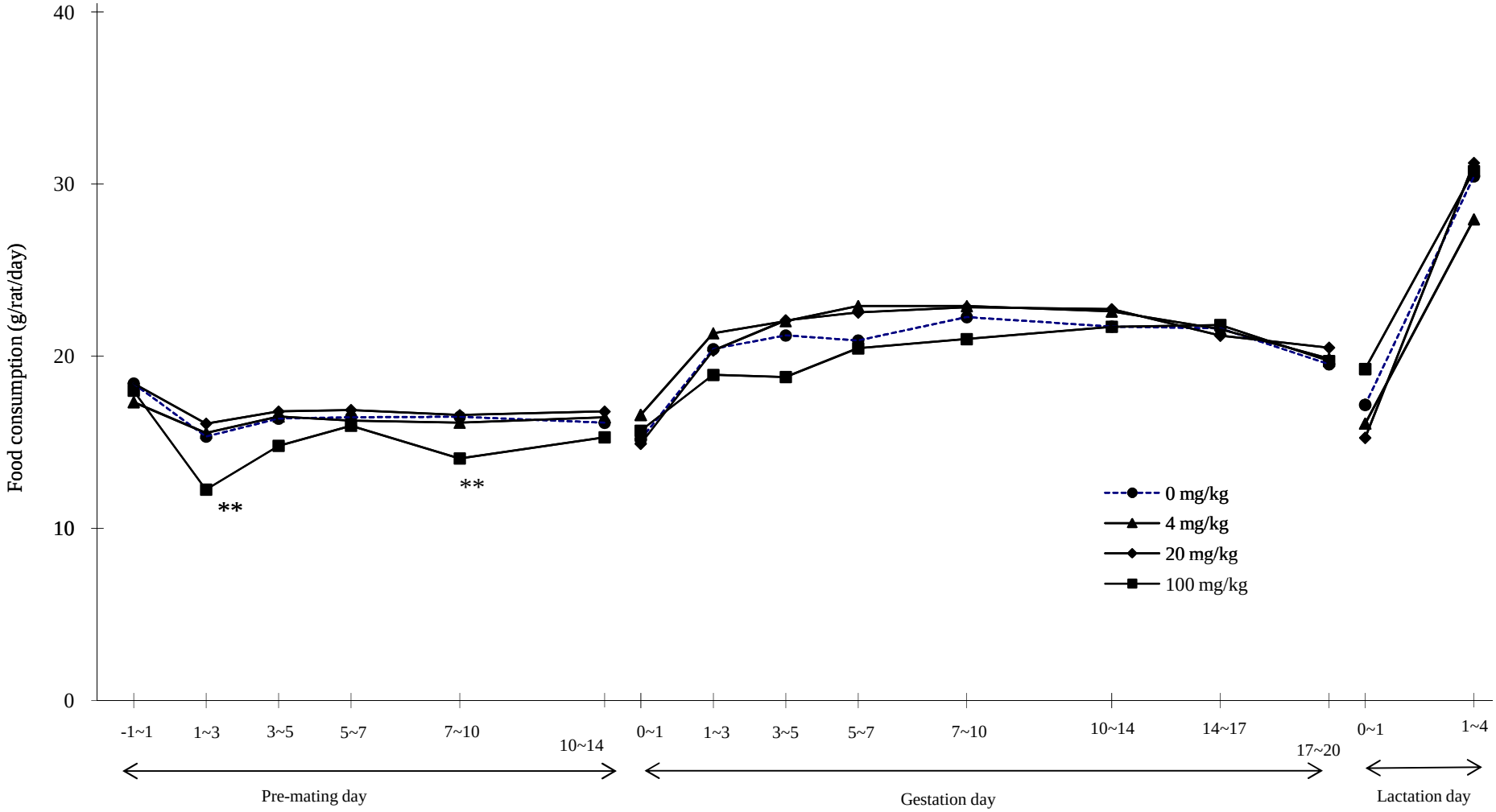


Figure 5 Food consunption of female rats

indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

** : Significantly different from the 0 mg/kg group at p ≦ 0.01

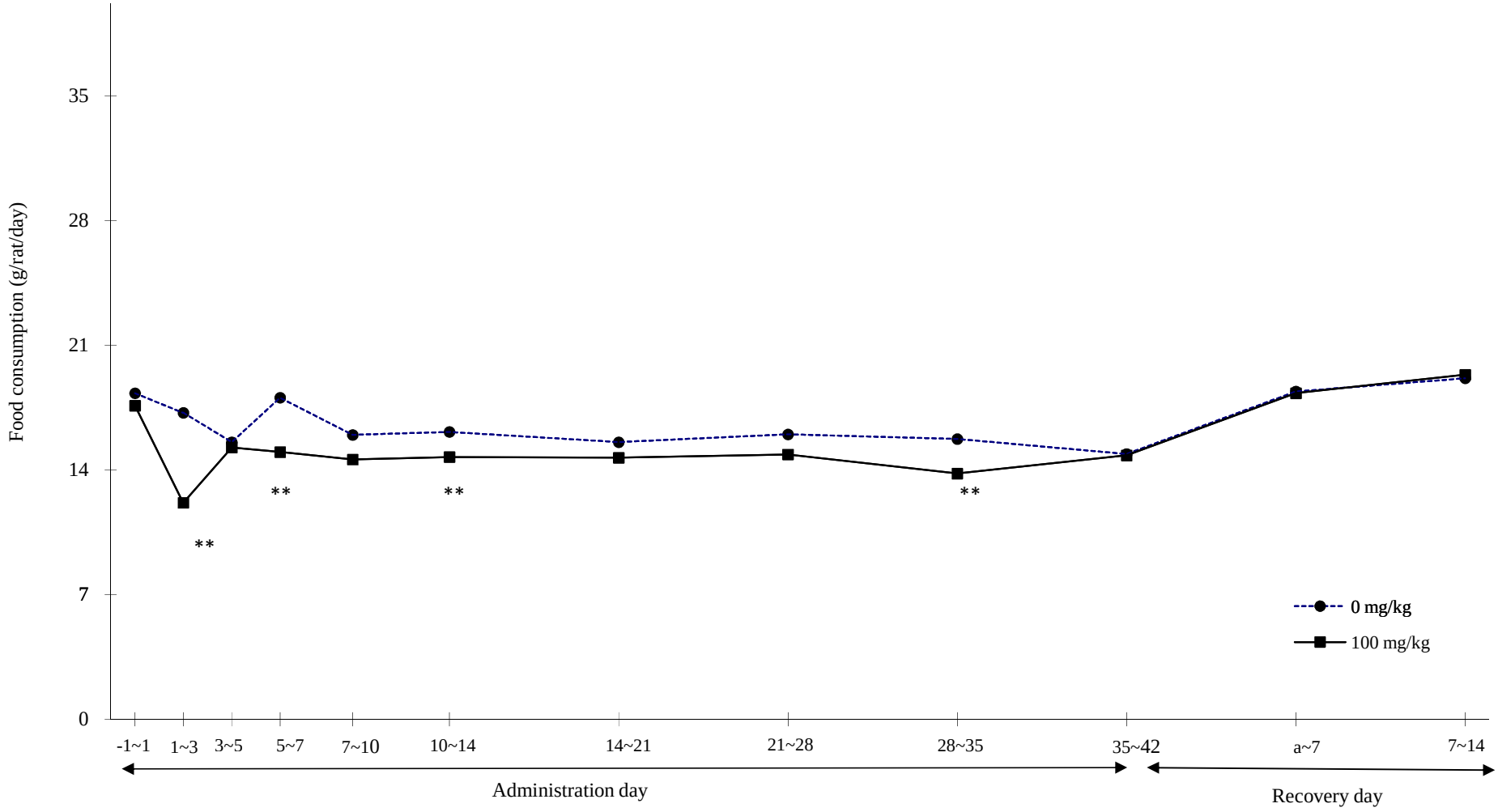


Figure 6 Food consumption of female rats in the satellite group

indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

** : Significantly different from the 0 mg/kg group at $p \leqq 0.01$

a: Day 42 of administration

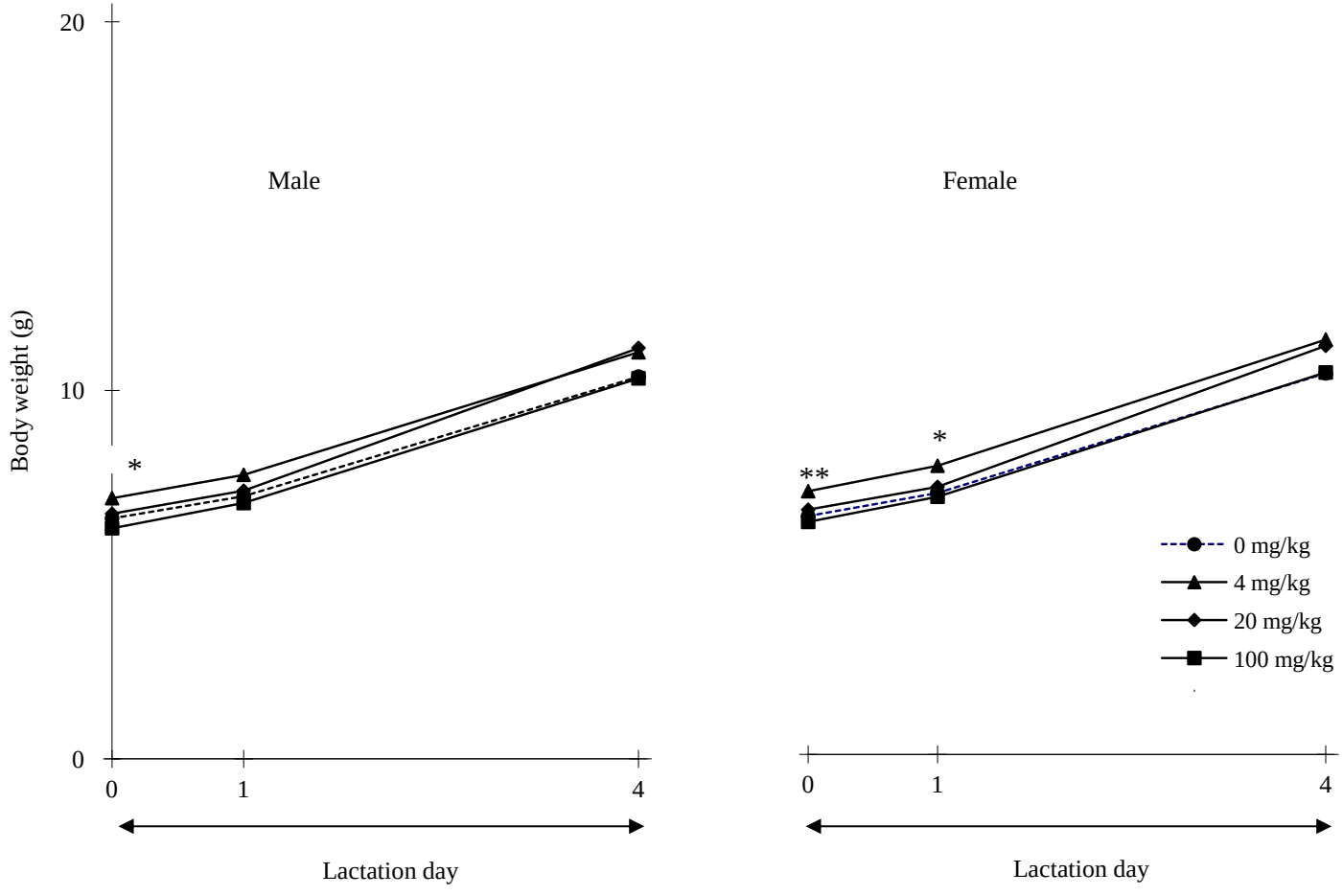


Figure 7 Body Weight changes of pups

indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

* : Significantly different from the 0 mg/kg group at P ≦ 0.05

** : Significantly different from the 0 mg/kg group at P ≦ 0.01

Table 1 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- General appearance of male rats -

Group	Findings	Administration period (day) 1-22	23-24	25-42	Autopsy day
0 mg/kg	Number of animals examined	12	12	12	7
	No abnormal findings	12	11	12	7
	Reddish urine	0	1	0	0
4 mg/kg	Number of animals examined	12	12	12	12
	No abnormal findings	12	12	12	12
20 mg/kg	Number of animals examined	12	12	12	12
	No abnormal findings	12	12	12	12
100 mg/kg	Number of animals examined	12	12	12	7
	No abnormal findings	12	12	12	7

Group	Findings	Recovery period (day) 1-14	Autopsy day
0 mg/kg	Number of animals examined	5	5
	No abnormal findings	5	5
100 mg/kg	Number of animals examined	5	5
	No abnormal findings	5	5

Values are number of animals with findings.

Table 2-1 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- General appearance of female rats in pre-mating period -

Group	Findings	Pre-mating period (day)					
		1-6	7-10	11-14	15	16	17
0 mg/kg	Number of animals examined	12	12	12	8	4	2
	No abnormal findings	12	12	12	8	4	2
4 mg/kg	Number of animals examined	12	12	12	8	7	3
	No abnormal findings	12	12	12	8	7	3
20 mg/kg	Number of animals examined	12	12	12	9	4	2
	No abnormal findings	12	11	12	9	4	2
	Fracture of rigth upper incisors	0	1	0	0	0	0
100 mg/kg	Number of animals examined	12	12	12	11	6	2
	No abnormal findings	12	12	12	11	6	2

Values are number of animal with findings.

Table 2-2 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- General appearance of female rats in gestation period -

Group	Findings	Gestation period (day)				
		0-9	10	11-21	22	23
0 mg/kg	Number of animals examined	12	12	12	5	0
	No abnormal findings	12	12	12	5	0
4 mg/kg	Number of animals examined	12	12	12	6	0
	No abnormal findings	12	12	12	6	0
20 mg/kg	Number of animals examined	12	12	12	4	1
	No abnormal findings	12	12	12	4	1
100 mg/kg	Number of animals examined	12	12	12	2	0
	No abnormal findings	12	11	12	2	0
	Mucous feces	0	1	0	0	0
	Pale Greenish stool	0	1	0	0	0

Values are number of animal with findings.

Table 2-3 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- General appearance of female rats in lactation period -

Group	Findings	Lactation period (day)					Autopsy day
		0	1	2	3	4	
0 mg/kg	Number of animals examined	12	12	12	12	11	11
	No abnormal findings	11	11	11	11	11	11
	Soil of perigenital fur	1	1	1	1	0	0
	Soil of perianal fur	1	1	1	1	0	0
	Soil of perioral fur	0	1	1	1	0	0
	Soil of periocular fur	0	1	1	1	0	0
	Mucous feces	0	1	1	0	0	0
	Hypothermia	0	0	1	0	0	0
	Dead	0	0	0	1	0	0
4 mg/kg	Number of animals examined	12	12	12	12	12	12
	No abnormal findings	12	12	12	12	12	12
20 mg/kg	Number of animals examined	12	12	12	12	12	12
	No abnormal findings	11	10	10	10	10	11
	Fracture of left upper incisors	0	1	1	1	1	0
	Subcutaneous mass, left side of inguinal region	1	1	1	1	1	1
100 mg/kg	Number of animals examined	12	12	12	12	12	12
	No abnormal findings	12	12	12	12	12	12

Values are number of animal with findings.

Table 3 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- General appearance of female rats in the satellite group -

Group	Findings	Administration period (day)					Autopsy day	Recovery period (day)	Autopsy day
		1-8	9	10-28	29	30-42		1-14	
0 mg/kg	Number of animals examined	10	10	10	10	10	5	5	5
	No abnormal findings	10	10	10	10	10	5	5	5
100 mg/kg	Number of animals examined	10	10	10	10	10	5	5	5
	No abnormal findings	10	9	10	9	10	5	5	5
	Mucous feces	0	1	0	1	0	0	0	0

Values are number of animal with findings.

Table 4-1-1 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Detailed clinical observation of male rats -

				In the cage					
							Stereotype		Bizarre behavior
Period	Group	Number of animals	Category No.	Body position/ Posture 1	Respiratory pattern 1	Tremor/ Convulsion 1	Rolling 0	Repetitive circling 0	Biting/ Selfmutilation 1
Days of administration									
Pre -	0 mg/kg	12		12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	12
Day 7	0 mg/kg	12		12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	12
Day 14	0 mg/kg	12		12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	12
Day 21	0 mg/kg	12		12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	12
Day 28	0 mg/kg	12		12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	12

Category : The category number observed in each item.

Pre : Pre-administration.

Table 4-1-2 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Detailed clinical observation of male rats -

				In the cage					
							Stereotype		Bizarre behavior
Period	Group	Number of animals	Category No.	Body position/ Posture 1	Respiratory pattern 1	Tremor/ Convulsion 1	Rolling 0	Repetitive circling 0	Biting/ Selfmutilation 1
Days of administration									
Day 35	0 mg/kg	12		12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	12
Day 42	0 mg/kg	12		12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	12
Days of recovery									
Day 7	0 mg/kg	5		5	5	5	5	5	5
	100 mg/kg	5		5	5	5	5	5	5
Day 14	0 mg/kg	5		5	5	5	5	5	5
	100 mg/kg	5		5	5	5	5	5	5

Category : The category number observed in each item.

Table 4-2-1 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Detailed clinical observation of male rats -

				On the hand											
				Ease of											
Period	Group	Number of animals	Category No.	Removal 1	Handling 1	Muscle tone 2	Piloerection 1	Fur 1	Eyes 1	Mucous membranes 0	Skin 1	Pupil size 1	Lacrimation 1	Salivation 1	Secretions/ Excretions 0
Days of administration															
Pre -	0 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
Day 7	0 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
Day 14	0 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
Day 21	0 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
Day 28	0 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12

Category : The category number observed in each item.

Pre : Pre-administration.

Table 4-2-2 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Detailed clinical observation of male rats -

Period	Group	Number of animals	Category No.	On the hand: Ease of Removal 1	Ease of Handling 1	Muscle tone 2	Piloerection 1	Fur 1	Eyes 1	Mucous membranes 0	Skin 1	Pupil size 1	Lacrimation 1	Salivation 1	Secretions/ Excretions 0
Days of administration															
Day 35	0 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
Day 42	0 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
Days of recovery															
Day 7	0 mg/kg	5		5	5	5	5	5	5	5	5	5	5	5	5
	100 mg/kg	5		5	5	5	5	5	5	5	5	5	5	5	5
Day 14	0 mg/kg	5		5	5	5	5	5	5	5	5	5	5	5	5
	100 mg/kg	5		5	5	5	5	5	5	5	5	5	5	5	5

Category : The category number observed in each item.

Table 4-3-1 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Detailed clinical observation of male rats -

				In the open-field												
												Stereotype		Bizarre behavior		
Period	Group	Number of animals	Category No.	Gait 1	Co-ordination of movement 1	Reactivity to environmental stimuli 1	Searching 1	Urination 0	Urination 1	Defecation 0	Defecation 1	Excessive grooming 0	Unusual head movement 0	Walking backward 1	Vocaliza-tion 1	Aggression 1
Days of administration																
Pre -	0 mg/kg	12		12	12	12	12	12	0	12	0	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	0	11	1	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	0	11	1	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	11	1	12	0	12	12	12	12	12
Day 7	0 mg/kg	12		12	12	12	12	10	2	12	0	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	10	2	12	0	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	0	12	0	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	10	2	12	0	12	12	12	12	12
Day 14	0 mg/kg	12		12	12	12	12	11	1	12	0	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	10	2	11	1	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	0	12	0	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	11	1	12	0	12	12	12	12	12
Day 21	0 mg/kg	12		12	12	12	12	11	1	12	0	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	0	12	0	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	11	1	11	1	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	0	12	0	12	12	12	12	12
Day 28	0 mg/kg	12		12	12	12	12	11	1	12	0	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	11	1	12	0	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	0	12	0	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	0	12	0	12	12	12	12	12

Category : The category number observed in each item.

Pre : Pre-administration.

Table 4-3-2 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Detailed clinical observation of male rats -

			In the open-field												
											Stereotype		Bizarre behavior		
Period	Group	Number of animals	Category No.	Gait 1	Co-ordination of movement 1	Reactivity to environmental stimuli 1	Searching 1	Urination 0	Urination 1	Defecation 0	Excessive grooming 0	Unusual head movement 0	Walking backward 1	Vocaliza-tion 1	Aggression 1
Days of administration															
Day 35	0 mg/kg	12		12	12	12	12	11	1	12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	0	12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	11	1	12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	0	12	12	12	12	12	12
Day 42	0 mg/kg	12		12	12	12	12	11	1	12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	0	12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	0	12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	0	12	12	12	12	12	12
Days of recovery															
Day 7	0 mg/kg	5		5	5	5	5	5	0	5	5	5	5	5	5
	100 mg/kg	5		5	5	5	5	5	0	5	5	5	5	5	5
Day 14	0 mg/kg	5		5	5	5	5	5	0	5	5	5	5	5	5
	100 mg/kg	5		5	5	5	5	4	1	5	5	5	5	5	5

Category : The category number observed in each item.

Table 5-1-1 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Detailed clinical observation of female rats -

				In the cage					
							Stereotype		Bizarre behavior
Period	Group	Number of animals	Category No.	Body position/ Posture 1	Respiratory pattern 1	Tremor/ Convulsion 1	Rolling 0	Repetitive circling 0	Biting/ Selfmutilation 1
Days of administration									
Pre -	0 mg/kg	12		12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	12
Day 7	0 mg/kg	12		12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	12
Day 14	0 mg/kg	12		12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	12
Day 21	0 mg/kg	12		12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	12
Day 28	0 mg/kg	12		12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	12

Category : The category number observed in each item.

Pre : Pre-administration.

Table 5-1-2 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Detailed clinical observation of female rats -

				In the cage					
							Stereotype		Bizarre behavior
Period	Group	Number of animals	Category No.	Body position/ Posture 1	Respiratory pattern 1	Tremor/ Convulsion 1	Rolling 0	Repetitive circling 0	Biting/ Selfmutilation 1
Days of administration									
Day 35	0 mg/kg	12		12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	12
Day 42	0 mg/kg	8		8	8	8	8	8	8
	4 mg/kg	9		9	9	9	9	9	9
	20 mg/kg	10		10	10	10	10	10	10
	100 mg/kg	11		11	11	11	11	11	11

Category : The category number observed in each item.

Table 5-2-1 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Detailed clinical observation of female rats -

				On the hand											
				Ease of											
Period	Group	Number of animals	Category No.	Removal 1	Handling 1	Muscle tone 2	Piloerection 1	Fur 1	Eyes 1	Mucous membranes 0	Skin 1	Pupil size 1	Lacrimation 1	Salivation 1	Secretions/ Excretions 0
Days of administration															
Pre -	0 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
Day 7	0 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
Day 14	0 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
Day 21	0 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
Day 28	0 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12

Category : The category number observed in each item.

Pre : Pre-administration.

Table 5-2-2 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Detailed clinical observation of female rats -

				On the hand											
				Ease of											
Period	Group	Number of animals	Category No.	Removal 1	Handling 1	Muscle tone 2	Piloerection 1	Fur 1	Eyes 1	Mucous membranes 0	Skin 1	Pupil size 1	Lacrimation 1	Salivation 1	Secretions/ Excretions 0
Days of administration															
Day 35	0 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12	12
Day 42	0 mg/kg	8		8	8	8	8	8	8	8	8	8	8	8	8
	4 mg/kg	9		9	9	9	9	9	9	9	9	9	9	9	9
	20 mg/kg	10		10	10	10	10	10	10	10	10	10	10	10	10
	100 mg/kg	11		11	11	11	11	11	11	11	11	11	11	11	11

Category : The category number observed in each item.

Table 5-3-1 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Detailed clinical observation of female rats -

				In the open-field												
												Stereotype		Bizarre behavior		
Period	Group	Number of animals	Category No.	Gait 1	Co-ordination of movement 1	Reactivity to environmental stimuli 1	Searching 1	Urination 0	Urination 1	Defecation 0	Excessive grooming 0	Unusual head movement 0	Walking backward 1	Vocaliza-tion 1	Aggression 1
Days of administration															
Pre -	0 mg/kg	12		12	12	12	12	10	2	12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	0	12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	0	12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	10	2	12	12	12	12	12	12
Day 7	0 mg/kg	12		12	12	12	12	9	3	12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	11	1	12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	9	3	12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	10	2	12	12	12	12	12	12
Day 14	0 mg/kg	12		12	12	12	12	11	1	12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	11	1	12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	0	12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	0	12	12	12	12	12	12
Day 21	0 mg/kg	12		12	12	12	12	12	0	12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	0	12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	0	12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	0	12	12	12	12	12	12
Day 28	0 mg/kg	12		12	12	12	12	11	1	12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	0	12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	0	12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	0	12	12	12	12	12	12

Category : The category number observed in each item.

Pre : Pre-administration.

Table 5-3-2 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Detailed clinical observation of female rats -

				In the open-field										
										Stereotype		Bizarre behavior		
Period	Group	Number of animals	Category No.	Gait 1	Co-ordination of movement 1	Reactivity to environmental stimuli 1	Searching 1	Urination 0	Defecation 0	Excessive grooming 0	Unusual head movement 0	Walking backward 1	Vocaliza-tion 1	Aggression 1
Days of administration														
Day 35	0 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12
	4 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12
	20 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12
	100 mg/kg	12		12	12	12	12	12	12	12	12	12	12	12
Day 42	0 mg/kg	8		8	8	8	8	8	8	8	8	8	8	8
	4 mg/kg	9		9	9	9	9	9	9	9	9	9	9	9
	20 mg/kg	10		10	10	10	10	10	10	10	10	10	10	10
	100 mg/kg	11		11	11	11	11	11	11	11	11	11	11	11

Category : The category number observed in each item.

Table 6-1-1 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Detailed clinical observation of female rats in the satellite group -

				In the cage					
							Stereotype		Bizarre behavior
Period	Group	Number of animals	Category No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
				1	1	1	0	0	1
Days of administration									
Pre -	0 mg/kg	10		10	10	10	10	10	10
	100 mg/kg	10		10	10	10	10	10	10
Day 7	0 mg/kg	10		10	10	10	10	10	10
	100 mg/kg	10		10	10	10	10	10	10
Day 14	0 mg/kg	10		10	10	10	10	10	10
	100 mg/kg	10		10	10	10	10	10	10
Day 21	0 mg/kg	10		10	10	10	10	10	10
	100 mg/kg	10		10	10	10	10	10	10
Day 28	0 mg/kg	10		10	10	10	10	10	10
	100 mg/kg	10		10	10	10	10	10	10

Category : The category number observed in each item.

Pre : Pre-administration.

Table 6-1-2 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Detailed clinical observation of female rats in the satellite group -

				In the cage					
							Stereotype		Bizarre behavior
Period	Group	Number of animals	Category No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
				1	1	1	0	0	1
Days of administration									
Day 35	0 mg/kg	10		10	10	10	10	10	10
	100 mg/kg	10		10	10	10	10	10	10
Day 42	0 mg/kg	10		10	10	10	10	10	10
	100 mg/kg	10		10	10	10	10	10	10
Days of recovery									
Day 7	0 mg/kg	5		5	5	5	5	5	5
	100 mg/kg	5		5	5	5	5	5	5
Day 14	0 mg/kg	5		5	5	5	5	5	5
	100 mg/kg	5		5	5	5	5	5	5

Category : The category number observed in each item.

Table 6-2-1 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Detailed clinical observation of female rats in the satellite group -

				On the hand											
				Ease of											
Period	Group	Number of animals	Category No.	Removal 1	Handling 1	Muscle tone 2	Piloerection 1	Fur 1	Eyes 1	Mucous membranes 0	Skin 1	Pupil size 1	Lacrimation 1	Salivation 1	Secretions/ Excretions 0
Days of administration															
Pre -	0 mg/kg	10		10	10	10	10	10	10	10	10	10	10	10	10
	100 mg/kg	10		10	10	10	10	10	10	10	10	10	10	10	10
Day 7	0 mg/kg	10		10	10	10	10	10	10	10	10	10	10	10	10
	100 mg/kg	10		10	10	10	10	10	10	10	10	10	10	10	10
Day 14	0 mg/kg	10		10	10	10	10	10	10	10	10	10	10	10	10
	100 mg/kg	10		10	10	10	10	10	10	10	10	10	10	10	10
Day 21	0 mg/kg	10		10	10	10	10	10	10	10	10	10	10	10	10
	100 mg/kg	10		10	10	10	10	10	10	10	10	10	10	10	10
Day 28	0 mg/kg	10		10	10	10	10	10	10	10	10	10	10	10	10
	100 mg/kg	10		10	10	10	10	10	10	10	10	10	10	10	10

Category : The category number observed in each item.

Pre : Pre-administration.

Table 6-2-2 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Detailed clinical observation of female rats in the satellite group -

				On the hand											
				Ease of											
Period	Group	Number of animals	Category No.	Removal 1	Handling 1	Muscle tone 2	Piloerection 1	Fur 1	Eyes 1	Mucous membranes 0	Skin 1	Pupil size 1	Lacrimation 1	Salivation 1	Secretions/ Excretions 0
Days of administration															
Day 35	0 mg/kg	10		10	10	10	10	10	10	10	10	10	10	10	10
	100 mg/kg	10		10	10	10	10	10	10	10	10	10	10	10	10
Day 42	0 mg/kg	10		10	10	10	10	10	10	10	10	10	10	10	10
	100 mg/kg	10		10	10	10	10	10	10	10	10	10	10	10	10
Days of recovery															
Day 7	0 mg/kg	5		5	5	5	5	5	5	5	5	5	5	5	5
	100 mg/kg	5		5	5	5	5	5	5	5	5	5	5	5	5
Day 14	0 mg/kg	5		5	5	5	5	5	5	5	5	5	5	5	5
	100 mg/kg	5		5	5	5	5	5	5	5	5	5	5	5	5

Category : The category number observed in each item.

Table 6-3-1 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Detailed clinical observation of female rats in the satellite group -

				In the open-field												
											Stereotype		Bizarre behavior			
Period	Group	Number of animals	Category No.	Gait 1	Co-ordination of movement 1	Reactivity to environmental stimuli 1	Searching 1	Urination 0	Urination 1	Defecation 0	Excessive grooming 0	Unusual head movement 0	Walking backward 1	Vocaliza-tion 1	Aggression 1
Days of administration															
Pre -	0 mg/kg	10		10	10	10	10	10	0	10	10	10	10	10	10
	100 mg/kg	10		10	10	10	10	10	0	10	10	10	10	10	10
Day 7	0 mg/kg	10		10	10	10	10	9	1	10	10	10	10	10	10
	100 mg/kg	10		10	10	10	10	9	1	10	10	10	10	10	10
Day 14	0 mg/kg	10		10	10	10	10	10	0	10	10	10	10	10	10
	100 mg/kg	10		10	10	10	10	10	0	10	10	10	10	10	10
Day 21	0 mg/kg	10		10	10	10	10	9	1	10	10	10	10	10	10
	100 mg/kg	10		10	10	10	10	9	1	10	10	10	10	10	10
Day 28	0 mg/kg	10		10	10	10	10	10	0	10	10	10	10	10	10
	100 mg/kg	10		10	10	10	10	10	0	10	10	10	10	10	10

Category : The category number observed in each item.

Pre : Pre-administration.

Table 6-3-2 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Detailed clinical observation of female rats in the satellite group -

				In the open-field												
											Stereotype		Bizarre behavior			
Period	Group	Number of animals	Category No.	Gait 1	Co-ordination of movement 1	Reactivity to environmental stimuli 1	Searching 1	Urination 0	Urination 1	Defecation 0	Excessive grooming 0	Unusual head movement 0	Walking backward 1	Vocalization 1	Aggression 1
Days of administration															
Day 35	0 mg/kg	10		10	10	10	10	9	1	10	10	10	10	10	10
	100 mg/kg	10		10	10	10	10	10	0	10	10	10	10	10	10
Day 42	0 mg/kg	10		10	10	10	10	10	0	10	10	10	10	10	10
	100 mg/kg	10		10	10	10	10	9	1	10	10	10	10	10	10
Days of recovery															
Day 7	0 mg/kg	5		5	5	5	5	5	0	5	5	5	5	5	5
	100 mg/kg	5		5	5	5	5	5	0	5	5	5	5	5	5
Day 14	0 mg/kg	5		5	5	5	5	4	1	5	5	5	5	5	5
	100 mg/kg	5		5	5	5	5	4	1	5	5	5	5	5	5

Category : The category number observed in each item.

Table 7-1 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Functional test of male rats -

Period	Group	Number of animals	Category No.	Reactivity					Righting reflex
				Visual	Touch	Auditory	Pain	Proprioceptive	
				4	2	1	2	1	1
Administration period									
Week 6	0 mg/kg	5		5	5	5	5	5	5
	4 mg/kg	5		5	5	5	5	5	5
	20 mg/kg	5		5	5	5	5	5	5
	100 mg/kg	5		5	5	5	5	5	5
Recovery period									
Week 2	0 mg/kg	5		5	5	5	5	5	5
	100 mg/kg	5		5	5	5	5	5	5

Category No. : The category number observed in each item.

Values are expressed as the number of animals.

Visual reactivity : approach response.
Touch reactivity : touch response.
Auditory reactivity : response to Galton's whistle.
Pain reactivity : tail pinch response.
Proprioceptive reactivity : returning from enforced posture.
Righting reflex : landing performance from 30 cm above.

Table 7-2 indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Functional test of male rats -

Period	Group	Number of animals		Grip strength		Motor activity measurements (count)						
				Forelimb (g)	Hindlimb (g)	0'-10'	10'-20'	20'-30'	30'-40'	40'-50'	50'-60'	Total
Administration period												
Week 6	0 mg/kg	5	Mean	1564.26	499.72	486.8	332.6	218.6	150.6	145.6	154.2	1488.4
			S.D.	176.77	80.65	234.6	97.5	77.7	134.8	118.2	113.6	488.4
	4 mg/kg	5	Mean	1616.86	529.82	793.0	505.6	298.2	202.0	167.2	79.0	2045.0
			S.D.	157.33	42.65	245.6	179.5	207.3	149.1	139.9	82.0	966.1
	20 mg/kg	5	Mean	1523.34	521.74	769.4	442.4	318.4	237.8	219.6	123.4	2111.0
			S.D.	177.72	47.24	352.1	202.5	174.6	129.2	130.2	91.7	1028.2
	100 mg/kg	5	Mean	1214.66**	523.28	642.8	395.0	238.4	189.8	118.4	75.4	1659.8
			S.D.	124.04	74.67	345.0	152.7	156.7	232.8	120.8	104.5	986.9
Recovery period												
Week 2	0 mg/kg	5	Mean	1692.74	490.34	611.0	365.2	284.0	232.8	274.0	254.6	2021.6
			S.D.	188.02	95.81	79.4	86.6	104.3	149.6	118.6	138.2	517.3
	100 mg/kg	5	Mean	1675.58	451.60	611.2	314.6	283.6	216.0	155.6	249.8	1830.8
			S.D.	214.78	60.54	229.9	126.8	165.6	117.0	94.6	139.7	647.5

** : Significantly different from the 0 mg/kg group at $p \leqq 0.01$ (Dunnett's test).

Table 8-1 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Functional test of female rats -

Period	Group	Number of animals	Category	Reactivity					Righting reflex
				Visual	Touch	Auditory	Pain	Proprioceptive	
				4	2	1	2	1	1
Lactation period									
	0 mg/kg	5		5	5	5	5	5	5
Day 4	4 mg/kg	5		5	5	5	5	5	5
	20 mg/kg	5		5	5	5	5	5	5
	100 mg/kg	5		5	5	5	5	5	5

Category No. : The category number observed in each item.

Values are expressed as the number of animals.

Visual reactivity : approach response.
Touch reactivity : touch response.
Auditory reactivity : response to Galton's whistle.
Pain reactivity : tail pinch response.
Proprioceptive reactivity : returning from enforced posture.
Righting reflex : landing performance from 30 cm above.

Table 8-2 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Functional test of female rats -

Period	Group	Number of animals		Grip strength		Motor activity measurements (count)						
				Forelimb (g)	Hindlimb (g)	0'-10'	10'-20'	20'-30'	30'-40'	40'-50'	50'-60'	Total
Lactation period												
	0 mg/kg	5	Mean	1345.04	411.48	379.6	268.4	184.0	121.6	80.2	104.2	1138.0
Day 4			S.D.	107.84	73.01	163.2	167.3	154.9	142.0	77.0	123.6	581.5
	4 mg/kg	5	Mean	1224.00	409.60	692.0	397.4	392.4	416.2	181.0	393.8*	2472.8*
			S.D.	99.55	60.06	270.6	163.8	252.7	335.3	96.1	190.5	815.7
	20 mg/kg	5	Mean	1335.34	409.58	559.4	215.0	141.8	109.8	135.8	88.6	1250.4
			S.D.	91.54	75.53	200.4	239.3	228.7	184.9	141.1	170.5	1057.4
	100 mg/kg	5	Mean	1394.12	375.94	446.2	81.0	74.8	22.4	0.6	21.2	646.2
			S.D.	106.38	49.56	210.0	47.7	54.0	31.0	0.9	47.4	214.0

* : Significantly different from the 0 mg/kg group at $p \leqq 0.05$ (Dunnett's test).

Table 9-1 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Functional test of female rats in the satellite group -

Period	Group	Number of animals	Category	Reactivity					Righting reflex
				Visual	Touch	Auditory	Pain	Proprioceptive	
				4	2	1	2	1	1
Administration period									
Week 6	0 mg/kg	5		5	5	5	5	5	5
	100 mg/kg	5		5	5	5	5	5	5
Recovery period									
Week 2	0 mg/kg	5		5	5	5	5	5	5
	100 mg/kg	5		5	5	5	5	5	5

Category No. : The category number observed in each item.
Values are expressed as the number of animals.

Visual reactivity : approach response.
Touch reactivity : touch response.
Auditory reactivity : response to Galton's whistle.
Pain reactivity : tail pinch response.
Proprioceptive reactivity : returning from enforced posture.
Righting reflex : landing performance from 30 cm above.

Table 9-2 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Functional test of female rats in the satellite group -

Period	Group	Number of animals		Grip strength Forelimb (g)	Grip strength Hindlimb (g)	Motor activity measurements (count) 0'-10'	10'-20'	20'-30'	30'-40'	40'-50'	50'-60'	Total
Administration period												
Week 6	0 mg/kg	5	Mean	1184.40	408.54	1033.0	616.6	557.6	408.6	246.4	65.2	2927.4
			S.D.	157.76	47.64	285.0	187.3	330.6	260.5	311.5	62.4	1053.1
	100 mg/kg	5	Mean	1276.86	411.34	920.4	664.8	483.8	332.4	265.6	247.0+	2914.0
			S.D.	107.97	71.71	515.5	406.0	447.7	394.1	308.0	220.3	2240.7
Recovery period												
Week 2	0 mg/kg	5	Mean	1365.80	404.72	949.2	711.0	355.2	370.0	274.2	418.8	3078.4
			S.D.	174.20	36.38	351.0	229.5	101.8	235.2	186.6	182.3	751.4
	100 mg/kg	5	Mean	1461.66	413.46	857.2	507.0	294.4	365.6	236.8	262.2	2523.2
			S.D.	59.98	48.12	431.4	406.8	214.2	246.2	295.0	233.4	1800.0

+ : Significantly different from the 0 mg/kg group at P≦0.05 (Steel's test).

Table 10 indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Body weight of male rats -

Group	Number of animals		Body weight (g) Administration day 1	3	5	7	10	14	21	28	35	42	Body weight gain(g) 1-42	%
0 mg/kg	12	Mean	379.3	390.4	401.7	410.9	422.3	442.2	470.5	493.7	519.8	534.3	155.0	40.651
		S.D.	16.5	16.6	17.4	19.6	19.8	24.2	25.7	32.6	36.2	46.0	31.2	6.816
4 mg/kg	12	Mean	378.7	387.8	398.8	409.0	420.4	436.9	463.9	489.6	516.8	535.6	156.9	41.393
		S.D.	16.8	17.6	17.2	20.1	22.3	21.8	25.9	29.7	30.6	31.2	17.6	3.748
20 mg/kg	12	Mean	376.1	385.9	396.2	405.8	417.3	435.7	461.5	485.0	507.0	524.3	148.3	39.399
		S.D.	14.3	14.3	15.1	15.8	17.4	18.1	19.4	21.1	29.0	32.2	24.6	6.198
100 mg/kg	12	Mean	378.5	374.7	387.8	396.7	405.2	421.1	442.6*	465.4*	490.2	505.4	126.9*	33.490**
		S.D.	14.6	17.7	18.0	19.1	22.8	23.3	23.4	26.5	29.2	28.6	18.2	4.309

Group	Number of animals		Body weight(g) Recovery day 7	14	Body weight gain (g) a-14	%
0 mg/kg	5	Mean	539.0	547.8	22.0	4.194
		S.D.	23.3	27.0	6.0	1.135
100 mg/kg	5	Mean	515.0	526.0	21.8	4.326
		S.D.	16.2	15.6	6.7	1.327

Body weight gain (%) = (body weight gain / body weight on day 1 or day 42) x 100.

a: Day 42 of administration.

* : Significantly different from the 0 mg/kg group at P≦ 0.05 (Dunnett's test).

** : Significantly different from the 0 mg/kg group at P≦ 0.01 (Dunnett's test).

Table 11-1 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Body weight of female rats in pre-mating period -

Group	Number of animals		Body weight(g) Pre-mating day 1	3	5	7	10	14	Body weight gain(g) 1-14	%
0 mg/kg	12	Mean	243.0	245.5	251.5	254.3	259.9	266.3	23.3	9.602
		S.D.	10.5	11.9	10.4	12.6	12.4	13.4	6.5	2.647
4 mg/kg	12	Mean	241.6	245.8	250.3	255.1	256.4	265.8	24.2	9.968
		S.D.	11.2	10.5	11.8	11.4	13.3	16.7	9.1	3.559
20 mg/kg	12	Mean	241.5	245.2	249.6	254.2	256.3	264.9	23.4	9.664
		S.D.	7.6	11.7	10.6	12.9	12.7	14.2	9.9	4.017
100 mg/kg	12	Mean	242.3	239.8	243.2	247.4	248.1	253.7	11.3**	4.733**
		S.D.	12.1	12.7	12.4	11.7	11.1	12.0	7.5	3.161

Body weight gain (%) = (body weight gain / body weight on day 1) x 100.

** : Significantly different from the 0 mg/kg group at P≦0.01 (Dunnett's test).

Table 11-2 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Body weight of female rats in gestation period -

Group	Number of animals		Body weight (g) Gestation day 0	1	3	5	7	10	14	17	20	Body weight gain(g) 0-20	%
0 mg/kg	12	Mean	270.8	276.2	291.9	300.8	308.3	325.9	348.9	383.5	433.3	162.4	60.298
		S.D.	15.2	13.7	13.1	14.3	16.1	15.2	17.1	19.3	20.3	21.0	9.674
4 mg/kg	12	Mean	273.5	280.9	294.8	304.5	314.2	331.3	353.1	384.7	430.2	156.7	57.348
		S.D.	16.2	18.2	17.1	20.8	19.7	21.6	22.9	24.1	27.0	16.8	5.875
20 mg/kg	12	Mean	270.9	275.5	288.3	299.5	311.8	327.3	351.8	384.1	434.1	163.2	60.228
		S.D.	14.4	16.0	16.1	17.9	20.2	18.4	21.5	23.7	29.2	19.9	6.721
100 mg/kg	12	Mean	257.5	265.0	278.3	284.0*	293.3	308.6	329.6	364.1	407.3*	149.8	58.242
		S.D.	12.8	13.0	14.1	13.4	13.6	16.1	18.6	19.4	23.4	16.4	6.460

Body weight gain (%) = (body weight gain / body weight on day 0) x 100.

* : Significantly different from the 0 mg/kg group at P≦0.05 (Dunnett's test).

Table 11-3 indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Body weight of female rats in lactation period -

Group	Number of animals		Body weight (g) Lactation day 0	1	4	Body weight gain (g) 0-4	%
					(11)	(11)	(11)
0 mg/kg	12	Mean	322.4	323.4	343.5	16.1	5.035
		S.D.	27.0	28.2	18.5	10.1	3.315
4 mg/kg	12	Mean	324.5	322.5	332.7	8.2	2.644
		S.D.	23.4	27.1	30.0	24.0	7.638
20 mg/kg	12	Mean	326.0	322.9	342.6	16.6	5.343
		S.D.	26.5	23.9	18.2	15.0	4.478
100 mg/kg	12	Mean	307.1	307.6	326.7	19.6	6.610
		S.D.	22.9	21.3	20.5	17.7	5.841

Body weight gain (%) = (body weight gain / body weight on day 0) x 100.
The number in the parenthese is the number of animals used for the measurement.

Table 12 indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Body weight of female rats in the satellite group -

Group	Number of animals		Body weight (g) Administration day 1	3	5	7	10	14	21	28	35	42	Body weight gain(g) 1-42	%
0 mg/kg	10	Mean	239.4	245.1	249.4	255.1	260.0	265.8	274.3	282.2	295.4	301.8	62.4	26.087
		S.D.	9.4	7.6	8.9	8.7	8.8	7.3	8.5	9.9	11.4	12.9	7.6	3.139
100 mg/kg	10	Mean	239.5	237.1*	240.9	245.0*	247.2*	253.4**	263.2*	270.1*	274.0**	283.5*	44.0+	18.453+
		S.D.	10.4	9.1	9.6	9.3	11.2	11.2	9.0	11.7	15.7	17.6	16.3	7.073

Group	Number of animals		Body weight (g) Recovery day 7	14	Body weight gain(g) a-14	%
0 mg/kg	5	Mean	309.8	310.4	9.2	3.052
		S.D.	14.1	13.5	4.8	1.600
100 mg/kg	5	Mean	295.4	302.8	17.2	6.016*
		S.D.	17.8	22.6	6.9	2.363

Body weight gain (%) = (body weight gain / body weight on day 1 or day 42) x 100.
a: Day 42 of administration.
* : Significantly different from the 0 mg/kg group at p≦0.05 (Dunnett's test).
** : Significantly different from the 0 mg/kg group at P≦0.01 (Dunnett's test).
+ : Significantly different from the 0 mg/kg group at P≦0.05 (Steel's test).

Table 13 indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Food consumption of male rats -

Group	Number of animals		Food consumption (g/rat/day) Administration day -1～1	1～3	3～5	5～7	7～10	10～14	21～28	28～35	35～42
0 mg/kg	12	Mean	25.92	22.75	23.67	22.96	22.30	22.93	22.37	22.12	21.47
		S.D.	2.78	1.83	1.51	1.79	1.71	2.27	2.36	2.50	3.31
4 mg/kg	12	Mean	26.08	23.13	23.67	23.13	22.56	22.52	22.33	22.08	22.33
		S.D.	3.00	1.87	2.29	2.12	2.25	1.94	2.18	2.07	1.88
20 mg/kg	12	Mean	25.67	22.42	23.25	22.42	21.78	22.04	21.52	20.74	20.88
		S.D.	2.02	1.94	1.48	1.64	1.47	1.69	1.34	1.85	1.55
100 mg/kg	12	Mean	25.50	15.88**	22.79	21.96	20.86	21.05	21.48	21.57	21.43
		S.D.	2.32	3.37	2.39	2.33	2.55	1.85	1.84	2.08	2.21

Group	Number of animals		Food consumption (g/rat/day) Recovery day a～7	7～14
0 mg/kg	5	Mean	25.56	27.68
		S.D.	1.13	1.15
100 mg/kg	5	Mean	23.08	26.64
		S.D.	2.34	3.34

a: Day 42 of administration.

** : Significantly different from the 0 mg/kg group at $p \leqq 0.01$ (Dunnett's test).

Table 14-1 indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Food consumption of female rats in pre-mating period -

Group	Number of animals		Food consumption (g/rat/day) Pre-mating day -1～1	1～3	3～5	5～7	7～10	10～14
0 mg/kg	12	Mean	18.42	15.33	16.38	16.46	16.48	16.13
		S.D.	2.94	2.10	1.82	2.08	1.41	1.09
4 mg/kg	12	Mean	17.33	15.54	16.50	16.25	16.14	16.45
		S.D.	3.31	1.97	2.14	1.48	2.18	1.75
20 mg/kg	12	Mean	18.42	16.08	16.79	16.88	16.58	16.79
		S.D.	2.54	2.24	1.76	2.23	1.26	1.58
100 mg/kg	12	Mean	18.00	12.25**	14.79	15.96	14.06**	15.29
		S.D.	2.83	2.62	2.03	1.20	1.65	1.20

** : Significantly different from the 0 mg/kg group at $p \leqq 0.01$ (Dunnett's test).

Table 14-2 indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Food consumption of female rats in gestation period -

Group	Number of animals		Food consumption (g/rat/day) Gestation day 0～1	1～3	3～5	5～7	7～10	10～14	14～17	17～20
0 mg/kg	12	Mean	15.17	20.42	21.21	20.92	22.28	21.73	21.62	19.53
		S.D.	2.12	3.37	2.57	1.77	1.71	2.17	1.96	1.53
4 mg/kg	12	Mean	16.58	21.33	22.04	22.92	22.92	22.60	21.57	19.87
		S.D.	2.47	1.61	2.94	2.32	1.99	2.35	1.82	1.66
20 mg/kg	12	Mean	14.92	20.33	22.08	22.54	22.85	22.73	21.19	20.50
		S.D.	3.15	1.83	2.30	2.31	2.42	2.45	2.49	1.82
100 mg/kg	12	Mean	15.67	18.92	18.79	20.46	21.00	21.71	21.82	19.73
		S.D.	2.23	2.19	1.95	1.62	1.94	2.38	1.89	1.75

Table 14-3 indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Food consumption of female rats in lactation period -

Group	Number of animals		Food consumption (g/rat/day) Lactation day 0～1	1～4
				(11)
0 mg/kg	12	Mean	17.17	30.45
		S.D.	6.85	2.96
4 mg/kg	12	Mean	16.08	27.96
		S.D.	8.34	9.80
20 mg/kg	12	Mean	15.25	31.23
		S.D.	7.15	3.20
100 mg/kg	12	Mean	19.25	30.76
		S.D.	5.36	3.96

The number in the parenthese is the number of animals used for the measurement.

Table 15 indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Food consumption of female rats in the satellite group -

Group	Number of animals		Food consumption (g/rat/day) Administration period (day) -1～1	1～3	3～5	5～7	7～10	10～14	14～21	21～28	28～35	35～42
0 mg/kg	10	Mean	18.30	17.20	15.55	18.05	15.96	16.13	15.55	15.99	15.73	14.89
		S.D.	2.91	1.38	1.72	1.04	1.42	0.74	0.81	0.98	0.96	1.40
100 mg/kg	10	Mean	17.60	12.15**	15.25	15.00**	14.58	14.72**	14.68	14.86	13.79**	14.81
		S.D.	2.22	1.75	2.68	1.37	2.11	1.00	1.05	1.70	1.68	1.82

Group	Number of animals		Food consumption (g/rat/day) Recovery day a～7	7～14
0 mg/kg	5	Mean	18.40	19.14
		S.D.	1.70	0.63
100 mg/kg	5	Mean	18.30	19.34
		S.D.	1.87	2.59

a: Day 42 of administration.

** : Significantly different from the 0 mg/kg group at $p \leqq 0.01$ (Dunnett's test).

Table 16-1-1 indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Urinary findings of male rats at Week 6 of administration -

Group	Number of animals	pH						Protein		Glucose	Ketone body	Urobilinogen	Bilirubin	Occult blood			Color	Specific gravity			Urine volume (mL/21hr, mean±S.D.)
		6.0	6.5	7.0	7.5	8.0	8.5	±	+	-	-	0.1 EU/dL	-	-	±	+	A	1.031-1.040	1.041-1.050	1.050<	
0 mg/kg	5	0	0	0	0	2	3	2	3	5	5	5	5	4	0	1	5	0	4	1	9.20 ± 1.96
4 mg/kg	5	0	0	0	0	4	1	2	3	5	5	5	5	4	1	0	5	0	1	4	8.00 ± 2.09
20 mg/kg	5	0	0	0	0	3	2	4	1	5	5	5	5	4	1	0	5	0	2	3	7.80 ± 0.76
100 mg/kg	5	1	0	1	0	0	3	5	0	5	5	5	5	4	1	0	5	2	1	2	12.80 ± 4.31

Values are number of animals with findings.
- ; Normal , ± ; Slight , + ; Moderate .
Color : A = Pale yellow or yellow

Table 16-1-2 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Urinary findings of male rats at Week 6 of administration -

		Urinary sediments						
				Epithelial cell				
Group	Number of animals	RBC	WBC	Squamous		Round	Small round	Cast
		−	−	−	±	−	−	−
0 mg/kg	5	5	5	3	2	5	5	5
4 mg/kg	5	5	5	5	0	5	5	5
20 mg/kg	5	5	5	4	1	5	5	5
100 mg/kg	5	5	5	4	1	5	5	5

Values are number of animals with findings.
- ; Normal , ± ; Slight .

Table 16-2-1 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Urinary findings of male rats at Week 2 of recovery -

Group	Number of animals	pH		Protein			Glucose	Ketone body	Urobili-nogen	Bili-rubin	Occult blood	Color	Specific gravity			Urine volume (mL/21hr, mean±S.D.)
		8.0	8.5	±	+	2+	-	-	0.1 EU/dL	-	-	A	1.031-1.040	1.041-1.050	1.050<	
0 mg/kg	5	1	4	3	1	1	5	5	5	5	5	5	0	2	3	11.00 ± 4.72
100 mg/kg	5	0	5	1	3	1	5	5	5	5	5	5	1	1	3	11.30 ± 3.21

Values are number of animals with findings.
- ; Normal , ± ; Slight , + ; Moderate , 2+ ; Severe .
Color : A = Pale yellow or yellow

Table 16-2-2 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Urinary findings of male rats at Week 2 of recovery -

		Urinary sediments							
					Epithelial cell				
	Number of	RBC		WBC	Squamous		Round	Small round	Cast
Group	animals	—	±	—	—	±	—	—	—
0 mg/kg	5	5	0	5	4	1	5	5	5
100 mg/kg	5	4	1	5	3	2	5	5	5

Values are number of animals with findings.
- ; Normal , ± ; Slight .

Table 17-1-1 indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Urinary findings of female rats in the satellite group at Week 6 of administration -

Group	Number of animals	pH					Protein			Glucose	Ketone body	Urobilinogen	Bilirubin	Occult	Color	Specific gravity			Urine volume (mL/21hr, mean±S.D.)
		6.0	6.5	7.0	7.5	8.0	±	+	2+	-	-	0.1 EU/dL	-	-	A	1.031-1.040	1.041-1.050	1.050<	
0 mg/kg	5	1	2	0	0	2	0	4	1	5	5	5	5	5	5	0	3	2	7.04 ± 2.45
100 mg/kg	5	1	1	1	1	1	[3	2	0]+	5	5	5	5	5	5	2	0	3	7.94 ± 4.50

Values are number of animals with findings.
- ; Normal , ± ; Slight , + ; Moderate , 2+ ; Severe .
Color : A = Pale yellow or yellow
+ : Significantly different from the 0 mg/kg group at P ≦ 0.05 (Steel's test).

Table 17-1-2 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Urinary findings of female rats in the satellite group at Week 6 of administration -

		Urinary sediments						
				Epithelial cell				
				Squamous			Small	
Group	Number of animals	RBC —	WBC —	— —	± ±	Round —	round —	Cast —
0 mg/kg	5	5	5	5	0	5	5	5
100 mg/kg	5	5	5	2	3 +	5	5	5

Values are number of animals with findings.
- ; Normal , ± ; Slight .
+ : Significantly different from the 0 mg/kg group at P≦0.05 (Steel's test).

Table 17-2-1 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Urinary findings of female rats in the satellite group at Week 2 of recovery -

Group	Number of animals	pH						Protein			Glucose	Ketone body	Urobili-nogen	Bili-rubin	Occult blood	Color	Specific gravity		Urine volume (mL/21hr, mean±S.D.)
		6.0	6.5	7.0	7.5	8.0	8.5	-	±	+	-	-	0.1 EU/dL	-	-	A	1.041-1.050	1.050<	
0 mg/kg	5	1	0	1	1	0	2	0	4	1	5	5	5	5	5	5	0	5	7.80 ± 2.25
100 mg/kg	5	1	1	0	1	1	1	3	1	1	5	5	5	5	5	5	3	2	9.40 ± 4.34

Values are number of animals with findings.
-, Normal ; ±, Slight ; +, Moderate.
Color : A = Pale yellow or yellow

Table 17-2-2 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Urinary findings of female rats in the satellite group at Week 2 of recovery -

		Urinary sediments						
				Epithelial cell				
				Squamous			Small	
Group	Number of animals	RBC —	WBC —	—	±	Round —	round —	Cast —
0 mg/kg	5	5	5	2	3	5	5	5
100 mg/kg	5	5	5	5	0	5	5	5

Values are number of animals with findings.
-, Normal ; ±, Slight .
+ : Significantly different from the 0 mg/kg group at P≦0.05 (Steel's test).

Table 18-1-1 indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Hematological findings of male rats after Week 6 of administration -

Group	Number of animals		WBC $10^2/\mu L$	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Platelet $10^4/\mu L$
0 mg/kg	5	Mean	62.44	831.8	14.90	41.88	50.34	17.92	35.60	108.82
		S.D.	19.98	17.6	0.47	1.29	1.61	0.50	0.39	10.69
4 mg/kg	5	Mean	65.86	836.0	15.04	42.78	51.20	18.00	35.16	113.34
		S.D.	20.77	22.7	0.15	0.68	1.37	0.43	0.51	15.38
20 mg/kg	5	Mean	56.90	795.8	14.52	41.68	52.44	18.24	34.82*	114.02
		S.D.	15.74	27.9	0.54	1.40	2.06	0.62	0.59	10.17
100 mg/kg	5	Mean	68.24	789.8	14.32	41.44	52.48	18.14	34.56**	97.44
		S.D.	21.90	39.4	0.70	2.11	1.52	0.46	0.27	6.42

* : Significantly different from the 0 mg/kg group at $p \leqq 0.05$ (Dunnett's test).
** : Significantly different from the 0 mg/kg group at $p \leqq 0.01$ (Dunnett's test).

Table 18-1-2 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Hematological findings of male rats after Week 6 of administration -

Group	Number of animals		Reticulo-cyte %	PT sec	APTT sec	Differential count of WBC (10^2/μL)					Heinz Body %	Met-hemoglobin %
						Neutrophil	Lympho-cyte	Monocyte	Eosinophil	Basophil		
0 mg/kg	5	Mean	2.688	25.04	28.70	9.82	49.70	1.84	1.08	0.00	0.00	1.90
		S.D.	0.545	3.23	1.36	4.43	15.62	0.55	0.48	0.00	0.00	0.25
4 mg/kg	5	Mean	3.160	21.76	26.68+	14.06	48.36	2.52	0.92	0.00	0.00	1.66
		S.D.	0.414	2.76	0.36	7.05	15.38	0.69	0.16	0.00	0.00	0.22
20 mg/kg	5	Mean	3.110	23.82	28.68	10.10	44.24	1.82	0.74	0.00	0.00	1.88
		S.D.	0.314	3.80	2.78	2.37	14.26	0.52	0.09	0.00	0.00	0.11
100 mg/kg	5	Mean	4.026**	32.68	32.58	12.96	52.52	1.84	0.92	0.00	0.00	1.98
		S.D.	0.461	8.55	3.18	1.92	21.44	0.11	0.11	0.00	0.00	0.52

+ : Significantly different from the 0 mg/kg group at $p \leqq 0.05$ (Steel's test).

** : Significantly different from the 0 mg/kg group at $p \leqq 0.01$ (Dunnett's test).

Table 18-2 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Hematological findings of male rats afetr Week 2 of recovery -

Group	Number of animals		WBC $10^2/\mu L$	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Platelet $10^4/\mu L$
0 mg/kg	5	Mean	72.42	867.4	15.26	42.90	49.54	17.62	35.58	110.14
		S.D.	21.51	47.3	0.38	0.83	2.08	0.61	0.53	13.43
100 mg/kg	5	Mean	69.38	858.8	15.40	43.28	50.38	17.94	35.60	117.06
		S.D.	24.88	19.5	0.49	1.56	1.71	0.49	0.46	12.20

Group	Number of animals		Reticulo-cyte %	PT sec	APTT sec	Differential count of WBC ($10^2/\mu L$)					Heinz Body %	Met-hemoglobin %
						Neutrophil	Lympho-cyte	Monocyte	Eosinophil	Basophil		
0 mg/kg	5	Mean	2.616	22.70	25.40	10.10	58.32	2.62	1.38	0.00	0.00	1.56
		S.D.	0.335	2.96	1.74	5.69	17.13	0.89	0.48	0.00	0.00	0.25
100 mg/kg	5	Mean	3.000	25.30	27.64*	8.02	57.86	2.48	1.02	0.00	0.00	1.62
		S.D.	0.610	4.81	1.18	2.11	24.29	0.51	0.13	0.00	0.00	0.22

* : Significantly different from the 0 mg/kg group at $p \leqq 0.05$ (Dunnett's test).

Table 19-1 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Hematological findings of female rats at Day 5 of lactation -

Group	Number of animals		WBC $10^2/\mu L$	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Platelet $10^4/\mu L$
0 mg/kg	5	Mean	70.20	665.0	12.76	37.40	56.34	19.20	34.12	132.78
		S.D.	10.53	41.4	0.64	1.41	2.83	0.46	1.03	14.93
4 mg/kg	5	Mean	64.14	624.0	12.10	35.72	57.64	19.44	33.86	113.40
		S.D.	26.07	69.3	0.97	2.09	4.75	0.86	1.25	11.88
20 mg/kg	5	Mean	67.26	663.8	12.70	37.30	56.26	19.14	34.08	121.90
		S.D.	14.45	33.0	0.41	1.38	2.97	0.54	0.83	9.47
100 mg/kg	5	Mean	68.32	634.6	12.54	37.56	59.28	19.80	33.40	118.04
		S.D.	25.88	34.8	0.52	1.72	3.23	0.99	0.39	12.97

Table 19-2 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Hematological findings of female rats at Day 5 of lactation -

Group	Number of animals		Reticulo-cyte %	PT sec	APTT sec	Differential count of WBC (10^2/μL)				
						Neutrophil	Lympho-cyte	Monocyte	Eosinophil	Basophil
0 mg/kg	5	Mean	8.536	17.02	19.86	19.56	47.86	2.28	0.50	0.00
		S.D.	0.908	0.87	1.66	3.48	8.51	0.78	0.41	0.00
4 mg/kg	5	Mean	9.892	16.82	20.54	19.62	42.72	1.50	0.28	0.02
		S.D.	4.389	0.73	2.12	5.52	22.01	0.69	0.16	0.04
20 mg/kg	5	Mean	8.522	17.04	18.90	24.72	40.20	1.92	0.42	0.00
		S.D.	1.379	0.67	1.08	7.84	8.21	0.53	0.23	0.00
100 mg/kg	5	Mean	10.902	16.90	19.98	24.08	41.54	2.42	0.28	0.00
		S.D.	2.330	1.08	1.65	13.66	12.86	1.09	0.19	0.00

Table 20-1 indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Hematological findings of female rats in the satellite group after Week 6 of administration -

Group	Number of animals		WBC $10^2/\mu L$	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Platelet $10^4/\mu L$
0 mg/kg	5	Mean	40.36	801.2	14.46	40.96	51.16	18.04	35.30	110.22
		S.D.	7.12	40.8	0.61	1.42	1.65	0.35	0.51	12.72
100 mg/kg	5	Mean	39.12	757.8	14.06	40.44	53.36	18.56	34.78	106.36
		S.D.	15.64	25.5	0.84	2.77	2.53	0.73	0.34	9.22

Group	Number of animals		Reticulo-cyte %	PT sec	APTT sec	Differential count of WBC ($10^2/\mu L$)					Heinz Body %	Met-hemoglobin %
						Neutrophil	Lympho-cyte	Monocyte	Eosinophil	Basophil		
0 mg/kg	5	Mean	2.882	16.60	18.56	5.42	33.24	1.30	0.40	0.00	0.00	1.26
		S.D.	0.577	0.88	0.61	1.55	7.04	0.43	0.07	0.00	0.00	0.31
100 mg/kg	5	Mean	3.844*	17.30	23.36++	7.34	30.06	1.38	0.34	0.00	0.00	1.52
		S.D.	0.518	2.68	3.42	2.78	13.18	0.94	0.21	0.00	0.00	0.46

* : Significantly different from the 0 mg/kg group at $p \leqq 0.05$ (Dunnett's test).
++ : Significantly different from the 0 mg/kg group at $p \leqq 0.01$ (Steel's test).

Table 20-2 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Hematological findings of female rats in the satellite group after Week 2 of recovery -

Group	Number of animals		WBC $10^2/\mu L$	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Platelet $10^4/\mu L$
0 mg/kg	5	Mean	27.46	785.8	14.40	41.14	52.36	18.34	35.00	102.52
		S.D.	5.18	14.4	0.37	1.31	1.89	0.52	0.23	5.41
100 mg/kg	5	Mean	34.64	771.4	14.38	41.02	53.22	18.64	35.06	103.70
		S.D.	4.73	23.9	0.52	1.83	2.34	0.59	0.47	13.99

Group	Number of animals		Reticulo-cyte %	PT sec	APTT sec	Differential count of WBC ($10^2/\mu L$)					Heinz Body %	Met-hemoglobin %
						Neutrophil	Lympho-cyte	Monocyte	Eosinophil	Basophil		
0 mg/kg	5	Mean	2.654	17.44	18.66	4.40	21.14	1.32	0.60	0.00	0.00	1.36
		S.D.	0.367	0.90	0.83	1.08	4.14	0.34	0.23	0.00	0.00	0.36
100 mg/kg	5	Mean	2.706	17.06	19.40	6.78	26.20	1.22	0.44	0.00	0.00	1.28
		S.D.	0.626	1.11	1.25	3.84	6.20	0.37	0.09	0.00	0.00	0.13

Table 21-1-1 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

-Biochemical findings of male rats after Week 6 of administration -

Group	Number of animals		TP g/dL	Albumin g/dL	A/G ratio	Protein fraction (%)					AST IU/L	ALT IU/L	ALP IU/L	γ -GTP IU/L	T-Bil mg/dL
						Albumin	Globulin								
							α_1	α_2	β	γ					
0 mg/kg	5	Mean	5.12	2.640	1.070	51.60	20.30	7.50	16.10	4.50	73.0	33.2	418.0	0.40	0.048
		S.D.	0.23	0.096	0.066	1.53	2.05	0.26	0.60	0.70	21.9	6.3	117.6	0.10	0.008
4 mg/kg	5	Mean	4.98	2.552	1.060	51.38	20.98	7.22	15.82	4.60	59.4	27.2	412.6	0.40	0.046
		S.D.	0.28	0.105	0.066	1.59	1.57	0.29	0.88	0.66	5.2	2.9	117.3	0.12	0.009
20 mg/kg	5	Mean	5.04	2.558	1.040	50.88	20.68	7.80	16.22	4.42	62.4	26.8	412.6	0.36	0.048
		S.D.	0.26	0.063	0.114	2.70	3.14	0.83	0.99	0.63	6.7	2.8	106.1	0.18	0.008
100 mg/kg	5	Mean	4.90	2.596	1.134	53.12	18.40	7.72	16.42	4.34	59.6	29.8	321.4	0.34	0.060
		S.D.	0.27	0.114	0.072	1.59	2.47	0.52	0.61	0.30	10.5	12.1	61.9	0.15	0.012

Table 21-1-2 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

-Biochemical findings of male rats after Week 6 of administration -

Group	Number of animals		TBA μmol/L	Glucose mg/dL	T-Cho mg/dL	TG mg/dL	UN mg/dL	Crea mg/dL	Na mEq/L	K mEq/L	Cl mEq/L	Ca mg/dL	IP mg/dL
0 mg/kg	5	Mean	11.58	149.0	53.4	30.2	12.56	0.370	144.4	4.400	105.2	9.76	7.02
		S.D.	5.69	22.1	8.2	22.1	0.98	0.077	0.5	0.359	0.8	0.48	0.95
4 mg/kg	5	Mean	18.12	150.2	51.0	31.6	13.22	0.354	144.2	4.474	105.6	9.44	7.30
		S.D.	9.12	18.6	4.7	9.3	0.91	0.018	2.2	0.247	1.8	0.23	0.73
20 mg/kg	5	Mean	8.08	136.4	52.6	20.8	12.92	0.346	144.8	4.398	105.8	9.68	7.00
		S.D.	5.43	17.3	11.5	7.9	1.23	0.033	1.1	0.198	1.3	0.29	0.63
100 mg/kg	5	Mean	11.90	138.2	56.0	23.6	11.84	0.322	144.6	4.178	105.2	9.50	6.80
		S.D.	11.30	17.6	7.1	4.3	1.55	0.047	0.5	0.318	1.3	0.49	0.95

Table 21-2 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

. -Biochemical findings of male rats after Week 2 of recovery -

Group	Number of animals		TP g/dL	Albumin g/dL	A/G ratio	Protein fraction (%)					AST IU/L	ALT IU/L	ALP IU/L	γ -GTP IU/L	T-Bil mg/dL
						Albumin	Globulin								
							α_1	α_2	β	γ					
0 mg/kg	5	Mean	5.22	2.442	0.888	46.88	22.28	7.60	17.50	5.74	59.2	30.4	337.2	0.40	0.058
		S.D.	0.27	0.187	0.119	3.46	2.26	0.67	0.68	1.43	9.4	6.5	64.5	0.22	0.008
100 mg/kg	5	Mean	5.38	2.530	0.894	47.10	23.72	7.44	16.74	5.00	51.4	23.4	270.6	0.44	0.056
		S.D.	0.27	0.119	0.115	3.12	2.46	0.53	0.78	0.85	6.9	5.0	47.8	0.21	0.005

Group	Number of animals		TBA μmol/L	Glucose mg/dL	T-Cho mg/dL	TG mg/dL	UN mg/dL	Crea mg/dL	Na mEq/L	K mEq/L	Cl mEq/L	Ca mg/dL	IP mg/dL
0 mg/kg	5	Mean	8.96	160.4	55.8	34.2	15.70	0.368	144.0	4.598	105.4	9.58	6.90
		S.D.	3.54	25.4	14.6	4.8	1.46	0.045	1.4	0.158	1.1	0.18	0.59
100 mg/kg	5	Mean	8.90	136.0	59.6	40.2	15.74	0.370	144.8	4.886	105.4	9.70	7.08
		S.D.	4.31	14.9	5.3	13.9	1.40	0.019	1.3	0.252	1.5	0.27	0.20

Table 22-1 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

-Biochemical findings of female rats at Day 5 of lactation -

Group	Number of animals		TP g/dL	Albumin g/dL	A/G ratio	Protein fraction (%)					AST IU/L	ALT IU/L	ALP IU/L	γ -GTP IU/L	T-Bil mg/dL
						Albumin	Globulin								
							α_1	α_2	β	γ					
0 mg/kg	5	Mean	5.34	2.774	1.088	51.96	18.98	8.20	16.34	4.52	77.8	43.4	201.0	0.72	0.036
		S.D.	0.22	0.240	0.107	2.43	1.53	0.82	1.65	0.86	19.3	15.7	34.7	0.11	0.009
4 mg/kg	5	Mean	5.28	2.708	1.052	51.32	18.08	9.32	16.80	4.48	76.8	41.6	254.4	0.50	0.040
		S.D.	0.20	0.143	0.080	1.93	2.57	1.25	1.50	1.13	10.1	6.3	119.1	0.32	0.012
20 mg/kg	5	Mean	5.40	2.690	1.002	49.94	19.62	8.94	16.92	4.58	80.8	43.6	185.2	0.60	0.036
		S.D.	0.42	0.089	0.091	2.26	2.41	1.44	0.73	0.87	10.5	2.3	35.8	0.19	0.005
100 mg/kg	5	Mean	5.20	2.606	1.006	50.18	18.54	9.00	17.34	4.94	75.8	37.4	204.4	0.60	0.050
		S.D.	0.25	0.165	0.055	1.39	0.50	1.19	0.66	0.90	17.0	1.7	31.8	0.30	0.033

Table 22-2 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

-Biochemical findings of female rats at Day 5 of lactation -

Group	Number of animals		TBA μmol/L	Glucose mg/dL	T-Cho mg/dL	TG mg/dL	UN mg/dL	Crea mg/dL	Na mEq/L	K mEq/L	Cl mEq/L	Ca mg/dL	IP mg/dL
0 mg/kg	5	Mean	10.06	116.0	56.0	38.0	15.62	0.374	142.6	4.506	104.6	10.46	8.92
		S.D.	7.26	2.5	8.9	6.6	2.09	0.018	0.9	0.212	1.8	0.25	0.48
4 mg/kg	5	Mean	11.26	121.2	59.6	38.4	15.22	0.382	142.4	4.342	105.4	10.24	8.76
		S.D.	6.98	8.2	9.4	10.8	2.63	0.034	1.3	0.144	1.8	0.31	0.84
20 mg/kg	5	Mean	10.78	121.4	63.4	50.4	16.32	0.370	142.8	4.394	105.4	10.48	8.58
		S.D.	3.17	6.9	8.2	15.9	3.35	0.026	1.1	0.242	1.5	0.36	0.59
100 mg/kg	5	Mean	14.26	118.8	57.2	33.0	14.40	0.356	142.6	4.428	105.2	10.12	8.24
		S.D.	10.48	3.8	2.9	18.3	3.62	0.015	0.5	0.178	1.9	0.45	0.69

Table 23-1 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Biochemical findings of female rats in the satellite group after Week 6 of administration -

Group	Number of animals		TP g/dL	Albumin g/dL	A/G ratio	Protein fraction (%)					AST IU/L	ALT IU/L	ALP IU/L	γ-GTP IU/L	T-Bil mg/dL
						Albumin	Globulin								
							α_1	α_2	β	γ					
0 mg/kg	5	Mean	5.64	3.230	1.346	57.26	16.70	6.16	14.10	5.78	74.2	29.6	189.4	0.64	0.056
		S.D.	0.34	0.353	0.158	2.78	1.19	0.32	1.12	1.79	33.0	18.2	31.3	0.19	0.009
100 mg/kg	5	Mean	5.56	3.114	1.278	56.02	16.36	6.66	15.02	5.94	62.2	24.4	165.6	0.68	0.052
		S.D.	0.32	0.236	0.115	2.04	1.07	0.88	1.04	1.17	11.2	5.9	39.6	0.24	0.011

Group	Number of animals		TBA μmol/L	Glucose mg/dL	T-Cho mg/dL	TG mg/dL	UN mg/dL	Crea mg/dL	Na mEq/L	K mEq/L	Cl mEq/L	Ca mg/dL	IP mg/dL
0 mg/kg	5	Mean	9.68	126.0	59.8	19.8	17.78	0.404	144.2	4.082	106.4	10.10	7.46
		S.D.	4.23	17.8	10.2	5.4	1.81	0.040	0.8	0.125	0.9	0.20	0.53
100 mg/kg	5	Mean	9.22	122.0	60.2	16.4	14.72**	0.376	144.2	4.140	106.4	9.90	7.26
		S.D.	2.21	10.1	14.5	8.1	0.89	0.040	0.8	0.305	1.1	0.34	0.91

** : Significantly different from the 0 mg/kg group at P≦0.01 (Dunnett's test).

Table 23-2 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Biochemical findings of female rats in the satellite group after Week 2 of recovery -

Group	Number of animals		TP g/dL	Albumin g/dL	A/G ratio	Protein fraction (%)					AST IU/L	ALT IU/L	ALP IU/L	γ-GTP IU/L	T-Bil mg/dL
						Albumin	Globulin α_1	Globulin α_2	Globulin β	Globulin γ					
0 mg/kg	5	Mean	5.96	3.190	1.154	53.52	18.94	6.12	15.52	5.90	63.6	33.0	143.2	0.70	0.072
		S.D.	0.31	0.131	0.082	1.73	0.71	0.47	1.08	0.97	8.4	6.0	39.6	0.28	0.013
100 mg/kg	5	Mean	5.86	3.378	1.364*	57.64**	15.86**	6.02	14.96	5.52	57.0	24.8	115.2	0.44	0.062
		S.D.	0.57	0.343	0.119	2.09	1.92	0.38	1.66	0.68	11.3	9.1	20.1	0.05	0.011

Group	Number of animals		TBA μmol/L	Glucose mg/dL	T-Cho mg/dL	TG mg/dL	UN mg/dL	Crea mg/dL	Na mEq/L	K mEq/L	Cl mEq/L	Ca mg/dL	IP mg/dL
0 mg/kg	5	Mean	14.20	132.0	79.6	39.8	18.70	0.406	143.0	4.290	104.6	10.18	6.90
		S.D.	8.64	2.5	7.7	18.5	1.16	0.036	1.6	0.070	1.1	0.26	1.22
100 mg/kg	5	Mean	8.78	124.8	75.4	30.8	17.86	0.384	143.6	4.106*	105.4	10.04	7.34
		S.D.	4.48	6.5	15.8	14.5	1.07	0.032	0.9	0.111	0.9	0.27	1.14

* : Significantly different from the 0 mg/kg group at $p \leqq 0.05$ (Dunnett's test).
** : Significantly different from the 0 mg/kg group at $p \leqq 0.01$ (Dunnett's test).

Table 24 indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Gross findings of male rats -

	After Week 6 of administration				After Week 2 of recovery	
Group	0 mg/kg	4 mg/kg	20 mg/kg	100 mg/kg	0 mg/kg	100 mg/kg
Number of animals examined	7	12	12	7	5	5
No abnormal findings	6	11	12	5	5	5
Organ : Findings						
Epididymis : Yellowish white mass, cauda (unilateral)	1	0	0	0	0	0
Epididymis : Yellowish white patch, cauda (unilateral)	0	1	0	2	0	0

Values are number of animals with findings.

Table 25 indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Gross findings of female rats at Day 5 of lactation -

	Group	0 mg/kg	4 mg/kg	20 mg/kg	100 mg/kg
Number of animals examined		12	12	12	12
Number of pregnant animals		12	12	12	12
No abnormal findings		10	10	11	11
Organ :	Findings				
Forestomach :	Black patch, mucosa	1[a]	0	0	0
	Thickening (crateriform), mucosa	0	1	0	0
	Recessed area, mucosa	0	1	0	0
	Adhesion, adipose tissue	0	1	0	0
Glandular stomach :	Black patch, mucosa	1[a]	1	0	0
Stomach :	White mass, limiting ridge	1	0	0	0
	Thickening, limiting ridge	0	1	0	0
Liver :	Yellowish brown discoloration	0	1	0	0
Spleen :	Atrophy	1[a]	0	0	0
Thymus :	Atrophy	1[a]	1	0	0
Adrenal :	Hypertrophy (bilateral)	1[a]	0	0	0
Kidney :	Dilatation, renel pelvis (unilateral)	0	0	0	1
Skin of left inguinal region :	Subcutaneous greenish brown mass	0	0	1	0

Values are number of animals with findings.

a : Findings with a dead animal on Day 3 of lactation .

Table 26 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Gross findings of female rats in the satellite group -

	After Week 6 of administration		After Week 2 of recovery	
Group	0 mg/kg	100 mg/kg	0 mg/kg	100 mg/kg
Number of animals examined	5	5	5	5
No abnormal findings	4	4	5	5
Organ ： Findings				
Glandular stomach ： Black patch, mucosa	1	0	0	0
Elevated area, mucosa	0	1	0	0

Values are number of animals with findings.

Table 27-1 indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Organ weight of male rats at end of administration after Week 6 of administration -

Group	Number of animals		Body weight g	Liver g	Liver %	Kidney g	Kidney %	Spleen g	Spleen %	Heart g	Heart %	Brain g	Brain %	Pituitary gland mg	Pituitary gland 10^{-3}%	Thymus mg	Thymus 10^{-3}%
0 mg/kg	7	Mean	513.6	13.329	2.580	3.464	0.674	0.840	0.161	1.517	0.296	2.211	0.434	13.39	2.629	311.4	60.744
		S.D.	55.7	2.380	0.232	0.375	0.026	0.213	0.031	0.165	0.010	0.022	0.045	1.75	0.411	100.3	18.584
4 mg/kg	12	Mean	511.6	13.873	2.704	3.413	0.666	0.742	0.143	1.457	0.286	2.160	0.423	13.22	2.582	303.5	59.251
		S.D.	28.9	1.487	0.169	0.407	0.052	0.117	0.020	0.100	0.016	0.093	0.025	1.60	0.264	68.6	12.667
20 mg/kg	12	Mean	500.3	13.158	2.629	3.298	0.661	0.797	0.160	1.438	0.289	2.207	0.441	13.34	2.673	309.5	61.560
		S.D.	28.9	1.278	0.181	0.261	0.047	0.130	0.022	0.100	0.017	0.059	0.024	1.16	0.241	93.5	16.711
100 mg/kg	7	Mean	481.0	12.956	2.694	3.326	0.691	0.814	0.166	1.419	0.294	2.237	0.467	12.49	2.591	282.0	59.134
		S.D.	35.0	1.256	0.177	0.316	0.044	0.181	0.026	0.131	0.022	0.029	0.030	1.46	0.173	65.8	15.472

Group	Number of animals		Thyroid mg	Thyroid 10^{-3}%	Adrenal mg	Adrenal 10^{-3}%	Testis g	Testis %	Epididymis g	Epididymis %	Prostate mg	Prostate 10^{-3}%	Seminal vesicle g	Seminal vesicle %
0 mg/kg	7	Mean	23.41	4.570	68.9	13.463	3.466	0.677	1.454	0.283	835.3	163.824	2.263	0.444
		S.D.	5.18	0.896	9.0	1.748	0.259	0.056	0.215	0.035	193.7	37.229	0.370	0.075
4 mg/kg	12	Mean	23.58	4.613	68.3	13.369	3.263	0.638	1.412	0.276	762.8	148.895	2.378	0.467
		S.D.	4.34	0.821	10.8	2.207	0.153	0.035	0.118	0.019	190.4	34.912	0.171	0.042
20 mg/kg	12	Mean	24.40	4.885	64.3	12.866	3.381	0.676	1.403	0.282	756.5	152.120	2.283	0.458
		S.D.	3.37	0.677	9.0	1.823	0.158	0.049	0.084	0.023	172.9	38.136	0.214	0.053
100 mg/kg	7	Mean	20.59	4.303	61.4	12.816	3.313	0.691	1.374	0.289	772.4	160.303	2.247	0.469
		S.D.	3.05	0.743	7.9	1.809	0.216	0.056	0.124	0.030	225.3	46.766	0.297	0.058

Table 27-2 indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Organ weight of male rats after Week 2 of recovery -

Group	Number of animals		Body weight g	Liver g	Liver %	Kidney g	Kidney %	Spleen g	Spleen %	Heart g	Heart %	Brain g	Brain %	Pituitary gland mg	Pituitary gland 10^{-3}%	Thymus mg	Thymus 10^{-3}%
0 mg/kg	5	Mean	517.2	13.472	2.604	3.236	0.628	0.766	0.152	1.510	0.294	2.212	0.428	12.72	2.472	331.6	64.186
		S.D.	26.1	1.066	0.167	0.221	0.031	0.106	0.019	0.098	0.023	0.058	0.026	1.29	0.372	62.1	12.425
100 mg/kg	5	Mean	497.0	12.380	2.490	3.242	0.652	0.698	0.142	1.386*	0.278	2.168	0.438	13.46	2.700	316.0	63.672
		S.D.	18.0	1.002	0.141	0.369	0.063	0.056	0.015	0.051	0.015	0.128	0.016	2.24	0.390	77.3	15.965

Group	Number of animals		Thyroid mg	Thyroid 10^{-3}%	Adrenal mg	Adrenal 10^{-3}%	Testis g	Testis %	Epididymis g	Epididymis %	Prostate mg	Prostate 10^{-3}%	Seminal vesicle g	Seminal vesicle %
0 mg/kg	5	Mean	25.94	5.030	56.6	10.940	3.338	0.648	1.362	0.264	972.4	188.832	2.254	0.436
		S.D.	4.06	0.844	4.7	0.614	0.218	0.034	0.045	0.011	71.4	22.403	0.236	0.041
100 mg/kg	5	Mean	23.00	4.616	60.2	12.068	3.224	0.648	1.428	0.286*	673.0*	136.042*	1.926*	0.388
		S.D.	3.82	0.648	10.6	1.664	0.218	0.050	0.077	0.015	197.2	42.242	0.126	0.033

* : Significantly different from the 0 mg/kg group at $p \leqq 0.05$ (Dunnett's test).

Table 28 indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Organ weight of female rats at Day 5 of lactation -

Group	Number of animals		Body weight g	Liver g	Liver %	Kidney g	Kidney %	Spleen g	Spleen %	Heart g	Heart %	Brain g	Brain %	Pituitary gland mg	Pituitary gland 10^{-3}%	Thymus mg	Thymus 10^{-3}%
0 mg/kg	11	Mean	320.1	10.461	3.270	2.111	0.659	0.795	0.245	1.038	0.326	2.071	0.649	18.54	5.815	246.6	77.213
		S.D.	21.2	0.997	0.239	0.192	0.046	0.144	0.033	0.077	0.030	0.068	0.034	2.17	0.808	51.9	16.524
4 mg/kg	12	Mean	315.2	10.343	3.294	2.130	0.681	0.767	0.243	1.003	0.319	2.045	0.653	17.10	5.446	221.1	69.038
		S.D.	26.4	0.790	0.265	0.129	0.066	0.205	0.062	0.116	0.029	0.058	0.059	1.89	0.639	86.8	23.974
20 mg/kg	12	Mean	314.3	10.527	3.358	2.129	0.678	0.759	0.242	0.988	0.314	2.032	0.648	16.98	5.413	208.2	66.263
		S.D.	18.5	0.513	0.199	0.150	0.037	0.131	0.042	0.079	0.029	0.072	0.036	1.91	0.614	47.9	15.110
100 mg/kg	12	Mean	296.3*	10.172	3.430	2.093	0.708	0.752	0.253	0.978	0.331	2.038	0.691	16.87	5.708	216.5	72.911
		S.D.	18.7	0.939	0.190	0.104	0.029	0.169	0.053	0.104	0.029	0.060	0.034	1.99	0.720	53.7	17.192

Group	Number of animals		Thyroid mg	Thyroid 10^{-3}%	Adrenal mg	Adrenal 10^{-3}%	Ovary mg	Ovary 10^{-3}%	Uterus g	Uterus %
0 mg/kg	11	Mean	17.29	5.403	82.0	25.706	127.5	39.912	0.742	0.231
		S.D.	2.23	0.572	5.0	2.133	14.7	4.584	0.113	0.031
4 mg/kg	12	Mean	16.48	5.231	82.2	26.261	118.9	37.843	0.737	0.235
		S.D.	3.24	0.932	11.3	4.328	12.1	3.680	0.089	0.041
20 mg/kg	12	Mean	17.19	5.492	81.8	26.009	116.0	37.197	0.707	0.224
		S.D.	2.27	0.832	10.1	2.692	19.4	7.529	0.062	0.024
100 mg/kg	12	Mean	18.19	6.116	80.7	27.203	116.8	39.363	0.693	0.233
		S.D.	4.08	1.160	7.3	1.411	12.4	2.950	0.059	0.020

* : Significantly different from the 0 mg/kg group at $p \leqq 0.05$ (Dunnett's test).

Table 29-1 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Organ weight of female rats in the satellite group after Week 6 of administration -

Group	Number of animals		Body weight g	Liver g	Liver %	Kidney g	Kidney %	Spleen g	Spleen %	Heart g	Heart %	Brain g	Brain %	Pituitary gland mg	Pituitary gland 10^{-3}%	Thymus mg	Thymus 10^{-3}%
0 mg/kg	5	Mean	286.8	7.156	2.498	1.840	0.640	0.558	0.194	0.920	0.322	1.976	0.688	15.22	5.302	305.4	107.292
		S.D.	13.1	0.413	0.154	0.077	0.020	0.069	0.025	0.045	0.028	0.101	0.035	2.49	0.780	66.2	26.998
100 mg/kg	5	Mean	264.0*	7.488	2.834**	1.852	0.702	0.514	0.194	0.844*	0.320	1.978	0.752*	16.22	6.128	254.2	95.960
		S.D.	11.9	0.506	0.102	0.200	0.083	0.079	0.024	0.043	0.014	0.026	0.039	2.26	0.675	44.9	14.192

Group	Number of animals		Thyroid mg	Thyroid 10^{-3}%	Adrenal mg	Adrenal 10^{-3}%	Ovary mg	Ovary 10^{-3}%	Uterus g	Uterus %
0 mg/kg	5	Mean	16.30	5.718	74.2	25.778	106.6	37.038	0.820	0.288
		S.D.	4.24	1.627	15.2	4.349	21.0	6.135	0.205	0.080
100 mg/kg	5	Mean	16.00	6.058	72.0	27.294	112.0	42.392	0.708	0.268
		S.D.	2.05	0.688	10.4	3.852	22.5	7.975	0.256	0.089

* : Significantly different from the 0 mg/kg group at $p \leqq 0.05$ (Dunnett's test).

** : Significantly different from the 0 mg/kg group at $p \leqq 0.01$ (Dunnett's test).

Table 29-2 indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Organ weight of female rats in the satellite group after Week 2 of recovery -

Group	Number of animals		Body weight g	Liver g	Liver %	Kidney g	Kidney %	Spleen g	Spleen %	Heart g	Heart %	Brain g	Brain %	Pituitary gland mg	Pituitary gland 10^{-3}%	Thymus mg	Thymus 10^{-3}%
0 mg/kg	5	Mean	293.8	7.428	2.534	1.910	0.652	0.538	0.184	0.990	0.336	2.056	0.702	17.04	5.798	246.6	83.246
		S.D.	10.6	0.309	0.142	0.116	0.018	0.094	0.035	0.050	0.019	0.069	0.050	2.41	0.788	94.1	29.104
100 mg/kg	5	Mean	281.6	7.632	2.700	2.004	0.716	0.552	0.198	0.894*	0.316	2.060	0.738	16.82	5.940	302.4	107.810
		S.D.	22.2	1.164	0.244	0.085	0.060	0.068	0.028	0.046	0.013	0.095	0.085	3.39	0.800	26.4	11.904

Group	Number of animals		Thyroid mg	Thyroid 10^{-3}%	Adrenal mg	Adrenal 10^{-3}%	Ovary mg	Ovary 10^{-3}%	Uterus g	Uterus %
0 mg/kg	5	Mean	15.98	5.446	67.8	23.118	93.0	31.716	0.538	0.184
		S.D.	3.27	1.112	5.4	2.265	15.4	5.461	0.053	0.019
100 mg/kg	5	Mean	14.20	5.068	73.8	26.176	77.6	27.942	0.786++	0.280+
		S.D.	1.44	0.649	14.2	4.400	13.2	6.635	0.202	0.074

* : Significantly different from the 0 mg/kg group at p≦ 0.05 (Dunnett's test).

+ : Significantly different from the 0 mg/kg group at P≦ 0.05 (Steel's test).

++ : Significantly different from the 0 mg/kg group at P≦ 0.01 (Steel's test).

Table 30-1 indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Histopathological findings of male rats afer Week 6 of administration -

		Group	0 mg/kg	4 mg/kg	20 mg/kg	100 mg/kg
Number of animals examined			7	12	12	7
Organ: Findings		Grade				
Lung:	Aggregation, macrophage, alveolar	+	1	-	-	2
	Mineralization, artery	+	1	-	-	1
Liver:	Microgranuloma	+	1	-	-	2
	Fatty change, periportal	+	2	-	-	0
Heart:	Inflammation, focal	+	4	-	-	3
Kidney:	Eosinophilic body, proximal tubbular epithelium	+	1	2	1	4
	Basophilic change, tubular epithelium	+	1	1	0	1
	Cyst	+	0	0	1	0
Epididymis:	Granuloma, spermatic	+	0	1 (1)	-	2
		++	1	0 (1)	-	0
Prostate:	Cellular infiltration, inflammatory cell	+	1	[9]$^{+}$	4	[6]$^{+}$
		++	0	0	3	0
Pituitary gland:	Cyst, pars distalis	+	1	-	-	0
Eyeball:	Retinal rosette	+	0	-	-	2
Harderian gland:	Cellular infiltration, mononuclear cell	+	0	-	-	1

Values are the number of animals with findings.
Values in parentheses are the number of animals examined.
-: Not applicable.
Grade; +: slight change, ++: moderate change, +++: severe change.
[ ] $^{+}$: Significantly different from the 0 mg/kg group at P≦0.05 (Steel's test).

Table 30-2 indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Histopathological findings of male rats after Week 2 of recovery -

		Group	0 mg/kg	100 mg/kg
Number of animals examined			5	5
Organ: Findings		Grade		
Lung:	Aggregation, macrophage, alveolar	+	2	0
	Metaplasia, osseous, alveoli	+	1	1
	Mineralization, artery	+	3	1
Pancreas:	Atrophy, acinar cell, focal	+	2	0
Liver:	Microgranuloma	+	1	2
	Fatty change, periportal	+	2	0
Heart:	Inflammation, focal	+	1	1
Kidney:	Eosinophilic body, proximal tubular epithelium	+	0	1
	Basophilic change, tubular epithelium	+	1	0
Prostate:	Cellular infiltration, inflammatory cell	+	2	3
Pituitary gland:	Cyst, pars distalis	+	0	1
	Cyst, pars intermedia	+	0	1
Eyeball:	Atrophy, retina, focal	+	1	0
	Retinal rosette	+	0	1
Harderian gland:	Cellular infiltration, mononuclear cell	+	0	1

Values are the number of animals with findings.

Grade; +: slight change, ++: moderate change, +++: severe change.

Table 31 indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Histopathological findings of female rats at Day 5 of lactation -

		Group	0 mg/kg	4 mg/kg	20 mg/kg	100 mg/kg
Number of animals examined			12	12	12	12
Organ: Findings		Grade				
Lung:	Aggregation, macrophage, alveolar	+	1	-	-	2
Forestomach:	Erosion	+	1[a]	0 (1)	-	0
	Ulcer	++	0	1 (1)	-	0
Stomach, limiting ridge:	Cyst, squamous cell	+	1	0 (1)	-	0
	Hyperplasia, squamous cell	++	0	1 (1)	-	0
Glandular stomach:	Erosion	+	1[a]	1 (1)	-	0
Liver:	Microgranuloma	+	2	0 (1)	-	4
	Necrosis, focal	+	1	0 (1)	-	1
	Fatty change, periportal	++	0	1 (1)	-	0
Kidney:	Dilatation, tubule, cortex	+	1[a]	0	0	0
	Cellular infiltration, inflammatory cell, renal pelvic mucosa	+	1	0	0	0
	Fatty change, tubular epithelium	+	0	1	0	0
	Dilatation, renal pelvis	+	0	0	0	1
Spleen:	Atrophy, follicle	++	1[a]	-	-	0
	Deposit, hemosiderin	+	1[a]	-	-	0
Thymus:	Atrophy	++	1[a]	1 (1)	-	0
Pituitary gland:	Cyst, pars distalis	+	0	-	-	1
Adrenal:	Necrosis, cortical cell, with cellular infiltration, inflammatory cell	+++	1[a]	-	-	0
Eyeball:	Cellular infiltration, neutrophil, ciliary body and iris	+	0	-	-	1
Mammary gland:	Hyperplasia, with inflammation	+	0	-	1 (1)	0

Values are the number of animals with findings.
Values in parentheses are the number of animals examined.
-: Not applicable.
Grade; +: slight change, ++: moderate change, +++: severe change.
a : Findings with a dead animal on Day 3 of lactation .

Table 32-1 indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Histopathological findings of female rats in the satellite group after Week 6 of administration -

		Group	Control	100 mg/kg
Number of animals examined			5	5
Organ: Findings		Grade		
Lung:	Aggregation, macrophage, alveolar	+	0	1
Glandular stomach:	Erosion	+	1	0
	Ductal tissue, ectopic, submucosa	+	0	1
Liver:	Microgranuloma	+	1	0
	Fatty change, periportal	+	0	1
Heart:	Inflammation, focal	+	1	0
Kidney:	Cellular infiltration, inflammatory cell, renal pelvic mucosa	+	1	0
Harderian gland:	Cellular infiltration, mononuclear cell	+	0	1

Values are the number of animals with findings.

Grade; +: slight change, ++: moderate change, +++: severe change.

Table 32-2 indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Histopathological findings of female rats n the satellite group after Week 2 of recovery -

		Group	0 mg/kg	100 mg/kg
Number of animals examined			5	5
Organ: Findings		Grade		
Lung:	Aggregation, macrophage, alveolar	+	3	0
	Mineralization, artery	+	3	1
	Metaplasia, osseous, alveoli	+	1	0
Pancreas:	Atrophy, acinar cell, focal	+	0	1
Liver:	Microgranuloma	+	0	1
Kidney:	Cellular infiltration, inflammatory cell, renal pelvic mucosa	+	1	0

Values are the number of animals with findings.

Grade; +: slight change, ++: moderate change, +++: severe change.

Table 33 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Reproduction performance in parental rats -

Group	Estrous cycle: Length (days) Mean	Estrous cycle: Length (days) S.D.	Estrous cycle: Abnormal estrous cycle Incidence	Estrous cycle: Abnormal estrous cycle (%)	Copulation index: Male Incidence (%)	Copulation index: Female Incidence (%)	Fertility index Incidence (%)	Gestation index Incidence (%)	Gestation length (days) Mean	Gestation length (days) S.D.	Nursing index Incidence (%)
0 mg/kg	4.23	0.36	0/12	(0.0)	12/12 (100.0)	12/12 (100.0)	12/12 (100.0)	12/12 (100.0)	22.4	0.5	11/12 (91.7)
4 mg/kg	4.03	0.09	0/12	(0.0)	12/12 (100.0)	12/12 (100.0)	12/12 100.0)	12/12 100.0)	22.5	0.5	12/12 (100.0)
20 mg/kg	4.00	0.00	0/12	(0.0)	12/12 (100.0)	12/12 (100.0)	12/12 (100.0)	12/12 (100.0)	22.4	0.7	12/12 (100.0)
100 mg/kg	4.41	0.68	0/12	(0.0)	12/12 (100.0)	12/12 (100.0)	12/12 (100.0)	12/12 (100.0)	22.2	0.4	12/12 (100.0)

Abnormal estrous cycle = (number of female with abnormal estrous cycle / number of females examined) x 100.
Copulation index = (number of copulated animals / number of animals mated) x 100.
Fertility index = (number of pregnant females / number of copulated females) x 100.
Gestation index = (number of females with live pups / number of pregnant females) x 100.
Nursing index = (number of females nursing live pups on lactation day 4 / number of females with live pups delivery) x 100.

Table 34 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Pregnancy and litter data of rats -

Group	Number of Dams		Number of corpora lutea	Number of implantation sites	Implantation index (%)	Delivery index (%)	Lactation day 0						Lactation day 4		
							Number of total pups born	Number of total dead pups	Number of total live pups	Sex ratio		Live birth index (%)	Number of total live pups	Sex ratio	Viability index (%)
										Pups born	Live pups				
														(11)	
0 mg/kg	12	Mean	16.7	16.2	97.141	97.477	15.8	1.3	14.4	0.565	0.583	92.477	13.8	0.547	89.955
		S.D.	1.9	1.9	5.662	4.746	2.0	4.0	3.8	0.130	0.172	22.415	4.8	0.109	28.655
4 mg/kg	12	Mean	15.6	15.2	97.298	92.798	14.1	0.0	14.1	0.526	0.526	100.000	14.0	0.523	99.479
		S.D.	1.2	1.3	3.372	8.374	1.8	0.0	1.8	0.138	0.138	0.000	1.8	0.139	1.804
20 mg/kg	12	Mean	16.0	15.8	98.989	92.978	14.8	0.5	14.3	0.520	0.508	97.261	14.1	0.509	98.888
		S.D.	1.1	1.1	2.362	15.116	2.7	1.2	2.7	0.170	0.178	6.286	2.7	0.175	2.596
100 mg/kg	12	Mean	16.3	15.9	98.001	94.957	15.1	0.2	14.9	0.535	0.537	98.889	14.8	0.537	98.915
		S.D.	1.1	1.2	3.882	5.994	1.1	0.6	1.2	0.108	0.110	3.848	1.2	0.106	2.548

Implantation index = (Number of implantation sites / number of corpora lutea) x 100.
Delivery index = (Number of pups born / number of implantation sites) x 100.
Sex ratio on Lactation day 0 = (number of male pups born / number of pups born) and (number of live male pups / number of live pups).
Sex ratio on Lactation day 4 = number of live male pups / number of live pups.
Live birth index = (Number of live pups on lactation day 0 / number of pups born) x 100.
Viability index = (Number of live pups on lactation day 4 / number of live pups on lactation day 0) x 100.

The number in the parenthese is the number of animals used for the measurement.

Table 35 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- General appearance of pups -

Group	Findings	Male					Female				
		Lactation day					Lactation day				
		0	1	2	3	4	0	1	2	3	4
0 mg/kg	Number of pups examined	109	98	94	93	93	80	75	73	73	73
	No abnormal findings	98	94	93	93	93	75	73	73	73	73
	Milk-band negative	4	0	0	0	0	0	0	0	0	0
	Death	11	4	1	0	0	5	2	0	0	0
	Milk-band negative	8	4	0	-	-	5	0	-	-	-
	Milk-band not examined	3	0	1	-	-	0	0	-	-	-
	Lost	0	0	0	-	-	0	2	-	-	-
4 mg/kg	Number of pups examined	88	88	88	88	88	81	81	81	81	81
	No abnormal findings	88	88	88	88	87	81	81	81	81	81
	Death	0	0	0	0	1	0	0	0	0	0
	Milk-band negative	-	-	-	-	1	-	-	-	-	-
	Lost	-	-	-	-	0	-	-	-	-	-
20 mg/kg	Number of pups examined	95	90	89	89	89	82	81	81	80	80
	No abnormal findings	90	89	89	89	89	81	81	80	80	80
	Death	5	1	0	0	0	1	0	1	0	0
	Milk-band positive	1	1	-	-	-	0	-	0	-	-
	Milk-band negative	1	0	-	-	-	0	-	1	-	-
	Milk-band not examined	3	0	-	-	-	1	-	0	-	-
100 mg/kg	Number of pups examined	97	96	96	95	95	84	83	82	82	82
	No abnormal findings	96	96	95	95	95	83	82	82	82	82
	Death	1	0	1	0	0	1	1	0	0	0
	Milk-band negative	1	-	1	-	-	1	0	-	-	-
	Lost	0	-	0	-	-	0	1	-	-	-

Values are number of animals with findings.
- : Not applicable.

Table 36 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Body weights of pups -

Group	Number of animals		Body weight (g) Male Lactation day 0	1	4	Female Lactation day 0	1	4
				(11)	(11)	(11)	(11)	(11)
0 mg/kg	12	Mean	6.53	7.13	10.37	6.09	6.68	9.74
		S.D.	0.53	0.76	1.31	0.50	0.75	1.45
4 mg/kg	12	Mean	7.08*	7.71	11.03	6.73**	7.38*	10.60
		S.D.	0.70	0.93	1.84	0.61	0.87	1.71
20 mg/kg	12	Mean	6.65	7.28	11.15	6.25	6.83	10.44
		S.D.	0.44	0.73	1.72	0.38	0.49	1.23
100 mg/kg	12	Mean	6.26	6.94	10.33	5.94	6.58	9.76
		S.D.	0.35	0.48	0.90	0.35	0.46	0.89

The number in the parenthese is the number of animals used for the measurement.
* : Significantly different from the 0 mg/kg group at P ≦0.05 (Dunnett's test).
** : Significantly different from the 0 mg/kg group at P ≦0.01 (Dunnett's test).

Table 37 indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (SR11087)

- Gross findings of pups -

Item	Group	Male				Female			
		0 mg/kg	4 mg/kg	20 mg/kg	100 mg/kg	0 mg/kg	4 mg/kg	20 mg/kg	100 mg/kg
Findings of dead pups during days 0-4 of lactation									
Number of pups examined		16	1	5	2	5	0	2	1
No abnormal findings		12	1	3	2	5	0	0	1
Liver : Yellowish white discoloration		0	0	0	0	0	0	1	0
Spleen : Pale discoloration		0	0	0	0	0	0	1	0
Intraperitoneum : Autolysis		4	0	2	0	0	0	1	0
Findings of pups euthanized on day 4 of lactation									
Number of pups examined		93	87	89	95	73	81	80	82
No abnormal findings		93	87	89	95	72	81	80	82
Liver : Yellowish white patch, middle lobe		0	0	0	0	1	0	0	0

Values are number of pups with findings.

INDIVIDUAL DATA 1-1

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

General appearance ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg

Animal No.	Administration period (day)																																							
	1		2		3		4		5		6		7		8		9		10		11		12		13		14		15		16		17		18		19		20		21	
	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P
101	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
102	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
103	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
104	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
105	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
106	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
107	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
108	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
109	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
110	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
111	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
112	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

Animal No.	Administration period (day)																																						Autopsy day
	22		23		24		25		26		27		28		29		30		31		32		33		34		35		36		37		38		39		40		41		42	
	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A
101	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
102	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
103	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
104	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#
105	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#
106	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#
107	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#
108	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#
109	N	N	Re	Re	Re	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
110	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
111	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
112	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : No abnormal findings. A : AM.

Re : Reddish urine. P : PM.

: Not applicable .

INDIVIDUAL DATA 1-2

STUDY NO. SR11087 TITLE : indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

General appearance ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg

Animal No.	Recovery period (day)																												Autopsy day
	1		2		3		4		5		6		7		8		9		10		11		12		13		14		
	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A
101	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#
102	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#
103	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#
104	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
105	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
106	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
107	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
108	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
109	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#
110	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#
111	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#
112	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#

N : No abnormal findings. A : AM.

: Not applicable . P : PM.

INDIVIDUAL DATA 1-3

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

General appearance ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg

Animal No.	Administration period (day)																																							
	1		2		3		4		5		6		7		8		9		10		11		12		13		14		15		16		17		18		19		20		21	
	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P
201	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
202	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
203	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
204	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
205	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
206	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
207	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
208	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
209	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
210	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
211	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
212	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

Animal No.	Administration period (day)																																								Autopsy day
	22		23		24		25		26		27		28		29		30		31		32		33		34		35		36		37		38		39		40		41		42		
	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A
201	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
202	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
203	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
204	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
205	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
206	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
207	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
208	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
209	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
210	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
211	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
212	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : No abnormal findings.

A : AM.

P : PM.

INDIVIDUAL DATA 1-4

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

General appearance ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg

Animal No.	Administration period (day)																																			
	1		2		3		4		5		6		7		8		9		10		11		12		13		14		15		16		17		18		19		20		21	
	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P
301	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
302	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
303	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
304	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
305	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
306	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
307	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
308	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
309	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
310	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
311	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
312	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

Animal No.	Administration period (day)																																				Autopsy day
	22		23		24		25		26		27		28		29		30		31		32		33		34		35		36		37		38		39		40		41		42		
	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A
301	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
302	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
303	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
304	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
305	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
306	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
307	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
308	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
309	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
310	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
311	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
312	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : No abnormal findings.

A : AM.

P : PM.

INDIVIDUAL DATA 1-5

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

General appearance ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg

Animal No.	Administration period (day)																																							
	1		2		3		4		5		6		7		8		9		10		11		12		13		14		15		16		17		18		19		20		21	
	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P
401	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
402	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
403	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
404	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
405	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
406	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
407	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
408	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
409	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
410	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
411	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
412	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

Animal No.	Administration period (day)																																						Autopsy day
	22		23		24		25		26		27		28		29		30		31		32		33		34		35		36		37		38		39		40		41		42	
	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A
401	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#
402	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
403	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
404	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#
405	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
406	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#
407	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
408	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
409	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
410	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
411	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#
412	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#

N : No abnormal findings. A : AM.

: Not applicable . P : PM.

INDIVIDUAL DATA 1-6

STUDY NO. SR11087 TITLE : indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

General appearance ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg

Animal No.	Recovery period (day)																												Autopsy day
	1		2		3		4		5		6		7		8		9		10		11		12		13		14		
	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A
401	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
402	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#
403	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#
404	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
405	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#
406	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
407	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#
408	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#
409	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#
410	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#
411	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
412	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : No abnormal findings. A : AM.

: Not applicable . P : PM.

INDIVIDUAL DATA 2-1-1

STUDY NO. SR11087 TITLE : indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

General appearance ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg

Animal No.	Pre-mating period (day)																															
	1		2		3		4		5		6		7		8		9		10		11		12		13		14		15		16		17	
	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P
151	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#	#	#
152	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#	#	#
153	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
154	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#
155	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#
156	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
157	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
158	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
159	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#	#	#
160	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#
161	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#	#	#
162	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#

N : No abnormal findings. A : AM.

: Not applicable (Copulated) . P : PM.

INDIVIDUAL DATA 2-1-2

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

General appearance ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg

Animal No.	Pre-mating period (day)																															
	1		2		3		4		5		6		7		8		9		10		11		12		13		14		15		16		17	
	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P
251	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
252	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
253	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
254	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
255	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
256	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#	#	#
257	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#	#	#
258	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
259	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#
260	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#	#	#
261	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
262	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#	#	#

N : No abnormal findings. A : AM.

: Not applicable (Copulated) . P : PM.

INDIVIDUAL DATA 2-1-3

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

General appearance ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg

Animal No.	Pre-mating period (day)																															
	1		2		3		4		5		6		7		8		9		10		11		12		13		14		15		16		17	
	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P
351	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
352	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#
353	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#	#	#
354	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
355	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#	#	#
356	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#
357	N	N	N	N	N	N	N	N	N	N	N	N	N	Fr	Fr	Fr	Fr	Fr	Fr	Fr	N	N	N	N	N	N	N	N	#	#	#	#	#	#
358	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#
359	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#
360	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#
361	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
362	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : No abnormal findings. A : AM.

Fr : Fracture of rigth upper incisors P : PM.

: Not applicable (Copulated) .

INDIVIDUAL DATA 2-1-4

STUDY NO. SR11087 TITLE : indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

General appearance ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg

Animal No.	Pre-mating period (day)																															
	1		2		3		4		5		6		7		8		9		10		11		12		13		14		15		16		17	
	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P
451	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#
452	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#
453	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
454	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
455	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
456	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#	#	#
457	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#
458	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#
459	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
460	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
461	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
462	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#

N : No abnormal findings. A : AM.

: Not applicable (Copulated) . P : PM.

INDIVIDUAL DATA 2-2-1

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

General appearance ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg

Animal No.	Gestation period (day)																																													
	0		1		2		3		4		5		6		7		8		9		10		11		12		13		14		15		16		17		18		19		20		21		22	
	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P
151	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
152	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
153	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
154	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
155	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
156	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
157	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
158	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
159	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
160	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
161	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
162	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : No abnormal findings. A : AM.

: Not applicable. P : PM.

INDIVIDUAL DATA 2-2-2
STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
General appearance ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg

	Gestation period (day)																																													
Animal No.	0		1		2		3		4		5		6		7		8		9		10		11		12		13		14		15		16		17		18		19		20		21		22	
	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P
251	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
252	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
253	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
254	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
255	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
256	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
257	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
258	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
259	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
260	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
261	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
262	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#

N : No abnormal findings.
: Not applicable.

A : AM.
P : PM.

INDIVIDUAL DATA 2-2-3

STUDY NO. SR11087 TITLE : indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

General appearance ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg

Animal No.	Gestation period (day)																																											
	0		1		2		3		4		5		6		7		8		9		10		11		12		13		14		15		16		17		18		19		20		21		22		23	
	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P
351	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#
352	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#
353	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
354	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
355	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#
356	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
357	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#
358	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#
359	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
360	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#
361	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#
362	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#	#	#

N : No abnormal findings.

: Not applicable.

A : AM.

P : PM.

INDIVIDUAL DATA 2-2-4

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

General appearance ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg

	Gestation period (day)																																													
Animal No.	0		1		2		3		4		5		6		7		8		9		10		11		12		13		14		15		16		17		18		19		20		21		22	
	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P
451	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
452	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
453	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
454	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
455	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
456	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
457	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Mf. Pg	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
458	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
459	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
460	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
461	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#
462	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#	#

N : No abnormal findings.

Mf : Mucous feces

Pg : Pale Greenish stool

: Not applicable.

A : AM.

P : PM.

INDIVIDUAL DATA 2-3-1

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

General appearance ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg

Animal No.	Lactation period (day)										Autopsy day
	0		1		2		3		4		
	A	P	A	P	A	P	A	P	A	P	A
151	N	N	N	N	N	N	N	N	N	N	N
152	N	N	N	N	N	N	N	N	N	N	N
153	N	N	N	N	N	N	N	N	N	N	N
154	N	N	N	N	N	N	N	N	N	N	N
155	Sg.Sp	Sg.Sp	Sg.Sp	Mf.Sg.Sp So.Sc	Mf.Sg.Sp So.Sc	Mf.Sg.Sp So.Sc.Ho	D.Sg.Sp So.Sc	#	#	#	#
156	N	N	N	N	N	N	N	N	N	N	N
157	N	N	N	N	N	N	N	N	N	N	N
158	N	N	N	N	N	N	N	N	N	N	N
159	N	N	N	N	N	N	N	N	N	N	N
160	N	N	N	N	N	N	N	N	N	N	N
161	N	N	N	N	N	N	N	N	N	N	N
162	N	N	N	N	N	N	N	N	N	N	N

N: No abnormal findings.

D : Dead

Sg : Soil of perigenital fur

Sp : Soil of perianal fur

So : Soil of perioral fur

Sc : Soil of periocular fur

Mf : Mucous feces

Ho : Hypothermia

: Not applicable.

A : AM.

P : PM.

INDIVIDUAL DATA 2-3-2

STUDY NO. SR11087 TITLE : indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

General appearance ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg

Animal No.	Lactation period (day)										Autopsy day
	0		1		2		3		4		
	A	P	A	P	A	P	A	P	A	P	A
251	N	N	N	N	N	N	N	N	N	N	N
252	N	N	N	N	N	N	N	N	N	N	N
253	N	N	N	N	N	N	N	N	N	N	N
254	N	N	N	N	N	N	N	N	N	N	N
255	N	N	N	N	N	N	N	N	N	N	N
256	N	N	N	N	N	N	N	N	N	N	N
257	N	N	N	N	N	N	N	N	N	N	N
258	N	N	N	N	N	N	N	N	N	N	N
259	N	N	N	N	N	N	N	N	N	N	N
260	N	N	N	N	N	N	N	N	N	N	N
261	N	N	N	N	N	N	N	N	N	N	N
262	N	N	N	N	N	N	N	N	N	N	N

N : No abnormal findings.

A : AM.
P : PM.

INDIVIDUAL DATA 2-3-3

STUDY NO. SR11087 TITLE : indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

General appearance ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg

Animal No.	Lactation period (day)										Autopsy day
	0		1		2		3		4		
	A	P	A	P	A	P	A	P	A	P	A
351	N	N	N	N	N	N	N	N	N	N	N
352	N	N	N	N	N	N	N	N	N	N	N
353	N	N	N	Fl	Fl	Fl	Fl	Fl	Fl	Fl	N
354	N	N	N	N	N	N	N	N	N	N	N
355	N	N	N	N	N	N	N	N	N	N	N
356	N	N	N	N	N	N	N	N	N	N	N
357	N	N	N	N	N	N	N	N	N	N	N
358	N	N	N	N	N	N	N	N	N	N	N
359	N	N	N	N	N	N	N	N	N	N	N
360	N	N	N	N	N	N	N	N	N	N	N
361	Sui (30×20×15)	Sui (30×20×15)	Sui (30×20×15)	Sui (30×20×15)	Sui (30×20×15)	Sui (30×20×15)	Sui (20×10×10)	Sui (20×10×10)	Sui (15×10×5)	Sui (15×10×5)	Sui (15×10×5)
362	N	N	N	N	N	N	N	N	N	N	N

N : No abnormal findings.

Fl : Fracture of left upper incisors

Sui : Subcutaneous mass, left side of inguinal region (size, mm)

A : AM.

P : PM.

INDIVIDUAL DATA 2-3-4

STUDY NO. SR11087 TITLE : indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

General appearance ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg

Animal No.	Lactation period (day)										Autopsy day
	0		1		2		3		4		
	A	P	A	P	A	P	A	P	A	P	A
451	N	N	N	N	N	N	N	N	N	N	N
452	N	N	N	N	N	N	N	N	N	N	N
453	N	N	N	N	N	N	N	N	N	N	N
454	N	N	N	N	N	N	N	N	N	N	N
455	N	N	N	N	N	N	N	N	N	N	N
456	N	N	N	N	N	N	N	N	N	N	N
457	N	N	N	N	N	N	N	N	N	N	N
458	N	N	N	N	N	N	N	N	N	N	N
459	N	N	N	N	N	N	N	N	N	N	N
460	N	N	N	N	N	N	N	N	N	N	N
461	N	N	N	N	N	N	N	N	N	N	N
462	N	N	N	N	N	N	N	N	N	N	N

N : No abnormal findings.

A : AM.
P : PM.

INDIVIDUAL DATA 3-1

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

General appearance ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 0 mg/kg

Animal No.	Administration period (day)																																			
	1		2		3		4		5		6		7		8		9		10		11		12		13		14		15		16		17		18		19		20		21	
	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P
163	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
164	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
165	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
166	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
167	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
168	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
169	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
170	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
171	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
172	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

Animal No.	Administration period (day)																																				Autopsy day
	22		23		24		25		26		27		28		29		30		31		32		33		34		35		36		37		38		39		40		41		42		
	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A
163	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
164	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
165	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
166	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
167	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
168	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#
169	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#
170	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#
171	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#
172	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#

N : No abnormal findings. A : AM.

: Not applicable . P : PM.

INDIVIDUAL DATA 3-2

STUDY NO. SR11087 TITLE : indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

General appearance ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 0 mg/kg

Animal No.	Recovery period (day)																										Autopsy day
	1		2		3		4		5		6		7		8		9		10		11		12		13		14		
	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A
168	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
169	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
170	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
171	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
172	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : No abnormal findings.

A : AM.

P : PM.

INDIVIDUAL DATA 3-3

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

General appearance ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 100 mg/kg

Animal No.	Administration period (day)																																			
	1		2		3		4		5		6		7		8		9		10		11		12		13		14		15		16		17		18		19		20		21	
	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P
463	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
464	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
465	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
466	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
467	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
468	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
469	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
470	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
471	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Mf	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
472	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

Animal No.	Administration period (day)																																				Autopsy day
	22		23		24		25		26		27		28		29		30		31		32		33		34		35		36		37		38		39		40		41		42		
	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A
463	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
464	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
465	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
466	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
467	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
468	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#
469	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#
470	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#
471	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Mf	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#
472	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	#

N : No abnormal findings.

Mf : Mucous feces.

: Not applicable .

A : AM.

P : PM.

INDIVIDUAL DATA 3-4

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

General appearance ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 100 mg/kg

Animal No.	Recovery period (day)																										Autopsy day
	1		2		3		4		5		6		7		8		9		10		11		12		13		14		
	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A	P	A
468	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
469	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
470	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
471	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
472	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N : No abnormal findings.

A : AM.

P : PM.

Definitions for detailed clinical observations

Item	Category No.					
In the cage:						
Body position/Posture						
	1; Normal (sitting, etc.)	2; Sleeping	3; Crouching	4; Prone, lateral	5; Standing, jumping	6; Cataleptic
Respiratory pattern						
	1; Normal	2; Slightly abnormal, rapid or slow	3; Moderately abnormal, difficult to breath	4; Severe abnormal, labored	5; Dyspnea	
Tremor / Convulsion						
	1; Not present	2; Irregularly, only the legs	3; Durable, only the legs	4; Clonic, systemic	5; Tonic, systemic	
Stereotype						
Rolling	0; Not present	1; Sometimes	2; Frequently			
Repetitive circling						
	0; Not present	1; Sometimes	2; Frequently			
Bizarre behavior						
Biting/Selfmutilation						
	1; Not present	2; Present				
On the hand: while removing the animal from its cage						
Handling : Removal from cage						
	1; Very easy	2; Easy	3; Slightly difficult	4; Difficult	5; Very difficult	
Treating : Reactivity to handling						
	1; Very easy	2; Easy	3; Slightly difficult	4; Difficult	5; Very difficult	
Muscle tone	1; Low	2; Normal	3; High			
Piloerection	1; Not present	2; Slightly present, around head and back	3; Slightly present, systemic	4; Severely present, systemic		
Fur	1; Normal	2; Slightly stained	3; Stained			
Eyes	1; Not present, normal	2; Slight ptosis, half closed	3; Ptosis	4; Closed		
Mucous membranes						
	-1; Dark purplish appearance, cyanosis		0; Normal	1; Red appearance		

(to be continued)

(Continued 1)

Item	Category No.			
Skin	0; Pale appearance, cyanosis	1; Normal	2; Red appearance	
Pupil size	1; Normal	2; Slightly mydriatic	3; Mydriatic	
Lacrimation	1; Not present	2; Wet around the eye	3; Wet	4; Severely wet
Salivation	1; Not present	2; Wet around the mouth	3; Wet	4; Severely wet
Secretions/Excretions				
	0; Not present	1; Present		
In the open-field: when placed the animal in an open-field				
Gait	0; Not moved	1; Normal	2; Difficult to walk	3; Unable to walk, paralytic
Co-ordination of movement				
	0; staggering (ataxic)	1; Normal		
Reactivity to environmental stimuli				
	0; Not present	1; present (to noise, etc.)		
Searching	0; Not present	1; present (sniffing, standing, etc.)		
Urination	0; Not present	1; Present		
Defecation	0; Not present	1; Present		
Stereotype				
Excessive grooming				
	0; Not present	1; Sometimes	2; Frequently	
Unusual head movement				
	0; Not present	1; Sometimes	2; Frequently	
Bizarre behavior				
Walking backward				
	1; Not present	2; Present		
Vocalization	1; Not present, sometimes	2; Present, frequently		
Aggression	1; Not present	2; Present		

(to be continued)

(Continued 2)

Item	Category No.				
On the desk: stimulus reactivity					
Visual reactivity: approach response					
	1; Jumping	2; Turning away	3; No reaction	4; Approach	5; Attack
Touch reactivity: touch response					
	1; Hyposensitive	2; Turning away	3; Hypersensitive		
Auditory reactivity: response to Galton's whistle					
	0; No reaction	1; Normal, moving the auricle	2; Sensitive, moving the body	3; Hypersensitive, surprising and jumping	
Pain reactivity: tail pinch response					
	0; No reaction	1; Dull, vocalizing	2; Normal, vocalizing and turning back	3; Hypersensitive attacking or jumping	
Proprioceptive reactivity: returning from enforced posture					
	0; No returning	1; Returning			
Righting reflex: landing performance from 30 cm above					
	1; Normal, landing by foot	2; Abnormal, landing by body			
Others					
Grip strength: measuring by CPU gage®					
	expressed by mean values (g) from 3 trials; forelimb and hindlimb				
Motor activity measurements : measuring by SUPERMEX and CompACT AMS					
	expressed by total counts for 60 minutes at 10 minutes' intervals				

INDIVIDUAL DATA 4-1-1

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Pre-administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
101	1	1	1	0	0	1
102	1	1	1	0	0	1
103	1	1	1	0	0	1
104	1	1	1	0	0	1
105	1	1	1	0	0	1
106	1	1	1	0	0	1
107	1	1	1	0	0	1
108	1	1	1	0	0	1
109	1	1	1	0	0	1
110	1	1	1	0	0	1
111	1	1	1	0	0	1
112	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 4-1-2

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Pre-administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
101	1	1	2	1	1	1	0	1	1	1	1	0
102	1	1	2	1	1	1	0	1	1	1	1	0
103	1	1	2	1	1	1	0	1	1	1	1	0
104	1	1	2	1	1	1	0	1	1	1	1	0
105	1	1	2	1	1	1	0	1	1	1	1	0
106	1	1	2	1	1	1	0	1	1	1	1	0
107	1	1	2	1	1	1	0	1	1	1	1	0
108	1	1	2	1	1	1	0	1	1	1	1	0
109	1	1	2	1	1	1	0	1	1	1	1	0
110	1	1	2	1	1	1	0	1	1	1	1	0
111	1	1	2	1	1	1	0	1	1	1	1	0
112	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-1-3

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Pre-administration

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
101	1	1	1	1	0	0	0	0	1	1	1
102	1	1	1	1	0	0	0	0	1	1	1
103	1	1	1	1	0	0	0	0	1	1	1
104	1	1	1	1	0	0	0	0	1	1	1
105	1	1	1	1	0	0	0	0	1	1	1
106	1	1	1	1	0	0	0	0	1	1	1
107	1	1	1	1	0	0	0	0	1	1	1
108	1	1	1	1	0	0	0	0	1	1	1
109	1	1	1	1	0	0	0	0	1	1	1
110	1	1	1	1	0	0	0	0	1	1	1
111	1	1	1	1	0	0	0	0	1	1	1
112	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-1-4

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : Pre-administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
201	1	1	1	0	0	1
202	1	1	1	0	0	1
203	1	1	1	0	0	1
204	1	1	1	0	0	1
205	1	1	1	0	0	1
206	1	1	1	0	0	1
207	1	1	1	0	0	1
208	1	1	1	0	0	1
209	1	1	1	0	0	1
210	1	1	1	0	0	1
211	1	1	1	0	0	1
212	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 4-1-5

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : Pre-administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
201	1	1	2	1	1	1	0	1	1	1	1	0
202	1	1	2	1	1	1	0	1	1	1	1	0
203	1	1	2	1	1	1	0	1	1	1	1	0
204	1	1	2	1	1	1	0	1	1	1	1	0
205	1	1	2	1	1	1	0	1	1	1	1	0
206	1	1	2	1	1	1	0	1	1	1	1	0
207	1	1	2	1	1	1	0	1	1	1	1	0
208	1	1	2	1	1	1	0	1	1	1	1	0
209	1	1	2	1	1	1	0	1	1	1	1	0
210	1	1	2	1	1	1	0	1	1	1	1	0
211	1	1	2	1	1	1	0	1	1	1	1	0
212	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-1-6

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : Pre-administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
201	1	1	1	1	0	0	0	0	1	1	1
202	1	1	1	1	0	0	0	0	1	1	1
203	1	1	1	1	0	1	0	0	1	1	1
204	1	1	1	1	0	0	0	0	1	1	1
205	1	1	1	1	0	0	0	0	1	1	1
206	1	1	1	1	0	0	0	0	1	1	1
207	1	1	1	1	0	0	0	0	1	1	1
208	1	1	1	1	0	0	0	0	1	1	1
209	1	1	1	1	0	0	0	0	1	1	1
210	1	1	1	1	0	0	0	0	1	1	1
211	1	1	1	1	0	0	0	0	1	1	1
212	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-1-7

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : Pre-administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
301	1	1	1	0	0	1
302	1	1	1	0	0	1
303	1	1	1	0	0	1
304	1	1	1	0	0	1
305	1	1	1	0	0	1
306	1	1	1	0	0	1
307	1	1	1	0	0	1
308	1	1	1	0	0	1
309	1	1	1	0	0	1
310	1	1	1	0	0	1
311	1	1	1	0	0	1
312	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 4-1-8

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : Pre-administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
301	1	1	2	1	1	1	0	1	1	1	1	0
302	1	1	2	1	1	1	0	1	1	1	1	0
303	1	1	2	1	1	1	0	1	1	1	1	0
304	1	1	2	1	1	1	0	1	1	1	1	0
305	1	1	2	1	1	1	0	1	1	1	1	0
306	1	1	2	1	1	1	0	1	1	1	1	0
307	1	1	2	1	1	1	0	1	1	1	1	0
308	1	1	2	1	1	1	0	1	1	1	1	0
309	1	1	2	1	1	1	0	1	1	1	1	0
310	1	1	2	1	1	1	0	1	1	1	1	0
311	1	1	2	1	1	1	0	1	1	1	1	0
312	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-1-9

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : Pre-administration

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
301	1	1	1	1	0	0	0	0	1	1	1
302	1	1	1	1	0	0	0	0	1	1	1
303	1	1	1	1	0	0	0	0	1	1	1
304	1	1	1	1	0	0	0	0	1	1	1
305	1	1	1	1	0	0	0	0	1	1	1
306	1	1	1	1	0	0	0	0	1	1	1
307	1	1	1	1	0	0	0	0	1	1	1
308	1	1	1	1	0	0	0	0	1	1	1
309	1	1	1	1	0	0	0	0	1	1	1
310	1	1	1	1	0	1	0	0	1	1	1
311	1	1	1	1	0	0	0	0	1	1	1
312	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-1-10

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Pre-administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
401	1	1	1	0	0	1
402	1	1	1	0	0	1
403	1	1	1	0	0	1
404	1	1	1	0	0	1
405	1	1	1	0	0	1
406	1	1	1	0	0	1
407	1	1	1	0	0	1
408	1	1	1	0	0	1
409	1	1	1	0	0	1
410	1	1	1	0	0	1
411	1	1	1	0	0	1
412	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 4-1-11

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Pre-administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
401	1	1	2	1	1	1	0	1	1	1	1	0
402	1	1	2	1	1	1	0	1	1	1	1	0
403	1	1	2	1	1	1	0	1	1	1	1	0
404	1	1	2	1	1	1	0	1	1	1	1	0
405	1	1	2	1	1	1	0	1	1	1	1	0
406	1	1	2	1	1	1	0	1	1	1	1	0
407	1	1	2	1	1	1	0	1	1	1	1	0
408	1	1	2	1	1	1	0	1	1	1	1	0
409	1	1	2	1	1	1	0	1	1	1	1	0
410	1	1	2	1	1	1	0	1	1	1	1	0
411	1	1	2	1	1	1	0	1	1	1	1	0
412	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-1-12

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Pre-administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
401	1	1	1	1	0	0	0	0	1	1	1
402	1	1	1	1	1	0	0	0	1	1	1
403	1	1	1	1	0	0	0	0	1	1	1
404	1	1	1	1	0	0	0	0	1	1	1
405	1	1	1	1	0	0	0	0	1	1	1
406	1	1	1	1	0	0	0	0	1	1	1
407	1	1	1	1	0	0	0	0	1	1	1
408	1	1	1	1	0	0	0	0	1	1	1
409	1	1	1	1	0	0	0	0	1	1	1
410	1	1	1	1	0	0	0	0	1	1	1
411	1	1	1	1	0	0	0	0	1	1	1
412	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-2-1

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Day 7 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
101	1	1	1	0	0	1
102	1	1	1	0	0	1
103	1	1	1	0	0	1
104	1	1	1	0	0	1
105	1	1	1	0	0	1
106	1	1	1	0	0	1
107	1	1	1	0	0	1
108	1	1	1	0	0	1
109	1	1	1	0	0	1
110	1	1	1	0	0	1
111	1	1	1	0	0	1
112	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 4-2-2

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Day 7 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
101	1	1	2	1	1	1	0	1	1	1	1	0
102	1	1	2	1	1	1	0	1	1	1	1	0
103	1	1	2	1	1	1	0	1	1	1	1	0
104	1	1	2	1	1	1	0	1	1	1	1	0
105	1	1	2	1	1	1	0	1	1	1	1	0
106	1	1	2	1	1	1	0	1	1	1	1	0
107	1	1	2	1	1	1	0	1	1	1	1	0
108	1	1	2	1	1	1	0	1	1	1	1	0
109	1	1	2	1	1	1	0	1	1	1	1	0
110	1	1	2	1	1	1	0	1	1	1	1	0
111	1	1	2	1	1	1	0	1	1	1	1	0
112	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-2-3

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Day 7 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
101	1	1	1	1	1	0	0	0	1	1	1
102	1	1	1	1	0	0	0	0	1	1	1
103	1	1	1	1	0	0	0	0	1	1	1
104	1	1	1	1	0	0	0	0	1	1	1
105	1	1	1	1	0	0	0	0	1	1	1
106	1	1	1	1	0	0	0	0	1	1	1
107	1	1	1	1	0	0	0	0	1	1	1
108	1	1	1	1	0	0	0	0	1	1	1
109	1	1	1	1	0	0	0	0	1	1	1
110	1	1	1	1	1	0	0	0	1	1	1
111	1	1	1	1	0	0	0	0	1	1	1
112	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-2-4

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : Day 7 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
201	1	1	1	0	0	1
202	1	1	1	0	0	1
203	1	1	1	0	0	1
204	1	1	1	0	0	1
205	1	1	1	0	0	1
206	1	1	1	0	0	1
207	1	1	1	0	0	1
208	1	1	1	0	0	1
209	1	1	1	0	0	1
210	1	1	1	0	0	1
211	1	1	1	0	0	1
212	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 4-2-5

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : Day 7 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
201	1	1	2	1	1	1	0	1	1	1	1	0
202	1	1	2	1	1	1	0	1	1	1	1	0
203	1	1	2	1	1	1	0	1	1	1	1	0
204	1	1	2	1	1	1	0	1	1	1	1	0
205	1	1	2	1	1	1	0	1	1	1	1	0
206	1	1	2	1	1	1	0	1	1	1	1	0
207	1	1	2	1	1	1	0	1	1	1	1	0
208	1	1	2	1	1	1	0	1	1	1	1	0
209	1	1	2	1	1	1	0	1	1	1	1	0
210	1	1	2	1	1	1	0	1	1	1	1	0
211	1	1	2	1	1	1	0	1	1	1	1	0
212	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-2-6

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : Day 7 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
201	1	1	1	1	1	0	0	0	1	1	1
202	1	1	1	1	0	0	0	0	1	1	1
203	1	1	1	1	1	0	0	0	1	1	1
204	1	1	1	1	0	0	0	0	1	1	1
205	1	1	1	1	0	0	0	0	1	1	1
206	1	1	1	1	0	0	0	0	1	1	1
207	1	1	1	1	0	0	0	0	1	1	1
208	1	1	1	1	0	0	0	0	1	1	1
209	1	1	1	1	0	0	0	0	1	1	1
210	1	1	1	1	0	0	0	0	1	1	1
211	1	1	1	1	0	0	0	0	1	1	1
212	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-2-7

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : Day 7 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
301	1	1	1	0	0	1
302	1	1	1	0	0	1
303	1	1	1	0	0	1
304	1	1	1	0	0	1
305	1	1	1	0	0	1
306	1	1	1	0	0	1
307	1	1	1	0	0	1
308	1	1	1	0	0	1
309	1	1	1	0	0	1
310	1	1	1	0	0	1
311	1	1	1	0	0	1
312	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 4-2-8

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : Day 7 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
301	1	1	2	1	1	1	0	1	1	1	1	0
302	1	1	2	1	1	1	0	1	1	1	1	0
303	1	1	2	1	1	1	0	1	1	1	1	0
304	1	1	2	1	1	1	0	1	1	1	1	0
305	1	1	2	1	1	1	0	1	1	1	1	0
306	1	1	2	1	1	1	0	1	1	1	1	0
307	1	1	2	1	1	1	0	1	1	1	1	0
308	1	1	2	1	1	1	0	1	1	1	1	0
309	1	1	2	1	1	1	0	1	1	1	1	0
310	1	1	2	1	1	1	0	1	1	1	1	0
311	1	1	2	1	1	1	0	1	1	1	1	0
312	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-2-9

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : Day 7 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
301	1	1	1	1	0	0	0	0	1	1	1
302	1	1	1	1	0	0	0	0	1	1	1
303	1	1	1	1	0	0	0	0	1	1	1
304	1	1	1	1	0	0	0	0	1	1	1
305	1	1	1	1	0	0	0	0	1	1	1
306	1	1	1	1	0	0	0	0	1	1	1
307	1	1	1	1	0	0	0	0	1	1	1
308	1	1	1	1	0	0	0	0	1	1	1
309	1	1	1	1	0	0	0	0	1	1	1
310	1	1	1	1	0	0	0	0	1	1	1
311	1	1	1	1	0	0	0	0	1	1	1
312	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-2-10

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Day 7 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
401	1	1	1	0	0	1
402	1	1	1	0	0	1
403	1	1	1	0	0	1
404	1	1	1	0	0	1
405	1	1	1	0	0	1
406	1	1	1	0	0	1
407	1	1	1	0	0	1
408	1	1	1	0	0	1
409	1	1	1	0	0	1
410	1	1	1	0	0	1
411	1	1	1	0	0	1
412	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 4-2-11

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Day 7 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
401	1	1	2	1	1	1	0	1	1	1	1	0
402	1	1	2	1	1	1	0	1	1	1	1	0
403	1	1	2	1	1	1	0	1	1	1	1	0
404	1	1	2	1	1	1	0	1	1	1	1	0
405	1	1	2	1	1	1	0	1	1	1	1	0
406	1	1	2	1	1	1	0	1	1	1	1	0
407	1	1	2	1	1	1	0	1	1	1	1	0
408	1	1	2	1	1	1	0	1	1	1	1	0
409	1	1	2	1	1	1	0	1	1	1	1	0
410	1	1	2	1	1	1	0	1	1	1	1	0
411	1	1	2	1	1	1	0	1	1	1	1	0
412	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-2-12

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Day 7 of administration

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
401	1	1	1	1	1	0	0	0	1	1	1
402	1	1	1	1	0	0	0	0	1	1	1
403	1	1	1	1	0	0	0	0	1	1	1
404	1	1	1	1	0	0	0	0	1	1	1
405	1	1	1	1	0	0	0	0	1	1	1
406	1	1	1	1	0	0	0	0	1	1	1
407	1	1	1	1	0	0	0	0	1	1	1
408	1	1	1	1	0	0	0	0	1	1	1
409	1	1	1	1	0	0	0	0	1	1	1
410	1	1	1	1	0	0	0	0	1	1	1
411	1	1	1	1	1	0	0	0	1	1	1
412	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-3-1

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Day 14 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
101	1	1	1	0	0	1
102	1	1	1	0	0	1
103	1	1	1	0	0	1
104	1	1	1	0	0	1
105	1	1	1	0	0	1
106	1	1	1	0	0	1
107	1	1	1	0	0	1
108	1	1	1	0	0	1
109	1	1	1	0	0	1
110	1	1	1	0	0	1
111	1	1	1	0	0	1
112	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 4-3-2

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Day 14 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
101	1	1	2	1	1	1	0	1	1	1	1	0
102	1	1	2	1	1	1	0	1	1	1	1	0
103	1	1	2	1	1	1	0	1	1	1	1	0
104	1	1	2	1	1	1	0	1	1	1	1	0
105	1	1	2	1	1	1	0	1	1	1	1	0
106	1	1	2	1	1	1	0	1	1	1	1	0
107	1	1	2	1	1	1	0	1	1	1	1	0
108	1	1	2	1	1	1	0	1	1	1	1	0
109	1	1	2	1	1	1	0	1	1	1	1	0
110	1	1	2	1	1	1	0	1	1	1	1	0
111	1	1	2	1	1	1	0	1	1	1	1	0
112	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-3-3

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Day 14 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
101	1	1	1	1	1	0	0	0	1	1	1
102	1	1	1	1	0	0	0	0	1	1	1
103	1	1	1	1	0	0	0	0	1	1	1
104	1	1	1	1	0	0	0	0	1	1	1
105	1	1	1	1	0	0	0	0	1	1	1
106	1	1	1	1	0	0	0	0	1	1	1
107	1	1	1	1	0	0	0	0	1	1	1
108	1	1	1	1	0	0	0	0	1	1	1
109	1	1	1	1	0	0	0	0	1	1	1
110	1	1	1	1	0	0	0	0	1	1	1
111	1	1	1	1	0	0	0	0	1	1	1
112	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-3-4

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : Day 14 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
201	1	1	1	0	0	1
202	1	1	1	0	0	1
203	1	1	1	0	0	1
204	1	1	1	0	0	1
205	1	1	1	0	0	1
206	1	1	1	0	0	1
207	1	1	1	0	0	1
208	1	1	1	0	0	1
209	1	1	1	0	0	1
210	1	1	1	0	0	1
211	1	1	1	0	0	1
212	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 4-3-5

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : Day 14 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
201	1	1	2	1	1	1	0	1	1	1	1	0
202	1	1	2	1	1	1	0	1	1	1	1	0
203	1	1	2	1	1	1	0	1	1	1	1	0
204	1	1	2	1	1	1	0	1	1	1	1	0
205	1	1	2	1	1	1	0	1	1	1	1	0
206	1	1	2	1	1	1	0	1	1	1	1	0
207	1	1	2	1	1	1	0	1	1	1	1	0
208	1	1	2	1	1	1	0	1	1	1	1	0
209	1	1	2	1	1	1	0	1	1	1	1	0
210	1	1	2	1	1	1	0	1	1	1	1	0
211	1	1	2	1	1	1	0	1	1	1	1	0
212	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-3-6

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : Day 14 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
201	1	1	1	1	1	0	0	0	1	1	1
202	1	1	1	1	0	0	0	0	1	1	1
203	1	1	1	1	1	0	0	0	1	1	1
204	1	1	1	1	0	0	0	0	1	1	1
205	1	1	1	1	0	0	0	0	1	1	1
206	1	1	1	1	0	1	0	0	1	1	1
207	1	1	1	1	0	0	0	0	1	1	1
208	1	1	1	1	0	0	0	0	1	1	1
209	1	1	1	1	0	0	0	0	1	1	1
210	1	1	1	1	0	0	0	0	1	1	1
211	1	1	1	1	0	0	0	0	1	1	1
212	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-3-7

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : Day 14 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
301	1	1	1	0	0	1
302	1	1	1	0	0	1
303	1	1	1	0	0	1
304	1	1	1	0	0	1
305	1	1	1	0	0	1
306	1	1	1	0	0	1
307	1	1	1	0	0	1
308	1	1	1	0	0	1
309	1	1	1	0	0	1
310	1	1	1	0	0	1
311	1	1	1	0	0	1
312	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 4-3-8

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : Day 14 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
301	1	1	2	1	1	1	0	1	1	1	1	0
302	1	1	2	1	1	1	0	1	1	1	1	0
303	1	1	2	1	1	1	0	1	1	1	1	0
304	1	1	2	1	1	1	0	1	1	1	1	0
305	1	1	2	1	1	1	0	1	1	1	1	0
306	1	1	2	1	1	1	0	1	1	1	1	0
307	1	1	2	1	1	1	0	1	1	1	1	0
308	1	1	2	1	1	1	0	1	1	1	1	0
309	1	1	2	1	1	1	0	1	1	1	1	0
310	1	1	2	1	1	1	0	1	1	1	1	0
311	1	1	2	1	1	1	0	1	1	1	1	0
312	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-3-9

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : Day 14 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
301	1	1	1	1	0	0	0	0	1	1	1
302	1	1	1	1	0	0	0	0	1	1	1
303	1	1	1	1	0	0	0	0	1	1	1
304	1	1	1	1	0	0	0	0	1	1	1
305	1	1	1	1	0	0	0	0	1	1	1
306	1	1	1	1	0	0	0	0	1	1	1
307	1	1	1	1	0	0	0	0	1	1	1
308	1	1	1	1	0	0	0	0	1	1	1
309	1	1	1	1	0	0	0	0	1	1	1
310	1	1	1	1	0	0	0	0	1	1	1
311	1	1	1	1	0	0	0	0	1	1	1
312	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-3-10

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Day 14 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
401	1	1	1	0	0	1
402	1	1	1	0	0	1
403	1	1	1	0	0	1
404	1	1	1	0	0	1
405	1	1	1	0	0	1
406	1	1	1	0	0	1
407	1	1	1	0	0	1
408	1	1	1	0	0	1
409	1	1	1	0	0	1
410	1	1	1	0	0	1
411	1	1	1	0	0	1
412	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 4-3-11

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Day 14 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
401	1	1	2	1	1	1	0	1	1	1	1	0
402	1	1	2	1	1	1	0	1	1	1	1	0
403	1	1	2	1	1	1	0	1	1	1	1	0
404	1	1	2	1	1	1	0	1	1	1	1	0
405	1	1	2	1	1	1	0	1	1	1	1	0
406	1	1	2	1	1	1	0	1	1	1	1	0
407	1	1	2	1	1	1	0	1	1	1	1	0
408	1	1	2	1	1	1	0	1	1	1	1	0
409	1	1	2	1	1	1	0	1	1	1	1	0
410	1	1	2	1	1	1	0	1	1	1	1	0
411	1	1	2	1	1	1	0	1	1	1	1	0
412	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-3-12

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Day 14 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
401	1	1	1	1	0	0	0	0	1	1	1
402	1	1	1	1	0	0	0	0	1	1	1
403	1	1	1	1	0	0	0	0	1	1	1
404	1	1	1	1	0	0	0	0	1	1	1
405	1	1	1	1	0	0	0	0	1	1	1
406	1	1	1	1	0	0	0	0	1	1	1
407	1	1	1	1	0	0	0	0	1	1	1
408	1	1	1	1	0	0	0	0	1	1	1
409	1	1	1	1	1	0	0	0	1	1	1
410	1	1	1	1	0	0	0	0	1	1	1
411	1	1	1	1	0	0	0	0	1	1	1
412	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-4-1

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Day 21 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
101	1	1	1	0	0	1
102	1	1	1	0	0	1
103	1	1	1	0	0	1
104	1	1	1	0	0	1
105	1	1	1	0	0	1
106	1	1	1	0	0	1
107	1	1	1	0	0	1
108	1	1	1	0	0	1
109	1	1	1	0	0	1
110	1	1	1	0	0	1
111	1	1	1	0	0	1
112	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 4-4-2

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Day 21 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
101	1	1	2	1	1	1	0	1	1	1	1	0
102	1	1	2	1	1	1	0	1	1	1	1	0
103	1	1	2	1	1	1	0	1	1	1	1	0
104	1	1	2	1	1	1	0	1	1	1	1	0
105	1	1	2	1	1	1	0	1	1	1	1	0
106	1	1	2	1	1	1	0	1	1	1	1	0
107	1	1	2	1	1	1	0	1	1	1	1	0
108	1	1	2	1	1	1	0	1	1	1	1	0
109	1	1	2	1	1	1	0	1	1	1	1	0
110	1	1	2	1	1	1	0	1	1	1	1	0
111	1	1	2	1	1	1	0	1	1	1	1	0
112	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-4-3

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Day 21 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
101	1	1	1	1	1	0	0	0	1	1	1
102	1	1	1	1	0	0	0	0	1	1	1
103	1	1	1	1	0	0	0	0	1	1	1
104	1	1	1	1	0	0	0	0	1	1	1
105	1	1	1	1	0	0	0	0	1	1	1
106	1	1	1	1	0	0	0	0	1	1	1
107	1	1	1	1	0	0	0	0	1	1	1
108	1	1	1	1	0	0	0	0	1	1	1
109	1	1	1	1	0	0	0	0	1	1	1
110	1	1	1	1	0	0	0	0	1	1	1
111	1	1	1	1	0	0	0	0	1	1	1
112	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-4-4

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : Day 21 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
201	1	1	1	0	0	1
202	1	1	1	0	0	1
203	1	1	1	0	0	1
204	1	1	1	0	0	1
205	1	1	1	0	0	1
206	1	1	1	0	0	1
207	1	1	1	0	0	1
208	1	1	1	0	0	1
209	1	1	1	0	0	1
210	1	1	1	0	0	1
211	1	1	1	0	0	1
212	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 4-4-5

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : Day 21 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
201	1	1	2	1	1	1	0	1	1	1	1	0
202	1	1	2	1	1	1	0	1	1	1	1	0
203	1	1	2	1	1	1	0	1	1	1	1	0
204	1	1	2	1	1	1	0	1	1	1	1	0
205	1	1	2	1	1	1	0	1	1	1	1	0
206	1	1	2	1	1	1	0	1	1	1	1	0
207	1	1	2	1	1	1	0	1	1	1	1	0
208	1	1	2	1	1	1	0	1	1	1	1	0
209	1	1	2	1	1	1	0	1	1	1	1	0
210	1	1	2	1	1	1	0	1	1	1	1	0
211	1	1	2	1	1	1	0	1	1	1	1	0
212	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-4-6

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : Day 21 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
201	1	1	1	1	0	0	0	0	1	1	1
202	1	1	1	1	0	0	0	0	1	1	1
203	1	1	1	1	0	0	0	0	1	1	1
204	1	1	1	1	0	0	0	0	1	1	1
205	1	1	1	1	0	0	0	0	1	1	1
206	1	1	1	1	0	0	0	0	1	1	1
207	1	1	1	1	0	0	0	0	1	1	1
208	1	1	1	1	0	0	0	0	1	1	1
209	1	1	1	1	0	0	0	0	1	1	1
210	1	1	1	1	0	0	0	0	1	1	1
211	1	1	1	1	0	0	0	0	1	1	1
212	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-4-7

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : Day 21 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
301	1	1	1	0	0	1
302	1	1	1	0	0	1
303	1	1	1	0	0	1
304	1	1	1	0	0	1
305	1	1	1	0	0	1
306	1	1	1	0	0	1
307	1	1	1	0	0	1
308	1	1	1	0	0	1
309	1	1	1	0	0	1
310	1	1	1	0	0	1
311	1	1	1	0	0	1
312	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 4-4-8

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : Day 21 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
301	1	1	2	1	1	1	0	1	1	1	1	0
302	1	1	2	1	1	1	0	1	1	1	1	0
303	1	1	2	1	1	1	0	1	1	1	1	0
304	1	1	2	1	1	1	0	1	1	1	1	0
305	1	1	2	1	1	1	0	1	1	1	1	0
306	1	1	2	1	1	1	0	1	1	1	1	0
307	1	1	2	1	1	1	0	1	1	1	1	0
308	1	1	2	1	1	1	0	1	1	1	1	0
309	1	1	2	1	1	1	0	1	1	1	1	0
310	1	1	2	1	1	1	0	1	1	1	1	0
311	1	1	2	1	1	1	0	1	1	1	1	0
312	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-4-9

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : Day 21 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
301	1	1	1	1	1	0	0	0	1	1	1
302	1	1	1	1	0	0	0	0	1	1	1
303	1	1	1	1	0	0	0	0	1	1	1
304	1	1	1	1	0	1	0	0	1	1	1
305	1	1	1	1	0	0	0	0	1	1	1
306	1	1	1	1	0	0	0	0	1	1	1
307	1	1	1	1	0	0	0	0	1	1	1
308	1	1	1	1	0	0	0	0	1	1	1
309	1	1	1	1	0	0	0	0	1	1	1
310	1	1	1	1	0	0	0	0	1	1	1
311	1	1	1	1	0	0	0	0	1	1	1
312	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-4-10

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Day 21 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
401	1	1	1	0	0	1
402	1	1	1	0	0	1
403	1	1	1	0	0	1
404	1	1	1	0	0	1
405	1	1	1	0	0	1
406	1	1	1	0	0	1
407	1	1	1	0	0	1
408	1	1	1	0	0	1
409	1	1	1	0	0	1
410	1	1	1	0	0	1
411	1	1	1	0	0	1
412	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 4-4-11

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Day 21 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
401	1	1	2	1	1	1	0	1	1	1	1	0
402	1	1	2	1	1	1	0	1	1	1	1	0
403	1	1	2	1	1	1	0	1	1	1	1	0
404	1	1	2	1	1	1	0	1	1	1	1	0
405	1	1	2	1	1	1	0	1	1	1	1	0
406	1	1	2	1	1	1	0	1	1	1	1	0
407	1	1	2	1	1	1	0	1	1	1	1	0
408	1	1	2	1	1	1	0	1	1	1	1	0
409	1	1	2	1	1	1	0	1	1	1	1	0
410	1	1	2	1	1	1	0	1	1	1	1	0
411	1	1	2	1	1	1	0	1	1	1	1	0
412	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-4-12

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Day 21 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
401	1	1	1	1	0	0	0	0	1	1	1
402	1	1	1	1	0	0	0	0	1	1	1
403	1	1	1	1	0	0	0	0	1	1	1
404	1	1	1	1	0	0	0	0	1	1	1
405	1	1	1	1	0	0	0	0	1	1	1
406	1	1	1	1	0	0	0	0	1	1	1
407	1	1	1	1	0	0	0	0	1	1	1
408	1	1	1	1	0	0	0	0	1	1	1
409	1	1	1	1	0	0	0	0	1	1	1
410	1	1	1	1	0	0	0	0	1	1	1
411	1	1	1	1	0	0	0	0	1	1	1
412	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-5-1

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Day 28 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
101	1	1	1	0	0	1
102	1	1	1	0	0	1
103	1	1	1	0	0	1
104	1	1	1	0	0	1
105	1	1	1	0	0	1
106	1	1	1	0	0	1
107	1	1	1	0	0	1
108	1	1	1	0	0	1
109	1	1	1	0	0	1
110	1	1	1	0	0	1
111	1	1	1	0	0	1
112	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 4-5-2

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Day 28 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
101	1	1	2	1	1	1	0	1	1	1	1	0
102	1	1	2	1	1	1	0	1	1	1	1	0
103	1	1	2	1	1	1	0	1	1	1	1	0
104	1	1	2	1	1	1	0	1	1	1	1	0
105	1	1	2	1	1	1	0	1	1	1	1	0
106	1	1	2	1	1	1	0	1	1	1	1	0
107	1	1	2	1	1	1	0	1	1	1	1	0
108	1	1	2	1	1	1	0	1	1	1	1	0
109	1	1	2	1	1	1	0	1	1	1	1	0
110	1	1	2	1	1	1	0	1	1	1	1	0
111	1	1	2	1	1	1	0	1	1	1	1	0
112	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-5-3

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Day 28 of administration

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
101	1	1	1	1	0	0	0	0	1	1	1
102	1	1	1	1	0	0	0	0	1	1	1
103	1	1	1	1	0	0	0	0	1	1	1
104	1	1	1	1	0	0	0	0	1	1	1
105	1	1	1	1	0	0	0	0	1	1	1
106	1	1	1	1	0	0	0	0	1	1	1
107	1	1	1	1	0	0	0	0	1	1	1
108	1	1	1	1	0	0	0	0	1	1	1
109	1	1	1	1	0	0	0	0	1	1	1
110	1	1	1	1	1	0	0	0	1	1	1
111	1	1	1	1	0	0	0	0	1	1	1
112	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-5-4

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : Day 28 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
201	1	1	1	0	0	1
202	1	1	1	0	0	1
203	1	1	1	0	0	1
204	1	1	1	0	0	1
205	1	1	1	0	0	1
206	1	1	1	0	0	1
207	1	1	1	0	0	1
208	1	1	1	0	0	1
209	1	1	1	0	0	1
210	1	1	1	0	0	1
211	1	1	1	0	0	1
212	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 4-5-5

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : Day 28 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
201	1	1	2	1	1	1	0	1	1	1	1	0
202	1	1	2	1	1	1	0	1	1	1	1	0
203	1	1	2	1	1	1	0	1	1	1	1	0
204	1	1	2	1	1	1	0	1	1	1	1	0
205	1	1	2	1	1	1	0	1	1	1	1	0
206	1	1	2	1	1	1	0	1	1	1	1	0
207	1	1	2	1	1	1	0	1	1	1	1	0
208	1	1	2	1	1	1	0	1	1	1	1	0
209	1	1	2	1	1	1	0	1	1	1	1	0
210	1	1	2	1	1	1	0	1	1	1	1	0
211	1	1	2	1	1	1	0	1	1	1	1	0
212	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-5-6

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : Day 28 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
201	1	1	1	1	1	0	0	0	1	1	1
202	1	1	1	1	0	0	0	0	1	1	1
203	1	1	1	1	0	0	0	0	1	1	1
204	1	1	1	1	0	0	0	0	1	1	1
205	1	1	1	1	0	0	0	0	1	1	1
206	1	1	1	1	0	0	0	0	1	1	1
207	1	1	1	1	0	0	0	0	1	1	1
208	1	1	1	1	0	0	0	0	1	1	1
209	1	1	1	1	0	0	0	0	1	1	1
210	1	1	1	1	0	0	0	0	1	1	1
211	1	1	1	1	0	0	0	0	1	1	1
212	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-5-7

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : Day 28 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
301	1	1	1	0	0	1
302	1	1	1	0	0	1
303	1	1	1	0	0	1
304	1	1	1	0	0	1
305	1	1	1	0	0	1
306	1	1	1	0	0	1
307	1	1	1	0	0	1
308	1	1	1	0	0	1
309	1	1	1	0	0	1
310	1	1	1	0	0	1
311	1	1	1	0	0	1
312	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 4-5-8

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : Day 28 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
301	1	1	2	1	1	1	0	1	1	1	1	0
302	1	1	2	1	1	1	0	1	1	1	1	0
303	1	1	2	1	1	1	0	1	1	1	1	0
304	1	1	2	1	1	1	0	1	1	1	1	0
305	1	1	2	1	1	1	0	1	1	1	1	0
306	1	1	2	1	1	1	0	1	1	1	1	0
307	1	1	2	1	1	1	0	1	1	1	1	0
308	1	1	2	1	1	1	0	1	1	1	1	0
309	1	1	2	1	1	1	0	1	1	1	1	0
310	1	1	2	1	1	1	0	1	1	1	1	0
311	1	1	2	1	1	1	0	1	1	1	1	0
312	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-5-9

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : Day 28 of administration

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
301	1	1	1	1	0	0	0	0	1	1	1
302	1	1	1	1	0	0	0	0	1	1	1
303	1	1	1	1	0	0	0	0	1	1	1
304	1	1	1	1	0	0	0	0	1	1	1
305	1	1	1	1	0	0	0	0	1	1	1
306	1	1	1	1	0	0	0	0	1	1	1
307	1	1	1	1	0	0	0	0	1	1	1
308	1	1	1	1	0	0	0	0	1	1	1
309	1	1	1	1	0	0	0	0	1	1	1
310	1	1	1	1	0	0	0	0	1	1	1
311	1	1	1	1	0	0	0	0	1	1	1
312	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-5-10

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Day 28 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
401	1	1	1	0	0	1
402	1	1	1	0	0	1
403	1	1	1	0	0	1
404	1	1	1	0	0	1
405	1	1	1	0	0	1
406	1	1	1	0	0	1
407	1	1	1	0	0	1
408	1	1	1	0	0	1
409	1	1	1	0	0	1
410	1	1	1	0	0	1
411	1	1	1	0	0	1
412	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 4-5-11

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Day 28 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
401	1	1	2	1	1	1	0	1	1	1	1	0
402	1	1	2	1	1	1	0	1	1	1	1	0
403	1	1	2	1	1	1	0	1	1	1	1	0
404	1	1	2	1	1	1	0	1	1	1	1	0
405	1	1	2	1	1	1	0	1	1	1	1	0
406	1	1	2	1	1	1	0	1	1	1	1	0
407	1	1	2	1	1	1	0	1	1	1	1	0
408	1	1	2	1	1	1	0	1	1	1	1	0
409	1	1	2	1	1	1	0	1	1	1	1	0
410	1	1	2	1	1	1	0	1	1	1	1	0
411	1	1	2	1	1	1	0	1	1	1	1	0
412	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-5-12

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Day 28 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
401	1	1	1	1	0	0	0	0	1	1	1
402	1	1	1	1	0	0	0	0	1	1	1
403	1	1	1	1	0	0	0	0	1	1	1
404	1	1	1	1	0	0	0	0	1	1	1
405	1	1	1	1	0	0	0	0	1	1	1
406	1	1	1	1	0	0	0	0	1	1	1
407	1	1	1	1	0	0	0	0	1	1	1
408	1	1	1	1	0	0	0	0	1	1	1
409	1	1	1	1	0	0	0	0	1	1	1
410	1	1	1	1	0	0	0	0	1	1	1
411	1	1	1	1	0	0	0	0	1	1	1
412	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-6-1

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Day 35 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
101	1	1	1	0	0	1
102	1	1	1	0	0	1
103	1	1	1	0	0	1
104	1	1	1	0	0	1
105	1	1	1	0	0	1
106	1	1	1	0	0	1
107	1	1	1	0	0	1
108	1	1	1	0	0	1
109	1	1	1	0	0	1
110	1	1	1	0	0	1
111	1	1	1	0	0	1
112	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 4-6-2

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Day 35 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
101	1	1	2	1	1	1	0	1	1	1	1	0
102	1	1	2	1	1	1	0	1	1	1	1	0
103	1	1	2	1	1	1	0	1	1	1	1	0
104	1	1	2	1	1	1	0	1	1	1	1	0
105	1	1	2	1	1	1	0	1	1	1	1	0
106	1	1	2	1	1	1	0	1	1	1	1	0
107	1	1	2	1	1	1	0	1	1	1	1	0
108	1	1	2	1	1	1	0	1	1	1	1	0
109	1	1	2	1	1	1	0	1	1	1	1	0
110	1	1	2	1	1	1	0	1	1	1	1	0
111	1	1	2	1	1	1	0	1	1	1	1	0
112	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-6-3

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Day 35 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
101	1	1	1	1	1	0	0	0	1	1	1
102	1	1	1	1	0	0	0	0	1	1	1
103	1	1	1	1	0	0	0	0	1	1	1
104	1	1	1	1	0	0	0	0	1	1	1
105	1	1	1	1	0	0	0	0	1	1	1
106	1	1	1	1	0	0	0	0	1	1	1
107	1	1	1	1	0	0	0	0	1	1	1
108	1	1	1	1	0	0	0	0	1	1	1
109	1	1	1	1	0	0	0	0	1	1	1
110	1	1	1	1	0	0	0	0	1	1	1
111	1	1	1	1	0	0	0	0	1	1	1
112	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-6-4

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : Day 35 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
201	1	1	1	0	0	1
202	1	1	1	0	0	1
203	1	1	1	0	0	1
204	1	1	1	0	0	1
205	1	1	1	0	0	1
206	1	1	1	0	0	1
207	1	1	1	0	0	1
208	1	1	1	0	0	1
209	1	1	1	0	0	1
210	1	1	1	0	0	1
211	1	1	1	0	0	1
212	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 4-6-5

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : Day 35 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
201	1	1	2	1	1	1	0	1	1	1	1	0
202	1	1	2	1	1	1	0	1	1	1	1	0
203	1	1	2	1	1	1	0	1	1	1	1	0
204	1	1	2	1	1	1	0	1	1	1	1	0
205	1	1	2	1	1	1	0	1	1	1	1	0
206	1	1	2	1	1	1	0	1	1	1	1	0
207	1	1	2	1	1	1	0	1	1	1	1	0
208	1	1	2	1	1	1	0	1	1	1	1	0
209	1	1	2	1	1	1	0	1	1	1	1	0
210	1	1	2	1	1	1	0	1	1	1	1	0
211	1	1	2	1	1	1	0	1	1	1	1	0
212	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-6-6

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : Day 35 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
201	1	1	1	1	0	0	0	0	1	1	1
202	1	1	1	1	0	0	0	0	1	1	1
203	1	1	1	1	0	0	0	0	1	1	1
204	1	1	1	1	0	0	0	0	1	1	1
205	1	1	1	1	0	0	0	0	1	1	1
206	1	1	1	1	0	0	0	0	1	1	1
207	1	1	1	1	0	0	0	0	1	1	1
208	1	1	1	1	0	0	0	0	1	1	1
209	1	1	1	1	0	0	0	0	1	1	1
210	1	1	1	1	0	0	0	0	1	1	1
211	1	1	1	1	0	0	0	0	1	1	1
212	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-6-7

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : Day 35 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
301	1	1	1	0	0	1
302	1	1	1	0	0	1
303	1	1	1	0	0	1
304	1	1	1	0	0	1
305	1	1	1	0	0	1
306	1	1	1	0	0	1
307	1	1	1	0	0	1
308	1	1	1	0	0	1
309	1	1	1	0	0	1
310	1	1	1	0	0	1
311	1	1	1	0	0	1
312	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 4-6-8

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : Day 35 of administration

	On the hand											
	Ease of											
Animal No.	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
301	1	1	2	1	1	1	0	1	1	1	1	0
302	1	1	2	1	1	1	0	1	1	1	1	0
303	1	1	2	1	1	1	0	1	1	1	1	0
304	1	1	2	1	1	1	0	1	1	1	1	0
305	1	1	2	1	1	1	0	1	1	1	1	0
306	1	1	2	1	1	1	0	1	1	1	1	0
307	1	1	2	1	1	1	0	1	1	1	1	0
308	1	1	2	1	1	1	0	1	1	1	1	0
309	1	1	2	1	1	1	0	1	1	1	1	0
310	1	1	2	1	1	1	0	1	1	1	1	0
311	1	1	2	1	1	1	0	1	1	1	1	0
312	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-6-9

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : Day 35 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
301	1	1	1	1	1	0	0	0	1	1	1
302	1	1	1	1	0	0	0	0	1	1	1
303	1	1	1	1	0	0	0	0	1	1	1
304	1	1	1	1	0	0	0	0	1	1	1
305	1	1	1	1	0	0	0	0	1	1	1
306	1	1	1	1	0	0	0	0	1	1	1
307	1	1	1	1	0	0	0	0	1	1	1
308	1	1	1	1	0	0	0	0	1	1	1
309	1	1	1	1	0	0	0	0	1	1	1
310	1	1	1	1	0	0	0	0	1	1	1
311	1	1	1	1	0	0	0	0	1	1	1
312	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-6-10

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Day 35 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
401	1	1	1	0	0	1
402	1	1	1	0	0	1
403	1	1	1	0	0	1
404	1	1	1	0	0	1
405	1	1	1	0	0	1
406	1	1	1	0	0	1
407	1	1	1	0	0	1
408	1	1	1	0	0	1
409	1	1	1	0	0	1
410	1	1	1	0	0	1
411	1	1	1	0	0	1
412	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 4-6-11

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Day 35 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
401	1	1	2	1	1	1	0	1	1	1	1	0
402	1	1	2	1	1	1	0	1	1	1	1	0
403	1	1	2	1	1	1	0	1	1	1	1	0
404	1	1	2	1	1	1	0	1	1	1	1	0
405	1	1	2	1	1	1	0	1	1	1	1	0
406	1	1	2	1	1	1	0	1	1	1	1	0
407	1	1	2	1	1	1	0	1	1	1	1	0
408	1	1	2	1	1	1	0	1	1	1	1	0
409	1	1	2	1	1	1	0	1	1	1	1	0
410	1	1	2	1	1	1	0	1	1	1	1	0
411	1	1	2	1	1	1	0	1	1	1	1	0
412	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-6-12

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Day 35 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
401	1	1	1	1	0	0	0	0	1	1	1
402	1	1	1	1	0	0	0	0	1	1	1
403	1	1	1	1	0	0	0	0	1	1	1
404	1	1	1	1	0	0	0	0	1	1	1
405	1	1	1	1	0	0	0	0	1	1	1
406	1	1	1	1	0	0	0	0	1	1	1
407	1	1	1	1	0	0	0	0	1	1	1
408	1	1	1	1	0	0	0	0	1	1	1
409	1	1	1	1	0	0	0	0	1	1	1
410	1	1	1	1	0	0	0	0	1	1	1
411	1	1	1	1	0	0	0	0	1	1	1
412	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-7-1

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Day 42 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
101	1	1	1	0	0	1
102	1	1	1	0	0	1
103	1	1	1	0	0	1
104	1	1	1	0	0	1
105	1	1	1	0	0	1
106	1	1	1	0	0	1
107	1	1	1	0	0	1
108	1	1	1	0	0	1
109	1	1	1	0	0	1
110	1	1	1	0	0	1
111	1	1	1	0	0	1
112	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 4-7-2

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Day 42 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
101	1	1	2	1	1	1	0	1	1	1	1	0
102	1	1	2	1	1	1	0	1	1	1	1	0
103	1	1	2	1	1	1	0	1	1	1	1	0
104	1	1	2	1	1	1	0	1	1	1	1	0
105	1	1	2	1	1	1	0	1	1	1	1	0
106	1	1	2	1	1	1	0	1	1	1	1	0
107	1	1	2	1	1	1	0	1	1	1	1	0
108	1	1	2	1	1	1	0	1	1	1	1	0
109	1	1	2	1	1	1	0	1	1	1	1	0
110	1	1	2	1	1	1	0	1	1	1	1	0
111	1	1	2	1	1	1	0	1	1	1	1	0
112	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-7-3

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Day 42 of administration

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
101	1	1	1	1	1	0	0	0	1	1	1
102	1	1	1	1	0	0	0	0	1	1	1
103	1	1	1	1	0	0	0	0	1	1	1
104	1	1	1	1	0	0	0	0	1	1	1
105	1	1	1	1	0	0	0	0	1	1	1
106	1	1	1	1	0	0	0	0	1	1	1
107	1	1	1	1	0	0	0	0	1	1	1
108	1	1	1	1	0	0	0	0	1	1	1
109	1	1	1	1	0	0	0	0	1	1	1
110	1	1	1	1	0	0	0	0	1	1	1
111	1	1	1	1	0	0	0	0	1	1	1
112	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-7-4

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : Day 42 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
201	1	1	1	0	0	1
202	1	1	1	0	0	1
203	1	1	1	0	0	1
204	1	1	1	0	0	1
205	1	1	1	0	0	1
206	1	1	1	0	0	1
207	1	1	1	0	0	1
208	1	1	1	0	0	1
209	1	1	1	0	0	1
210	1	1	1	0	0	1
211	1	1	1	0	0	1
212	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 4-7-5

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : Day 42 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
201	1	1	2	1	1	1	0	1	1	1	1	0
202	1	1	2	1	1	1	0	1	1	1	1	0
203	1	1	2	1	1	1	0	1	1	1	1	0
204	1	1	2	1	1	1	0	1	1	1	1	0
205	1	1	2	1	1	1	0	1	1	1	1	0
206	1	1	2	1	1	1	0	1	1	1	1	0
207	1	1	2	1	1	1	0	1	1	1	1	0
208	1	1	2	1	1	1	0	1	1	1	1	0
209	1	1	2	1	1	1	0	1	1	1	1	0
210	1	1	2	1	1	1	0	1	1	1	1	0
211	1	1	2	1	1	1	0	1	1	1	1	0
212	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-7-6

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : Day 42 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
201	1	1	1	1	0	0	0	0	1	1	1
202	1	1	1	1	0	0	0	0	1	1	1
203	1	1	1	1	0	0	0	0	1	1	1
204	1	1	1	1	0	0	0	0	1	1	1
205	1	1	1	1	0	0	0	0	1	1	1
206	1	1	1	1	0	0	0	0	1	1	1
207	1	1	1	1	0	0	0	0	1	1	1
208	1	1	1	1	0	0	0	0	1	1	1
209	1	1	1	1	0	0	0	0	1	1	1
210	1	1	1	1	0	0	0	0	1	1	1
211	1	1	1	1	0	0	0	0	1	1	1
212	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-7-7

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : Day 42 of administration

Animal No.	In the cage					
				Stereotype		Bizarre behavior
	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
301	1	1	1	0	0	1
302	1	1	1	0	0	1
303	1	1	1	0	0	1
304	1	1	1	0	0	1
305	1	1	1	0	0	1
306	1	1	1	0	0	1
307	1	1	1	0	0	1
308	1	1	1	0	0	1
309	1	1	1	0	0	1
310	1	1	1	0	0	1
311	1	1	1	0	0	1
312	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 4-7-8

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : Day 42 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
301	1	1	2	1	1	1	0	1	1	1	1	0
302	1	1	2	1	1	1	0	1	1	1	1	0
303	1	1	2	1	1	1	0	1	1	1	1	0
304	1	1	2	1	1	1	0	1	1	1	1	0
305	1	1	2	1	1	1	0	1	1	1	1	0
306	1	1	2	1	1	1	0	1	1	1	1	0
307	1	1	2	1	1	1	0	1	1	1	1	0
308	1	1	2	1	1	1	0	1	1	1	1	0
309	1	1	2	1	1	1	0	1	1	1	1	0
310	1	1	2	1	1	1	0	1	1	1	1	0
311	1	1	2	1	1	1	0	1	1	1	1	0
312	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-7-9

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : Day 42 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
301	1	1	1	1	0	0	0	0	1	1	1
302	1	1	1	1	0	0	0	0	1	1	1
303	1	1	1	1	0	0	0	0	1	1	1
304	1	1	1	1	0	0	0	0	1	1	1
305	1	1	1	1	0	0	0	0	1	1	1
306	1	1	1	1	0	0	0	0	1	1	1
307	1	1	1	1	0	0	0	0	1	1	1
308	1	1	1	1	0	0	0	0	1	1	1
309	1	1	1	1	0	0	0	0	1	1	1
310	1	1	1	1	0	0	0	0	1	1	1
311	1	1	1	1	0	0	0	0	1	1	1
312	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-7-10

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Day 42 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
401	1	1	1	0	0	1
402	1	1	1	0	0	1
403	1	1	1	0	0	1
404	1	1	1	0	0	1
405	1	1	1	0	0	1
406	1	1	1	0	0	1
407	1	1	1	0	0	1
408	1	1	1	0	0	1
409	1	1	1	0	0	1
410	1	1	1	0	0	1
411	1	1	1	0	0	1
412	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 4-7-11

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Day 42 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
401	1	1	2	1	1	1	0	1	1	1	1	0
402	1	1	2	1	1	1	0	1	1	1	1	0
403	1	1	2	1	1	1	0	1	1	1	1	0
404	1	1	2	1	1	1	0	1	1	1	1	0
405	1	1	2	1	1	1	0	1	1	1	1	0
406	1	1	2	1	1	1	0	1	1	1	1	0
407	1	1	2	1	1	1	0	1	1	1	1	0
408	1	1	2	1	1	1	0	1	1	1	1	0
409	1	1	2	1	1	1	0	1	1	1	1	0
410	1	1	2	1	1	1	0	1	1	1	1	0
411	1	1	2	1	1	1	0	1	1	1	1	0
412	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-7-12

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Day 42 of administration

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
401	1	1	1	1	0	0	0	0	1	1	1
402	1	1	1	1	0	0	0	0	1	1	1
403	1	1	1	1	0	0	0	0	1	1	1
404	1	1	1	1	0	0	0	0	1	1	1
405	1	1	1	1	0	0	0	0	1	1	1
406	1	1	1	1	0	0	0	0	1	1	1
407	1	1	1	1	0	0	0	0	1	1	1
408	1	1	1	1	0	0	0	0	1	1	1
409	1	1	1	1	0	0	0	0	1	1	1
410	1	1	1	1	0	0	0	0	1	1	1
411	1	1	1	1	0	0	0	0	1	1	1
412	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 4-8-1

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Day 7 of recovery

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
104	1	1	1	0	0	1
105	1	1	1	0	0	1
106	1	1	1	0	0	1
107	1	1	1	0	0	1
108	1	1	1	0	0	1
N	5	5	5	5	5	5

INDIVIDUAL DATA 4-8-2

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Day 7 of recovery

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
104	1	1	2	1	1	1	0	1	1	1	1	0
105	1	1	2	1	1	1	0	1	1	1	1	0
106	1	1	2	1	1	1	0	1	1	1	1	0
107	1	1	2	1	1	1	0	1	1	1	1	0
108	1	1	2	1	1	1	0	1	1	1	1	0
N	5	5	5	5	5	5	5	5	5	5	5	5

INDIVIDUAL DATA 4-8-3

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Day 7 of recovery

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
104	1	1	1	1	0	0	0	0	1	1	1
105	1	1	1	1	0	0	0	0	1	1	1
106	1	1	1	1	0	0	0	0	1	1	1
107	1	1	1	1	0	0	0	0	1	1	1
108	1	1	1	1	0	0	0	0	1	1	1
N	5	5	5	5	5	5	5	5	5	5	5

INDIVIDUAL DATA 4-8-4

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Day 7 of recovery

Animal No.	In the cage					
				Stereotype		Bizarre behavior
	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
401	1	1	1	0	0	1
404	1	1	1	0	0	1
406	1	1	1	0	0	1
411	1	1	1	0	0	1
412	1	1	1	0	0	1
N	5	5	5	5	5	5

INDIVIDUAL DATA 4-8-5

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Day 7 of recovery

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
401	1	1	2	1	1	1	0	1	1	1	1	0
404	1	1	2	1	1	1	0	1	1	1	1	0
406	1	1	2	1	1	1	0	1	1	1	1	0
411	1	1	2	1	1	1	0	1	1	1	1	0
412	1	1	2	1	1	1	0	1	1	1	1	0
N	5	5	5	5	5	5	5	5	5	5	5	5

INDIVIDUAL DATA 4-8-6

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Day 7 of recovery

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
401	1	1	1	1	0	0	0	0	1	1	1
404	1	1	1	1	0	0	0	0	1	1	1
406	1	1	1	1	0	0	0	0	1	1	1
411	1	1	1	1	0	0	0	0	1	1	1
412	1	1	1	1	0	0	0	0	1	1	1
N	5	5	5	5	5	5	5	5	5	5	5

INDIVIDUAL DATA 4-9-1

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Day 14 of recovery

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
104	1	1	1	0	0	1
105	1	1	1	0	0	1
106	1	1	1	0	0	1
107	1	1	1	0	0	1
108	1	1	1	0	0	1
N	5	5	5	5	5	5

INDIVIDUAL DATA 4-9-2

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Day 14 of recovery

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
104	1	1	2	1	1	1	0	1	1	1	1	0
105	1	1	2	1	1	1	0	1	1	1	1	0
106	1	1	2	1	1	1	0	1	1	1	1	0
107	1	1	2	1	1	1	0	1	1	1	1	0
108	1	1	2	1	1	1	0	1	1	1	1	0
N	5	5	5	5	5	5	5	5	5	5	5	5

INDIVIDUAL DATA 4-9-3

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Day 14 of recovery

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
104	1	1	1	1	0	0	0	0	1	1	1
105	1	1	1	1	0	0	0	0	1	1	1
106	1	1	1	1	0	0	0	0	1	1	1
107	1	1	1	1	0	0	0	0	1	1	1
108	1	1	1	1	0	0	0	0	1	1	1
N	5	5	5	5	5	5	5	5	5	5	5

INDIVIDUAL DATA 4-9-4

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Day 14 of recovery

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
401	1	1	1	0	0	1
404	1	1	1	0	0	1
406	1	1	1	0	0	1
411	1	1	1	0	0	1
412	1	1	1	0	0	1
N	5	5	5	5	5	5

INDIVIDUAL DATA 4-9-5

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Day 14 of recovery

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
401	1	1	2	1	1	1	0	1	1	1	1	0
404	1	1	2	1	1	1	0	1	1	1	1	0
406	1	1	2	1	1	1	0	1	1	1	1	0
411	1	1	2	1	1	1	0	1	1	1	1	0
412	1	1	2	1	1	1	0	1	1	1	1	0
N	5	5	5	5	5	5	5	5	5	5	5	5

INDIVIDUAL DATA 4-9-6

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Day 14 of recovery

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
401	1	1	1	1	0	0	0	0	1	1	1
404	1	1	1	1	0	0	0	0	1	1	1
406	1	1	1	1	1	0	0	0	1	1	1
411	1	1	1	1	0	0	0	0	1	1	1
412	1	1	1	1	0	0	0	0	1	1	1
N	5	5	5	5	5	5	5	5	5	5	5

INDIVIDUAL DATA 5-1-1

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg PERIOD : Pre-administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
151	1	1	1	0	0	1
152	1	1	1	0	0	1
153	1	1	1	0	0	1
154	1	1	1	0	0	1
155	1	1	1	0	0	1
156	1	1	1	0	0	1
157	1	1	1	0	0	1
158	1	1	1	0	0	1
159	1	1	1	0	0	1
160	1	1	1	0	0	1
161	1	1	1	0	0	1
162	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 5-1-2

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg PERIOD : Pre-administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
151	1	1	2	1	1	1	0	1	1	1	1	0
152	1	1	2	1	1	1	0	1	1	1	1	0
153	1	1	2	1	1	1	0	1	1	1	1	0
154	1	1	2	1	1	1	0	1	1	1	1	0
155	1	1	2	1	1	1	0	1	1	1	1	0
156	1	1	2	1	1	1	0	1	1	1	1	0
157	1	1	2	1	1	1	0	1	1	1	1	0
158	1	1	2	1	1	1	0	1	1	1	1	0
159	1	1	2	1	1	1	0	1	1	1	1	0
160	1	1	2	1	1	1	0	1	1	1	1	0
161	1	1	2	1	1	1	0	1	1	1	1	0
162	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-1-3

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg PERIOD : Pre-administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
151	1	1	1	1	0	0	0	0	1	1	1
152	1	1	1	1	0	0	0	0	1	1	1
153	1	1	1	1	0	0	0	0	1	1	1
154	1	1	1	1	0	0	0	0	1	1	1
155	1	1	1	1	0	0	0	0	1	1	1
156	1	1	1	1	1	0	0	0	1	1	1
157	1	1	1	1	0	0	0	0	1	1	1
158	1	1	1	1	0	0	0	0	1	1	1
159	1	1	1	1	0	0	0	0	1	1	1
160	1	1	1	1	0	0	0	0	1	1	1
161	1	1	1	1	1	0	0	0	1	1	1
162	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-1-4

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg PERIOD : Pre-administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
251	1	1	1	0	0	1
252	1	1	1	0	0	1
253	1	1	1	0	0	1
254	1	1	1	0	0	1
255	1	1	1	0	0	1
256	1	1	1	0	0	1
257	1	1	1	0	0	1
258	1	1	1	0	0	1
259	1	1	1	0	0	1
260	1	1	1	0	0	1
261	1	1	1	0	0	1
262	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 5-1-5

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg PERIOD : Pre-administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
251	1	1	2	1	1	1	0	1	1	1	1	0
252	1	1	2	1	1	1	0	1	1	1	1	0
253	1	1	2	1	1	1	0	1	1	1	1	0
254	1	1	2	1	1	1	0	1	1	1	1	0
255	1	1	2	1	1	1	0	1	1	1	1	0
256	1	1	2	1	1	1	0	1	1	1	1	0
257	1	1	2	1	1	1	0	1	1	1	1	0
258	1	1	2	1	1	1	0	1	1	1	1	0
259	1	1	2	1	1	1	0	1	1	1	1	0
260	1	1	2	1	1	1	0	1	1	1	1	0
261	1	1	2	1	1	1	0	1	1	1	1	0
262	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-1-6

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg PERIOD : Pre-administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
251	1	1	1	1	0	0	0	0	1	1	1
252	1	1	1	1	0	0	0	0	1	1	1
253	1	1	1	1	0	0	0	0	1	1	1
254	1	1	1	1	0	0	0	0	1	1	1
255	1	1	1	1	0	0	0	0	1	1	1
256	1	1	1	1	0	0	0	0	1	1	1
257	1	1	1	1	0	0	0	0	1	1	1
258	1	1	1	1	0	0	0	0	1	1	1
259	1	1	1	1	0	0	0	0	1	1	1
260	1	1	1	1	0	0	0	0	1	1	1
261	1	1	1	1	0	0	0	0	1	1	1
262	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-1-7

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg PERIOD : Pre-administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
351	1	1	1	0	0	1
352	1	1	1	0	0	1
353	1	1	1	0	0	1
354	1	1	1	0	0	1
355	1	1	1	0	0	1
356	1	1	1	0	0	1
357	1	1	1	0	0	1
358	1	1	1	0	0	1
359	1	1	1	0	0	1
360	1	1	1	0	0	1
361	1	1	1	0	0	1
362	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 5-1-8

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg PERIOD : Pre-administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
351	1	1	2	1	1	1	0	1	1	1	1	0
352	1	1	2	1	1	1	0	1	1	1	1	0
353	1	1	2	1	1	1	0	1	1	1	1	0
354	1	1	2	1	1	1	0	1	1	1	1	0
355	1	1	2	1	1	1	0	1	1	1	1	0
356	1	1	2	1	1	1	0	1	1	1	1	0
357	1	1	2	1	1	1	0	1	1	1	1	0
358	1	1	2	1	1	1	0	1	1	1	1	0
359	1	1	2	1	1	1	0	1	1	1	1	0
360	1	1	2	1	1	1	0	1	1	1	1	0
361	1	1	2	1	1	1	0	1	1	1	1	0
362	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-1-9

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg PERIOD : Pre-administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
351	1	1	1	1	0	0	0	0	1	1	1
352	1	1	1	1	0	0	0	0	1	1	1
353	1	1	1	1	0	0	0	0	1	1	1
354	1	1	1	1	0	0	0	0	1	1	1
355	1	1	1	1	0	0	0	0	1	1	1
356	1	1	1	1	0	0	0	0	1	1	1
357	1	1	1	1	0	0	0	0	1	1	1
358	1	1	1	1	0	0	0	0	1	1	1
359	1	1	1	1	0	0	0	0	1	1	1
360	1	1	1	1	0	0	0	0	1	1	1
361	1	1	1	1	0	0	0	0	1	1	1
362	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-1-10

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg PERIOD : Pre-administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
451	1	1	1	0	0	1
452	1	1	1	0	0	1
453	1	1	1	0	0	1
454	1	1	1	0	0	1
455	1	1	1	0	0	1
456	1	1	1	0	0	1
457	1	1	1	0	0	1
458	1	1	1	0	0	1
459	1	1	1	0	0	1
460	1	1	1	0	0	1
461	1	1	1	0	0	1
462	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 5-1-11

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg PERIOD : Pre-administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
451	1	1	2	1	1	1	0	1	1	1	1	0
452	1	1	2	1	1	1	0	1	1	1	1	0
453	1	1	2	1	1	1	0	1	1	1	1	0
454	1	1	2	1	1	1	0	1	1	1	1	0
455	1	1	2	1	1	1	0	1	1	1	1	0
456	1	1	2	1	1	1	0	1	1	1	1	0
457	1	1	2	1	1	1	0	1	1	1	1	0
458	1	1	2	1	1	1	0	1	1	1	1	0
459	1	1	2	1	1	1	0	1	1	1	1	0
460	1	1	2	1	1	1	0	1	1	1	1	0
461	1	1	2	1	1	1	0	1	1	1	1	0
462	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-1-12

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg PERIOD : Pre-administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
451	1	1	1	1	1	0	0	0	1	1	1
452	1	1	1	1	0	0	0	0	1	1	1
453	1	1	1	1	0	0	0	0	1	1	1
454	1	1	1	1	0	0	0	0	1	1	1
455	1	1	1	1	0	0	0	0	1	1	1
456	1	1	1	1	0	0	0	0	1	1	1
457	1	1	1	1	0	0	0	0	1	1	1
458	1	1	1	1	0	0	0	0	1	1	1
459	1	1	1	1	0	0	0	0	1	1	1
460	1	1	1	1	0	0	0	0	1	1	1
461	1	1	1	1	0	0	0	0	1	1	1
462	1	1	1	1	1	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-2-1

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg PERIOD : Day 7 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
151	1	1	1	0	0	1
152	1	1	1	0	0	1
153	1	1	1	0	0	1
154	1	1	1	0	0	1
155	1	1	1	0	0	1
156	1	1	1	0	0	1
157	1	1	1	0	0	1
158	1	1	1	0	0	1
159	1	1	1	0	0	1
160	1	1	1	0	0	1
161	1	1	1	0	0	1
162	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 5-2-2

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg PERIOD : Day 7 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
151	1	1	2	1	1	1	0	1	1	1	1	0
152	1	1	2	1	1	1	0	1	1	1	1	0
153	1	1	2	1	1	1	0	1	1	1	1	0
154	1	1	2	1	1	1	0	1	1	1	1	0
155	1	1	2	1	1	1	0	1	1	1	1	0
156	1	1	2	1	1	1	0	1	1	1	1	0
157	1	1	2	1	1	1	0	1	1	1	1	0
158	1	1	2	1	1	1	0	1	1	1	1	0
159	1	1	2	1	1	1	0	1	1	1	1	0
160	1	1	2	1	1	1	0	1	1	1	1	0
161	1	1	2	1	1	1	0	1	1	1	1	0
162	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-2-3

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg PERIOD : Day 7 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
151	1	1	1	1	1	0	0	0	1	1	1
152	1	1	1	1	1	0	0	0	1	1	1
153	1	1	1	1	0	0	0	0	1	1	1
154	1	1	1	1	0	0	0	0	1	1	1
155	1	1	1	1	0	0	0	0	1	1	1
156	1	1	1	1	0	0	0	0	1	1	1
157	1	1	1	1	0	0	0	0	1	1	1
158	1	1	1	1	0	0	0	0	1	1	1
159	1	1	1	1	1	0	0	0	1	1	1
160	1	1	1	1	0	0	0	0	1	1	1
161	1	1	1	1	0	0	0	0	1	1	1
162	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-2-4

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg PERIOD : Day 7 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
251	1	1	1	0	0	1
252	1	1	1	0	0	1
253	1	1	1	0	0	1
254	1	1	1	0	0	1
255	1	1	1	0	0	1
256	1	1	1	0	0	1
257	1	1	1	0	0	1
258	1	1	1	0	0	1
259	1	1	1	0	0	1
260	1	1	1	0	0	1
261	1	1	1	0	0	1
262	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 5-2-5

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg PERIOD : Day 7 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
251	1	1	2	1	1	1	0	1	1	1	1	0
252	1	1	2	1	1	1	0	1	1	1	1	0
253	1	1	2	1	1	1	0	1	1	1	1	0
254	1	1	2	1	1	1	0	1	1	1	1	0
255	1	1	2	1	1	1	0	1	1	1	1	0
256	1	1	2	1	1	1	0	1	1	1	1	0
257	1	1	2	1	1	1	0	1	1	1	1	0
258	1	1	2	1	1	1	0	1	1	1	1	0
259	1	1	2	1	1	1	0	1	1	1	1	0
260	1	1	2	1	1	1	0	1	1	1	1	0
261	1	1	2	1	1	1	0	1	1	1	1	0
262	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-2-6

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg PERIOD : Day 7 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
251	1	1	1	1	0	0	0	0	1	1	1
252	1	1	1	1	0	0	0	0	1	1	1
253	1	1	1	1	0	0	0	0	1	1	1
254	1	1	1	1	0	0	0	0	1	1	1
255	1	1	1	1	0	0	0	0	1	1	1
256	1	1	1	1	0	0	0	0	1	1	1
257	1	1	1	1	0	0	0	0	1	1	1
258	1	1	1	1	0	0	0	0	1	1	1
259	1	1	1	1	0	0	0	0	1	1	1
260	1	1	1	1	0	0	0	0	1	1	1
261	1	1	1	1	0	0	0	0	1	1	1
262	1	1	1	1	1	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-2-7

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg PERIOD : Day 7 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
351	1	1	1	0	0	1
352	1	1	1	0	0	1
353	1	1	1	0	0	1
354	1	1	1	0	0	1
355	1	1	1	0	0	1
356	1	1	1	0	0	1
357	1	1	1	0	0	1
358	1	1	1	0	0	1
359	1	1	1	0	0	1
360	1	1	1	0	0	1
361	1	1	1	0	0	1
362	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 5-2-8

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg PERIOD : Day 7 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
351	1	1	2	1	1	1	0	1	1	1	1	0
352	1	1	2	1	1	1	0	1	1	1	1	0
353	1	1	2	1	1	1	0	1	1	1	1	0
354	1	1	2	1	1	1	0	1	1	1	1	0
355	1	1	2	1	1	1	0	1	1	1	1	0
356	1	1	2	1	1	1	0	1	1	1	1	0
357	1	1	2	1	1	1	0	1	1	1	1	0
358	1	1	2	1	1	1	0	1	1	1	1	0
359	1	1	2	1	1	1	0	1	1	1	1	0
360	1	1	2	1	1	1	0	1	1	1	1	0
361	1	1	2	1	1	1	0	1	1	1	1	0
362	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-2-9

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg PERIOD : Day 7 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
351	1	1	1	1	0	0	0	0	1	1	1
352	1	1	1	1	0	0	0	0	1	1	1
353	1	1	1	1	0	0	0	0	1	1	1
354	1	1	1	1	0	0	0	0	1	1	1
355	1	1	1	1	1	0	0	0	1	1	1
356	1	1	1	1	0	0	0	0	1	1	1
357	1	1	1	1	1	0	0	0	1	1	1
358	1	1	1	1	1	0	0	0	1	1	1
359	1	1	1	1	0	0	0	0	1	1	1
360	1	1	1	1	0	0	0	0	1	1	1
361	1	1	1	1	0	0	0	0	1	1	1
362	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-2-10

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg PERIOD : Day 7 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
451	1	1	1	0	0	1
452	1	1	1	0	0	1
453	1	1	1	0	0	1
454	1	1	1	0	0	1
455	1	1	1	0	0	1
456	1	1	1	0	0	1
457	1	1	1	0	0	1
458	1	1	1	0	0	1
459	1	1	1	0	0	1
460	1	1	1	0	0	1
461	1	1	1	0	0	1
462	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 5-2-11

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg PERIOD : Day 7 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
451	1	1	2	1	1	1	0	1	1	1	1	0
452	1	1	2	1	1	1	0	1	1	1	1	0
453	1	1	2	1	1	1	0	1	1	1	1	0
454	1	1	2	1	1	1	0	1	1	1	1	0
455	1	1	2	1	1	1	0	1	1	1	1	0
456	1	1	2	1	1	1	0	1	1	1	1	0
457	1	1	2	1	1	1	0	1	1	1	1	0
458	1	1	2	1	1	1	0	1	1	1	1	0
459	1	1	2	1	1	1	0	1	1	1	1	0
460	1	1	2	1	1	1	0	1	1	1	1	0
461	1	1	2	1	1	1	0	1	1	1	1	0
462	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-2-12

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg PERIOD : Day 7 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
451	1	1	1	1	1	0	0	0	1	1	1
452	1	1	1	1	0	0	0	0	1	1	1
453	1	1	1	1	0	0	0	0	1	1	1
454	1	1	1	1	0	0	0	0	1	1	1
455	1	1	1	1	0	0	0	0	1	1	1
456	1	1	1	1	0	0	0	0	1	1	1
457	1	1	1	1	0	0	0	0	1	1	1
458	1	1	1	1	0	0	0	0	1	1	1
459	1	1	1	1	0	0	0	0	1	1	1
460	1	1	1	1	0	0	0	0	1	1	1
461	1	1	1	1	0	0	0	0	1	1	1
462	1	1	1	1	1	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-3-1

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg PERIOD : Day 14 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
151	1	1	1	0	0	1
152	1	1	1	0	0	1
153	1	1	1	0	0	1
154	1	1	1	0	0	1
155	1	1	1	0	0	1
156	1	1	1	0	0	1
157	1	1	1	0	0	1
158	1	1	1	0	0	1
159	1	1	1	0	0	1
160	1	1	1	0	0	1
161	1	1	1	0	0	1
162	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 5-3-2

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg PERIOD : Day 14 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
151	1	1	2	1	1	1	0	1	1	1	1	0
152	1	1	2	1	1	1	0	1	1	1	1	0
153	1	1	2	1	1	1	0	1	1	1	1	0
154	1	1	2	1	1	1	0	1	1	1	1	0
155	1	1	2	1	1	1	0	1	1	1	1	0
156	1	1	2	1	1	1	0	1	1	1	1	0
157	1	1	2	1	1	1	0	1	1	1	1	0
158	1	1	2	1	1	1	0	1	1	1	1	0
159	1	1	2	1	1	1	0	1	1	1	1	0
160	1	1	2	1	1	1	0	1	1	1	1	0
161	1	1	2	1	1	1	0	1	1	1	1	0
162	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-3-3

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg PERIOD : Day 14 of administration

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
151	1	1	1	1	0	0	0	0	1	1	1
152	1	1	1	1	0	0	0	0	1	1	1
153	1	1	1	1	0	0	0	0	1	1	1
154	1	1	1	1	0	0	0	0	1	1	1
155	1	1	1	1	0	0	0	0	1	1	1
156	1	1	1	1	0	0	0	0	1	1	1
157	1	1	1	1	0	0	0	0	1	1	1
158	1	1	1	1	0	0	0	0	1	1	1
159	1	1	1	1	1	0	0	0	1	1	1
160	1	1	1	1	0	0	0	0	1	1	1
161	1	1	1	1	0	0	0	0	1	1	1
162	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-3-4

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg PERIOD : Day 14 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
251	1	1	1	0	0	1
252	1	1	1	0	0	1
253	1	1	1	0	0	1
254	1	1	1	0	0	1
255	1	1	1	0	0	1
256	1	1	1	0	0	1
257	1	1	1	0	0	1
258	1	1	1	0	0	1
259	1	1	1	0	0	1
260	1	1	1	0	0	1
261	1	1	1	0	0	1
262	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 5-3-5

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg PERIOD : Day 14 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
251	1	1	2	1	1	1	0	1	1	1	1	0
252	1	1	2	1	1	1	0	1	1	1	1	0
253	1	1	2	1	1	1	0	1	1	1	1	0
254	1	1	2	1	1	1	0	1	1	1	1	0
255	1	1	2	1	1	1	0	1	1	1	1	0
256	1	1	2	1	1	1	0	1	1	1	1	0
257	1	1	2	1	1	1	0	1	1	1	1	0
258	1	1	2	1	1	1	0	1	1	1	1	0
259	1	1	2	1	1	1	0	1	1	1	1	0
260	1	1	2	1	1	1	0	1	1	1	1	0
261	1	1	2	1	1	1	0	1	1	1	1	0
262	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-3-6

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg PERIOD : Day 14 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
251	1	1	1	1	0	0	0	0	1	1	1
252	1	1	1	1	0	0	0	0	1	1	1
253	1	1	1	1	0	0	0	0	1	1	1
254	1	1	1	1	0	0	0	0	1	1	1
255	1	1	1	1	1	0	0	0	1	1	1
256	1	1	1	1	0	0	0	0	1	1	1
257	1	1	1	1	0	0	0	0	1	1	1
258	1	1	1	1	0	0	0	0	1	1	1
259	1	1	1	1	0	0	0	0	1	1	1
260	1	1	1	1	0	0	0	0	1	1	1
261	1	1	1	1	0	0	0	0	1	1	1
262	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-3-7

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg PERIOD : Day 14 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
351	1	1	1	0	0	1
352	1	1	1	0	0	1
353	1	1	1	0	0	1
354	1	1	1	0	0	1
355	1	1	1	0	0	1
356	1	1	1	0	0	1
357	1	1	1	0	0	1
358	1	1	1	0	0	1
359	1	1	1	0	0	1
360	1	1	1	0	0	1
361	1	1	1	0	0	1
362	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 5-3-8

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg PERIOD : Day 14 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
351	1	1	2	1	1	1	0	1	1	1	1	0
352	1	1	2	1	1	1	0	1	1	1	1	0
353	1	1	2	1	1	1	0	1	1	1	1	0
354	1	1	2	1	1	1	0	1	1	1	1	0
355	1	1	2	1	1	1	0	1	1	1	1	0
356	1	1	2	1	1	1	0	1	1	1	1	0
357	1	1	2	1	1	1	0	1	1	1	1	0
358	1	1	2	1	1	1	0	1	1	1	1	0
359	1	1	2	1	1	1	0	1	1	1	1	0
360	1	1	2	1	1	1	0	1	1	1	1	0
361	1	1	2	1	1	1	0	1	1	1	1	0
362	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-3-9

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg PERIOD : Day 14 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
351	1	1	1	1	0	0	0	0	1	1	1
352	1	1	1	1	0	0	0	0	1	1	1
353	1	1	1	1	0	0	0	0	1	1	1
354	1	1	1	1	0	0	0	0	1	1	1
355	1	1	1	1	0	0	0	0	1	1	1
356	1	1	1	1	0	0	0	0	1	1	1
357	1	1	1	1	0	0	0	0	1	1	1
358	1	1	1	1	0	0	0	0	1	1	1
359	1	1	1	1	0	0	0	0	1	1	1
360	1	1	1	1	0	0	0	0	1	1	1
361	1	1	1	1	0	0	0	0	1	1	1
362	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-3-10

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg PERIOD : Day 14 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
451	1	1	1	0	0	1
452	1	1	1	0	0	1
453	1	1	1	0	0	1
454	1	1	1	0	0	1
455	1	1	1	0	0	1
456	1	1	1	0	0	1
457	1	1	1	0	0	1
458	1	1	1	0	0	1
459	1	1	1	0	0	1
460	1	1	1	0	0	1
461	1	1	1	0	0	1
462	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 5-3-11

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg PERIOD : Day 14 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
451	1	1	2	1	1	1	0	1	1	1	1	0
452	1	1	2	1	1	1	0	1	1	1	1	0
453	1	1	2	1	1	1	0	1	1	1	1	0
454	1	1	2	1	1	1	0	1	1	1	1	0
455	1	1	2	1	1	1	0	1	1	1	1	0
456	1	1	2	1	1	1	0	1	1	1	1	0
457	1	1	2	1	1	1	0	1	1	1	1	0
458	1	1	2	1	1	1	0	1	1	1	1	0
459	1	1	2	1	1	1	0	1	1	1	1	0
460	1	1	2	1	1	1	0	1	1	1	1	0
461	1	1	2	1	1	1	0	1	1	1	1	0
462	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-3-12

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg PERIOD : Day 14 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
451	1	1	1	1	0	0	0	0	1	1	1
452	1	1	1	1	0	0	0	0	1	1	1
453	1	1	1	1	0	0	0	0	1	1	1
454	1	1	1	1	0	0	0	0	1	1	1
455	1	1	1	1	0	0	0	0	1	1	1
456	1	1	1	1	0	0	0	0	1	1	1
457	1	1	1	1	0	0	0	0	1	1	1
458	1	1	1	1	0	0	0	0	1	1	1
459	1	1	1	1	0	0	0	0	1	1	1
460	1	1	1	1	0	0	0	0	1	1	1
461	1	1	1	1	0	0	0	0	1	1	1
462	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-4-1

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg PERIOD : Day 21 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
151	1	1	1	0	0	1
152	1	1	1	0	0	1
153	1	1	1	0	0	1
154	1	1	1	0	0	1
155	1	1	1	0	0	1
156	1	1	1	0	0	1
157	1	1	1	0	0	1
158	1	1	1	0	0	1
159	1	1	1	0	0	1
160	1	1	1	0	0	1
161	1	1	1	0	0	1
162	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 5-4-2

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg PERIOD : Day 21 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
151	1	1	2	1	1	1	0	1	1	1	1	0
152	1	1	2	1	1	1	0	1	1	1	1	0
153	1	1	2	1	1	1	0	1	1	1	1	0
154	1	1	2	1	1	1	0	1	1	1	1	0
155	1	1	2	1	1	1	0	1	1	1	1	0
156	1	1	2	1	1	1	0	1	1	1	1	0
157	1	1	2	1	1	1	0	1	1	1	1	0
158	1	1	2	1	1	1	0	1	1	1	1	0
159	1	1	2	1	1	1	0	1	1	1	1	0
160	1	1	2	1	1	1	0	1	1	1	1	0
161	1	1	2	1	1	1	0	1	1	1	1	0
162	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-4-3

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg PERIOD : Day 21 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
151	1	1	1	1	0	0	0	0	1	1	1
152	1	1	1	1	0	0	0	0	1	1	1
153	1	1	1	1	0	0	0	0	1	1	1
154	1	1	1	1	0	0	0	0	1	1	1
155	1	1	1	1	0	0	0	0	1	1	1
156	1	1	1	1	0	0	0	0	1	1	1
157	1	1	1	1	0	0	0	0	1	1	1
158	1	1	1	1	0	0	0	0	1	1	1
159	1	1	1	1	0	0	0	0	1	1	1
160	1	1	1	1	0	0	0	0	1	1	1
161	1	1	1	1	0	0	0	0	1	1	1
162	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-4-4

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg PERIOD : Day 21 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
251	1	1	1	0	0	1
252	1	1	1	0	0	1
253	1	1	1	0	0	1
254	1	1	1	0	0	1
255	1	1	1	0	0	1
256	1	1	1	0	0	1
257	1	1	1	0	0	1
258	1	1	1	0	0	1
259	1	1	1	0	0	1
260	1	1	1	0	0	1
261	1	1	1	0	0	1
262	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 5-4-5

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg PERIOD : Day 21 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
251	1	1	2	1	1	1	0	1	1	1	1	0
252	1	1	2	1	1	1	0	1	1	1	1	0
253	1	1	2	1	1	1	0	1	1	1	1	0
254	1	1	2	1	1	1	0	1	1	1	1	0
255	1	1	2	1	1	1	0	1	1	1	1	0
256	1	1	2	1	1	1	0	1	1	1	1	0
257	1	1	2	1	1	1	0	1	1	1	1	0
258	1	1	2	1	1	1	0	1	1	1	1	0
259	1	1	2	1	1	1	0	1	1	1	1	0
260	1	1	2	1	1	1	0	1	1	1	1	0
261	1	1	2	1	1	1	0	1	1	1	1	0
262	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-4-6

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg PERIOD : Day 21 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
251	1	1	1	1	0	0	0	0	1	1	1
252	1	1	1	1	0	0	0	0	1	1	1
253	1	1	1	1	0	0	0	0	1	1	1
254	1	1	1	1	0	0	0	0	1	1	1
255	1	1	1	1	0	0	0	0	1	1	1
256	1	1	1	1	0	0	0	0	1	1	1
257	1	1	1	1	0	0	0	0	1	1	1
258	1	1	1	1	0	0	0	0	1	1	1
259	1	1	1	1	0	0	0	0	1	1	1
260	1	1	1	1	0	0	0	0	1	1	1
261	1	1	1	1	0	0	0	0	1	1	1
262	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-4-7

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg PERIOD : Day 21 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
351	1	1	1	0	0	1
352	1	1	1	0	0	1
353	1	1	1	0	0	1
354	1	1	1	0	0	1
355	1	1	1	0	0	1
356	1	1	1	0	0	1
357	1	1	1	0	0	1
358	1	1	1	0	0	1
359	1	1	1	0	0	1
360	1	1	1	0	0	1
361	1	1	1	0	0	1
362	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 5-4-8

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg PERIOD : Day 21 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
351	1	1	2	1	1	1	0	1	1	1	1	0
352	1	1	2	1	1	1	0	1	1	1	1	0
353	1	1	2	1	1	1	0	1	1	1	1	0
354	1	1	2	1	1	1	0	1	1	1	1	0
355	1	1	2	1	1	1	0	1	1	1	1	0
356	1	1	2	1	1	1	0	1	1	1	1	0
357	1	1	2	1	1	1	0	1	1	1	1	0
358	1	1	2	1	1	1	0	1	1	1	1	0
359	1	1	2	1	1	1	0	1	1	1	1	0
360	1	1	2	1	1	1	0	1	1	1	1	0
361	1	1	2	1	1	1	0	1	1	1	1	0
362	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-4-9

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg PERIOD : Day 21 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
351	1	1	1	1	0	0	0	0	1	1	1
352	1	1	1	1	0	0	0	0	1	1	1
353	1	1	1	1	0	0	0	0	1	1	1
354	1	1	1	1	0	0	0	0	1	1	1
355	1	1	1	1	0	0	0	0	1	1	1
356	1	1	1	1	0	0	0	0	1	1	1
357	1	1	1	1	0	0	0	0	1	1	1
358	1	1	1	1	0	0	0	0	1	1	1
359	1	1	1	1	0	0	0	0	1	1	1
360	1	1	1	1	0	0	0	0	1	1	1
361	1	1	1	1	0	0	0	0	1	1	1
362	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-4-10

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg PERIOD : Day 21 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
451	1	1	1	0	0	1
452	1	1	1	0	0	1
453	1	1	1	0	0	1
454	1	1	1	0	0	1
455	1	1	1	0	0	1
456	1	1	1	0	0	1
457	1	1	1	0	0	1
458	1	1	1	0	0	1
459	1	1	1	0	0	1
460	1	1	1	0	0	1
461	1	1	1	0	0	1
462	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 5-4-11

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg PERIOD : Day 21 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
451	1	1	2	1	1	1	0	1	1	1	1	0
452	1	1	2	1	1	1	0	1	1	1	1	0
453	1	1	2	1	1	1	0	1	1	1	1	0
454	1	1	2	1	1	1	0	1	1	1	1	0
455	1	1	2	1	1	1	0	1	1	1	1	0
456	1	1	2	1	1	1	0	1	1	1	1	0
457	1	1	2	1	1	1	0	1	1	1	1	0
458	1	1	2	1	1	1	0	1	1	1	1	0
459	1	1	2	1	1	1	0	1	1	1	1	0
460	1	1	2	1	1	1	0	1	1	1	1	0
461	1	1	2	1	1	1	0	1	1	1	1	0
462	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-4-12

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg PERIOD : Day 21 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
451	1	1	1	1	0	0	0	0	1	1	1
452	1	1	1	1	0	0	0	0	1	1	1
453	1	1	1	1	0	0	0	0	1	1	1
454	1	1	1	1	0	0	0	0	1	1	1
455	1	1	1	1	0	0	0	0	1	1	1
456	1	1	1	1	0	0	0	0	1	1	1
457	1	1	1	1	0	0	0	0	1	1	1
458	1	1	1	1	0	0	0	0	1	1	1
459	1	1	1	1	0	0	0	0	1	1	1
460	1	1	1	1	0	0	0	0	1	1	1
461	1	1	1	1	0	0	0	0	1	1	1
462	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-5-1

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg PERIOD : Day 28 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
151	1	1	1	0	0	1
152	1	1	1	0	0	1
153	1	1	1	0	0	1
154	1	1	1	0	0	1
155	1	1	1	0	0	1
156	1	1	1	0	0	1
157	1	1	1	0	0	1
158	1	1	1	0	0	1
159	1	1	1	0	0	1
160	1	1	1	0	0	1
161	1	1	1	0	0	1
162	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 5-5-2

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg PERIOD : Day 28 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
151	1	1	2	1	1	1	0	1	1	1	1	0
152	1	1	2	1	1	1	0	1	1	1	1	0
153	1	1	2	1	1	1	0	1	1	1	1	0
154	1	1	2	1	1	1	0	1	1	1	1	0
155	1	1	2	1	1	1	0	1	1	1	1	0
156	1	1	2	1	1	1	0	1	1	1	1	0
157	1	1	2	1	1	1	0	1	1	1	1	0
158	1	1	2	1	1	1	0	1	1	1	1	0
159	1	1	2	1	1	1	0	1	1	1	1	0
160	1	1	2	1	1	1	0	1	1	1	1	0
161	1	1	2	1	1	1	0	1	1	1	1	0
162	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-5-3

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg PERIOD : Day 28 of administration

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
151	1	1	1	1	0	0	0	0	1	1	1
152	1	1	1	1	0	0	0	0	1	1	1
153	1	1	1	1	0	0	0	0	1	1	1
154	1	1	1	1	1	0	0	0	1	1	1
155	1	1	1	1	0	0	0	0	1	1	1
156	1	1	1	1	0	0	0	0	1	1	1
157	1	1	1	1	0	0	0	0	1	1	1
158	1	1	1	1	0	0	0	0	1	1	1
159	1	1	1	1	0	0	0	0	1	1	1
160	1	1	1	1	0	0	0	0	1	1	1
161	1	1	1	1	0	0	0	0	1	1	1
162	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-5-4

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg PERIOD : Day 28 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
251	1	1	1	0	0	1
252	1	1	1	0	0	1
253	1	1	1	0	0	1
254	1	1	1	0	0	1
255	1	1	1	0	0	1
256	1	1	1	0	0	1
257	1	1	1	0	0	1
258	1	1	1	0	0	1
259	1	1	1	0	0	1
260	1	1	1	0	0	1
261	1	1	1	0	0	1
262	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 5-5-5

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg PERIOD : Day 28 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
251	1	1	2	1	1	1	0	1	1	1	1	0
252	1	1	2	1	1	1	0	1	1	1	1	0
253	1	1	2	1	1	1	0	1	1	1	1	0
254	1	1	2	1	1	1	0	1	1	1	1	0
255	1	1	2	1	1	1	0	1	1	1	1	0
256	1	1	2	1	1	1	0	1	1	1	1	0
257	1	1	2	1	1	1	0	1	1	1	1	0
258	1	1	2	1	1	1	0	1	1	1	1	0
259	1	1	2	1	1	1	0	1	1	1	1	0
260	1	1	2	1	1	1	0	1	1	1	1	0
261	1	1	2	1	1	1	0	1	1	1	1	0
262	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-5-6

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg PERIOD : Day 28 of administration

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
251	1	1	1	1	0	0	0	0	1	1	1
252	1	1	1	1	0	0	0	0	1	1	1
253	1	1	1	1	0	0	0	0	1	1	1
254	1	1	1	1	0	0	0	0	1	1	1
255	1	1	1	1	0	0	0	0	1	1	1
256	1	1	1	1	0	0	0	0	1	1	1
257	1	1	1	1	0	0	0	0	1	1	1
258	1	1	1	1	0	0	0	0	1	1	1
259	1	1	1	1	0	0	0	0	1	1	1
260	1	1	1	1	0	0	0	0	1	1	1
261	1	1	1	1	0	0	0	0	1	1	1
262	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-5-7

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg PERIOD : Day 28 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
351	1	1	1	0	0	1
352	1	1	1	0	0	1
353	1	1	1	0	0	1
354	1	1	1	0	0	1
355	1	1	1	0	0	1
356	1	1	1	0	0	1
357	1	1	1	0	0	1
358	1	1	1	0	0	1
359	1	1	1	0	0	1
360	1	1	1	0	0	1
361	1	1	1	0	0	1
362	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 5-5-8

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg PERIOD : Day 28 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
351	1	1	2	1	1	1	0	1	1	1	1	0
352	1	1	2	1	1	1	0	1	1	1	1	0
353	1	1	2	1	1	1	0	1	1	1	1	0
354	1	1	2	1	1	1	0	1	1	1	1	0
355	1	1	2	1	1	1	0	1	1	1	1	0
356	1	1	2	1	1	1	0	1	1	1	1	0
357	1	1	2	1	1	1	0	1	1	1	1	0
358	1	1	2	1	1	1	0	1	1	1	1	0
359	1	1	2	1	1	1	0	1	1	1	1	0
360	1	1	2	1	1	1	0	1	1	1	1	0
361	1	1	2	1	1	1	0	1	1	1	1	0
362	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-5-9

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg PERIOD : Day 28 of administration

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
351	1	1	1	1	0	0	0	0	1	1	1
352	1	1	1	1	0	0	0	0	1	1	1
353	1	1	1	1	0	0	0	0	1	1	1
354	1	1	1	1	0	0	0	0	1	1	1
355	1	1	1	1	0	0	0	0	1	1	1
356	1	1	1	1	0	0	0	0	1	1	1
357	1	1	1	1	0	0	0	0	1	1	1
358	1	1	1	1	0	0	0	0	1	1	1
359	1	1	1	1	0	0	0	0	1	1	1
360	1	1	1	1	0	0	0	0	1	1	1
361	1	1	1	1	0	0	0	0	1	1	1
362	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-5-10

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg PERIOD : Day 28 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
451	1	1	1	0	0	1
452	1	1	1	0	0	1
453	1	1	1	0	0	1
454	1	1	1	0	0	1
455	1	1	1	0	0	1
456	1	1	1	0	0	1
457	1	1	1	0	0	1
458	1	1	1	0	0	1
459	1	1	1	0	0	1
460	1	1	1	0	0	1
461	1	1	1	0	0	1
462	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 5-5-11

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg PERIOD : Day 28 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
451	1	1	2	1	1	1	0	1	1	1	1	0
452	1	1	2	1	1	1	0	1	1	1	1	0
453	1	1	2	1	1	1	0	1	1	1	1	0
454	1	1	2	1	1	1	0	1	1	1	1	0
455	1	1	2	1	1	1	0	1	1	1	1	0
456	1	1	2	1	1	1	0	1	1	1	1	0
457	1	1	2	1	1	1	0	1	1	1	1	0
458	1	1	2	1	1	1	0	1	1	1	1	0
459	1	1	2	1	1	1	0	1	1	1	1	0
460	1	1	2	1	1	1	0	1	1	1	1	0
461	1	1	2	1	1	1	0	1	1	1	1	0
462	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-5-12

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg PERIOD : Day 28 of administration

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
451	1	1	1	1	0	0	0	0	1	1	1
452	1	1	1	1	0	0	0	0	1	1	1
453	1	1	1	1	0	0	0	0	1	1	1
454	1	1	1	1	0	0	0	0	1	1	1
455	1	1	1	1	0	0	0	0	1	1	1
456	1	1	1	1	0	0	0	0	1	1	1
457	1	1	1	1	0	0	0	0	1	1	1
458	1	1	1	1	0	0	0	0	1	1	1
459	1	1	1	1	0	0	0	0	1	1	1
460	1	1	1	1	0	0	0	0	1	1	1
461	1	1	1	1	0	0	0	0	1	1	1
462	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-6-1

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg PERIOD : Day 35 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
151	1	1	1	0	0	1
152	1	1	1	0	0	1
153	1	1	1	0	0	1
154	1	1	1	0	0	1
155	1	1	1	0	0	1
156	1	1	1	0	0	1
157	1	1	1	0	0	1
158	1	1	1	0	0	1
159	1	1	1	0	0	1
160	1	1	1	0	0	1
161	1	1	1	0	0	1
162	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 5-6-2

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg PERIOD : Day 35 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
151	1	1	2	1	1	1	0	1	1	1	1	0
152	1	1	2	1	1	1	0	1	1	1	1	0
153	1	1	2	1	1	1	0	1	1	1	1	0
154	1	1	2	1	1	1	0	1	1	1	1	0
155	1	1	2	1	1	1	0	1	1	1	1	0
156	1	1	2	1	1	1	0	1	1	1	1	0
157	1	1	2	1	1	1	0	1	1	1	1	0
158	1	1	2	1	1	1	0	1	1	1	1	0
159	1	1	2	1	1	1	0	1	1	1	1	0
160	1	1	2	1	1	1	0	1	1	1	1	0
161	1	1	2	1	1	1	0	1	1	1	1	0
162	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-6-3

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg PERIOD : Day 35 of administration

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
151	1	1	1	1	0	0	0	0	1	1	1
152	1	1	1	1	0	0	0	0	1	1	1
153	1	1	1	1	0	0	0	0	1	1	1
154	1	1	1	1	0	0	0	0	1	1	1
155	1	1	1	1	0	0	0	0	1	1	1
156	1	1	1	1	0	0	0	0	1	1	1
157	1	1	1	1	0	0	0	0	1	1	1
158	1	1	1	1	0	0	0	0	1	1	1
159	1	1	1	1	0	0	0	0	1	1	1
160	1	1	1	1	0	0	0	0	1	1	1
161	1	1	1	1	0	0	0	0	1	1	1
162	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-6-4

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg PERIOD : Day 35 of administration

Animal No.	In the cage					
				Stereotype		Bizarre behavior
	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
251	1	1	1	0	0	1
252	1	1	1	0	0	1
253	1	1	1	0	0	1
254	1	1	1	0	0	1
255	1	1	1	0	0	1
256	1	1	1	0	0	1
257	1	1	1	0	0	1
258	1	1	1	0	0	1
259	1	1	1	0	0	1
260	1	1	1	0	0	1
261	1	1	1	0	0	1
262	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 5-6-5

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg PERIOD : Day 35 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
251	1	1	2	1	1	1	0	1	1	1	1	0
252	1	1	2	1	1	1	0	1	1	1	1	0
253	1	1	2	1	1	1	0	1	1	1	1	0
254	1	1	2	1	1	1	0	1	1	1	1	0
255	1	1	2	1	1	1	0	1	1	1	1	0
256	1	1	2	1	1	1	0	1	1	1	1	0
257	1	1	2	1	1	1	0	1	1	1	1	0
258	1	1	2	1	1	1	0	1	1	1	1	0
259	1	1	2	1	1	1	0	1	1	1	1	0
260	1	1	2	1	1	1	0	1	1	1	1	0
261	1	1	2	1	1	1	0	1	1	1	1	0
262	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-6-6

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg PERIOD : Day 35 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
251	1	1	1	1	0	0	0	0	1	1	1
252	1	1	1	1	0	0	0	0	1	1	1
253	1	1	1	1	0	0	0	0	1	1	1
254	1	1	1	1	0	0	0	0	1	1	1
255	1	1	1	1	0	0	0	0	1	1	1
256	1	1	1	1	0	0	0	0	1	1	1
257	1	1	1	1	0	0	0	0	1	1	1
258	1	1	1	1	0	0	0	0	1	1	1
259	1	1	1	1	0	0	0	0	1	1	1
260	1	1	1	1	0	0	0	0	1	1	1
261	1	1	1	1	0	0	0	0	1	1	1
262	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-6-7

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg PERIOD : Day 35 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
351	1	1	1	0	0	1
352	1	1	1	0	0	1
353	1	1	1	0	0	1
354	1	1	1	0	0	1
355	1	1	1	0	0	1
356	1	1	1	0	0	1
357	1	1	1	0	0	1
358	1	1	1	0	0	1
359	1	1	1	0	0	1
360	1	1	1	0	0	1
361	1	1	1	0	0	1
362	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 5-6-8

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg PERIOD : Day 35 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
351	1	1	2	1	1	1	0	1	1	1	1	0
352	1	1	2	1	1	1	0	1	1	1	1	0
353	1	1	2	1	1	1	0	1	1	1	1	0
354	1	1	2	1	1	1	0	1	1	1	1	0
355	1	1	2	1	1	1	0	1	1	1	1	0
356	1	1	2	1	1	1	0	1	1	1	1	0
357	1	1	2	1	1	1	0	1	1	1	1	0
358	1	1	2	1	1	1	0	1	1	1	1	0
359	1	1	2	1	1	1	0	1	1	1	1	0
360	1	1	2	1	1	1	0	1	1	1	1	0
361	1	1	2	1	1	1	0	1	1	1	1	0
362	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-6-9

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg PERIOD : Day 35 of administration

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
351	1	1	1	1	0	0	0	0	1	1	1
352	1	1	1	1	0	0	0	0	1	1	1
353	1	1	1	1	0	0	0	0	1	1	1
354	1	1	1	1	0	0	0	0	1	1	1
355	1	1	1	1	0	0	0	0	1	1	1
356	1	1	1	1	0	0	0	0	1	1	1
357	1	1	1	1	0	0	0	0	1	1	1
358	1	1	1	1	0	0	0	0	1	1	1
359	1	1	1	1	0	0	0	0	1	1	1
360	1	1	1	1	0	0	0	0	1	1	1
361	1	1	1	1	0	0	0	0	1	1	1
362	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-6-10

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg PERIOD : Day 35 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
451	1	1	1	0	0	1
452	1	1	1	0	0	1
453	1	1	1	0	0	1
454	1	1	1	0	0	1
455	1	1	1	0	0	1
456	1	1	1	0	0	1
457	1	1	1	0	0	1
458	1	1	1	0	0	1
459	1	1	1	0	0	1
460	1	1	1	0	0	1
461	1	1	1	0	0	1
462	1	1	1	0	0	1
N	12	12	12	12	12	12

INDIVIDUAL DATA 5-6-11

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg PERIOD : Day 35 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
451	1	1	2	1	1	1	0	1	1	1	1	0
452	1	1	2	1	1	1	0	1	1	1	1	0
453	1	1	2	1	1	1	0	1	1	1	1	0
454	1	1	2	1	1	1	0	1	1	1	1	0
455	1	1	2	1	1	1	0	1	1	1	1	0
456	1	1	2	1	1	1	0	1	1	1	1	0
457	1	1	2	1	1	1	0	1	1	1	1	0
458	1	1	2	1	1	1	0	1	1	1	1	0
459	1	1	2	1	1	1	0	1	1	1	1	0
460	1	1	2	1	1	1	0	1	1	1	1	0
461	1	1	2	1	1	1	0	1	1	1	1	0
462	1	1	2	1	1	1	0	1	1	1	1	0
N	12	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-6-12

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg PERIOD : Day 35 of administration

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
451	1	1	1	1	0	0	0	0	1	1	1
452	1	1	1	1	0	0	0	0	1	1	1
453	1	1	1	1	0	0	0	0	1	1	1
454	1	1	1	1	0	0	0	0	1	1	1
455	1	1	1	1	0	0	0	0	1	1	1
456	1	1	1	1	0	0	0	0	1	1	1
457	1	1	1	1	0	0	0	0	1	1	1
458	1	1	1	1	0	0	0	0	1	1	1
459	1	1	1	1	0	0	0	0	1	1	1
460	1	1	1	1	0	0	0	0	1	1	1
461	1	1	1	1	0	0	0	0	1	1	1
462	1	1	1	1	0	0	0	0	1	1	1
N	12	12	12	12	12	12	12	12	12	12	12

INDIVIDUAL DATA 5-7-1

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg PERIOD : Day 42 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
151	#	#	#	#	#	#
152	1	1	1	0	0	1
153	1	1	1	0	0	1
154	1	1	1	0	0	1
155[a]	#	#	#	#	#	#
156	1	1	1	0	0	1
157	1	1	1	0	0	1
158	1	1	1	0	0	1
159	#	#	#	#	#	#
160	1	1	1	0	0	1
161	#	#	#	#	#	#
162	1	1	1	0	0	1
N	8	8	8	8	8	8

: Not applicable.

a : Died on Day 3 of Lactation .

INDIVIDUAL DATA 5-7-2

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg PERIOD : Day 42 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
151	#	#	#	#	#	#	#	#	#	#	#	#
152	1	1	2	1	1	1	0	1	1	1	1	0
153	1	1	2	1	1	1	0	1	1	1	1	0
154	1	1	2	1	1	1	0	1	1	1	1	0
155[a]	#	#	#	#	#	#	#	#	#	#	#	#
156	1	1	2	1	1	1	0	1	1	1	1	0
157	1	1	2	1	1	1	0	1	1	1	1	0
158	1	1	2	1	1	1	0	1	1	1	1	0
159	#	#	#	#	#	#	#	#	#	#	#	#
160	1	1	2	1	1	1	0	1	1	1	1	0
161	#	#	#	#	#	#	#	#	#	#	#	#
162	1	1	2	1	1	1	0	1	1	1	1	0
N	8	8	8	8	8	8	8	8	8	8	8	8

: Not applicable.

a : Died on Day 3 of Lactation .

INDIVIDUAL DATA 5-7-3

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg PERIOD : Day 42 of administration

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
151	#	#	#	#	#	#	#	#	#	#	#
152	1	1	1	1	0	0	0	0	1	1	1
153	1	1	1	1	0	0	0	0	1	1	1
154	1	1	1	1	0	0	0	0	1	1	1
155[a]	#	#	#	#	#	#	#	#	#	#	#
156	1	1	1	1	0	0	0	0	1	1	1
157	1	1	1	1	0	0	0	0	1	1	1
158	1	1	1	1	0	0	0	0	1	1	1
159	#	#	#	#	#	#	#	#	#	#	#
160	1	1	1	1	0	0	0	0	1	1	1
161	#	#	#	#	#	#	#	#	#	#	#
162	1	1	1	1	0	0	0	0	1	1	1
N	8	8	8	8	8	8	8	8	8	8	8

: Not applicable.

a : Died on Day 3 of Lactation .

INDIVIDUAL DATA 5-7-4

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg PERIOD : Day 42 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
251	1	1	1	0	0	1
252	1	1	1	0	0	1
253	1	1	1	0	0	1
254	1	1	1	0	0	1
255	1	1	1	0	0	1
256	#	#	#	#	#	#
257	#	#	#	#	#	#
258	1	1	1	0	0	1
259	1	1	1	0	0	1
260	1	1	1	0	0	1
261	1	1	1	0	0	1
262	#	#	#	#	#	#
N	9	9	9	9	9	9

: Not applicable.

INDIVIDUAL DATA 5-7-5

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg PERIOD : Day 42 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
251	1	1	2	1	1	1	0	1	1	1	1	0
252	1	1	2	1	1	1	0	1	1	1	1	0
253	1	1	2	1	1	1	0	1	1	1	1	0
254	1	1	2	1	1	1	0	1	1	1	1	0
255	1	1	2	1	1	1	0	1	1	1	1	0
256	#	#	#	#	#	#	#	#	#	#	#	#
257	#	#	#	#	#	#	#	#	#	#	#	#
258	1	1	2	1	1	1	0	1	1	1	1	0
259	1	1	2	1	1	1	0	1	1	1	1	0
260	1	1	2	1	1	1	0	1	1	1	1	0
261	1	1	2	1	1	1	0	1	1	1	1	0
262	#	#	#	#	#	#	#	#	#	#	#	#
N	9	9	9	9	9	9	9	9	9	9	9	9

: Not applicable.

INDIVIDUAL DATA 5-7-6

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg PERIOD : Day 42 of administration

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
251	1	1	1	1	0	0	0	0	1	1	1
252	1	1	1	1	0	0	0	0	1	1	1
253	1	1	1	1	0	0	0	0	1	1	1
254	1	1	1	1	0	0	0	0	1	1	1
255	1	1	1	1	0	0	0	0	1	1	1
256	#	#	#	#	#	#	#	#	#	#	#
257	#	#	#	#	#	#	#	#	#	#	#
258	1	1	1	1	0	0	0	0	1	1	1
259	1	1	1	1	0	0	0	0	1	1	1
260	1	1	1	1	0	0	0	0	1	1	1
261	1	1	1	1	0	0	0	0	1	1	1
262	#	#	#	#	#	#	#	#	#	#	#
N	9	9	9	9	9	9	9	9	9	9	9

: Not applicable.

INDIVIDUAL DATA 5-7-7

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg PERIOD : Day 42 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
351	1	1	1	0	0	1
352	1	1	1	0	0	1
353	1	1	1	0	0	1
354	1	1	1	0	0	1
355	#	#	#	#	#	#
356	1	1	1	0	0	1
357	#	#	#	#	#	#
358	1	1	1	0	0	1
359	1	1	1	0	0	1
360	1	1	1	0	0	1
361	1	1	1	0	0	1
362	1	1	1	0	0	1
N	10	10	10	10	10	10

: Not applicable.

INDIVIDUAL DATA 5-7-8

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg PERIOD : Day 42 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
351	1	1	2	1	1	1	0	1	1	1	1	0
352	1	1	2	1	1	1	0	1	1	1	1	0
353	1	1	2	1	1	1	0	1	1	1	1	0
354	1	1	2	1	1	1	0	1	1	1	1	0
355	#	#	#	#	#	#	#	#	#	#	#	#
356	1	1	2	1	1	1	0	1	1	1	1	0
357	#	#	#	#	#	#	#	#	#	#	#	#
358	1	1	2	1	1	1	0	1	1	1	1	0
359	1	1	2	1	1	1	0	1	1	1	1	0
360	1	1	2	1	1	1	0	1	1	1	1	0
361	1	1	2	1	1	1	0	1	1	1	1	0
362	1	1	2	1	1	1	0	1	1	1	1	0
N	10	10	10	10	10	10	10	10	10	10	10	10

: Not applicable.

INDIVIDUAL DATA 5-7-9

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg PERIOD : Day 42 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
351	1	1	1	1	0	0	0	0	1	1	1
352	1	1	1	1	0	0	0	0	1	1	1
353	1	1	1	1	0	0	0	0	1	1	1
354	1	1	1	1	0	0	0	0	1	1	1
355	#	#	#	#	#	#	#	#	#	#	#
356	1	1	1	1	0	0	0	0	1	1	1
357	#	#	#	#	#	#	#	#	#	#	#
358	1	1	1	1	0	0	0	0	1	1	1
359	1	1	1	1	0	0	0	0	1	1	1
360	1	1	1	1	0	0	0	0	1	1	1
361	1	1	1	1	0	0	0	0	1	1	1
362	1	1	1	1	0	0	0	0	1	1	1
N	10	10	10	10	10	10	10	10	10	10	10

: Not applicable.

INDIVIDUAL DATA 5-7-10

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg PERIOD : Day 42 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
451	1	1	1	0	0	1
452	1	1	1	0	0	1
453	1	1	1	0	0	1
454	1	1	1	0	0	1
455	1	1	1	0	0	1
456	#	#	#	#	#	#
457	1	1	1	0	0	1
458	1	1	1	0	0	1
459	1	1	1	0	0	1
460	1	1	1	0	0	1
461	1	1	1	0	0	1
462	1	1	1	0	0	1
N	11	11	11	11	11	11

: Not applicable.

INDIVIDUAL DATA 5-7-11

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg PERIOD : Day 42 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
451	1	1	2	1	1	1	0	1	1	1	1	0
452	1	1	2	1	1	1	0	1	1	1	1	0
453	1	1	2	1	1	1	0	1	1	1	1	0
454	1	1	2	1	1	1	0	1	1	1	1	0
455	1	1	2	1	1	1	0	1	1	1	1	0
456	#	#	#	#	#	#	#	#	#	#	#	#
457	1	1	2	1	1	1	0	1	1	1	1	0
458	1	1	2	1	1	1	0	1	1	1	1	0
459	1	1	2	1	1	1	0	1	1	1	1	0
460	1	1	2	1	1	1	0	1	1	1	1	0
461	1	1	2	1	1	1	0	1	1	1	1	0
462	1	1	2	1	1	1	0	1	1	1	1	0
N	11	11	11	11	11	11	11	11	11	11	11	11

: Not applicable.

INDIVIDUAL DATA 5-7-12

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg PERIOD : Day 42 of administration

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
451	1	1	1	1	0	0	0	0	1	1	1
452	1	1	1	1	0	0	0	0	1	1	1
453	1	1	1	1	0	0	0	0	1	1	1
454	1	1	1	1	0	0	0	0	1	1	1
455	1	1	1	1	0	0	0	0	1	1	1
456	#	#	#	#	#	#	#	#	#	#	#
457	1	1	1	1	0	0	0	0	1	1	1
458	1	1	1	1	0	0	0	0	1	1	1
459	1	1	1	1	0	0	0	0	1	1	1
460	1	1	1	1	0	0	0	0	1	1	1
461	1	1	1	1	0	0	0	0	1	1	1
462	1	1	1	1	0	0	0	0	1	1	1
N	11	11	11	11	11	11	11	11	11	11	11

: Not applicable.

INDIVIDUAL DATA 6-1-1

STUDY NO. SR11087 TITLE: indene indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg PERIOD : Pre-administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
163	1	1	1	0	0	1
164	1	1	1	0	0	1
165	1	1	1	0	0	1
166	1	1	1	0	0	1
167	1	1	1	0	0	1
168	1	1	1	0	0	1
169	1	1	1	0	0	1
170	1	1	1	0	0	1
171	1	1	1	0	0	1
172	1	1	1	0	0	1
N	10	10	10	10	10	10

INDIVIDUAL DATA 6-1-2

STUDY NO. SR11087 TITLE: indene indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg PERIOD : Pre-administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
163	1	1	2	1	1	1	0	1	1	1	1	0
164	1	1	2	1	1	1	0	1	1	1	1	0
165	1	1	2	1	1	1	0	1	1	1	1	0
166	1	1	2	1	1	1	0	1	1	1	1	0
167	1	1	2	1	1	1	0	1	1	1	1	0
168	1	1	2	1	1	1	0	1	1	1	1	0
169	1	1	2	1	1	1	0	1	1	1	1	0
170	1	1	2	1	1	1	0	1	1	1	1	0
171	1	1	2	1	1	1	0	1	1	1	1	0
172	1	1	2	1	1	1	0	1	1	1	1	0
N	10	10	10	10	10	10	10	10	10	10	10	10

INDIVIDUAL DATA 6-1-3

STUDY NO. SR11087 TITLE: indene indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg PERIOD : Pre-administration

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
163	1	1	1	1	0	0	0	0	1	1	1
164	1	1	1	1	0	0	0	0	1	1	1
165	1	1	1	1	0	0	0	0	1	1	1
166	1	1	1	1	0	0	0	0	1	1	1
167	1	1	1	1	0	0	0	0	1	1	1
168	1	1	1	1	0	0	0	0	1	1	1
169	1	1	1	1	0	0	0	0	1	1	1
170	1	1	1	1	0	0	0	0	1	1	1
171	1	1	1	1	0	0	0	0	1	1	1
172	1	1	1	1	0	0	0	0	1	1	1
N	10	10	10	10	10	10	10	10	10	10	10

INDIVIDUAL DATA 6-1-4

STUDY NO. SR11087 TITLE: indene indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg PERIOD : Pre-administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
463	1	1	1	0	0	1
464	1	1	1	0	0	1
465	1	1	1	0	0	1
466	1	1	1	0	0	1
467	1	1	1	0	0	1
468	1	1	1	0	0	1
469	1	1	1	0	0	1
470	1	1	1	0	0	1
471	1	1	1	0	0	1
472	1	1	1	0	0	1
N	10	10	10	10	10	10

INDIVIDUAL DATA 6-1-5

STUDY NO. SR11087 TITLE: indene indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg PERIOD : Pre-administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
463	1	1	2	1	1	1	0	1	1	1	1	0
464	1	1	2	1	1	1	0	1	1	1	1	0
465	1	1	2	1	1	1	0	1	1	1	1	0
466	1	1	2	1	1	1	0	1	1	1	1	0
467	1	1	2	1	1	1	0	1	1	1	1	0
468	1	1	2	1	1	1	0	1	1	1	1	0
469	1	1	2	1	1	1	0	1	1	1	1	0
470	1	1	2	1	1	1	0	1	1	1	1	0
471	1	1	2	1	1	1	0	1	1	1	1	0
472	1	1	2	1	1	1	0	1	1	1	1	0
N	10	10	10	10	10	10	10	10	10	10	10	10

INDIVIDUAL DATA 6-1-6

STUDY NO. SR11087 TITLE: indene indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg PERIOD : Pre-administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
463	1	1	1	1	0	0	0	0	1	1	1
464	1	1	1	1	0	0	0	0	1	1	1
465	1	1	1	1	0	0	0	0	1	1	1
466	1	1	1	1	0	0	0	0	1	1	1
467	1	1	1	1	0	0	0	0	1	1	1
468	1	1	1	1	0	0	0	0	1	1	1
469	1	1	1	1	0	0	0	0	1	1	1
470	1	1	1	1	0	0	0	0	1	1	1
471	1	1	1	1	0	0	0	0	1	1	1
472	1	1	1	1	0	0	0	0	1	1	1
N	10	10	10	10	10	10	10	10	10	10	10

INDIVIDUAL DATA 6-2-1

STUDY NO. SR11087 TITLE: indene indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg PERIOD : Day 7 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
163	1	1	1	0	0	1
164	1	1	1	0	0	1
165	1	1	1	0	0	1
166	1	1	1	0	0	1
167	1	1	1	0	0	1
168	1	1	1	0	0	1
169	1	1	1	0	0	1
170	1	1	1	0	0	1
171	1	1	1	0	0	1
172	1	1	1	0	0	1
N	10	10	10	10	10	10

INDIVIDUAL DATA 6-2-2

STUDY NO. SR11087 TITLE: indene indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg PERIOD : Day 7 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
163	1	1	2	1	1	1	0	1	1	1	1	0
164	1	1	2	1	1	1	0	1	1	1	1	0
165	1	1	2	1	1	1	0	1	1	1	1	0
166	1	1	2	1	1	1	0	1	1	1	1	0
167	1	1	2	1	1	1	0	1	1	1	1	0
168	1	1	2	1	1	1	0	1	1	1	1	0
169	1	1	2	1	1	1	0	1	1	1	1	0
170	1	1	2	1	1	1	0	1	1	1	1	0
171	1	1	2	1	1	1	0	1	1	1	1	0
172	1	1	2	1	1	1	0	1	1	1	1	0
N	10	10	10	10	10	10	10	10	10	10	10	10

INDIVIDUAL DATA 6-2-3

STUDY NO. SR11087 TITLE: indene indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg PERIOD : Day 7 of administration

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
163	1	1	1	1	0	0	0	0	1	1	1
164	1	1	1	1	0	0	0	0	1	1	1
165	1	1	1	1	0	0	0	0	1	1	1
166	1	1	1	1	0	0	0	0	1	1	1
167	1	1	1	1	0	0	0	0	1	1	1
168	1	1	1	1	0	0	0	0	1	1	1
169	1	1	1	1	0	0	0	0	1	1	1
170	1	1	1	1	1	0	0	0	1	1	1
171	1	1	1	1	0	0	0	0	1	1	1
172	1	1	1	1	0	0	0	0	1	1	1
N	10	10	10	10	10	10	10	10	10	10	10

INDIVIDUAL DATA 6-2-4

STUDY NO. SR11087 TITLE: indene indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg PERIOD : Day 7 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
463	1	1	1	0	0	1
464	1	1	1	0	0	1
465	1	1	1	0	0	1
466	1	1	1	0	0	1
467	1	1	1	0	0	1
468	1	1	1	0	0	1
469	1	1	1	0	0	1
470	1	1	1	0	0	1
471	1	1	1	0	0	1
472	1	1	1	0	0	1
N	10	10	10	10	10	10

INDIVIDUAL DATA 6-2-5

STUDY NO. SR11087 TITLE: indene indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg PERIOD : Day 7 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
463	1	1	2	1	1	1	0	1	1	1	1	0
464	1	1	2	1	1	1	0	1	1	1	1	0
465	1	1	2	1	1	1	0	1	1	1	1	0
466	1	1	2	1	1	1	0	1	1	1	1	0
467	1	1	2	1	1	1	0	1	1	1	1	0
468	1	1	2	1	1	1	0	1	1	1	1	0
469	1	1	2	1	1	1	0	1	1	1	1	0
470	1	1	2	1	1	1	0	1	1	1	1	0
471	1	1	2	1	1	1	0	1	1	1	1	0
472	1	1	2	1	1	1	0	1	1	1	1	0
N	10	10	10	10	10	10	10	10	10	10	10	10

INDIVIDUAL DATA 6-2-6

STUDY NO. SR11087 TITLE: indene indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg PERIOD : Day 7 of administration

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
463	1	1	1	1	0	0	0	0	1	1	1
464	1	1	1	1	1	0	0	0	1	1	1
465	1	1	1	1	0	0	0	0	1	1	1
466	1	1	1	1	0	0	0	0	1	1	1
467	1	1	1	1	0	0	0	0	1	1	1
468	1	1	1	1	0	0	0	0	1	1	1
469	1	1	1	1	0	0	0	0	1	1	1
470	1	1	1	1	0	0	0	0	1	1	1
471	1	1	1	1	0	0	0	0	1	1	1
472	1	1	1	1	0	0	0	0	1	1	1
N	10	10	10	10	10	10	10	10	10	10	10

INDIVIDUAL DATA 6-3-1

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg PERIOD : Day 14 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
163	1	1	1	0	0	1
164	1	1	1	0	0	1
165	1	1	1	0	0	1
166	1	1	1	0	0	1
167	1	1	1	0	0	1
168	1	1	1	0	0	1
169	1	1	1	0	0	1
170	1	1	1	0	0	1
171	1	1	1	0	0	1
172	1	1	1	0	0	1
N	10	10	10	10	10	10

INDIVIDUAL DATA 6-3-2

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg PERIOD : Day 14 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
163	1	1	2	1	1	1	0	1	1	1	1	0
164	1	1	2	1	1	1	0	1	1	1	1	0
165	1	1	2	1	1	1	0	1	1	1	1	0
166	1	1	2	1	1	1	0	1	1	1	1	0
167	1	1	2	1	1	1	0	1	1	1	1	0
168	1	1	2	1	1	1	0	1	1	1	1	0
169	1	1	2	1	1	1	0	1	1	1	1	0
170	1	1	2	1	1	1	0	1	1	1	1	0
171	1	1	2	1	1	1	0	1	1	1	1	0
172	1	1	2	1	1	1	0	1	1	1	1	0
N	10	10	10	10	10	10	10	10	10	10	10	10

INDIVIDUAL DATA 6-3-3

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg PERIOD : Day 14 of administration

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
163	1	1	1	1	0	0	0	0	1	1	1
164	1	1	1	1	0	0	0	0	1	1	1
165	1	1	1	1	0	0	0	0	1	1	1
166	1	1	1	1	0	0	0	0	1	1	1
167	1	1	1	1	0	0	0	0	1	1	1
168	1	1	1	1	0	0	0	0	1	1	1
169	1	1	1	1	0	0	0	0	1	1	1
170	1	1	1	1	0	0	0	0	1	1	1
171	1	1	1	1	0	0	0	0	1	1	1
172	1	1	1	1	0	0	0	0	1	1	1
N	10	10	10	10	10	10	10	10	10	10	10

INDIVIDUAL DATA 6-3-4

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg PERIOD : Day 14 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
463	1	1	1	0	0	1
464	1	1	1	0	0	1
465	1	1	1	0	0	1
466	1	1	1	0	0	1
467	1	1	1	0	0	1
468	1	1	1	0	0	1
469	1	1	1	0	0	1
470	1	1	1	0	0	1
471	1	1	1	0	0	1
472	1	1	1	0	0	1
N	10	10	10	10	10	10

INDIVIDUAL DATA 6-3-5

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg PERIOD : Day 14 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
463	1	1	2	1	1	1	0	1	1	1	1	0
464	1	1	2	1	1	1	0	1	1	1	1	0
465	1	1	2	1	1	1	0	1	1	1	1	0
466	1	1	2	1	1	1	0	1	1	1	1	0
467	1	1	2	1	1	1	0	1	1	1	1	0
468	1	1	2	1	1	1	0	1	1	1	1	0
469	1	1	2	1	1	1	0	1	1	1	1	0
470	1	1	2	1	1	1	0	1	1	1	1	0
471	1	1	2	1	1	1	0	1	1	1	1	0
472	1	1	2	1	1	1	0	1	1	1	1	0
N	10	10	10	10	10	10	10	10	10	10	10	10

INDIVIDUAL DATA 6-3-6

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg PERIOD : Day 14 of administration

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
463	1	1	1	1	0	0	0	0	1	1	1
464	1	1	1	1	0	0	0	0	1	1	1
465	1	1	1	1	0	0	0	0	1	1	1
466	1	1	1	1	0	0	0	0	1	1	1
467	1	1	1	1	0	0	0	0	1	1	1
468	1	1	1	1	0	0	0	0	1	1	1
469	1	1	1	1	0	0	0	0	1	1	1
470	1	1	1	1	0	0	0	0	1	1	1
471	1	1	1	1	0	0	0	0	1	1	1
472	1	1	1	1	0	0	0	0	1	1	1
N	10	10	10	10	10	10	10	10	10	10	10

INDIVIDUAL DATA 6-4-1

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg PERIOD : Day 21 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
163	1	1	1	0	0	1
164	1	1	1	0	0	1
165	1	1	1	0	0	1
166	1	1	1	0	0	1
167	1	1	1	0	0	1
168	1	1	1	0	0	1
169	1	1	1	0	0	1
170	1	1	1	0	0	1
171	1	1	1	0	0	1
172	1	1	1	0	0	1
N	10	10	10	10	10	10

INDIVIDUAL DATA 6-4-2

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg PERIOD : Day 21 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
163	1	1	2	1	1	1	0	1	1	1	1	0
164	1	1	2	1	1	1	0	1	1	1	1	0
165	1	1	2	1	1	1	0	1	1	1	1	0
166	1	1	2	1	1	1	0	1	1	1	1	0
167	1	1	2	1	1	1	0	1	1	1	1	0
168	1	1	2	1	1	1	0	1	1	1	1	0
169	1	1	2	1	1	1	0	1	1	1	1	0
170	1	1	2	1	1	1	0	1	1	1	1	0
171	1	1	2	1	1	1	0	1	1	1	1	0
172	1	1	2	1	1	1	0	1	1	1	1	0
N	10	10	10	10	10	10	10	10	10	10	10	10

INDIVIDUAL DATA 6-4-3

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg PERIOD : Day 21 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
163	1	1	1	1	0	0	0	0	1	1	1
164	1	1	1	1	0	0	0	0	1	1	1
165	1	1	1	1	0	0	0	0	1	1	1
166	1	1	1	1	0	0	0	0	1	1	1
167	1	1	1	1	1	0	0	0	1	1	1
168	1	1	1	1	0	0	0	0	1	1	1
169	1	1	1	1	0	0	0	0	1	1	1
170	1	1	1	1	0	0	0	0	1	1	1
171	1	1	1	1	0	0	0	0	1	1	1
172	1	1	1	1	0	0	0	0	1	1	1
N	10	10	10	10	10	10	10	10	10	10	10

INDIVIDUAL DATA 6-4-4

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg PERIOD : Day 21 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
463	1	1	1	0	0	1
464	1	1	1	0	0	1
465	1	1	1	0	0	1
466	1	1	1	0	0	1
467	1	1	1	0	0	1
468	1	1	1	0	0	1
469	1	1	1	0	0	1
470	1	1	1	0	0	1
471	1	1	1	0	0	1
472	1	1	1	0	0	1
N	10	10	10	10	10	10

INDIVIDUAL DATA 6-4-5

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg PERIOD : Day 21 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
463	1	1	2	1	1	1	0	1	1	1	1	0
464	1	1	2	1	1	1	0	1	1	1	1	0
465	1	1	2	1	1	1	0	1	1	1	1	0
466	1	1	2	1	1	1	0	1	1	1	1	0
467	1	1	2	1	1	1	0	1	1	1	1	0
468	1	1	2	1	1	1	0	1	1	1	1	0
469	1	1	2	1	1	1	0	1	1	1	1	0
470	1	1	2	1	1	1	0	1	1	1	1	0
471	1	1	2	1	1	1	0	1	1	1	1	0
472	1	1	2	1	1	1	0	1	1	1	1	0
N	10	10	10	10	10	10	10	10	10	10	10	10

INDIVIDUAL DATA 6-4-6

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg PERIOD : Day 21 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
463	1	1	1	1	0	0	0	0	1	1	1
464	1	1	1	1	1	0	0	0	1	1	1
465	1	1	1	1	0	0	0	0	1	1	1
466	1	1	1	1	0	0	0	0	1	1	1
467	1	1	1	1	0	0	0	0	1	1	1
468	1	1	1	1	0	0	0	0	1	1	1
469	1	1	1	1	0	0	0	0	1	1	1
470	1	1	1	1	0	0	0	0	1	1	1
471	1	1	1	1	0	0	0	0	1	1	1
472	1	1	1	1	0	0	0	0	1	1	1
N	10	10	10	10	10	10	10	10	10	10	10

INDIVIDUAL DATA 6-5-1

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg PERIOD : Day 28 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
163	1	1	1	0	0	1
164	1	1	1	0	0	1
165	1	1	1	0	0	1
166	1	1	1	0	0	1
167	1	1	1	0	0	1
168	1	1	1	0	0	1
169	1	1	1	0	0	1
170	1	1	1	0	0	1
171	1	1	1	0	0	1
172	1	1	1	0	0	1
N	10	10	10	10	10	10

INDIVIDUAL DATA 6-5-2

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg PERIOD : Day 28 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
163	1	1	2	1	1	1	0	1	1	1	1	0
164	1	1	2	1	1	1	0	1	1	1	1	0
165	1	1	2	1	1	1	0	1	1	1	1	0
166	1	1	2	1	1	1	0	1	1	1	1	0
167	1	1	2	1	1	1	0	1	1	1	1	0
168	1	1	2	1	1	1	0	1	1	1	1	0
169	1	1	2	1	1	1	0	1	1	1	1	0
170	1	1	2	1	1	1	0	1	1	1	1	0
171	1	1	2	1	1	1	0	1	1	1	1	0
172	1	1	2	1	1	1	0	1	1	1	1	0
N	10	10	10	10	10	10	10	10	10	10	10	10

INDIVIDUAL DATA 6-5-3

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg PERIOD : Day 28 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
163	1	1	1	1	0	0	0	0	1	1	1
164	1	1	1	1	0	0	0	0	1	1	1
165	1	1	1	1	0	0	0	0	1	1	1
166	1	1	1	1	0	0	0	0	1	1	1
167	1	1	1	1	0	0	0	0	1	1	1
168	1	1	1	1	0	0	0	0	1	1	1
169	1	1	1	1	0	0	0	0	1	1	1
170	1	1	1	1	0	0	0	0	1	1	1
171	1	1	1	1	0	0	0	0	1	1	1
172	1	1	1	1	0	0	0	0	1	1	1
N	10	10	10	10	10	10	10	10	10	10	10

INDIVIDUAL DATA 6-5-4

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg PERIOD : Day 28 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
463	1	1	1	0	0	1
464	1	1	1	0	0	1
465	1	1	1	0	0	1
466	1	1	1	0	0	1
467	1	1	1	0	0	1
468	1	1	1	0	0	1
469	1	1	1	0	0	1
470	1	1	1	0	0	1
471	1	1	1	0	0	1
472	1	1	1	0	0	1
N	10	10	10	10	10	10

INDIVIDUAL DATA 6-5-5

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg PERIOD : Day 28 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
463	1	1	2	1	1	1	0	1	1	1	1	0
464	1	1	2	1	1	1	0	1	1	1	1	0
465	1	1	2	1	1	1	0	1	1	1	1	0
466	1	1	2	1	1	1	0	1	1	1	1	0
467	1	1	2	1	1	1	0	1	1	1	1	0
468	1	1	2	1	1	1	0	1	1	1	1	0
469	1	1	2	1	1	1	0	1	1	1	1	0
470	1	1	2	1	1	1	0	1	1	1	1	0
471	1	1	2	1	1	1	0	1	1	1	1	0
472	1	1	2	1	1	1	0	1	1	1	1	0
N	10	10	10	10	10	10	10	10	10	10	10	10

INDIVIDUAL DATA 6-5-6

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg PERIOD : Day 28 of administration

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
463	1	1	1	1	0	0	0	0	1	1	1
464	1	1	1	1	0	0	0	0	1	1	1
465	1	1	1	1	0	0	0	0	1	1	1
466	1	1	1	1	0	0	0	0	1	1	1
467	1	1	1	1	0	0	0	0	1	1	1
468	1	1	1	1	0	0	0	0	1	1	1
469	1	1	1	1	0	0	0	0	1	1	1
470	1	1	1	1	0	0	0	0	1	1	1
471	1	1	1	1	0	0	0	0	1	1	1
472	1	1	1	1	0	0	0	0	1	1	1
N	10	10	10	10	10	10	10	10	10	10	10

INDIVIDUAL DATA 6-6-1

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg PERIOD : Day 35 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
163	1	1	1	0	0	1
164	1	1	1	0	0	1
165	1	1	1	0	0	1
166	1	1	1	0	0	1
167	1	1	1	0	0	1
168	1	1	1	0	0	1
169	1	1	1	0	0	1
170	1	1	1	0	0	1
171	1	1	1	0	0	1
172	1	1	1	0	0	1
N	10	10	10	10	10	10

INDIVIDUAL DATA 6-6-2

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg PERIOD : Day 35 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
163	1	1	2	1	1	1	0	1	1	1	1	0
164	1	1	2	1	1	1	0	1	1	1	1	0
165	1	1	2	1	1	1	0	1	1	1	1	0
166	1	1	2	1	1	1	0	1	1	1	1	0
167	1	1	2	1	1	1	0	1	1	1	1	0
168	1	1	2	1	1	1	0	1	1	1	1	0
169	1	1	2	1	1	1	0	1	1	1	1	0
170	1	1	2	1	1	1	0	1	1	1	1	0
171	1	1	2	1	1	1	0	1	1	1	1	0
172	1	1	2	1	1	1	0	1	1	1	1	0
N	10	10	10	10	10	10	10	10	10	10	10	10

INDIVIDUAL DATA 6-6-3

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg PERIOD : Day 35 of administration

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
163	1	1	1	1	0	0	0	0	1	1	1
164	1	1	1	1	0	0	0	0	1	1	1
165	1	1	1	1	0	0	0	0	1	1	1
166	1	1	1	1	1	0	0	0	1	1	1
167	1	1	1	1	0	0	0	0	1	1	1
168	1	1	1	1	0	0	0	0	1	1	1
169	1	1	1	1	0	0	0	0	1	1	1
170	1	1	1	1	0	0	0	0	1	1	1
171	1	1	1	1	0	0	0	0	1	1	1
172	1	1	1	1	0	0	0	0	1	1	1
N	10	10	10	10	10	10	10	10	10	10	10

INDIVIDUAL DATA 6-6-4

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg PERIOD : Day 35 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
463	1	1	1	0	0	1
464	1	1	1	0	0	1
465	1	1	1	0	0	1
466	1	1	1	0	0	1
467	1	1	1	0	0	1
468	1	1	1	0	0	1
469	1	1	1	0	0	1
470	1	1	1	0	0	1
471	1	1	1	0	0	1
472	1	1	1	0	0	1
N	10	10	10	10	10	10

INDIVIDUAL DATA 6-6-5

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg PERIOD : Day 35 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
463	1	1	2	1	1	1	0	1	1	1	1	0
464	1	1	2	1	1	1	0	1	1	1	1	0
465	1	1	2	1	1	1	0	1	1	1	1	0
466	1	1	2	1	1	1	0	1	1	1	1	0
467	1	1	2	1	1	1	0	1	1	1	1	0
468	1	1	2	1	1	1	0	1	1	1	1	0
469	1	1	2	1	1	1	0	1	1	1	1	0
470	1	1	2	1	1	1	0	1	1	1	1	0
471	1	1	2	1	1	1	0	1	1	1	1	0
472	1	1	2	1	1	1	0	1	1	1	1	0
N	10	10	10	10	10	10	10	10	10	10	10	10

INDIVIDUAL DATA 6-6-6

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg PERIOD : Day 35 of administration

	In the open-field										
							Stereotype		Bizarre behavior		
Animal No.	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
463	1	1	1	1	0	0	0	0	1	1	1
464	1	1	1	1	0	0	0	0	1	1	1
465	1	1	1	1	0	0	0	0	1	1	1
466	1	1	1	1	0	0	0	0	1	1	1
467	1	1	1	1	0	0	0	0	1	1	1
468	1	1	1	1	0	0	0	0	1	1	1
469	1	1	1	1	0	0	0	0	1	1	1
470	1	1	1	1	0	0	0	0	1	1	1
471	1	1	1	1	0	0	0	0	1	1	1
472	1	1	1	1	0	0	0	0	1	1	1
N	10	10	10	10	10	10	10	10	10	10	10

INDIVIDUAL DATA 6-7-1

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg PERIOD : Day 42 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
163	1	1	1	0	0	1
164	1	1	1	0	0	1
165	1	1	1	0	0	1
166	1	1	1	0	0	1
167	1	1	1	0	0	1
168	1	1	1	0	0	1
169	1	1	1	0	0	1
170	1	1	1	0	0	1
171	1	1	1	0	0	1
172	1	1	1	0	0	1
N	10	10	10	10	10	10

INDIVIDUAL DATA 6-7-2

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg PERIOD : Day 42 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
163	1	1	2	1	1	1	0	1	1	1	1	0
164	1	1	2	1	1	1	0	1	1	1	1	0
165	1	1	2	1	1	1	0	1	1	1	1	0
166	1	1	2	1	1	1	0	1	1	1	1	0
167	1	1	2	1	1	1	0	1	1	1	1	0
168	1	1	2	1	1	1	0	1	1	1	1	0
169	1	1	2	1	1	1	0	1	1	1	1	0
170	1	1	2	1	1	1	0	1	1	1	1	0
171	1	1	2	1	1	1	0	1	1	1	1	0
172	1	1	2	1	1	1	0	1	1	1	1	0
N	10	10	10	10	10	10	10	10	10	10	10	10

INDIVIDUAL DATA 6-7-3

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg PERIOD : Day 42 of administration

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
163	1	1	1	1	0	0	0	0	1	1	1
164	1	1	1	1	0	0	0	0	1	1	1
165	1	1	1	1	0	0	0	0	1	1	1
166	1	1	1	1	0	0	0	0	1	1	1
167	1	1	1	1	0	0	0	0	1	1	1
168	1	1	1	1	0	0	0	0	1	1	1
169	1	1	1	1	0	0	0	0	1	1	1
170	1	1	1	1	0	0	0	0	1	1	1
171	1	1	1	1	0	0	0	0	1	1	1
172	1	1	1	1	0	0	0	0	1	1	1
N	10	10	10	10	10	10	10	10	10	10	10

INDIVIDUAL DATA 6-7-4

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg PERIOD : Day 42 of administration

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
463	1	1	1	0	0	1
464	1	1	1	0	0	1
465	1	1	1	0	0	1
466	1	1	1	0	0	1
467	1	1	1	0	0	1
468	1	1	1	0	0	1
469	1	1	1	0	0	1
470	1	1	1	0	0	1
471	1	1	1	0	0	1
472	1	1	1	0	0	1
N	10	10	10	10	10	10

INDIVIDUAL DATA 6-7-5

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg PERIOD : Day 42 of administration

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
463	1	1	2	1	1	1	0	1	1	1	1	0
464	1	1	2	1	1	1	0	1	1	1	1	0
465	1	1	2	1	1	1	0	1	1	1	1	0
466	1	1	2	1	1	1	0	1	1	1	1	0
467	1	1	2	1	1	1	0	1	1	1	1	0
468	1	1	2	1	1	1	0	1	1	1	1	0
469	1	1	2	1	1	1	0	1	1	1	1	0
470	1	1	2	1	1	1	0	1	1	1	1	0
471	1	1	2	1	1	1	0	1	1	1	1	0
472	1	1	2	1	1	1	0	1	1	1	1	0
N	10	10	10	10	10	10	10	10	10	10	10	10

INDIVIDUAL DATA 6-7-6

STUDY NO. SR11087 TITLE: indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg PERIOD : Day 42 of administration

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
463	1	1	1	1	0	0	0	0	1	1	1
464	1	1	1	1	0	0	0	0	1	1	1
465	1	1	1	1	0	0	0	0	1	1	1
466	1	1	1	1	0	0	0	0	1	1	1
467	1	1	1	1	0	0	0	0	1	1	1
468	1	1	1	1	0	0	0	0	1	1	1
469	1	1	1	1	0	0	0	0	1	1	1
470	1	1	1	1	0	0	0	0	1	1	1
471	1	1	1	1	0	0	0	0	1	1	1
472	1	1	1	1	1	0	0	0	1	1	1
N	10	10	10	10	10	10	10	10	10	10	10

INDIVIDUAL DATA 6-8-1

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg PERIOD : Day 7 of recovery

Animal No.	In the cage					
				Stereotype		Bizarre behavior
	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
168	1	1	1	0	0	1
169	1	1	1	0	0	1
170	1	1	1	0	0	1
171	1	1	1	0	0	1
172	1	1	1	0	0	1
N	5	5	5	5	5	5

INDIVIDUAL DATA 6-8-2

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg PERIOD : Day 7 of recovery

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
168	1	1	2	1	1	1	0	1	1	1	1	0
169	1	1	2	1	1	1	0	1	1	1	1	0
170	1	1	2	1	1	1	0	1	1	1	1	0
171	1	1	2	1	1	1	0	1	1	1	1	0
172	1	1	2	1	1	1	0	1	1	1	1	0
N	5	5	5	5	5	5	5	5	5	5	5	5

INDIVIDUAL DATA 6-8-3

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg PERIOD : Day 7 of recovery

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
168	1	1	1	1	0	0	0	0	1	1	1
169	1	1	1	1	0	0	0	0	1	1	1
170	1	1	1	1	0	0	0	0	1	1	1
171	1	1	1	1	0	0	0	0	1	1	1
172	1	1	1	1	0	0	0	0	1	1	1
N	5	5	5	5	5	5	5	5	5	5	5

INDIVIDUAL DATA 6-8-4

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg PERIOD : Day 7 of recovery

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
468	1	1	1	0	0	1
469	1	1	1	0	0	1
470	1	1	1	0	0	1
471	1	1	1	0	0	1
472	1	1	1	0	0	1
N	5	5	5	5	5	5

INDIVIDUAL DATA 6-8-5

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg PERIOD : Day 7 of recovery

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
468	1	1	2	1	1	1	0	1	1	1	1	0
469	1	1	2	1	1	1	0	1	1	1	1	0
470	1	1	2	1	1	1	0	1	1	1	1	0
471	1	1	2	1	1	1	0	1	1	1	1	0
472	1	1	2	1	1	1	0	1	1	1	1	0
N	5	5	5	5	5	5	5	5	5	5	5	5

INDIVIDUAL DATA 6-8-6

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg PERIOD : Day 7 of recovery

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
468	1	1	1	1	0	0	0	0	1	1	1
469	1	1	1	1	0	0	0	0	1	1	1
470	1	1	1	1	0	0	0	0	1	1	1
471	1	1	1	1	0	0	0	0	1	1	1
472	1	1	1	1	0	0	0	0	1	1	1
N	5	5	5	5	5	5	5	5	5	5	5

INDIVIDUAL DATA 6-9-1

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg PERIOD : Day 14 of recovery

	In the cage					
				Stereotype		Bizarre behavior
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
168	1	1	1	0	0	1
169	1	1	1	0	0	1
170	1	1	1	0	0	1
171	1	1	1	0	0	1
172	1	1	1	0	0	1
N	5	5	5	5	5	5

INDIVIDUAL DATA 6-9-2

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg PERIOD : Day 14 of recovery

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
168	1	1	2	1	1	1	0	1	1	1	1	0
169	1	1	2	1	1	1	0	1	1	1	1	0
170	1	1	2	1	1	1	0	1	1	1	1	0
171	1	1	2	1	1	1	0	1	1	1	1	0
172	1	1	2	1	1	1	0	1	1	1	1	0
N	5	5	5	5	5	5	5	5	5	5	5	5

INDIVIDUAL DATA 6-9-3

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg PERIOD : Day 14 of recovery

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
168	1	1	1	1	0	0	0	0	1	1	1
169	1	1	1	1	0	0	0	0	1	1	1
170	1	1	1	1	0	0	0	0	1	1	1
171	1	1	1	1	0	0	0	0	1	1	1
172	1	1	1	1	1	0	0	0	1	1	1
N	5	5	5	5	5	5	5	5	5	5	5

INDIVIDUAL DATA 6-9-4

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg PERIOD : Day 14 of recovery

Animal No.	In the cage					
				Stereotype		Bizarre behavior
	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Biting/ Selfmutilation
468	1	1	1	0	0	1
469	1	1	1	0	0	1
470	1	1	1	0	0	1
471	1	1	1	0	0	1
472	1	1	1	0	0	1
N	5	5	5	5	5	5

INDIVIDUAL DATA 6-9-5

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg PERIOD : Day 14 of recovery

Animal No.	On the hand											
	Ease of											
	Removal	Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacrimation	Salivation	Secretions/ Excretions
468	1	1	2	1	1	1	0	1	1	1	1	0
469	1	1	2	1	1	1	0	1	1	1	1	0
470	1	1	2	1	1	1	0	1	1	1	1	0
471	1	1	2	1	1	1	0	1	1	1	1	0
472	1	1	2	1	1	1	0	1	1	1	1	0
N	5	5	5	5	5	5	5	5	5	5	5	5

INDIVIDUAL DATA 6-9-6

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Detailed clinical observations ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg PERIOD : Day 14 of recovery

Animal No.	In the open-field										
							Stereotype		Bizarre behavior		
	Gait	Co-ordination of movement	Reactivity to environmental stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
468	1	1	1	1	0	0	0	0	1	1	1
469	1	1	1	1	0	0	0	0	1	1	1
470	1	1	1	1	0	0	0	0	1	1	1
471	1	1	1	1	1	0	0	0	1	1	1
472	1	1	1	1	0	0	0	0	1	1	1
N	5	5	5	5	5	5	5	5	5	5	5

INDIVIDUAL DATA 7-1-1

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Functional test ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Week 6 of administration

Animal No.	Reactivity					Righting reflex
	Visual	Touch	Auditory	Pain	Proprioceptive	
104	4	2	1	2	1	1
105	4	2	1	2	1	1
106	4	2	1	2	1	1
107	4	2	1	2	1	1
108	4	2	1	2	1	1
N	5	5	5	5	5	5

INDIVIDUAL DATA 7-1-2

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Functional test ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : Week 6 of administration

Animal No.	Reactivity					Righting reflex
	Visual	Touch	Auditory	Pain	Proprioceptive	
203	4	2	1	2	1	1
205	4	2	1	2	1	1
207	4	2	1	2	1	1
208	4	2	1	2	1	1
209	4	2	1	2	1	1
N	5	5	5	5	5	5

INDIVIDUAL DATA 7-1-3

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Functional test ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : Week 6 of administration

Animal No.	Reactivity					Righting reflex
	Visual	Touch	Auditory	Pain	Proprioceptive	
301	4	2	1	2	1	1
303	4	2	1	2	1	1
305	4	2	1	2	1	1
306	4	2	1	2	1	1
312	4	2	1	2	1	1
N	5	5	5	5	5	5

INDIVIDUAL DATA 7-1-4

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Functional test ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Week 6 of administration

Animal No.	Reactivity					Righting reflex
	Visual	Touch	Auditory	Pain	Proprioceptive	
401	4	2	1	2	1	1
404	4	2	1	2	1	1
406	4	2	1	2	1	1
411	4	2	1	2	1	1
412	4	2	1	2	1	1
N	5	5	5	5	5	5

INDIVIDUAL DATA 7-2-1

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Functional test ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Week 2 of recovery

Animal No.	Reactivity					Righting reflex
	Visual	Touch	Auditory	Pain	Proprioceptive	
104	4	2	1	2	1	1
105	4	2	1	2	1	1
106	4	2	1	2	1	1
107	4	2	1	2	1	1
108	4	2	1	2	1	1
N	5	5	5	5	5	5

INDIVIDUAL DATA 7-2-2

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Functional test ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Week 2 of recovery

Animal No.	Reactivity					Righting reflex
	Visual	Touch	Auditory	Pain	Proprioceptive	
401	4	2	1	2	1	1
404	4	2	1	2	1	1
406	4	2	1	2	1	1
411	4	2	1	2	1	1
412	4	2	1	2	1	1
N	5	5	5	5	5	5

INDIVIDUAL DATA 7-3-1

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Functional test ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Week 6 of administration

Animal No.	Grip strength (g)		Motor activity measurements (count)						
	Forelimb	Hindlimb	0'-10'	10'-20'	20'-30'	30'-40'	40'-50'	50'-60'	Total
104	1353.7	430.3	557	370	180	125	35	58	1325
105	1458.3	454.3	272	186	135	46	51	15	705
106	1519.0	452.3	548	387	262	143	280	281	1901
107	1714.0	537.7	244	287	331	380	265	231	1738
108	1776.3	624.0	813	433	185	59	97	186	1773
N	5	5	5	5	5	5	5	5	5
MEAN	1564.26	499.72	486.8	332.6	218.6	150.6	145.6	154.2	1488.4
S.D.	176.77	80.65	234.6	97.5	77.7	134.8	118.2	113.6	488.4

INDIVIDUAL DATA 7-3-2

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Functional test ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : Week 6 of administration

Animal No.	Grip strength (g)		Motor activity measurements (count)						
	Forelimb	Hindlimb	0'-10'	10'-20'	20'-30'	30'-40'	40'-50'	50'-60'	Total
203	1682.3	529.7	726	507	215	81	128	131	1788
205	1466.0	483.7	571	336	97	104	78	9	1195
207	1469.7	504.3	929	612	466	361	195	63	2626
208	1625.3	534.7	589	328	145	95	40	0	1197
209	1841.0	596.7	1150	745	568	369	395	192	3419
N	5	5	5	5	5	5	5	5	5
MEAN	1616.86	529.82	793.0	505.6	298.2	202.0	167.2	79.0	2045.0
S.D.	157.33	42.65	245.6	179.5	207.3	149.1	139.9	82.0	966.1

INDIVIDUAL DATA 7-3-3

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Functional test ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : Week 6 of administration

Animal No.	Grip strength (g)		Motor activity measurements (count)						
	Forelimb	Hindlimb	0'-10'	10'-20'	20'-30'	30'-40'	40'-50'	50'-60'	Total
301	1704.3	498.7	449	297	173	128	140	104	1291
303	1246.0	514.7	542	322	228	220	150	77	1539
305	1595.7	575.3	1016	620	517	426	404	125	3108
306	1460.7	459.0	1263	702	499	300	307	276	3347
312	1610.0	561.0	577	271	175	115	97	35	1270
N	5	5	5	5	5	5	5	5	5
MEAN	1523.34	521.74	769.4	442.4	318.4	237.8	219.6	123.4	2111.0
S.D.	177.72	47.24	352.1	202.5	174.6	129.2	130.2	91.7	1028.2

INDIVIDUAL DATA 7-3-4

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Functional test ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Week 6 of administration

Animal No.	Grip strength (g)		Motor activity measurements (count)						
	Forelimb	Hindlimb	0'-10'	10'-20'	20'-30'	30'-40'	40'-50'	50'-60'	Total
401	1195.3	432.7	277	196	153	47	55	2	730
404	1104.7	585.7	742	384	93	15	0	0	1234
406	1114.7	572.0	752	592	446	506	122	105	2523
411	1249.3	574.7	1114	487	365	372	318	246	2902
412	1409.3	451.3	329	316	135	9	97	24	910
N	5	5	5	5	5	5	5	5	5
MEAN	1214.66**	523.28	642.8	395.0	238.4	189.8	118.4	75.4	1659.8
S.D.	124.04	74.67	345.0	152.7	156.7	232.8	120.8	104.5	986.9

** : Significantly different from the 0 mg/kg group at $p \leqq 0.01$ (Dunnett's test).

INDIVIDUAL DATA 7-4-1

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Functional test ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : Satellite 0 mg/kg PERIOD : Week 2 of recovery

Animal No.	Grip strength (g)		Motor activity measurements (count)						
	Forelimb	Hindlimb	0'-10'	10'-20'	20'-30'	30'-40'	40'-50'	50'-60'	Total
104	1465.0	507.0	501	281	243	232	288	211	1756
105	1822.7	438.7	638	499	394	416	426	501	2874
106	1522.0	384.0	674	353	192	242	111	181	1753
107	1766.0	482.0	557	392	398	274	329	187	2137
108	1888.0	640.0	685	301	193	0	216	193	1588
N	5	5	5	5	5	5	5	5	5
MEAN	1692.74	490.34	611.0	365.2	284.0	232.8	274.0	254.6	2021.6
S.D.	188.02	95.81	79.4	86.6	104.3	149.6	118.6	138.2	517.3

INDIVIDUAL DATA 7-4-2

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Functional test ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : Satellite 100 mg/kg PERIOD : Week 2 of recovery

Animal No.	Grip strength (g)		Motor activity measurements (count)						
	Forelimb	Hindlimb	0'-10'	10'-20'	20'-30'	30'-40'	40'-50'	50'-60'	Total
401	1448.3	500.0	533	395	371	395	200	163	2057
404	1454.3	378.0	761	185	131	178	11	266	1532
406	1765.3	449.7	453	263	152	86	114	132	1200
411	1930.7	522.3	932	494	527	164	250	483	2850
412	1779.3	408.0	377	236	237	257	203	205	1515
N	5	5	5	5	5	5	5	5	5
MEAN	1675.58	451.60	611.2	314.6	283.6	216.0	155.6	249.8	1830.8
S.D.	214.78	60.54	229.9	126.8	165.6	117.0	94.6	139.7	647.5

INDIVIDUAL DATA 8-1-1

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Functional test ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg PERIOD : Day 4 of lactation

Animal No.	Reactivity					Righting reflex
	Visual	Touch	Auditory	Pain	Proprioceptive	
151	4	2	1	2	1	1
152	4	2	1	2	1	1
154	4	2	1	2	1	1
159	4	2	1	2	1	1
161	4	2	1	2	1	1
N	5	5	5	5	5	5

INDIVIDUAL DATA 8-1-2

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Functional test ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg PERIOD : Day 4 of lactation

Animal No.	Reactivity					Righting reflex
	Visual	Touch	Auditory	Pain	Proprioceptive	
256	4	2	1	2	1	1
257	4	2	1	2	1	1
259	4	2	1	2	1	1
260	4	2	1	2	1	1
262	4	2	1	2	1	1
N	5	5	5	5	5	5

INDIVIDUAL DATA 8-1-3

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Functional test ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg PERIOD : Day 4 of lactation

Animal No.	Reactivity					Righting reflex
	Visual	Touch	Auditory	Pain	Proprioceptive	
352	4	2	1	2	1	1
355	4	2	1	2	1	1
357	4	2	1	2	1	1
358	4	2	1	2	1	1
360	4	2	1	2	1	1
N	5	5	5	5	5	5

INDIVIDUAL DATA 8-1-4

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Functional test ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg PERIOD : Day 4 of lactation

Animal No.	Reactivity					Righting reflex
	Visual	Touch	Auditory	Pain	Proprioceptive	
451	4	2	1	2	1	1
452	4	2	1	2	1	1
456	4	2	1	2	1	1
458	4	2	1	2	1	1
462	4	2	1	2	1	1
N	5	5	5	5	5	5

INDIVIDUAL DATA 8-2-1

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Functional test ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Day 4 of lactation

Animal No.	Grip strength (g)		Motor activity measurements (count)						
	Forelimb	Hindlimb	0'-10'	10'-20'	20'-30'	30'-40'	40'-50'	50'-60'	Total
151	1181.3	327.7	336	235	368	84	141	127	1291
152	1356.0	380.0	666	256	52	0	0	5	979
154	1311.3	421.7	287	125	92	118	97	86	805
159	1415.3	526.0	342	553	337	363	163	303	2061
161	1461.3	402.0	267	173	71	43	0	0	554
N	5	5	5	5	5	5	5	5	5
MEAN	1345.04	411.48	379.6	268.4	184.0	121.6	80.2	104.2	1138.0
S.D.	107.84	73.01	163.2	167.3	154.9	142.0	77.0	123.6	581.5

INDIVIDUAL DATA 8-2-2

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Functional test ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : Day 4 of lactation

Animal No.	Grip strength (g)		Motor activity measurements (count)						
	Forelimb	Hindlimb	0'-10'	10'-20'	20'-30'	30'-40'	40'-50'	50'-60'	Total
256	1256.0	451.7	394	402	393	438	321	278	2226
257	1087.0	348.0	554	438	113	284	123	352	1864
259	1360.7	432.7	1101	336	552	285	106	613	2993
260	1190.0	472.3	799	180	183	98	242	163	1665
262	1226.3	343.3	612	631	721	976	113	563	3616
N	5	5	5	5	5	5	5	5	5
MEAN	1224.00	409.60	692.0	397.4	392.4	416.2	181.0	393.8*	2472.8*
S.D.	99.55	60.06	270.6	163.8	252.7	335.3	96.1	190.5	815.7

* : Significantly different from the 0 mg/kg group at $p \leqq 0.05$ (Dunnett's test).

INDIVIDUAL DATA 8-2-3

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Functional test ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : Day 4 of lactation

Animal No.	Grip strength (g)		Motor activity measurements (count)						
	Forelimb	Hindlimb	0'-10'	10'-20'	20'-30'	30'-40'	40'-50'	50'-60'	Total
352	1180.3	396.3	744	83	7	43	155	0	1032
355	1387.7	301.0	719	626	529	439	336	391	3040
357	1385.0	490.0	269	44	0	0	0	52	365
358	1399.7	472.3	620	223	173	23	187	0	1226
360	1324.0	388.3	445	99	0	44	1	0	589
N	5	5	5	5	5	5	5	5	5
MEAN	1335.34	409.58	559.4	215.0	141.8	109.8	135.8	88.6	1250.4
S.D.	91.54	75.53	200.4	239.3	228.7	184.9	141.1	170.5	1057.4

INDIVIDUAL DATA 8-2-4

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Functional test ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Day 4 of lactation

Animal No.	Grip strength (g)		Motor activity measurements (count)						
	Forelimb	Hindlimb	0'-10'	10'-20'	20'-30'	30'-40'	40'-50'	50'-60'	Total
451	1408.3	383.7	374	11	42	0	1	0	428
452	1492.0	302.0	447	67	83	50	0	106	753
456	1261.0	432.3	163	114	124	62	0	0	463
458	1311.0	357.7	505	135	0	0	0	0	640
462	1498.3	404.0	742	78	125	0	2	0	947
N	5	5	5	5	5	5	5	5	5
MEAN	1394.12	375.94	446.2	81.0	74.8	22.4	0.6	21.2	646.2
S.D.	106.38	49.56	210.0	47.7	54.0	31.0	0.9	47.4	214.0

INDIVIDUAL DATA 9-1-1

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Functional test ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg PERIOD : Week 6 of administration

Animal No.	Reactivity					Righting reflex
	Visual	Touch	Auditory	Pain	Proprioceptive	
168	4	2	1	2	1	1
169	4	2	1	2	1	1
170	4	2	1	2	1	1
171	4	2	1	2	1	1
172	4	2	1	2	1	1
N	5	5	5	5	5	5

INDIVIDUAL DATA 9-1-2

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Functional test ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg PERIOD : Week 6 of administration

Animal No.	Reactivity					Righting reflex
	Visual	Touch	Auditory	Pain	Proprioceptive	
468	4	2	1	2	1	1
469	4	2	1	2	1	1
470	4	2	1	2	1	1
471	4	2	1	2	1	1
472	4	2	1	2	1	1
N	5	5	5	5	5	5

INDIVIDUAL DATA 9-2-1

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Functional test ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg PERIOD : Week 2 of recovery

Animal No.	Reactivity					Righting reflex
	Visual	Touch	Auditory	Pain	Proprioceptive	
168	4	2	1	2	1	1
169	4	2	1	2	1	1
170	4	2	1	2	1	1
171	4	2	1	2	1	1
172	4	2	1	2	1	1
N	5	5	5	5	5	5

INDIVIDUAL DATA 9-2-2

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Functional test ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg PERIOD : Week 2 of recovery

Animal No.	Reactivity					Righting reflex
	Visual	Touch	Auditory	Pain	Proprioceptive	
468	4	2	1	2	1	1
469	4	2	1	2	1	1
470	4	2	1	2	1	1
471	4	2	1	2	1	1
472	4	2	1	2	1	1
N	5	5	5	5	5	5

INDIVIDUAL DATA 9-3-1

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Functional test ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : Satellite 0 mg/kg PERIOD : Week 6 of administration

Animal No.	Grip strength (g)		Motor activity measurements (count)						
	Forelimb	Hindlimb	0'-10'	10'-20'	20'-30'	30'-40'	40'-50'	50'-60'	Total
168	1129.7	458.3	669	331	202	101	80	83	1466
169	1266.0	452.7	945	853	848	455	0	0	3101
170	1293.3	353.7	1427	648	286	291	47	3	2702
171	1302.0	368.0	1180	596	945	809	743	144	4417
172	931.0	410.0	944	655	507	387	362	96	2951
N	5	5	5	5	5	5	5	5	5
MEAN	1184.40	408.54	1033.0	616.6	557.6	408.6	246.4	65.2	2927.4
S.D.	157.76	47.64	285.0	187.3	330.6	260.5	311.5	62.4	1053.1

INDIVIDUAL DATA 9-3-2

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Functional test ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : Satellite 100 mg/kg PERIOD : Week 6 of administration

Animal No.	Grip strength (g)		Motor activity measurements (count)						
	Forelimb	Hindlimb	0'-10'	10'-20'	20'-30'	30'-40'	40'-50'	50'-60'	Total
468	1412.0	467.7	558	372	224	163	176	178	1671
469	1243.3	413.0	778	381	65	0	0	168	1392
470	1121.3	473.3	1794	1302	1212	1001	794	637	6740
471	1275.7	295.0	936	841	576	352	237	156	3098
472	1332.0	407.7	536	428	342	146	121	96	1669
N	5	5	5	5	5	5	5	5	5
MEAN	1276.86	411.34	920.4	664.8	483.8	332.4	265.6	247.0+	2914.0
S.D.	107.97	71.71	515.5	406.0	447.7	394.1	308.0	220.3	2240.7

+ : Significantly different from the 0 mg/kg group at P $\leqq$ 0.05 (Steel's test).

INDIVIDUAL DATA 9-4-1

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Functional test ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg PERIOD : Week 2 of recovery

Animal	Grip strength (g)		Motor activity measurements (count)						
No.	Forelimb	Hindlimb	0'-10'	10'-20'	20'-30'	30'-40'	40'-50'	50'-60'	Total
168	1161.7	376.0	842	576	204	491	348	521	2982
169	1314.0	366.3	449	384	304	284	295	228	1944
170	1639.7	457.7	1240	841	402	0	0	641	3124
171	1387.3	418.3	888	795	404	482	509	234	3312
172	1326.3	405.3	1327	959	462	593	219	470	4030
N	5	5	5	5	5	5	5	5	5
MEAN	1365.80	404.72	949.2	711.0	355.2	370.0	274.2	418.8	3078.4
S.D.	174.20	36.38	351.0	229.5	101.8	235.2	186.6	182.3	751.4

INDIVIDUAL DATA 9-4-2

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Functional test ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg PERIOD : Week 2 of recovery

Animal No.	Grip strength (g)		Motor activity measurements (count)						
	Forelimb	Hindlimb	0'-10'	10'-20'	20'-30'	30'-40'	40'-50'	50'-60'	Total
468	1467.3	347.7	353	220	132	160	84	100	1049
469	1547.7	483.3	722	273	93	237	21	128	1474
470	1414.3	416.3	1118	755	429	524	400	368	3594
471	1482.7	413.7	1454	1105	599	721	679	626	5184
472	1396.3	406.3	639	182	219	186	0	89	1315
N	5	5	5	5	5	5	5	5	5
MEAN	1461.66	413.46	857.2	507.0	294.4	365.6	236.8	262.2	2523.2
S.D.	59.98	48.12	431.4	406.8	214.2	246.2	295.0	233.4	1800.0

INDIVIDUAL DATA 10-1

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Body weight ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg

	Body weight(g)										Body weight gain(g)		Body weight(g)		Body weight gain(g)	
	Administration day												Recovery day			
Animal No.	1	3	5	7	10	14	21	28	35	42	1-42	%	7	14	42-R14	%
101	348	357	370	376	390	407	432	442	464	447	99	28.45	#	#	#	#
102	365	377	389	399	404	422	443	463	487	509	144	39.45	#	#	#	#
103	362	376	380	386	398	408	444	462	484	505	143	39.50	#	#	#	#
104	373	381	399	400	409	429	452	470	495	503	130	34.85	515	522	19	3.78
105	369	381	391	399	413	426	456	475	496	493	124	33.60	512	515	22	4.46
106	381	395	407	415	425	444	470	489	521	534	153	40.16	556	564	30	5.62
107	381	392	397	410	427	450	477	502	525	547	166	43.57	557	572	25	4.57
108	387	396	407	419	433	452	489	518	544	552	165	42.64	555	566	14	2.54
109	389	400	412	422	432	453	481	507	528	552	163	41.90	#	#	#	#
110	395	404	419	433	445	479	514	550	585	615	220	55.70	#	#	#	#
111	404	414	429	440	456	478	506	537	569	592	188	46.53	#	#	#	#
112	398	412	420	432	436	458	482	509	540	563	165	41.46	#	#	#	#
N	12	12	12	12	12	12	12	12	12	12	12	12	5	5	5	5
MEAN	379.3	390.4	401.7	410.9	422.3	442.2	470.5	493.7	519.8	534.3	155.0	40.651	539.0	547.8	22.0	4.194
S.D.	16.5	16.6	17.4	19.6	19.8	24.2	25.7	32.6	36.2	46.0	31.2	6.816	23.3	27.0	6.0	1.135

R14 : Recovery day 14.

: Not applicable.

INDIVIDUAL DATA 10-2

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Body weight ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg

	Body weight(g)										Body weight gain(g)	
	Administration day											
Animal No.	1	3	5	7	10	14	21	28	35	42	1-42	%
201	358	364	372	383	392	409	430	455	484	495	137	38.27
202	354	360	373	371	377	396	426	441	469	499	145	40.96
203	363	373	384	397	412	425	448	470	500	523	160	44.08
204	373	380	395	407	419	439	459	490	519	535	162	43.43
205	377	391	401	411	425	443	456	482	504	522	145	38.46
206	365	374	384	395	401	421	442	466	483	496	131	35.89
207	396	404	415	425	435	452	482	511	545	558	162	40.91
208	383	393	402	408	417	428	452	472	502	520	137	35.77
209	381	391	407	414	430	448	487	514	535	553	172	45.14
210	390	402	415	433	444	463	500	533	556	575	185	47.44
211	397	410	418	437	452	470	496	521	549	575	178	44.84
212	407	412	420	427	441	449	489	520	555	576	169	41.52
N	12	12	12	12	12	12	12	12	12	12	12	12
MEAN	378.7	387.8	398.8	409.0	420.4	436.9	463.9	489.6	516.8	535.6	156.9	41.393
S.D.	16.8	17.6	17.2	20.1	22.3	21.8	25.9	29.7	30.6	31.2	17.6	3.748

INDIVIDUAL DATA 10-3

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Body weight ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg

	Body weight(g)										Body weight gain(g)	
	Administration day											
Animal No.	1	3	5	7	10	14	21	28	35	42	1-42	%
301	362	377	388	397	412	431	465	488	510	522	160	44.20
302	364	374	379	387	395	413	435	458	465	480	116	31.87
303	368	384	395	407	418	439	467	497	523	537	169	45.92
304	362	369	379	389	399	416	441	453	467	475	113	31.22
305	372	378	387	402	412	431	457	481	501	514	142	38.17
306	376	391	398	404	414	441	465	492	507	512	136	36.17
307	380	384	390	395	403	418	449	472	490	510	130	34.21
308	357	364	379	388	399	414	439	467	487	515	158	44.26
309	396	406	420	432	443	466	498	524	565	590	194	48.99
310	386	403	413	426	440	457	482	499	524	548	162	41.97
311	391	395	410	419	439	453	484	511	542	562	171	43.73
312	399	406	416	423	433	449	456	478	503	527	128	32.08
N	12	12	12	12	12	12	12	12	12	12	12	12
MEAN	376.1	385.9	396.2	405.8	417.3	435.7	461.5	485.0	507.0	524.3	148.3	39.399
S.D.	14.3	14.3	15.1	15.8	17.4	18.1	19.4	21.1	29.0	32.2	24.6	6.198

INDIVIDUAL DATA 10-4

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Body weight ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg

	Body weight(g)										Body weight gain(g)		Body weight(g)		Body weight gain(g)	
	Administration day												Recovery day			
Animal No.	1	3	5	7	10	14	21	28	35	42	1-42	%	7	14	42-R14	%
401	367	367	380	391	399	418	438	460	483	497	130	35.42	498	511	14	2.82
402	358	348	361	372	378	395	417	442	458	477	119	33.24	#	#	#	#
403	365	347	361	366	365	383	406	420	443	456	91	24.93	#	#	#	#
404	363	363	377	386	389	405	428	444	465	486	123	33.88	501	512	26	5.35
405	372	367	381	387	397	408	425	438	463	476	104	27.96	#	#	#	#
406	376	367	378	385	403	416	449	474	504	512	136	36.17	518	527	15	2.93
407	386	382	393	405	418	441	469	497	528	540	154	39.90	#	#	#	#
408	385	387	399	413	424	443	468	494	514	527	142	36.88	#	#	#	#
409	378	378	391	396	397	409	423	455	484	514	136	35.98	#	#	#	#
410	405	396	412	429	448	465	481	504	536	554	149	36.79	#	#	#	#
411	387	397	407	412	420	430	451	475	495	504	117	30.23	520	531	27	5.36
412	400	397	414	418	424	440	456	482	509	522	122	30.50	538	549	27	5.17
N	12	12	12	12	12	12	12	12	12	12	12	12	5	5	5	5
MEAN	378.5	374.7	387.8	396.7	405.2	421.1	442.6*	465.4*	490.2	505.4	126.9*	33.490**	515.0	526.0	21.8	4.326
S.D.	14.6	17.7	18.0	19.1	22.8	23.3	23.4	26.5	29.2	28.6	18.2	4.309	16.2	15.6	6.7	1.327

R14 : Recovery day 14.

: Not applicable.

* : Significantly different from the 0 mg/kg group at P ≦ 0.05 (Dunnett's test).

** : Significantly different from the 0 mg/kg group at P ≦ 0.01 (Dunnett's test).

INDIVIDUAL DATA 11-1-1

STUDY NO. SR11087 TITLE : indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Body weight ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg

	Body weight(g) on pre-mating period						Body weight gain(g)	
	Administration day							
Animal No.	1	3	5	7	10	14	1-14	%
151	229	223	237	231	250	253	24	10.48
152	226	233	237	240	243	254	28	12.39
153	238	249	250	259	259	266	28	11.76
154	246	248	251	255	258	264	18	7.32
155	236	238	245	247	251	254	18	7.63
156	241	238	244	248	245	251	10	4.15
157	239	243	254	251	260	263	24	10.04
158	250	263	255	270	270	275	25	10.00
159	247	244	255	251	258	263	16	6.48
160	250	251	253	261	270	277	27	10.80
161	249	251	263	261	268	281	32	12.85
162	265	265	274	277	287	295	30	11.32
N	12	12	12	12	12	12	12	12
MEAN	243.0	245.5	251.5	254.3	259.9	266.3	23.3	9.602
S.D.	10.5	11.9	10.4	12.6	12.4	13.4	6.5	2.647

INDIVIDUAL DATA 11-1-2

STUDY NO. SR11087 TITLE : indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Body weight ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg

	Body weight(g) on pre-mating period						Body weight gain(g)	
	Administration day							
Animal No.	1	3	5	7	10	14	1-14	%
251	222	234	230	237	238	241	19	8.56
252	222	231	228	241	241	247	25	11.26
253	235	236	242	244	238	244	9	3.83
254	238	251	248	261	260	267	29	12.18
255	241	246	253	261	259	272	31	12.86
256	243	234	250	245	258	267	24	9.88
257	244	241	255	250	259	268	24	9.84
258	248	262	256	268	270	277	29	11.69
259	248	258	259	270	269	280	32	12.90
260	251	253	260	261	261	272	21	8.37
261	247	249	254	255	245	255	8	3.24
262	260	255	268	268	279	299	39	15.00
N	12	12	12	12	12	12	12	12
MEAN	241.6	245.8	250.3	255.1	256.4	265.8	24.2	9.968
S.D.	11.2	10.5	11.8	11.4	13.3	16.7	9.1	3.559

INDIVIDUAL DATA 11-1-3

STUDY NO. SR11087 TITLE : indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Body weight ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg

	Body weight(g) on pre-mating period						Body weight gain(g)	
	Administration day							
Animal No.	1	3	5	7	10	14	1-14	%
351	226	227	230	236	231	235	9	3.98
352	232	233	234	238	237	245	13	5.60
353	240	234	243	242	247	257	17	7.08
354	240	250	250	262	263	276	36	15.00
355	238	235	248	245	257	266	28	11.76
356	244	248	252	256	259	263	19	7.79
357	239	238	245	243	252	263	24	10.04
358	244	251	258	264	267	277	33	13.52
359	246	252	254	258	262	267	21	8.54
360	245	250	254	265	269	280	35	14.29
361	249	267	259	276	273	284	35	14.06
362	255	257	268	265	258	266	11	4.31
N	12	12	12	12	12	12	12	12
MEAN	241.5	245.2	249.6	254.2	256.3	264.9	23.4	9.664
S.D.	7.6	11.7	10.6	12.9	12.7	14.2	9.9	4.017

INDIVIDUAL DATA 11-1-4

STUDY NO. SR11087 TITLE : indene: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Body weight ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg

	Body weight(g) on pre-mating period						Body weight gain(g)	
	Administration day							
Animal No.	1	3	5	7	10	14	1-14	%
451	221	217	224	231	231	238	17	7.69
452	233	226	228	234	233	238	5	2.15
453	228	238	231	242	241	247	19	8.33
454	242	243	240	249	249	251	9	3.72
455	235	223	239	238	242	244	9	3.83
456	241	242	241	250	239	246	5	2.07
457	241	238	246	245	255	268	27	11.20
458	246	241	246	240	252	256	10	4.07
459	248	248	245	254	254	256	8	3.23
460	260	255	260	258	257	259	-1	-0.38
461	252	247	252	255	255	264	12	4.76
462	261	260	266	273	269	277	16	6.13
N	12	12	12	12	12	12	12	12
MEAN	242.3	239.8	243.2	247.4	248.1	253.7	11.3**	4.733**
S.D.	12.1	12.7	12.4	11.7	11.1	12.0	7.5	3.161

** : Significantly different from the 0 mg/kg group at $P \leqq 0.01$ (Dunnett's test).

INDIVIDUAL DATA 11-2-1

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Body weight ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg

	Body weight(g)									Body weight gain(g)	
	Gestation day										
Animal No.	0	1	3	5	7	10	14	17	20	0-20	%
151	256	263	280	292	295	317	347	384	430	174	67.97
152	257	262	279	284	289	307	332	362	415	158	61.48
153	276	283	297	297	304	322	348	381	421	145	52.54
154	259	264	281	294	304	321	340	379	430	171	66.02
155	257	263	277	293	299	323	348	381	436	179	69.65
156	268	273	281	289	294	310	326	354	399	131	48.88
157	268	273	294	300	311	328	361	408	468	200	74.63
158	281	290	306	314	325	338	356	382	429	148	52.67
159	260	270	288	301	311	330	357	393	452	192	73.85
160	277	278	300	297	306	318	336	373	424	147	53.07
161	284	289	301	312	312	332	344	378	428	144	50.70
162	307	306	319	337	349	365	392	427	467	160	52.12
N	12	12	12	12	12	12	12	12	12	12	12
MEAN	270.8	276.2	291.9	300.8	308.3	325.9	348.9	383.5	433.3	162.4	60.298
S.D.	15.2	13.7	13.1	14.3	16.1	15.2	17.1	19.3	20.3	21.0	9.674

INDIVIDUAL DATA 11-2-2

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Body weight ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg

	Body weight(g)									Body weight gain(g)	
	Gestation day										
Animal No.	0	1	3	5	7	10	14	17	20	0-20	%
251	245	252	266	266	276	292	308	337	377	132	53.88
252	250	248	266	270	281	294	318	353	401	151	60.40
253	261	271	287	296	306	326	345	374	414	153	58.62
254	272	276	291	301	310	329	356	396	446	174	63.97
255	291	303	308	324	328	352	378	409	464	173	59.45
256	264	277	288	299	309	321	342	373	423	159	60.23
257	273	281	292	305	320	332	370	405	462	189	69.23
258	294	300	316	321	332	352	372	407	445	151	51.36
259	280	290	307	319	323	339	358	385	422	142	50.71
260	282	287	304	319	332	342	368	399	436	154	54.61
261	276	280	294	300	313	334	343	367	411	135	48.91
262	294	306	319	334	340	363	379	411	461	167	56.80
N	12	12	12	12	12	12	12	12	12	12	12
MEAN	273.5	280.9	294.8	304.5	314.2	331.3	353.1	384.7	430.2	156.7	57.348
S.D.	16.2	18.2	17.1	20.8	19.7	21.6	22.9	24.1	27.0	16.8	5.875

INDIVIDUAL DATA 11-2-3

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Body weight ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg

	Body weight(g)									Body weight gain(g)	
	Gestation day										
Animal No.	0	1	3	5	7	10	14	17	20	0-20	%
351	250	253	268	276	285	301	324	361	401	151	60.40
352	251	247	264	273	283	301	319	349	402	151	60.16
353	261	263	272	277	288	309	327	347	382	121	46.36
354	278	282	296	305	314	326	350	377	423	145	52.16
355	273	280	285	294	306	324	349	382	421	148	54.21
356	263	266	283	297	310	319	344	377	431	168	63.88
357	260	272	279	294	303	330	349	392	446	186	71.54
358	287	287	299	312	333	350	380	417	470	183	63.76
359	269	279	291	307	317	336	361	387	442	173	64.31
360	282	287	301	315	328	340	369	409	467	185	65.60
361	281	287	304	312	326	331	362	394	454	173	61.57
362	296	303	318	332	348	361	387	417	470	174	58.78
N	12	12	12	12	12	12	12	12	12	12	12
MEAN	270.9	275.5	288.3	299.5	311.8	327.3	351.8	384.1	434.1	163.2	60.228
S.D.	14.4	16.0	16.1	17.9	20.2	18.4	21.5	23.7	29.2	19.9	6.721

INDIVIDUAL DATA 11-2-4

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Body weight ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg

	Body weight(g)									Body weight gain(g)	
	Gestation day										
Animal No.	0	1	3	5	7	10	14	17	20	0-20	%
451	242	247	251	259	272	278	295	328	374	132	54.55
452	241	249	257	270	280	295	316	351	396	155	64.32
453	256	261	286	284	292	310	335	372	422	166	64.84
454	255	266	277	277	284	300	317	353	400	145	56.86
455	251	257	271	274	284	300	314	345	361	110	43.82
456	244	254	270	278	283	302	327	359	413	169	69.26
457	253	259	283	289	295	305	321	354	394	141	55.73
458	267	272	282	289	301	314	342	377	420	153	57.30
459	260	270	280	285	295	309	335	370	421	161	61.92
460	264	273	290	295	304	321	336	374	413	149	56.44
461	276	284	296	306	316	337	362	394	438	162	58.70
462	281	288	296	302	314	332	355	392	436	155	55.16
N	12	12	12	12	12	12	12	12	12	12	12
MEAN	257.5	265.0	278.3	284.0*	293.3	308.6	329.6	364.1	407.3*	149.8	58.242
S.D.	12.8	13.0	14.1	13.4	13.6	16.1	18.6	19.4	23.4	16.4	6.460

* : Significantly different from the 0 mg/kg group at P ≦ 0.05 (Dunnett's test).

INDIVIDUAL DATA 11-3-1

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Body weight ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg

	Body weight(g)			Body weight gain(g)	
	Lactation day				
Animal No.	0	1	4	0-4	%
151	322	331	337	15	4.66
152	297	309	327	30	10.10
153	324	327	344	20	6.17
154	328	337	348	20	6.10
155[a]	268	257	#	#	#
156	302	301	330	28	9.27
157	338	333	355	17	5.03
158	324	322	330	6	1.85
159	338	347	362	24	7.10
160	319	326	334	15	4.70
161	328	316	325	-3	-0.91
162	381	375	386	5	1.31
N	12	12	11	11	11
MEAN	322.4	323.4	343.5	16.1	5.035
S.D.	27.0	28.2	18.5	10.1	3.315

a : Died on Day 3 of Lactation .

: Not applicable.

INDIVIDUAL DATA 11-3-2

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Body weight ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg

	Body weight(g)			Body weight gain(g)	
	Lactation day				
Animal No.	0	1	4	0-4	%
251	288	297	329	41	14.24
252	294	271	293	-1	-0.34
253	331	331	333	2	0.60
254	326	330	335	9	2.76
255	323	308	268	-55	-17.03
256	306	298	325	19	6.21
257	342	338	354	12	3.51
258	344	352	360	16	4.65
259	352	342	351	-1	-0.28
260	348	347	348	0	0.00
261	294	299	318	24	8.16
262	346	357	378	32	9.25
N	12	12	12	12	12
MEAN	324.5	322.5	332.7	8.2	2.644
S.D.	23.4	27.1	30.0	24.0	7.638

INDIVIDUAL DATA 11-3-3

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Body weight ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg

	Body weight(g)			Body weight gain(g)	
	Lactation day				
Animal No.	0	1	4	0-4	%
351	300	301	322	22	7.33
352	303	313	331	28	9.24
353	314	324	323	9	2.87
354	319	322	346	27	8.46
355	317	302	349	32	10.09
356	301	285	314	13	4.32
357	331	333	344	13	3.93
358	371	367	376	5	1.35
359	313	306	335	22	7.03
360	328	325	356	28	8.54
361	331	339	354	23	6.95
362	384	358	361	-23	-5.99
N	12	12	12	12	12
MEAN	326.0	322.9	342.6	16.6	5.343
S.D.	26.5	23.9	18.2	15.0	4.478

INDIVIDUAL DATA 11-3-4

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Body weight ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg

	Body weight(g)			Body weight gain(g)	
	Lactation day				
Animal No.	0	1	4	0-4	%
451	282	291	312	30	10.64
452	305	296	312	7	2.30
453	309	291	322	13	4.21
454	296	297	304	8	2.70
455	282	285	314	32	11.35
456	293	302	333	40	13.65
457	276	281	305	29	10.51
458	320	328	362	42	13.13
459	334	322	315	-19	-5.69
460	306	316	335	29	9.48
461	341	345	361	20	5.87
462	341	337	345	4	1.17
N	12	12	12	12	12
MEAN	307.1	307.6	326.7	19.6	6.610
S.D.	22.9	21.3	20.5	17.7	5.841

INDIVIDUAL DATA 12-1

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Body weight ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg

	Body weight(g)										Body weight gain(g)		Body weight gain(g)		Body weight gain(g)	
	Administration day												Recovery day			
Animal No.	1	3	5	7	10	14	21	28	35	42	1-42	%	7	14	42-R14	%
163	224	231	235	236	243	251	258	260	274	282	58	25.89	#	#	#	#
164	230	243	241	252	254	260	267	284	296	298	68	29.57	#	#	#	#
165	239	242	247	250	257	265	275	277	290	300	61	25.52	#	#	#	#
166	248	261	251	269	271	275	272	292	310	309	61	24.60	#	#	#	#
167	251	246	263	258	268	270	279	287	309	323	72	28.69	#	#	#	#
168	227	242	239	252	254	262	272	288	295	292	65	28.63	291	295	3	1.03
169	241	245	250	256	261	267	278	281	294	297	56	23.24	310	310	13	4.38
170	242	251	256	260	258	264	277	282	290	304	62	25.62	313	319	15	4.93
171	244	247	254	257	263	268	274	276	287	292	48	19.67	305	300	8	2.74
172	248	243	258	261	271	276	291	295	309	321	73	29.44	330	328	7	2.18
N	10	10	10	10	10	10	10	10	10	10	10	10	5	5	5	5
MEAN	239.4	245.1	249.4	255.1	260.0	265.8	274.3	282.2	295.4	301.8	62.4	26.087	309.8	310.4	9.2	3.052
S.D.	9.4	7.6	8.9	8.7	8.8	7.3	8.5	9.9	11.4	12.9	7.6	3.139	14.1	13.5	4.8	1.600

R14 : Recovery day 14.

: Not applicable.

INDIVIDUAL DATA 12-2

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Body weight ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg

	Body weight(g)										Body weight gain(g)		Body weight gain(g)		Body weight gain(g)	
	Administration day												Recovery day			
Animal No.	1	3	5	7	10	14	21	28	35	42	1-42	%	7	14	42-R14	%
463	215	224	218	226	221	226	243	248	252	251	36	16.74	#	#	#	#
464	238	230	241	238	248	257	265	273	272	288	50	21.01	#	#	#	#
465	249	235	246	249	255	261	273	282	270	290	41	16.47	#	#	#	#
466	241	242	240	243	253	258	266	267	280	289	48	19.92	#	#	#	#
467	250	249	246	255	252	259	263	273	284	289	39	15.60	#	#	#	#
468	230	237	238	248	250	258	269	287	302	306	76	33.04	311	322	16	5.23
469	239	226	237	243	235	243	259	264	264	269	30	12.55	284	292	23	8.55
470	243	243	251	252	259	264	274	279	291	306	63	25.93	318	331	25	8.17
471	245	251	252	257	252	257	264	271	271	283	38	15.51	285	291	8	2.83
472	245	234	240	239	247	251	256	257	254	264	19	7.76	279	278	14	5.30
N	10	10	10	10	10	10	10	10	10	10	10	10	5	5	5	5
MEAN	239.5	237.1*	240.9	245.0*	247.2*	253.4**	263.2*	270.1*	274.0**	283.5*	44.0+	18.453+	295.4	302.8	17.2	6.016*
S.D.	10.4	9.1	9.6	9.3	11.2	11.2	9.0	11.7	15.7	17.6	16.3	7.073	17.8	22.6	6.9	2.363

R14 : Recovery day 14.

: Not applicable.

* : Significantly different from the 0 mg/kg group at p ≦ 0.05 (Dunnett's test).

** : Significantly different from the 0 mg/kg group at P ≦ 0.01 (Dunnett's test).

+ : Significantly different from the 0 mg/kg group at P ≦ 0.05 (Steel's test).

INDIVIDUAL DATA 13-1

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Food consumption ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg

Food consmuption (g/rat/day)

	Administration day									Recovery day	
Animal No.	-1～1	1～3	3～5	5～7	7～10	10～14	21～28	28～35	35～42	a～7	7～14
101	19.0	18.0	20.0	19.5	19.7	20.0	19.1	18.3	12.9	#	#
102	27.0	22.0	23.5	22.0	21.0	21.3	21.1	20.3	20.9	#	#
103	25.0	23.5	23.5	22.0	22.0	22.5	22.4	21.1	21.7	#	#
104	28.0	23.0	25.0	23.0	21.7	23.3	22.4	22.9	22.2 [b]	26.1	27.5
105	25.0	21.5	21.5	20.5	20.3	20.0	20.0	19.9	18.8 [b]	23.9	27.2
106	25.0	23.0	24.5	23.5	22.0	23.5	22.3	22.0	22.3 [b]	26.3	27.0
107	28.0	23.5	24.0	23.5	24.0	24.3	23.0	23.0	22.8 [b]	26.6	29.7
108	29.0	22.5	25.0	24.0	23.3	23.8	23.1	22.6	20.3 [b]	24.9	27.0
109	25.0	23.0	23.5	23.5	21.0	21.5	20.4	20.3	21.4	#	#
110	24.0	23.0	24.5	26.0	25.3	28.5	28.4	27.9	26.0	#	#
111	27.0	24.5	24.0	23.0	24.3	23.0	22.3	22.4	23.7	#	#
112	29.0	25.5	25.0	25.0	23.0	23.5	23.9	24.7	24.6	#	#
N	12	12	12	12	12	12	12	12	12	5	5
MEAN	25.92	22.75	23.67	22.96	22.30	22.93	22.37	22.12	21.47	25.56	27.68
S.D.	2.78	1.83	1.51	1.79	1.71	2.27	2.36	2.50	3.31	1.13	1.15

a: Day 42 of administration.

b : Data is the mean value of 6 days due to urinary examination .

: Not applicable.

INDIVIDUAL DATA 13-2

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Food consumption ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg

Food consmuption (g/rat/day)

Animal No.	Administration day -1～1	1～3	3～5	5～7	7～10	10～14	21～28	28～35	35～42
201	23.0	23.0	20.5	22.0	22.0	21.8	21.6	21.7	21.0
202	23.0	21.0	21.0	19.5	19.0	19.3	21.3	21.1	22.7
203	25.0	23.5	24.0	24.0	23.0	22.3	21.6	21.3	24.5 [a]
204	25.0	20.0	24.5	22.5	22.0	22.3	21.7	21.1	21.3
205	25.0	23.0	22.5	23.0	21.7	22.3	20.9	20.7	22.2 [a]
206	22.0	21.0	21.5	20.5	19.7	20.5	20.7	19.4	19.1
207	27.0	25.0	25.5	25.5	24.7	24.5	25.0	24.4	22.7 [a]
208	27.0	22.0	22.0	21.0	20.3	20.0	18.7	19.6	20.8 [a]
209	27.0	25.5	25.5	24.5	26.0	25.3	23.9	23.6	22.2 [a]
210	27.0	23.0	24.0	23.5	22.3	22.8	22.4	21.9	21.3
211	29.0	25.5	24.5	26.5	25.0	24.3	23.1	23.7	24.0
212	33.0	25.0	28.5	25.0	25.0	24.8	27.0	26.4	26.1
N	12	12	12	12	12	12	12	12	12
MEAN	26.08	23.13	23.67	23.13	22.56	22.52	22.33	22.08	22.33
S.D.	3.00	1.87	2.29	2.12	2.25	1.94	2.18	2.07	1.88

a : Data is the mean value of 6 days due to urinary examination .

INDIVIDUAL DATA 13-3

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Food consumption ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg

Food consmuption (g/rat/day)

Animal No.	Administration day -1～1	1～3	3～5	5～7	7～10	10～14	21～28	28～35	35～42
301	27.0	24.5	24.0	23.0	22.0	21.8	20.1	19.1	19.2 [a]
302	26.0	22.0	23.0	22.5	20.3	19.8	20.3	18.1	18.1
303	26.0	24.5	23.5	22.0	21.0	21.3	22.3	21.4	21.0 [a]
304	23.0	23.0	22.5	22.0	22.0	21.0	20.4	19.0	19.7
305	22.0	19.0	20.5	23.5	21.3	23.0	22.4	21.3	21.7 [a]
306	25.0	24.0	23.0	22.0	21.7	23.0	21.1	19.7	19.7 [a]
307	24.0	20.5	20.5	18.5	19.0	19.3	19.9	18.7	19.9
308	25.0	19.5	24.0	21.0	21.0	20.8	21.1	20.9	21.1
309	28.0	24.0	25.0	23.5	22.7	25.0	23.3	23.9	23.1
310	26.0	24.0	24.0	24.5	24.0	23.0	20.7	21.4	22.6
311	27.0	22.5	24.0	24.5	24.3	24.0	23.7	23.4	22.1
312	29.0	21.5	25.0	22.0	22.0	22.5	22.9	22.0	22.3 [a]
N	12	12	12	12	12	12	12	12	12
MEAN	25.67	22.42	23.25	22.42	21.78	22.04	21.52	20.74	20.88
S.D.	2.02	1.94	1.48	1.64	1.47	1.69	1.34	1.85	1.55

a : Data is the mean value of 6 days due to urinary examination .

INDIVIDUAL DATA 13-4

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Food consumption ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg

Food consmuption (g/rat/day)

	Administration day									Recovery day	
Animal No.	-1～1	1～3	3～5	5～7	7～10	10～14	21～28	28～35	35～42	a～7	7～14
401	26.0	18.0	23.0	23.0	21.3	21.0	20.3	21.3	21.3 [b]	21.0	23.5
402	23.0	12.5	18.5	20.0	19.7	19.8	20.0	19.3	19.9	#	#
403	23.0	9.5	19.5	19.5	17.0	18.8	18.0	18.1	17.3	#	#
404	23.0	14.5	21.5	19.5	19.7	19.5	20.4	20.4	19.8 [b]	21.7	23.8
405	25.0	15.0	23.0	21.5	20.3	19.5	20.4	20.1	20.6	#	#
406	26.0	13.0	22.5	20.5	21.0	21.3	22.3	22.9	21.8 [b]	23.1	27.7
407	27.0	19.5	24.5	23.5	23.3	23.8	24.4	24.4	23.4	#	#
408	28.0	16.5	24.0	25.0	23.0	22.8	23.0	22.3	22.6	#	#
409	26.0	18.0	23.5	21.0	18.0	20.0	22.3	22.7	24.1	#	#
410	29.0	14.0	27.5	27.0	25.7	23.8	22.9	23.1	23.6	#	#
411	22.0	19.0	21.5	20.5	18.3	19.3	20.4	19.6	18.8 [b]	22.6	26.5
412	28.0	21.0	24.5	22.5	23.0	23.0	23.4	24.6	24.0 [b]	27.0	31.7
N	12	12	12	12	12	12	12	12	12	5	5
MEAN	25.50	15.88**	22.79	21.96	20.86	21.05	21.48	21.57	21.43	23.08	26.64
S.D.	2.32	3.37	2.39	2.33	2.55	1.85	1.84	2.08	2.21	2.34	3.34

a: Day 42 of administration.

b : Data is the mean value of 6 days due to urinary examination .

: Not applicable.

** : Significantly different from the 0 mg/kg group at $p \leqq 0.01$ (Dunnett's test).

INDIVIDUAL DATA 14-1-1

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Food consumption ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg

Food consumption (g/rat/day) on pre-mating period

	Administration day					
Animal No.	-1～1	1～3	3～5	5～7	7～10	10～14
151	22.0	12.5	17.0	14.0	18.7	16.8
152	15.0	16.5	15.5	14.0	15.7	16.5
153	16.0	16.5	16.0	18.5	15.7	16.8
154	18.0	17.5	16.0	18.5	15.3	16.0
155	18.0	15.0	14.0	17.5	14.0	14.8
156	20.0	12.0	16.0	14.0	16.3	16.3
157	18.0	13.5	19.5	15.5	15.3	15.0
158	12.0	19.0	15.0	20.0	16.7	17.3
159	20.0	13.5	17.5	15.0	17.0	13.8
160	20.0	16.5	13.5	18.5	16.7	16.0
161	22.0	16.0	17.5	16.0	17.7	17.3
162	20.0	15.5	19.0	16.0	18.7	17.0
N	12	12	12	12	12	12
MEAN	18.42	15.33	16.38	16.46	16.48	16.13
S.D.	2.94	2.10	1.82	2.08	1.41	1.09

INDIVIDUAL DATA 14-1-2

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Food consumption ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg

Food consumption (g/rat/day) on pre-mating period

	Administration day					
Animal No.	-1～1	1～3	3～5	5～7	7～10	10～14
251	12.0	15.0	12.5	15.5	13.3	13.3
252	12.0	16.5	12.5	16.5	13.7	14.8
253	18.0	13.5	16.5	13.5	15.0	15.3
254	14.0	17.0	15.5	17.0	14.3	15.5
255	18.0	15.5	17.5	16.0	16.3	17.8
256	21.0	13.0	18.0	16.0	18.7	16.3
257	20.0	15.5	19.5	16.0	17.0	16.3
258	16.0	18.0	16.0	18.5	16.3	17.0
259	20.0	19.5	17.0	18.5	16.7	18.3
260	18.0	15.0	18.0	15.5	16.7	17.5
261	17.0	13.0	17.0	14.5	14.7	15.5
262	22.0	15.0	18.0	17.5	21.0	19.8
N	12	12	12	12	12	12
MEAN	17.33	15.54	16.50	16.25	16.14	16.45
S.D.	3.31	1.97	2.14	1.48	2.18	1.75

INDIVIDUAL DATA 14-1-3

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Food consumption ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg

Food consumption (g/rat/day) on pre-mating period

	Administration day					
Animal No.	-1～1	1～3	3～5	5～7	7～10	10～14
351	18.0	13.5	16.5	14.5	14.7	14.0
352	18.0	17.5	15.5	17.0	16.0	15.8
353	18.0	13.0	17.5	13.5	16.3	16.0
354	17.0	18.0	18.0	19.0	17.3	19.0
355	19.0	14.5	17.5	16.0	17.7	17.5
356	23.0	16.0	16.0	17.0	16.3	16.3
357	17.0	14.5	17.0	15.0	19.0	16.3
358	21.0	20.0	18.5	21.0	17.0	18.0
359	16.0	16.5	14.0	17.0	15.0	14.5
360	18.0	16.5	15.0	18.0	16.0	17.3
361	14.0	19.0	15.5	19.5	15.7	18.3
362	22.0	14.0	20.5	15.0	18.0	18.5
N	12	12	12	12	12	12
MEAN	18.42	16.08	16.79	16.88	16.58	16.79
S.D.	2.54	2.24	1.76	2.23	1.26	1.58

INDIVIDUAL DATA 14-1-4

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Food consumption ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg

Food consumption (g/rat/day) on pre-mating period

	Administration day					
Animal No.	-1～1	1～3	3～5	5～7	7～10	10～14
451	17.0	11.0	13.5	16.0	13.7	14.8
452	17.0	10.5	12.5	14.5	12.7	13.5
453	11.0	15.5	13.0	16.0	13.3	15.0
454	17.0	14.5	14.0	15.5	14.7	15.8
455	17.0	6.5	17.0	15.5	13.3	13.8
456	17.0	13.0	13.0	16.5	11.3	14.3
457	21.0	14.5	17.0	17.0	16.3	17.8
458	20.0	10.5	17.0	16.5	17.3	15.8
459	19.0	14.0	12.0	16.5	14.7	14.8
460	22.0	12.5	17.5	14.0	15.0	16.3
461	20.0	10.0	15.0	15.0	13.7	15.3
462	18.0	14.5	16.0	18.5	12.7	16.3
N	12	12	12	12	12	12
MEAN	18.00	12.25**	14.79	15.96	14.06**	15.29
S.D.	2.83	2.62	2.03	1.20	1.65	1.20

** : Significantly different from the 0 mg/kg group at $p \leqq 0.01$ (Dunnett's test).

INDIVIDUAL DATA 14-2-1

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Food consumption ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg

Food consumption (g/rat/day)

	Gestation day							
Animal No.	0～1	1～3	3～5	5～7	7～10	10～14	14～17	17～20
151	16.0	21.0	22.0	21.0	23.7	24.0	22.3	19.3
152	15.0	21.0	18.5	20.0	20.7	20.3	21.0	19.7
153	17.0	21.0	18.0	21.0	21.3	20.8	20.7	18.0
154	15.0	22.0	24.5	23.0	23.7	21.3	21.7	21.3
155	14.0	19.0	22.0	21.5	24.7	23.3	22.7	19.0
156	16.0	18.5	18.0	19.0	19.3	18.5	19.0	18.0
157	12.0	11.0	20.0	21.5	21.3	25.3	26.7	21.0
158	19.0	24.5	22.5	23.5	24.3	22.3	19.7	19.0
159	13.0	20.5	23.0	19.5	21.3	21.8	21.3	21.7
160	12.0	23.0	18.0	17.5	20.7	19.0	20.3	17.7
161	17.0	21.5	23.5	20.5	23.0	19.8	21.3	18.0
162	16.0	22.0	24.5	23.0	23.3	24.3	22.7	21.7
N	12	12	12	12	12	12	12	12
MEAN	15.17	20.42	21.21	20.92	22.28	21.73	21.62	19.53
S.D.	2.12	3.37	2.57	1.77	1.71	2.17	1.96	1.53

INDIVIDUAL DATA 14-2-2

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Food consumption ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg

Food consumption (g/rat/day)

Animal No.	Gestation day 0～1	1～3	3～5	5～7	7～10	10～14	14～17	17～20
251	14.0	19.5	15.5	17.5	18.0	18.3	19.0	17.7
252	11.0	20.0	20.5	22.5	21.7	22.3	20.7	21.0
253	16.0	22.0	21.5	24.0	23.0	23.0	21.3	20.7
254	15.0	20.0	21.0	22.0	22.3	22.5	22.0	20.7
255	16.0	21.5	23.5	23.0	23.0	22.5	22.0	20.7
256	19.0	19.5	22.0	22.5	21.7	19.5	18.7	18.0
257	18.0	21.0	23.5	25.5	26.0	27.0	25.0	21.3
258	19.0	22.0	21.5	24.0	24.0	24.5	23.7	21.3
259	19.0	22.5	23.5	20.5	23.0	22.5	22.0	20.3
260	19.0	24.0	26.5	26.5	24.7	25.0	22.7	17.7
261	16.0	20.0	19.5	24.0	23.3	20.8	20.0	17.3
262	17.0	24.0	26.0	23.0	24.3	23.3	21.7	21.7
N	12	12	12	12	12	12	12	12
MEAN	16.58	21.33	22.04	22.92	22.92	22.60	21.57	19.87
S.D.	2.47	1.61	2.94	2.32	1.99	2.35	1.82	1.66

INDIVIDUAL DATA 14-2-3

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Food consumption ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg

Food consumption (g/rat/day)

	Gestation day							
Animal No.	0～1	1～3	3～5	5～7	7～10	10～14	14～17	17～20
351	13.0	19.0	19.0	19.5	19.7	19.0	20.3	18.0
352	11.0	20.5	21.5	22.5	22.7	21.8	19.0	21.3
353	15.0	18.0	19.0	20.0	20.3	20.3	18.0	17.3
354	14.0	21.0	21.5	21.5	22.0	21.8	19.3	18.7
355	18.0	20.0	21.5	22.0	23.3	23.0	21.0	19.7
356	13.0	19.5	22.0	22.5	22.3	22.0	21.7	21.3
357	18.0	20.5	22.5	23.0	25.3	22.8	22.7	20.7
358	16.0	22.0	25.0	25.5	27.0	28.5	26.3	23.3
359	15.0	19.0	22.0	21.0	22.3	22.8	19.0	21.0
360	17.0	19.0	21.5	23.0	21.3	24.5	24.3	23.0
361	9.0	20.5	22.0	22.0	21.0	21.3	19.7	20.7
362	20.0	25.0	27.5	28.0	27.0	25.0	23.0	21.0
N	12	12	12	12	12	12	12	12
MEAN	14.92	20.33	22.08	22.54	22.85	22.73	21.19	20.50
S.D.	3.15	1.83	2.30	2.31	2.42	2.45	2.49	1.82

INDIVIDUAL DATA 14-2-4

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Food consumption ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg

Food consumption (g/rat/day)

	Gestation day							
Animal No.	0～1	1～3	3～5	5～7	7～10	10～14	14～17	17～20
451	11.0	15.5	18.5	19.0	19.0	18.0	19.0	18.0
452	17.0	17.5	18.0	20.0	20.3	20.3	21.7	19.3
453	18.0	24.5	19.5	22.5	23.0	23.3	22.3	21.3
454	17.0	18.0	16.0	18.0	19.7	21.8	20.3	19.3
455	15.0	18.5	16.5	19.0	20.7	19.5	20.7	15.3
456	15.0	17.0	18.0	19.0	18.7	21.0	20.7	19.7
457	15.0	20.0	22.0	20.5	22.3	21.5	22.7	19.7
458	16.0	20.0	21.5	22.0	24.7	26.5	24.0	21.0
459	15.0	18.5	18.0	21.0	18.3	22.5	22.7	21.0
460	14.0	19.5	18.0	22.5	21.3	19.0	19.7	19.7
461	20.0	19.5	21.5	22.5	22.7	22.8	25.7	20.7
462	15.0	18.5	18.0	19.5	21.3	24.3	22.3	21.7
N	12	12	12	12	12	12	12	12
MEAN	15.67	18.92	18.79	20.46	21.00	21.71	21.82	19.73
S.D.	2.23	2.19	1.95	1.62	1.94	2.38	1.89	1.75

INDIVIDUAL DATA 14-3-1

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Food consumption ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg

	Food consumption (g/rat/day)	
	Lactation day	
Animal No.	0～1	1～4
151	14.0	27.0
152	24.0	34.0
153	26.0	33.7
154	19.0	28.0
155[a]	0.0	#
156	18.0	33.0
157	16.0	34.7
158	15.0	27.0
159	24.0	29.3
160	21.0	28.0
161	15.0	29.0
162	14.0	31.3
N	12	11
MEAN	17.17	30.45
S.D.	6.85	2.96

a : Died on Day 3 of Lactation .

: Not applicable.

INDIVIDUAL DATA 14-3-2

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Food consumption ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg

	Food consumption (g/rat/day)	
	Lactation day	
Animal No.	0～1	1～4
251	26.0	39.0
252	2.0	24.3
253	24.0	31.7
254	21.0	27.7
255	0.0	0.0
256	8.0	29.7
257	17.0	33.7
258	18.0	29.7
259	18.0	27.3
260	21.0	24.7
261	17.0	32.0
262	21.0	35.7
N	12	12
MEAN	16.08	27.96
S.D.	8.34	9.80

INDIVIDUAL DATA 14-3-3

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Food consumption ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg

	Food consumption (g/rat/day)	
	Lactation day	
Animal No.	0～1	1～4
351	18.0	34.3
352	24.0	33.3
353	16.0	29.3
354	20.0	35.0
355	4.0	31.3
356	6.0	27.3
357	20.0	32.3
358	26.0	36.0
359	7.0	29.0
360	14.0	30.0
361	18.0	31.7
362	10.0	25.3
N	12	12
MEAN	15.25	31.23
S.D.	7.15	3.20

INDIVIDUAL DATA 14-3-4

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Food consumption ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg

	Food consumption (g/rat/day)	
	Lactation day	
Animal No.	0～1	1～4
451	23.0	31.7
452	24.0	31.0
453	7.0	28.0
454	21.0	27.0
455	18.0	34.0
456	21.0	34.3
457	14.0	30.0
458	28.0	37.0
459	17.0	21.7
460	17.0	31.7
461	19.0	32.7
462	22.0	30.0
N	12	12
MEAN	19.25	30.76
S.D.	5.36	3.96

INDIVIDUAL DATA 15-1

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Food consumption ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 0 mg/kg

Food consumption (g/rat/day)

	Administration day										Recovery day	
Animal No.	-1～1	1～3	3～5	5～7	7～10	10～14	14～21	21～28	28～35	35～42	a～7	7～14
163	18.0	16.5	14.0	17.0	13.7	16.0	14.6	15.3	15.7	15.0	#	#
164	14.0	16.0	14.5	18.0	15.3	15.8	15.3	16.6	16.1	15.0	#	#
165	22.0	17.0	16.5	18.0	17.0	16.8	16.0	16.4	14.9	14.7	#	#
166	15.0	19.5	13.5	18.0	15.0	15.3	14.6	16.0	15.0	13.7	#	#
167	22.0	15.5	19.5	17.0	18.3	15.5	16.3	17.6	17.7	17.9	#	#
168	15.0	17.5	16.5	18.0	17.3	17.3	16.4	17.0	15.3	14.7 [b]	16.1	18.3
169	21.0	17.0	14.5	17.0	16.0	16.0	15.0	14.9	14.7	12.5 [b]	17.6	18.8
170	19.0	19.5	16.0	18.5	14.3	15.8	16.3	14.7	15.9	15.8 [b]	20.7	19.3
171	19.0	17.5	15.0	18.5	16.0	15.5	14.6	15.0	15.1	14.3 [b]	18.9	19.3
172	18.0	16.0	15.5	20.5	16.7	17.3	16.4	16.4	16.9	15.3 [b]	18.7	20.0
N	10	10	10	10	10	10	10	10	10	10	5	5
MEAN	18.30	17.20	15.55	18.05	15.96	16.13	15.55	15.99	15.73	14.89	18.40	19.14
S.D.	2.91	1.38	1.72	1.04	1.42	0.74	0.81	0.98	0.96	1.40	1.70	0.63

a: Day 42 of administration.

b : Data is the mean value of 6 days due to urinary examination .

: Not applicable.

INDIVIDUAL DATA 15-2

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Food consumption ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : Satellite 100 mg/kg

Food consumption (g/rat/day)

	Administration day										Recovery day	
Animal No.	-1～1	1～3	3～5	5～7	7～10	10～14	14～21	21～28	28～35	35～42	a～7	7～14
463	16.0	13.5	10.5	14.5	11.7	14.3	14.6	14.0	12.6	12.6	#	#
464	19.0	11.5	16.5	14.0	15.0	15.3	14.0	14.7	13.3	14.9	#	#
465	19.0	11.5	17.0	15.0	16.7	16.5	15.7	15.7	13.9	15.3	#	#
466	17.0	11.0	14.0	15.0	14.0	14.8	14.0	14.9	14.9	14.0	#	#
467	18.0	13.5	14.5	16.5	13.3	14.0	14.1	14.7	14.0	14.3	#	#
468	13.0	12.5	14.5	16.0	15.7	16.0	15.9	17.6	16.1	15.5 [b]	17.9	20.0
469	16.0	9.5	14.0	13.5	12.0	13.3	13.4	12.9	11.7	14.0 [b]	17.0	17.7
470	21.0	15.0	21.0	15.0	18.7	15.0	16.7	17.4	16.7	19.2 [b]	21.6	23.3
471	19.0	13.5	15.0	17.5	14.0	14.0	14.1	14.4	12.4	15.3 [b]	17.6	19.2
472	18.0	10.0	15.5	13.0	14.7	14.0	14.3	12.3	12.3	13.0 [b]	17.4	16.5
N	10	10	10	10	10	10	10	10	10	10	5	5
MEAN	17.60	12.15**	15.25	15.00**	14.58	14.72**	14.68	14.86	13.79**	14.81	18.30	19.34
S.D.	2.22	1.75	2.68	1.37	2.11	1.00	1.05	1.70	1.68	1.82	1.87	2.59

a: Day 42 of administration.

b : Data is the mean value of 6 days due to urinary examination .

: Not applicable.

** : Significantly different from the 0 mg/kg group at $p \leqq 0.01$ (Dunnett's test).

INDIVIDUAL DATA 16-1-1

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Urinary findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Week 6 of administration

Animal No.	pH	Protein	Glucose	Ketone body	Urobili-nogen EU/dL	Bili-rubin	Occult blood	Color	Specific gravity	Urine volume mL/21hr
104	8.5	+	−	−	0.1	−	+	A	1.050<	6.5
105	8.5	±	−	−	0.1	−	−	A	1.048	8.0
106	8.5	+	−	−	0.1	−	−	A	1.048	10.0
107	8.0	+	−	−	0.1	−	−	A	1.047	10.0
108	8.0	±	−	−	0.1	−	−	A	1.045	11.5
N	5	5	5	5	5	5	5	5	5	5
MEAN										9.20
S.D.										1.96

- ; Normal , ± ; Slight , + ; Moderate .

Color : A = Pale yellow or yellow.

INDIVIDUAL DATA 16-1-2

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Urinary findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Week 6 of administration

	Urinary sediments					
			Epithelial cell			
Animal No.	RBC	WBC	Squamous	Round	Small round	Cast
104	—	—	—	—	—	—
105	—	—	—	—	—	—
106	—	—	±	—	—	—
107	—	—	—	—	—	—
108	—	—	±	—	—	—
N	5	5	5	5	5	5

- ; Normal , ± ; Slight .

INDIVIDUAL DATA 16-1-3
STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Urinary findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : Week 6 of administration

Animal No.	pH	Protein	Glucose	Ketone body	Urobili-nogen EU/dL	Bili-rubin	Occult blood	Color	Specific gravity	Urine volume mL/21hr
203	8.0	+	−	−	0.1	−	−	A	1.050<	5.5
205	8.0	±	−	−	0.1	−	−	A	1.045	11.0
207	8.5	±	−	−	0.1	−	±	A	1.050<	9.0
208	8.0	+	−	−	0.1	−	−	A	1.050<	7.0
209	8.0	+	−	−	0.1	−	−	A	1.050<	7.5
N	5	5	5	5	5	5	5	5	5	5
MEAN										8.00
S.D.										2.09

- ; Normal , ± ; Slight , + ; Moderate .
Color : A = Pale yellow or yellow.

INDIVIDUAL DATA 16-1-4

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Urinary findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : Week 6 of administration

	Urinary sediments					
			Epithelial cell			
Animal No.	RBC	WBC	Squamous	Round	Small round	Cast
203	—	—	—	—	—	—
205	—	—	—	—	—	—
207	—	—	—	—	—	—
208	—	—	—	—	—	—
209	—	—	—	—	—	—
N	5	5	5	5	5	5

- ; Normal .

INDIVIDUAL DATA 16-1-5
STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Urinary findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : Week 6 of administration

Animal No.	pH	Protein	Glucose	Ketone body	Urobili-nogen EU/dL	Bili-rubin	Occult blood	Color	Specific gravity	Urine volume mL/21hr
301	8.5	+	−	−	0.1	−	−	A	1.050	8.0
303	8.0	±	−	−	0.1	−	−	A	1.050<	7.0
305	8.0	±	−	−	0.1	−	±	A	1.050<	7.5
306	8.5	±	−	−	0.1	−	−	A	1.050<	7.5
312	8.0	±	−	−	0.1	−	−	A	1.050	9.0
N	5	5	5	5	5	5	5	5	5	5
MEAN										7.80
S.D.										0.76

- ; Normal , ± ; Slight , + ; Moderate .
Color : A = Pale yellow or yellow.

INDIVIDUAL DATA 16-1-6

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Urinary findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : Week 6 of administration

	Urinary sediments					
			Epithelial cell			
Animal No.	RBC	WBC	Squamous	Round	Small round	Cast
301	—	—	—	—	—	—
303	—	—	—	—	—	—
305	—	—	±	—	—	—
306	—	—	—	—	—	—
312	—	—	—	—	—	—
N	5	5	5	5	5	5

- ; Normal , ± ; Slight .

INDIVIDUAL DATA 16-1-7

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Urinary findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Week 6 of administration

Animal No.	pH	Protein	Glucose	Ketone body	Urobili-nogen EU/dL	Bili-rubin	Occult blood	Color	Specific gravity	Urine volume mL/21hr
401	8.5	±	−	−	0.1	−	−	A	1.048	11.0
404	7.0	±	−	−	0.1	−	−	A	1.035	17.5
406	8.5	±	−	−	0.1	−	±	A	1.050<	11.0
411	6.0	±	−	−	0.1	−	−	A	1.050<	7.5
412	8.5	±	−	−	0.1	−	−	A	1.040	17.0
N	5	5	5	5	5	5	5	5	5	5
MEAN										12.80
S.D.										4.31

- ; Normal , ± ; Slight .

Color : A = Pale yellow or yellow.

INDIVIDUAL DATA 16-1-8

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Urinary findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Week 6 of administration

	Urinary sediments					
			Epithelial cell			
Animal No.	RBC	WBC	Squamous	Round	Small round	Cast
401	—	—	—	—	—	—
404	—	—	—	—	—	—
406	—	—	±	—	—	—
411	—	—	—	—	—	—
412	—	—	—	—	—	—
N	5	5	5	5	5	5

- ; Normal , ± ; Slight .

INDIVIDUAL DATA 16-2-1
STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Urinary findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Week 2 of recovery

Animal No.	pH	Protein	Glucose	Ketone body	Urobili-nogen EU/dL	Bili-rubin	Occult blood	Color	Specific gravity	Urine volume mL/21hr
104	8.5	2+	−	−	0.1	−	−	A	1.050<	9.5
105	8.5	+	−	−	0.1	−	−	A	1.050<	6.5
106	8.5	±	−	−	0.1	−	−	A	1.050<	7.0
107	8.0	±	−	−	0.1	−	−	A	1.047	16.5
108	8.5	±	−	−	0.1	−	−	A	1.045	15.5
N	5	5	5	5	5	5	5	5	5	5
MEAN										11.00
S.D.										4.72

- ; Normal , ± ; Slight , + ; Moderate , 2+ ; Severe .
Color : A = Pale yellow or yellow.

INDIVIDUAL DATA 16-2-2

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Urinary findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : Week 2 of recovery

	Urinary sediments					
			Epithelial cell			
Animal No	RBC	WBC	Squamous	Round	Small round	Cast
104	—	—	—	—	—	—
105	—	—	—	—	—	—
106	—	—	—	—	—	—
107	—	—	—	—	—	—
108	—	—	±	—	—	—
N	5	5	5	5	5	5

- ; Normal , ± ; Slight .

INDIVIDUAL DATA 16-2-3
STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Urinary findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Week 2 of recovery

Animal No.	pH	Protein	Glucose	Ketone body	Urobili-nogen EU/dL	Bili-rubin	Occult blood	Color	Specific gravity	Urine volume mL/21hr
401	8.5	+	−	−	0.1	−	−	A	1.049	10.0
404	8.5	±	−	−	0.1	−	−	A	1.038	17.0
406	8.5	2+	−	−	0.1	−	−	A	1.050<	9.5
411	8.5	+	−	−	0.1	−	−	A	1.050<	9.5
412	8.5	+	−	−	0.1	−	−	A	1.050<	10.5
N	5	5	5	5	5	5	5	5	5	5
MEAN										11.30
S.D.										3.21

- ; Normal , ± ; Slight , + ; Moderate , 2+ ; Severe .
Color : A = Pale yellow or yellow.

INDIVIDUAL DATA 16-2-4

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Urinary findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : Week 2 of recovery

	Urinary sediments					
			Epithelial cell			
Animal No	RBC	WBC	Squamous	Round	Small round	Cast
401	—	—	—	—	—	—
404	—	—	—	—	—	—
406	—	—	±	—	—	—
411	±	—	—	—	—	—
412	—	—	±	—	—	—
N	5	5	5	5	5	5

- ; Normal , ± ; Slight .

INDIVIDUAL DATA 17-1-1

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Urinary findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 0 mg/kg PERIOD : Week 6 of administration

Animal No.	pH	Protein	Glucose	Ketone body	Urobili-nogen EU/dL	Bili-rubin	Occult blood	Color	Specific gravity	Urine volume mL/21hr
168	6.0	+	−	−	0.1	−	−	A	1.050<	5.7
169	6.5	+	−	−	0.1	−	−	A	1.050<	4.0
170	8.0	+	−	−	0.1	−	−	A	1.048	9.0
171	6.5	+	−	−	0.1	−	−	A	1.047	6.5
172	8.0	2+	−	−	0.1	−	−	A	1.044	10.0
N	5	5	5	5	5	5	5	5	5	5
MEAN										7.04
S.D.										2.45

- ; Normal , + ; Moderate , 2+ ; Severe .

Color : A = Pale yellow or yellow.

INDIVIDUAL DATA 17-1-2

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Urinary findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 0 mg/kg PERIOD : Week 6 of administration

	Urinary sediments					
			Epithelial cell			
Animal No.	RBC	WBC	Squamous	Round	Small round	Cast
168	—	—	—	—	—	—
169	—	—	—	—	—	—
170	—	—	—	—	—	—
171	—	—	—	—	—	—
172	—	—	—	—	—	—
N	5	5	5	5	5	5

- ; Normal .

INDIVIDUAL DATA 17-1-3
STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Urinary findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 100 mg/kg PERIOD : Week 6 of administration

Animal No.	pH	Protein	Glucose	Ketone body	Urobili-nogen EU/dL	Bili-rubin	Occult blood	Color	Specific gravity	Urine volume mL/21hr
468	6.0	+	−	−	0.1	−	−	A	1.050<	5.2
469	7.5	±	−	−	0.1	−	−	A	1.050<	4.0
470	7.0	+	−	−	0.1	−	−	A	1.038	14.0
471	8.0	±	−	−	0.1	−	−	A	1.050<	5.0
472	6.5	±	−	−	0.1	−	−	A	1.035	11.5
N	5	5	5	5	5	5	5	5	5	5
MEAN										7.94
S.D.										4.50

- ; Normal , ± ; Slight , + ; Moderate .
Color : A = Pale yellow or yellow.

INDIVIDUAL DATA 17-1-4

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Urinary findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 100 mg/kg PERIOD : Week 6 of administration

	Urinary sediments					
			Epithelial cell			
Animal No.	RBC	WBC	Squamous	Round	Small round	Cast
468	—	—	±	—	—	—
469	—	—	—	—	—	—
470	—	—	±	—	—	—
471	—	—	—	—	—	—
472	—	—	±	—	—	—
N	5	5	5	5	5	5

- ; Normal , ± ; Slight .

INDIVIDUAL DATA 17-2-1

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Urinary findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 0 mg/kg PERIOD : Week 2 of recovery

Animal No.	pH	Protein	Glucose	Ketone body	Urobili-nogen EU/dL	Bili-rubin	Occult blood	Color	Specific gravity	Urine volume mL/21hr
168	8.5	±	−	−	0.1	−	−	A	1.050<	5.0
169	6.0	±	−	−	0.1	−	−	A	1.050<	6.0
170	8.5	+	−	−	0.1	−	−	A	1.050<	10.5
171	7.5	±	−	−	0.1	−	−	A	1.050<	8.5
172	7.0	±	−	−	0.1	−	−	A	1.050<	9.0
N	5	5	5	5	5	5	5	5	5	5
MEAN										7.80
S.D.										2.25

- ; Normal , ± ; Slight , + ; Moderate .

Color : A = Pale yellow or yellow.

INDIVIDUAL DATA 17-2-2

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Urinary findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 0 mg/kg PERIOD : Week 2 of recovery

	Urinary sediments					
			Epithelial cell			
Animal No.	RBC	WBC	Squamous	Round	Small round	Cast
168	—	—	±	—	—	—
169	—	—	—	—	—	—
170	—	—	—	—	—	—
171	—	—	±	—	—	—
172	—	—	±	—	—	—
N	5	5	5	5	5	5

- ; Normal , ± ; Slight .

INDIVIDUAL DATA 17-2-3

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Urinary findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 100 mg/kg PERIOD : Week 2 of recovery

Animal No.	pH	Protein	Glucose	Ketone body	Urobili-nogen EU/dL	Bili-rubin	Occult blood	Color	Specific gravity	Urine volume mL/21hr
468	6.0	−	−	−	0.1	−	−	A	1.050<	6.5
469	8.0	+	−	−	0.1	−	−	A	1.043	10.5
470	8.5	±	−	−	0.1	−	−	A	1.042	14.0
471	6.5	−	−	−	0.1	−	−	A	1.050<	3.5
472	7.5	−	−	−	0.1	−	−	A	1.041	12.5
N	5	5	5	5	5	5	5	5	5	5
MEAN										9.40
S.D.										4.34

- ; Normal , ± ; Slight , + ; Moderate .

Color : A = Pale yellow or yellow.

INDIVIDUAL DATA 17-2-4

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Urinary findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 100 mg/kg PERIOD : Week 2 of recovery

	Urinary sediments					
			Epithelial cell			
Animal No.	RBC	WBC	Squamous	Round	Small round	Cast
468	—	—	—	—	—	—
469	—	—	—	—	—	—
470	—	—	—	—	—	—
471	—	—	—	—	—	—
472	—	—	—	—	—	—
N	5	5	5	5	5	5

- ; Normal .

INDIVIDUAL DATA 18-1-1

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Hematological findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : after Week 6 of administration

Animal No.	WBC $10^2/\mu L$	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Platelet $10^4/\mu L$
101	43.3	840	14.9	41.2	49.0	17.7	36.2	91.9
102	54.1	822	15.1	42.8	52.1	18.4	35.3	113.9
103	47.0	857	15.1	42.2	49.2	17.6	35.8	120.0
109	84.6	811	14.1	40.0	49.3	17.4	35.3	112.3
110	83.2	829	15.3	43.2	52.1	18.5	35.4	106.0
N	5	5	5	5	5	5	5	5
MEAN	62.44	831.8	14.90	41.88	50.34	17.92	35.60	108.82
S.D.	19.98	17.6	0.47	1.29	1.61	0.50	0.39	10.69

INDIVIDUAL DATA 18-1-2

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Hematological findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : after Week 6 of administration

Animal No.	Reticulo-cyte %	PT sec	APTT sec	Differential count of WBC ($10^2/\mu L$)					Heinz Body %	Met-hemoglobin %
				Neutrophil	Lympho-cyte	Monocyte	Eosinophil	Basophil		
101	1.91	28.3	30.6	3.1	38.5	1.0	0.7	0.0	0.0	1.9
102	2.63	28.5	28.6	10.6	40.5	2.1	0.9	0.0	0.0	1.9
103	2.49	24.1	27.7	8.5	36.1	1.6	0.8	0.0	0.0	2.3
109	3.15	23.0	27.2	15.0	65.6	2.1	1.9	0.0	0.0	1.6
110	3.26	21.3	29.4	11.9	67.8	2.4	1.1	0.0	0.0	1.8
N	5	5	5	5	5	5	5	5	5	5
MEAN	2.688	25.04	28.70	9.82	49.70	1.84	1.08	0.00	0.00	1.90
S.D.	0.545	3.23	1.36	4.43	15.62	0.55	0.48	0.00	0.00	0.25

INDIVIDUAL DATA 18-1-3

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Hematological findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : after Week 6 of administration

Animal No.	WBC $10^2/\mu L$	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Platelet $10^4/\mu L$
201	96.4	856	15.2	42.6	49.8	17.8	35.7	127.8
202	56.0	804	15.0	43.0	53.5	18.7	34.9	96.7
204	77.7	821	14.9	41.7	50.8	18.1	35.7	131.5
206	53.2	854	15.2	43.5	50.9	17.8	34.9	106.4
210	46.0	845	14.9	43.1	51.0	17.6	34.6	104.3
N	5	5	5	5	5	5	5	5
MEAN	65.86	836.0	15.04	42.78	51.20	18.00	35.16	113.34
S.D.	20.77	22.7	0.15	0.68	1.37	0.43	0.51	15.38

INDIVIDUAL DATA 18-1-4

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Hematological findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : after Week 6 of administration

Animal No.	Reticulo-cyte %	PT sec	APTT sec	Differential count of WBC ($10^2/\mu L$)					Heinz Body %	Met-hemoglobin %
				Neutrophil	Lympho-cyte	Monocyte	Eosinophil	Basophil		
201	2.57	21.1	27.2	25.3	66.4	3.5	1.2	0.0	0.0	1.5
202	3.65	26.0	26.8	7.0	46.2	1.9	0.9	0.0	0.0	1.9
204	3.44	21.7	26.4	12.8	61.9	2.1	0.9	0.0	0.0	1.5
206	3.03	18.3	26.3	15.5	33.9	3.0	0.8	0.0	0.0	1.9
210	3.11	21.7	26.7	9.7	33.4	2.1	0.8	0.0	0.0	1.5
N	5	5	5	5	5	5	5	5	5	5
MEAN	3.160	21.76	26.68+	14.06	48.36	2.52	0.92	0.00	0.00	1.66
S.D.	0.414	2.76	0.36	7.05	15.38	0.69	0.16	0.00	0.00	0.22

+ : Significantly different from the 0 mg/kg group at $p \leqq 0.05$ (Steel's test).

INDIVIDUAL DATA 18-1-5

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Hematological findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : after Week 6 of administration

Animal No.	WBC $10^2/\mu L$	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Platelet $10^4/\mu L$
302	48.4	829	14.3	40.5	48.9	17.2	35.3	124.8
304	63.1	809	15.2	42.7	52.8	18.8	35.6	100.3
307	77.7	787	14.4	41.7	53.0	18.3	34.5	122.2
308	35.9	754	13.8	40.1	53.2	18.3	34.4	107.6
309	59.4	800	14.9	43.4	54.3	18.6	34.3	115.2
N	5	5	5	5	5	5	5	5
MEAN	56.90	795.8	14.52	41.68	52.44	18.24	34.82*	114.02
S.D.	15.74	27.9	0.54	1.40	2.06	0.62	0.59	10.17

* : Significantly different from the 0 mg/kg group at $p \leqq 0.05$ (Dunnett's test).

INDIVIDUAL DATA 18-1-6

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Hematological findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : after Week 6 of administration

Animal No.	Reticulo-cyte %	PT sec	APTT sec	Differential count of WBC ($10^2/\mu L$)					Heinz Body %	Met-hemoglobin %
				Neutrophil	Lympho-cyte	Monocyte	Eosinophil	Basophil		
302	3.00	20.8	32.0	9.3	36.2	2.1	0.8	0.0	0.0	2.0
304	2.75	24.2	26.8	8.0	52.8	1.5	0.8	0.0	0.0	1.9
307	3.37	29.7	31.0	12.1	62.9	2.0	0.7	0.0	0.0	1.9
308	2.93	24.3	28.2	8.0	26.2	1.1	0.6	0.0	0.0	1.7
309	3.50	20.1	25.4	13.1	43.1	2.4	0.8	0.0	0.0	1.9
N	5	5	5	5	5	5	5	5	5	5
MEAN	3.110	23.82	28.68	10.10	44.24	1.82	0.74	0.00	0.00	1.88
S.D.	0.314	3.80	2.78	2.37	14.26	0.52	0.09	0.00	0.00	0.11

INDIVIDUAL DATA 18-1-7

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Hematological findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : after Week 6 of administration

Animal No.	WBC $10^2/\mu L$	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Platelet $10^4/\mu L$
402	59.4	852	15.3	44.2	51.9	18.0	34.6	87.6
403	50.9	782	13.6	39.2	50.1	17.4	34.7	97.5
405	56.0	794	14.6	42.8	53.9	18.4	34.1	95.8
407	69.4	777	14.4	41.4	53.3	18.5	34.8	102.8
408	105.5	744	13.7	39.6	53.2	18.4	34.6	103.5
N	5	5	5	5	5	5	5	5
MEAN	68.24	789.8	14.32	41.44	52.48	18.14	34.56**	97.44
S.D.	21.90	39.4	0.70	2.11	1.52	0.46	0.27	6.42

** : Significantly different from the 0 mg/kg group at $p \leqq 0.01$ (Dunnett's test).

INDIVIDUAL DATA 18-1-8

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Hematological findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : after Week 6 of administration

Animal No.	Reticulo-cyte %	PT sec	APTT sec	Differential count of WBC ($10^2/\mu L$)					Heinz Body %	Met-hemoglobin %
				Neutrophil	Lympho-cyte	Monocyte	Eosinophil	Basophil		
402	3.67	33.2	30.9	15.0	41.5	1.8	1.1	0.0	0.0	1.9
403	4.11	33.9	33.2	11.9	36.4	1.7	0.9	0.0	0.0	2.5
405	3.50	40.4	34.0	10.3	43.0	1.8	0.9	0.0	0.0	1.9
407	4.18	18.3	28.2	14.5	52.2	1.9	0.8	0.0	0.0	2.4
408	4.67	37.6	36.6	13.1	89.5	2.0	0.9	0.0	0.0	1.2
N	5	5	5	5	5	5	5	5	5	5
MEAN	4.026**	32.68	32.58	12.96	52.52	1.84	0.92	0.00	0.00	1.98
S.D.	0.461	8.55	3.18	1.92	21.44	0.11	0.11	0.00	0.00	0.52

** : Significantly different from the 0 mg/kg group at $p \leqq 0.01$ (Dunnett's test).

INDIVIDUAL DATA 18-2-1

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Hematological findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : after Week 2 of recovery

Animal No.	WBC $10^2/\mu L$	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Platelet $10^4/\mu L$
104	92.4	939	15.8	43.7	46.5	16.8	36.2	124.6
105	49.2	837	15.3	42.5	50.8	18.3	36.0	122.7
106	85.2	892	15.4	43.6	48.9	17.3	35.3	94.3
107	86.4	842	14.8	41.7	49.5	17.6	35.5	109.1
108	48.9	827	15.0	43.0	52.0	18.1	34.9	100.0
N	5	5	5	5	5	5	5	5
MEAN	72.42	867.4	15.26	42.90	49.54	17.62	35.58	110.14
S.D.	21.51	47.3	0.38	0.83	2.08	0.61	0.53	13.43

INDIVIDUAL DATA 18-2-2

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Hematological findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : after Week 2 of recovery

Animal No.	Reticulo-cyte %	PT sec	APTT sec	Differential count of WBC ($10^2/\mu L$)					Heinz Body %	Met-hemoglobin %
				Neutrophil	Lympho-cyte	Monocyte	Eosinophil	Basophil		
104	2.89	23.2	24.6	8.2	79.4	3.4	1.4	0.0	0.0	1.8
105	2.63	23.8	27.7	4.8	42.2	1.3	0.9	0.0	0.0	1.8
106	2.60	18.9	24.0	18.9	61.3	3.2	1.8	0.0	0.0	1.5
107	2.89	20.9	23.9	12.4	69.0	3.1	1.9	0.0	0.0	1.2
108	2.07	26.7	26.8	6.2	39.7	2.1	0.9	0.0	0.0	1.5
N	5	5	5	5	5	5	5	5	5	5
MEAN	2.616	22.70	25.40	10.10	58.32	2.62	1.38	0.00	0.00	1.56
S.D.	0.335	2.96	1.74	5.69	17.13	0.89	0.48	0.00	0.00	0.25

INDIVIDUAL DATA 18-2-3

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Hematological findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : after Week 2 of recovery

Animal No.	WBC $10^2/\mu L$	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Platelet $10^4/\mu L$
401	108.8	883	15.4	42.8	48.5	17.4	36.0	125.7
404	68.5	864	15.4	43.5	50.3	17.8	35.4	123.4
406	70.5	850	15.7	45.0	52.9	18.5	34.9	95.8
411	57.7	831	14.6	40.9	49.2	17.6	35.7	122.3
412	41.4	866	15.9	44.2	51.0	18.4	36.0	118.1
N	5	5	5	5	5	5	5	5
MEAN	69.38	858.8	15.40	43.28	50.38	17.94	35.60	117.06
S.D.	24.88	19.5	0.49	1.56	1.71	0.49	0.46	12.20

INDIVIDUAL DATA 18-2-4

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Hematological findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : after Week 2 of recovery

Animal No.	Reticulo-cyte %	PT sec	APTT sec	Differential count of WBC ($10^2/\mu L$)					Heinz Body %	Met-hemoglobin %
				Neutrophil	Lympho-cyte	Monocyte	Eosinophil	Basophil		
401	2.34	22.0	26.3	7.4	97.3	3.0	1.1	0.0	0.0	1.5
404	2.69	30.1	28.5	6.7	57.9	2.9	1.0	0.0	0.0	1.5
406	3.91	31.0	29.2	11.7	55.4	2.6	0.8	0.0	0.0	1.8
411	3.28	22.0	27.2	7.7	46.9	2.0	1.1	0.0	0.0	1.9
412	2.78	21.4	27.0	6.6	31.8	1.9	1.1	0.0	0.0	1.4
N	5	5	5	5	5	5	5	5	5	5
MEAN	3.000	25.30	27.64*	8.02	57.86	2.48	1.02	0.00	0.00	1.62
S.D.	0.610	4.81	1.18	2.11	24.29	0.51	0.13	0.00	0.00	0.22

* : Significantly different from the 0 mg/kg group at $p \leqq 0.05$ (Dunnett's test).

INDIVIDUAL DATA 19-1

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Hematological findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg PERIOD : Day 5 of lactation

Animal No.	WBC $10^2/\mu L$	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Platelet $10^4/\mu L$
151	68.5	730	13.6	37.9	51.9	18.6	35.9	129.2
152	60.8	626	12.2	36.4	58.1	19.5	33.5	129.2
154	68.9	678	13.3	39.6	58.4	19.6	33.6	119.5
159	88.1	655	12.3	36.1	55.1	18.8	34.1	127.5
161	64.7	636	12.4	37.0	58.2	19.5	33.5	158.5
N	5	5	5	5	5	5	5	5
MEAN	70.20	665.0	12.76	37.40	56.34	19.20	34.12	132.78
S.D.	10.53	41.4	0.64	1.41	2.83	0.46	1.03	14.93

INDIVIDUAL DATA 19-2

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Hematological findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg PERIOD : Day 5 of lactation

Animal No.	Reticulo-cyte %	PT sec	APTT sec	Differential count of WBC ($10^2/\mu L$)				
				Neutrophil	Lympho-cyte	Monocyte	Eosinophil	Basophil
151	7.37	16.9	21.2	19.1	46.6	2.6	0.2	0.0
152	9.12	18.5	19.6	21.4	38.2	0.9	0.3	0.0
154	8.89	16.8	18.6	20.7	44.9	2.8	0.5	0.0
159	7.80	16.7	18.0	22.8	61.5	2.6	1.2	0.0
161	9.50	16.2	21.9	13.8	48.1	2.5	0.3	0.0
N	5	5	5	5	5	5	5	5
MEAN	8.536	17.02	19.86	19.56	47.86	2.28	0.50	0.00
S.D.	0.908	0.87	1.66	3.48	8.51	0.78	0.41	0.00

INDIVIDUAL DATA 19-3

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Hematological findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg PERIOD : Day 5 of lactation

Animal No.	WBC $10^2/\mu L$	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Platelet $10^4/\mu L$
256	63.5	630	12.1	35.2	55.9	19.2	34.4	109.0
257	108.8	511	10.6	33.4	65.4	20.7	31.7	131.3
259	56.3	701	13.1	38.0	54.2	18.7	34.5	118.5
260	47.9	635	11.9	34.2	53.9	18.7	34.8	107.7
262	44.2	643	12.8	37.8	58.8	19.9	33.9	100.5
N	5	5	5	5	5	5	5	5
MEAN	64.14	624.0	12.10	35.72	57.64	19.44	33.86	113.40
S.D.	26.07	69.3	0.97	2.09	4.75	0.86	1.25	11.88

INDIVIDUAL DATA 19-4

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Hematological findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg PERIOD : Day 5 of lactation

Animal No.	Reticulo-cyte %	PT sec	APTT sec	Differential count of WBC ($10^2/\mu L$)				
				Neutrophil	Lympho-cyte	Monocyte	Eosinophil	Basophil
256	9.25	16.2	19.5	24.5	38.3	0.5	0.2	0.0
257	17.08	17.8	22.4	25.0	81.5	2.1	0.1	0.1
259	5.95	16.1	23.1	19.6	34.5	1.7	0.5	0.0
260	6.85	16.7	18.1	17.4	28.0	2.1	0.4	0.0
262	10.33	17.3	19.6	11.6	31.3	1.1	0.2	0.0
N	5	5	5	5	5	5	5	5
MEAN	9.892	16.82	20.54	19.62	42.72	1.50	0.28	0.02
S.D.	4.389	0.73	2.12	5.52	22.01	0.69	0.16	0.04

INDIVIDUAL DATA 19-5

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Hematological findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg PERIOD : Day 5 of lactation

Animal No.	WBC $10^2/\mu L$	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Platelet $10^4/\mu L$
352	72.5	699	13.2	38.1	54.5	18.9	34.6	134.5
355	67.3	651	12.2	34.9	53.6	18.7	35.0	116.2
357	49.8	651	12.7	38.3	58.8	19.5	33.2	122.2
358	58.7	622	12.4	37.4	60.1	19.9	33.2	109.9
360	88.0	696	13.0	37.8	54.3	18.7	34.4	126.7
N	5	5	5	5	5	5	5	5
MEAN	67.26	663.8	12.70	37.30	56.26	19.14	34.08	121.90
S.D.	14.45	33.0	0.41	1.38	2.97	0.54	0.83	9.47

INDIVIDUAL DATA 19-6

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Hematological findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg PERIOD : Day 5 of lactation

Animal No.	Reticulo-cyte %	PT sec	APTT sec	Differential count of WBC ($10^2/\mu L$)				
				Neutrophil	Lympho-cyte	Monocyte	Eosinophil	Basophil
352	7.38	16.6	17.3	32.5	37.7	1.6	0.7	0.0
355	8.25	17.6	20.0	25.1	39.8	2.2	0.2	0.0
357	10.88	16.7	18.4	12.6	35.6	1.4	0.2	0.0
358	7.72	16.4	19.1	22.8	33.6	1.7	0.6	0.0
360	8.38	17.9	19.7	30.6	54.3	2.7	0.4	0.0
N	5	5	5	5	5	5	5	5
MEAN	8.522	17.04	18.90	24.72	40.20	1.92	0.42	0.00
S.D.	1.379	0.67	1.08	7.84	8.21	0.53	0.23	0.00

INDIVIDUAL DATA 19-7

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Hematological findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg PERIOD : Day 5 of lactation

Animal No.	WBC $10^2/\mu L$	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Platelet $10^4/\mu L$
451	42.2	605	11.9	35.7	59.0	19.7	33.3	129.2
452	55.3	647	12.1	35.9	55.5	18.7	33.7	123.7
456	54.2	682	13.1	39.7	58.2	19.2	33.0	129.2
458	84.7	596	12.7	38.4	64.4	21.3	33.1	103.5
462	105.2	643	12.9	38.1	59.3	20.1	33.9	104.6
N	5	5	5	5	5	5	5	5
MEAN	68.32	634.6	12.54	37.56	59.28	19.80	33.40	118.04
S.D.	25.88	34.8	0.52	1.72	3.23	0.99	0.39	12.97

INDIVIDUAL DATA 19-8

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Hematological findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg PERIOD : Day 5 of lactation

Animal No.	Reticulo-cyte %	PT sec	APTT sec	Differential count of WBC ($10^2/\mu L$)				
				Neutrophil	Lympho-cyte	Monocyte	Eosinophil	Basophil
451	11.48	16.3	18.9	12.1	28.4	1.6	0.1	0.0
452	8.23	16.0	20.4	21.7	30.7	2.7	0.2	0.0
456	11.47	17.7	19.6	10.3	42.1	1.6	0.2	0.0
458	14.19	16.1	22.6	35.8	46.3	2.0	0.6	0.0
462	9.14	18.4	18.4	40.5	60.2	4.2	0.3	0.0
N	5	5	5	5	5	5	5	5
MEAN	10.902	16.90	19.98	24.08	41.54	2.42	0.28	0.00
S.D.	2.330	1.08	1.65	13.66	12.86	1.09	0.19	0.00

INDIVIDUAL DATA 20-1-1

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Hematological findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 0 mg/kg PERIOD : after Week 6 of administration

Animal No.	WBC $10^2/\mu L$	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Platelet $10^4/\mu L$
163	41.0	811	14.3	40.3	49.7	17.6	35.5	113.6
164	40.4	755	14.0	40.7	53.9	18.5	34.4	127.8
165	49.9	851	15.4	43.1	50.6	18.1	35.7	100.8
166	40.7	825	14.7	41.4	50.2	17.8	35.5	113.7
167	29.8	764	13.9	39.3	51.4	18.2	35.4	95.2
N	5	5	5	5	5	5	5	5
MEAN	40.36	801.2	14.46	40.96	51.16	18.04	35.30	110.22
S.D.	7.12	40.8	0.61	1.42	1.65	0.35	0.51	12.72

INDIVIDUAL DATA 20-1-2

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Hematological findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 0 mg/kg PERIOD : after Week 6 of administration

Animal No.	Reticulo-cyte %	PT sec	APTT sec	Differential count of WBC ($10^2/\mu L$)					Heinz Body %	Met-hemoglobin %
				Neutrophil	Lympho-cyte	Monocyte	Eosinophil	Basophil		
163	2.64	16.6	18.6	3.4	36.4	0.7	0.5	0.0	0.0	1.2
164	2.11	15.5	19.4	5.3	33.4	1.3	0.4	0.0	0.0	1.6
165	2.77	16.2	17.7	6.0	42.3	1.2	0.4	0.0	0.0	1.5
166	3.57	16.8	18.7	7.6	30.9	1.9	0.3	0.0	0.0	0.8
167	3.32	17.9	18.4	4.8	23.2	1.4	0.4	0.0	0.0	1.2
N	5	5	5	5	5	5	5	5	5	5
MEAN	2.882	16.60	18.56	5.42	33.24	1.30	0.40	0.00	0.00	1.26
S.D.	0.577	0.88	0.61	1.55	7.04	0.43	0.07	0.00	0.00	0.31

INDIVIDUAL DATA 20-1-3

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Hematological findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 100 mg/kg PERIOD : after Week 6 of administration

Animal No.	WBC $10^2/\mu L$	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Platelet $10^4/\mu L$
463	19.6	742	13.1	37.3	50.3	17.7	35.1	99.9
464	27.9	735	13.2	37.6	51.2	18.0	35.1	122.6
465	59.6	775	14.7	42.3	54.6	19.0	34.8	104.3
466	44.4	743	14.5	41.9	56.4	19.5	34.6	102.9
467	44.1	794	14.8	43.1	54.3	18.6	34.3	102.1
N	5	5	5	5	5	5	5	5
MEAN	39.12	757.8	14.06	40.44	53.36	18.56	34.78	106.36
S.D.	15.64	25.5	0.84	2.77	2.53	0.73	0.34	9.22

INDIVIDUAL DATA 20-1-4

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Hematological findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 100 mg/kg PERIOD : after Week 6 of administration

Animal No.	Reticulo-cyte %	PT sec	APTT sec	Differential count of WBC ($10^2/\mu L$)					Heinz Body %	Met-hemoglobin %
				Neutrophil	Lympho-cyte	Monocyte	Eosinophil	Basophil		
463	3.41	14.9	23.0	3.5	15.2	0.7	0.2	0.0	0.0	2.2
464	3.51	21.7	26.0	7.5	19.6	0.7	0.1	0.0	0.0	1.8
465	4.05	17.7	27.6	8.5	47.8	2.8	0.5	0.0	0.0	1.2
466	4.66	15.6	20.6	6.2	37.1	0.8	0.3	0.0	0.0	1.2
467	3.59	16.6	19.6	11.0	30.6	1.9	0.6	0.0	0.0	1.2
N	5	5	5	5	5	5	5	5	5	5
MEAN	3.844*	17.30	23.36++	7.34	30.06	1.38	0.34	0.00	0.00	1.52
S.D.	0.518	2.68	3.42	2.78	13.18	0.94	0.21	0.00	0.00	0.46

* : Significantly different from the 0 mg/kg group at $p \leqq 0.05$ (Dunnett's test).

++ : Significantly different from the 0 mg/kg group at $p \leqq 0.01$ (Steel's test).

INDIVIDUAL DATA 20-2-1

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Hematological findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 0 mg/kg PERIOD : after Week 2 of recovery

Animal No.	WBC $10^2/\mu L$	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Platelet $10^4/\mu L$
168	25.4	777	13.9	39.5	50.8	17.9	35.2	105.5
169	30.8	795	14.2	40.3	50.7	17.9	35.2	95.5
170	34.7	802	14.5	41.3	51.5	18.1	35.1	108.5
171	21.9	789	14.9	42.9	54.4	18.9	34.7	104.8
172	24.5	766	14.5	41.7	54.4	18.9	34.8	98.3
N	5	5	5	5	5	5	5	5
MEAN	27.46	785.8	14.40	41.14	52.36	18.34	35.00	102.52
S.D.	5.18	14.4	0.37	1.31	1.89	0.52	0.23	5.41

INDIVIDUAL DATA 20-2-2

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Hematological findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 0 mg/kg PERIOD : after Week 2 of recovery

Animal No.	Reticulo-cyte %	PT sec	APTT sec	Differential count of WBC ($10^2/\mu L$)					Heinz Body %	Met-hemoglobin %
				Neutrophil	Lympho-cyte	Monocyte	Eosinophil	Basophil		
168	2.85	17.8	17.7	5.0	18.7	1.1	0.6	0.0	0.0	1.6
169	2.86	17.9	18.5	4.3	24.7	1.4	0.4	0.0	0.0	1.6
170	2.04	18.3	18.1	5.9	26.4	1.4	1.0	0.0	0.0	1.2
171	2.93	16.0	19.7	3.5	17.0	0.9	0.5	0.0	0.0	1.6
172	2.59	17.2	19.3	3.3	18.9	1.8	0.5	0.0	0.0	0.8
N	5	5	5	5	5	5	5	5	5	5
MEAN	2.654	17.44	18.66	4.40	21.14	1.32	0.60	0.00	0.00	1.36
S.D.	0.367	0.90	0.83	1.08	4.14	0.34	0.23	0.00	0.00	0.36

INDIVIDUAL DATA 20-2-3

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Hematological findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 100 mg/kg PERIOD : after Week 2 of recovery

Animal No.	WBC $10^2/\mu L$	RBC $10^4/\mu L$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Platelet $10^4/\mu L$
468	33.7	751	14.5	42.1	56.1	19.3	34.4	90.7
469	35.7	808	14.7	41.9	51.9	18.2	35.1	89.4
470	36.3	750	13.5	38.0	50.7	18.0	35.5	119.9
471	40.2	779	14.4	40.6	52.1	18.5	35.5	102.7
472	27.3	769	14.8	42.5	55.3	19.2	34.8	115.8
N	5	5	5	5	5	5	5	5
MEAN	34.64	771.4	14.38	41.02	53.22	18.64	35.06	103.70
S.D.	4.73	23.9	0.52	1.83	2.34	0.59	0.47	13.99

INDIVIDUAL DATA 20-2-4

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Hematological findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 100 mg/kg PERIOD : after Week 2 of recovery

Animal No.	Reticulo-cyte %	PT sec	APTT sec	Differential count of WBC ($10^2/\mu L$)					Heinz Body %	Met-hemoglobin %
				Neutrophil	Lympho-cyte	Monocyte	Eosinophil	Basophil		
468	3.52	16.0	19.9	9.6	22.5	1.1	0.5	0.0	0.0	1.2
469	2.97	18.3	19.1	4.6	29.5	1.2	0.4	0.0	0.0	1.2
470	1.95	16.2	21.3	12.1	22.0	1.7	0.5	0.0	0.0	1.3
471	2.87	16.6	18.1	3.6	35.6	0.7	0.3	0.0	0.0	1.2
472	2.22	18.2	18.6	4.0	21.4	1.4	0.5	0.0	0.0	1.5
N	5	5	5	5	5	5	5	5	5	5
MEAN	2.706	17.06	19.40	6.78	26.20	1.22	0.44	0.00	0.00	1.28
S.D.	0.626	1.11	1.25	3.84	6.20	0.37	0.09	0.00	0.00	0.13

INDIVIDUAL DATA 21-1-1

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Biochemical findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : after Week 6 of administration

Animal No.	TP g/dL	Albumin g/dL	A/G ratio	Protein fraction (%)					AST IU/L	ALT IU/L	ALP IU/L	γ-GTP IU/L	T-Bil mg/dL
				Albumin	Globulin								
					α_1	α_2	β	γ					
101	5.0	2.68	1.17	53.8	17.5	7.4	15.9	5.4	62	28	443	0.3	0.06
102	5.2	2.71	1.08	52.0	21.6	7.4	15.5	3.5	111	43	421	0.5	0.04
103	5.2	2.60	1.00	49.9	22.3	7.2	16.1	4.5	72	30	319	0.4	0.05
109	4.8	2.49	1.08	51.9	18.8	7.9	17.1	4.3	58	29	308	0.5	0.05
110	5.4	2.72	1.02	50.4	21.3	7.6	15.9	4.8	62	36	599	0.3	0.04
N	5	5	5	5	5	5	5	5	5	5	5	5	5
MEAN	5.12	2.640	1.070	51.60	20.30	7.50	16.10	4.50	73.0	33.2	418.0	0.40	0.048
S.D.	0.23	0.096	0.066	1.53	2.05	0.26	0.60	0.70	21.9	6.3	117.6	0.10	0.008

INDIVIDUAL DATA 21-1-2

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Biochemical findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : after Week 6 of administration

Animal No.	TBA μmol/L	Glucose mg/dL	T-Cho mg/dL	TG mg/dL	UN mg/dL	Crea mg/dL	Na mEq/L	K mEq/L	Cl mEq/L	Ca mg/dL	IP mg/dL
101	5.6	136	45	9	11.4	0.38	145	3.87	106	9.2	5.7
102	20.1	185	46	12	14.1	0.49	144	4.82	104	9.8	7.9
103	14.3	147	59	23	12.7	0.34	144	4.51	105	9.8	7.3
109	9.1	150	64	49	12.3	0.36	144	4.55	106	9.5	6.4
110	8.8	127	53	58	12.3	0.28	145	4.25	105	10.5	7.8
N	5	5	5	5	5	5	5	5	5	5	5
MEAN	11.58	149.0	53.4	30.2	12.56	0.370	144.4	4.400	105.2	9.76	7.02
S.D.	5.69	22.1	8.2	22.1	0.98	0.077	0.5	0.359	0.8	0.48	0.95

INDIVIDUAL DATA 21-1-3

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Biochemical findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : after Week 6 of administration

Animal No.	TP g/dL	Albumin g/dL	A/G ratio	Protein fraction (%)					AST IU/L	ALT IU/L	ALP IU/L	γ-GTP IU/L	T-Bil mg/dL
				Albumin	Globulin								
					α_1	α_2	β	γ					
201	5.3	2.66	1.01	50.2	21.3	7.2	16.6	4.7	61	32	392	0.3	0.04
202	4.6	2.42	1.12	52.8	19.7	7.6	15.6	4.3	67	26	382	0.4	0.04
204	5.1	2.66	1.09	52.2	22.9	6.8	14.4	3.7	59	25	394	0.6	0.05
206	5.1	2.51	0.97	49.2	21.9	7.3	16.1	5.5	53	25	607	0.3	0.06
210	4.8	2.51	1.11	52.5	19.1	7.2	16.4	4.8	57	28	288	0.4	0.04
N	5	5	5	5	5	5	5	5	5	5	5	5	5
MEAN	4.98	2.552	1.060	51.38	20.98	7.22	15.82	4.60	59.4	27.2	412.6	0.40	0.046
S.D.	0.28	0.105	0.066	1.59	1.57	0.29	0.88	0.66	5.2	2.9	117.3	0.12	0.009

INDIVIDUAL DATA 21-1-4

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Biochemical findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : after Week 6 of administration

Animal No.	TBA μmol/L	Glucose mg/dL	T-Cho mg/dL	TG mg/dL	UN mg/dL	Crea mg/dL	Na mEq/L	K mEq/L	Cl mEq/L	Ca mg/dL	IP mg/dL
201	24.7	161	56	22	12.8	0.35	143	4.23	104	9.3	6.3
202	23.6	170	56	33	14.7	0.38	142	4.53	105	9.2	7.4
204	10.4	153	46	32	12.9	0.35	143	4.87	104	9.4	7.0
206	25.7	146	49	25	13.4	0.36	146	4.33	107	9.8	7.5
210	6.2	121	48	46	12.3	0.33	147	4.41	108	9.5	8.3
N	5	5	5	5	5	5	5	5	5	5	5
MEAN	18.12	150.2	51.0	31.6	13.22	0.354	144.2	4.474	105.6	9.44	7.30
S.D.	9.12	18.6	4.7	9.3	0.91	0.018	2.2	0.247	1.8	0.23	0.73

INDIVIDUAL DATA 21-1-5

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Biochemical findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : after Week 6 of administration

				Protein fraction (%)									
					Globulin								
Animal No.	TP g/dL	Albumin g/dL	A/G ratio	Albumin	α_1	α_2	β	γ	AST IU/L	ALT IU/L	ALP IU/L	γ-GTP IU/L	T-Bil mg/dL
302	5.3	2.52	0.90	47.5	22.3	8.3	17.3	4.6	59	25	400	0.3	0.06
304	4.7	2.49	1.12	53.0	16.8	8.8	17.2	4.2	59	31	580	0.5	0.04
307	5.0	2.54	1.04	50.9	22.9	7.0	15.5	3.7	55	24	348	0.2	0.04
308	4.9	2.65	1.18	54.0	17.8	8.0	16.0	4.2	69	26	433	0.2	0.05
309	5.3	2.59	0.96	49.0	23.6	6.9	15.1	5.4	70	28	302	0.6	0.05
N	5	5	5	5	5	5	5	5	5	5	5	5	5
MEAN	5.04	2.558	1.040	50.88	20.68	7.80	16.22	4.42	62.4	26.8	412.6	0.36	0.048
S.D.	0.26	0.063	0.114	2.70	3.14	0.83	0.99	0.63	6.7	2.8	106.1	0.18	0.008

INDIVIDUAL DATA 21-1-6

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Biochemical findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : after Week 6 of administration

Animal No.	TBA μmol/L	Glucose mg/dL	T-Cho mg/dL	TG mg/dL	UN mg/dL	Crea mg/dL	Na mEq/L	K mEq/L	Cl mEq/L	Ca mg/dL	IP mg/dL
302	17.6	150	51	22	12.0	0.32	143	4.41	104	9.5	6.2
304	4.0	152	68	25	11.4	0.34	145	4.28	107	9.3	7.0
307	6.8	138	44	20	13.2	0.32	145	4.57	106	9.7	7.4
308	5.6	133	60	8	13.5	0.40	146	4.13	107	9.9	6.6
309	6.4	109	40	29	14.5	0.35	145	4.60	105	10.0	7.8
N	5	5	5	5	5	5	5	5	5	5	5
MEAN	8.08	136.4	52.6	20.8	12.92	0.346	144.8	4.398	105.8	9.68	7.00
S.D.	5.43	17.3	11.5	7.9	1.23	0.033	1.1	0.198	1.3	0.29	0.63

INDIVIDUAL DATA 21-1-7

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Biochemical findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : after Week 6 of administration

				Protein fraction (%)									
					Globulin								
Animal No.	TP g/dL	Albumin g/dL	A/G ratio	Albumin	α_1	α_2	β	γ	AST IU/L	ALT IU/L	ALP IU/L	γ-GTP IU/L	T-Bil mg/dL
402	4.9	2.61	1.14	53.3	19.2	7.3	15.8	4.4	58	24	337	0.4	0.06
403	4.6	2.50	1.19	54.4	15.1	8.4	17.4	4.7	54	26	327	0.5	0.06
405	5.0	2.72	1.21	54.7	17.1	7.9	16.1	4.2	48	21	253	0.1	0.05
407	5.3	2.69	1.03	50.8	21.7	7.1	16.5	3.9	62	27	277	0.4	0.08
408	4.7	2.46	1.10	52.4	18.9	7.9	16.3	4.5	76	51	413	0.3	0.05
N	5	5	5	5	5	5	5	5	5	5	5	5	5
MEAN	4.90	2.596	1.134	53.12	18.40	7.72	16.42	4.34	59.6	29.8	321.4	0.34	0.060
S.D.	0.27	0.114	0.072	1.59	2.47	0.52	0.61	0.30	10.5	12.1	61.9	0.15	0.012

INDIVIDUAL DATA 21-1-8

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Biochemical findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : after Week 6 of administration

Animal No.	TBA μmol/L	Glucose mg/dL	T-Cho mg/dL	TG mg/dL	UN mg/dL	Crea mg/dL	Na mEq/L	K mEq/L	Cl mEq/L	Ca mg/dL	IP mg/dL
402	6.7	153	48	26	12.9	0.36	145	3.86	104	9.2	5.3
403	5.5	153	53	26	13.5	0.37	144	4.52	107	8.9	6.9
405	4.0	138	64	28	11.9	0.29	145	4.44	105	9.4	7.2
407	31.4	137	52	18	11.4	0.33	145	3.84	104	10.0	6.7
408	11.9	110	63	20	9.5	0.26	144	4.23	106	10.0	7.9
N	5	5	5	5	5	5	5	5	5	5	5
MEAN	11.90	138.2	56.0	23.6	11.84	0.322	144.6	4.178	105.2	9.50	6.80
S.D.	11.30	17.6	7.1	4.3	1.55	0.047	0.5	0.318	1.3	0.49	0.95

INDIVIDUAL DATA 21-2-1

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Biochemical findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : after Week 2 of recovery

				Protein fraction (%)									
					Globulin								
Animal No.	TP g/dL	Albumin g/dL	A/G ratio	Albumin	α_1	α_2	β	γ	AST IU/L	ALT IU/L	ALP IU/L	γ-GTP IU/L	T-Bil mg/dL
104	5.4	2.67	0.98	49.6	21.6	6.9	16.8	5.1	71	37	406	0.5	0.05
105	5.1	2.54	1.00	49.9	19.8	8.0	17.3	5.0	50	22	305	0.1	0.07
106	5.4	2.50	0.87	46.4	24.5	7.0	17.0	5.1	63	33	394	0.7	0.06
107	4.8	2.27	0.89	47.2	20.7	8.5	18.4	5.2	63	35	331	0.4	0.06
108	5.4	2.23	0.70	41.3	24.8	7.6	18.0	8.3	49	25	250	0.3	0.05
N	5	5	5	5	5	5	5	5	5	5	5	5	5
MEAN	5.22	2.442	0.888	46.88	22.28	7.60	17.50	5.74	59.2	30.4	337.2	0.40	0.058
S.D.	0.27	0.187	0.119	3.46	2.26	0.67	0.68	1.43	9.4	6.5	64.5	0.22	0.008

INDIVIDUAL DATA 21-2-2

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Biochemical findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : after Week 2 of recovery

Animal No.	TBA μmol/L	Glucose mg/dL	T-Cho mg/dL	TG mg/dL	UN mg/dL	Crea mg/dL	Na mEq/L	K mEq/L	Cl mEq/L	Ca mg/dL	IP mg/dL
104	6.5	205	43	34	14.7	0.35	142	4.76	105	9.4	5.9
105	11.2	144	63	32	18.0	0.44	145	4.60	107	9.4	7.1
106	7.9	157	78	34	15.4	0.38	143	4.55	104	9.7	6.9
107	13.9	148	46	42	14.3	0.32	145	4.36	106	9.6	7.4
108	5.3	148	49	29	16.1	0.35	145	4.72	105	9.8	7.2
N	5	5	5	5	5	5	5	5	5	5	5
MEAN	8.96	160.4	55.8	34.2	15.70	0.368	144.0	4.598	105.4	9.58	6.90
S.D.	3.54	25.4	14.6	4.8	1.46	0.045	1.4	0.158	1.1	0.18	0.59

INDIVIDUAL DATA 21-2-3

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Biochemical findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : after Week 2 of recovery

				Protein fraction (%)									
					Globulin								
Animal No.	TP g/dL	Albumin g/dL	A/G ratio	Albumin	α_1	α_2	β	γ	AST IU/L	ALT IU/L	ALP IU/L	γ-GTP IU/L	T-Bil mg/dL
401	5.2	2.68	1.06	51.5	20.4	7.6	16.2	4.3	59	32	353	0.3	0.06
404	5.1	2.46	0.93	48.2	23.3	7.7	16.3	4.5	49	22	240	0.2	0.06
406	5.4	2.58	0.91	47.6	23.2	6.9	16.1	6.2	56	23	256	0.4	0.06
411	5.4	2.37	0.78	43.9	24.5	8.1	17.9	5.6	52	21	268	0.7	0.05
412	5.8	2.56	0.79	44.3	27.2	6.9	17.2	4.4	41	19	236	0.6	0.05
N	5	5	5	5	5	5	5	5	5	5	5	5	5
MEAN	5.38	2.530	0.894	47.10	23.72	7.44	16.74	5.00	51.4	23.4	270.6	0.44	0.056
S.D.	0.27	0.119	0.115	3.12	2.46	0.53	0.78	0.85	6.9	5.0	47.8	0.21	0.005

INDIVIDUAL DATA 21-2-4

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Biochemical findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : after Week 2 of recovery

Animal No.	TBA μmol/L	Glucose mg/dL	T-Cho mg/dL	TG mg/dL	UN mg/dL	Crea mg/dL	Na mEq/L	K mEq/L	Cl mEq/L	Ca mg/dL	IP mg/dL
401	10.4	150	58	42	14.1	0.37	144	4.82	104	9.6	7.1
404	14.6	129	53	40	17.2	0.38	144	4.84	107	9.3	7.1
406	9.5	121	57	38	14.4	0.37	147	4.63	107	9.7	6.9
411	7.1	126	64	21	16.4	0.39	144	4.83	105	9.9	7.4
412	2.9	154	66	60	16.6	0.34	145	5.31	104	10.0	6.9
N	5	5	5	5	5	5	5	5	5	5	5
MEAN	8.90	136.0	59.6	40.2	15.74	0.370	144.8	4.886	105.4	9.70	7.08
S.D.	4.31	14.9	5.3	13.9	1.40	0.019	1.3	0.252	1.5	0.27	0.20

INDIVIDUAL DATA 22-1

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Biochemical findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg PERIOD : Day 5 of lactation

				Protein fraction (%)									
					Globulin								
Animal No.	TP g/dL	Albumin g/dL	A/G ratio	Albumin	α_1	α_2	β	γ	AST IU/L	ALT IU/L	ALP IU/L	γ-GTP IU/L	T-Bil mg/dL
151	5.6	3.12	1.26	55.8	18.2	7.1	14.8	4.1	112	70	172	0.7	0.05
152	5.4	2.76	1.05	51.2	20.3	8.7	16.1	3.7	72	44	230	0.9	0.03
154	5.0	2.46	0.98	49.4	18.1	8.5	19.0	5.0	67	31	198	0.7	0.03
159	5.4	2.84	1.11	52.6	17.4	7.6	16.6	5.8	72	33	242	0.7	0.03
161	5.3	2.69	1.04	50.8	20.9	9.1	15.2	4.0	66	39	163	0.6	0.04
N	5	5	5	5	5	5	5	5	5	5	5	5	5
MEAN	5.34	2.774	1.088	51.96	18.98	8.20	16.34	4.52	77.8	43.4	201.0	0.72	0.036
S.D.	0.22	0.240	0.107	2.43	1.53	0.82	1.65	0.86	19.3	15.7	34.7	0.11	0.009

INDIVIDUAL DATA 22-2

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Biochemical findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg PERIOD : Day 5 of lactation

Animal No.	TBA μmol/L	Glucose mg/dL	T-Cho mg/dL	TG mg/dL	UN mg/dL	Crea mg/dL	Na mEq/L	K mEq/L	Cl mEq/L	Ca mg/dL	IP mg/dL
151	22.2	118	55	33	13.4	0.38	142	4.78	103	10.7	9.2
152	8.3	117	60	41	18.4	0.40	143	4.23	104	10.6	9.0
154	4.1	118	44	29	14.1	0.37	142	4.55	107	10.1	8.6
159	10.6	115	68	43	17.1	0.37	142	4.60	103	10.6	9.5
161	5.1	112	53	44	15.1	0.35	144	4.37	106	10.3	8.3
N	5	5	5	5	5	5	5	5	5	5	5
MEAN	10.06	116.0	56.0	38.0	15.62	0.374	142.6	4.506	104.6	10.46	8.92
S.D.	7.26	2.5	8.9	6.6	2.09	0.018	0.9	0.212	1.8	0.25	0.48

INDIVIDUAL DATA 22-3

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Biochemical findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg PERIOD : Day 5 of lactation

				Protein fraction (%)									
					Globulin								
Animal No.	TP g/dL	Albumin g/dL	A/G ratio	Albumin	α_1	α_2	β	γ	AST IU/L	ALT IU/L	ALP IU/L	γ-GTP IU/L	T-Bil mg/dL
256	5.3	2.70	1.03	50.9	16.8	10.9	17.2	4.2	86	48	236	0.9	0.04
257	5.6	2.94	1.10	52.4	20.5	8.3	14.9	3.9	64	38	135	0.3	0.06
259	5.1	2.63	1.06	51.6	15.7	10.4	18.8	3.5	74	36	383	0.5	0.03
260	5.1	2.71	1.14	53.4	16.2	8.2	15.8	6.4	72	37	372	0.1	0.03
262	5.3	2.56	0.93	48.3	21.2	8.8	17.3	4.4	88	49	146	0.7	0.04
N	5	5	5	5	5	5	5	5	5	5	5	5	5
MEAN	5.28	2.708	1.052	51.32	18.08	9.32	16.80	4.48	76.8	41.6	254.4	0.50	0.040
S.D.	0.20	0.143	0.080	1.93	2.57	1.25	1.50	1.13	10.1	6.3	119.1	0.32	0.012

INDIVIDUAL DATA 22-4

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Biochemical findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg PERIOD : Day 5 of lactation

Animal No.	TBA μmol/L	Glucose mg/dL	T-Cho mg/dL	TG mg/dL	UN mg/dL	Crea mg/dL	Na mEq/L	K mEq/L	Cl mEq/L	Ca mg/dL	IP mg/dL
256	14.3	126	60	29	14.3	0.35	141	4.42	103	10.3	9.4
257	22.1	119	75	55	13.2	0.35	143	4.34	104	10.7	8.9
259	7.3	124	50	30	19.3	0.43	143	4.15	106	9.9	9.2
260	7.6	108	58	35	13.0	0.40	141	4.27	107	10.0	7.3
262	5.0	129	55	43	16.3	0.38	144	4.53	107	10.3	9.0
N	5	5	5	5	5	5	5	5	5	5	5
MEAN	11.26	121.2	59.6	38.4	15.22	0.382	142.4	4.342	105.4	10.24	8.76
S.D.	6.98	8.2	9.4	10.8	2.63	0.034	1.3	0.144	1.8	0.31	0.84

INDIVIDUAL DATA 22-5

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Biochemical findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg PERIOD : Day 5 of lactation

				Protein fraction (%)									
					Globulin								
Animal No.	TP g/dL	Albumin g/dL	A/G ratio	Albumin	α_1	α_2	β	γ	AST IU/L	ALT IU/L	ALP IU/L	γ-GTP IU/L	T-Bil mg/dL
352	5.3	2.70	1.04	50.9	17.6	11.0	16.8	3.7	94	41	194	0.8	0.03
355	6.0	2.80	0.87	46.6	22.3	7.4	17.8	5.9	78	46	238	0.5	0.04
357	4.9	2.57	1.11	52.6	18.7	8.1	16.7	3.9	66	46	139	0.8	0.03
358	5.2	2.64	1.03	50.6	17.4	9.8	17.4	4.8	87	43	177	0.4	0.04
360	5.6	2.74	0.96	49.0	22.1	8.4	15.9	4.6	79	42	178	0.5	0.04
N	5	5	5	5	5	5	5	5	5	5	5	5	5
MEAN	5.40	2.690	1.002	49.94	19.62	8.94	16.92	4.58	80.8	43.6	185.2	0.60	0.036
S.D.	0.42	0.089	0.091	2.26	2.41	1.44	0.73	0.87	10.5	2.3	35.8	0.19	0.005

INDIVIDUAL DATA 22-6

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Biochemical findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg PERIOD : Day 5 of lactation

Animal No.	TBA μmol/L	Glucose mg/dL	T-Cho mg/dL	TG mg/dL	UN mg/dL	Crea mg/dL	Na mEq/L	K mEq/L	Cl mEq/L	Ca mg/dL	IP mg/dL
352	8.2	124	64	46	19.2	0.41	143	4.26	106	10.5	8.9
355	16.3	132	64	73	18.4	0.36	143	4.06	103	11.0	9.3
357	10.0	120	51	55	11.4	0.36	144	4.68	107	10.4	8.2
358	9.9	116	74	29	14.3	0.34	141	4.43	106	10.0	7.8
360	9.5	115	64	49	18.3	0.38	143	4.54	105	10.5	8.7
N	5	5	5	5	5	5	5	5	5	5	5
MEAN	10.78	121.4	63.4	50.4	16.32	0.370	142.8	4.394	105.4	10.48	8.58
S.D.	3.17	6.9	8.2	15.9	3.35	0.026	1.1	0.242	1.5	0.36	0.59

INDIVIDUAL DATA 22-7

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Biochemical findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg PERIOD : Day 5 of lactation

				Protein fraction (%)									
					Globulin								
Animal No.	TP g/dL	Albumin g/dL	A/G ratio	Albumin	α_1	α_2	β	γ	AST IU/L	ALT IU/L	ALP IU/L	γ-GTP IU/L	T-Bil mg/dL
451	5.0	2.53	1.03	50.8	18.4	9.3	16.6	4.9	61	36	168	0.6	0.02
452	4.9	2.45	1.00	50.1	17.9	9.5	18.0	4.5	80	40	175	0.5	0.02
456	5.5	2.86	1.08	52.0	18.3	8.6	16.7	4.4	63	38	219	0.5	0.09
458	5.2	2.51	0.93	48.2	19.1	10.4	17.9	4.4	72	37	217	0.3	0.04
462	5.4	2.68	0.99	49.8	19.0	7.2	17.5	6.5	103	36	243	1.1	0.08
N	5	5	5	5	5	5	5	5	5	5	5	5	5
MEAN	5.20	2.606	1.006	50.18	18.54	9.00	17.34	4.94	75.8	37.4	204.4	0.60	0.050
S.D.	0.25	0.165	0.055	1.39	0.50	1.19	0.66	0.90	17.0	1.7	31.8	0.30	0.033

INDIVIDUAL DATA 22-8

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Biochemical findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg PERIOD : Day 5 of lactation

Animal No.	TBA μmol/L	Glucose mg/dL	T-Cho mg/dL	TG mg/dL	UN mg/dL	Crea mg/dL	Na mEq/L	K mEq/L	Cl mEq/L	Ca mg/dL	IP mg/dL
451	12.6	121	59	38	12.9	0.35	142	4.72	106	9.7	8.1
452	11.9	118	59	22	14.0	0.34	143	4.34	106	9.7	8.1
456	32.4	124	54	63	18.6	0.38	142	4.44	102	10.8	9.2
458	8.3	117	60	19	17.1	0.35	143	4.25	105	10.2	8.5
462	6.1	114	54	23	9.4	0.36	143	4.39	107	10.2	7.3
N	5	5	5	5	5	5	5	5	5	5	5
MEAN	14.26	118.8	57.2	33.0	14.40	0.356	142.6	4.428	105.2	10.12	8.24
S.D.	10.48	3.8	2.9	18.3	3.62	0.015	0.5	0.178	1.9	0.45	0.69

INDIVIDUAL DATA 23-1-1

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Biochemical findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 0 mg/kg PERIOD : after Week 6 of administration

Animal No.	TP g/dL	Albumin g/dL	A/G ratio	Protein fraction (%)					AST IU/L	ALT IU/L	ALP IU/L	γ-GTP IU/L	T-Bil mg/dL
				Albumin	Globulin								
					α_1	α_2	β	γ					
163	5.8	3.29	1.31	56.8	18.4	5.7	14.3	4.8	65	28	180	0.7	0.05
164	6.1	3.74	1.59	61.4	15.2	6.5	12.5	4.4	133	61	158	0.4	0.05
165	5.7	3.33	1.40	58.4	16.1	6.2	14.9	4.4	58	23	185	0.9	0.05
166	5.3	2.92	1.24	55.4	16.7	6.0	13.5	8.4	56	15	182	0.5	0.07
167	5.3	2.87	1.19	54.3	17.1	6.4	15.3	6.9	59	21	242	0.7	0.06
N	5	5	5	5	5	5	5	5	5	5	5	5	5
MEAN	5.64	3.230	1.346	57.26	16.70	6.16	14.10	5.78	74.2	29.6	189.4	0.64	0.056
S.D.	0.34	0.353	0.158	2.78	1.19	0.32	1.12	1.79	33.0	18.2	31.3	0.19	0.009

INDIVIDUAL DATA 23-1-2

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Biochemical findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 0 mg/kg PERIOD : after Week 6 of administration

Animal No.	TBA μmol/L	Glucose mg/dL	T-Cho mg/dL	TG mg/dL	UN mg/dL	Crea mg/dL	Na mEq/L	K mEq/L	Cl mEq/L	Ca mg/dL	IP mg/dL
163	15.0	148	74	18	17.6	0.36	143	4.16	106	10.0	7.3
164	13.3	118	61	27	20.8	0.45	145	4.18	106	10.4	7.8
165	6.8	142	64	23	17.2	0.37	144	4.04	108	10.2	6.6
166	5.3	113	49	13	15.9	0.40	145	4.15	106	10.0	7.7
167	8.0	109	51	18	17.4	0.44	144	3.88	106	9.9	7.9
N	5	5	5	5	5	5	5	5	5	5	5
MEAN	9.68	126.0	59.8	19.8	17.78	0.404	144.2	4.082	106.4	10.10	7.46
S.D.	4.23	17.8	10.2	5.4	1.81	0.040	0.8	0.125	0.9	0.20	0.53

INDIVIDUAL DATA 23-1-3

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Biochemical findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 100 mg/kg PERIOD : after Week 6 of administration

Animal No.	TP g/dL	Albumin g/dL	A/G ratio	Protein fraction (%)					AST IU/L	ALT IU/L	ALP IU/L	γ-GTP IU/L	T-Bil mg/dL
				Albumin	Globulin								
					α_1	α_2	β	γ					
463	6.0	3.27	1.20	54.6	18.2	5.5	15.1	6.6	57	26	191	0.4	0.05
464	5.4	3.05	1.30	56.5	15.5	7.2	16.3	4.5	58	25	174	1.0	0.04
465	5.3	2.90	1.20	54.7	16.0	7.6	15.2	6.5	63	18	208	0.7	0.05
466	5.8	3.44	1.47	59.4	16.3	6.0	13.4	4.9	81	33	107	0.8	0.07
467	5.3	2.91	1.22	54.9	15.8	7.0	15.1	7.2	52	20	148	0.5	0.05
N	5	5	5	5	5	5	5	5	5	5	5	5	5
MEAN	5.56	3.114	1.278	56.02	16.36	6.66	15.02	5.94	62.2	24.4	165.6	0.68	0.052
S.D.	0.32	0.236	0.115	2.04	1.07	0.88	1.04	1.17	11.2	5.9	39.6	0.24	0.011

INDIVIDUAL DATA 23-1-4

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Biochemical findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 100 mg/kg PERIOD : after Week 6 of administration

Animal No.	TBA μmol/L	Glucose mg/dL	T-Cho mg/dL	TG mg/dL	UN mg/dL	Crea mg/dL	Na mEq/L	K mEq/L	Cl mEq/L	Ca mg/dL	IP mg/dL
463	6.2	121	85	23	15.1	0.38	143	4.26	105	9.6	7.7
464	8.1	121	52	10	15.0	0.41	145	4.62	108	9.7	8.2
465	9.1	116	48	9	14.2	0.34	144	3.88	107	9.7	6.5
466	11.2	139	57	13	15.8	0.42	144	3.99	106	10.1	6.1
467	11.5	113	59	27	13.5	0.33	145	3.95	106	10.4	7.8
N	5	5	5	5	5	5	5	5	5	5	5
MEAN	9.22	122.0	60.2	16.4	14.72**	0.376	144.2	4.140	106.4	9.90	7.26
S.D.	2.21	10.1	14.5	8.1	0.89	0.040	0.8	0.305	1.1	0.34	0.91

** : Significantly different from the 0 mg/kg group at P ≦0.01 (Dunnett's test).

INDIVIDUAL DATA 23-2-1

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Biochemical findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 0 mg/kg PERIOD : after Week 2 of recovery

				Protein fraction (%)									
					Globulin								
Animal No.	TP g/dL	Albumin g/dL	A/G ratio	Albumin	α_1	α_2	β	γ	AST IU/L	ALT IU/L	ALP IU/L	γ-GTP IU/L	T-Bil mg/dL
168	5.9	3.09	1.10	52.3	19.0	6.4	15.5	6.8	75	42	118	0.4	0.09
169	6.5	3.40	1.09	52.2	18.4	5.9	17.0	6.5	70	36	93	0.8	0.08
170	5.9	3.18	1.17	53.8	18.2	5.7	15.8	6.5	58	31	154	0.9	0.07
171	5.8	3.07	1.12	52.9	20.0	6.8	15.3	5.0	56	27	154	1.0	0.06
172	5.7	3.21	1.29	56.4	19.1	5.8	14.0	4.7	59	29	197	0.4	0.06
N	5	5	5	5	5	5	5	5	5	5	5	5	5
MEAN	5.96	3.190	1.154	53.52	18.94	6.12	15.52	5.90	63.6	33.0	143.2	0.70	0.072
S.D.	0.31	0.131	0.082	1.73	0.71	0.47	1.08	0.97	8.4	6.0	39.6	0.28	0.013

INDIVIDUAL DATA 23-2-2

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Biochemical findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 0 mg/kg PERIOD : after Week 2 of recovery

Animal No.	TBA μmol/L	Glucose mg/dL	T-Cho mg/dL	TG mg/dL	UN mg/dL	Crea mg/dL	Na mEq/L	K mEq/L	Cl mEq/L	Ca mg/dL	IP mg/dL
168	28.2	130	79	40	17.3	0.38	141	4.40	104	10.1	5.8
169	14.7	131	86	53	18.2	0.42	142	4.27	103	10.5	5.6
170	14.0	136	76	62	19.9	0.37	144	4.22	105	10.0	7.0
171	6.6	133	69	16	19.9	0.46	145	4.31	105	9.9	8.5
172	7.5	130	88	28	18.2	0.40	143	4.25	106	10.4	7.6
N	5	5	5	5	5	5	5	5	5	5	5
MEAN	14.20	132.0	79.6	39.8	18.70	0.406	143.0	4.290	104.6	10.18	6.90
S.D.	8.64	2.5	7.7	18.5	1.16	0.036	1.6	0.070	1.1	0.26	1.22

INDIVIDUAL DATA 23-2-3

STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Biochemical findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 100 mg/kg PERIOD : after Week 2 of recovery

Animal No.	TP g/dL	Albumin g/dL	A/G ratio	Protein fraction (%) Albumin	Globulin α_1	Globulin α_2	Globulin β	Globulin γ	AST IU/L	ALT IU/L	ALP IU/L	γ-GTP IU/L	T-Bil mg/dL
468	6.1	3.41	1.27	55.9	17.2	6.2	15.8	4.9	50	23	109	0.4	0.06
469	5.2	2.89	1.24	55.5	14.7	6.3	17.1	6.4	49	19	127	0.4	0.06
470	6.7	3.85	1.35	57.4	18.5	5.4	12.6	6.1	76	40	91	0.4	0.06
471	5.7	3.44	1.53	60.5	13.9	5.9	14.7	5.0	51	17	143	0.5	0.05
472	5.6	3.30	1.43	58.9	15.0	6.3	14.6	5.2	59	25	106	0.5	0.08
N	5	5	5	5	5	5	5	5	5	5	5	5	5
MEAN	5.86	3.378	1.364*	57.64**	15.86**	6.02	14.96	5.52	57.0	24.8	115.2	0.44	0.062
S.D.	0.57	0.343	0.119	2.09	1.92	0.38	1.66	0.68	11.3	9.1	20.1	0.05	0.011

* : Significantly different from the 0 mg/kg group at $p \leqq 0.05$ (Dunnett's test).

** : Significantly different from the 0 mg/kg group at $p \leqq 0.01$ (Dunnett's test).

INDIVIDUAL DATA 23-2-4
STUDY NO. SR11087 TITLE: indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Biochemical findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 100 mg/kg PERIOD : after Week 2 of recovery

Animal No.	TBA μmol/L	Glucose mg/dL	T-Cho mg/dL	TG mg/dL	UN mg/dL	Crea mg/dL	Na mEq/L	K mEq/L	Cl mEq/L	Ca mg/dL	IP mg/dL
468	6.2	127	81	38	16.5	0.40	143	4.12	106	10.2	5.7
469	13.2	135	59	22	17.2	0.33	143	4.02	105	9.7	7.4
470	14.1	122	98	53	19.3	0.41	143	3.97	104	10.4	6.8
471	5.0	122	77	22	18.0	0.40	145	4.24	106	9.9	8.4
472	5.4	118	62	19	18.3	0.38	144	4.18	106	10.0	8.4
N	5	5	5	5	5	5	5	5	5	5	5
MEAN	8.78	124.8	75.4	30.8	17.86	0.384	143.6	4.106*	105.4	10.04	7.34
S.D.	4.48	6.5	15.8	14.5	1.07	0.032	0.9	0.111	0.9	0.27	1.14

* : Significantly different from the 0 mg/kg group at $p \leqq 0.05$ (Dunnett's test).

INDIVIDUAL DATA 24-1-1
STUDY NO. SR11087 TITLE : indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Gross findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : after Week 6 of administration

Animal No.	Findings	Other description
101	No abnormal findings	Euthanasia on next day of Day 42 of administration
102	No abnormal findings	Euthanasia on next day of Day 42 of administration
103	No abnormal findings	Euthanasia on next day of Day 42 of administration
109	Epididymis (left) : Yellowish white mass, cauda (15 x 10 x 5, mm)	Euthanasia on next day of Day 42 of administration
110	No abnormal findings	Euthanasia on next day of Day 42 of administration
111	No abnormal findings	Euthanasia on next day of Day 42 of administration
112	No abnormal findings	Euthanasia on next day of Day 42 of administration

INDIVIDUAL DATA 24-1-2
STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Gross findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : after Week 6 of administration

Animal No.	Findings	Other description
201	No abnormal findings	Euthanasia on next day of Day 42 of administration
202	No abnormal findings	Euthanasia on next day of Day 42 of administration
203	No abnormal findings	Euthanasia on next day of Day 42 of administration
204	No abnormal findings	Euthanasia on next day of Day 42 of administration
205	No abnormal findings	Euthanasia on next day of Day 42 of administration
206	No abnormal findings	Euthanasia on next day of Day 42 of administration
207	No abnormal findings	Euthanasia on next day of Day 42 of administration
208	Epididymis (left) : Yellowish white patch, cauda (5 x 5, mm)	Euthanasia on next day of Day 42 of administration
209	No abnormal findings	Euthanasia on next day of Day 42 of administration
210	No abnormal findings	Euthanasia on next day of Day 42 of administration
211	No abnormal findings	Euthanasia on next day of Day 42 of administration
212	No abnormal findings	Euthanasia on next day of Day 42 of administration

INDIVIDUAL DATA 24-1-3

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Gross findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : after Week 6 of administration

Animal No.	Findings	Other description
301	No abnormal findings	Euthanasia on next day of Day 42 of administration
302	No abnormal findings	Euthanasia on next day of Day 42 of administration
303	No abnormal findings	Euthanasia on next day of Day 42 of administration
304	No abnormal findings	Euthanasia on next day of Day 42 of administration
305	No abnormal findings	Euthanasia on next day of Day 42 of administration
306	No abnormal findings	Euthanasia on next day of Day 42 of administration
307	No abnormal findings	Euthanasia on next day of Day 42 of administration
308	No abnormal findings	Euthanasia on next day of Day 42 of administration
309	No abnormal findings	Euthanasia on next day of Day 42 of administration
310	No abnormal findings	Euthanasia on next day of Day 42 of administration
311	No abnormal findings	Euthanasia on next day of Day 42 of administration
312	No abnormal findings	Euthanasia on next day of Day 42 of administration

INDIVIDUAL DATA 24-1-4
STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Gross findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : after Week 6 of administration

Animal No.	Findings	Other description
402	No abnormal findings	Euthanasia on next day of Day 42 of administration
403	No abnormal findings	Euthanasia on next day of Day 42 of administration
405	Epididymis (right) : Yellowish white patch, cauda (3 x 3, mm)	Euthanasia on next day of Day 42 of administration
407	No abnormal findings	Euthanasia on next day of Day 42 of administration
408	No abnormal findings	Euthanasia on next day of Day 42 of administration
409	Epididymis (left) : Yellowish white patch, cauda (3 x 2, mm)	Euthanasia on next day of Day 42 of administration
410	No abnormal findings	Euthanasia on next day of Day 42 of administration

INDIVIDUAL DATA 24-2-1
STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Gross findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : after Week 2 of recovery

Animal No.	Findings	Other description
104	No abnormal findings	Euthanasia on next day of Day 14 of recovery
105	No abnormal findings	Euthanasia on next day of Day 14 of recovery
106	No abnormal findings	Euthanasia on next day of Day 14 of recovery
107	No abnormal findings	Euthanasia on next day of Day 14 of recovery
108	No abnormal findings	Euthanasia on next day of Day 14 of recovery

INDIVIDUAL DATA 24-2-2
STUDY NO. SR11087 TITLE : indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Gross findings ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : after Week 2 of recovery

Animal No.	Findings	Other description
401	No abnormal findings	Euthanasia on next day of Day 14 of recovery
404	No abnormal findings	Euthanasia on next day of Day 14 of recovery
406	No abnormal findings	Euthanasia on next day of Day 14 of recovery
411	No abnormal findings	Euthanasia on next day of Day 14 of recovery
412	No abnormal findings	Euthanasia on next day of Day 14 of recovery

INDIVIDUAL DATA 25-1-1
STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Gross findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg PERIOD : Day 5 of lactation

Animal No.	Findings	Other description
151	No abnormal findings	Euthanasia on Day 5 of lactation
152	No abnormal findings	Euthanasia on Day 5 of lactation
153	No abnormal findings	Euthanasia on Day 5 of lactation
154	No abnormal findings	Euthanasia on Day 5 of lactation
155	Forestomach : Black patch, mucosa, multifocal (less than 3×3, mm) Glandular stomach : Black patch, mucosa, multifocal (less than 2×2, mm) Spleen : Atrophy Thymus : Atrophy Adrenal (right and left) : Hypertrophy	Died on Day 3 of Lactation
156	No abnormal findings	Euthanasia on Day 5 of lactation
157	No abnormal findings	Euthanasia on Day 5 of lactation
158	No abnormal findings	Euthanasia on Day 5 of lactation
159	No abnormal findings	Euthanasia on Day 5 of lactation
160	No abnormal findings	Euthanasia on Day 5 of lactation
161	No abnormal findings	Euthanasia on Day 5 of lactation
162	Stomach : White mass, limiting ridge (1×1×1, mm)	Euthanasia on Day 5 of lactation

INDIVIDUAL DATA 25-1-2

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Gross findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg PERIOD : Day 5 of lactation

Animal No.	Findings	Other description
251	No abnormal findings	Euthanasia on Day 5 of lactation
252	No abnormal findings	Euthanasia on Day 5 of lactation
253	No abnormal findings	Euthanasia on Day 5 of lactation
254	No abnormal findings	Euthanasia on Day 5 of lactation
255	Stomach : Thickening, limiting ridge	Euthanasia on Day 5 of lactation
	Forestomach : Thickening, mucosa (crateriform)	
	Recessed area, mucosa	
	Adhesion, adipose tissue	
	Liver : Yellowish brown discoloration	
	Thymus : Atrophy	
256	No abnormal findings	Euthanasia on Day 5 of lactation
257	No abnormal findings	Euthanasia on Day 5 of lactation
258	No abnormal findings	Euthanasia on Day 5 of lactation
259	Glandular stomach : Black patch, mucosa (6×3, mm)	Euthanasia on Day 5 of lactation
260	No abnormal findings	Euthanasia on Day 5 of lactation
261	No abnormal findings	Euthanasia on Day 5 of lactation
262	No abnormal findings	Euthanasia on Day 5 of lactation

INDIVIDUAL DATA 25-1-3
STUDY NO. SR11087 TITLE : indene ：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Gross findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg PERIOD : Day 5 of lactation

Animal No.	Findings	Other description
351	No abnormal findings	Euthanasia on Day 5 of lactation
352	No abnormal findings	Euthanasia on Day 5 of lactation
353	No abnormal findings	Euthanasia on Day 5 of lactation
354	No abnormal findings	Euthanasia on Day 5 of lactation
355	No abnormal findings	Euthanasia on Day 5 of lactation
356	No abnormal findings	Euthanasia on Day 5 of lactation
357	No abnormal findings	Euthanasia on Day 5 of lactation
358	No abnormal findings	Euthanasia on Day 5 of lactation
359	No abnormal findings	Euthanasia on Day 5 of lactation
360	No abnormal findings	Euthanasia on Day 5 of lactation
361	Skin of left inguinal region : Subcutaneous greenish brown mass (15×10×5, mm)	Euthanasia on Day 5 of lactation
362	No abnormal findings	Euthanasia on Day 5 of lactation

INDIVIDUAL DATA 25-1-4
STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Gross findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg PERIOD : Day 5 of lactation

Animal No.	Findings	Other description
451	Kidney (left) : Dilatation, renal pelvis	Euthanasia on Day 5 of lactation
452	No abnormal findings	Euthanasia on Day 5 of lactation
453	No abnormal findings	Euthanasia on Day 5 of lactation
454	No abnormal findings	Euthanasia on Day 5 of lactation
455	No abnormal findings	Euthanasia on Day 5 of lactation
456	No abnormal findings	Euthanasia on Day 5 of lactation
457	No abnormal findings	Euthanasia on Day 5 of lactation
458	No abnormal findings	Euthanasia on Day 5 of lactation
459	No abnormal findings	Euthanasia on Day 5 of lactation
460	No abnormal findings	Euthanasia on Day 5 of lactation
461	No abnormal findings	Euthanasia on Day 5 of lactation
462	No abnormal findings	Euthanasia on Day 5 of lactation

INDIVIDUAL DATA 26-1-1
STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Gross findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 0 mg/kg PERIOD : after Week 6 of administration

Animal No.	Findings	Other description
163	Glandular stomach : Black patch, mucosa (2 x 1, mm)	Euthanasia on next day of Day 42 of administration
164	No abnormal findings	Euthanasia on next day of Day 42 of administration
165	No abnormal findings	Euthanasia on next day of Day 42 of administration
166	No abnormal findings	Euthanasia on next day of Day 42 of administration
167	No abnormal findings	Euthanasia on next day of Day 42 of administration

INDIVIDUAL DATA 26-1-2
STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Gross findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 100 mg/kg PERIOD : after Week 6 of administration

Animal No.	Findings	Other description
463	No abnormal findings	Euthanasia on next day of Day 42 of administration
464	Glandular stomach : Elevated area, mucosa (2 x 2, mm)	Euthanasia on next day of Day 42 of administration
465	No abnormal findings	Euthanasia on next day of Day 42 of administration
466	No abnormal findings	Euthanasia on next day of Day 42 of administration
467	No abnormal findings	Euthanasia on next day of Day 42 of administration

INDIVIDUAL DATA 26-2-1
STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Gross findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 0 mg/kg PERIOD : after Week 2 of recovery

Animal No.	Findings	Other description
168	No abnormal findings	Euthanasia on next day of Day 14 of recovery
169	No abnormal findings	Euthanasia on next day of Day 14 of recovery
170	No abnormal findings	Euthanasia on next day of Day 14 of recovery
171	No abnormal findings	Euthanasia on next day of Day 14 of recovery
172	No abnormal findings	Euthanasia on next day of Day 14 of recovery

INDIVIDUAL DATA 26-2-2
STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Gross findings ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 100 mg/kg PERIOD : after Week 2 of recovery

Animal No.	Findings	Other description
468	No abnormal findings	Euthanasia on next day of Day 14 of recovery
469	No abnormal findings	Euthanasia on next day of Day 14 of recovery
470	No abnormal findings	Euthanasia on next day of Day 14 of recovery
471	No abnormal findings	Euthanasia on next day of Day 14 of recovery
472	No abnormal findings	Euthanasia on next day of Day 14 of recovery

INDIVIDUAL DATA 27-1-1

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weights ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : After Week 6 of administration

	Body weight	Liver		Kidney		Spleen		Heart		Brain		Pituitary gland		Thymus		Thyroid		Adrenal	
Animal No.	g	g	%	g	%	g	%	g	%	g	%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%
101	429	9.41	2.19	2.92	0.68	0.79	0.18	1.23	0.29	2.18	0.51	11.2	2.61	215	50.12	23.1	5.38	53	12.35
102	476	11.65	2.45	3.30	0.69	0.66	0.14	1.42	0.30	2.20	0.46	16.0	3.36	283	59.45	23.2	4.87	68	14.29
103	474	12.71	2.68	3.18	0.67	0.60	0.13	1.41	0.30	2.20	0.46	13.4	2.83	349	73.63	21.3	4.49	79	16.67
109	529	14.05	2.66	3.37	0.64	0.86	0.16	1.64	0.31	2.21	0.42	13.7	2.59	505	95.46	15.9	3.01	75	14.18
110	583	16.92	2.90	3.93	0.67	0.96	0.16	1.64	0.28	2.24	0.38	12.3	2.11	343	58.83	29.0	4.97	74	12.69
111	567	13.97	2.46	3.67	0.65	1.24	0.22	1.65	0.29	2.21	0.39	15.2	2.68	263	46.38	31.1	5.49	72	12.70
112	537	14.59	2.72	3.88	0.72	0.77	0.14	1.63	0.30	2.24	0.42	11.9	2.22	222	41.34	20.3	3.78	61	11.36
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	513.6	13.329	2.580	3.464	0.674	0.840	0.161	1.517	0.296	2.211	0.434	13.39	2.629	311.4	60.744	23.41	4.570	68.9	13.463
S.D.	55.7	2.380	0.232	0.375	0.026	0.213	0.031	0.165	0.010	0.022	0.045	1.75	0.411	100.3	18.584	5.18	0.896	9.0	1.748

INDIVIDUAL DATA 27-1-2

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weights ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : After Week 6 of administration

Animal No.	Body weight	Testis		Epididymis		Prostate		Seminal vesicle	
	g	g	%	g	%	mg	10^{-3}%	g	%
101	429	3.06	0.71	1.36	0.32	871	203.03	2.08	0.48
102	476	3.50	0.74	1.24	0.26	672	141.18	2.35	0.49
103	474	3.48	0.73	1.30	0.27	793	167.30	2.45	0.52
109	529	3.50	0.66	1.82	0.34	736	139.13	2.00	0.38
110	583	3.50	0.60	1.47	0.25	616	105.66	2.22	0.38
111	567	3.92	0.69	1.67	0.29	1175	207.23	2.94	0.52
112	537	3.30	0.61	1.32	0.25	984	183.24	1.80	0.34
N	7	7	7	7	7	7	7	7	7
MEAN	513.6	3.466	0.677	1.454	0.283	835.3	163.824	2.263	0.444
S.D.	55.7	0.259	0.056	0.215	0.035	193.7	37.229	0.370	0.075

INDIVIDUAL DATA 27-1-3

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weights ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : After Week 6 of administration

Animal No.	Body weight	Liver		Kidney		Spleen		Heart		Brain		Pituitary gland		Thymus		Thyroid		Adrenal	
	g	g	%	g	%	g	%	g	%	g	%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%
201	481	12.22	2.54	2.78	0.58	0.76	0.16	1.49	0.31	2.00	0.42	13.7	2.85	259	53.85	24.9	5.18	52	10.81
202	473	12.45	2.63	2.95	0.62	0.70	0.15	1.41	0.30	2.21	0.47	10.4	2.20	297	62.79	21.8	4.61	64	13.53
203	498	13.86	2.78	3.62	0.73	0.65	0.13	1.37	0.28	2.10	0.42	13.3	2.67	250	50.20	20.4	4.10	91	18.27
204	508	13.03	2.56	3.20	0.63	0.73	0.14	1.53	0.30	2.13	0.42	12.2	2.40	425	83.66	23.7	4.67	75	14.76
205	505	13.43	2.66	3.49	0.69	0.76	0.15	1.36	0.27	2.21	0.44	12.5	2.48	385	76.24	32.5	6.44	58	11.49
206	473	12.07	2.55	2.89	0.61	0.48	0.10	1.35	0.29	2.08	0.44	12.4	2.62	224	47.36	21.0	4.44	69	14.59
207	539	15.36	2.85	3.82	0.71	0.78	0.14	1.33	0.25	2.07	0.38	13.7	2.54	326	60.48	25.8	4.79	62	11.50
208	496	12.70	2.56	3.28	0.66	0.66	0.13	1.40	0.28	2.24	0.45	14.7	2.96	237	47.78	18.1	3.65	64	12.90
209	527	16.09	3.05	3.46	0.66	0.94	0.18	1.54	0.29	2.13	0.40	11.3	2.14	240	45.54	19.9	3.78	84	15.94
210	550	14.42	2.62	3.54	0.64	0.74	0.13	1.54	0.28	2.32	0.42	16.4	2.98	263	47.82	19.1	3.47	65	11.82
211	535	14.47	2.70	3.84	0.72	0.87	0.16	1.51	0.28	2.16	0.40	13.7	2.56	380	71.03	27.1	5.07	71	13.27
212	554	16.37	2.95	4.09	0.74	0.83	0.15	1.65	0.30	2.27	0.41	14.3	2.58	356	64.26	28.6	5.16	64	11.55
N	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
MEAN	511.6	13.873	2.704	3.413	0.666	0.742	0.143	1.457	0.286	2.160	0.423	13.22	2.582	303.5	59.251	23.58	4.613	68.3	13.369
S.D.	28.9	1.487	0.169	0.407	0.052	0.117	0.020	0.100	0.016	0.093	0.025	1.60	0.264	68.6	12.667	4.34	0.821	10.8	2.207

INDIVIDUAL DATA 27-1-4

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weights ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 4 mg/kg PERIOD : After Week 6 of administration

Animal No.	Body weight	Testis		Epididymis		Prostate		Seminal vesicle	
	g	g	%	g	%	mg	10^{-3}%	g	%
201	481	3.15	0.65	1.23	0.26	732	152.18	2.37	0.49
202	473	3.15	0.67	1.39	0.29	698	147.57	2.40	0.51
203	498	3.26	0.65	1.49	0.30	444	89.16	2.58	0.52
204	508	3.30	0.65	1.37	0.27	917	180.51	2.22	0.44
205	505	3.35	0.66	1.32	0.26	999	197.82	2.37	0.47
206	473	2.97	0.63	1.23	0.26	639	135.10	2.29	0.48
207	539	3.09	0.57	1.34	0.25	737	136.73	2.72	0.50
208	496	3.42	0.69	1.54	0.31	758	152.82	2.40	0.48
209	527	3.50	0.66	1.50	0.28	464	88.05	2.47	0.47
210	550	3.42	0.62	1.56	0.28	1021	185.64	2.29	0.42
211	535	3.29	0.61	1.55	0.29	963	180.00	2.39	0.45
212	554	3.25	0.59	1.42	0.26	782	141.16	2.04	0.37
N	12	12	12	12	12	12	12	12	12
MEAN	511.6	3.263	0.638	1.412	0.276	762.8	148.895	2.378	0.467
S.D.	28.9	0.153	0.035	0.118	0.019	190.4	34.912	0.171	0.042

INDIVIDUAL DATA 27-1-5

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weights ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : After Week 6 of administration

Animal No.	Body weight	Liver		Kidney		Spleen		Heart		Brain		Pituitary gland		Thymus		Thyroid		Adrenal	
	g	g	%	g	%	g	%	g	%	g	%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%
301	497	13.33	2.68	3.48	0.70	0.73	0.15	1.28	0.26	2.19	0.44	12.1	2.43	196	39.44	25.2	5.07	57	11.47
302	459	13.20	2.88	3.12	0.68	0.78	0.17	1.43	0.31	2.22	0.48	12.7	2.77	254	55.34	27.1	5.90	63	13.73
303	515	13.24	2.57	3.27	0.63	0.61	0.12	1.48	0.29	2.23	0.43	13.0	2.52	362	70.29	21.8	4.23	57	11.07
304	456	11.84	2.60	3.08	0.68	0.80	0.18	1.26	0.28	2.07	0.45	13.3	2.92	273	59.87	23.1	5.07	71	15.57
305	489	12.10	2.47	3.17	0.65	0.90	0.18	1.36	0.28	2.26	0.46	13.3	2.72	222	45.40	19.0	3.89	48	9.82
306	493	12.07	2.45	3.53	0.72	0.75	0.15	1.51	0.31	2.17	0.44	13.3	2.70	276	55.98	29.2	5.92	63	12.78
307	491	12.99	2.65	3.13	0.64	0.78	0.16	1.47	0.30	2.18	0.44	12.5	2.55	408	83.10	22.3	4.54	62	12.63
308	488	12.16	2.49	2.89	0.59	0.77	0.16	1.39	0.28	2.29	0.47	14.4	2.95	361	73.98	22.3	4.57	76	15.57
309	553	14.37	2.60	3.13	0.57	1.13	0.20	1.56	0.28	2.19	0.40	12.6	2.28	404	73.06	24.2	4.38	69	12.48
310	523	15.54	2.97	3.71	0.71	0.66	0.13	1.55	0.30	2.26	0.43	16.3	3.12	230	43.98	23.4	4.47	60	11.47
311	540	15.18	2.81	3.71	0.69	0.84	0.16	1.44	0.27	2.17	0.40	14.2	2.63	494	91.48	31.2	5.78	81	15.00
312	500	11.88	2.38	3.36	0.67	0.81	0.16	1.53	0.31	2.25	0.45	12.4	2.48	234	46.80	24.0	4.80	64	12.80
N	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
MEAN	500.3	13.158	2.629	3.298	0.661	0.797	0.160	1.438	0.289	2.207	0.441	13.34	2.673	309.5	61.560	24.40	4.885	64.3	12.866
S.D.	28.9	1.278	0.181	0.261	0.047	0.130	0.022	0.100	0.017	0.059	0.024	1.16	0.241	93.5	16.711	3.37	0.677	9.0	1.823

INDIVIDUAL DATA 27-1-6

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weights ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 20 mg/kg PERIOD : After Week 6 of administration

Animal No.	Body weight	Testis		Epididymis		Prostate		Seminal vesicle	
	g	g	%	g	%	mg	10^{-3}%	g	%
301	497	3.68	0.74	1.27	0.26	689	138.63	2.25	0.45
302	459	3.27	0.71	1.44	0.31	895	194.99	2.34	0.51
303	515	3.42	0.66	1.26	0.24	644	125.05	2.56	0.50
304	456	3.26	0.71	1.44	0.32	912	200.00	2.60	0.57
305	489	3.48	0.71	1.46	0.30	1102	225.36	1.96	0.40
306	493	3.55	0.72	1.47	0.30	622	126.17	2.45	0.50
307	491	3.26	0.66	1.37	0.28	562	114.46	2.23	0.45
308	488	3.52	0.72	1.34	0.27	625	128.07	2.13	0.44
309	553	3.28	0.59	1.53	0.28	933	168.72	2.43	0.44
310	523	3.36	0.64	1.35	0.26	763	145.89	2.34	0.45
311	540	3.38	0.63	1.45	0.27	547	101.30	2.19	0.41
312	500	3.11	0.62	1.46	0.29	784	156.80	1.92	0.38
N	12	12	12	12	12	12	12	12	12
MEAN	500.3	3.381	0.676	1.403	0.282	756.5	152.120	2.283	0.458
S.D.	28.9	0.158	0.049	0.084	0.023	172.9	38.136	0.214	0.053

INDIVIDUAL DATA 27-1-7

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weights ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : After Week 6 of administration

	Body weight	Liver		Kidney		Spleen		Heart		Brain		Pituitary gland		Thymus		Thyroid		Adrenal	
Animal No.	g	g	%	g	%	g	%	g	%	g	%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%
402	452	11.08	2.45	3.03	0.67	0.74	0.16	1.22	0.27	2.20	0.49	11.4	2.52	252	55.75	26.0	5.75	47	10.40
403	433	11.24	2.60	3.00	0.69	0.61	0.14	1.28	0.30	2.22	0.51	10.4	2.40	352	81.29	19.4	4.48	63	14.55
405	455	13.59	2.99	3.18	0.70	0.60	0.13	1.51	0.33	2.23	0.49	11.5	2.53	302	66.37	17.6	3.87	65	14.29
407	514	14.25	2.77	3.27	0.64	1.05	0.20	1.60	0.31	2.24	0.44	14.3	2.78	344	66.93	18.8	3.66	58	11.28
408	500	13.54	2.71	3.91	0.78	0.92	0.18	1.42	0.28	2.27	0.45	14.1	2.82	324	64.80	23.4	4.68	63	12.60
409	487	13.53	2.78	3.37	0.69	0.78	0.16	1.48	0.30	2.22	0.46	13.1	2.69	181	37.17	18.3	3.76	73	14.99
410	526	13.46	2.56	3.52	0.67	1.00	0.19	1.42	0.27	2.28	0.43	12.6	2.40	219	41.63	20.6	3.92	61	11.60
N	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7
MEAN	481.0	12.956	2.694	3.326	0.691	0.814	0.166	1.419	0.294	2.237	0.467	12.49	2.591	282.0	59.134	20.59	4.303	61.4	12.816
S.D.	35.0	1.256	0.177	0.316	0.044	0.181	0.026	0.131	0.022	0.029	0.030	1.46	0.173	65.8	15.472	3.05	0.743	7.9	1.809

INDIVIDUAL DATA 27-1-8

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weights ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : After Week 6 of administration

Animal No.	Body weight	Testis		Epididymis		Prostate		Seminal vesicle	
	g	g	%	g	%	mg	10^{-3}%	g	%
402	452	2.96	0.65	1.41	0.31	990	219.03	2.35	0.52
403	433	3.34	0.77	1.32	0.30	391	90.30	1.85	0.43
405	455	3.28	0.72	1.30	0.29	886	194.73	2.26	0.50
407	514	3.17	0.62	1.26	0.25	903	175.68	1.96	0.38
408	500	3.38	0.68	1.63	0.33	918	183.60	2.75	0.55
409	487	3.66	0.75	1.39	0.29	527	108.21	2.17	0.45
410	526	3.40	0.65	1.31	0.25	792	150.57	2.39	0.45
N	7	7	7	7	7	7	7	7	7
MEAN	481.0	3.313	0.691	1.374	0.289	772.4	160.303	2.247	0.469
S.D.	35.0	0.216	0.056	0.124	0.030	225.3	46.766	0.297	0.058

INDIVIDUAL DATA 27-2-1

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weights ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : After Week 2 of recovery

Animal No.	Body weight	Liver		Kidney		Spleen		Heart		Brain		Pituitary gland		Thymus		Thyroid		Adrenal	
	g	g	%	g	%	g	%	g	%	g	%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%
104	498	14.01	2.81	3.28	0.66	0.78	0.16	1.54	0.31	2.22	0.45	13.5	2.71	235	47.19	29.2	5.86	57	11.45
105	481	11.80	2.45	2.92	0.61	0.70	0.15	1.48	0.31	2.23	0.46	14.4	2.99	380	79.00	25.3	5.26	50	10.40
106	535	13.78	2.58	3.13	0.59	0.67	0.13	1.37	0.26	2.21	0.41	12.4	2.32	309	57.76	24.4	4.56	58	10.84
107	539	13.17	2.44	3.35	0.62	0.74	0.14	1.52	0.28	2.28	0.42	12.3	2.28	348	64.56	30.5	5.66	63	11.69
108	533	14.60	2.74	3.50	0.66	0.94	0.18	1.64	0.31	2.12	0.40	11.0	2.06	386	72.42	20.3	3.81	55	10.32
N	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
MEAN	517.2	13.472	2.604	3.236	0.628	0.766	0.152	1.510	0.294	2.212	0.428	12.72	2.472	331.6	64.186	25.94	5.030	56.6	10.940
S.D.	26.1	1.066	0.167	0.221	0.031	0.106	0.019	0.098	0.023	0.058	0.026	1.29	0.372	62.1	12.425	4.06	0.844	4.7	0.614

INDIVIDUAL DATA 27-2-2

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weights ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 0 mg/kg PERIOD : After Week 2 of recovery

Animal No.	Body weight	Testis		Epididymis		Prostate		Seminal vesicle	
	g	g	%	g	%	mg	10^{-3}%	g	%
104	498	3.42	0.69	1.37	0.28	983	197.39	2.03	0.41
105	481	3.06	0.64	1.31	0.27	1071	222.66	2.26	0.47
106	535	3.19	0.60	1.32	0.25	947	177.01	2.15	0.40
107	539	3.62	0.67	1.41	0.26	987	183.12	2.65	0.49
108	533	3.40	0.64	1.40	0.26	874	163.98	2.18	0.41
N	5	5	5	5	5	5	5	5	5
MEAN	517.2	3.338	0.648	1.362	0.264	972.4	188.832	2.254	0.436
S.D.	26.1	0.218	0.034	0.045	0.011	71.4	22.403	0.236	0.041

INDIVIDUAL DATA 27-2-3

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weights ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : After Week 2 of recovery

Animal No.	Body weight	Liver		Kidney		Spleen		Heart		Brain		Pituitary gland		Thymus		Thyroid		Adrenal	
	g	g	%	g	%	g	%	g	%	g	%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%
401	485	11.36	2.34	2.71	0.56	0.77	0.16	1.38	0.28	2.17	0.45	10.2	2.10	405	83.51	19.0	3.92	54	11.13
404	483	11.77	2.44	3.01	0.62	0.67	0.14	1.32	0.27	1.96	0.41	13.0	2.69	272	56.31	19.1	3.95	54	11.18
406	488	12.88	2.64	3.51	0.72	0.71	0.15	1.45	0.30	2.17	0.44	13.0	2.66	234	47.95	23.6	4.84	57	11.68
411	503	12.02	2.39	3.41	0.68	0.72	0.14	1.42	0.28	2.24	0.45	15.9	3.16	392	77.93	26.9	5.35	57	11.33
412	526	13.87	2.64	3.57	0.68	0.62	0.12	1.36	0.26	2.30	0.44	15.2	2.89	277	52.66	26.4	5.02	79	15.02
N	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
MEAN	497.0	12.380	2.490	3.242	0.652	0.698	0.142	1.386*	0.278	2.168	0.438	13.46	2.700	316.0	63.672	23.00	4.616	60.2	12.068
S.D.	18.0	1.002	0.141	0.369	0.063	0.056	0.015	0.051	0.015	0.128	0.016	2.24	0.390	77.3	15.965	3.82	0.648	10.6	1.664

* : Significantly different from the 0 mg/kg group at $p \leqq 0.05$ (Dunnett's test).

INDIVIDUAL DATA 27-2-4

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weights ANIMAL : Rat, Crl:CD(SD) SEX : Male GROUP : 100 mg/kg PERIOD : After Week 2 of recovery

Animal No.	Body weight	Testis		Epididymis		Prostate		Seminal vesicle	
	g	g	%	g	%	mg	10^{-3}%	g	%
401	485	3.32	0.68	1.34	0.28	656	135.26	1.96	0.40
404	483	3.40	0.70	1.52	0.31	626	129.61	1.93	0.40
406	488	2.88	0.59	1.36	0.28	1010	206.97	2.01	0.41
411	503	3.38	0.67	1.48	0.29	503	100.00	2.02	0.40
412	526	3.14	0.60	1.44	0.27	570	108.37	1.71	0.33
N	5	5	5	5	5	5	5	5	5
MEAN	497.0	3.224	0.648	1.428	0.286*	673.0*	136.042*	1.926*	0.388
S.D.	18.0	0.218	0.050	0.077	0.015	197.2	42.242	0.126	0.033

* : Significantly different from the 0 mg/kg group at $p \leqq 0.05$ (Dunnett's test).

INDIVIDUAL DATA 28-1

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weights ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg PERIOD : Day 5 of lactation

	Body weight	Liver		Kidney		Spleen		Heart		Brain		Pituitary gland		Thymus		Thyroid		Adrenal	
Animal No.	g	g	%	g	%	g	%	g	%	g	%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%
151	318	9.12	2.87	1.80	0.57	0.62	0.19	0.98	0.31	2.14	0.67	18.8	5.91	293	92.14	19.3	6.07	78	24.53
152	298	11.02	3.70	1.95	0.65	0.87	0.29	1.06	0.36	1.97	0.66	22.7	7.62	249	83.56	17.3	5.81	83	27.85
153	318	10.53	3.31	2.16	0.68	0.81	0.25	0.97	0.31	1.96	0.62	19.3	6.07	284	89.31	16.4	5.16	84	26.42
154	320	9.96	3.11	2.04	0.64	0.75	0.23	1.06	0.33	2.04	0.64	20.7	6.47	312	97.50	15.9	4.97	80	25.00
155[a]	(241)	(11.11)	#	(1.93)	#	(0.23)	#	(1.16)	#	(2.04)	#	(17.5)	#	(55)	#	(15.5)	#	(228)	#
156	299	9.15	3.06	2.08	0.70	0.75	0.25	0.92	0.31	2.06	0.69	16.9	5.65	172	57.53	17.7	5.92	85	28.43
157	318	10.96	3.45	2.05	0.64	0.80	0.25	0.98	0.31	2.16	0.68	18.8	5.91	138	43.40	17.0	5.35	87	27.36
158	317	11.07	3.49	2.39	0.75	0.69	0.22	1.07	0.34	2.03	0.64	17.1	5.39	244	76.97	18.4	5.80	76	23.97
159	348	11.33	3.26	2.24	0.64	0.87	0.25	1.06	0.30	2.13	0.61	15.0	4.31	224	64.37	15.5	4.45	74	21.26
160	314	9.48	3.02	2.18	0.69	0.76	0.24	1.01	0.32	2.09	0.67	18.1	5.76	256	81.53	14.9	4.75	80	25.48
161	302	10.14	3.36	1.91	0.63	0.67	0.22	1.20	0.40	2.06	0.68	16.4	5.43	273	90.40	15.2	5.03	84	27.81
162	369	12.31	3.34	2.42	0.66	1.16	0.31	1.11	0.30	2.14	0.58	20.1	5.45	268	72.63	22.6	6.12	91	24.66
N	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
MEAN	320.1	10.461	3.270	2.111	0.659	0.795	0.245	1.038	0.326	2.071	0.649	18.54	5.815	246.6	77.213	17.29	5.403	82.0	25.706
S.D.	21.2	0.997	0.239	0.192	0.046	0.144	0.033	0.077	0.030	0.068	0.034	2.17	0.808	51.9	16.524	2.23	0.572	5.0	2.133

a : Died on Day 3 of Lactation .

Values in parentheses are excluded from the statistical calculation (reference data).

: Not applicable.

INDIVIDUAL DATA 28-2

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weights ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg PERIOD : Day 5 of lactation

Animal No.	Body weight	Ovary		Uterus	
	g	mg	10^{-3}%	g	%
151	318	129	40.57	0.70	0.22
152	298	139	46.64	0.76	0.26
153	318	138	43.40	0.65	0.20
154	320	110	34.38	0.69	0.22
155[a]	(241)	(91)	#	(1.71)	#
156	299	109	36.45	0.56	0.19
157	318	145	45.60	0.90	0.28
158	317	116	36.59	0.61	0.19
159	348	131	37.64	0.91	0.26
160	314	106	33.76	0.78	0.25
161	302	135	44.70	0.77	0.25
162	369	145	39.30	0.83	0.22
N	11	11	11	11	11
MEAN	320.1	127.5	39.912	0.742	0.231
S.D.	21.2	14.7	4.584	0.113	0.031

a : Died on Day 3 of Lactation .

Values in parentheses are excluded from the statistical calculation (reference data).

: Not applicable.

INDIVIDUAL DATA 28-3

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weights ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg PERIOD : Day 5 of lactation

	Body weight	Liver		Kidney		Spleen		Heart		Brain		Pituitary gland		Thymus		Thyroid		Adrenal	
Animal No.	g	g	%	g	%	g	%	g	%	g	%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%
251	284	9.56	3.37	1.92	0.68	0.67	0.24	0.88	0.31	1.99	0.70	18.4	6.48	255	89.79	17.6	6.20	78	27.46
252	281	9.73	3.46	2.03	0.72	1.04	0.37	0.98	0.35	2.06	0.73	16.6	5.91	107	38.08	11.3	4.02	76	27.05
253	318	9.17	2.88	2.23	0.70	0.63	0.20	1.04	0.33	2.03	0.64	17.2	5.41	233	73.27	15.8	4.97	113	35.53
254	329	10.31	3.13	2.17	0.66	0.83	0.25	1.01	0.31	2.01	0.61	16.0	4.86	248	75.38	13.5	4.10	81	24.62
255	268	10.16	3.79	2.16	0.81	0.52	0.19	0.87	0.32	2.11	0.79	13.4	5.00	85	31.72	16.6	6.19	87	32.46
256	313	10.18	3.25	1.99	0.64	0.68	0.22	0.96	0.31	1.91	0.61	16.1	5.14	118	37.70	16.6	5.30	73	23.32
257	338	12.38	3.66	2.17	0.64	1.26	0.37	1.31	0.39	2.10	0.62	19.5	5.77	263	77.81	17.2	5.09	85	25.15
258	329	10.38	3.16	2.29	0.70	0.73	0.22	1.00	0.30	2.08	0.63	19.0	5.78	182	55.32	12.3	3.74	67	20.36
259	328	10.48	3.20	1.99	0.61	0.76	0.23	1.09	0.33	2.08	0.63	14.8	4.51	273	83.23	17.1	5.21	79	24.09
260	340	10.47	3.08	2.16	0.64	0.71	0.21	0.94	0.28	2.03	0.60	18.5	5.44	255	75.00	22.7	6.68	84	24.71
261	301	10.46	3.48	2.35	0.78	0.57	0.19	0.93	0.31	2.03	0.67	19.2	6.38	236	78.41	16.0	5.32	86	28.57
262	353	10.84	3.07	2.10	0.59	0.80	0.23	1.03	0.29	2.11	0.60	16.5	4.67	398	112.75	21.0	5.95	77	21.81
N	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
MEAN	315.2	10.343	3.294	2.130	0.681	0.767	0.243	1.003	0.319	2.045	0.653	17.10	5.446	221.1	69.038	16.48	5.231	82.2	26.261
S.D.	26.4	0.790	0.265	0.129	0.066	0.205	0.062	0.116	0.029	0.058	0.059	1.89	0.639	86.8	23.974	3.24	0.932	11.3	4.328

INDIVIDUAL DATA 28-4

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weights ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg PERIOD : Day 5 of lactation

Animal No.	Body weight	Ovary		Uterus	
	g	mg	10^{-3}%	g	%
251	284	106	37.32	0.67	0.24
252	281	109	38.79	0.87	0.31
253	318	105	33.02	0.61	0.19
254	329	106	32.22	0.74	0.22
255	268	118	44.03	0.83	0.31
256	313	132	42.17	0.86	0.27
257	338	129	38.17	0.76	0.22
258	329	138	41.95	0.65	0.20
259	328	124	37.80	0.73	0.22
260	340	132	38.82	0.65	0.19
261	301	107	35.55	0.67	0.22
262	353	121	34.28	0.80	0.23
N	12	12	12	12	12
MEAN	315.2	118.9	37.843	0.737	0.235
S.D.	26.4	12.1	3.680	0.089	0.041

INDIVIDUAL DATA 28-5

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weights ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg PERIOD : Day 5 of lactation

	Body weight	Liver		Kidney		Spleen		Heart		Brain		Pituitary gland		Thymus		Thyroid		Adrenal	
Animal No.	g	g	%	g	%	g	%	g	%	g	%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%
351	296	9.76	3.30	2.03	0.69	0.58	0.20	0.98	0.33	1.95	0.66	15.1	5.10	263	88.85	17.1	5.78	73	24.66
352	299	10.42	3.48	2.03	0.68	0.69	0.23	0.97	0.32	1.92	0.64	15.7	5.25	166	55.52	19.6	6.56	76	25.42
353	305	10.43	3.42	2.02	0.66	0.74	0.24	0.95	0.31	2.15	0.70	17.5	5.74	235	77.05	15.5	5.08	73	23.93
354	306	11.31	3.70	2.17	0.71	1.00	0.33	0.80	0.26	1.99	0.65	16.5	5.39	173	56.54	20.8	6.80	89	29.08
355	317	11.09	3.50	2.09	0.66	0.71	0.22	0.97	0.31	2.10	0.66	17.0	5.36	196	61.83	19.7	6.21	81	25.55
356	291	10.67	3.67	2.12	0.73	0.73	0.25	1.05	0.36	1.98	0.68	19.1	6.56	196	67.35	17.5	6.01	83	28.52
357	317	10.07	3.18	2.09	0.66	0.94	0.30	1.11	0.35	2.03	0.64	16.3	5.14	280	88.33	14.3	4.51	73	23.03
358	349	10.91	3.13	2.41	0.69	0.68	0.19	1.02	0.29	2.06	0.59	19.8	5.67	196	56.16	16.9	4.84	106	30.37
359	305	9.66	3.17	2.23	0.73	0.59	0.19	0.97	0.32	2.01	0.66	17.1	5.61	109	35.74	13.3	4.36	74	24.26
360	322	10.40	3.23	1.94	0.60	0.73	0.23	0.96	0.30	2.09	0.65	12.9	4.01	196	60.87	16.0	4.97	80	24.84
361	316	10.63	3.36	2.02	0.64	0.83	0.26	1.09	0.34	2.12	0.67	19.0	6.01	230	72.78	19.0	6.01	94	29.75
362	348	10.97	3.15	2.40	0.69	0.89	0.26	0.98	0.28	1.98	0.57	17.8	5.11	258	74.14	16.6	4.77	79	22.70
N	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
MEAN	314.3	10.527	3.358	2.129	0.678	0.759	0.242	0.988	0.314	2.032	0.648	16.98	5.413	208.2	66.263	17.19	5.492	81.8	26.009
S.D.	18.5	0.513	0.199	0.150	0.037	0.131	0.042	0.079	0.029	0.072	0.036	1.91	0.614	47.9	15.110	2.27	0.832	10.1	2.692

INDIVIDUAL DATA 28-6

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weights ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg PERIOD : Day 5 of lactation

Animal No.	Body weight	Ovary		Uterus	
	g	mg	10^{-3}%	g	%
351	296	115	38.85	0.76	0.26
352	299	127	42.47	0.64	0.21
353	305	93	30.49	0.74	0.24
354	306	155	50.65	0.69	0.23
355	317	103	32.49	0.64	0.20
356	291	139	47.77	0.79	0.27
357	317	115	36.28	0.77	0.24
358	349	114	32.66	0.78	0.22
359	305	130	42.62	0.62	0.20
360	322	98	30.43	0.63	0.20
361	316	114	36.08	0.71	0.22
362	348	89	25.57	0.71	0.20
N	12	12	12	12	12
MEAN	314.3	116.0	37.197	0.707	0.224
S.D.	18.5	19.4	7.529	0.062	0.024

INDIVIDUAL DATA 28-7

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weights ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg PERIOD : Day 5 of lactation

	Body weight	Liver		Kidney		Spleen		Heart		Brain		Pituitary gland		Thymus		Thyroid		Adrenal	
Animal No.	g	g	%	g	%	g	%	g	%	g	%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%
451	278	8.81	3.17	1.98	0.71	0.97	0.35	0.74	0.27	1.96	0.71	16.2	5.83	260	93.53	13.9	5.00	79	28.42
452	284	8.98	3.16	1.91	0.67	0.61	0.21	1.12	0.39	2.09	0.74	17.9	6.30	162	57.04	17.1	6.02	73	25.70
453	287	9.71	3.38	2.00	0.70	0.75	0.26	1.01	0.35	2.03	0.71	16.5	5.75	170	59.23	17.8	6.20	78	27.18
454	287	9.89	3.45	2.12	0.74	0.65	0.23	0.94	0.33	1.97	0.69	14.3	4.98	147	51.22	16.3	5.68	75	26.13
455	283	9.92	3.51	2.11	0.75	0.56	0.20	0.96	0.34	1.98	0.70	18.3	6.47	293	103.53	17.5	6.18	70	24.73
456	286	11.07	3.87	2.08	0.73	0.86	0.30	1.01	0.35	2.09	0.73	17.1	5.98	196	68.53	14.6	5.10	77	26.92
457	279	9.45	3.39	2.07	0.74	0.53	0.19	0.92	0.33	1.94	0.70	16.1	5.77	164	58.78	17.6	6.31	81	29.03
458	314	11.06	3.52	2.20	0.70	1.04	0.33	1.03	0.33	2.07	0.66	16.2	5.16	225	71.66	30.0	9.55	87	27.71
459	295	9.60	3.25	2.01	0.68	0.73	0.25	0.94	0.32	2.09	0.71	14.5	4.92	183	62.03	17.3	5.86	81	27.46
460	304	10.68	3.51	2.19	0.72	0.65	0.21	0.90	0.30	2.04	0.67	22.0	7.24	289	95.07	16.9	5.56	82	26.97
461	333	11.69	3.51	2.19	0.66	0.96	0.29	1.06	0.32	2.11	0.63	16.6	4.98	282	84.68	19.3	5.80	88	26.43
462	326	11.20	3.44	2.25	0.69	0.71	0.22	1.11	0.34	2.08	0.64	16.7	5.12	227	69.63	20.0	6.13	97	29.75
N	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
MEAN	296.3*	10.172	3.430	2.093	0.708	0.752	0.253	0.978	0.331	2.038	0.691	16.87	5.708	216.5	72.911	18.19	6.116	80.7	27.203
S.D.	18.7	0.939	0.190	0.104	0.029	0.169	0.053	0.104	0.029	0.060	0.034	1.99	0.720	53.7	17.192	4.08	1.160	7.3	1.411

* : Significantly different from the 0 mg/kg group at P≦ 0.05 (Dunnett's test).

INDIVIDUAL DATA 28-8

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weights ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg PERIOD : Day 5 of lactation

Animal No.	Body weight	Ovary		Uterus	
	g	mg	10^{-3}%	g	%
451	278	109	39.21	0.65	0.23
452	284	108	38.03	0.59	0.21
453	287	119	41.46	0.78	0.27
454	287	114	39.72	0.75	0.26
455	283	121	42.76	0.63	0.22
456	286	122	42.66	0.74	0.26
457	279	89	31.90	0.65	0.23
458	314	124	39.49	0.65	0.21
459	295	112	37.97	0.69	0.23
460	304	114	37.50	0.71	0.23
461	333	133	39.94	0.73	0.22
462	326	136	41.72	0.75	0.23
N	12	12	12	12	12
MEAN	296.3	116.8	39.363	0.693	0.233
S.D.	18.7	12.4	2.950	0.059	0.020

INDIVIDUAL DATA 29-1-1

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weights ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 0 mg/kg PERIOD : After Week 6 of administration

Animal No.	Body weight	Liver		Kidney		Spleen		Heart		Brain		Pituitary gland		Thymus		Thyroid		Adrenal	
	g	g	%	g	%	g	%	g	%	g	%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%
163	268	6.93	2.59	1.78	0.66	0.53	0.20	0.93	0.35	1.85	0.69	13.8	5.15	372	138.81	19.9	7.43	68	25.37
164	284	7.73	2.72	1.86	0.65	0.57	0.20	0.99	0.35	2.02	0.71	17.9	6.30	264	92.96	14.5	5.11	70	24.65
165	286	6.77	2.37	1.74	0.61	0.49	0.17	0.92	0.32	1.93	0.67	12.7	4.44	380	132.87	20.6	7.20	60	20.98
166	292	6.90	2.36	1.90	0.65	0.67	0.23	0.88	0.30	2.12	0.73	13.8	4.73	276	94.52	10.2	3.49	73	25.00
167	304	7.45	2.45	1.92	0.63	0.53	0.17	0.88	0.29	1.96	0.64	17.9	5.89	235	77.30	16.3	5.36	100	32.89
N	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
MEAN	286.8	7.156	2.498	1.840	0.640	0.558	0.194	0.920	0.322	1.976	0.688	15.22	5.302	305.4	107.292	16.30	5.718	74.2	25.778
S.D.	13.1	0.413	0.154	0.077	0.020	0.069	0.025	0.045	0.028	0.101	0.035	2.49	0.780	66.2	26.998	4.24	1.627	15.2	4.349

INDIVIDUAL DATA 29-1-2

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weights ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 0 mg/kg PERIOD : After Week 6 of administration

Animal No.	Body weight	Ovary		Uterus		Estrous cycle
	g	mg	10^{-3}%	g	%	
163	268	91	33.96	1.04	0.39	II
164	284	110	38.73	0.62	0.22	V
165	286	80	27.97	0.97	0.34	V
166	292	121	41.44	0.59	0.20	V
167	304	131	43.09	0.88	0.29	II
N	5	5	5	5	5	
MEAN	286.8	106.6	37.038	0.820	0.288	
S.D.	13.1	21.0	6.135	0.205	0.080	

II : Proestrus. V : Diestrus.

INDIVIDUAL DATA 29-1-3

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weights ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 100 mg/kg PERIOD : After Week 6 of administration

Animal No.	Body weight	Liver		Kidney		Spleen		Heart		Brain		Pituitary gland		Thymus		Thyroid		Adrenal	
	g	g	%	g	%	g	%	g	%	g	%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%
463	243	6.67	2.74	1.80	0.74	0.40	0.16	0.79	0.33	1.99	0.82	13.4	5.51	194	79.84	14.5	5.97	68	27.98
464	269	8.00	2.97	1.78	0.66	0.54	0.20	0.84	0.31	1.98	0.74	19.0	7.06	312	115.99	16.2	6.02	90	33.46
465	268	7.79	2.91	1.98	0.74	0.47	0.18	0.91	0.34	1.97	0.74	15.2	5.67	228	85.07	18.6	6.94	70	26.12
466	272	7.48	2.75	1.59	0.58	0.56	0.21	0.84	0.31	2.01	0.74	18.0	6.62	268	98.53	17.2	6.32	63	23.16
467	268	7.50	2.80	2.11	0.79	0.60	0.22	0.84	0.31	1.94	0.72	15.5	5.78	269	100.37	13.5	5.04	69	25.75
N	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
MEAN	264.0*	7.488	2.834**	1.852	0.702	0.514	0.194	0.844*	0.320	1.978	0.752*	16.22	6.128	254.2	95.960	16.00	6.058	72.0	27.294
S.D.	11.9	0.506	0.102	0.200	0.083	0.079	0.024	0.043	0.014	0.026	0.039	2.26	0.675	44.9	14.192	2.05	0.688	10.4	3.852

* : Significantly different from the 0 mg/kg group at $p \leqq 0.05$ (Dunnett's test).

** : Significantly different from the 0 mg/kg group at $p \leqq 0.01$ (Dunnett's test).

INDIVIDUAL DATA 29-1-4

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weights ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 100 mg/kg PERIOD : After Week 6 of administration

Animal No.	Body weight	Ovary		Uterus		Estrous cycle
	g	mg	10^{-3}%	g	%	
463	243	95	39.09	0.46	0.19	V
464	269	134	49.81	0.96	0.36	Ⅲ
465	268	129	48.13	0.55	0.21	Ⅲ
466	272	82	30.15	1.01	0.37	Ⅱ
467	268	120	44.78	0.56	0.21	V
N	5	5	5	5	5	
MEAN	264.0*	112.0	42.392	0.708	0.268	
S.D.	11.9	22.5	7.975	0.256	0.089	

II : Proestrus. III : Estrus. V : Diestrus.

* : Significantly different from the 0 mg/kg group at $p \leqq 0.05$ (Dunnett's test).

INDIVIDUAL DATA 29-2-1

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weights ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 0 mg/kg PERIOD : After Week 2 of recovery

Animal No.	Body weight	Liver		Kidney		Spleen		Heart		Brain		Pituitary gland		Thymus		Thyroid		Adrenal	
	g	g	%	g	%	g	%	g	%	g	%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%
168	280	7.21	2.58	1.78	0.64	0.51	0.18	0.93	0.33	2.17	0.78	17.4	6.21	189	67.50	15.7	5.61	65	23.21
169	297	7.75	2.61	1.97	0.66	0.45	0.15	1.04	0.35	2.04	0.69	20.4	6.87	200	67.34	17.3	5.82	70	23.57
170	300	7.04	2.35	1.91	0.64	0.56	0.19	0.99	0.33	1.99	0.66	16.3	5.43	304	101.33	10.5	3.50	62	20.67
171	286	7.71	2.70	1.82	0.64	0.69	0.24	1.04	0.36	2.06	0.72	13.7	4.79	157	54.90	17.5	6.12	76	26.57
172	306	7.43	2.43	2.07	0.68	0.48	0.16	0.95	0.31	2.02	0.66	17.4	5.69	383	125.16	18.9	6.18	66	21.57
N	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
MEAN	293.8	7.428	2.534	1.910	0.652	0.538	0.184	0.990	0.336	2.056	0.702	17.04	5.798	246.6	83.246	15.98	5.446	67.8	23.118
S.D.	10.6	0.309	0.142	0.116	0.018	0.094	0.035	0.050	0.019	0.069	0.050	2.41	0.788	94.1	29.104	3.27	1.112	5.4	2.265

INDIVIDUAL DATA 29-2-2

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weights ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 0 mg/kg PERIOD : After Week 2 of recovery

Animal No.	Body weight	Ovary		Uterus		Estrous cycle
	g	mg	10^{-3}%	g	%	
168	280	99	35.36	0.55	0.20	Ⅲ
169	297	77	25.93	0.51	0.17	Ⅳ
170	300	116	38.67	0.62	0.21	Ⅴ
171	286	91	31.82	0.48	0.17	Ⅳ
172	306	82	26.80	0.53	0.17	Ⅳ
N	5	5	5	5	5	
MEAN	293.8	93.0	31.716	0.538	0.184	
S.D.	10.6	15.4	5.461	0.053	0.019	

III : Estrus. IV : Metestrus. V : Diestrus.

INDIVIDUAL DATA 29-2-3

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weights ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 100 mg/kg PERIOD : After Week 2 of recovery

Animal No.	Body weight	Liver		Kidney		Spleen		Heart		Brain		Pituitary gland		Thymus		Thyroid		Adrenal	
	g	g	%	g	%	g	%	g	%	g	%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%	mg	10^{-3}%
468	301	8.16	2.71	2.06	0.68	0.64	0.21	0.94	0.31	2.04	0.68	18.2	6.05	312	103.65	13.6	4.52	78	25.91
469	272	6.42	2.36	2.01	0.74	0.56	0.21	0.91	0.33	1.99	0.73	13.6	5.00	256	94.12	13.1	4.82	55	20.22
470	308	9.25	3.00	1.93	0.63	0.45	0.15	0.93	0.30	1.99	0.65	22.1	7.18	317	102.92	15.8	5.13	92	29.87
471	272	7.72	2.84	2.11	0.78	0.55	0.20	0.85	0.31	2.06	0.76	15.2	5.59	307	112.87	12.8	4.71	65	23.90
472	255	6.61	2.59	1.91	0.75	0.56	0.22	0.84	0.33	2.22	0.87	15.0	5.88	320	125.49	15.7	6.16	79	30.98
N	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
MEAN	281.6	7.632	2.700	2.004	0.716	0.552	0.198	0.894*	0.316	2.060	0.738	16.82	5.940	302.4	107.810	14.20	5.068	73.8	26.176
S.D.	22.2	1.164	0.244	0.085	0.060	0.068	0.028	0.046	0.013	0.095	0.085	3.39	0.800	26.4	11.904	1.44	0.649	14.2	4.400

* : Significantly different from the 0 mg/kg group at P≦0.05 (Dunnett's test).

INDIVIDUAL DATA 29-2-4

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Organ weights ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : satellite 100 mg/kg PERIOD : After Week 2 of recovery

Animal No.	Body weight	Ovary		Uterus		Estrous cycle
	g	mg	10^{-3}%	g	%	
468	301	78	25.91	0.90	0.30	III
469	272	77	28.31	1.09	0.40	II
470	308	58	18.83	0.65	0.21	V
471	272	80	29.41	0.65	0.24	III
472	255	95	37.25	0.64	0.25	V
N	5	5	5	5	5	
MEAN	281.6	77.6	27.942	0.786++	0.280+	
S.D.	22.2	13.2	6.635	0.202	0.074	

II : Proestrus. III : Estrus. V : Diestrus.

+ : Significantly different from the 0 mg/kg group at P≦0.05 (Steel's test).

++ : Significantly different from the 0 mg/kg group at P≦0.01 (Steel's test).

INDIVIDUAL DATA 30-1-1

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Histopathological findings ANIMAL: Rat, Crl: CD (SD) SEX: Male GROUP: 0 mg/kg PERIOD: after Week 6 of administration

Animal No.		101	102	103	109	110	111	112
Organ: Findings								
Lung:	Aggregation, macrophage, alveolar	-	-	-	-	-	-	+
	Mineralization, artery	-	-	-	-	+	-	-
Trachea:		N	N	N	N	N	N	N
Right submandibular gland:		N	N	N	N	N	N	N
Left submandibular gland:		N	N	N	N	N	N	N
Esophagus:		N	N	N	N	N	N	N
Forestomach:		N	N	N	N	N	N	N
Stomach, limiting ridge:		N	N	N	N	N	N	N
Glandular stomach:		N	N	N	N	N	N	N
Duodenum:		N	N	N	N	N	N	N
Jejunum:		N	N	N	N	N	N	N
Ileum (including Peyer's patch):		N	N	N	N	N	N	N
Cecum:		N	N	N	N	N	N	N
Colon:		N	N	N	N	N	N	N
Rectum:		N	N	N	N	N	N	N
Pancreas:		N	N	N	N	N	N	N
Liver:	Microgranuloma	-	-	-	-	-	-	+
	Fatty change, periportal	-	-	-	-	+[a]	-	+[a]
Heart:	Inflammation, focal	-	+	-	+	+	+	-
Right kidney:	Eosinophilic body, proximal tubular epithelium	-	-	-	+[b]	-	-	-
Left kidney:	Eosinophilic body, proximal tubular epithelium	-	-	-	+[b]	-	-	-
	Basophilic change, tubular epithelium	-	+	-	-	-	-	-
Urinary bladder:		N	N	N	N	N	N	N
Right testis:		N	N	N	N	N	N	N
Left testis:		N	N	N	N	N	N	N
Right epididymis:	Granuloma, spermatic	-	-	-	+	-	-	-
Left epididymis:	Granuloma, spermatic	-	-	-	++	-	-	-
Prostate:	Cellular infiltration, inflammatory cell	-	-	-	-	+	-	-
Right seminal vesicle:		N	N	N	N	N	N	N
Left seminal vesicle:		N	N	N	N	N	N	N
Right coagulating gland:		N	N	N	N	N	N	N
Left coagulating gland:		N	N	N	N	N	N	N

N: No abnormal findings, -: normal, +: slight change, ++: moderate change, +++: severe change.
a: Oil red O stain positive.
b: Alpha-2u-globulin antibody positive.

INDIVIDUAL DATA 30-1-2

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Histopathological findings ANIMAL: Rat, Crl: CD (SD) SEX: Male GROUP: 0 mg/kg PERIOD: after Week 6 of administration

Animal No.		101	102	103	109	110	111	112
Organ: Findings								
Cerebrum:		N	N	N	N	N	N	N
Cerebellum:		N	N	N	N	N	N	N
Pons:		N	N	N	N	N	N	N
Spinal cord:		N	N	N	N	N	N	N
Sciatic nerve:		N	N	N	N	N	N	N
Spleen:		N	N	N	N	N	N	N
Thymus:		N	N	N	N	N	N	N
Bone marrow of right femur:		N	N	N	N	N	N	N
Right submandibular lymph node:		N	N	N	N	N	N	N
Left submandibular lymph node:		N	N	N	N	N	N	N
Mesenteric lymph node:		N	N	N	N	N	N	N
Pituitary gland:	Cyst, pars distalis	+	-	-	-	-	-	-
Right thyroid:		N	N	N	N	N	N	N
Left thyroid:		N	N	N	N	N	N	N
Right parathyroid:		N	N	N	N	N	N	N
Left parathyroid:		N	N	N	N	N	N	N
Right adrenal:		N	N	N	N	N	N	N
Left adrenal:		N	N	N	N	N	N	N
Right eyeball:		N	N	N	N	N	N	N
Left eyeball:		N	N	N	N	N	N	N
Right Harderian gland:		N	N	N	N	N	N	N
Left Harderian gland:		N	N	N	N	N	N	N
Skeletal muscle:		N	N	N	N	N	N	N
Right femur:		N	N	N	N	N	N	N

N: No abnormal findings, -: normal, +: slight change, ++: moderate change.

INDIVIDUAL DATA 30-1-3

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Histopathological findings ANIMAL: Rat, Crl: CD (SD) SEX: Male GROUP: 4 mg/kg PERIOD: after Week 6 of administration

Animal No.			201	202	203	204	205	206	207	208	209	210	211	212
Organ: Findings														
	Right kidney:	Eosinophilic body, proximal tubular epithelium	-	-	-	-	+	-	-	-	-	+[a]	-	-
		Basophilic change, tubular epithelium	-	-	-	+	-	-	-	-	-	-	-	-
	Left kidney:	Eosinophilic body, proximal tubular epithelium	-	-	-	-	+	-	-	-	-	+[a]	-	-
	Left epididymis:	Granuloma, spermatic	*	*	*	*	*	*	*	+	*	*	*	*
	Prostate:	Cellular infiltration, inflammatory cell	+	-	+	-	+	+	+	+	+	-	+	+

N: No abnormal findings, -: normal, +: slight change, ++: moderate change, +++: severe change.

a: Alpha-2u-globulin antibody positive.

*: Not examined.

INDIVIDUAL DATA 30-1-4

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Histopathological findings ANIMAL: Rat, Crl: CD (SD) SEX: Male GROUP: 20 mg/kg PERIOD: after Week 6 of administration

Animal No.			301	302	303	304	305	306	307	308	309	310	311	312
Organ: Findings														
	Right kidney:	Eosinophilic body, proximal tubular epithelium	-	-	-	+[a]	-	-	-	-	-	-	-	-
		Cyst	-	-	-	-	-	-	-	-	-	-	-	+
	Left kidney:	Eosinophilic body, proximal tubular epithelium	-	-	-	+[a]	-	-	-	-	-	-	-	-
	Prostate:	Cellular infiltration, inflammatory cell	-	+	++	-	-	+	++	++	-	-	+	+

N: No abnormal findings, -: normal, +: slight change, ++: moderate change, +++: severe change.
a: Alpha-2u-globulin antibody positive.

INDIVIDUAL DATA 30-1-5

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Histopathological findings ANIMAL: Rat, Crl: CD (SD) SEX: Male GROUP: 100 mg/kg PERIOD: after Week 6 of administration

Animal No.		402	403	405	407	408	409	410
Organ: Findings								
Lung:	Aggregation, macrophage, alveolar	-	+	-	+	-	-	-
	Mineralization, artery	-	-	-	-	+	-	-
Trachea:		N	N	N	N	N	N	N
Right submandibular gland:		N	N	N	N	N	N	N
Left submandibular gland:		N	N	N	N	N	N	N
Esophagus:		N	N	N	N	N	N	N
Forestomach:		N	N	N	N	N	N	N
Stomach, limiting ridge:		N	N	N	N	N	N	N
Glandular stomach:		N	N	N	N	N	N	N
Duodenum:		N	N	N	N	N	N	N
Jejunum:		N	N	N	N	N	N	N
Ileum (including Peyer's patch):		N	N	N	N	N	N	N
Cecum:		N	N	N	N	N	N	N
Colon:		N	N	N	N	N	N	N
Rectum:		N	N	N	N	N	N	N
Pancreas:		N	N	N	N	N	N	N
Liver:	Microgranuloma	+	-	-	+	-	-	-
Heart:	Inflammation, focal	+	-	-	+	+	-	-
Right kidney:	Eosinophilic body, proximal tubular epithelium	-	+[a]	-	+	-	+	+
	Basophilic change, tubular epithelium	-	+	-	-	-	-	-
Left kidney:	Eosinophilic body, proximal tubular epithelium	-	+[a]	-	+	-	+	+
Urinary bladder:		N	N	N	N	N	N	N
Right testis:		N	N	N	N	N	N	N
Left testis:		N	N	N	N	N	N	N
Right epididymis:	Granuloma, spermatic	-	-	+	-	-	-	-
Left epididymis:	Granuloma, spermatic	-	-	-	-	-	+	-
Prostate:	Cellular infiltration, inflammatory cell	-	+	+	+	+	+	+
Right seminal vesicle:		N	N	N	N	N	N	N
Left seminal vesicle:		N	N	N	N	N	N	N
Right coagulating gland:		N	N	N	N	N	N	N
Left coagulating gland:		N	N	N	N	N	N	N

N: No abnormal findings, -: normal, +: slight change, ++: moderate change, +++: severe change.
a: Alpha-2u-globulin antibody positive.

INDIVIDUAL DATA 30-1-6

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Histopathological findings ANIMAL: Rat, Crl: CD (SD) SEX: Male GROUP: 100 mg/kg PERIOD: after Week 6 of administration

Animal No.		402	403	405	407	408	409	410
Organ: Findings								
Cerebrum:		N	N	N	N	N	N	N
Cerebellum:		N	N	N	N	N	N	N
Pons:		N	N	N	N	N	N	N
Spinal cord:		N	N	N	N	N	N	N
Sciatic nerve:		N	N	N	N	N	N	N
Spleen:		N	N	N	N	N	N	N
Thymus:		N	N	N	N	N	N	N
Bone marrow of right femur:		N	N	N	N	N	N	N
Right submandibular lymph node:		N	N	N	N	N	N	N
Left submandibular lymph node:		N	N	N	N	N	N	N
Mesenteric lymph node:		N	N	N	N	N	N	N
Pituitary gland:		N	N	N	N	N	N	N
Right thyroid:		N	N	N	N	N	N	N
Left thyroid:		N	N	N	N	N	N	N
Right parathyroid:		N	N	N	N	N	N	N
Left parathyroid:		N	N	N	**	N	N	N
Right adrenal:		N	N	N	N	N	N	N
Left adrenal:		N	N	N	N	N	N	N
Right eyeball:	Retinal rosette	+	-	+	-	-	-	-
Left eyeball:	Retinal rosette	-	-	+	-	-	-	-
Right Harderian gland:	Cellular infiltration, mononuclear cell	-	-	-	-	-	-	+
Left Harderian gland:		N	N	N	N	N	N	N
Skeletal muscle:		N	N	N	N	N	N	N
Right femur:		N	N	N	N	N	N	N

N: No abnormal findings, -: normal, +: slight change, ++: moderate change, +++: severe change.

**: Not examined because of missing.

INDIVIDUAL DATA 30-2-1

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Histopathological findings ANIMAL: Rat, Crl: CD (SD) SEX: Male GROUP: 0 mg/kg PERIOD: afer Week 2 of recovery

Animal No.		104	105	106	107	108
Organ: Findings						
Lung:	Aggregation, macrophage, alveolar	-	+	-	-	+
	Metaplasia, osseous, alveoli	-	+	-	-	-
	Mineralization, artery	+	-	+	+	-
Trachea:		N	N	N	N	N
Right submandibular gland:		N	N	N	N	N
Left submandibular gland:		N	N	N	N	N
Esophagus:		N	N	N	N	N
Forestomach:		N	N	N	N	N
Stomach, limiting ridge:		N	N	N	N	N
Glandular stomach:		N	N	N	N	N
Duodenum:		N	N	N	N	N
Jejunum:		N	N	N	N	N
Ileum (including Peyer's patch):		N	N	N	N	N
Cecum:		N	N	N	N	N
Colon:		N	N	N	N	N
Rectum:		N	N	N	N	N
Pancreas:	Atrophy, acinar cell, focal	+	-	-	+	-
Liver:	Microgranuloma	-	-	-	+	-
	Fatty change, periportal	-	-	+[a]	-	+[a]
Heart:	Inflammation, focal	-	-	-	-	+
Right kidney:	Basophilic change, tubular epithelium	+	-	-	-	-
Left kidney:		N	N	N	N	N
Urinary bladder:		N	N	N	N	N
Right testis:		N	N	N	N	N
Left testis:		N	N	N	N	N
Right epididymis:		N	N	N	N	N
Left epididymis:		N	N	N	N	N
Prostate:	Cellular infiltration, inflammatory cell	+	-	+	-	-
Right seminal vesicle:		N	N	N	N	N
Left seminal vesicle:		N	N	N	N	N
Right coagulating gland:		N	N	N	N	N
Left coagulating gland:		N	N	N	N	N

N: No abnormal findings, -: normal, +: slight change, ++: moderate change, +++: severe change.
a: Oil red O stain positive.

INDIVIDUAL DATA 30-2-2

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Histopathological findings ANIMAL: Rat, Crl: CD (SD) SEX: Male GROUP: 0 mg/kg PERIOD: afer Week 2 of recovery

Animal No.		104	105	106	107	108
Organ: Findings						
Cerebrum:		N	N	N	N	N
Cerebellum:		N	N	N	N	N
Pons:		N	N	N	N	N
Spinal cord:		N	N	N	N	N
Sciatic nerve:		N	N	N	N	N
Spleen:		N	N	N	N	N
Thymus:		N	N	N	N	N
Bone marrow of right femur:		N	N	N	N	N
Right submandibular lymph node:		N	N	N	N	N
Left submandibular lymph node:		N	N	N	N	N
Mesenteric lymph node:		N	N	N	N	N
Pituitary gland:		N	N	N	N	N
Right thyroid:		N	N	N	N	N
Left thyroid:		N	N	N	N	N
Right parathyroid:		N	N	N	N	N
Left parathyroid:		N	N	N	N	N
Right adrenal:		N	N	N	N	N
Left adrenal:		N	N	N	N	N
Right eyeball:		N	N	N	N	N
Left eyeball:	Atrophy, retina, focal	-	-	-	-	+
Right Harderian gland:		N	N	N	N	N
Left Harderian gland:		N	N	N	N	N
Skeletal muscle:		N	N	N	N	N
Right femur:		N	N	N	N	N

N: No abnormal findings, -: normal, +: slight change, ++: moderate change, +++: severe change.

INDIVIDUAL DATA 30-2-3

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Histopathological findings ANIMAL: Rat, Crl: CD (SD) SEX: Male GROUP: 100 mg/kg PERIOD: afer Week 2 of recovery

Animal No.			401	404	406	411	412
Organ: Findings							
	Lung:	Metaplasia, osseous, alveoli	-	-	+	-	-
		Mineralization, artery	-	+	-	-	-
	Trachea:		N	N	N	N	N
	Right submandibular gland:		N	N	N	N	N
	Left submandibular gland:		N	N	N	N	N
	Esophagus:		N	N	N	N	N
	Forestomach:		N	N	N	N	N
	Stomach, limiting ridge:		N	N	N	N	N
	Glandular stomach:		N	N	N	N	N
	Duodenum:		N	N	N	N	N
	Jejunum:		N	N	N	N	N
	Ileum (including Peyer's patch):		N	N	N	N	N
	Cecum:		N	N	N	N	N
	Colon:		N	N	N	N	N
	Rectum:		N	N	N	N	N
	Pancreas:		N	N	N	N	N
	Liver:	Microgranuloma	-	+	+	-	-
	Heart:	Inflammation, focal	-	-	-	-	+
	Right kidney:	Eosinophilic body, proximal tubular epithelium	-	+[a]	-	-	-
	Left kidney:	Eosinophilic body, proximal tubular epithelium	-	+[a]	-	-	-
	Urinary bladder:		N	N	N	N	N
	Right testis:		N	N	N	N	N
	Left testis:		N	N	N	N	N
	Right epididymis:		N	N	N	N	N
	Left epididymis:		N	N	N	N	N
	Prostate:	Cellular infiltration, inflammatory cell	+	+	-	-	+
	Right seminal vesicle:		N	N	N	N	N
	Left seminal vesicle:		N	N	N	N	N
	Right coagulating gland:		N	N	N	N	N
	Left coagulating gland:		N	N	N	N	N

N: No abnormal findings, -: normal, +: slight change, ++: moderate change, +++: severe change.

a: Alpha-2u-globulin antibody positive.

INDIVIDUAL DATA 30-2-4

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Histopathological findings ANIMAL: Rat, Crl: CD (SD) SEX: Male GROUP: 100 mg/kg PERIOD: afer Week 2 of recovery

Animal No.			401	404	406	411	412
Organ: Findings							
	Cerebrum:		N	N	N	N	N
	Cerebellum:		N	N	N	N	N
	Pons:		N	N	N	N	N
	Spinal cord:		N	N	N	N	N
	Sciatic nerve:		N	N	N	N	N
	Spleen:		N	N	N	N	N
	Thymus:		N	N	N	N	N
	Bone marrow of right femur:		N	N	N	N	N
	Right submandibular lymph node:		N	N	N	N	N
	Left submandibular lymph node:		N	N	N	N	N
	Mesenteric lymph node:		N	N	N	N	N
	Pituitary gland:	Cyst, pars distalis	-	+	-	-	-
		Cyst, pars intermedia	-	-	+	-	-
	Right thyroid:		N	N	N	N	N
	Left thyroid:		N	N	N	N	N
	Right parathyroid:		N	**	N	N	N
	Left parathyroid:		N	N	N	N	N
	Right adrenal:		N	N	N	N	N
	Left adrenal:		N	N	N	N	N
	Right eyeball:	Retinal rosette	-	+	-	-	-
	Left eyeball:		N	N	N	N	N
	Right Harderian gland:		N	N	N	N	N
	Left Harderian gland:	Cellular infiltration, mononuclear cell	+	-	-	-	-
	Skeletal muscle:		N	N	N	N	N
	Right femur:		N	N	N	N	N

N: No abnormal findings, -: normal, +: slight change, ++: moderate change, +++: severe change.

**: Not examined because of missing.

INDIVIDUAL DATA 31-1

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Histopathological findings ANIMAL: Rat, Crl: CD (SD) SEX: Female GROUP: 0 mg/kg PERIOD: Day 5 of lactation

Animal No.		151	152	153	154	155[a]	156	157	158	159	160	161	162
Organ: Findings													
Lung:	Aggregation, macrophage. alveolar	-	-	-	-	-	-	-	+	-	-	-	-
Trachea:		N	N	N	N	N	N	N	N	N	N	N	N
Right submandibular gland:		N	N	N	N	N	N	N	N	N	N	N	N
Left submandibular gland:		N	N	N	N	N	N	N	N	N	N	N	N
Esophagus:		N	N	N	N	N	N	N	N	N	N	N	N
Forestomach:	Erosion	-	-	-	-	+	-	-	-	-	-	-	-
Stomach, limiting ridge:	Cyst, squamous cell	-	-	-	-	-	-	-	-	-	-	-	+
Glandular stomach:	Erosion	-	-	-	-	+	-	-	-	-	-	-	-
Duodenum:		N	N	N	N	N	N	N	N	N	N	N	N
Jejunum:		N	N	N	N	#	N	N	N	N	N	N	N
Ileum (including Peyer's patch):		N	N	N	N	#	N	N	N	N	N	N	N
Cecum:		N	N	N	N	#	N	N	N	N	N	N	N
Colon:		N	N	N	N	N	N	N	N	N	N	N	N
Rectum:		N	N	N	N	N	N	N	N	N	N	N	N
Pancreas:		N	N	N	N	N	N	N	N	N	N	N	N
Liver:	Microgranuloma	+	-	+	-	-	-	-	-	-	-	-	-
	Necrosis, focal	-	-	-	-	-	-	-	-	-	-	+	-
Heart:		N	N	N	N	N	N	N	N	N	N	N	N
Right kidney:	Dilatation, tubule, cortex	-	-	-	-	+	-	-	-	-	-	-	-
	Cellular infiltration, inflammatory cell, renal pelvic mucosa	-	-	-	+	-	-	-	-	-	-	-	-
Left kidney:	Dilatation, tubule, cortex	-	-	-	-	+	-	-	-	-	-	-	-
Urinary bladder:		N	N	N	N	N	N	N	N	N	N	N	N
Right overy:		N	N	N	N	N	N	N	N	N	N	N	N
Left ovary:		N	N	N	N	N	N	N	N	N	N	N	N
Right uterine horn:		N	N	N	N	N	N	N	N	N	N	N	N
Left uterin horn:		N	N	N	N	N	N	N	N	N	N	N	N
Uterine cervix:		N	N	N	N	N	N	N	N	N	N	N	N
Vagina;		N	N	N	N	N	N	N	N	N	N	N	N

N: No abnormal findings, -: normal, +: slight change, ++: moderate change, +++: severe change.

a: Died on Day 3 of lactation.

#: Autolysis.

INDIVIDUAL DATA 31-2

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Histopathological findings ANIMAL: Rat, Crl: CD (SD) SEX: Female GROUP: 0 mg/kg PERIOD: Day 5 of lactation

Animal No.		151	152	153	154	155[a]	156	157	158	159	160	161	162
Organ: Findings													
Cerebrum:		N	N	N	N	N	N	N	N	N	N	N	N
Cerebellum:		N	N	N	N	N	N	N	N	N	N	N	N
Pons:		N	N	N	N	N	N	N	N	N	N	N	N
Spinal cord:		N	N	N	N	N	N	N	N	N	N	N	N
Sciatic nerve:		N	N	N	N	N	N	N	N	N	N	N	N
Spleen:	Atrophy, follicle	-	-	-	-	++	-	-	-	-	-	-	-
	Deposit, hemosiderin	-	-	-	-	+	-	-	-	-	-	-	-
Thymus:	Atrophy	-	-	-	-	++	-	-	-	-	-	-	-
Bone marrow of right femur:		N	N	N	N	N	N	N	N	N	N	N	N
Right submandibular lymph node:		N	N	N	N	#	N	N	N	N	N	N	N
Left submandibular lymph node:		N	N	N	N	#	N	N	N	N	N	N	N
Mesenteric lymph node:		N	N	N	N	#	N	N	N	N	N	N	N
Pituitary gland:		N	N	N	N	#	N	N	N	N	N	N	N
Right thyroid:		N	N	N	N	#	N	N	N	N	N	N	N
Left thyroid:		N	N	N	N	#	N	N	N	N	N	N	N
Right parathyroid:		N	N	N	N	N	N	N	N	N	N	N	N
Left parathyroid:		N	N	N	N	N	**	N	N	N	N	N	N
Right adrenal:	Necrosis, cortical cell, with cellular infiltration, inflammatory cell	N	N	N	N	+++	N	N	N	N	N	N	N
Left adrenal:	Necrosis, cortical cell, with cellular infiltration, inflammatory cell	N	N	N	N	+	N	N	N	N	N	N	N
Right eyeball:		N	N	N	N	N	N	N	N	N	N	N	N
Left eyeball:		N	N	N	N	N	N	N	N	N	N	N	N
Right Harderian gland:		N	N	N	N	N	N	N	N	N	N	N	N
Left Harderian gland:		N	N	N	N	N	N	N	N	N	N	N	N
Skeletal muscle:		N	N	N	N	N	N	N	N	N	N	N	N
Right femur:		N	N	N	N	N	N	N	N	N	N	N	N
Mammary gland:		N	N	N	N	N	N	N	N	N	N	N	N

a: Dead on day 1 of lactation.

N: No abnormal findings, -: normal, +: slight change, ++: moderate change, +++: severe change.

#: Autolysis.

**: Not examined because of missing.

INDIVIDUAL DATA 31-3

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Histopathological findings ANIMAL: Rat, Crl: CD (SD) SEX: Female GROUP: 4 mg/kg PERIOD: Day 5 of lactation

Animal No.		251	252	253	254	255	256	257	258	259	260	261	262
Organ: Findings													
Forestomach:	Ulcer	*	*	*	*	++	*	*	*	*	*	*	*
Stomach, limiting ridge:	Hyperplasia, squamous cell	*	*	*	*	++	*	*	*	*	*	*	*
Glandular stomach:	Erosion	*	*	*	*	*	*	*	*	+	*	*	*
Liver:	Fatty change, periportal	*	*	*	*	++[a]	*	*	*	*	*	*	*
Right kidney:	Fatty change, tubular epithelium	-	-	-	-	+[a]	-	-	-	-	-	-	-
Left kidney:	Fatty change, tubular epithelium	-	-	-	-	+	-	-	-	-	-	-	-
Thymus:	Atrophy	*	*	*	*	++	*	*	*	*	*	*	*

N: No abnormal findings, -: normal, +: slight change, ++: moderate change, +++: severe change.

a: Oil red O stain positive.

*: Not examined.

INDIVIDUAL DATA 31-4

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Histopathological findings ANIMAL: Rat, Crl: CD (SD) SEX: Female GROUP: 20 mg/kg PERIOD: Day 5 of lactation

Animal No.		351	352	353	354	355	356	357	358	359	360	361	362
Organ: Findings													
Right kidney:		N	N	N	N	N	N	N	N	N	N	N	N
Left kidney:		N	N	N	N	N	N	N	N	N	N	N	N
Mammary gland:	Hyperplasia, with inflammation	*	*	*	*	*	*	*	*	*	*	+	*

N: No abnormal findings, -: normal, +: slight change, ++: moderate change, +++: severe change.

*: Not examined.

INDIVIDUAL DATA 31-5

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Histopathological findings ANIMAL: Rat, Crl: CD (SD) SEX: Female GROUP: 100 mg/kg PERIOD: Day 5 of lactation

Animal No.		451	452	453	454	455	456	457	458	459	460	461	462
Organ: Findings													
Lung:	Aggregation, macrophage. alveolar	-	+	-	+	-	-	-	-	-	-	-	-
Trachea:		N	N	N	N	N	N	N	N	N	N	N	N
Right submandibular gland:		N	N	N	N	N	N	N	N	N	N	N	N
Left submandibular gland:		N	N	N	N	N	N	N	N	N	N	N	N
Esophagus:		N	N	N	N	N	N	N	N	N	N	N	N
Forestomach:		N	N	N	N	N	N	N	N	N	N	N	N
Stomach, limiting ridge:		N	N	N	N	N	N	N	N	N	N	N	N
Glandular stomach:		N	N	N	N	N	N	N	N	N	N	N	N
Duodenum:		N	N	N	N	N	N	N	N	N	N	N	N
Jejunum:		N	N	N	N	N	N	N	N	N	N	N	N
Ileum (including Peyer's patch):		N	N	N	N	N	N	N	N	N	N	N	N
Cecum:		N	N	N	N	N	N	N	N	N	N	N	N
Colon:		N	N	N	N	N	N	N	N	N	N	N	N
Rectum:		N	N	N	N	N	N	N	N	N	N	N	N
Pancreas:		N	N	N	N	N	N	N	N	N	N	N	N
Liver:	Microgranuloma	+	-	-	-	-	+	-	+	-	+	-	-
	Necrosis, focal	+	-	-	-	-	-	-	-	-	-	-	-
Heart:		N	N	N	N	N	N	N	N	N	N	N	N
Right kidney:		N	N	N	N	N	N	N	N	N	N	N	N
Left kidney:	Dilatation, renal pelvis	+	-	-	-	-	-	-	-	-	-	-	-
Urinary bladder:		N	N	N	N	N	N	N	N	N	N	N	N
Right overy:		N	N	N	N	N	N	N	N	N	N	N	N
Left ovary:		N	N	N	N	N	N	N	N	N	N	N	N
Right uterine horn:		N	N	N	N	N	N	N	N	N	N	N	N
Left uterin horn:		N	N	N	N	N	N	N	N	N	N	N	N
Uterine cervix:		N	N	N	N	N	N	N	N	N	N	N	N
Vagina;		N	N	N	N	N	N	N	N	N	N	N	N

N: No abnormal findings, -: normal, +: slight change, ++: moderate change, +++: severe change.

INDIVIDUAL DATA 31-6

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Histopathological findings ANIMAL: Rat, Crl: CD (SD) SEX: Female GROUP: 100 mg/kg PERIOD: Day 5 of lactation

Animal No.		451	452	453	454	455	456	457	458	459	460	461	462
Organ: Findings													
Cerebrum:		N	N	N	N	N	N	N	N	N	N	N	N
Cerebellum:		N	N	N	N	N	N	N	N	N	N	N	N
Pons:		N	N	N	N	N	N	N	N	N	N	N	N
Spinal cord:		N	N	N	N	N	N	N	N	N	N	N	N
Sciatic nerve:		N	N	N	N	N	N	N	N	N	N	N	N
Spleen:		N	N	N	N	N	N	N	N	N	N	N	N
Thymus:		N	N	N	N	N	N	N	N	N	N	N	N
Bone marrow of right femur:		N	N	N	N	N	N	N	N	N	N	N	N
Right submandibular lymph node:		N	N	N	N	N	N	N	N	N	N	N	N
Left submandibular lymph node:		N	N	N	N	N	N	N	N	N	N	N	N
Mesenteric lymph node:		N	N	N	N	N	N	N	N	N	N	N	N
Pituitary gland:	Cyst, pars distalis	-	-	-	-	-	-	-	-	-	-	-	+
Right thyroid:		N	N	N	N	N	N	N	N	N	N	N	N
Left thyroid:		N	N	N	N	N	N	N	N	N	N	N	N
Right parathyroid:		N	N	N	N	N	N	N	N	N	N	N	N
Left parathyroid:		N	N	N	N	N	N	N	N	N	N	N	N
Right adrenal:		N	N	N	N	N	N	N	N	N	N	N	N
Left adrenal:		N	N	N	N	N	N	N	N	N	N	N	N
Right eyeball:		N	N	N	N	N	N	N	N	N	N	N	N
Left eyeball:	Cellular infiltration, neutrophil, ciliary body and iris	-	-	-	-	-	-	-	+	-	-	-	-
Right Harderian gland:		N	N	N	N	N	N	N	N	N	N	N	N
Left Harderian gland:		N	N	N	N	N	N	N	N	N	N	N	N
Skeletal muscle:		N	N	N	N	N	N	N	N	N	N	N	N
Right femur:		N	N	N	N	N	N	N	N	N	N	N	N
Mammary gland:		N	N	N	N	N	N	N	N	N	N	N	N

N: No abnormal findings, -: normal, +: slight change, ++: moderate change, +++: severe change.

INDIVIDUAL DATA 32-1-1

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Histopathological findings ANIMAL: Rat, Crl: CD (SD) SEX: Female GROUP: satellite 0 mg/kg PERIOD: after Week 6 of administration

Animal No.		163	164	165	166	167
Organ: Findings						
Lung:		N	N	N	N	N
Trachea:		N	N	N	N	N
Right submandibular gland:		N	N	N	N	N
Left submandibular gland:		N	N	N	N	N
Esophagus:		N	N	N	N	N
Forestomach:		N	N	N	N	N
Stomach, limiting ridge:		N	N	N	N	N
Glandular stomach:	Erosion	+	-	-	-	-
Duodenum:		N	N	N	N	N
Jejunum:		N	N	N	N	N
Ileum (including Peyer's patch):		N	N	N	N	N
Cecum:		N	N	N	N	N
Colon:		N	N	N	N	N
Rectum:		N	N	N	N	N
Pancreas:		N	N	N	N	N
Liver:	Microgranuloma	-	-	-	+	-
Heart:	Inflammation, focal	+	-	-	-	-
Right kidney:	Cellular infiltration, inflammatory cell, renal pelvic mucosa	-	-	+	-	-
Left kidney:		N	N	N	N	N
Urinary bladder:		N	N	N	N	N
Right overy:		N	N	N	N	N
Left ovary:		N	N	N	N	N
Right uterine horn:		N	N	N	N	N
Left uterin horn:		N	N	N	N	N
Uterine cervix:		N	N	N	N	N
Vagina;		N	N	N	N	N

N: No abnormal findings, -: normal, +: slight change, ++: moderate change, +++: severe change.

INDIVIDUAL DATA 32-1-2

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Histopathological findings ANIMAL: Rat, Crl: CD (SD) SEX: Female GROUP: satellite 0 mg/kg PERIOD: after Week 6 of administration

Animal No.	163	164	165	166	167
Organ: Findings					
Cerebrum:	N	N	N	N	N
Cerebellum:	N	N	N	N	N
Pons:	N	N	N	N	N
Spinal cord:	N	N	N	N	N
Sciatic nerve:	N	N	N	N	N
Spleen:	N	N	N	N	N
Thymus:	N	N	N	N	N
Bone marrow of right femur:	N	N	N	N	N
Right submandibular lymph node:	N	N	N	N	N
Left submandibular lymph node:	N	N	N	N	N
Mesenteric lymph node:	N	N	N	N	N
Pituitary gland:	N	N	N	N	N
Right thyroid:	N	N	N	N	N
Left thyroid:	N	N	N	N	N
Right parathyroid:	N	N	N	N	N
Left parathyroid:	**	N	N	N	N
Right adrenal:	N	N	N	N	N
Left adrenal:	N	N	N	N	N
Right eyeball:	N	N	N	N	N
Left eyeball:	N	N	N	N	N
Right Harderian gland:	N	N	N	N	N
Left Harderian gland:	N	N	N	N	N
Skeletal muscle:	N	N	N	N	N
Right femur:	N	N	N	N	N
Mammary gland:	N	N	N	N	N

N: No abnormal findings, -: normal, +: slight change, ++: moderate change, +++: severe change.
**: Not examined because of missing.

INDIVIDUAL DATA 32-1-3

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Histopathological findings ANIMAL: Rat, Crl: CD (SD) SEX: Female GROUP: satellite 100 mg/kg PERIOD: after Week 6 of administration

Animal No.		463	464	465	466	467
Organ: Findings						
Lung:	Aggregation, macrophage, alveolar	-	-	-	+	-
Trachea:		N	N	N	N	N
Right submandibular gland:		N	N	N	N	N
Left submandibular gland:		N	N	N	N	N
Esophagus:		N	N	N	N	N
Forestomach:		N	N	N	N	N
Stomach, limiting ridge:		N	N	N	N	N
Glandular stomach:	Ductal tissue, ectopic, submucosa	-	+	-	-	-
Duodenum:		N	N	N	N	N
Jejunum:		N	N	N	N	N
Ileum (including Peyer's patch):		N	N	N	N	N
Cecum:		N	N	N	N	N
Colon:		N	N	N	N	N
Rectum:		N	N	N	N	N
Pancreas:		N	N	N	N	N
Liver:	Fatty change, periportal	-	-	+[a]	-	-
Heart:		N	N	N	N	N
Right kidney:		N	N	N	N	N
Left kidney:		N	N	N	N	N
Urinary bladder:		N	N	N	N	N
Right overy:		N	N	N	N	N
Left ovary:		N	N	N	N	N
Right uterine horn:		N	N	N	N	N
Left uterin horn:		N	N	N	N	N
Uterine cervix:		N	N	N	N	N
Vagina;		N	N	N	N	N

N: No abnormal findings, -: normal, +: slight change, ++: moderate change, +++: severe change.

a: Oil red O stain positive.

INDIVIDUAL DATA 32-1-4

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Histopathological findings ANIMAL: Rat, Crl: CD (SD) SEX: Female GROUP: satellite 100 mg/kg PERIOD: after Week 6 of administration

Animal No.		463	464	465	466	467
Organ: Findings						
Cerebrum:		N	N	N	N	N
Cerebellum:		N	N	N	N	N
Pons:		N	N	N	N	N
Spinal cord:		N	N	N	N	N
Sciatic nerve:		N	N	N	N	N
Spleen:		N	N	N	N	N
Thymus:		N	N	N	N	N
Bone marrow of right femur:		N	N	N	N	N
Right submandibular lymph node:		N	N	N	N	N
Left submandibular lymph node:		N	N	N	N	N
Mesenteric lymph node:		N	N	N	N	N
Pituitary gland:		N	N	N	N	N
Right thyroid:		N	N	N	N	N
Left thyroid:		N	N	N	N	N
Right parathyroid:		N	N	N	N	N
Left parathyroid:		N	N	N	N	N
Right adrenal:		N	N	N	N	N
Left adrenal:		N	N	N	N	N
Right eyeball:		N	N	N	N	N
Left eyeball:		N	N	N	N	N
Right Harderian gland:	Cellular infiltration, mononuclear cell	-	-	-	+	-
Left Harderian gland:		N	N	N	N	N
Skeletal muscle:		N	N	N	N	N
Right femur:		N	N	N	N	N
Mammary gland:		N	N	N	N	N

N: No abnormal findings, -: normal, +: slight change, ++: moderate change, +++: severe change.

INDIVIDUAL DATA 32-2-1

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Histopathological findings ANIMAL: Rat, Crl: CD (SD) SEX: Female GROUP: satellite 0 mg/kg PERIOD: after Week 2 of recovery

Animal No.		168	169	170	171	172
Organ: Findings						
Lung:	Aggregation, macrophage, alveolar	+	-	+	+	-
	Mineralization, artery	+	-	+	+	-
	Metaplasia, osseous, alveoli	-	-	-	-	+
Trachea:		N	N	N	N	N
Right submandibular gland:		N	N	N	N	N
Left submandibular gland:		N	N	N	N	N
Esophagus:		N	N	N	N	N
Forestomach:		N	N	N	N	N
Stomach, limiting ridge:		N	N	N	N	N
Glandular stomach:		N	N	N	N	N
Duodenum:		N	N	N	N	N
Jejunum:		N	N	N	N	N
Ileum (including Peyer's patch):		N	N	N	N	N
Cecum:		N	N	N	N	N
Colon:		N	N	N	N	N
Rectum:		N	N	N	N	N
Pancreas:		N	N	N	N	N
Liver:		N	N	N	N	N
Heart:		N	N	N	N	N
Right kidney:	Cellular infiltration, inflammatory cell, renal pelvic mucosa	+	-	-	-	-
Left kidney:		N	N	N	N	N
Urinary bladder:		N	N	N	N	N
Right overy:		N	N	N	N	N
Left ovary:		N	N	N	N	N
Right uterine horn:		N	N	N	N	N
Left uterin horn:		N	N	N	N	N
Uterine cervix:		N	N	N	N	N
Vagina;		N	N	N	N	N

N: No abnormal findings, -: normal, +: slight change, ++: moderate change, +++: severe change.

INDIVIDUAL DATA 32-2-2

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Histopathological findings ANIMAL: Rat, Crl: CD (SD) SEX: Female GROUP: satellite 0 mg/kg PERIOD: after Week 2 of recovery

Animal No.	168	169	170	171	172
Organ: Findings					
Cerebrum:	N	N	N	N	N
Cerebellum:	N	N	N	N	N
Pons:	N	N	N	N	N
Spinal cord:	N	N	N	N	N
Sciatic nerve:	N	N	N	N	N
Spleen:	N	N	N	N	N
Thymus:	N	N	N	N	N
Bone marrow of right femur:	N	N	N	N	N
Right submandibular lymph node:	N	N	N	N	N
Left submandibular lymph node:	N	N	N	N	N
Mesenteric lymph node:	N	N	N	N	N
Pituitary gland:	N	N	N	N	N
Right thyroid:	N	N	N	N	N
Left thyroid:	N	N	N	N	N
Right parathyroid:	N	N	N	N	N
Left parathyroid:	**	N	N	N	N
Right adrenal:	N	N	N	N	N
Left adrenal:	N	N	N	N	N
Right eyeball:	N	N	N	N	N
Left eyeball:	N	N	N	N	N
Right Harderian gland:	N	N	N	N	N
Left Harderian gland:	N	N	N	N	N
Skeletal muscle:	N	N	N	N	N
Right femur:	N	N	N	N	N
Mammary gland:	N	N	N	N	N

N: No abnormal findings, -: normal, +: slight change, ++: moderate change, +++: severe change.

**: Not examined because of missing.

INDIVIDUAL DATA 32-2-3

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Histopathological findings ANIMAL: Rat, Crl: CD (SD) SEX: Female GROUP: satellite 100 mg/kg PERIOD: after Week 2 of recovery

Animal No.		468	469	470	471	472
Organ: Findings						
Lung:	Mineralization, artery	+	-	-	-	-
Trachea:		N	N	N	N	N
Right submandibular gland:		N	N	N	N	N
Left submandibular gland:		N	N	N	N	N
Esophagus:		N	N	N	N	N
Forestomach:		N	N	N	N	N
Stomach, limiting ridge:		N	N	N	N	N
Glandular stomach:		N	N	N	N	N
Duodenum:		N	N	N	N	N
Jejunum:		N	N	N	N	N
Ileum (including Peyer's patch):		N	N	N	N	N
Cecum:		N	N	N	N	N
Colon:		N	N	N	N	N
Rectum:		N	N	N	N	N
Pancreas:	Atrophy, acinar cell, focal	-	-	-	+	-
Liver:	Microgranuloma	-	+	-	-	-
Heart:		N	N	N	N	N
Right kidney:		N	N	N	N	N
Left kidney:		N	N	N	N	N
Urinary bladder:		N	N	N	N	N
Right overy:		N	N	N	N	N
Left ovary:		N	N	N	N	N
Right uterine horn:		N	N	N	N	N
Left uterin horn:		N	N	N	N	N
Uterine cervix:		N	N	N	N	N
Vagina;		N	N	N	N	N

N: No abnormal findings, -: normal, +: slight change, ++: moderate change, +++: severe change.

INDIVIDUAL DATA 32-2-4

STUDY NO. SR11087 TITLE: indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Histopathological findings ANIMAL: Rat, Crl: CD (SD) SEX: Female GROUP: satellite 100 mg/kg PERIOD: after Week 2 of recovery

Animal No.	468	469	470	471	472
Organ: Findings					
Cerebrum:	N	N	N	N	N
Cerebellum:	N	N	N	N	N
Pons:	N	N	N	N	N
Spinal cord:	N	N	N	N	N
Sciatic nerve:	N	N	N	N	N
Spleen:	N	N	N	N	N
Thymus:	N	N	N	N	N
Bone marrow of right femur:	N	N	N	N	N
Right submandibular lymph node:	N	N	N	N	N
Left submandibular lymph node:	N	N	N	N	N
Mesenteric lymph node:	N	N	N	N	N
Pituitary gland:	N	N	N	N	N
Right thyroid:	N	N	N	N	N
Left thyroid:	N	N	N	N	N
Right parathyroid:	N	**	**	N	N
Left parathyroid:	N	N	N	N	N
Right adrenal:	N	N	N	N	N
Left adrenal:	N	N	N	N	N
Right eyeball:	N	N	N	N	N
Left eyeball:	N	N	N	N	N
Right Harderian gland:	N	N	N	N	N
Left Harderian gland:	N	N	N	N	N
Skeletal muscle:	N	N	N	N	N
Right femur:	N	N	N	N	N
Mammary gland:	N	N	N	N	N

N: No abnormal findings, -: normal, +: slight change, ++: moderate change, +++: severe change.

**: Not examined because of missing.

INDIVIDUAL DATA 33-1-1

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Estrous cycle ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg

Animal No.	Administration day 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
	Pre-mating period														Mating period			
151	V	II	III	IV	V	II	III	IV	V	II	III	IV	V	II	IIIC	#	#	#
152	III	IV	V	V	II	III	IV	V	V	II	III	IV	V	V	IIIC	#	#	#
153	III	IV	V	II	III	IV	V	II	III	IV	V	II	III	III	IV	V	II	IIIC
154	IV	V	II	III	IV	V	II	III	IV	V	II	III	IV	V	II	IIIC	#	#
155	IV	V	II	III	IV	V	II	III	IV	V	II	III	IV	V	II	IIIC	#	#
156	V	III	IV	V	V	III	IV	V	V	III	IV	V	V	III	IV	V	II	IIIC
157	II	III	IV	V	II	II	III	IV	V	II	II	III	IV	V	V	II	IIIC	#
158	III	IV	V	II	III	IV	V	II	III	IV	V	II	III	IV	V	II	IIIC	#
159	V	II	III	IV	V	II	III	IV	V	II	III	IV	V	II	IIIC	#	#	#
160	IV	V	II	III	IV	V	II	III	IV	V	II	III	IV	V	II	IIIC	#	#
161	V	II	III	IV	V	II	III	IV	V	II	III	IV	V	II	IIIC	#	#	#
162	II	III	IV	V	V	II	III	IV	V	V	II	III	IV	V	V	IIIC	#	#

II : Proestrus. III : Estrus. IV : Metestrus. V : Diestrus. C : Copulated.

: Not applicable.

INDIVIDUAL DATA 33-1-2

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Estrous cycle ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg

Animal No.	Administration day 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
	Pre-mating period														Mating period			
251	III	IV	V	II	III	IV	V	II	III	IV	V	II	III	IV	V	II	IIIC	#
252	III	IV	V	II	III	IV	V	II	III	IV	V	II	III	IV	V	II	IIIC	#
253	II	III	IV	V	II	III	IV	V	II	III	IV	V	II	III	IV	V	II	IIIC
254	III	IV	V	V	III	IV	V	II	III	IV	V	II	III	IV	V	II	IIIC	#
255	II	III	IV	V	II	III	IV	V	II	III	IV	V	II	III	IV	V	II	IIIC
256	V	II	III	IV	V	V	III	IV	V	II	III	IV	V	V	IIIC	#	#	#
257	V	II	III	IV	V	II	III	IV	V	II	III	IV	V	II	IIIC	#	#	#
258	III	IV	V	II	III	IV	V	II	III	IV	V	II	III	IV	V	II	IIIC	#
259	IV	V	II	III	IV	V	V	III	IV	V	II	III	IV	V	V	IIIC	#	#
260	II	III	IV	V	II	III	IV	V	V	III	III	IV	V	V	IIIC	#	#	#
261	II	III	IV	V	II	III	IV	V	II	III	IV	V	II	III	IV	V	II	IIIC
262	V	II	III	IV	V	II	III	IV	V	II	III	IV	V	II	IIIC	#	#	#

II : Proestrus. III : Estrus. IV : Metestrus. V : Diestrus. C : Copulated.

: Not applicable.

INDIVIDUAL DATA 33-1-3

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Estrous cycle ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg

Animal No.	Administration day 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
	Pre-mating period														Mating period			
351	II	III	IV	V	V	III	IV	V	II	III	IV	V	II	III	IV	V	II	IIIC
352	IV	V	II	III	IV	V	V	III	IV	V	V	III	IV	V	II	IIIC	#	#
353	V	II	III	IV	V	II	III	IV	V	II	III	IV	V	II	IIIC	#	#	#
354	III	IV	V	II	III	IV	V	II	III	IV	V	II	III	IV	V	II	IIIC	#
355	V	II	III	IV	V	II	III	IV	V	II	III	IV	V	II	IIIC	#	#	#
356	IV	V	II	III	IV	V	II	III	IV	V	II	III	IV	V	II	IIIC	#	#
357	V	II	III	IV	V	II	III	IV	V	II	III	IV	V	V	IIIC	#	#	#
358	IV	V	II	III	IV	V	V	III	IV	V	V	III	IV	V	II	IIIC	#	#
359	IV	V	II	III	IV	V	V	III	IV	V	II	III	IV	V	II	IIIC	#	#
360	IV	V	II	III	IV	V	V	III	IV	V	II	III	IV	V	II	IIIC	#	#
361	III	IV	V	II	III	IV	V	V	III	IV	V	II	III	IV	V	II	IIIC	#
362	II	III	IV	V	V	III	IV	V	V	III	IV	V	II	III	IV	V	II	IIIC

II : Proestrus. III : Estrus. IV : Metestrus. V : Diestrus. C : Copulated.

: Not applicable.

INDIVIDUAL DATA 33-1-4

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Estrous cycle ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg

Animal No.	Administration day 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
	Pre-mating period														Mating period			
451	V	II	III	III	IV	V	II	III	IV	V	II	III	IV	V	II	IIIC	#	#
452	V	II	III	III	IV	V	II	III	IV	V	II	III	IV	V	II	IIIC	#	#
453	III	IV	V	II	III	IV	V	II	III	IV	V	II	III	IV	V	II	IIIC	#
454	III	IV	V	II	III	IV	V	II	III	IV	V	II	III	IV	V	II	IIIC	#
455	V	II	III	IV	V	II	III	III	IV	V	V	III	III	IV	V	II	IIIC	#
456	IV	V	II	III	IV	V	V	V	III	III	IV	V	II	III	IIIC	#	#	#
457	V	II	III	IV	V	V	II	II	IV	V	II	III	IV	V	II	IIIC	#	#
458	V	II	III	IV	V	V	II	III	IV	V	II	III	IV	V	II	IIIC	#	#
459	IV	V	V	III	IV	V	V	V	III	IV	V	II	III	IV	V	II	IIIC	#
460	II	III	IV	V	II	III	IV	V	II	III	IV	V	II	III	IV	V	II	IIIC
461	V	II	III	IV	V	II	IV	V	II	III	IV	V	II	III	IV	V	II	IIIC
462	V	II	III	III	IV	V	V	II	III	IV	V	V	V	V	V	IIIC	#	#

II : Proestrus. III : Estrus. IV : Metestrus. V : Diestrus. C : Copulated.

: Not applicable.

INDIVIDUAL DATA 33-2-1

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Reproduction performance ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg

Female No.	Estrous cycle		Paired male No.	Copulation	Pregnancy	Parturition	Gestation length (days)	Nursing
	Normal or Abnormal	Mean cycle Length (days)						
151	Normal	4.0	101	+	+	+	22	+
152	Normal	4.7	102	+	+	+	23	+
153	Normal	4.3	103	+	+	+	23	+
154	Normal	4.0	104	+	+	+	22	+
155	Normal	4.0	105	+	+	+	23	-
156	Normal	4.0	106	+	+	+	23	+
157	Normal	5.0	107	+	+	+	22	+
158	Normal	4.0	108	+	+	+	22	+
159	Normal	4.0	109	+	+	+	22	+
160	Normal	4.0	110	+	+	+	22	+
161	Normal	4.0	111	+	+	+	22	+
162	Normal	4.7	112	+	+	+	23	+
N		12					12	
MEAN		4.23					22.4	
S.D.		0.36					0.5	

Abnormal estrous cycle (%)	Copulation index (%)		Fertility index (%)	Gestation index (%)	Nursing index (%)
	Male	Female			
0/12 (0.0)	12/12 (100.0)	12/12 (100.0)	12/12 (100.0)	12/12 (100.0)	11/12 (91.7)

Estrous cycle : Female rats cycling normally ; Defined as having a cycle length between 4 and 6 days.

Copulation, pregnancy, parturition and nursing : + ; Positive, - ; Negative.

Copulation index = (number of copulated animals / number of animals mated) x 100.

Fertility index = (number of pregnant females / number of copulated females) x 100.

Gestation index = (number of females with live pups / number of pregnant females) x 100.

Nursing index = (number of females nursing live pups on lactation day 4 / number of females with live pups delivery) x 100.

INDIVIDUAL DATA 33-2-2

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Reproduction performance ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg

Female No.	Estrous cycle		Paired male No.	Copulation	Pregnancy	Parturition	Gestation length (days)	Nursing
	Normal or Abnormal	Mean cycle Length (days)						
251	Normal	4.0	201	+	+	+	23	+
252	Normal	4.0	202	+	+	+	22	+
253	Normal	4.0	203	+	+	+	23	+
254	Normal	4.0	204	+	+	+	22	+
255	Normal	4.0	205	+	+	+	23	+
256	Normal	4.0	206	+	+	+	22	+
257	Normal	4.0	207	+	+	+	22	+
258	Normal	4.0	208	+	+	+	23	+
259	Normal	4.0	209	+	+	+	22	+
260	Normal	4.3	210	+	+	+	23	+
261	Normal	4.0	211	+	+	+	23	+
262	Normal	4.0	212	+	+	+	22	+
N		12					12	
MEAN		4.03					22.5	
S.D.		0.09					0.5	

Abnormal estrous cycle (%)	Copulation index (%)		Fertility index (%)	Gestation index (%)	Nursing index (%)
	Male	Female			
0/12 (0.0)	12/12 (100.0)	12/12 (100.0)	12/12 (100.0)	12/12 (100.0)	12/12 (100.0)

Estrous cycle : Female rats cycling normally ; Defined as having a cycle length between 4 and 6 days.

Copulation, pregnancy, parturition and nursing : + ; Positive.

Copulation index = (number of copulated animals / number of animals mated) x 100.

Fertility index = (number of pregnant females / number of copulated females) x 100.

Gestation index = (number of females with live pups / number of pregnant females) x 100.

Nursing index = (number of females nursing live pups on lactation day 4 / number of females with live pups delivery) x 100.

INDIVIDUAL DATA 33-2-3
STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
Reproduction performance ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg

Female No.	Estrous cycle		Paired male No.	Copulation	Pregnancy	Parturition	Gestation length (days)	Nursing
	Normal or Abnormal	Mean cycle Length (days)						
351	Normal	4.0	301	+	+	+	22	+
352	Normal	4.0	302	+	+	+	22	+
353	Normal	4.0	303	+	+	+	24	+
354	Normal	4.0	304	+	+	+	23	+
355	Normal	4.0	305	+	+	+	22	+
356	Normal	4.0	306	+	+	+	23	+
357	Normal	4.0	307	+	+	+	22	+
358	Normal	4.0	308	+	+	+	22	+
359	Normal	4.0	309	+	+	+	23	+
360	Normal	4.0	310	+	+	+	22	+
361	Normal	4.0	311	+	+	+	22	+
362	Normal	4.0	312	+	+	+	22	+
N		12					12	
MEAN		4.00					22.4	
S.D.		0.00					0.7	

Abnormal estrous cycle (%)	Copulation index (%)		Fertility index (%)	Gestation index (%)	Nursing index (%)
	Male	Female			
0/12 (0.0)	12/12 (100.0)	12/12 (100.0)	12/12 (100.0)	12/12 (100.0)	12/12 (100.0)

Estrous cycle : Female rats cycling normally ; Defined as having a cycle length between 4 and 6 days.
Copulation, pregnancy, parturition and nursing : + ; Positive.
Copulation index = (number of copulated animals / number of animals mated) x 100.
Fertility index = (number of pregnant females / number of copulated females) x 100.
Gestation index = (number of females with live pups / number of pregnant females) x 100.
Nursing index = (number of females nursing live pups on lactation day 4 / number of females with live pups delivery) x 100.

INDIVIDUAL DATA 33-2-4

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Reproduction performance ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg

Female No.	Estrous cycle		Paired male No.	Copulation	Pregnancy	Parturition	Gestation length (days)	Nursing
	Normal or Abnormal	Mean cycle Length (days)						
451	Normal	4.0	401	+	+	+	22	+
452	Normal	4.0	402	+	+	+	22	+
453	Normal	4.0	403	+	+	+	22	+
454	Normal	4.0	404	+	+	+	22	+
455	Normal	4.7	405	+	+	+	23	+
456	Normal	5.5	406	+	+	+	22	+
457	Normal	4.3	407	+	+	+	23	+
458	Normal	4.3	408	+	+	+	22	+
459	Normal	4.3	409	+	+	+	22	+
460	Normal	4.0	410	+	+	+	22	+
461	Normal	3.8	411	+	+	+	22	+
462	Normal	6.0	412	+	+	+	22	+
N		12					12	
MEAN		4.41					22.2	
S.D.		0.68					0.4	

Abnormal estrous cycle (%)	Copulation index (%)		Fertility index (%)	Gestation index (%)	Nursing index (%)
	Male	Female			
0/12 (0.0)	12/12 (100.0)	12/12 (100.0)	12/12 (100.0)	12/12 (100.0)	12/12 (100.0)

Estrous cycle : Female rats cycling normally ; Defined as having a cycle length between 4 and 6 days.

Copulation, pregnancy, parturition and nursing : + ; Positive.

Copulation index = (number of copulated animals / number of animals mated) x 100.

Fertility index = (number of pregnant females / number of copulated females) x 100.

Gestation index = (number of females with live pups / number of pregnant females) x 100.

Nursing index = (number of females nursing live pups on lactation day 4 / number of females with live pups delivery) x 100.

INDIVIDUAL DATA 34-1

STUDY NO. SR11087 TITLE : indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Pregnancy and litter data ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg

Dam No.	Number of corpora lutea	Number of implantation sites	Implantation index (%)	Delivery index (%)	Lactation Day 0										Lactation Day 4				
					Number of pups born				Number of live pups			Sex Ratio		Live birth index (%)	Number of live pups				Viability index (%)
					Total	Male	Female	Dead	Total	Male	Female	Pups born	Live pups		Total	Male	Female	Sex Ratio	
151	15	15	100.00	100.00	15	8	7	0	15	8	7	0.53	0.53	100.00	15	8	7	0.53	100.00
152	16	16	100.00	100.00	16	7	9	2	14	6	8	0.44	0.43	87.50	14	6	8	0.43	100.00
153	18	15	83.33	93.33	14	7	7	0	14	7	7	0.50	0.50	100.00	14	7	7	0.50	100.00
154	15	15	100.00	100.00	15	7	8	0	15	7	8	0.47	0.47	100.00	15	7	8	0.47	100.00
155	18	18	100.00	100.00	18	14	4	14	4	4	0	0.78	1.00	22.22	0	#	#	#	0.00
156	14	14	100.00	100.00	14	8	6	0	14	8	6	0.57	0.57	100.00	14	8	6	0.57	100.00
157	21	21	100.00	100.00	21	17	4	0	21	17	4	0.81	0.81	100.00	21	17	4	0.81	100.00
158	16	16	100.00	100.00	16	9	7	0	16	9	7	0.56	0.56	100.00	15	8	7	0.53	93.75
159	15	15	100.00	100.00	15	9	6	0	15	9	6	0.60	0.60	100.00	15	9	6	0.60	100.00
160	17	15	88.24	100.00	15	8	7	0	15	8	7	0.53	0.53	100.00	15	8	7	0.53	100.00
161	18	18	100.00	88.89	16	10	6	0	16	10	6	0.63	0.63	100.00	16	10	6	0.63	100.00
162	17	16	94.12	87.50	14	5	9	0	14	5	9	0.36	0.36	100.00	12	5	7	0.42	85.71
N	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	11	11	11	12
MEAN	16.7	16.2	97.141	97.477	15.8	9.1	6.7	1.3	14.4	8.2	6.3	0.565	0.583	92.477	13.8	8.5	6.6	0.547	89.955
S.D.	1.9	1.9	5.662	4.746	2.0	3.3	1.6	4.0	3.8	3.3	2.3	0.130	0.172	22.415	4.8	3.1	1.1	0.109	28.655

Implantation index = (number of implantation sites / number of corpora lutea) x 100.

Delivery index = (number of pups born / number of implantation sites) x 100.

Sex ratio on Lactation day 0 = (number of male pups born / number of pups born) and (number of live male pups / number of live pups).

Sex ratio on Lactation day 4 = number of live male pups / number of live pups.

Live birth index = (number of live pups on lactation day 0 / number of pups born) x 100.

Viability index = (number of live pups on lactation day 4 / number of live pups on lactation day 0) x 100.

: Not applicable.

INDIVIDUAL DATA 34-2

STUDY NO. SR11087 TITLE : indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Pregnancy and litter data ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg

Dam No.	Number of corpora lutea	Number of implantation sites	Implantation index (%)	Delivery index (%)	Lactation Day 0										Lactation Day 4				
					Number of pups born				Number of live pups			Sex Ratio		Live birth index (%)	Number of live pups				Viability index (%)
					Total	Male	Female	Dead	Total	Male	Female	Pups born	Live pups		Total	Male	Female	Sex Ratio	
251	13	12	92.31	100.00	12	8	4	0	12	8	4	0.67	0.67	100.00	12	8	4	0.67	100.00
252	16	15	93.75	100.00	15	9	6	0	15	9	6	0.60	0.60	100.00	15	9	6	0.60	100.00
253	15	15	100.00	80.00	12	7	5	0	12	7	5	0.58	0.58	100.00	12	7	5	0.58	100.00
254	18	17	94.44	100.00	17	9	8	0	17	9	8	0.53	0.53	100.00	17	9	8	0.53	100.00
255	16	16	100.00	100.00	16	8	8	0	16	8	8	0.50	0.50	100.00	15	7	8	0.47	93.75
256	16	16	100.00	100.00	16	8	8	0	16	8	8	0.50	0.50	100.00	16	8	8	0.50	100.00
257	15	15	100.00	100.00	15	5	10	0	15	5	10	0.33	0.33	100.00	15	5	10	0.33	100.00
258	15	15	100.00	86.67	13	5	8	0	13	5	8	0.38	0.38	100.00	13	5	8	0.38	100.00
259	15	14	93.33	78.57	11	7	4	0	11	7	4	0.64	0.64	100.00	11	7	4	0.64	100.00
260	16	16	100.00	87.50	14	6	8	0	14	6	8	0.43	0.43	100.00	14	6	8	0.43	100.00
261	16	15	93.75	93.33	14	5	9	0	14	5	9	0.36	0.36	100.00	14	5	9	0.36	100.00
262	16	16	100.00	87.50	14	11	3	0	14	11	3	0.79	0.79	100.00	14	11	3	0.79	100.00
N	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
MEAN	15.6	15.2	97.298	92.798	14.1	7.3	6.8	0.0	14.1	7.9	6.8	0.526	0.526	100.000	14.0	7.3	6.8	0.523	99.479
S.D.	1.2	1.3	3.372	8.374	1.8	1.9	2.3	0.0	1.8	2.0	2.3	0.138	0.138	0.000	1.8	1.9	2.3	0.139	1.804

Implantation index = (number of implantation sites / number of corpora lutea) x 100.

Delivery index = (number of pups born / number of implantation sites) x 100.

Sex ratio on Lactation day 0 = (number of male pups born / number of pups born) and (number of live male pups / number of live pups).

Sex ratio on Lactation day 4 = number of live male pups / number of live pups.

Live birth index = (number of live pups on lactation day 0 / number of pups born) x 100.

Viability index = (number of live pups on lactation day 4 / number of live pups on lactation day 0) x 100.

INDIVIDUAL DATA 34-3

STUDY NO. SR11087 TITLE : indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Pregnancy and litter data ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg

Dam No.	Number of corpora lutea	Number of implantation sites	Implantation index (%)	Delivery index (%)	Lactation Day 0										Lactation Day 4				
					Number of pups born				Number of live pups			Sex Ratio		Live birth index (%)	Number of live pups				Viability index (%)
					Total	Male	Female	Dead	Total	Male	Female	Pups born	Live pups		Total	Male	Female	Sex Ratio	
351	16	16	100.00	93.75	15	9	6	0	15	9	6	0.60	0.60	100.00	15	9	6	0.60	100.00
352	16	15	93.75	93.33	14	9	5	0	14	9	5	0.64	0.64	100.00	14	9	5	0.64	100.00
353	15	15	100.00	46.67	7	1	6	0	7	1	6	0.14	0.14	100.00	7	1	6	0.14	100.00
354	15	15	100.00	100.00	15	11	4	0	15	11	4	0.73	0.73	100.00	14	10	4	0.71	93.33
355	14	14	100.00	100.00	14	9	5	0	14	9	5	0.64	0.64	100.00	14	9	5	0.64	100.00
356	17	17	100.00	88.24	15 [a]	6	8	4 [a]	11	4	7	0.43	0.36	78.57	11	4	7	0.36	100.00
357	15	15	100.00	100.00	15	7	8	0	15	7	8	0.47	0.47	100.00	14	7	7	0.50	93.33
358	16	16	100.00	93.75	15	10	5	0	15	10	5	0.67	0.67	100.00	15	10	5	0.67	100.00
359	17	16	94.12	100.00	16	6	10	0	16	6	10	0.38	0.38	100.00	16	6	10	0.38	100.00
360	17	17	100.00	100.00	17	6	11	1	16	5	11	0.35	0.31	94.12	16	5	11	0.31	100.00
361	18	18	100.00	100.00	18	10	8	1	17	9	8	0.56	0.53	94.44	17	9	8	0.53	100.00
362	16	16	100.00	100.00	16	10	6	0	16	10	6	0.63	0.63	100.00	16	10	6	0.63	100.00
N	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
MEAN	16.0	15.8	98.989	92.978	14.8	7.8	6.8	0.5	14.3	7.5	6.8	0.520	0.508	97.261	14.1	7.4	6.7	0.509	98.888
S.D.	1.1	1.1	2.362	15.116	2.7	2.8	2.2	1.2	2.7	3.0	2.1	0.170	0.178	6.286	2.7	2.9	2.1	0.175	2.596

Implantation index = (number of implantation sites / number of corpora lutea) x 100.

Delivery index = (number of pups born / number of implantation sites) x 100.

Sex ratio on Lactation day 0 = (number of male pups born / number of pups born) and (number of live male pups / number of live pups).

Sex ratio on Lactation day 4 = number of live male pups / number of live pups.

Live birth index = (number of live pups on lactation day 0 / number of pups born) x 100.

Viability index = (number of live pups on lactation day 4 / number of live pups on lactation day 0) x 100.

a : Including one pup that was not distinguished its sex because of maternal cannibalism (it was excluded from calculatiom of sex ratio).

INDIVIDUAL DATA 34-4

STUDY NO. SR11087 TITLE : indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Pregnancy and litter data ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg

Dam No.	Number of corpora lutea	Number of implantation sites	Implantation index (%)	Delivery index (%)	Lactation Day 0										Lactation Day 4				
					Number of pups born				Number of live pups			Sex Ratio		Live birth index (%)	Number of live pups				Viability index (%)
					Total	Male	Female	Dead	Total	Male	Female	Pups born	Live pups		Total	Male	Female	Sex Ratio	
451	15	15	100.00	93.33	14	6	8	0	14	6	8	0.43	0.43	100.00	13	6	7	0.46	92.86
452	15	15	100.00	100.00	15	9	6	0	15	9	6	0.60	0.60	100.00	15	9	6	0.60	100.00
453	17	17	100.00	100.00	17	10	7	0	17	10	7	0.59	0.59	100.00	16	9	7	0.56	94.12
454	16	16	100.00	100.00	16	9	7	0	16	9	7	0.56	0.56	100.00	16	9	7	0.56	100.00
455	15	15	100.00	93.33	14	8	6	0	14	8	6	0.57	0.57	100.00	14	8	6	0.57	100.00
456	17	17	100.00	100.00	17	7	10	0	17	7	10	0.41	0.41	100.00	17	7	10	0.41	100.00
457	17	15	88.24	100.00	15	8	7	0	15	8	7	0.53	0.53	100.00	15	8	7	0.53	100.00
458	16	16	100.00	93.75	15	10	5	0	15	10	5	0.67	0.67	100.00	15	10	5	0.67	100.00
459	18	17	94.44	88.24	15	9	6	2	13	8	5	0.60	0.62	86.67	13	8	5	0.62	100.00
460	15	14	93.33	100.00	14	9	5	0	14	9	5	0.64	0.64	100.00	14	9	5	0.64	100.00
461	16	16	100.00	87.50	14	4	10	0	14	4	10	0.29	0.29	100.00	14	4	10	0.29	100.00
462	18	18	100.00	83.33	15	8	7	0	15	8	7	0.53	0.53	100.00	15	8	7	0.53	100.00
N	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
MEAN	16.3	15.9	98.001	94.957	15.1	8.1	7.0	0.2	14.9	8.0	6.9	0.535	0.537	98.889	14.8	7.9	6.8	0.537	98.915
S.D.	1.1	1.2	3.882	5.994	1.1	1.7	1.7	0.6	1.2	1.7	1.7	0.108	0.110	3.848	1.2	1.6	1.7	0.106	2.548

Implantation index = (number of implantation sites / number of corpora lutea) x 100.

Delivery index = (number of pups born / number of implantation sites) x 100.

Sex ratio on Lactation day 0 = (number of male pups born / number of pups born) and (number of live male pups / number of live pups).

Sex ratio on Lactation day 4 = number of live male pups / number of live pups.

Live birth index = (number of live pups on lactation day 0 / number of pups born) x 100.

Viability index = (number of live pups on lactation day 4 / number of live pups on lactation day 0) x 100.

INDIVIDUAL DATA 35-1
STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
General appearance , pups ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg

Dam No.	Day of lactation period	Male		Female	
		Number of pups	Finding and number of animals with findings	Number of pups	Finding and number of animals with findings
151	0-4	8	No abnormal findings ; 8	7	No abnormal findings ; 7
152	0	7	Death(milk-band negative) ; 1, No abnormal findings ; 6	9	Death(milk-band negative) ; 1, No abnormal findings ; 8
	1-4	6	No abnormal findings ; 6	8	No abnormal findings ; 8
153	0-4	7	No abnormal findings ; 7	7	No abnormal findings ; 7
154	0-4	7	No abnormal findings ; 7	8	No abnormal findings ; 8
155	0	14	Death(milk-band negative) ; 7 , Death(milk-band not examined because of autolysis of abdominal cavity) ; 3 , Milk-band negative ; 4	4	Death(milk-band negative) ; 4
	1	4	Death(milk-band negative) ; 4	#	#
156	0-4	8	No abnormal findings ; 8	6	No abnormal findings ; 6
157	0-4	17	No abnormal findings ; 17	4	No abnormal findings ; 4
158	0,1	9	No abnormal findings ; 9	7	No abnormal findings ; 7
	2	9	Death(milk-band not examined because of autolysis of abdominal cavity) ; 1 , No abnormal findings ; 8	7	No abnormal findings ; 7
	3,4	8	No abnormal findings ; 8	7	No abnormal findings ; 7
159	0-4	9	No abnormal findings ; 9	6	No abnormal findings ; 6
160	0-4	8	No abnormal findings ; 8	7	No abnormal findings ; 7
161	0-4	10	No abnormal findings ; 10	6	No abnormal findings ; 6
162	0	5	No abnormal findings ; 5	9	No abnormal findings ; 9
	1	5	No abnormal findings ; 5	9	Death (lost) ; 2, No abnormal findings ; 7
	2-4	5	No abnormal findings ; 5	7	No abnormal findings ; 7

: Not applicable.

INDIVIDUAL DATA 35-2
STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
General appearance , pups ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg

Dam No.	Day of lactation period	Male		Female	
		Number of pups	Finding and number of animals with findings	Number of pups	Finding and number of animals with findings
251	0-4	8	No abnormal findings ; 8	4	No abnormal findings ; 4
252	0-4	9	No abnormal findings ; 9	6	No abnormal findings ; 6
253	0-4	7	No abnormal findings ; 7	5	No abnormal findings ; 5
254	0-4	9	No abnormal findings ; 9	8	No abnormal findings ; 8
255	0-3	8	No abnormal findings ; 8	8	No abnormal findings ; 8
	4	8	Death(milk-band negative) ; 1, No abnormal findings ; 7	8	No abnormal findings ; 8
256	0-4	8	No abnormal findings ; 8	8	No abnormal findings ; 8
257	0-4	5	No abnormal findings ; 5	10	No abnormal findings ; 10
258	0-4	5	No abnormal findings ; 5	8	No abnormal findings ; 8
259	0-4	7	No abnormal findings ; 7	4	No abnormal findings ; 4
260	0-4	6	No abnormal findings ; 6	8	No abnormal findings ; 8
261	0-4	5	No abnormal findings ; 5	9	No abnormal findings ; 9
262	0-4	11	No abnormal findings ; 11	3	No abnormal findings ; 3

INDIVIDUAL DATA 35-3
STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
General appearance , pups ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg

Dam No.	Day of lactation period	Male		Female	
		Number of pups	Finding and number of animals with findings	Number of pups	Finding and number of animals with findings
351	0-4	9	No abnormal findings ; 9	6	No abnormal findings ; 6
352	0-4	9	No abnormal findings ; 9	5	No abnormal findings ; 5
353	0-4	1	No abnormal findings ; 1	6	No abnormal findings ; 6
354	0	11	No abnormal findings ; 11	4	No abnormal findings ; 4
	1	11	Death(milk-band positive) ; 1, No abnormal findings ; 10	4	No abnormal findings ; 4
	2-4	10	No abnormal findings ; 10	4	No abnormal findings ; 4
355	0-4	9	No abnormal findings ; 9	5	No abnormal findings ; 5
356	0	7[a]	Death(milk-band not examined because of autolysis of abdominal cavity) ; 1 , Death(milk-band not examined because of maternal cannibalism) ; 1 , Death(milk-band positive) ; 1 , No abnormal findings ; 4	8	Death(milk-band not examined because of autolysis of abdominal cavity) ; 1 , No abnormal findings ; 7
	1-4	4	No abnormal findings ; 4	7	No abnormal findings ; 7
357	0,1	7	No abnormal findings ; 7	8	No abnormal findings ; 8
	2	7	No abnormal findings ; 7	8	Death(milk-band negative) ; 1, No abnormal findings ; 7
	3,4	7	No abnormal findings ; 7	7	No abnormal findings ; 7
358	0-4	10	No abnormal findings ; 10	5	No abnormal findings ; 5
359	0-4	6	No abnormal findings ; 6	10	No abnormal findings ; 10
360	0	6	Death(milk-band negative) ; 1, No abnormal findings ; 5	11	No abnormal findings ; 11
	1-4	5	No abnormal findings ; 5	11	No abnormal findings ; 11
361	0	10	Death(milk-band not examined because of autolysis of abdominal cavity) ; 1 , No abnormal findings ; 9	8	No abnormal findings ; 8
	1-4	9	No abnormal findings ; 9	8	No abnormal findings ; 8
362	0-4	10	No abnormal findings ; 10	6	No abnormal findings ; 6

a : Including one pup that was not distinguished its sex because of maternal cannibalism.

INDIVIDUAL DATA 35-4
STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats
General appearance , pups ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg

Dam No.	Day of lactation period	Male		Female	
		Number of pups	Finding and number of animals with findings	Number of pups	Finding and number of animals with findings
451	0	6	No abnormal findings ; 6	8	No abnormal findings ; 8
	1	6	No abnormal findings ; 6	8	Death (lost) ; 1, No abnormal findings ; 7
	2-4	6	No abnormal findings ; 6	7	No abnormal findings ; 7
452	0-4	9	No abnormal findings ; 9	6	No abnormal findings ; 6
453	0,1	10	No abnormal findings ; 10	7	No abnormal findings ; 7
	2	10	Death(milk-band negative) ; 1, No abnormal findings ; 9	7	No abnormal findings ; 7
	3,4	9	No abnormal findings ; 9	7	No abnormal findings ; 7
454	0-4	9	No abnormal findings ; 9	7	No abnormal findings ; 7
455	0-4	8	No abnormal findings ; 8	6	No abnormal findings ; 6
456	0-4	7	No abnormal findings ; 7	10	No abnormal findings ; 10
457	0-4	8	No abnormal findings ; 8	7	No abnormal findings ; 7
458	0-4	10	No abnormal findings ; 10	5	No abnormal findings ; 5
459	0	9	Death(milk-band negative) ; 1, No abnormal findings ; 8	6	Death(milk-band negative) ; 1, No abnormal findings ; 5
	1-4	8	No abnormal findings ; 8	5	No abnormal findings ; 5
460	0-4	9	No abnormal findings ; 9	5	No abnormal findings ; 5
461	0-4	4	No abnormal findings ; 4	10	No abnormal findings ; 10
462	0-4	8	No abnormal findings ; 8	7	No abnormal findings ; 7

INDIVIDUAL DATA 36-1

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Body weight, pups ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg

	Body weight (g)											
	Male						Female					
	Lactation day						Lactation day					
	0		1		4		0		1		4	
Dam No.	n	Mean	n	Mean	n	Mean	n	Mean	n	Mean	n	Mean
151	8	6.3	8	6.6	8	9.3	7	6.0	7	6.3	7	8.9
152	6	7.4	6	8.2	6	11.8	8	6.6	8	7.2	8	10.3
153	7	7.2	7	8.1	7	11.8	7	6.4	7	7.2	7	11.0
154	7	6.4	7	6.5	7	9.4	8	6.0	8	6.2	8	8.7
155	4	6.3	#	#	#	#	#	#	#	#	#	#
156	8	6.7	8	7.2	8	10.4	6	6.2	6	6.7	6	9.7
157	17	5.6	17	6.1	17	8.6	4	5.0	4	5.4	4	7.1
158	9	6.0	9	6.4	8	9.7	7	5.6	7	6.0	7	8.7
159	9	6.5	9	7.1	9	9.9	6	6.5	6	6.9	6	10.3
160	8	6.6	8	7.1	8	10.2	7	6.5	7	7.0	7	10.2
161	10	6.1	10	6.8	10	10.0	6	5.7	6	6.4	6	9.5
162	5	7.2	5	8.3	5	13.0	9	6.5	7	8.2	7	12.7
N		12		11		11		11		11		11
MEAN		6.53		7.13		10.37		6.09		6.68		9.74
S.D.		0.53		0.76		1.31		0.50		0.75		1.45
S.E.		0.15		0.23		0.39		0.15		0.22		0.44

n : Number of pups.

: Not applicable.

INDIVIDUAL DATA 36-2

STUDY NO. SR11087 TITLE : indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Body weight, pups ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg

	Body weight (g)											
	Male						Female					
	Lactation day						Lactation day					
	0		1		4		0		1		4	
Dam No.	n	Mean	n	Mean	n	Mean	n	Mean	n	Mean	n	Mean
251	8	8.2	8	9.1	8	13.8	4	7.4	4	8.4	4	12.9
252	9	6.1	9	6.2	9	8.8	6	5.9	6	6.1	6	8.6
253	7	7.6	7	8.7	7	13.3	5	7.1	5	8.3	5	13.1
254	9	6.5	9	7.0	9	9.7	8	6.1	8	6.7	8	9.2
255	8	6.8	8	6.8	7	7.4	8	6.6	8	6.6	8	7.3
256	8	6.2	8	6.7	8	9.7	8	6.0	8	6.3	8	9.6
257	5	6.9	5	7.6	5	11.2	10	6.6	10	7.3	10	10.6
258	5	8.2	5	9.0	5	12.3	8	8.0	8	8.9	8	12.0
259	7	6.9	7	7.6	7	11.6	4	6.7	4	7.5	4	11.4
260	6	7.3	6	8.0	6	11.4	8	6.9	8	7.7	8	10.9
261	5	7.5	5	8.2	5	11.6	9	7.0	9	7.5	9	10.7
262	11	6.7	11	7.6	11	11.6	3	6.4	3	7.2	3	10.9
N		12		12		12		12		12		12
MEAN		7.08*		7.71		11.03		6.73**		7.38*		10.60
S.D.		0.70		0.93		1.84		0.61		0.87		1.71
S.E.		0.20		0.27		0.53		0.18		0.25		0.49

* : Significantly different from the 0 mg/kg group at P≦0.05 (Dunnett's test).

** : Significantly different from the 0 mg/kg group at P≦0.01 (Dunnett's test).

n : Number of pups.

INDIVIDUAL DATA 36-3

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Body weight, pups ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg

	Body weight (g)											
	Male						Female					
	Lactation day						Lactation day					
	0		1		4		0		1		4	
Dam No.	n	Mean	n	Mean	n	Mean	n	Mean	n	Mean	n	Mean
351	9	6.5	9	7.0	9	10.2	6	6.2	6	6.7	6	9.7
352	9	6.7	9	7.1	9	10.5	5	6.2	5	6.6	5	9.8
353	1	7.8	1	9.3	1	16.1	6	6.7	6	7.7	6	13.7
354	11	7.0	10	7.7	10	11.3	4	7.1	4	7.7	4	11.0
355	9	6.2	9	6.8	9	10.1	5	6.0	5	6.5	5	9.7
356	4	6.7	4	7.5	4	11.9	7	6.4	7	7.1	7	11.0
357	7	6.4	7	7.3	7	11.6	8	5.9	8	6.8	7	11.3
358	10	6.7	10	7.4	10	11.6	5	6.2	5	6.9	5	10.6
359	6	6.8	6	7.2	6	10.3	10	6.3	10	6.9	10	9.9
360	5	6.5	5	6.7	5	10.5	11	6.2	11	6.6	11	10.0
361	9	6.1	9	6.5	9	9.7	8	5.6	8	6.0	8	9.2
362	10	6.4	10	6.8	10	10.0	6	6.2	6	6.5	6	9.4
N		12		12		12		12		12		12
MEAN		6.65		7.28		11.15		6.25		6.83		10.44
S.D.		0.44		0.73		1.72		0.38		0.49		1.23
S.E.		0.13		0.21		0.50		0.11		0.14		0.35

n : Number of pups.

INDIVIDUAL DATA 36-4

STUDY NO. SR11087 TITLE : indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Body weight, pups ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg

	Body weight (g)											
	Male						Female					
	Lactation day						Lactation day					
	0		1		4		0		1		4	
Dam No.	n	Mean	n	Mean	n	Mean	n	Mean	n	Mean	n	Mean
451	6	6.3	6	7.1	6	11.1	8	5.7	7	6.7	7	10.3
452	9	5.9	9	6.7	9	10.2	6	5.7	6	6.5	6	9.8
453	10	6.0	10	6.3	9	9.5	7	5.5	7	6.0	7	8.8
454	9	5.8	9	6.4	9	8.8	7	5.5	7	5.9	7	8.4
455	8	6.0	8	6.8	8	10.2	6	5.8	6	6.6	6	10.0
456	7	6.0	7	6.4	7	9.4	10	5.6	10	6.0	10	9.0
457	8	6.0	8	6.5	8	9.6	7	6.1	7	6.5	7	9.0
458	10	6.7	10	7.3	10	10.7	5	6.5	5	6.8	5	9.8
459	8	6.6	8	7.3	8	10.6	5	6.1	5	6.5	5	9.9
460	9	6.4	9	7.3	9	11.5	5	6.2	5	7.2	5	11.2
461	4	6.7	4	7.7	4	11.8	10	6.4	10	7.4	10	11.3
462	8	6.7	8	7.5	8	10.5	7	6.2	7	6.9	7	9.6
N		12		12		12		12		12		12
MEAN		6.26		6.94		10.33		5.94		6.58		9.76
S.D.		0.35		0.48		0.90		0.35		0.46		0.89
S.E.		0.10		0.14		0.26		0.10		0.13		0.26

n : Number of pups.

INDIVIDUAL DATA 37-1

STUDY NO. SR11087 TITLE : indene : Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Gross findings of dead pups on lactation day 0-4 ANIMAL : Rat, Crl:CD(SD)

Group	Dam No.	Day of death	Number of pups		Findings
			Male	Female	
0 mg/kg	152	0	1	1	No abnormal findings
	155	0	7	4	No abnormal findings
		0	3	0	Intraperitoneum : Autolysis
		1	4	0	No abnormal findings
	158	2	1	0	Intraperitoneum : Autolysis
4 mg/kg	255	4	1	0	No abnormal findings
20 mg/kg	354	1	1	0	No abnormal findings
	356[a]	0	1	0	No abnormal findings
		0	1	1	Intraperitoneum : Autolysis
	357	2	0	1	Liver : Yellowish white discoloration
					Spleen : Pale discoloration
	360	0	1	0	No abnormal findings
	361	0	1	0	Intraperitoneum : Autolysis
100 mg/kg	453	2	1	0	No abnormal findings
	459	0	1	1	No abnormal findings

a : Not distinguished sex of one fetus.

INDIVIDUAL DATA 37-2-1

STUDY NO. SR11087 TITLE : indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Gross findings of pups euthanized on day 4 of lactation ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 0 mg/kg

Dam No.	Number of pups		Findings
	Male	Female	
151	8	7	Female ; Liver : Yellowish white patch, middle lobe (3×3, mm), 1
152	6	8	No abnormal findings
153	7	7	No abnormal findings
154	7	8	No abnormal findings
156	8	6	No abnormal findings
157	17	4	No abnormal findings
158	8	7	No abnormal findings
159	9	6	No abnormal findings
160	8	7	No abnormal findings
161	10	6	No abnormal findings
162	5	7	No abnormal findings

INDIVIDUAL DATA 37-2-2

STUDY NO. SR11087 TITLE : indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Gross findings of pups euthanized on day 4 of lactation ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 4 mg/kg

Dam No.	Number of pups		Findings
	Male	Female	
251	8	4	No abnormal findings
252	9	6	No abnormal findings
253	7	5	No abnormal findings
254	9	8	No abnormal findings
255	7	8	No abnormal findings
256	8	8	No abnormal findings
257	5	10	No abnormal findings
258	5	8	No abnormal findings
259	7	4	No abnormal findings
260	6	8	No abnormal findings
261	5	9	No abnormal findings
262	11	3	No abnormal findings

INDIVIDUAL DATA 37-2-3

STUDY NO. SR11087 TITLE : indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Gross findings of pups euthanized on day 4 of lactation ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 20 mg/kg

Dam No.	Number of pups		Findings
	Male	Female	
351	9	6	No abnormal findings
352	9	5	No abnormal findings
353	1	6	No abnormal findings
354	10	4	No abnormal findings
355	9	5	No abnormal findings
356	4	7	No abnormal findings
357	7	7	No abnormal findings
358	10	5	No abnormal findings
359	6	10	No abnormal findings
360	5	11	No abnormal findings
361	9	8	No abnormal findings
362	10	6	No abnormal findings

INDIVIDUAL DATA 37-2-4

STUDY NO. SR11087 TITLE : indene：Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats

Gross findings of pups euthanized on day 4 of lactation ANIMAL : Rat, Crl:CD(SD) SEX : Female GROUP : 100 mg/kg

Dam No.	Number of pups		Findings
	Male	Female	
451	6	7	No abnormal findings
452	9	6	No abnormal findings
453	9	7	No abnormal findings
454	9	7	No abnormal findings
455	8	6	No abnormal findings
456	7	10	No abnormal findings
457	8	7	No abnormal findings
458	10	5	No abnormal findings
459	8	5	No abnormal findings
460	9	5	No abnormal findings
461	4	10	No abnormal findings
462	8	7	No abnormal findings

試験成績書

2012年02月27日

東京化成工業株式会社 品質保証[redacted]
〒103-0023
東京都中央区日本橋本町4丁目10[redacted]
TEL: 03(5640)8860 FAX: 03[redacted]

製品名: Indene				[redacted]
製品コード: I0354	等級: GR	製品ロット: IG5TI	判定: 合格	

項目	結果	規格値
純度(GC)	98.9 %	98.0 %以上
比重 (20/20)	0.9964	0.9950 ～ 0.9990
屈折率 n20/D	1.5756	1.5740 ～ 1.5780

報 告 書

整理 No. V 0442
2012 年 02 月 28 日

(株)化合物安全性研究所
安全性研究部
[redacted]

東京化成工業株式会社 深谷工場
分析センター
〒366-0816 埼玉県深谷市樫合 725 番地
TEL 048-571-3466
FAX 048-571-1810
[redacted]

試料名 インデンの分析につきましてご報告致します。

分析試料
I0354 インデン　Lot . IG5TI [東京化成工業(株) 製]

1. 純度(GC)
(1) 分析条件
カ ラ ム　：50%Diphenyl 50%Dimethylpolysiloxane
3.0μm×15m×0.32mm
カラム温度：最初 140℃で 10 分間保ち、その後 20℃/min で 240℃まで昇温し、その温度に 5 分間保つ。
気化室温度：250℃
検出器温度：250℃
ｷｬﾘｱｰ ｶﾞｽ：ﾍﾘｳﾑ 線速度 30cm/sec.
検 出 器：FID
注 入 法：ｽﾌﾟﾘｯﾄ法　ｽﾌﾟﾘｯﾄ比 (1：300)
注 入 量：試料 0.1μℓ
定 量 法：未補正面積百分率法
機　　器：HP6890

(2) 結果 (未補正面積百分率) 添付データ 2 枚
①98.85%　②98.84%　平均 98.8%

2. 比重 SG^{20}_{20}　0.9965
測定装置：京都電子製 DA-505

3. 屈折率 n^{20}_{D}　1.5756
測定装置：京都電子製 RA-500N

この報告書に関するご質問は[redacted]までお願い致します。

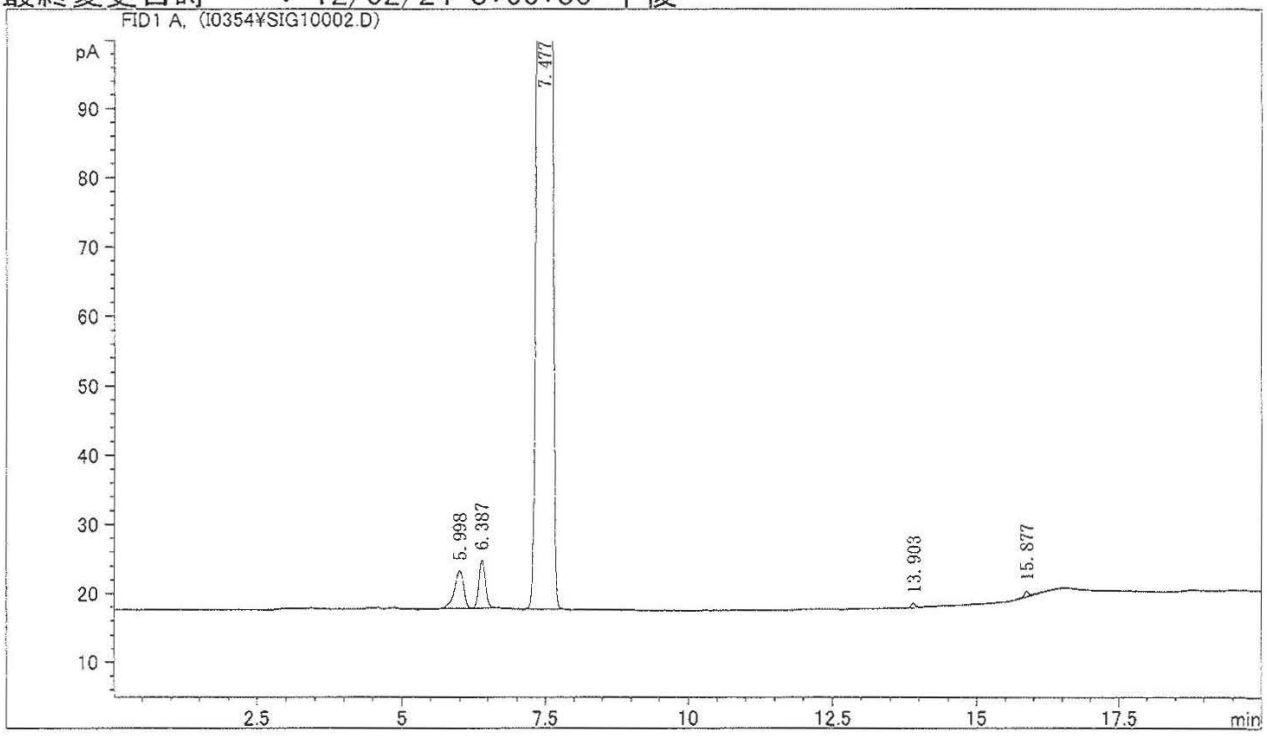
[redacted]

ﾃﾞｰﾀ ﾌｧｲﾙ C:¥HPCHEM¥1¥DATA¥I0354¥SIG10002.D ｻﾝﾌﾟﾙ名: V0442

BUNCE
I0354 Indene (Lot. IG5TI)

注入日 : 12/02/24 4:20:57 午後
ｻﾝﾌﾟﾙ名 : V0442
ｵﾍﾟﾚｰﾀ :
ﾊﾞｲｱﾙ : 1
注入回数 : 1
注入量 : 外部

ﾒｿｯﾄﾞ : C:¥HPCHEM¥1¥METHODS¥I0354.M
最終変更日時 : 12/02/24 3:00:36 午後



面積 ﾊﾟｰｾﾝﾄ ﾚﾎﾟｰﾄ

表示順 : ｼｸﾞﾅﾙ
倍率 : 1.0000
希釈率 : 1.0000

ｼｸﾞﾅﾙ 1: FID1 A,

ﾋﾟｰｸ #	RT [min]	ﾀｲﾌﾟ	幅 [min]	面積 [pA*s]	高さ [pA]	面積 %
1	5.998	BP	0.1677	63.39194	5.54994	0.57589
2	6.387	VB	0.1232	55.39537	6.96586	0.50324
3	7.477	BB	0.1497	1.08809e4	1141.03516	98.84806
4	13.903	PB	0.0681	2.74232	6.34009e-1	0.02491
5	15.877	PB	0.0904	5.27274	8.45213e-1	0.04790
ﾄｰﾀﾙ :				1.10077e4	1155.03018	

拡張 ｲﾝﾃｸﾞﾚｰｼｮﾝ

*** End of Report ***

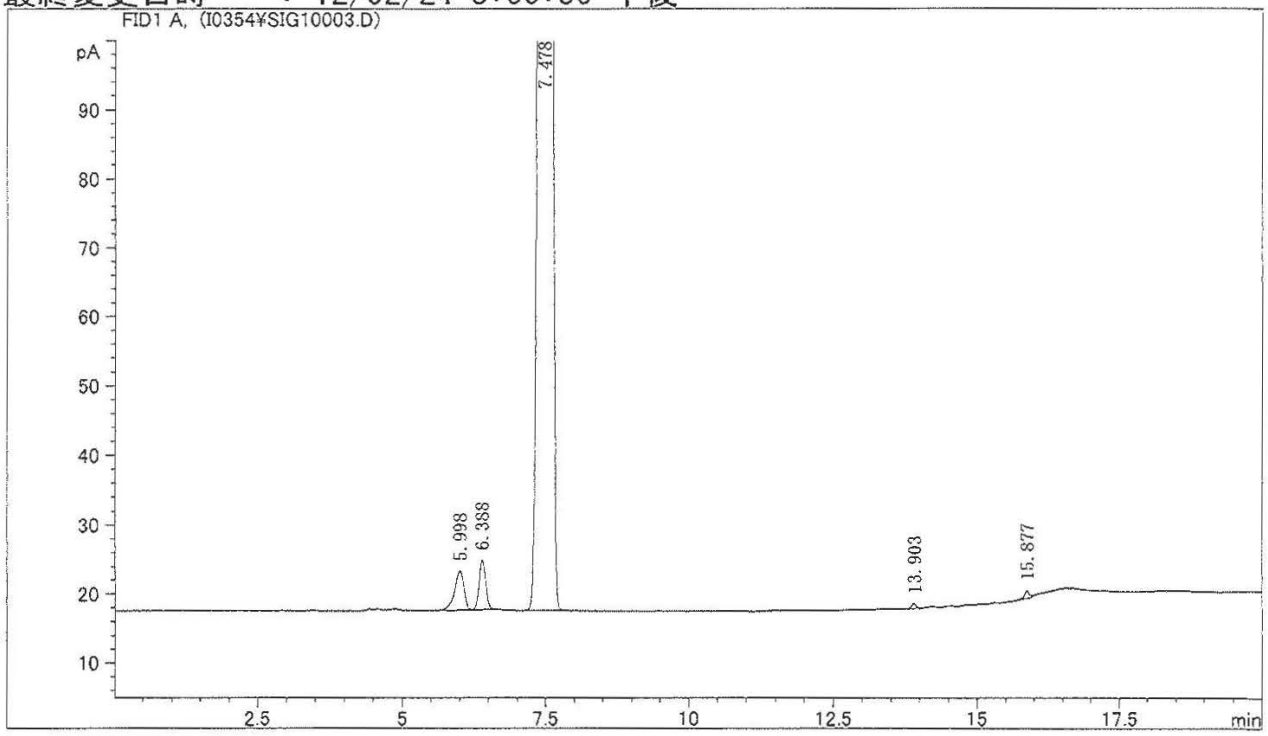
装置 1 12/02/24 5:46:51 午後 ﾍﾟｰｼﾞ 1 / 1

ﾃﾞｰﾀ ﾌｧｲﾙ C:¥HPCHEM¥1¥DATA¥I0354¥SIG10003.D ｻﾝﾌﾟﾙ名: V0442

BUNCE
I0354 Indene (Lot. IG5TI)

注入日 : 12/02/24 4:54:03 午後
ｻﾝﾌﾟﾙ名 : V0442
ｵﾍﾟﾚｰﾀ :
ﾊﾞｲｱﾙ : 1
注入回数 : 1
注入量 : 外部

ﾒｿｯﾄﾞ : C:¥HPCHEM¥1¥METHODS¥I0354.M
最終変更日時 : 12/02/24 3:00:36 午後



面積 ﾊﾟｰｾﾝﾄ ﾚﾎﾟｰﾄ

表示順 : ｼｸﾞﾅﾙ
倍率 : 1.0000
希釈率 : 1.0000

ｼｸﾞﾅﾙ 1: FID1 A,

ﾋﾟｰｸ #	RT [min]	ﾀｲﾌﾟ	幅 [min]	面積 [pA*s]	高さ [pA]	面積 %
1	5.998	BP	0.1667	65.25051	5.71965	0.56858
2	6.388	VP	0.1247	57.85248	7.27971	0.50412
3	7.478	BB	0.1494	1.13432e4	1192.07361	98.84256
4	13.903	BP	0.0722	3.09219	7.01883e-1	0.02694
5	15.877	PV	0.0891	6.63274	1.10663	0.05780

ﾄｰﾀﾙ : 1.14760e4 1206.88149

拡張 ｲﾝﾃｸﾞﾚｰｼｮﾝ

*** End of Report ***

装置 1 12/02/24 5:46:18 午後 ﾍﾟｰｼﾞ 1 / 1

添付資料 3 B-5517

CERTIFICATE OF ANALYSIS
(Stability of Indene in Test Solutions)

Study No.: A-1715
Analytical Facility: Gotemba Laboratory, Bozo Research Center Inc.
Date of Analysis: August 4, 2005 (Initial)
August 5, 2005 (After storage for 24 hours at room temperature)
August 13, 2005 (After storage for 24 hours at room temperature following 8 days in a cold place)
Analytical Method: GC

Test Article: Indene (Lot No. Y3545289)
Vehicle: Corn oil
Nominal Concentration: 0.1 mg/mL and 200 mg/mL
Form of Sample: Solution
Date of Preparation: August 4, 2005
Prepared by: [redacted]
Storage Condition: Brown bottle, room temperature and cold place
Acceptance Criteria: Residual ratio (the ratios of the mean measured concentrations after storage to initial) is within 100 ± 10%

Results:

Prepared concentration (mg/mL)	Measured concentration (mg/mL)		
	Initial	After storage*	After storage**
0.100	0.0997	0.101	0.100
	0.101	0.101	0.101
	0.0980	0.101	0.101
Mean	0.0996	0.101	0.101
Residual ratio (%)	–	101.4	101.4
200	199	202	201
	199	202	198
	199	202	199
Mean	199	202	199
Residual ratio (%)	–	101.5	100.0

*: 24 hours at room temperature
**: 24 hours at room temperature following 8 days in a cold place

Judgment: It was confirmed that these test solutions were stable for 24 hours at room temperature following 8 days in a cold place.

This study was conducted in compliance with the following GLP regulations:
"Regulations of Testing Facilities for Studies on New Chemical Substances etc."
YakuShokuHatsu No. 1121003, Heisei 15-11-17 SeiKyoKu No. 3, KanHoKiHatsu No. 031121004, November 21, 2003, Revised on April 30, 2004.

Analyst: [redacted] Date: August 15, 2005
Study Director: [redacted] Date: August 15, 2005

分析証明書番号：1441

濃度確認試験　分析証明書

試　　験　　名　：　indene のラットにおける反復投与毒性･生殖発生毒性併合試験
試　験　番　号　：　SR11087
被 験 物 質 名　：　indene
ロ ッ ト 番 号　：　IG5TI
媒　　体　：　トウモロコシ油
調 製 年 月 日　：　2011 年 10 月 7 日
分析試験実施時期　：　雄の初回調製時
測 定 年 月 日　：　2011 年 10 月 7 日
測 定 方 法　：　HPLC 法
試 験 成 績　：

調製液 表示濃度	測定の 繰返し数	調製液 被験物質濃度 (v/v%)	調製液 平均値 ±標準偏差	調製液 変動係数 (%)	調製液 含有率 (%)
0.08 v/v%	1	0.0788	0.0783 ± 0.00061	0.8	97.9
	2	0.0776			
	3	0.0784			
0.4 v/v%	1	0.390	0.395 ± 0.0042	1.1	98.8
	2	0.396			
	3	0.398			
2 v/v%	1	2.02	2.04 ± 0.015	0.7	102.0
	2	2.05			
	3	2.04			

判　定　基　準　：　含有率が 90 ～ 110%、変動係数が 5%以下の場合を適とする。
合　否　判　定　：　適
備　　考　：　－

試験施設　株式会社 化合物安全性研究所

化学分析担当者：[redacted]　2011 年 10 月 7 日

化学分析責任者：[redacted]　2011 年 10 月 7 日

分析証明書番号：1458

濃度確認試験　分析証明書

試　験　名　：indene のラットにおける反復投与毒性・生殖発生毒性併合試験
試験番号　：SR11087
被験物質名　：indene
ロット番号　：IG5TI
媒　体　：トウモロコシ油
調製年月日　：2011 年 11 月 16 日
分析試験実施時期　：雄の最終回調製時
測定年月日　：2011 年 11 月 16 日
測定方法　：HPLC 法
試験成績　：

調製液表示濃度	測定の繰返し数	調製液 被験物質濃度 (v/v%)	調製液 平均値 ±標準偏差	調製液 変動係数 (%)	調製液 含有率 (%)
0.08 v/v%	1	0.0756	0.0759 ± 0.00046	0.6	94.9
	2	0.0764			
	3	0.0756			
0.4 v/v%	1	0.388	0.385 ± 0.0023	0.6	96.3
	2	0.384			
	3	0.384			
2 v/v%	1	1.95	1.94 ± 0.006	0.3	97.0
	2	1.94			
	3	1.94			

判定基準　：含有率が 90 ～ 110%、変動係数が 5%以下の場合を適とする。
合否判定　：適
備　考　：－

試験施設　株式会社 化合物安全性研究所

化学分析担当者：[redacted]　2011 年 11 月 17 日

化学分析責任者：[redacted]　2011 年 11 月 17 日

被験物質調製液の濃度分析方法

1. 使用機器

高速液体クロマトグラフ(HPLC)

UV-VIS Detector	L-4200	株式会社 日立製作所
Intelligent Pump	L-6200	株式会社 日立製作所
Column Oven	L-5025	株式会社 日立製作所
Autosampler	AS-2000	株式会社 日立製作所
Degasser	ERC-3315α	株式会社 イーアールシー
データ処理装置	Empower 2	日本ウォーターズ 株式会社
電子式上皿天秤	GH-202	株式会社 エー・アンド・デイ

2. 標準物質(遮光容器に入れ、冷凍保存)

インデン(被験物質)	Lot No.IG5TI	東京化成工業株式会社

3. 試薬

テトラヒドロフラン(安定剤不含)

	HPLC 用	和光純薬工業株式会社
アセトニトリル	HPLC 用	関東化学株式会社
蒸留水	大量分取液体クロマトグラフィー用	関東化学株式会社

4. 調製（以下の割合で調製、調製日を 0 日として起算）

(1) 標準溶液(0.002%)

被験物質の 100 μL を 100 mL 容のメスフラスコに量りとり、テトラヒドロフランで定容して 0.1%溶液を調製した(標準原液)。標準原液の 1 mL を正確に 50 mL 容のメスフラスコに採取し、テトラヒドロフランで定容して 0.002%溶液とした(標準溶液)。調製は 1 回、HPLC への注入は 3 回とした。調製後は当日中に使用した。

(2) 試料溶液

1) 各被験物質調製液を採取し、被験物質の最終濃度が 0.0005～0.02%の範囲内(可能な場合は 0.002%付近)、媒体の割合が 10%以下となるようにテトラヒドロフランを加えたものを試料溶液とした。

2) 試料溶液の調製は 3 回、HPLC への注入は各 1 回とした。

(3) 移動相

アセトニトリル 700 mL に蒸留水 300 mL を加え、十分に混合したものを移動相とした。調製後は室温で保存し、2 日以内に使用した。

(4)オートサンプラ洗浄液

テトラヒドロフラン 500 mL に蒸留水 500 mL を加え、十分に混合したものをオートサンプラ洗浄液とした。調製後は室温で保存し、2 日以内に使用した。

(5) 洗浄用注入液

テトラヒドロフランそのものを洗浄用注入液とした。

5. HPLC 条件

カラム	: L-column ODS、5 μm、4.6 mm I.D.×250 mm、 一般財団法人 化学物質評価研究機構
移動相	: アセトニトリル/蒸留水 (70 : 30)
ｵｰﾄｻﾝﾌﾟﾗ洗浄液	: テトラヒドロフラン/蒸留水 (50 : 50)
洗浄用注入液	: テトラヒドロフラン
測定波長	: 250 nm
カラム温度	: 35℃
流量	: 1 mL/min
注入量	: 10 μL
ｵｰﾄｻﾝﾌﾟﾗ温度	: 10℃
分析時間	: 11 分

6. システム適合性試験

測定日ごとに標準溶液を連続して 6 回注入した。インデンのピーク面積および保持時間について変動係数を求めた。

7. 計算

Empower 2 を用いて標準溶液のピーク面積と濃度から作成した検量線より、各試料溶液の測定濃度を求め、以下の式より調製液中の被験物質濃度、変動係数および含有率を算出した。

被験物質濃度(%)＝ 測定濃度(%)×希釈係数

$$\text{変動係数}(\%) = \frac{\text{標準偏差}}{\text{平均値}} \times 100$$

$$\text{含有率}(\%) = \frac{\text{被験物質濃度平均値}}{\text{調製液の表示濃度}} \times 100$$

8. 数値の表示

(1) 調製液の被験物質濃度は四捨五入して有効数字 3 桁に丸めた。

(2) 変動係数および含有率は四捨五入して小数点以下第 1 位に丸めた。

9. 判定基準

(1) 濃度確認試験：含有率が 90～110%、変動係数が 5%以下の場合を適とした。

(2) システム適合性試験：変動係数が2%以下の場合を適とした。本試験では、ピーク面積における変動係数が 0.2～0.4%、保持時間における変動係数が 0.0%であり、いずれも判定基準内であった。