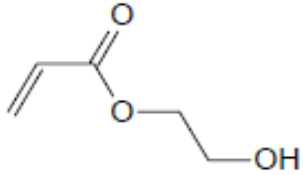
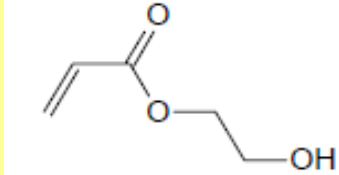


| 項目名 | 和訳結果(SIDS Dossier) | 原文(SIDS Dossier) |
|-----|--------------------|------------------|
|-----|--------------------|------------------|

1. 一般情報
GENERAL INFORMATION

1.01 物質情報
SUBSTANCE INFORMATION

| | | |
|------------|---|--|
| CAS番号 | 818-61-1 | 818-61-1 |
| 物質名(日本語名) | アクリル酸ヒドロキシエチル | |
| 物質名(英名) | | Hydroxyethyl acrylate |
| 別名等 | | |
| 国内適用法令の番号 | | |
| 国内適用法令物質名 | | |
| OECD/HPV名称 | | |
| 分子式 | C5H8O3 | C5H8O3 |
| 構造式 |  |  |
| 備考 | | |

1.02 安全性情報収集計画書/報告書作成者に関する情報
SPONSOR INFORMATION

| | | |
|-----------------|--|--|
| 機関名 | OECD/HPVプログラム(SIAM20)により収集された情報 (http://cs3-hq.oecd.org/scripts/hpv/) | OECD/HPV Program, SIDS Dossier, assessed at SIAM20- APR-2005 http://ecb.jrc.ec.europa.eu/esis/index.php?PGM=hpv |
| 代表者名 | | |
| 所在地及び連絡先 | | |
| 担当者氏名 | | |
| 担当者連絡先(住所) | | |
| 担当者連絡先(電話番号) | | |
| 担当者連絡先(メールアドレス) | | |
| 報告書作成日 | | |
| 備考 | スポンサー国: 米国 | Sponsor Country: United States |

1.03 カテゴリー評価
DETAILS ON CHEMICAL CATEGORY

1.1 一般的な物質情報
GENERAL SUBSTANCE INFORMATION

| | | |
|---------------------|----------------------------|---|
| 物質のタイプ | 有機物 | organic |
| 物質の色・におい・形状等の情報 | 色: 薄黄色または無色、におい: 強い刺激臭、甘味臭 | Colour: Pale yellow or colorless, Odour: Pungent, sweet |
| 物理的状態(20°C、1013hPa) | 液体 | liquid |
| 純度(重量/重量%) | 96.5 - 99 % w/w | 96.5 - 99 % w/w |
| 出典 | | |
| 備考 | | |

1.2 不純物
IMPURITIES

1.3 添加物
ADDITIVES

1.4 別名
SYNONYMS

1.5 製造・輸入量
QUANTITY

| | | |
|--------|----------------------|------------------------------------|
| 製造・輸入量 | 2001年に <= 15000 トン製造 | <= - 15000 tonnes produced in 2001 |
| 報告年 | | |
| 出典 | (2) | (2) |
| 備考 | (1) 制限なく信頼性あり | (1) valid without restriction |

1.6 用途情報
USE PATTERN

| | | |
|--------|------------------------------|---|
| 主な用途情報 | 用途タイプ : タイプ カテゴリ : 非拡散的用途 | Type of use : type Category : Non dispersive use |
| 工業的用途 | | |
| 用途分類 | | |
| 出典 | | |
| 備考 | | |
| 主な用途情報 | 用途タイプ : タイプ カテゴリ : 閉鎖系で使用 | Type of use : type Category : Use in closed system |

| | | |
|-------|--|--|
| | | |
| 工業的用途 | | |
| | | |
| 用途分類 | | |
| 出典 | | |
| 備考 | | |

| | | |
|--------|--|---|
| 主な用途情報 | 用途タイプ : タイプ カテゴリ : 結果としてマトリックス中に含まれるような用途 | Type of use : type Category : Use resulting in inclusion into or onto matrix |
| | | |
| 工業的用途 | | |
| | | |
| 用途分類 | | |
| 出典 | | |
| 備考 | | |

| | | |
|--------|---------------------------------|---|
| 主な用途情報 | 用途タイプ : 工業 カテゴリ : 化学工業:合成に使用 | Type of use : industrial Category : Chemical industry: used in synthesis |
| | | |
| 工業的用途 | | |
| | | |
| 用途分類 | | |
| 出典 | | |
| 備考 | | |

| | | |
|--------|---------------------------------|--|
| 主な用途情報 | 用途タイプ : 工業 カテゴリ : 塗料、漆、ワニス工業 | Type of use : industrial Category : Paints, lacquers and varnishes industry |
| | | |
| 工業的用途 | | |
| | | |
| 用途分類 | | |
| 出典 | | |
| 備考 | | |

1.7 環境および人への暴露情報 SOURCES OF EXPOSURE

1.8 追加情報 ADDITIONAL INFORMATION

2. 物理化学的性状 PHYSICAL CHEMICAL DATA

2.1 融点 MELTING POINT

| | | |
|----------|--|--|
| 試験物質名 | | |
| CAS番号 | | |
| 純度等 | | |
| 注釈 | | |
| 方法 | | |
| GLP | | |
| 試験を行った年 | | |
| 試験条件 | | |
| 結果 | | |
| 融点: °C | -60.2°C | -60.2 ° C |
| 分解: °C | | |
| | | |
| 昇華: °C | | |
| | | |
| 結論 | | |
| 注釈 | DIPPRに引用された実験値: 正確な値は -60.15であり。結果の表には四捨五入した値である | Experimental value cited in DIPPR: Precise value was -60.15, rounded in value field. |
| 信頼性スコア | (2) 制限付で信頼性あり | (2) valid with restrictions |
| 信頼性の判断根拠 | ハンドブック又はデータ集からのデータ | Data from Handbook or collection of data |
| 出典 | | |
| 引用文献 | (12) | (12) |
| 備考 | フラグ: SIDSエンドポイントに重要な試験 | Flag: Critical study for SIDS endpoint |

2.2 沸点 BOILING POINT

| | | |
|---------|-------------------|---------------------|
| 試験物質名 | | |
| CAS番号 | | |
| 純度等 | | |
| 注釈 | | |
| 方法 | その他の方法 | other |
| GLP | データなし | no data |
| 試験を行った年 | 1993 | 1993 |
| 試験条件 | | |
| 結果 | | |
| 沸点: °C | 210 °C (1013 hPa) | 210 ° C at 1013 hPa |
| 圧力 | | |

| | | |
|----------|-------------------------|--|
| 分解: °C | | |
| 結論 | | |
| 注釈 | | |
| 信頼性スコア | (2) 制限付で信頼性あり | (2) valid with restrictions |
| 信頼性の判断根拠 | 信頼できるハンドブック又はデータ集からのデータ | Data from Reliable Handbook or compilation of data |
| 出典 | | |
| 引用文献 | (14)(15) | (14)(15) |
| 備考 | フラグ: SIDSエンドポイントに重要な試験 | Flag: Critical study for SIDS endpoint |

2.3 密度(比重)

DENSITY(RELATIVE DENSITY)

| | | |
|----------|-------------------------|-----------------------------|
| 試験物質名 | | |
| CAS番号 | | |
| 純度等 | | |
| 注釈 | | |
| 方法 | | |
| GLP | データなし | no data |
| 試験を行った年 | 2002 | 2002 |
| 試験条件 | | |
| 結果 | 1.101 g/cm ³ | 1.101 g/cm ³ |
| タイプ | | |
| 温度(°C) | 25°C | 25 ° C |
| 注釈 | | |
| 信頼性スコア | (2) 制限付で信頼性あり | (2) valid with restrictions |
| 信頼性の判断根拠 | | |
| 出典 | | |
| 引用文献 | | |
| 備考 | | |

2.4 蒸気圧

VAPOUR PRESSURE

| | | |
|----------|------------------------|--|
| 試験物質名 | | |
| CAS番号 | | |
| 純度等 | | |
| 注釈 | | |
| 方法 | | |
| GLP | データなし | no data |
| 試験を行った年 | | |
| 試験条件 | | |
| 結果 | | |
| 蒸気圧 | 0.0697 hPa | .0697 hPa |
| 温度: °C | 25°C | 25 ° C |
| 分解: °C | | |
| 結論 | | |
| 注釈 | | |
| 信頼性スコア | (1) 制限なく信頼性あり | (1) valid without restriction |
| 信頼性の判断根拠 | ハンドブック又はデータ集からのデータ | Data from Handbook or collection of data |
| 出典 | | |
| 引用文献 | (17) | (17) |
| 備考 | フラグ: SIDSエンドポイントに重要な試験 | Flag: Critical study for SIDS endpoint |

2.5 分配係数(log Kow)

PARTITION COEFFICIENT

| | | |
|---------|---|--|
| 試験物質名 | | |
| CAS番号 | | |
| 純度等 | | |
| 注釈 | オクタノール-水 | octanol-water |
| 方法 | その他の方法(測定) | other (measured) |
| GLP | | |
| 試験を行った年 | 1982 | 1982 |
| 試験条件 | 2-HEAのn-オクタノール-水分分配係数を決定した。栓付きチューブに2-HEAを蒸留水で溶解(0.1mM)し、n-オクタノールを添加した(2.5 ml 水; 7.5 ml n-オクタノール)。チューブを室温で1時間シェーカーで激しく振とうした後2500 回転/分で30分間遠心分離した。水相中のエステルの量をガスクロマトグラム法により測定した。 | The n-octanol-water partition coefficient of 2-HEA was determined. 2-HEA was dissolved in distilled water (0.1 mM) and the water and n-octanol phases were mixed in stoppered tubes (2.5 ml water; 7.5 ml n-octanol). The tubes were shaken vigorously on a mechanical shaker for 1 h at room temperature, then cetrifuged at 2500 rev./min for 30 min. The amounts of esters in the water phase were analysed by gas-liquid chromatography. |
| 結果 | | |
| Log Kow | -0.21 | -0.21 |
| 温度: °C | 20°C | 20 ° C |
| 結論 | | |
| 注釈 | | |
| 信頼性スコア | (2) 制限付で信頼性あり | (2) valid with restrictions |

| | | |
|----------|---|---|
| 信頼性の判断根拠 | 一般的に認められた科学的標準法と合致しており、評価法として引用され、受け入れられている | Meets generally accepted scientific standards, well documented and acceptable for assessment. |
| 出典 | | |
| 引用文献 | (19) | (19) |
| 備考 | フラグ: SIDSエンドポイントに重要な試験 | Flag: Critical study for SIDS endpoint |

2.6.1 水溶解性(解離定数を含む)

WATER SOLUBILITY & DISSOCIATION CONSTANT

| | | |
|------------|-------------------------|--|
| 試験物質名 | | |
| CAS番号 | | |
| 純度等 | | |
| 注釈 | | |
| 方法 | | |
| GLP | | |
| 試験を行った年 | | |
| 試験条件 | | |
| 結果 | | |
| 水溶解度 | 999999 g/m ³ | 999999 g/m ³ |
| 温度: °C | | |
| pH | | |
| pH測定時の物質濃度 | | |
| 結論 | | miscible |
| 注釈 | | |
| 信頼性スコア | (2) 制限付で信頼性あり | (2) valid with restrictions |
| 信頼性の判断根拠 | ハンドブック又はデータ集からのデータ | Data from Handbook or collection of data |
| 出典 | | |
| 引用文献 | (22) | (22) |
| 備考 | フラグ: SIDSエンドポイントに重要な試験 | Flag: Critical study for SIDS endpoint |
| 解離定数 | | |
| 試験物質 | | |
| 同一性 | | |
| 方法 | | |
| 温度: °C | | |
| GLP | | |
| 試験条件 | | |
| 試験を行った年 | | |
| 結果 | | |
| 結論 | | |
| 注釈 | | |
| 信頼性スコア | | |
| 信頼性の判断根拠 | | |
| 出典 | | |
| 引用文献 | | |
| 備考 | | |

2.6.2 表面張力

SURFACE TENSION

2.7 引火点(液体)

FLASH POINT (LIQUIDS)

| | | |
|----------|-----------|------------|
| 試験物質名 | | |
| CAS番号 | | |
| 純度等 | | |
| 注釈 | クリーズドカップ法 | closed cup |
| 方法 | その他の方法 | other |
| GLP | データなし | no data |
| 試験を行った年 | 1993 | 1993 |
| 試験条件 | | |
| 結果 | | |
| 引火点: °C | 101°C | 101 ° C |
| 試験のタイプ | | |
| 結論 | | |
| 注釈 | | |
| 信頼性スコア | | |
| 信頼性の判断根拠 | | |
| 出典 | | |
| 引用文献 | (15) | (15) |
| 備考 | | |

2.8 自己燃焼性 (固体/気体)

AUTO FLAMMABILITY (SOLIDS/GASES)

2.9 引火性

FLAMMABILITY

| | | |
|-------|--|--|
| 試験物質名 | | |
| CAS番号 | | |
| 純度等 | | |

| | | |
|----------|---|---|
| 注釈 | | |
| 方法 | その他の方法:計算 | other: calculation |
| GLP | いいえ | no |
| 試験を行った年 | | |
| 試験条件 | 最小引火点限界値は100℃で1.8 %v/v、上限限界値は12.9 %v/vと推定されている。 | Lower flammability limit was estimated as 1.8 %v/v at 100 deg. C. Upper limit was estimated as 12.9 %v/v. |
| 結果 | | |
| 固体の場合 | | |
| 引火性が高い | | |
| 気体の場合 | | |
| 水との接触 | | |
| 結論 | 引火性 | flammable |
| 注釈 | | |
| 信頼性スコア | | |
| 信頼性の判断根拠 | | |
| 出典 | | |
| 引用文献 | (23)(15) | (23)(15) |
| 備考 | | |

2.10 爆発性 EXPLOSIVE PROPERTIES

2.11 酸化性 OXIDISING PROPERTIES

2.12 酸化還元ポテンシャル OXIDATION/REDUCTION POTENTIAL

2.13 その他の物理化学的性状に関する情報 ADDITIONAL INFORMATION

| | | |
|----------|-------------------------------------|---|
| 試験物質名 | | |
| CAS番号 | | |
| 純度等 | | |
| 注釈 | Henry則定数 | Henry's Law Constant |
| 方法 | | |
| GLP | | |
| 試験を行った年 | | |
| 試験条件 | | |
| 結果 | 0.073 Pa x m ⁻³ /モル(20℃) | 0.073 Pa x m ⁻³ /mol at 20 degrees C |
| 結論 | | |
| 注釈 | | |
| 信頼性スコア | (3) 信頼性なし | (3) invalid |
| 信頼性の判断根拠 | 評価には不十分な資料 | Documentation insufficient for assessment |
| 出典 | | |
| 引用文献 | (24) | (24) |
| 備考 | フラグ: SIDSエンドポイントに重要な試験 | Flag: Critical study for SIDS endpoint |

3. 環境運命と経路 ENVIRONMENTAL FATE AND PATHWAYS

3.1 安定性 STABILITY

3.1.1. 光分解 PHOTODEGRADATION

| | | |
|----------------|------------------------------------|---|
| 試験物質名 | | |
| CAS番号 | | |
| 純度等 | | |
| 注釈 | | |
| 方法 | その他の方法(計算) | other (calculated) |
| タイプ | 大気 | air |
| GLP | データなし | no data |
| 試験を行った年 | 1987 | 1987 |
| 光源と波長(nm) | | |
| 太陽光強度に基づいた相対強度 | 太陽光の強度に基づく | based on intensity of sunlight |
| 物質のスペクトル | | |
| 試験条件 | | |
| 結果 | | |
| 物質濃度 | | |
| 温度(℃) | 25℃ | 25 ° C |
| 直接光分解 | | |
| 半減期t1/2 | | |
| 分解度(%)と時間 | | |
| 量子収率 (%) | | |
| 間接光分解 | | |
| 増感剤(タイプ) | オゾン | O3 |
| 増感剤濃度 | 7000000000000 分子/cm³ | 7000000000000 molecule/cm³ |
| 速度定数 | 0.000000000000000000175 cm³/(分子・秒) | .000000000000000000175 cm³/(molecule*sec) |

| | | |
|---------------|---|---|
| 半減期 $t_{1/2}$ | 6.5 日 | 50 % after 6.5 day(s) |
| 分解生成物 | | |
| 結論 | | |
| 注釈 | <p>オゾン濃度が7×10^{11}分子/cm³としたときHEAとオゾンの反応によるHEAの大気中半減期は10 時間であった。25°Cでの速度定数は1.75×10^{-18} cm³/分子/秒と推定された。アクリル酸エチル及びその他のアクリル酸エステルは290nm以上の波長の光を僅かに吸収するので、HEAは直接光分解されるかもしれない(Brunn J. et al., 1976を参照)。</p> <p>Brunn J. et al. (1976) J. Prakt. Chem., 318: 745-755</p> | <p>Estimated atmospheric half-life for reaction of HEA with ozone at a concentration of 7×10^{11} molecules/cm³ is 10 hours. Rate constants estimated to be 1.75×10^{-18} cm³/molecule/sec at 25 deg. Celsius for ozone molecules. Based on slight absorption of light at wavelengths > 290 nm by ethyl acrylate and other acrylate esters. HEA may directly photolyze (see Brunn J. et al., 1976).</p> <p>Brunn J. et al. (1976) J. Prakt. Chem., 318: 745-755.</p> |
| 信頼性スコア | (2) 制限付で信頼性あり | (2) valid with restrictions |
| 信頼性の判断根拠 | 認められた計算法 | Accepted calculation method. |
| 出典 | | |
| 引用文献 | (25) | (25) |
| 備考 | | |

3.1.2. 水中安定性(加水分解性)

STABILITY IN WATER

| | | |
|-------|--|---|
| 試験物質名 | | |
| CAS番号 | | |
| 純度等 | | |
| 注釈 | 非生物学的 | abiotic |
| 方法 | <p>その他の方法:TSCA section 796.3500 「25°CにおけるpHの関数としての加水分解」</p> <p>加水分解はTSCAガイドラインT, section 796.3500「25°CにおけるpH の関数としての加水分解」に従って実施した。試験物質を1mM(15 ul 試験物質/150mL 溶液)以下の濃度になるように緩衝液に添加した。HEAの設定濃度は約110mg/Lであった。このHEAの濃度は少なくとも対水溶解度の数オーダー以下であった。この試験溶液10mLを10mLのラベル表示をした血清ビンに入れた後にテフロンコートしたゴム製セプタムとアルミ製シールで密封した。試験溶液を暗所で25°Cで28日間置いた。定期的に試験溶液を取り出しpH及び試験物質の残留量を測定した。各時点で試験試料を取り出しUV検出器付き逆相HPLCにより3連で測定した。pH11の試験試料については、分析に先立って20μ lの蟻酸を添加して試料のpHを5から6の範囲に調整した。これにより更なる加水分解を最小限に抑えた。</p> | <p>other: TSCA section 796.3500 Hydrolysis as a Function of pH at 25C</p> <p>Hydrolysis study was conducted following the TSCA guidelines, section 796.3500 Hydrolysis as a Function of pH at 25C. Test material was added to the buffered solutions at a concentration of less than 1 mM (15 ul test material/150mL solution). Approximate nominal concentration for HEA was 110 mg/L.. The concentration of HEA was at least several orders of magnitude below the water solubility (miscible in water). Portions (10mL) of the test solutions were transferred to uniquely labeled 10-mL serum bottles and sealed with Teflon-coated rubber septa and aluminum crimp seals. The test solutions were incubated in the dark for 28 days at 25+/-1C. Periodically, test solutions were removed for measurement of pH and the analysis of test material remaining in the solution. Single test samples were removed at each time point and analyzed in triplicate by reverse phase HPLC using UV detection. For test samples at pH 11, 20-ul portions of formic acid were added prior to analysis to adjust the sample to the pH range of 5 to 6 to minimize further hydrolysis.</p> |
| | <p>以下のサンプリングスケジュールはTSCAガイドラインに記載されている。</p> <p>方法1: 28日以内に60-70%の変換率となる場合、最低限6つの測定は加水分解度が20から70%になるような測定間隔とする。</p> <p>方法2: 反応が遅すぎで28日で加水分解をうまく追うことができないが、少なくとも20%の変換率に達するには十分な速度である場合、試験溶液は変換率が10%に達した後に15-20ポイントで分析しなければならない。</p> <p>方法3: 28日後においても変換率が20%以内の場合、28日後の試験物質の濃度を測定して半減期が>xであることを報告する。</p> <p>HEAの加水分解へのメチルエチルヒドロキノンの影響: HEAの重合を防止するために製造過程でメチルエチルヒドロキノン(MEHQ)が日常的に添加されている。それ故に、HEA加水分解へのMEHQの影響を調べた。異なる濃度のMEHAを含む2つHEA試料に対してpH11で加水分解速度を測定した。1つのHEA試料はMEHQ398ppmを含み、もう一つのHEA試料は275ppmのMEHAを含む。</p> | <p>The following sampling schedule is described in the TSCA guidelines:</p> <p>Procedure 1- If 60-70% conversion occurs within 28 days, then a minimum of six measurements will be made at regular intervals between 20 and 70% hydrolysis.</p> <p>Procedure 2- If the reaction is too slow to conveniently follow the hydrolysis to a high conversion in 28 days, but is still rapid enough to attain at least 20% conversion, then the test solution should be analyzed at 15- 20 time points at regular intervals after 10% conversion is attained.</p> <p>Procedure 3- If less than 20% conversion occurs after 28 days, then the concentration of test chemical after 28 days will be determined, and a half-life of >x days reported.</p> <p>Effect of Methyl Ether of Hydroquinone on Hydrolysis of HEA- Methyl ether of hydroquinone (MEHQ) is routinely added to HEA during manufacture to inhibit polymerization; therefore, the effect of MEHQ on the hydrolysis of HEA was evaluated. The hydrolysis rates at pH 11 for two different samples of HEA containing different concentrations of MEHQ were determined. The first sample of HEA contained 398 ppm MEHQ while the second sample contained 275 ppm MEHQ.</p> |

| | 各加水分解試験に対して試験物質濃度の自然対数値を時間の関数でプロットした。一定のpHでは直線となった。これは偽一次反応であることを示す。回帰直線の傾きが-Khなる。ここで、Khは偽一次反応の速度定数である。T1/2=ln 2/Khの関係式から加水分解の半減期が決定される。次の関係が緩衝液中の加水分解に当てはまる: Kh=Ka[H+]+Kb[OH-]+Kn。ここで、Ka、Kb及びKnはそれぞれ酸、塩基及び中性の二次反応定数であり、Khは偽一次反応定数の実測値である。所定のpHでこの式は3つの未知数Ka、Kb及びKnを含む。これらの3つの値を決定するには3つの式が必要である。これはpH3、7及び11の加水分解速度を測定することにより達成できる。 | For each hydrolysis experiment, the natural logarithm of the test substance concentration was plotted as a function of time. At a constant pH, a straight line was obtained, indicating pseudo-first order kinetics. The slope of the linear regression line was equal to -Kh, where Kh was the pseudo-first order rate constant. Using the relationship T1/2=ln 2/Kh, the half-life of the hydrolysis reaction was determined. The following relationship holds for hydrolysis reactions in buffered systems: Kh=Ka[H+]+Kb[OH-]+Kn where Ka, Kb, and Kn are the second-order rate constants for acid and base catalyzed, and neutral water hydrolysis reactions, respectively, and Kh is the measured pseudo-first order rate constant. At a given pH, the equation contains three unknowns, Ka, Kb, and Kn; therefore, three equations are required to determine the three unknown values. This was accomplished by measuring the hydrolysis rates at pH 3, 7 and 11. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|-------------------|--|---|------------------------|---------|----------------|----|---|-------|-----|-------|-----|---|-------|-----|-------|-----|---|-------|-----|-------|-----|----|-------|-----|-------|-----|----|-------|-----|-------|-----|----|-------|-----|-------|-----|---|-------|-----|-----|------|-----|---|------|-----|---|------|-----|-----|------|-----|---|------|-----|---|-----|-----|----|-------------------------|---------|------------------------|------|-----|---|---|------|--------|------|---|-------|-------|-------|--------|---|-------------|------------------|---------|------------------|---------|---|-------|-----|-------|-----|---|-------|-----|-------|-----|---|-------|-----|-------|-----|----|-------|-----|-------|-----|----|-------|-----|-------|-----|----|-------|-----|-------|-----|---|-------|-----|-----|------|-----|---|------|-----|---|------|-----|-----|------|-----|---|------|-----|---|-----|-----|----|----------------------------|------------------|------------------|------|-----|---|---|------|--------|------|---|-------|-------|-------|--------|
| GLP | はい | yes | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 試験を行った年 | 1997 | 1997 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 試験条件 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 結果 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 設定濃度 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 実測濃度 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 所定時間後の分解度(%、pH、温度 | | 93 % after 5 hour(s) at pH 11 and 25 ° C | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 半減期 | | t1/2 pH7 : > 270 day(s) at 25 ° C t1/2 pH 10.9 : = 1.2 hour(s) at 25 ° C | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 分解生成物 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | <p>緩衝液中のHEA (25°C)</p> <table><tr><th>時間 (日)</th><th>pH 3 平均mg/L</th><th>SD</th><th>pH 7 平均mg/L</th><th>SD</th></tr><tr><td>0</td><td>111.3</td><td>0.3</td><td>108.0</td><td>0.1</td></tr><tr><td>5</td><td>109.1</td><td>0.3</td><td>105.1</td><td>0.1</td></tr><tr><td>7</td><td>121.6</td><td>0.5</td><td>116.2</td><td>0.4</td></tr><tr><td>15</td><td>117.5</td><td>0.1</td><td>111.2</td><td>0.3</td></tr><tr><td>21</td><td>115.2</td><td>0.4</td><td>106.1</td><td>0.3</td></tr><tr><td>28</td><td>114.1</td><td>0.4</td><td>100.5</td><td>0.2</td></tr></table> <p>時間 pH 11 (時) 平均mg/L SD</p> <table><tr><td>0</td><td>108.1</td><td>1.4</td></tr><tr><td>0.5</td><td>85.3</td><td>0.3</td></tr><tr><td>1</td><td>61.8</td><td>0.0</td></tr><tr><td>2</td><td>36.3</td><td>0.0</td></tr><tr><td>3.5</td><td>14.5</td><td>0.2</td></tr><tr><td>4</td><td>11.0</td><td>0.0</td></tr><tr><td>5</td><td>6.5</td><td>0.1</td></tr></table> <p>HEAの加水分解試験の結果</p> <table><tr><th>pH</th><th>K(a) (日⁻¹)</th><th>半減期 (日)</th><th>相関係数 (r²)</th></tr><tr><td>2.84</td><td>nil</td><td>-</td><td>-</td></tr><tr><td>7.03</td><td>0.0025</td><td>>270</td><td>-</td></tr><tr><td>10.87</td><td>13.72</td><td>0.051</td><td>0.9994</td></tr></table> | 時間 (日) | pH 3 平均mg/L | SD | pH 7 平均mg/L | SD | 0 | 111.3 | 0.3 | 108.0 | 0.1 | 5 | 109.1 | 0.3 | 105.1 | 0.1 | 7 | 121.6 | 0.5 | 116.2 | 0.4 | 15 | 117.5 | 0.1 | 111.2 | 0.3 | 21 | 115.2 | 0.4 | 106.1 | 0.3 | 28 | 114.1 | 0.4 | 100.5 | 0.2 | 0 | 108.1 | 1.4 | 0.5 | 85.3 | 0.3 | 1 | 61.8 | 0.0 | 2 | 36.3 | 0.0 | 3.5 | 14.5 | 0.2 | 4 | 11.0 | 0.0 | 5 | 6.5 | 0.1 | pH | K(a) (日 ⁻¹) | 半減期 (日) | 相関係数 (r ²) | 2.84 | nil | - | - | 7.03 | 0.0025 | >270 | - | 10.87 | 13.72 | 0.051 | 0.9994 | <p>Hydrolysis of HEA in Buffered Solutions at 25C</p> <table><tr><th>Time (days)</th><th>pH 3 Ave mg/L</th><th>Std dev</th><th>pH 7 Ave mg/L</th><th>Std dev</th></tr><tr><td>0</td><td>111.3</td><td>0.3</td><td>108.0</td><td>0.1</td></tr><tr><td>5</td><td>109.1</td><td>0.3</td><td>105.1</td><td>0.1</td></tr><tr><td>7</td><td>121.6</td><td>0.5</td><td>116.2</td><td>0.4</td></tr><tr><td>15</td><td>117.5</td><td>0.1</td><td>111.2</td><td>0.3</td></tr><tr><td>21</td><td>115.2</td><td>0.4</td><td>106.1</td><td>0.3</td></tr><tr><td>28</td><td>114.1</td><td>0.4</td><td>100.5</td><td>0.2</td></tr></table> <p>Time pH 11 (hrs) Ave mg/L Std dev</p> <table><tr><td>0</td><td>108.1</td><td>1.4</td></tr><tr><td>0.5</td><td>85.3</td><td>0.3</td></tr><tr><td>1</td><td>61.8</td><td>0.0</td></tr><tr><td>2</td><td>36.3</td><td>0.0</td></tr><tr><td>3.5</td><td>14.5</td><td>0.2</td></tr><tr><td>4</td><td>11.0</td><td>0.0</td></tr><tr><td>5</td><td>6.5</td><td>0.1</td></tr></table> <p>Results for Hydrolysis Studies for HEA correlation coefficient (r2)</p> <table><tr><th>pH</th><th>K(a) (days⁻¹)</th><th>half-life (days)</th><th>coefficient (r2)</th></tr><tr><td>2.84</td><td>nil</td><td>-</td><td>-</td></tr><tr><td>7.03</td><td>0.0025</td><td>>270</td><td>-</td></tr><tr><td>10.87</td><td>13.72</td><td>0.051</td><td>0.9994</td></tr></table> | Time (days) | pH 3 Ave mg/L | Std dev | pH 7 Ave mg/L | Std dev | 0 | 111.3 | 0.3 | 108.0 | 0.1 | 5 | 109.1 | 0.3 | 105.1 | 0.1 | 7 | 121.6 | 0.5 | 116.2 | 0.4 | 15 | 117.5 | 0.1 | 111.2 | 0.3 | 21 | 115.2 | 0.4 | 106.1 | 0.3 | 28 | 114.1 | 0.4 | 100.5 | 0.2 | 0 | 108.1 | 1.4 | 0.5 | 85.3 | 0.3 | 1 | 61.8 | 0.0 | 2 | 36.3 | 0.0 | 3.5 | 14.5 | 0.2 | 4 | 11.0 | 0.0 | 5 | 6.5 | 0.1 | pH | K(a) (days ⁻¹) | half-life (days) | coefficient (r2) | 2.84 | nil | - | - | 7.03 | 0.0025 | >270 | - | 10.87 | 13.72 | 0.051 | 0.9994 |
| 時間 (日) | pH 3 平均mg/L | SD | pH 7 平均mg/L | SD | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 0 | 111.3 | 0.3 | 108.0 | 0.1 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 5 | 109.1 | 0.3 | 105.1 | 0.1 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 7 | 121.6 | 0.5 | 116.2 | 0.4 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 15 | 117.5 | 0.1 | 111.2 | 0.3 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 21 | 115.2 | 0.4 | 106.1 | 0.3 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 28 | 114.1 | 0.4 | 100.5 | 0.2 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 0 | 108.1 | 1.4 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 0.5 | 85.3 | 0.3 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 1 | 61.8 | 0.0 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 2 | 36.3 | 0.0 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 3.5 | 14.5 | 0.2 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 4 | 11.0 | 0.0 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 5 | 6.5 | 0.1 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| pH | K(a) (日 ⁻¹) | 半減期 (日) | 相関係数 (r ²) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 2.84 | nil | - | - | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 7.03 | 0.0025 | >270 | - | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 10.87 | 13.72 | 0.051 | 0.9994 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Time (days) | pH 3 Ave mg/L | Std dev | pH 7 Ave mg/L | Std dev | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 0 | 111.3 | 0.3 | 108.0 | 0.1 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 5 | 109.1 | 0.3 | 105.1 | 0.1 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 7 | 121.6 | 0.5 | 116.2 | 0.4 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 15 | 117.5 | 0.1 | 111.2 | 0.3 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 21 | 115.2 | 0.4 | 106.1 | 0.3 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 28 | 114.1 | 0.4 | 100.5 | 0.2 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 0 | 108.1 | 1.4 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 0.5 | 85.3 | 0.3 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 1 | 61.8 | 0.0 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 2 | 36.3 | 0.0 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 3.5 | 14.5 | 0.2 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 4 | 11.0 | 0.0 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 5 | 6.5 | 0.1 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| pH | K(a) (days ⁻¹) | half-life (days) | coefficient (r2) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 2.84 | nil | - | - | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 7.03 | 0.0025 | >270 | - | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 10.87 | 13.72 | 0.051 | 0.9994 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | <p>(a) 所定のpHで測定した偽一次反応速度定数</p> <p>Ka、Kb 及び二次速度定数Kn を決定した:</p> <p>Ka (M-1day-1)=nil, Kb (M-1day-1)=18,500 及び Kn (day-1)=5.18X10-4</p> <p>HEAはpH11で急速に加水分解され、その半減期は0.05日であった。対照的にpH3及び7での加水分解は遅く、半減期は230日以上であった。これらの結果はHEA中に高いpHで加水分解され易いエステル基を有していることで説明できる。HEAの加水分解の速度定数からpH8における半減期は35から40日と推定される。</p> <p>加水分解へのMEHQ阻害剤の効果-398 及び 275 ppm のMEHQ を含むHEA試料の半減期はそれぞれ1.34 及び1.30時間であった。このように、MEHQ濃度を45%以上増加させても半減期は3%しか長くならなかった。この結果は、275から398ppmにMEHQ濃度を変化させてもpH11における加水分解速度には僅かの影響しかないことを示す。この結果は、MEHQを10,000倍希釈したときに加水分解反応への影響を最小限度に抑えることができた事実と一致する。</p> | <p>(a) pseudo-first-order rate constant determined at indicated pH</p> <p>Calculated kA, kB and kN second order rate constants:</p> <p>Ka (M-1day-1)=nil, Kb (M-1day-1)=18,500 and Kn (day-1)=5.18X10-4</p> <p>HEA hydrolyzed rapidly at pH 11, with a half-life of 0.051 days. In contrast, slow hydrolysis was observed at pH 3 and pH 7, with half-lives greater than 230 days. These results were explained by the presence of ester functional groups in HEA which are more susceptible to hydrolysis at high pH. Based on the hydrolysis rate constant determined for HEA, half-lives of 35 to 40 days would be expected at pH 8.</p> <p>Effect of MEHQ inhibitor on hydrolysis- Samples of HEA containing 398 and 275 ppm MEHQ had half-lives of 1.34 and 1.30 hours, respectively. Thus, a 45% higher concentration of MEHQ resulted in only a 3% longer half-life. These results indicate that varying the MEHQ levels from 275 to 398 ppm in HEA had minimal effect on the rate of hydrolysis at pH 11. This observation was consistent with the fact that the MEHQ was diluted 10,000-fold in the test solutions, thereby minimizing any possible effect on the hydrolysis reaction.</p> | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 結論 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 注釈 | 試験物質はThe Dow Chemical Companyから得た。純度は98.52%との報告を受けた。 | Test material was received from The Dow Chemical Company with a reported purity of 98.52%. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

| | | |
|----------|------------------------------------|--|
| 信頼性スコア | (2) 制限付で信頼性あり | (2) valid with restrictions |
| 信頼性の判断根拠 | ガイドライン試験、ただし、試験物質の特性評価はGLPに準拠していない | Guideline study with the restriction that the test material was not characterized in accordance with GLPs. |
| 出典 | | |
| 引用文献 | (27) | (27) |
| 備考 | フラグ: SIDSエンドポイントに重要な試験 | Flag: Critical study for SIDS endpoint |

3.1.3. 土壌中安定性 STABILITY IN SOIL

| | | |
|-------------------|---|--|
| 試験物質名 | | |
| CAS番号 | | |
| 純度等 | | |
| 注釈 | | |
| 方法 | | |
| GLP | | |
| 試験を行った年 | | |
| 試験条件 | | |
| 試験期間 | | |
| 結果 | | |
| 試験のタイプ | | |
| | 水中スクリーニング試験での生分解性からHEAは土壌中で生分解されると考えられる。アクリル酸エチルの加水分解性から、HEAは特に、アルカリ性の土壌中において加水分解されると考えられる。土壌中に放出されたときHEAは土壌中での移動性は高く地下水中に入ることが予想される。 | Based on its biodegradability in aqueous screening tests, HEA may biodegrade in soil. Based on the hydrolyzability of ethyl acrylate, HEA may hydrolyze, especially in alkaline soils. If released into soil, HEA will be expected to exhibit a very high mobility in soil and may leach into groundwater. |
| 放射性ラベル | | |
| 濃度 | | |
| 土壌温度 °C | | |
| 土壌中pH | | |
| 土壌中湿度 (%) | | |
| 土壌のクラス | | |
| 粘土含量 (%) | | |
| 有機炭素 (%) | | |
| 陽イオン交換能 | | |
| 微生物バイオマス濃度 | | |
| 消失時間 (DT50, DT90) | | |
| 分解生成物 | | |
| 時間ごとの消失率 | | |
| 結論 | | |
| 注釈 | | |
| 信頼性スコア | | |
| 信頼性の判断根拠 | | |
| 出典 | | |
| 引用文献 | (30) (31) (32) (33) (34) | (30) (31) (32) (33) (34) |
| 備考 | | |

3.2. モニタリングデータ(環境) MONITORING DATA (ENVIRONMENT)

3.3. 移動と分配 TRANSPORT AND DISTRIBUTION

3.3.1 環境区分間の移動 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

| | | |
|-------|----------------|------------------------|
| 試験物質名 | | |
| CAS番号 | | |
| 純度等 | | |
| 注釈 | フガシティーモデル レベルI | fugacity model level I |

| | | |
|------------------------------|--|--|
| 方法 | その他の方法:レベル I モデル version 2.11 レベル I モデル version 2.11は、Canadian Environmental Modeling Centre, Trent University, Peterborough, Ontario, Canada から得た レベル I モデルの入力パラメーター: 性状、値、情報源の順に以下にリスト 温度 (°C): 25, デフォルト温度 化学タイプ: 1、タイプ 1 は化学物質が環境コンパートメントに分布されることを示す 分子量 (g/mol): 116.12, 分子式から計算 対水溶解度(g/m ³): 1.0 x 10+6 (混和)、IUCLID データセットに報告された測定値 蒸気圧 (25°C)(Pa): 6.97, DIPPR, Compilation of Pure Chemical Properties, AIChE, New York, NY 融点 (°C): -60.15 °C, DIPPR, Compilation of Pure Chemical Properties, AIChE, New York, NY Henry則定数の推定値 (H)(Pa m ³ /mol): 8.1 x 10-4、レベル I フガシティーモデルにより計算 Log Kow オクタノール-水分配係数: -0.21, Tani and Hashimoto (1982) Tox. Letters 11: 125-129. 推定排出量 (kg): 100,000、レベル I のデフォルト値 | other: Level I model version 2.11 Level I model version 2.11, Obtained from the Canadian Environmental Modeling Centre, Trent University, Peterborough, Ontario, Canada Input Parameters for Level I Model: Listed in the following order: Property: Value, Source of information. Data Temperature (degC): 25, Default environmental temperature Chemical Type: 1, Type 1 indicates chemical can partition into all environmental compartments Molecular Mass (g/mol): 116.12, Calculated from molecular structure Water Solubility (g/cubic m): 1.0 x 10+6 (miscible), Measured value reported in IUCLID dataset Vapor Pressure @ 25 deg C (Pa): 6.97, from DIPPR, Compilation of Pure Chemical Properties, AIChE, New York, NY Melting Point (OC): -60.15 deg C, from DIPPR, Compilation of Pure Chemical Properties, AIChE, New York, NY Estimated Henry's Law Constant (H)(Pa m ³ /mol): 8.1 x 10-4, Calculated by Level I Fugacity Model Log Kow Octanol-Water Partition Coefficient: -0.21, from Tani and Hashimoto (1982) Tox. Letters 11: 125-129. Simulated Emission (kg): 100,000, Level I Default |
| | トータル排出量を100,000kgとしたときの大気、水、土壌及び底質間での分布の予想値: 各層への分布の割合と量は、大気: 1.6 x 10-2, 16.3 kg、水: 99.9%, 1.0 x 10+5 kg、土壌: 5.5 x 10-2%, 54.6 kg、底質: 1.2 x 10-2%, 1.2 kg | Predicted equilibrium distribution among air, water, soil, and sediments with an emission scenario of 100,000 kg total emissions: Percentage and amount distributed to air: 1.6 x 10-2%; 16.3 kg; water: 99.9%; 1.0 x 10+5 kg; soil: 5.5 x 10-2%, 54.6 kg; sediment: 1.2 x 10-2%; 1.2 kg |
| 結果 | | |
| 媒体 | | |
| 試験を行った年 | | 2003 |
| 環境分布予測と媒体中濃度 (level III/III) | 大気: 0.016 % (フガシティーモデルレベル I) 水: 99.9 % (フガシティーモデルレベル I) 土壌: 0.055 % (フガシティーモデルレベル I) | Air : .016 % (Fugacity Model Level I) Water : 99.9 % (Fugacity Model Level I) Soil : .055 % (Fugacity Model Level I) |
| 結論 | HEAは非常に高い対水溶解をと大変低い蒸気圧及びlogKowを有している。これらの性状から移流と反応過程がないとき本物質は平衡状態では排他的に水コンパートメントに分布されることを示す。 | HEA has very high water solubility, very low vapor pressure, and very low log Kow. In the absence of advective and reactive processes, these properties dictate that the material will partition exclusively to the water compartment at equilibrium. |
| 注釈 | | |
| 信頼性スコア | (2) 制限付で信頼性あり | (2) valid with restrictions |
| 信頼性の判断根拠 | 認められた計算法 | Accepted calculation method. |
| 出典 | | |
| 引用文献 | (35) | (35) |
| 備考 | フラグ: SIDSエンドポイントに重要な試験 | Flag: Critical study for SIDS endpoint |

3.3.2 分配 DISTRIBUTION

3.4 好気性生分解性 AEROBIC BIODEGRADATION

| | | |
|-----------------|---|--|
| 試験物質名 | | |
| CAS番号 | | |
| 純度等 | | |
| 注釈 | 好氣的 | aerobic |
| 方法 | その他の方法: OECD ガイドライン301B 及び 指令 84/449/EEC, C.5 | other: according to OECD Guide-line 301B and Directive 84/449/EEC, C.5 |
| 培養期間 | | |
| 植種源 | 活性汚泥 | activated sludge |
| GLP | はい | yes |
| 試験を行った年 | 1984 | 1984 |
| 試験条件 | | |
| 試験物質濃度 | 20 mg/l及び10 mg/l | 20 mg/l related to Test substance 10 mg/l related to Test substance |
| 汚泥濃度 | | |
| 培養温度 °C | | |
| 対照物質および濃度(mg/L) | | |
| 分解度測定方法 | | |
| 分解度算出方法 | | |
| 結果 | | |
| 最終分解度(%) 日目 | | |
| 分解速度-1 | 80%、28日 | 80 (±) % after 28 day(s) |
| 分解速度-2 | | |
| 分解速度-3 | | |
| 分解速度-4 | | |

| | | |
|------------------------|---|---|
| 分解生成物 | | |
| 上記結果以外の分解度測定方法及びその結果 | | |
| 対象物質の7、14日目の分解度 その他 | 2-アクリル酸ヒドロキシエチルの28日後の生分解度は、10mg/lで78%及び20mg/lで80%であった。濃度が10mg/l及び20mg/lのとき、分解度が10%以上に達するまでの時間(lag period)はそれぞれ6.5日及び8.2日であり、これらのlag period以後10日以内にそれぞれ平均で72%及び75%に達した。対照物質の安息香酸ナトリウムは94%分解された。これにより植種源と試験条件の妥当性が確認された。それ故に、2-アクリル酸ヒドロキシエチルは厳しい条件下及び修正 Sturm試験条件下で易分解性と考えられる | 2-Hydroxyethyl acrylate attained 79% biodegradation after 28 days at a concentration of 10 mg/L and 80% biodegradation at a concentration of 20 mg/L. The lag periods required before greater than 10% biodegradation occurred were approximately 6.5 and 8.2 days, at the 10 and 20 mg/l concentrations, respectively. Within ten days following these lag periods, biodegradation averaged about 72 and 75% for the 10 and 20 mg/l reactions, respectively. The sodium benzoate control attained 94% degradation which confirmed the suitability of the inoculum and test conditions. Therefore, 2-hydroxyethyl acrylate can be considered as readily biodegradable under the strict terms and conditions of the Modified Sturm Test. |
| 結論 | 易分解性 | readily biodegradable |
| 注釈 | 試験方法の詳細に関しては英文を参照 | The study was conducted with 5-liter glass culture vessels that contained 3 liters of solution; the vessels were maintained in the dark at 21 degrees C +/- 1 degrees C for 28 days. Filtrate of activated sludge from a sewage treatment plant was added to the culture vessels at a final concentration of 1%. The test substance was incubated in the nutrient medium at a concentration of 10 or 20 mg/L. Concurrent controls consisted of nutrient medium alone as well as nutrient medium with 20 mg/L sodium benzoate. Degradation was measured by total inorganic carbon analysis of evolved CO2 in multiple samples from day 0 through day 28. The percentage degradation then was calculated from the total organic carbon (TOC) content of the test material; the carbon content of the test material was 52.5% based on analysis. |
| 信頼性スコア | (1) 制限なく信頼性あり | (1) valid without restriction |
| 信頼性の判断根拠 | GLPガイドライン試験 | GLP Guideline Study |
| 出典 | | |
| 引用文献 | (38) | (38) |
| 備考 | フラグ: SIDSエンドポイントに重要な試験 | Flag: Critical study for SIDS endpoint |

3.5. BOD-5、CODまたはBOD-5/COD比
BOD-5、COD OR RATIO BOD-5/COD

| | | |
|------------------------|---|---|
| 試験物質名 | | |
| CAS番号 | | |
| 純度等 | | |
| 注釈 | | |
| BOD5の算出方法 | その他の方法: ach Method Number 8000に基づく BODは、Standard Methods for the Examination of Water and Wastewater, APHA, 17th Edition, 1987の方法で測定された。試験物質は直接試験容器に添加した。試験濃度は、2、5、17、33、and 66 mg/Lとした。対照物質はデキストロースとグルタミン酸で調製した。植種源にはPolyseed (Polybac, Bethlehem, PA)を用いた。COD試験はHach Method Number 8000を基にした。HEAのストック溶液はナノポア水で設定濃度1mg/lに調製した。測定は3連で行った。対象溶液は安息香酸カリウムで調製した。 | other: based on Hach Method Number 8000 The BOD was performed based on the methods described in Standard Methods for the Examination of Water and Wastewater, APHA, 17th Edition, 1987. The test substance was administered to the test chambers by direct addition. The tested concentration range was 2, 5, 17, 33, and 66 mg/L. The reference standard was prepared using dextrose and glutamic acid. The biological seed was Polyseed (Polybac, Bethlehem, PA). The procedures for the COD test was based on Hach Method Number 8000. A stock solution of hydroxyethyl acrylate was prepared at a nominal concentration of 1 mg/ml in Nanopure water. Triplicate chemical oxygen demand determinations were performed on the stock solution. The reference standard was prepared using potassium hydrogen phthalate. |
| GLP | データなし | no data |
| 試験を行った年 | 1994 | 1994 |
| 試験条件 | | |
| 結果 | | |
| 濃度 | | |
| 結果 mgO ₂ /L | | |
| BOD/COD比 | COD: 1500 mg/g 物質 | COD: 1500 mg/g substance |
| その他 | | |
| 結論 | COD値は1500 mg/g +/- 0.0 mg/g 及び、ThOD値は1520 mg/gであった。COD対照物質は設定値の15%以内の許容範囲内であった。HEAは試験した濃度範囲で2.0 mg O ₂ /L (実際の値は<1.0 mg/L)以上の溶存酸素(DO)の減少を示さなかった。それ故に、BOD値の計算に十分なDO値の減少はなかった。DOの減少がなかったことはHEAにより微生物源が阻害されたことを示唆するかもしれない。希釈水及びグルコース-グルタミン酸コントロールの結果はそれぞれ0.15 mg O ₂ /L及び180 mg/Lであり、これらの値は試験が成立する許容範囲内であった。 | The COD was 1500 mg/g +/- 0.0 mg/g and the ThOD was 1520 mg/g. The results of the COD reference standards were within the acceptable range of 15% of nominal. HEA did not exhibit a dissolved oxygen (DO) depletion of greater than or equal to 2.0 mg O ₂ /L (actual was <1.0 mg/L) over the range of concentrations tested; therefore, there was insufficient DO depletion to calculate a BOD value. The absence of DO depletion may indicate inhibition of the microbial inoculum by HEA. The dilution water and glucose-glutamic acid control results were within the acceptable ranges established for the test with values of 0.15 mg O ₂ /L and 180 mg/L, respectively. |
| 注釈 | 試験物質はThe Dow Chemical Companyから得た | Test material was received from The Dow Chemical Company. |

| | | |
|----------|---|---|
| 信頼性スコア | (2) 制限付で信頼性あり | (2) valid with restrictions |
| 信頼性の判断根拠 | 一般的に認められた科学的標準法と合致しており、評価法として引用され、受け入れられている | Meets generally accepted scientific standards, well documented and acceptable for assessment. |
| 出典 | | |
| 引用文献 | (42) | (42) |
| 備考 | | |

3.6 生物濃縮性

BIOACCUMULATION

| | | |
|-------------|---|---|
| 試験物質名 | | |
| CAS番号 | | |
| 純度等 | | |
| 注釈 | | |
| 方法 | | |
| 生物種 | | |
| 暴露期間（日） | | |
| 曝露濃度 | | |
| 排泄期間 | | |
| GLP | | |
| 試験を行った年 | | |
| 分析方法 | | |
| 試験条件 | | |
| 被験物質溶液 | | |
| 対照物質 | | |
| 対照物質名及び分析方法 | | |
| | | |
| 試験方式／実施 | | |
| 結果 | | |
| 死亡率／行動 | | |
| 脂質含有量（%） | | |
| 試験中の被験物質濃度 | | |
| 濃縮係数 (BCF) | | |
| 取込／排泄定数 | | |
| 排泄時間 | | |
| 代謝物 | | |
| その他の観察 | | |
| 結論 | | |
| 注釈 | HEAは水生生物へ生物濃縮しないと考えられる。しかし、その関連文献はない。log Kow値が-0.21であることから、推奨される回帰式を用いてBCFは0.41と計算される。この結果は水生生物への生物濃縮は起こらないことを示す。 | It is unlikely that HEA bioaccumulates in aquatic organisms; however, there is no relevant literature available. Using the reported log Kow of -0.21, a bioconcentration factor (BCF) of 0.41 has been calculated using a recommended regression-derived equation, indicating that bioconcentration in aquatic organisms is unlikely to occur |
| 信頼性スコア | | |
| | | |
| 信頼性の判断根拠 | | |
| 出典 | | |
| 引用文献 | (45) (46) | (45) (46) |
| 備考 | | |

| 項目名 | 和訳結果 (SIDS Dossier) | 原文 (SIDS Dossier) |
|---------------------------------------|---|---|
| 4-1 魚への急性毒性 ACUTE TOXICITY TO FISH | | |
| 試験物質 | 入手源- Scientific Polymer Products, Inc. 純度- >97% (ガスクロマトグラフィーによる分析値) | Source- Scientific Polymer Products, Inc. Purity- >97% by gas liquid chromatography |
| 同一性 | | |
| 方法 | ※英文参照 | HEA concentrations were analyzed in the water sample from the fish exposure tanks via gas-liquid chromatography. Tests were initiated by adding 20 fish per treatment and control. Death was the major test endpoint. The number of dead fish was noted every 24 hours. Observations of fish behavior and toxic sign were made at 2-8, 24, 48, 72 and 96 hours. Upon test termination, individual control fish were weighed and measured. Four surviving fish each from the control, the lowest concentration and the concentration nearest the LC50 were preserved in 10% buffered formalin and kept for histological examination (no data presented by authors). The estimated LC50 and EC50 with corresponding 95% confidence intervals were calculated using the corrected average of the analyzed tank concentrations and the Trimmed Spearman-Kärber Method (Hamilton et al., 1977, Environ. Sci. Technol. 11:714-719). |
| GLP | データ無し | no data |
| 試験を行った年 | 1983 | 1983 |
| 魚種、系統、供給者 | <i>Pimephales promelas</i> (魚類, 淡水) | <i>Pimephales promelas</i> (Fish, fresh water) |
| エンドポイント | | |
| 試験物質の分析の有無 | 有り | yes |
| 試験物質の分析方法 | | |
| 結果の統計解析手法 | | |
| 試験条件 | | |
| 試験魚の月齢、体長、体重 | 齢: 28日齢 平均体長: 18.5 mm (SD 2.417) 平均体重: 0.110 gram (SD 0.0427) 負荷率: 1.100 grams/L | Age: 28 days Mean length: 18.5 mm (SD 2.417) Mean weight: 0.110 gram (SD 0.0427) Loading: 1.100 grams/L |
| 試験用水量あたりの魚体重 | | |
| 参照物質での感受性試験結果 | | |
| じゅん化条件 | | |
| 希釈水源 | | |
| 希釈水の化学的性質 | 温度: 24.5°C 溶存酸素: 7.1 mg/l 硬度: 44 mg/l CaCO3 アルカリ度: 49.8 mg/l CaCO3 タンク容量: 2 L 添加: 18 V/D pH: 7.69 | Temperature: 24.5 deg. C Dissolved oxygen: 7.1 mg/l Hardness: 44 mg/l CaCO3 Alkalinity: 49.8 mg/l CaCO3 Tank volume: 2 liter Additions: 18 V/D pH: 7.69 |
| 試験溶液(及び保存溶液)とその調製法 | | |
| 試験物質の溶液中での安定性 | | |
| 溶解助剤/溶剤の種類とその濃度 | | |
| 暴露容器 | | |
| 暴露期間 | 96時間 | 96 hour(s) |
| 試験方式 | 流水 | flow through |
| 換水率/換水頻度 | | |
| 連数、1連当たりの魚数 | | |
| 影響が観察された少なくとも1濃度区及び対照区における水質 | | |
| 試験温度範囲 | | |
| 照明の状態 | | |
| 平均測定濃度の計算方法 | | |
| 結果 | | |
| 設定濃度 | 0.0, 2.7, 4.2, 6.5, 10, 16 mg/l | 0.0, 2.7, 4.2, 6.5, 10, or 16 mg/l |
| 実測濃度 | <0.5, 3.18, 3.92, 5.92, 9.14, 16.1 mg/l | <0.5, 3.18, 3.92, 5.92, 9.14, or 16.1 mg/l |
| 生物学的影響観察 | | |
| 累積死亡率の表 | | |
| 統計的結果 | | |

| | | |
|---------------|---|---|
| 注釈 | <p>96時間 LC50は4.8 mg/L、96時間 EC50は4.7 mg/L (信頼限界:4.5-4.8)であった。16mg/L群の全ての魚が暴露24時間以内に死亡した。影響の見られた魚では、群泳行動の喪失及び水表面での螺旋遊泳が見られた。これらの魚は、多動傾向で、外部刺激に過剰反応し、暗色、奇形、浮腫がみられ、死亡前に平衡の喪失がみられた。</p> <p>NOEC = 4.2 mg/L。本試験はASTM (1980)ガイドラインに従い、流水式で実施された。設定濃度は2.7～16 mg/Lの範囲で、96時間での分析値は3.18～16.1 mg/Lであった。高用量の3濃度群 (5.92, 9.14 及び 16.1mg/L、測定値) で死亡がみられた。LC50は分析値に基づいて算出された。</p> | <p>The 96 hr LC50 was 4.8 mg/L and the 96 hr EC50 was 4.7 mg/L (conf. lim: 4.5-4.8). All fish died within 24 hours following exposure to the 16 mg/L concentration. Affected fish lost schooling behavior and swam near the tank surface in a corkscrew/spiral pattern. They were hyperactive and overreactive to external stimuli, were darkly colored and deformed, had edema, and lost equilibrium prior to death.</p> <p>The NOEC = 4.2 mg/L. This study followed ASTM (1980) guidelines using a flow-through design. Nominal exposure concentrations ranged from 2.7 to 16 mg/L and analyses at 96 hours ranged from 3.18 to 16.1 mg/L. Mortality occurred in the three highest concentrations (5.92, 9.14 and 16.1 mg/L, measured). The LC50 was determined based on analytical values.</p> |
| 対照区における死亡率 | | |
| 異常反応 | | |
| その他の観察結果 | | |
| 結論 | | |
| 結果 (96h-LC50) | <p>NOEC : = 4.2mg/l 測定値/設定値 LC50 : = 4.8mg/l 測定値/設定値 EC50 : = 4.7mg/l 測定値/設定値</p> | <p>NOEC : = 4.2mg/l measured/nominal LC50 : = 4.8mg/l measured/nominal EC50 : = 4.7mg/l measured/nominal</p> |
| 信頼性スコア | (2) 制限付で信頼性あり | (2) valid with restrictions |
| キースタディ | | |
| 信頼性の判断根拠 | 一般的に許容できる科学的基準に合致。よく文書化され評価に利用できる。 | Meets generally accepted scientific standards, well documented and acceptable for assessment. |
| 出典 | | |
| 引用文献 | (47) | (47) |
| 備考 | フラグ: SIDSエンドポイントにとって重要な試験 | Flag : Critical study for SIDS endpoint |

4-2 水生無脊椎動物への急性毒性 (例えばミジンコ)

ACUTE TOXICITY TO AQUATIC INVERTEBRATES (DAPHNIA)

| | | |
|------------------|---|---|
| 試験物質 | 1.1～1.4で規定 | as prescribed by 1.1 – 1.4 |
| 同一性 | | |
| 方法 | その他: OECDガイドライン202, part 1 及び Directive84/449/EEC, C2に従った | other: according to OECD Guide-line 202, part 1 and Directive 84/449/EEC, C2 |
| 方法 | ※英文参照 | <p>Test condition : Subsequent to a range-finding study, 2 replicate groups of 10 daphnia were exposed to an aqueous solution of the test material at nominal concentrations of 0.10, 0.18, 0.32, 0.56, 1.0, 1.8, 3.2, 5.6 and 10 mg/L.</p> <p>Additional duplicate groups of 10 daphnia were included as untreated controls. The daphnia were exposed under static conditions in glass jars that contained 200 ml of the test media. The daphnia were observed for immobilization at 24 and 48 hours of exposure. The temperature, pH and oxygen concentration of the test solutions were monitored throughout the study. The pH of the water in controls was 8.0 at 0 hr and 7.9 at 48 hr in both replicates; at all HEA concentrations the pH ranged from 8.1 to 8.2 at 0 hr and from 7.9 and 8.1 at 48 hr. The water temperature was constant at 22 degrees C. HEA is expected to be stable under these conditions.</p> |
| GLP | はい | yes |
| 試験を行った年 | 1992 | 1992 |
| 生物種、系統、供給者 | <i>Daphnia magna</i> (甲殻類) | <i>Daphnia magna</i> (Crustacea) |
| エンドポイント | | |
| 試験物質の分析の有無 | データ無し | no data |
| 試験物質の分析方法 | | |
| 結果の統計解析手法 | | |
| 試験条件 | | |
| 試験生物の起源、前処理、繁殖方法 | | |
| 参照物質での感受性試験結果 | | |
| 試験開始時の時間齢 | | |
| 希釈水源 | | |
| 希釈水の化学的性質 | | |

| | | |
|-----------------------------|---|--|
| 試験溶液(及び保存溶液)とその調製法 | | |
| 試験物質の溶液中での安定性 | | |
| 溶解助剤/溶剤の種類とその濃度 | | |
| 暴露容器 | | |
| 暴露期間 | 48時間 | 48 hour(s) |
| 試験方式 | | |
| 連数、1連当たりの試験生物数 | | |
| 対照区と影響が観察された少なくとも1濃度区における水質 | | |
| 試験温度範囲 | | |
| 照明の状態 | | |
| 平均測定濃度の計算方法 | | |
| 結果 | | |
| 設定濃度 | | |
| 実測濃度 | | |
| 遊泳阻害数 | | |
| 累積遊泳阻害数の表 | | |
| 注釈 | 試験物質への暴露により、0.56, 1.0, 1.8, 3.2, 5.6 及び10 mg/L 群でミジンコの遊泳阻害がみられた。一方、0.10, 0.18 及び0.32 mg/L群では遊泳阻害はみられなかった。未処理の対照群においても遊泳阻害は見られなかった。2-ヒドロキシエチルアクリレート(ミジンコの48時間半数影響設定濃度(EC50)は0.78 mg/L (95%信頼限界:0.64 - 0.95 mg/L)であった。NOECは0.32 mg/Lであった。 | Exposure to the test material resulted in immobilization in the daphnia in the 0.56, 1.0, 1.8, 3.2, 5.6 and 10 mg/L test groups. On the other hand, exposure to the test material at concentrations of 0.10, 0.18 and 0.32 mg/L did not result in immobilization. Also, exposure to the untreated control solutions did not result in immobilization. The 48-hour median effective nominal concentration (EC50) of 2-hydroxyethyl acrylate in Daphnia magna was 0.78 mg/L with 95% confidence limits of 0.64 - 0.95 mg/L. The noobserved-effect concentration was 0.32 mg/L. |
| 対照区における反応は妥当か | | |
| 対照区における反応の妥当性の考察 | | |
| 結論 | | |
| 結果(48h-EC50) | EC50 : = .78mg/l 測定値/設定値 | EC50 : = .78mg/l measured/nominal |
| 信頼性スコア | (1) 制限なく信頼性あり | (1) valid without restriction |
| キースタディ | | |
| 信頼性の判断根拠 | | |
| 出典 | | |
| 引用文献 | (54) | (54) |
| 備考 | フラグ: SIDSエンドポイントにとって重要な試験 | Flag : Critical study for SIDS endpoint |

4-3 水生植物への毒性(例えば藻類)

TOXICITY TO AQUATIC PLANTS e. g. ALGAE

| | | |
|-----------------|--|--|
| 試験物質 | 試験物質は99.23%の2-HEA | The test substance was 99.23% 2-HEA. |
| 同一性 | | |
| 方法 | EPA OPPTS 850.5400 OECDテストガイドライン201にも従った。 対照群のpH値は各容器において1.0以上の差はなく、7.49～8.48であった。水温は24 +/- 2 °C; 加水分解試験より、HEAはこれらの条件下では安定であると考えられる。 | EPA OPPTS 850.5400 Also conducted according to OECD Test Guideline 201. The pH-value in the control replicates increased not higher than 1.0 unit; from 7.49 to 8.48, water temperature was 24 +/- 2 degrees C; HEA is expected to be stable under these conditions based on hydrolysis studies. |
| GLP | はい | yes |
| 試験を行った年 | 2003 | 2003 |
| 生物種、系統、供給者 | <i>Selenastrum capricornutum</i> (藻類) <i>Selenastrum capriornutum</i> は <i>Pseudokirchneriella subcapitata</i> として知られている。 | <i>Selenastrum capricornutum</i> (Algae) <i>Selenastrum capriornutum</i> is now known as <i>Pseudokirchneriella subcapitata</i> |
| エンドポイント | その他: バイオマス及び生長速度 | other: biomass and growth rate |
| 毒性値算出に用いたデータの種類 | | |
| 試験物質の分析の有無 | 無し | no |
| 試験物質の分析方法 | | |
| 結果の統計解析手法 | | |
| 試験条件 | | |
| 試験施設での藻類継代培養方法 | | |

| 藻類の前培養の方法及び状況 | ※英文参照 | Preculture: A three day old preculture was used as inoculum. Incubation was performed in 500 mL erlenmeyer flasks with test medium under the same environmental conditions as described for the definitive test. For the start of the test the preculture was diluted test medium to receive an initial cell concentration of approximatley 1 x 10+4 cells/mL in the replicates. All algae were from the same source and had not been used in any previous studies. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|------------------------------------|---|---|------------------|------|----------------|-----------------------------|----------------|--|----------------|--|--|------|------|------|------|--|--|--|--|---|-----|----|-----|-----|--|--|--|--|-------|-----|----|-----|-----|-----|-----|--|--|------|-----|----|-----|-----|------|-----|--|--|-----|-----|----|-----|-----|----|------|--|--|---|-----|----|-----|-----|----|------|--|--|----|-----|-----|-----|-----|----|----|--|--|---|------------------------------------|------|------|------|------|----------------|-----------------------------|---|-----|----|-----|-----|--|--|-------|-----|----|-----|-----|-----|-----|------|-----|----|-----|-----|------|-----|-----|-----|----|-----|-----|----|------|---|-----|----|-----|-----|----|------|----|-----|-----|-----|-----|----|----|
| 参照物質での感受性試験結果 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 希釈水源 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 培地の化学的性質 | ※英文参照 | Test medium: Threefold concentrated medium according to OECD guideline (AAP medium). | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 試験溶液(及び保存溶液)とその調製法 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 試験物質の溶液中での安定性 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 溶解助剤/溶剤の種類とその濃度 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 暴露容器 | 試験容器:無菌の三角フラスコ、容量250 mL、脱脂綿で蓋 試験液量: 100 mL | Test container: Sterile erlenmeyer flasks, volume 250 mL, covered with cotton wool plugs. Test volume: 100 mL | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 暴露期間 | 96時間 | 96 hour(s) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 試験方式 | 止水 | Static | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 連数 | 各濃度3連。対照群は6連。 | Three replicates for each concentration level, 6 per control. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 各濃度区の少なくとも1連における試験開始時と終了時の水質 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 試験温度範囲 | 24 +/- 2 °C | 24 +/- 2 degrees C | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 照明の状態 | 光強度: 66.5 microE x m-2 +/- 10% 照明型: 24 時間/日 明 | Light intensity: 66.5 microE x m-2 +/- 10% Light regime: 24 h/d light | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 平均測定濃度の計算方法 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 結果 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 設定濃度 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 実測濃度 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 細胞密度 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 生長阻害率(%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 各濃度区における生長曲線 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| その他観察結果 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 注釈 | 設定濃度に基づく: バイオマス(生長曲線下面積)阻害: EbC50 (72時間) = 3.96 mg/L (95% CI = 3.53 - 4.44 mg/L) EbC50 (96時間) = 4.12 mg/L (95% CI = 3.75 - 4.52 mg/L) NOEC (72時間) = 0.625 mg/L LOEC (72時間) = 1.25 mg/L NOEC (96時間) = 0.625 mg/L LOEC (96時間) = 1.25 mg/L 生長阻害: ErC50 (72時間) = 8.81 mg/L (95% CI = 7.98 - 9.72 mg/L) ErC50 (96時間) = 8.26 mg/L (95% CI = 7.62 - 8.95 mg/L) NOEC (72時間) = 1.25 mg/L LOEC (72時間) = 2.5 mg/L NOEC (96時間) = 2.5 mg/L LOEC (96時間) = 5.0 mg/L | Based on nominal concentrations: Inhibition of Biomass (area under the curve): EbC50 (72h) = 3.96 mg/L (95% CI = 3.53 - 4.44 mg/L) EbC50 (96h) = 4.12 mg/L (95% CI = 3.75 - 4.52 mg/L) NOEC (72h) = 0.625 mg/L LOEC (72h) = 1.25 mg/L NOEC (96h) = 0.625 mg/L LOEC (96h) = 1.25 mg/L Inhibition of Growth: ErC50 (72h) = 8.81 mg/L (95% CI = 7.98 - 9.72 mg/L) ErC50 (96h) = 8.26 mg/L (95% CI = 7.62 - 8.95 mg/L) NOEC (72h) = 1.25 mg/L LOEC (72h) = 2.5 mg/L NOEC (96h) = 2.5 mg/L LOEC (96h) = 5.0 mg/L | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 注釈 | 予備試験において、バイオマスに基づく阻害は10, 100 及び 1000 mg/L群でそれぞれ98, 100 及び100%であった。生長速度に基づく阻害は72, 100 及び 100%であった。 暴露終了時に細胞を顕微鏡で観察した結果、形態学的な異常はみられなかった。環境条件(pH、水温)はガイドラインの要求に合致した。 | For the preliminary test, inhibition based on biomass was 98, 100 and 100% of control at 10, 100 and 1000 mg/L, respectively. Corresponding inhibition based on growth rate was 72, 100 and 100%. Microscopic evaluation of the cells at the end of the incubation period revealed no morphological abnormalities. Environmental conditions (pH, water temperature) met the guideline requirements. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 注釈 | 本試験における細胞密度、生長曲線下面積及び生長速度の要約を表に示す: <table><tr><th>設定濃度 (mg/L)</th><th colspan="4">平均細胞数 (x 10,000)</th><th colspan="2">バイオマス 阻害 (%)</th><th colspan="2">速度に 関連した阻害 (%)</th></tr><tr><th></th><th>24時間</th><th>48時間</th><th>72時間</th><th>96時間</th><th></th><th></th><th></th><th></th></tr><tr><td>0</td><td>8.3</td><td>46</td><td>201</td><td>453</td><td></td><td></td><td></td><td></td></tr><tr><td>0.625</td><td>7.6</td><td>48</td><td>202</td><td>389</td><td>6.1</td><td>1.9</td><td></td><td></td></tr><tr><td>1.25</td><td>7.2</td><td>43</td><td>170</td><td>395</td><td>13.4</td><td>1.5</td><td></td><td></td></tr><tr><td>2.5</td><td>7.3</td><td>29</td><td>138</td><td>362</td><td>27</td><td>2.62</td><td></td><td></td></tr><tr><td>5</td><td>5.6</td><td>19</td><td>111</td><td>252</td><td>46</td><td>11.1</td><td></td><td></td></tr><tr><td>10</td><td>4.2</td><td>5.5</td><td>7.5</td><td>6.4</td><td>96</td><td>68</td><td></td><td></td></tr></table> | 設定濃度 (mg/L) | 平均細胞数 (x 10,000) | | | | バイオマス 阻害 (%) | | 速度に 関連した阻害 (%) | | | 24時間 | 48時間 | 72時間 | 96時間 | | | | | 0 | 8.3 | 46 | 201 | 453 | | | | | 0.625 | 7.6 | 48 | 202 | 389 | 6.1 | 1.9 | | | 1.25 | 7.2 | 43 | 170 | 395 | 13.4 | 1.5 | | | 2.5 | 7.3 | 29 | 138 | 362 | 27 | 2.62 | | | 5 | 5.6 | 19 | 111 | 252 | 46 | 11.1 | | | 10 | 4.2 | 5.5 | 7.5 | 6.4 | 96 | 68 | | | The following table provides a summary of cell density, area under growth curves and growth rate for the definitive test: <table><tr><th>Nominal Average Cell Counts (mg/L)</th><th>24 h</th><th>48 h</th><th>72 h</th><th>96 h</th><th>Inhibition (%)</th><th>Rate-Related Inhibition (%)</th></tr><tr><td>0</td><td>8.3</td><td>46</td><td>201</td><td>453</td><td></td><td></td></tr><tr><td>0.625</td><td>7.6</td><td>48</td><td>202</td><td>389</td><td>6.1</td><td>1.9</td></tr><tr><td>1.25</td><td>7.2</td><td>43</td><td>170</td><td>395</td><td>13.4</td><td>1.5</td></tr><tr><td>2.5</td><td>7.3</td><td>29</td><td>138</td><td>362</td><td>27</td><td>2.62</td></tr><tr><td>5</td><td>5.6</td><td>19</td><td>111</td><td>252</td><td>46</td><td>11.1</td></tr><tr><td>10</td><td>4.2</td><td>5.5</td><td>7.5</td><td>6.4</td><td>96</td><td>68</td></tr></table> | Nominal Average Cell Counts (mg/L) | 24 h | 48 h | 72 h | 96 h | Inhibition (%) | Rate-Related Inhibition (%) | 0 | 8.3 | 46 | 201 | 453 | | | 0.625 | 7.6 | 48 | 202 | 389 | 6.1 | 1.9 | 1.25 | 7.2 | 43 | 170 | 395 | 13.4 | 1.5 | 2.5 | 7.3 | 29 | 138 | 362 | 27 | 2.62 | 5 | 5.6 | 19 | 111 | 252 | 46 | 11.1 | 10 | 4.2 | 5.5 | 7.5 | 6.4 | 96 | 68 |
| 設定濃度 (mg/L) | 平均細胞数 (x 10,000) | | | | バイオマス 阻害 (%) | | 速度に 関連した阻害 (%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | 24時間 | 48時間 | 72時間 | 96時間 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 0 | 8.3 | 46 | 201 | 453 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 0.625 | 7.6 | 48 | 202 | 389 | 6.1 | 1.9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 1.25 | 7.2 | 43 | 170 | 395 | 13.4 | 1.5 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 2.5 | 7.3 | 29 | 138 | 362 | 27 | 2.62 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 5 | 5.6 | 19 | 111 | 252 | 46 | 11.1 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 10 | 4.2 | 5.5 | 7.5 | 6.4 | 96 | 68 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Nominal Average Cell Counts (mg/L) | 24 h | 48 h | 72 h | 96 h | Inhibition (%) | Rate-Related Inhibition (%) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 0 | 8.3 | 46 | 201 | 453 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 0.625 | 7.6 | 48 | 202 | 389 | 6.1 | 1.9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 1.25 | 7.2 | 43 | 170 | 395 | 13.4 | 1.5 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 2.5 | 7.3 | 29 | 138 | 362 | 27 | 2.62 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 5 | 5.6 | 19 | 111 | 252 | 46 | 11.1 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 10 | 4.2 | 5.5 | 7.5 | 6.4 | 96 | 68 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

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| 対照区での生長は妥当か | | |
| 対照区における反応の妥当性の考察 | | |
| 結論 | | |
| 結果 (ErC50) | | |
| 結果 (NOEC) | | |
| 信頼性スコア | (1) 制限なく信頼性あり | (1) valid without restriction |
| キースタディ | | |
| 信頼性の判断根拠 | GLPガイドライン試験。制限無く信頼性あり | GLP Guideline Study, valid without restriction |
| 出典 | | |
| 引用文献 | | |
| 備考 | ※英文参照 | <p>Test condition :</p> <p>Application: At the test start fluorescence was measured after application of the test item. Application was carried out by adding appropriate volumes of the stock solution to the test replicates.</p> <p>Agitation: Test containers were placed on a rotary shaker and oscillated at approximately 100 rpm.</p> <p>Recovery of algae: After 96 h 5 mL alga suspension from the nominal concentration 10 mg/L and from the control were transferred to 100 mL untreated test medium and allowed to grow for further 3 – 4 d to determine whether the effect of the test item was reversible. The test medium and growing conditions were the same as used in the main test.</p> |
| | ※英文参照 | <p>TYPE AND FREQUENCY MEASUREMENT: Cell density was measured via Chlorophyll-a-fluorescence, excitation at 435 nm, emission at 685 nm. Each replicate was measured 6-fold. The cell density was measured at the beginning of the test and every 24 h. Filtrated culture medium was used as ground signal. The pH-value at the beginning of the test was measured out of one additional replicate of each concentration and control. At the end it was measured from a pool of all replicates. The water temperature was recorded hourly during the test. The room temperature was measured continuously by a hygrothermograph. Light intensity was measured prior to test start. Microscopic evaluation of the cells at the start and at the end of the incubation was determined. Also any unusual cell shapes, colour differences, differences in chloroplast morphology, flocculations, adherence of algae to test containers or aggregation of alga cell were observed.</p> |
| | ※英文参照 | <p>A preliminary test at concentrations of 2-HEA at 0, 1, 10, 100 and 1000 mg/L (2 replicates/concentration) was conducted in which biomass and growth rate were monitored at 0, 24, 48, 72 and 96 hours. Based on the results of the preliminary study, the definitive 96 hour static EC50 test was conducted with nominal concentrations of 0, 0.625, 1.25, 2.5, 5, and 10 mg/L.</p> |
| 備考 | フラグ: SIDSエンドポイントにとって重要な試験 | Flag : Critical study for SIDS endpoint |

4-4 微生物への毒性(例えばバクテリア)
TOXICITY TO MICROORGANISMS e. g. BACTERIA

4-5 水生生物への慢性毒性
CHRONIC TOXICITY TO AQUATIC ORGANISMS

A. 魚への慢性毒性
CHRONIC TOXICITY TO FISH

B. 水生無脊椎動物への慢性毒性
CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4-6 陸生生物への毒性
TOXICITY TO TERRESTRIAL ORGANISMS

A. 陸生植物への毒性
TOXICITY TO TERRESTRIAL PLANTS

B. 土壌生物への毒性
TOXICITY TO SOIL DWELLING ORGANISMS

C. 他の非哺乳類陸生種(鳥類を含む)への毒性
TOXICITY TO OTHER NON-MAMMALIAN TERRESTRIAL SPECIES (INCLUDING AVIAN)

4-6-1底生生物への毒性
TOXICITY TO SEDIMENT DWELLING ORGANISMS

4-7 生物学的影響モニタリング(食物連鎖による蓄積を含む)
BIOLOGICAL EFFECTS MONITORING (INCLUDING BIOMAGNIFICATION)

4-8 生体内物質変換と動態
BIOTRANSFORMATION AND KINETICS

4-9 追加情報
ADDITIONAL INFORMATION

| 項目名 | 和訳結果 (SIDS Dossier) | 原文 (SIDS Dossier) |
|-----|---------------------|-------------------|
|-----|---------------------|-------------------|

5-1 トキシコキネティクス、代謝、分布
TOXICOKINETICS, METABOLISM, and DISTRIBUTION

| | | |
|-----------|--|---|
| 試験物質名 | 他のTS | other TS |
| CAS番号 | | |
| 純度等 | <p>均一に標識した¹⁴C-HEAは非放射能が6.3 mCi/mmolで、HPLCで測定した放射化学純度は100%であった。放射化学純度は試験を通して測定し、100%から87%の範囲 (低い純度は吸入試験用のみ)であった。</p> <p>非標識のHEAはGCとIRでの測定により分子の純度は98.3%であった。</p> | <p>Uniformly labeled ¹⁴C-HEA had a specific activity of 6.3 mCi/mmol and a radiochemical purity of 100% as determined by HPLC. Radiochemical purity was evaluated throughout the study and ranged from 100% to 87% (lower purity for inhalation study only).</p> <p>Non-radiolabeled HEA had a molar purity of 98.3% as determined by GC and IR.</p> |
| 注釈 | | |
| 方法 | | |
| 方法／ガイドライン | | |
| 試験形態 | In vivo タイプ : トキシコキネティクス | In vivo Type : Toxicokinetics |
| GLP適合 | はい | yes |
| 試験をおこなった年 | | |
| 方法の概略 | ※英文参照 | <p>The disposition of ¹⁴C-HEA was determined following a single dose administration via the oral, intraperitoneal, dermal, and inhalation routes of exposure. Four male Fischer 344 rats (approx. 200g) were utilized per dose and route of exposure. Doses selected for the oral and IP studies were 2.5 and 50 mg/kg, respectively, which were prepared in distilled deionized water. The radiotracer was diluted with non-radiolabeled HEA to obtain a target radioactivity and concentration of 20 uCi and 1.75 and 36.7 mg/ml of dosing solution. The dose applied dermally was 12.5 mg/kg and each animal received approximately 15–20 uCi of activity. The dermal site was clipped of hair and a frame was attached to the skin with adhesive. The dermal dosing solution prepared in water was then applied to the skin and immediately covered with a piece of Teflon film. The dosed area was then wrapped with tape. The nose-only inhalation exposure concentration was 8 ppm ¹⁴C-HEA for a 6 hour period under dynamic flow-through conditions. Exposure HEA concentrations and radioactivity were monitored over the exposure period.</p> |
| 方法の概略 | ※英文参照 | <p>After administration or termination of exposure to ¹⁴C-HEA, rats from all groups were housed in metabolism cages. Urine and cage rinse was collected at 0–12, 12–24 and 24–48 hr, post-dosing or post-exposure. Feces were collected at 24 hr intervals for up to 48 hr post-dosing or postexposure. Expired organics and ¹⁴CO₂ were collected at 0.25,0.5,1,2,4,8, and 12 hr post administration and then at 12 hr intervals thereafter. All of the above sample were analyzed for radioactivity. Urine and feces were also collected from individual rats during the inhalation exposure. In addition, the combined ¹⁴CO₂ released into the inhalation chamber from the expired air of all 4 rats was trapped and analyzed after scrubbing ¹⁴CHEA from the chamber exhaust. Selected samples of urine were analyzed by HPLC to determine ¹⁴C metabolic profiles.</p> |
| 方法の概略 | ※英文参照 | <p>Blood concentration–time profiles were obtained from separate groups of animals so that expired ¹⁴CO₂ would not be lost while blood was collected from the animals in the metabolism cages. Blood samples for the ¹⁴Cplasma and red blood cell time course were collected at 0.25,0.5,1,2,4,6,8,12,16,24,30 and 48 hr after the administration of ¹⁴CHEA by the oral, IP and dermal routes. During the inhalation exposure, blood samples were collected at 0.25,0.5,1,2,4 and 6 hr, and 0.5,1,2,4,8,20,30 and 48 hr post inhalation exposure. Plasma and red blood cells were analyzed for radioactivity.</p> |
| 方法の概略 | ※英文参照 | <p>The rats were sacrificed 48 hr after administration or exposure to ¹⁴CHEA, and the radioactivity remaining in samples of blood, skin, and the carcass was quantified. For the dermal route of administration, the radioactivity associated with the skin at the dose site and all bandage material was also determined.</p> |

| | | |
|--------------|--|---|
| 方法の概略 | ※英文参照 | The half-lives for the CO ₂ excretion and the plasma radioactivity were determined from the slope of the line by regression analysis of the excretion time-course obtained from each treatment group. Statistical analysis of the data was limited to the calculation of means and standard deviations were appropriate. Pharmacokinetic analysis (calculation of half-lives, AUC's etc.) were carried out using standard methodologies. |
| 動物種 | ラット | Rat |
| 試験動物:系統 | | |
| 性別 | 雄 | Males |
| 細胞株 | | |
| 年齢 | | |
| 体重 | | |
| 試験動物数 | 4匹 | 4 |
| 曝露経路 | | |
| 溶媒(賦剤) | | |
| 投与量 | | |
| 統計手法 | | |
| 実際に投与された量 | | |
| 排泄経路 | | |
| 採取体液 | | |
| 採取組織 | | |
| 代謝産物 | | |
| 代謝産物 CAS No. | | |
| 結果 | | |
| 試験結果 | いったん全身的に利用可能になると、2-HEAは速やかに代謝され、体から排泄された。ラット血中でのHEAのin vitro半減期は約100秒であった。In vivoでは、[14C]-HEAの投与量の70%以上が投与又は暴露後12時間後までに排泄され、経口、腹腔内及び吸入の経路で尿中代謝物及び呼気中に[14C]-CO ₂ として排泄された。 | Once systemically available, 2-HEA was rapidly metabolized and eliminated from the body. The in vitro half-life of HEA in rat blood was approximately 100 seconds. In vivo, greater than 70% of the administered dose of [14C]-HEA was excreted by 12 hours post-dosing or post-exposure as urinary metabolites and as [14C]-CO ₂ in the expired air for the oral, i.p. and inhalation routes. |
| 試験結果 | 経口及び腹腔内経路を介して2.5 mg/kg投与後に、投与量の43-47%が尿中に、35-36%が呼気の14CO ₂ として排泄された。経口及び腹腔内経路を介しての50 mg/kgの投与では33-36%が尿中に、40-45%が14CO ₂ として呼気に排泄され、やや飽和した動態の証拠が示された。HEAの吸収率は経路依存性であるように思われ、経口又は腹腔内経路で投与した場合には4時間以内に完全に吸収された。 | Following the 2.5 mg/kg dose via the oral and IP routes, 43-47% of the dose was excreted in urine and 35-36% as expired 14CO ₂ . At 50 mg/kg dose via the oral and IP routes, there was some evidence of saturation kinetics, with 33-36% excreted in the urine and 40-45% expired as 14CO ₂ . The rate of absorption of HEA appeared to be route-dependent and was complete within 4 hours or less when given by oral or i.p. routes. |
| 試験結果 | 12.5 mg/kgの用量で経皮投与後には適用量の66%が48時間以内に徐々に吸収され、残りの33%は適用部位に留まった。いったん吸収されると、27%は尿中に、27%は14CO ₂ として呼気に排泄された。 | Following dermal administration of a dose of 12.5 mg/kg, 66% of the applied dose was slowly absorbed within 48 hours with the remaining 33% being associated with the application site. Once absorbed, 27% was excreted in the urine and 27% was expired as 14CO ₂ . |
| 試験結果 | 8 ppmのHEAに6時間吸入暴露後、48時間で回収された放射能の39%は尿中にHEA代謝物として、また41%は14CO ₂ として呼気排泄された。 | Following inhalation exposure to 8 ppm HEA for 6 hours, 39% of the radioactivity recovered at 48 hr was eliminated in the urine as metabolites of HEA and 41% was expired as 14CO ₂ . |
| 試験結果 | 全ての経路で、投与量又は回収された放射能の9-16%が組織及び屍体中で検出され、糞中には3%未満であった。尿中及び排出された14CO ₂ 中の放射能の消失半減期はそれぞれ約14時間及び17時間であった。血漿中の放射能の消失半減期は約26時間と算出され、親化合物を表してはいなかった。経路間には尿中代謝物の質的な違いはみられず、HEAの代謝運命には著しい経路依存性の差はないことが示唆された。 | For all routes 9-16% of the dose or recovered radioactivity was found in the tissues and carcass and less than 3% in the feces. The half-lives of elimination of radioactivity in the urine and expired 14CO ₂ were approximately 14 hours and 17 hours, respectively. The half-life of elimination of radioactivity in the plasma was determined to be approximately 26 hours and did not represent parent chemical. No qualitative differences in urinary metabolites between routes were observed, indicating no marked route-dependent differences in the metabolic fate of HEA. |
| 結論 | | |
| 結論 | | |
| 信頼性 | (1) 制限なく信頼性あり | (1) valid without restriction |
| 信頼性の判断根拠 | 一般に受入れられる科学的基準に合致し、十分詳細に記述されているGLP試験 | A GLP study that meets generally accepted scientific standards and is described in sufficient detail. |
| 出典 | | |
| 引用文献(元文献) | (57) | (57) |
| 備考 | | |
| 試験物質名 | | |
| CAS番号 | | |
| 純度等 | | |
| 注釈 | | |
| 方法 | | |
| 方法/ガイドライン | | |
| 試験形態 | In vivo タイプ：代謝 | In vivo Type：Metabolism |

| | | |
|--------------|---|---|
| GLP適合 | | |
| 試験をおこなった年 | | |
| 方法の概略 | | |
| 動物種 | ラット | rat |
| 試験動物:系統 | | |
| 性別 | 雄 | Males |
| 細胞株 | | |
| 年齢 | | |
| 体重 | | |
| 試験動物数 | | |
| 曝露経路 | 腹腔内 | i.p. |
| 溶媒(賦剤) | | |
| 投与量 | 42、104、208、又は 333 mg/kg 体重 | 42, 104, 208, or 333 mg/kg bw |
| 統計手法 | | |
| 実際に投与された量 | | |
| 排泄経路 | | |
| 採取体液 | | |
| 採取組織 | | |
| 代謝産物 | | |
| 代謝産物 CAS No. | | |
| 結果 | | |
| 試験結果 | <p>GSHは用量依存的に枯渇した。TOTPは肝臓GSHレベルに影響を示さなかった。TOTP前処置でのカルボキシルエステラーゼの抑制はHEAによるGSHの枯渇を促進した。</p> <p>グルタチオン (GSH) 枯渇の時間経過: - 経口LD50の25%での投与 - 投与後15、60及び120分で検査のため銅太を屠殺した</p> | <p>GSH was depleted in a dose-dependent manner; TOTP had no effect on hepatic GSH levels; inhibition of carboxylesterase with TOTP pretreatment enhanced the depletion of GSH by HEA;</p> <p>Time course of glutathione (GSH) depletion: - treatment with 25% of oral LD50 - animals were killed for examination at 15, 60, and 120 minutes posttreatment</p> |
| 試験結果 | <p>GSH枯渇に対する用量反応相関 - カルボキシルエステラーゼ阻害剤 (TOTP、125 mg/kg i.p.; 2-HEA投与の18時間前) による前処置のあり、又はなしで42、104、208、又は333 mg HEA/kgをip注射 - 動物を投与1時間後に検査のため屠殺した</p> | <p>Dose response relationship for GSH depletion: - injection of 42, 104, 208, or 333 mg HEA/kg i.p. with or without pretreatment with carboxyl esterase inhibitor (TOTP,125 mg/kg i.p.; 18 hours prior to 2-HEA) - animals were killed for examination 1 hour post-treatment</p> |
| 結論 | | |
| 結論 | | |
| 信頼性 | (2) 制限付きで信頼性あり | (2) valid with restrictions |
| 信頼性の判断根拠 | | |
| 出典 | Dow Benelux N.V. (Botlek) XA Botlek RT EUROPEAN COMMISSION – European Chemicals Bureau Ispra (VA) | Dow Benelux N.V. (Botlek) XA Botlek RT EUROPEAN COMMISSION – European Chemicals Bureau Ispra (VA) |
| 引用文献(元文献) | (58) | (58) |
| 備考 | | |

5-2 急性毒性 ACUTE TOXICITY

A. 急性経口毒性 ACUTE ORAL TOXICITY

| | | |
|--------------|--|--|
| 試験物質名 | 他のTS | other TS |
| CAS番号 | | |
| 純度等 | 純度のデータなし。試験物質はCelanese Corporationから入手した。 | No purity data. Test material was received from Celanese Corporation. |
| 注釈 | | |
| 方法 | | |
| 方法／ガイドライン | その他: Litchfield and Wilcoxin (1949). "A Simplified Method of Evaluating Dose-Effect Experiments." J. Pharm. & Exp. Ther. 96, 99. | other: Litchfield and Wilcoxin (1949). "A Simplified Method of Evaluating Dose-Effect Experiments." J. Pharm. & Exp. Ther. 96, 99. |
| GLP適合 | いいえ | no |
| 試験を行った年 | | |
| 試験系(種／系統) | ラット | rat |
| | Sprague-Dawley | Sprague-Dawley |
| 性別(雄:M、雌:F) | 雌雄 | male/female |
| 投与量 | 用量 (mg/kg): 266.7, 400, 600, 900、強制経口 | Doses (mg/kg): 266.7, 400, 600, 900, by gavage |
| 各用量群(性別)の動物数 | 動物数:16匹 | Number of animals: 16 |
| 溶媒(担体) | その他:水溶液 | other:aqueous solution |
| 投与経路 | | |
| | | |
| 観察期間(日) | | |

| | | |
|---------------------|--|--|
| その他の試験条件 | 英文参照 | TEST ORGANISMS -Source: Sprague Dawley rats, source unknown -Age: Unknown ("young") -Weight at study: 154-168 grams -Controls: None ADMINISTRATION: -Doses (mg/kg): 266.7, 400, 600, 900, by gavage, Animals were fasted for 16 hours prior to dosing. -Doses per time period: Single -Volume Administered: 10% (w/v) -Post dose observation period: 14 days EXAMINATIONS: A necropsy exam was conducted on all animals. |
| 統計学的処理 | | |
| 結果 | | |
| 各用量群での死亡数 | 死亡率: -死亡時間: 600 mg/kg (6-22 時間); 900 mg/kg (6-22 時間) -各用量での死亡数: 266.7 mg/kg (0/4); 400 mg/kg (0/4); 600 mg/kg (3/4); 900 mg/kg (4/4) | MORTALITY: -Time of death: 600 mg/kg (6-22 hours); 900 mg/kg (6-22 hours) -Number of deaths at each dose: 266.7 mg/kg (0/4); 400 mg/kg (0/4); 600 mg/kg (3/4); 900 mg/kg (4/4) |
| 臨床所見 | 臨床症状: -266.7 mg/kg 活動性低下、被毛粗剛 (開始、30 分後、持続時間 6-22 時間) -400 mg/kg 活動性低下及び被毛粗剛 (開始、30 分後、持続時間 2日間) 努力呼吸 (開始、1 時間後、持続時間 6-22時間) -600 mg/kg 活動性低下及び被毛粗剛 (開始、30 分後、持続時間 4日間; 努力呼吸及び筋肉の虚弱 (開始、1時間後、持続時間 2日間) -900 mg/kg 活動性低下及び被毛粗剛 (開始、30 分後、持続死亡まで); 努力呼吸及び筋肉の虚弱 (開始、1時間後、持続死亡まで) | CLINICAL SIGNS: -266.7 mg/kg hypoactivity, rough fur (onset, 30 min, duration 6-22 hr) -400 mg/kg hypoactivity & rough fur (onset, 30 min, duration 2 days) labored breathing (onset, 1 hr, duration 6-22 hr) -600 mg/kg hypoactivity & rough fur (onset, 30 min, duration 4 days); labored breathing & muscular weakness (onset, 1 hr, duration 2 days) -900 mg/kg hypoactivity & rough fur (onset, 30 min, duration until death); labored breathing & muscular weakness (onset, 1 hr, duration until death) |
| 剖検所見 | 剖検所見: -胃腸管の出血、14日間尾観察期間終了時には動物に肉眼的病理所見は認められなかった。 | NECROPSY FINDINGS: -Hemorrhages in the gastrointestinal tracts, no gross pathology observations were noted in animals at the end of the 14 day observation period. |
| その他 | 潜在的な標的器官: -明記なし 性特異的な差異: -明記なし | POTENTIAL TARGET ORGANS: -Not specified SEX-SPECIFIC DIFFERENCES: -None observed |
| 結論 | | |
| LD50値又はLC50値 | LD50= 548 mg/kg bw | LD50= 548 mg/kg bw |
| 雌雄のLD50値又はLC50値の違い等 | | |
| 注釈 | | |
| 信頼性 | (2) 制限付きで信頼性あり | (2) valid with restrictions |
| 信頼性の判断根拠 | 一般的に許容できる科学的基準を満たし、良好な文書で評価に受け入れられる。 | Meets generally accepted scientific standards, well documented and acceptable for assessment. |
| 出典 | | |
| 引用文献(元文献) | (59) | (59) |
| 備考 | フラグ : SIDSエンドポイントにとって重要な試験 | Flag : Critical study for SIDS endpoint |

B. 急性吸入毒性
ACUTE INHALATION TOXICITY

| | | |
|--------------|---------------------------|--|
| 試験物質名 | データなし | no data |
| CAS番号 | | |
| 純度等 | 試験物質の純度あるいは入手可能な分析値のデータなし | No purity data of test material or analysis available. |
| 注釈 | | |
| 方法 | | |
| 方法/ガイドライン | タイプ : その他: 飽和蒸気の暴露 | Type : other: saturated vapor exposures |
| GLP適合 | いいえ | no |
| 試験を行った年 | 1966 | 1966 |
| 試験系(種/系統) | ラット | rat |
| 性別(雄:M、雌:F) | | |
| 投与量 | 濃縮した蒸気 (1.87 mg/L)への単回暴露 | single exposures to concentrated vapor (1.87 mg/L) |
| 各用量群(性別)の動物数 | 動物数 : 6匹 | Number of animals : 6 |
| 溶媒(担体) | その他: なし | other: none |
| 投与経路 | | |
| 観察期間(日) | | |
| その他の試験条件 | 暴露時間 : 4時間 | Exposure time : 4 hour(s) |
| 統計学的処理 | | |

| 結果 | | |
|---------------------|---|--|
| 各用量群での死亡数 | | |
| 臨床所見 | <p>症状及び/又は症候群: 眼の刺激、下痢、末端の刺激。6匹の動物が試験された。濃縮蒸気はガス洗浄瓶の中で乾燥した空気を硝子板を通して2.5 l/分で通過させることにより発生させた。平均蒸気濃度は液体重量のロスから算出、または通気中の化学物質の実際の温度での蒸気圧から推定した。試験した濃度は1.87 mg/kg又は394 ppmであった。 4時間暴露は暴露した6匹中1匹の死亡を生じた。</p> | <p>Signs and/or symptoms: Ocular irritation, diarrhea, extremities irritated Six animals were tested. Concentrated vapor was generated in a gas washing bottle by passing dried air at 2.5 l/min through a fritted glass disc. Mean vapor concentration was calculated from the loss in weight of the liquid or estimated from the vapor pressure at the actual temperature of the chemical during aeration. Tested concentration was 1.87 mg/kg or 394 ppm. A 4 hour exposure resulted in death for 1 of 6 animals exposed.</p> |
| 剖検所見 | | |
| その他 | | |
| 結論 | | |
| LD50値又はLC50値 | | |
| 雌雄のLD50値又はLC50値の違い等 | | |
| 注釈 | | |
| 信頼性 | (2) 制限付きで信頼性あり | (2) valid with restrictions |
| 信頼性の判断根拠 | 一般的に許容できる科学的基準を満たし、良好な文書で評価に受け入れられる。 | Meets generally accepted scientific standards, well documented and acceptable for assessment. |
| 出典 | | |
| 引用文献(元文献) | (65) | (65) |
| 備考 | | |

C. 急性経皮毒性
ACUTE DERMAL TOXICITY

| | | |
|--------------|--|--|
| 試験物質名 | 1.1～1.4で規定 | as prescribed by 1.1 – 1.4 |
| CAS番号 | | |
| 純度等 | | |
| 注釈 | | |
| 方法 | | |
| 方法／ガイドライン | | |
| GLP適合 | はい | yes |
| 試験を行った年 | 1981 | 1981 |
| 試験系(種／系統) | ウサギ ニュージーランド白色 | rabbit New Zealand white |
| 性別(雄:M、雌:F) | 雌雄 | male/female |
| 投与量 | 63, 130, 160, 200, 250 mg/kg/bw | 63, 130, 160, 200, 250 mg/kg/bw |
| 各用量群(性別)の動物数 | 動物数 :20匹 | Number of animals : 20 |
| 溶媒(担体) | | other: none |
| 投与経路 | | |
| 観察期間(日) | | |
| その他の試験条件 | 英文参照 | The acute percutaneous absorption potential was evaluated by treating 2 male and 2 female rabbits per dose level with the undiluted test material. Following dosing to the intact skin (not abraded) the site of application was occluded with plastic wrap and left in place for 24 hours. At 24 hours postdosing the occlusion was removed and the dose site washed with mild soap and water to remove any unabsorbed test material. |
| 統計学的処理 | | |
| 結果 | | |
| 各用量群での死亡数 | 死亡率 用量群 死亡動物数/ (mg/kg bw) 投与動物数 63 0/4 130 0/4 160 3/4 200 4/4 250 4/4 | Mortality Dose group No. Dead/ (mg/kg bw) No. Dosed 63 0/4 130 0/4 160 3/4 200 4/4 250 4/4 |
| 臨床所見 | | |
| 剖検所見 | | |

| | | |
|---------------------|--|--|
| その他 | 急性経皮吸収KD50は分析値の移動平均法により算出した結果、154 mg/kg (131-174 mg/kg、95%信頼区間)であった。ウサギは試験物質の 63, 130, 160, 200 または 250 mg/kgで処置された。投与25時間後に10匹の動物の適用部位にみられた局所反応は顕著な発赤(10/10)、顕著な腫脹(10/10)及び軽度(4/10)または中等度の壊死(3/10)であった。試験群のウサギでは以下の毒性症状が生存中に観察された(影響のみられた用量を括弧内に示す):嗜眠(全用量)、運動性低下(63、160及び200 mg/kg)、食欲不振(63及び160 mg/kg)、及び速く浅い呼吸(250 mg/kg)。2週間の投与後の期間を生存したウサギではいくつかの皮膚傷害が剖検時に認められた。しかしながら、処置に関連した全身的な変化は肉眼検査で示されなかった。 | The acute percutaneous absorption LD50 was 154 mg/kg (131-174 mg/kg, 95% confidence interval) when calculated by the moving average method of analysis. Rabbits were treated with 63, 130, 160, 200 or 250 mg/kg of the test material. Topical responses observed on the application sites of 10 test animals 25 hours post-treatment included marked redness (10/10), marked swelling (10/10) and slight (4/10) or moderate necrosis (3/10). The following in-life signs of toxicity were observed in test rabbits (dose groups affected are in parentheses): lethargy (all), decreased activity (63, 160 and 200 mg/kg), loss of appetite (63 and 160 mg/kg) and rapid shallow breathing (250 mg/kg). In rabbits surviving the 2 week post-treatment interval there were some skin lesions noted at necropsy. However, there were no systemic treatment related changes seen upon gross examination. |
| 結論 | | |
| LD50値又はLC50値 | LD50= 154 mg/kg bw | LD50= 154 mg/kg bw |
| 雌雄のLD50値又はLC50値の違い等 | | |
| 注釈 | | |
| 信頼性 | (1) 制限なく信頼性あり | (1) valid without restriction |
| 信頼性の判断根拠 | GLP試験、一般的に許容できる科学的基準を満たし、十分詳細に記述されている。 | GLP study, meets generally accepted scientific standards and is described in sufficient detail. |
| 出典 | | |
| 引用文献(元文献) | (68) | (68) |
| 備考 | フラグ : SIDSエンドポイントにとって重要な試験 | Flag : Critical study for SIDS endpoint |

D. 急性毒性(その他の投与経路)

ACUTE TOXICITY, OTHER ROUTES

| | | |
|--------------|---|---|
| 試験物質名 | データなし | no data |
| CAS番号 | | |
| 純度等 | 利用できる純度はなし | No purity available |
| 注釈 | | |
| 方法 | | |
| 方法/ガイドライン | 群当たり5匹の雌のアルビノウサギが試験された。HEAの原液が1.0, 0.5, または 0.25 ml/kgで注射された。1 ml/kgの濃度では全ての動物が24時間以内に死亡した。 | Five female albino rats per group were tested. Undiluted HEA was injected at 1.0, 0.5, or 0.25 ml/kg. At the concentration of 1 ml/kg all animals died within 24 hours. |
| GLP適合 | いいえ | no |
| 試験を行った年 | 1966 | 1966 |
| 試験系(種/系統) | ラット | rat |
| 性別(雄:M、雌:F) | その他: アルビノ | other: albino |
| 投与量 | 雌 | female |
| 各用量群(性別)の動物数 | 動物数 : 15匹 | Number of animals : 15 |
| 溶媒(担体) | その他: なし | other: none |
| 投与経路 | 腹腔内 | i.p. |
| 観察期間(日) | | |
| その他の試験条件 | | |
| 統計学的処理 | | |
| 結果 | | |
| 各用量群での死亡数 | | |
| 臨床所見 | | |
| 剖検所見 | | |
| その他 | | |
| 結論 | | |
| 毒性値 | LC50= 620 mg/kg bw | LC50= 620 mg/kg bw |
| 注釈 | | |
| 信頼性 | (2) 制限付きで信頼性あり | (2) valid with restrictions |
| 信頼性の判断根拠 | 一般的に許容できる科学的基準を満たし、良好な文書で評価に受け入れられる。 | Meets generally accepted scientific standards, well documented and acceptable for assessment. |
| 出典 | | |
| 引用文献(元文献) | (65) | (65) |
| 備考 | | |

5-3 腐食性/刺激性

CORROSIVENESS/IRRITATION

A. 皮膚刺激/腐食

SKIN IRRITATION/CORROSION

| | | |
|-----------|-----------|---------------------|
| 試験物質名 | データなし | no data |
| CAS番号 | | |
| 純度等 | 利用可能な純度なし | No purity available |
| 注釈 | | |
| pH | | |
| 方法 | | |
| 方法/ガイドライン | | |

| | | |
|--------------|--|---|
| GLP適合 | データなし | no data |
| 試験を行った年 | 1981 | 1981 |
| 試験系(種/系統) | ウサギ | rabbit |
| 性別(雄:M、雌:F) | | |
| 投与量 | 濃度：希釈せず | Concentration：undiluted |
| 各用量群(性別)の動物数 | 動物数：6匹 | Number of animals：6 |
| 溶媒(担体) | その他：なし | other: none |
| 投与経路 | | |
| 観察期間(日) | | |
| その他の試験条件 | 暴露：閉塞 暴露時間：24時間 | Exposure：Occlusive Exposure time：24 hour(s) |
| その他の試験条件 | 英文参照 | Primary skin irritancy was assessed using albino rabbits. The test material was applied in 0.25 ml aliquots to areas of abraded and non-abraded shaved dorsal skin and the sites were covered for 24 hours with occlusive bandage. After removal of patches the remaining test material was washed off with water and the site scored using the "Draize" scoring system and again scored at 72 hours. The Draize score for primary irritation was 8 out of a possible highest score of 8. |
| 統計学的処理 | | |
| 結果 | | |
| 一次刺激スコア | PDII：8 | PDII：8 |
| 皮膚反応等 | | |
| その他 | HEAは皮膚の広範な領域に及ぶ壊死、皮下出血及び窪みのある浮腫を生じて重度の刺激性を示すことが明らかになった。皮膚の一つの領域の組織検査では表皮の壊死とともに深部の真皮及び皮下組織に深く広がる損傷及び出血部位が示された。 | HEA was found to be a severe irritant producing necrosis, subcutaneous haemorrhage and pitting oedema over a wide area of skin. Histological examination of one area of skin revealed epidermal necrosis together with areas of damage and haemorrhage extending deeply into the deep dermis and hypodermis. |
| 結論 | | |
| 皮膚刺激性 | 高度の刺激性あり | highly irritating |
| 皮膚腐食性 | | |
| 注釈 | 分類：刺激性あり | Classification：irritating |
| 信頼性 | (2) 制限付きで信頼性あり | (2) valid with restrictions |
| 信頼性の判断根拠 | 一般的に許容できる科学的基準を満たし、良好な文書で評価に受け入れられる。 | Meets generally accepted scientific standards, well documented and acceptable for assessment. |
| 出典 | | |
| 引用文献(元文献) | (73) | (73) |
| 備考 | フラグ：SIDSエンドポイントにとって重要な試験 | Flag：Critical study for SIDS endpoint |

B. 眼刺激/腐食
EYE IRRITATION/CORROSION

| | | |
|--------------|---|---|
| 試験物質名 | 他のTS | other TS |
| CAS番号 | | |
| 純度等 | 純度のデータなし。試験物質はCelanese Corporationから入手した。 | No purity data. Test material was received from Celanese Corporation. |
| 注釈 | | |
| 方法 | | |
| 方法/ガイドライン | Draize 法 | Draize Test |
| | Draize, J. H., Woodard, G. and Calvery, H.O. (1944) Methods for the study of irritation and toxicity of substances applied topically to the skin and mucous membranes. J. Pharmacol. Exp. Therapeut. 82: 377. | Draize, J. H., Woodard, G. and Calvery, H.O. (1944) Methods for the study of irritation and toxicity of substances applied topically to the skin and mucous membranes. J. Pharmacol. Exp. Therapeut. 82: 377. |
| 試験のタイプ | | |
| GLP適合 | いいえ | no |
| 試験を行った年 | 1974 | 1974 |
| 試験系(種/系統) | ウサギ | rabbit |
| 性別(雄:M、雌:F) | | |
| 投与量 | 濃度：希釈せず 用量：0.1 ml コメント：洗浄せず | Concentration：undiluted Dose：.1 ml Comment：not rinsed |
| 各用量群(性別)の動物数 | 動物数：6匹 | Number of animals：6 |
| 溶媒(担体) | | |
| 投与経路 | | |
| 観察期間(日) | | |

| | | |
|-----------|---|--|
| その他の試験条件 | 英文参照 | TEST ANIMALS: Strain: New Zealand Albino rabbits Sex: Unspecified Source: Unspecified Age: Unspecified Weight at study initiation: Unspecified Number of animals: Six Controls: No |
| その他の試験条件 | 英文参照 | ADMINISTRATION/EXPOSURE: Preparation of test substance: none, undiluted material Amount of substance instilled: 0.1 ml of undiluted HEA Vehicle: None Postexposure period: 14 days Eyes were unwashed following administration with undiluted HEA. EXAMINATIONS: Ophthalmoscopic examination: No Scoring system: As described by Draize, 110 points maximum score |
| 統計学的処理 | | |
| 結果 | | |
| 腐食 | | |
| 刺激点数: 角膜 | | |
| 刺激点数: 虹彩 | | |
| 刺激点数: 結膜 | | |
| その他 | 平均スコア: 角膜: 1 分 = 20.0, 1 時間 = 20.0, 24 時間 = 20.0, 72 時間 = 50.0, 7 日 = 53.3, 14 日 = 70.0 (最大スコア80のうち) 虹彩: 1 分 = 5.0, 1 時間 = 5.0, 24 時間 = 10.0, 72 時間 = 10.0, 7 日 = 10.0, 14 日 = 10.0 (最大スコア10のうち) 結膜: 1 分 = 12.0, 1 時間 = 18.0, 24 時間 = 20.0, 72 時間 = 20.0, 7 日 = 19.0, 14 日 = 16.7 (最大スコア20のうち) 全体の平均刺激スコア: (最大スコア110のうち) 1 分 = 37.0, 1 時間 = 43.0, 24 時間 = 50.0, 72 時間 = 80.0, 7 日 = 82.3, 14 日 = 96.7 | AVERAGE SCORES: Cornea: 1 min = 20.0, 1 hr = 20.0, 24 hr = 20.0, 72 hr = 50.0, 7 d = 53.3, 14 d = 70.0 (Out of a maximum score of 80) Iris: 1 min = 5.0, 1 hr = 5.0, 24 hr = 10.0, 72 hr = 10.0, 7 d = 10.0, 14 d = 10.0 (Out of a maximum score of 10) Conjunctiva: 1 min = 12.0, 1 hr = 18.0, 24 hr = 20.0, 72 hr = 20.0, 7 d = 19.0, 14 d = 16.7 (Out of a maximum score of 20) Overall average irritation scores: (Out of a maximum score of 110) 1 min = 37.0, 1 hr = 43.0, 24 hr = 50.0, 72 hr = 80.0, 7 d = 82.3, 14 d = 96.7 |
| その他 | 傷害の記述: 点眼後1分で数匹の動物に角膜の上皮の脱落が認められた。以下の影響が暴露後72時間及びそれ以後に認められた: 角膜の水疱、腐食及び/又は潰瘍 回復性: 利用可能な情報はない。傷害の記述から眼への損傷は永続的であるとみられる。 | DESCRIPTION OF LESIONS: Epithelial sloughing of the cornea was noted in some animals as soon as 1 minute after instillation. The following effects were noted in some animals at or past 72 hours postexposure: blister, corrosion and/or ulceration of the cornea. REVERSIBILITY: No information available, from the description of the lesions damage to the eye may be permanent. |
| 結論 | | |
| 眼刺激性 | 高度に刺激性あり | highly irritating |
| 眼腐食性 | | |
| 注釈 | | |
| 信頼性 | (2) 制限付きで信頼性あり | (2) valid with restrictions |
| 信頼性の判断根拠 | 一般的に許容できる科学的基準を満たし、良好な文書で評価に受け入れられる。 | Meets generally accepted scientific standards, well documented and acceptable for assessment. |
| 出典 | | |
| 引用文献(元文献) | (59) | (59) |
| 備考 | フラグ : SIDSエンドポイントにとって重要な試験 | Flag : Critical study for SIDS endpoint |

5-4 皮膚感作

SKIN SENSITISATION

| | | |
|-------------|---|---|
| 試験物質名 | 他のTS | other TS |
| CAS番号 | | |
| 純度等 | 試験物質はFluka AG (Glossop, Derbyshire, UK)から入手した。純度の特異的な値なし。しかし、著者は試験した化学物質の大部分は98%以上であると主張している。 | The test material was received from Fluka AG (Glossop, Derbyshire, UK). No specific value for purity; however, the authors state that the vast majority of the chemical tested were more than 98% pure. |
| 注釈 | | |
| 方法 | | |
| 方法/ガイドライン | その他: Basketter et al. (1991), Toxicology Methods 1, 30-43 に準じた。 | other: according to Basketter et al. (1991), Toxicology Methods 1, 30-43 |
| 試験のタイプ | マウス局所リンパ節アッセイ | Mouse local lymphnode assay |
| GLP適合 | データなし | no data |
| 試験を行った年 | 1992 | 1992 |
| 試験系(種/系統) | マウス | mouse |
| 性別(雄:M、雌:F) | | |

| | | |
|--------------|--|--|
| 投与量 | 濃度： 1回目：惹起 10% 2回目：惹起 25% 3回目：惹起 50% | Concentration : 1st: Challenge 10 % 2nd: Challenge 25 % 3rd: Challenge 50 % |
| 各用量群(性別)の動物数 | 動物数：12匹 | Number of animals : 12 |
| 溶媒(担体) | その他：アセトン：オリーブ油、4:1、v/v | other: acetone:olive oil, 4:1, v/v |
| 投与経路 | | |
| 観察期間(日) | | |
| その他の試験条件 | 英文参照 | The murine local lymph node assay was conducted as described by Basketter et al., 1991, Toxicology Methods 1, 30-43. Male and female CBA/Ca mice 8-12 weeks old were used. HEA was assayed at three consecutive concentrations (10, 25 and 50%). Groups of four mice were treated by a daily topical application of 25uL of each concentration on the dorsal surface of each ear for 3 consecutive days. Control animals were treated with the vehicle which was acetoneolive oil (4:1, v/v). Four to five days after the first topical application, all mice were injected i.v. through the tail vein with 250 uL phosphate buffered saline containing labelled methyl thymidine. After 5 hr the mice were killed by CO2 and the draining auricular lymph nodes were excised and pooled for each experimental group. Labelled methyl thymidine incorporation into lymph nodes was measured by beta-scintillation counting. A chemical was regarded as a sensitizer in the lymph node assay if at least one concentration of the chemical resulted in a three-fold or greater increase in H3TdR incorporation compared with control values. In addition, the data had to be compatible with a biological dose response although an allowance was made, especially at high doses, for either local toxicity or immunological suppression. Radiolabeled thymidine[3H]methyl thymidine (sp. act. 2.0 Ci/mmol) was purchased from Amersham International plc (Bucks, UK). |
| 統計学的処理 | | |
| 結果 | | |
| 試験結果 | 10、25または50%のHEAをマウスに投与後、リンパ節増殖についての試験群の対照群に対する比 (T/C)は9.0、8.2及びデータなしであった。従って、HEAは局所リンパ節アッセイにおいて陽性と判定された。 | Following administration of 10, 25 or 50% HEA to mice the ratios of test to control lymphocyte proliferation (T/C) were 9.0, 8.2 and no data, respectively. Therefore HEA was classified as positive in the local lymph node assay. |
| その他 | | |
| 結論 | | |
| 感作性 | 感作性あり | sensitizing |
| 注釈 | 分類：感作性あり | Classification : sensitizing |
| 信頼性 | (2) 制限付きで信頼性あり | (2) valid with restrictions |
| 信頼性の判断根拠 | 一般的に許容できる科学的基準を満たし、良好な文書で評価に受け入れられる。 | Meets generally accepted scientific standards, well documented and acceptable for assessment. |
| 出典 | | |
| 引用文献(元文献) | (80) | (80) |
| 備考 | フラグ：SIDSエンドポイントにとって重要な試験 | Flag : Critical study for SIDS endpoint |

5-5 反復投与毒性 REPEATED DOSE TOXICITY

| | | |
|--|-----------------|--------------------------------|
| 試験物質名 | アクリル酸2-ヒドロキシエチル | 2-hydroxyethyl acrylate |
| CAS番号 | | |
| 純度等 | 純度の情報は提供されていない | no purity information provided |
| 注釈 | | |
| 方法 | | |
| 方法／ガイドライン | その他：直接暴露 | other: dynamic exposure |
| GLP適合 | データなし | no data |
| 試験を行った年 | 1970 | 1970 |
| 試験系(種／系統) | ラット Sherman | rat Sherman |
| 性別(雄:M、雌:F) | 雄 | male |
| 投与量 | 対照、5、10、25 ppm | Control, 5, 10 or 25 ppm |
| 各用量群(性別)の動物数 | | |
| 溶媒(担体) | | |
| 投与経路 | 吸入 | inhalation |
| 対照群に対する処理 | 無処置対照群 | yes, concurrent no treatment |
| 投与期間(日)(OECD422等で、投与期間のデータ等がある場合、最長投与期間) | 28日間(最大21回暴露) | 28 days (up to 21 exposures) |
| 投与頻度 | 6時間/日、5日間/週 | 7 hours/day and 5 days/week |
| 回復期間(日) | 最大14日日間 | up to 14 days |

| | | |
|------------------------|--|---|
| 試験条件 | *英文参照 | <p>TEST ORGANISMS</p> <p>–Age: no data</p> <p>–Weight at study initiation: mean values ranged from 268–314 grams</p> <p>–Number of animals: 15–20 animals/group (5–10 animals/group for 10 dayinterim sacrifice)</p> <p>ADMINISTRATION/EXPOSURE</p> <p>–route: inhalation; whole body exposure</p> <p>SATELITE GROUPS AND REASONS THEY WERE ADDED: An interim sacrifice group of 5– 10 animals were exposed at the same concentrations for 7 hours/day for 10 days.</p> <p>CLINICAL OBSERVATIONS AND FREQUENCY: During exposures animals were observed closely for signs of irritation and toxicity.</p> <p>ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):</p> <p>–Macroscopic: organ weight: lung, liver, spleen, kidney and testes</p> <p>–Microscopic: yes</p> <p>EXPOSURE CONCENTRATIONS: 4.5 +/- 1.1, 10.6 +/- 1.4 and 22.5 +/- 3.9</p> <p>METHOD OF CHAMBER CONCENTRATIONS: Gas–liquid chromatography</p> |
| 統計学的処理 | | |
| 結果 | | |
| 体重、体重増加量 | <p>5 ppm群では有害影響はみられていない。</p> <p>10 ppm群で週の5日の暴露日のあいだに体重の減少を示したが、週末の暴露のない2日間で急速に回復した。20日の試験終了時の体重は有意に低値であった。</p> <p>25 ppm群では暴露期間中に急速に体重が減少したが、試験の12日までは続かなかった。生存例では回復期間で急速に回復した。</p> | <p>Body weights: The 5 ppm group showed no adverse effects. At 10 ppm, mean body weights decreased during the five exposure days of the week but showed a rapid recovery or a gain during the two no-exposure days of the weekend. At termination, mean body weight of rats exposed to 10 ppm for 20 days was significantly lower than controls. For the 25 ppm group, body weights rapidly decreased during the exposure period but after the exposures were discontinued on study day 12 the surviving animals quickly gained body weight over the recovery period.</p> |
| 摂餌量、飲水量 | | |
| 臨床所見(重篤度、所見の発現時期と持続時間) | <p>5 ppm群では有害影響はみられていない。</p> <p>10 ppm群では、軽度の鼻刺激と鼻汁がみられ、7回暴露後に肺の湿性のガラガラ音がみられた。</p> <p>25 ppm群では眼、鼻刺激、呼吸困難、上部気道の刺激を示す胃の膨満がみられ、これらの状態は暴露の継続に伴いより重篤となった。</p> | <p>Clinical signs: The 5 ppm group showed no adverse effects. Animals in the 10 ppm group exhibited mild nasal irritation and discharge and afterseven exposures, some animals acquired lung rattles. The animals in the 25 ppm group were observed with eye and nasal irritation followed by dyspnea and a bloated stomach which were indicative of an upper respiratory tract irritant. These conditions became more severe as the exposures continued.</p> |
| 眼科学的所見(発生率、重篤度) | | |
| 血液学的所見(発生率、重篤度) | | |
| 血液生化学的所見(発生率、重篤度) | | |
| 尿検査所見(発生率、重篤度) | | |
| 死亡数(率)、死亡時間 | <p>10ppm群の1例が15回の暴露で死亡、25 ppm群では合計8例が10回暴露日までに死亡し10回暴露の終了までにさらに9例が死亡した。3例のみが生存し暴露から回復した。</p> | <p>Mortality and time to death: One animal in the 10 ppm group died after 15 exposures. In the 25 ppm group, a total of 8 animals died during the 10 exposure days and following the termination of exposures after exposure day 10, an additional 9 animals died. Only 3 animals survived and recovered from the exposures.</p> |
| 剖検所見(発生率、重篤度) | | |
| 臓器重量 | <p>10 ppm群で肝臓、腎臓の相対重量が有意に高値を示した。同様の変化は5 ppm群でもみられた。これに対して、5 ppm群では心臓の相対重量は有意に低値であった。精巣の相対重量に影響はみられていない。</p> | <p>Organ to body weight ratios: Organ to body weight ratios of liver and kidneys were significantly higher for rats exposed to 10 ppm HEA. Similar elevation of liver to body weight ratio was also seen at 5 ppm. In contrast, heart to body weight ratios for the animals in the 5 ppm group were significantly lower. No changes occurred in the relative testes weight of HEA treated rats when compared to controls.</p> |

| | | |
|---------------------|--|---|
| 病理組織学的所見(発生率、重篤度) | 5、10、25ppmで潰瘍性角膜炎、慢性活動性気管支炎がみられ、限局性潰瘍性鼻炎、慢性活動性喉頭炎が10、25 ppmでみられた。25 ppmでの病変は5、10ppmより重篤であった。気管支肺炎と重篤な上部気道の病変は25 ppmの死亡原因となった。14日間の回復期間では潰瘍性鼻炎の欠如を除いてはあまり病変数の減少はみられなかった。 10 ppm群の20回暴露で9例中1例で精巣の萎縮が病理組織学的に観察された。この所見は、自然発生的で、吸入経路での慢性、発がん性試験での精巣影響の欠如と一致していると判断された。(Rampy L.W. et al. (1978) Toxicol. Appl. Pharmacol., 45:310). | Pathology findings: HEA produced ulcerative keratitis and chronic-active tracheitis at 5, 10 and 5 ppm. Focal ulcerative rhinitis and chronic-active laryngitis resulted from HEA exposure at 10 and 25 ppm. Lesions at the 25 ppm level were more severe than those at 10 and 5 ppm. Bronchopneumonia and severe upper respiratory lesions were responsible for the spontaneous deaths at the 25 ppm exposure. The 14-day recovery period did not significantly reduce the number of lesions observed, except for the absence of ulcerative rhinitis. Testicular atrophy was observed histopathologically in one of 9 rats exposed to 10 ppm HEA for 20 exposures. This was judged to be spontaneous and not related to HEA exposure and consistent with an absence of testicular effects in a chronic toxicity/carcinogenicity study conducted by the inhalation route (Rampy L.W. et al. (1978) Toxicol. Appl. Pharmacol., 45:310). |
| 実際に摂取された量 | | |
| 用量反応性 | | |
| 注釈 | | |
| 結論 | | |
| NOAEL (NOEL) | 5 ppm | 5 ppm |
| LOAEL (LOEL) | | |
| NOAEL/LOAELの推定根拠 | | |
| 雌雄のNOAEL(LOAEL)の違い等 | | |
| 注釈 | 結論 LOAELは5ppm 5 ppm群で角膜に刺激がみられた。 潰瘍性の角膜変化、鼻刺激、体重減少は10 ppm群でみられた。しかし、体重は暴露のない週末で回復した。25 ppm群では2日間で鼻刺激、呼吸の困難があり、急激な体重減少と呼吸不全により死亡した。 これらのデータは呼吸器系と眼が上記暴露により影響を受ける唯一の器官であることを示している。これらの結果に基づいて、労働者が長期間、反復して暴露される場合は、作業場での濃度を5 ppm以下に保つこと、TWAは1ppmを上回ってはいけないことを示唆している。 | Conclusion The LOAEL was 5 ppm. In the 5 ppm group, only irritation of the corneas was observed. Ulcerative corneal changes, nasal irritation and decreased body weight were found in the 10 ppm group; however, the animals were able to recover weight during the un-exposed weekend. Exposures of animals to 25 ppm resulted in considerable nasal irritation and severe respiratory distress within two days. Thereafter, the animals exhibited drastic loss of body weight and died of respiratory failure. These data indicate that the respiratory system and the eyes are the only systems likely to be affected by vapor exposure. Based on these results it is suggested that when worker's exposures are prolonged and repeated, the workroom concentrations be kept below 5 ppm and that the time weighed average of all exposures not exceed 1 ppm. |
| 信頼性 | (2) 制限付きで信頼性あり | (2) valid with restrictions |
| 信頼性の判断根拠 | 一般に認められた科学的な標準を満たし、文書で十分に裏付けられて評価にとって許容できる。試験物質の純度、分析は得られていない。 | Meets generally accepted scientific standards, well-documented and acceptable for assessment;no data on test material purity or analysis were available. |
| 出典 | | |
| 引用文献(元文献) | (95) | (95) |
| 備考 | フラグ :SIDSエンドポイントにとって重要な試験 | Flag : Critical study for SIDS endpoint |

5-6 *in vitro* 遺伝毒性
GENETIC TOXICITY IN VITRO

A. 遺伝子突然変異
GENE MUTATION

| | | |
|--------------|--|--|
| 試験物質名 | 他の物質 | other TS |
| CAS番号 | | |
| 純度等 | 純度の情報無し | No data on purity |
| 注釈 | 著者は、試験に使用された化学物質は最高の純度であると述べている。被験物質は和光純薬から入手したもの。 | The authors state that the chemicals used for testing were of the highest purity available. The test material was received from Wako Pure Chemical Industries, Ltd., Osaka, Japan. |
| 方法 | | |
| 方法／ガイドライン | 細菌の遺伝子突然変異試験 | Bacterial gene mutation assay |
| GLP適合 | 情報無し | no data |
| 試験を行った年 | 1996年 | 1996 |
| 細胞株又は検定菌 | 細菌 | bacterial |
| 代謝活性化(S9)の有無 | 有及び無 | with and without |
| 試験条件 | 原文参照 | Plate incorporation method. Test concentration : 0, 38, 75, 78, 150, 156, 300, 313, 600, 625, 1000, 1250, 2000, 2500, 3000, 4000 and 5000 ug/plate. |

| | | |
|-----------|---|--|
| 試験条件 | 原文参照 | Chemically-induced mutagenicity was performed using the four bacterial strains Salmonella typhimurium TA102 and TA2638 and Escherichia coli WP2/pKM101 and WP2 uvrA/pKM101. Compounds were tested for mutagenicity using the plate incorporation method with or without metabolic activation, essentially as described by Maron and Ames [Maron, D.M. and B. M. Ames (1983). Revised methods for the Salmonella mutagenicity test, Mutation Res., 113, 173-215]. Each bacterial strain was inoculated from the original stock cultures into nutrient broth, especially supplemented with 2 ug/ml tetracycline for TA 102, and cultured under conditions for growth culture. Within 2 hours of the end of the growth culture period, cultures were used for the mutagenicity assay as follows: 0.1 ml of a culture, 0.1 ml of a solution of test chemical, 0.5 ml of S9 mix and 2 ml of the amino-acid-supplemented molten soft agar were mixed uniformly and overlaid on a minimal glucose agar plate. A S9 mix was used for metabolic activation which contained 10% of S9 fraction which was prepared from livers of Sprague-Dawley rats induced by phenobarbital and 5,6-benzoflavone. The plates were incubated at 37C for 48 hours and colonies counted. Chemical were tested in at least two independent experiments using five dose levels and three plates per dose, and tests were performed in two laboratories per chemical to assess reproducibility. A dose of 5000ug/plate was used as the highest dose if no toxicity was observed. Positive controls were included in each experiment. |
| 結果 | | |
| 細胞毒性 | | |
| 代謝活性ありの場合 | | |
| 代謝活性なしの場合 | | |
| 変異原性 | | |
| 代謝活性ありの場合 | 陽性 | positive |
| 代謝活性なしの場合 | 陽性 | positive |
| 注釈 | 原文参照 | In two laboratories, 2-HEA was negative in the Salmonella typhimurium strains TA102 and TA2638 and positive in the Escherichia coli strain WP2/pKM101. Number of revertants/plate Dose TA102 TA2638 WP2/pKM101 WP2 uvrA/pKM101 ug/plate Lab 1 Lab 2 Lab 1 Lab 2 Lab 1 Lab 2 Lab 1 Lab 2 0 481 407 61 47 92 78 119 103 38 - 400 - - - - - - 75 - 425 - - - - - - 78 491 - - - - - - - 150 - 404 - - - - - - 156 486 - - - 103 - - - 300 - 391 - - - - - - 313 454 - 63 47 92 - 129 - 600 310a - - - - - - - 625 481 - 56 40 129 - 137 - 1000 - - - - - 78 - 85 1250 385a - 56 38 246 - 191 - 2000 - - - - - 121 - 95 2500 - - 53 43 247 - 388 - 3000 - - - - - 146 - 155 4000 - - - - - 151 - 194 5000 - - 33a 36a - 107 358 182 a= toxic not tested. All values are the average of three plates of the one experiment for each laboratory. |
| 結論 | | |
| 遺伝子突然変異 | 陽性 | positive |
| 注釈 | | |
| 信頼性 | (2)制限付きで有効 | (2) valid with restrictions |
| 信頼性の判断根拠 | 一般に受容できる科学的な標準法に合致し十分詳細に記載されている。 | Meets generally accepted scientific standards and is described in sufficient detail. |
| 出典 | OECD SIDS Dossier, 2005 | OECD SIDS Dossier, 2005 |
| 引用文献(元文献) | Watanabe, K., Sakamoto, K. and Sasaki, T. (1996). Comparisons on Chemically-Induced Mutagenicity Among Four Bacterial Strains, Salmonella Typhimurium TA102 and TA2638, and Escherichia coli WP2/pKM101 and WP2 uvrA/pKM101: Collaborative Study I. Mutation Research 361 (1996) 143-155. | Watanabe, K., Sakamoto, K. and Sasaki, T. (1996). Comparisons on Chemically-Induced Mutagenicity Among Four Bacterial Strains, Salmonella Typhimurium TA102 and TA2638, and Escherichia coli WP2/pKM101 and WP2 uvrA/pKM101: Collaborative Study I. Mutation Research 361 (1996) 143-155. |
| 備考 | フラグ : SIDSエンドポイントの重要な試験 | Flag : Critical study for SIDS endpoint |
| 試験物質名 | 他の物質 | other TS |
| CAS番号 | | |
| 純度等 | | |
| 注釈 | Rocryl 420 (HEA) は96.5%であった(Rohm and Haasによる試験)。 | Rocryl 420 (HEA) was 96.5% a.i. as tested by Rohm and Haas. |

| | | |
|--------------|--|--|
| 方法 | | |
| 方法／ガイドライン | エームス試験 | Ames test |
| GLP適合 | 情報無し | no data |
| 試験を行った年 | 1982年 | 1982 |
| 細胞株又は検定菌 | ネズミチフス菌 Salmonella typhimurium strains TA100 | Salmonella typhimurium strains TA100 |
| 代謝活性化(S9)の有無 | 有及び無 | with and without |
| 試験条件 | 原文参照 | Test concentration : 10, 50, 75, 100, 250, 500, 750, 1000, 2500, 7500 nl/plate |
| 結果 | | |
| 細胞毒性 | | |
| 代謝活性ありの場合 | | |
| 代謝活性なしの場合 | | |
| 変異原性 | | |
| 代謝活性ありの場合 | 陰性 | negative |
| 代謝活性なしの場合 | 陰性 | negative |
| 注釈 | 原文参照 | Inhibition of growth was seen at concentrations of 1000 nanoliters/plate and above with activation and 250 nanoliters/plate and above without activation. Rocryl 420 (HEA) did not demonstrate mutagenic activity on strain TA100. |
| 結論 | | |
| 遺伝子突然変異 | 陰性 | negative |
| 注釈 | | |
| 信頼性 | (2)制限付きで有効 | (2) valid with restrictions |
| 信頼性の判断根拠 | 単一の菌株が使用された。著者は、本被験物質が非変異原であるとする前に、追加の菌株の試験が必要であると述べている。 | Only one strain was used and authors state that additional strains would be necessary before this compound could be considered a non-mutagen. |
| 出典 | OECD SIDS Dossier, 2005 | OECD SIDS Dossier, 2005 |
| 引用文献(元文献) | Lohse, K.L. and Melly, J.G. (1982). Genetic Toxicology Report Number 82R-184 of Rohm and Haas Company. | Lohse, K.L. and Melly, J.G. (1982). Genetic Toxicology Report Number 82R-184 of Rohm and Haas Company. |
| 備考 | | |

| | | |
|--------------|---|--|
| 試験物質名 | 情報無し | no data |
| CAS番号 | | |
| 純度等 | | |
| 注釈 | | |
| 方法 | | |
| 方法／ガイドライン | マウスリンフォーマ試験、 他法: Turner N.T. et al. (1984) | Mouse lymphoma assay, other: Turner N.T. et al. (1984) |
| | (原文には、Cytogenetic assayと記載されているが、これは誤りと考えられるため、マウスリンフォーマ試験とした。) | |
| GLP適合 | 情報無し | no data |
| 試験を行った年 | | |
| 細胞株又は検定菌 | L5178Y マウスリンフォーマ細胞のTK+/- 3.7.2C ヘテロ接合体 | TK+/- 3.7.2C heterozygote of L5178Y mouse lymphoma cells |
| 代謝活性化(S9)の有無 | 無 | without |
| 試験条件 | 原文参照 | Test concentration : 0, 15, 18, or 20 microG/ml |
| 試験条件 | 原文参照 | L5178Y/TK+/- 3.7.2C cells were treated for 4 hours with 2-HEA (0, 15, 18 or 20 microG/ml) in DMSO according to Turner et al. (1984). No more than 100 microL DMSO was added to 10 ml culture and this concentration does not effect the cytotoxicity or mutagenicity of the culture. Cells were then centrifuged and washed and 10 microL M bromodeoxyuridine added. Cultures for micronucleus analysis were treated with 3 microg/ml cytochalasin B and harvested 12-13 hr later. Cultures for aberration analysis were incubated for 14-15 hr; 0.1 microL/ml colcemid being added for the last 2 hr. For a positive result, the response must be double that of the negative control for the experiment as well as that of the historic means for negative controls (quoted as being 4.45 + 2.11 aberrations/100 cells or 9.90 + 2.47 micronuclei/1000 cells). |
| 結果 | | |
| 細胞毒性 | | |
| 代謝活性ありの場合 | | |
| 代謝活性なしの場合 | | |
| 変異原性 | | |
| 代謝活性ありの場合 | | |
| 代謝活性なしの場合 | 陽性 | positive |

| | | |
|-----------|--|--|
| 注釈 | 原文参照 | A dose-related decrease in survival (calculated according to Clive & Spector, 1975) was seen up to a level of 15% at 20 microg/ml. This was considered adequate for examining the cytogenetic effects. The background number of total aberrations was 2/100 cells and that in the treated cultures was 99/100 cells. In the micronucleus test, a background of 13/1000 cells compared to 47/1000 in the treated culture was seen. The total mutant frequencies in the control and treated groups were $85 \times 10E6$ and $560 \times 10E6$ respectively. |
| 結論 | | |
| 遺伝子突然変異 | 陽性 | positive |
| 注釈 | | |
| 信頼性 | (2)制限付きで有効 | (2) valid with restrictions |
| 信頼性の判断根拠 | 一般に受容できる科学的な標準法に合致し十分詳細に記載されている。 | Meets generally accepted scientific standards and is described in sufficient detail. |
| 出典 | OECD SIDS Dossier, 2005 | OECD SIDS Dossier, 2005 |
| 引用文献(元文献) | Dearfield K.L. et al. (1989) Mutagenesis, 4: 381-393 | Dearfield K.L. et al. (1989) Mutagenesis, 4: 381-393 |
| 備考 | | |

| | | |
|--------------|--|---|
| 試験物質名 | 情報無し | no data |
| CAS番号 | | |
| 純度等 | | |
| 注釈 | | |
| 方法 | | |
| 方法／ガイドライン | マウスリンフォーマ試験、 他法: Turner N.T. et al. (1984) | Mouse lymphoma assay, other: Turner N.T. et al. (1984) |
| GLP適合 | 情報無し | no data |
| 試験を行った年 | 1984年 | 1984 |
| 細胞株又は検定菌 | L5178Y/ マウスリンフォーマ細胞のTK+/- 3.7.2C ヘテロ接合体 | TK+/- 3.7.2C heterozygote of L5178Y mouse lymphoma cells |
| 代謝活性化(S9)の有無 | 無 | without |
| 試験条件 | 原文参照 | Test concentration : 0, 6, 10-20 microG/ml |
| 試験条件 | | |
| 結果 | | |
| 細胞毒性 | | |
| 代謝活性ありの場合 | | |
| 代謝活性なしの場合 | | |
| 変異原性 | | |
| 代謝活性ありの場合 | | |
| 代謝活性なしの場合 | 陽性 | positive |
| 注釈 | 原文参照 | A dose-related decrease in survival was seen to a level of 6% at 20 microG/ml. The background mutant frequency was $89-102 \times 10E-6$ survivors/100 cells. In the test system, a concentration of 18 microG/ml was considered to produce an adequate survival rate (13%) for mutant frequency to be determined. The mutant frequency was $707 \times 10E-6$ survivors/100 cells, showing 2-HEA to be a mutagen. The ratio of small colonies/large colonies at this dose was 607/100 in comparison to the background ratio of 67/22; the large excess of small colonies indicating a possible cytogenic effect. L5178Y/TK+/- 3.7.2C cells were treated for 4 hours with 2-HEA (0, 6, 10-20 microG/ml) in DMSO according to Turner et al. (1984). No more than 100 microL DMSO was added to 10 ml culture and this concentration does not effect the cytotoxicity or mutagenicity of the culture. Cells were then centrifuged, washed, resuspended in fresh medium and maintained at 37 deg.C in log-phase growth for 2 days. They were then cloned with 1 microG/ml trifluorothymidine for 9-11 days at 37 deg.C, the colonies counted and the mutant frequency calculated. A positive response was defined as one in which the quantitated mutant frequency is >2x the background mutant frequency. The response must be consistent and observed at concentrations giving > 10% cell survival. |
| 結論 | | |
| 遺伝子突然変異 | 陽性 | positive |
| 注釈 | | |
| 信頼性 | (2)制限付きで有効 | (2) valid with restrictions |
| 信頼性の判断根拠 | 一般に受容できる科学的な標準法に合致し十分詳細に記載されている。 | Meets generally accepted scientific standards and is described in sufficient detail. |
| 出典 | OECD SIDS Dossier, 2005 | OECD SIDS Dossier, 2005 |
| 引用文献(元文献) | Dearfield K.L. et al. (1989) Mutagenesis, 4: 381-393 | Dearfield K.L. et al. (1989) Mutagenesis, 4: 381-393 |
| 備考 | | |

| | | |
|-------|------|---------|
| 試験物質名 | 情報無し | no data |
| CAS番号 | | |
| 純度等 | | |
| 注釈 | | |

| | | |
|--------------|--|--|
| 方法 | | |
| 方法／ガイドライン | Saccharomyces cerevisiaeの遺伝子突然変異 | Gene mutation in Saccharomyces cerevisiae |
| | | other |
| GLP適合 | 非適合 | no |
| 試験を行った年 | 1976年 | 1976 |
| 細胞株又は検定菌 | Saccharomyces cerevisiae D3 | Saccharomyces cerevisiae D3 |
| | | |
| 代謝活性化(S9)の有無 | 有及び無 | with and without |
| 試験条件 | 用量: データなし。 | Test concentration : no data specified |
| 試験条件 | | |
| 結果 | | |
| 細胞毒性 | | |
| 代謝活性ありの場合 | | |
| 代謝活性なしの場合 | | |
| 変異原性 | | |
| 代謝活性ありの場合 | | |
| 代謝活性なしの場合 | 陰性 | negative |
| 注釈 | | |
| 結論 | | |
| 遺伝子突然変異 | 陰性 | negative |
| 注釈 | | |
| 信頼性 | (2)制限付きで有効 | (2) valid with restrictions |
| 信頼性の判断根拠 | 一般に受容できる科学的な標準法に合致し十分詳細に記載されている。 | Meets generally accepted scientific standards and is described in sufficient detail. |
| 出典 | OECD SIDS Dossier, 2005 | OECD SIDS Dossier, 2005 |
| 引用文献(元文献) | Unpublished report of The Dow Chemical Company, 1976 | Unpublished report of The Dow Chemical Company, 1976 |
| 備考 | | |

B. 染色体異常
CHROMOSOMAL ABBERATION

5-7 *in vivo* 遺伝毒性
GENETIC TOXICITY IN VIVO

| | | |
|-------------|---|---|
| 試験物質名 | 他の物質 | other TS |
| CAS番号 | | |
| 純度等 | | |
| 注釈 | 2-Hydroxypropylacrylate (purity = 97.68%) | 2-Hydroxypropylacrylate (purity = 97.68%) |
| 方法 | | |
| 方法／ガイドライン | OECDガイドライン474「遺伝毒性:小核試験」 | OECD Guide-line 474 "Genetic Toxicology: Micronucleus |
| | | |
| 試験のタイプ | 小核試験 | Micronucleus assay |
| GLP適合 | 適合 | Yes |
| 試験を行った年 | 2000年 | 2000 |
| 試験系(種／系統) | マウス | mouse |
| | NMRI | NMRI |
| 性別(雄:M、雌:F) | 雌雄 | male/female |
| 投与量 | 0, 100, 300, 600 mg/kg bw | 0, 100, 300, 600 mg/kg bw |
| | | |
| 投与経路 | 強制経口 | gavage |
| | | |
| 試験期間 | 単回投与 | Single administration |
| 試験条件 | 原文参照 | Groups of 10 mice (5 of each sex) were administered a single p.o. dose of the test substance orally at concentrations of 100, 300 and 600 mg/kg body weight. The test substance was prepared in carboxymethylcellulose. The volume administered was 33.3 ml/kg body weight. Two additional groups of mice (5/sex/group) were used as the negative control and positive control. The negative control group received carboxymethylcellulose by gavage. The positive control group animals received a single i.p. injection of 10 ml/kg cyclophosphamide in 0.9% NaCl at 30 mg/kg b.w. Five males and five females from each group were sacrificed 24 hours after dosing. Forty eight hours after dosing five animals per sex from the 600 mg/kg dose level were killed. One bone marrow smear was prepared per animal from the tissue cleared from each femur. Stained smears were examined by light microscopy for incidence of micronucleated cells per 2000 polychromatic erythrocytes per animal. To describe a cytotoxic effect, the ratio of polychromatic to normochromatic erythrocytes was assessed by the examination of at least 1000 erythrocytes. Evaluation of Results: Cells were evaluated for large (aneugenic effects) and small (clastogenic effects) micronuclei. The test substance was classified as mutagenic if it induced either a statistically significant, doserelated increase in the number of micronucleated polychromatic erythrocytes or a reproducible, statistically significant positive response for at least one of the test points. |

| | | |
|---------------------|---|---|
| 試験条件 | 原文参照 | These data on 2-Hydroxypropyl acrylate as an analog of 2-hydroxyl ethyl acrylate. It is expected that a similar result as observed in this study would result if 2-hydroxyethyl acrylate were tested in this assay. An initial experiment to determine the toxicity of the test substance was conducted. Three male and three female mice were administered the test substance orally at 1000 mg/kg b.w. This dose resulted in only slight toxicity and was therefore chosen as the top dose. In the main experiment, two animals died within the first 6 hours of dosing at 1000 mg/kg b.w. so a dose of 600 mg/kg b.w. was chosen as the highest dose that could be used for analysis of micronuclei. All 10 mice at 1000 mg/kg b.w. died within 24 hours of dosing. |
| 統計学的処理 | | |
| 結果 | | |
| 性別及び投与量別の結果 | | |
| 遺伝毒性効果 | 陰性 | negative |
| NOAEL (NOEL) | | |
| LOAEL (LOEL) | | |
| 統計的結果 | | |
| 注釈 | 原文参照 | The ratio of normochromatic to polychromatic erythrocytes was slightly affected by the treatment with 2-hydroxypropylacrylate at a dose of 600 mg/kg b.w. (at 24 and 48 hours in male mice and at 48 hours in female mice). At this dose level, only slight toxic effects, as evidenced by reduced spontaneous reactivity, were obtained up to 6 hours after dosing. There was no increase in the frequency of micronuclei at any dose level at either 24- or 48-hours after dosing compared to the negative control group. Data are shown below: |
| 注釈 | 原文参照 | <p>Males</p> <p>24 hours Mean Micronuclei/2000 PCE Mean PCE/NCE All (%) Small (%) Negative control 3.2 (0.16) 2.8 (0.14) 1000/873.6 600 mg/kg 4.4 (0.22) 3.8 (0.19) 1000/1056.8 300 mg/kg 5.4 (0.27) 5.4 (0.27) 1000/1177.6 100 mg/kg 4.8 (0.24) 3.8 (0.19) 1000/974.6 Positive control 20.2 (1.01) 18.8 (0.94) 1000/739.6</p> <p>Females</p> <p>24 hours Mean Micronuclei/2000 PCE Mean PCE/NCE All (%) Small (%) Negative control 3.2 (0.16) 2.8 (0.14) 1000/737.4 600 mg/kg 2.8 (0.14) 2.0 (0.10) 1000/854.6 300 mg/kg 5.2 (0.26) 4.8 (0.24) 1000/773.8 100 mg/kg 3.2 (0.16) 2.8 (0.14) 1000/918.8 Positive control 19.6 (0.98) 18.4 (0.92) 1000/688.6</p> <p>48 hours Sex Mean Micronuclei/2000 PCE Mean PCE/NCE All (%) Small (%) 600 mg/kg Male 2.2 (0.11) 2.0 (0.10) 1000/986.2 600 mg/kg Female 2.2 (0.11) 1.8 (0.09) 1000/1065.4</p> |
| 結論 | | |
| <i>in vivo</i> 遺伝毒性 | 2-Hydroxypropyl acrylateはこの小核試験において変異原性が無いと結論された。 | It was concluded that 2-Hydroxypropyl acrylate is considered to be nonmutagenic in this micronucleus test |
| 注釈 | | |
| 信頼性 | (1)制限なしに有効 | (1) valid without restriction |
| 信頼性の判断根拠 | GLPガイドライン試験 | GLP guideline study |
| 出典 | OECD SIDS Dossier, 2005 | OECD SIDS Dossier, 2005 |
| 引用文献(元文献) | Hamann, U. (2000) Mammalian Micronucleus Test of Murine Bone Marrow Cells with 2-Hydroxypropylacrylate. BSL Bioservice Project No.: 991524 A. BSL Bioservice Scientific Laboratories GmbH, Planegg/Munich, Germany. | Hamann, U. (2000) Mammalian Micronucleus Test of Murine Bone Marrow Cells with 2-Hydroxypropylacrylate. BSL Bioservice Project No.: 991524 A. BSL Bioservice Scientific Laboratories GmbH, Planegg/Munich, Germany. |
| 備考 | フラグ: SIDSエンドポイントの重要な試験 | Flag: Critical study for SIDS endpoint |
| 試験物質名 | 2-Propenoic acid, 2-hydroxyethylester | 2-Propenoic acid, 2-hydroxyethylester |
| CAS番号 | 818-61-1 | 818-61-1 |
| 純度等 | 96.5 - 99 % w/w | 96.5 - 99 % w/w |
| 注釈 | | |
| 方法 | | |
| 方法/ガイドライン | 他 | other |
| 試験のタイプ | 染色体異常試験 | Cytogenetic assay |
| GLP適合 | 情報無し | no data |
| 試験を行った年 | 1977年 | 1977 |
| 試験系(種/系統) | ラット | rat |
| 性別(雄:M、雌:F) | 雌雄 | male/female |
| 投与量 | 0.5, or 5 ppm (2.37 or 23.7 mg/m3) | 0.5, or 5 ppm (2.37 or 23.7 mg/m3) |

| | | |
|---------------------|--|---|
| 投与経路 | 吸入 | inhalation |
| 試験期間 | 18ヶ月 | 18 months |
| 試験条件 | 原文参照 | Groups of 100 male and 100 female animals were exposed to HEA vapor at 0 (controls), 0.5 or 5 ppm for 6 hours/day, 5 days/week as part of the chronic toxicity/oncogenicity study. After the first year of treatment, 4 male and 4 female rats per group were injected intraperitoneally with colchicine (0.4 mg/kg) sacrificed four hours after injection and samples of bone marrow collected. Slides of the bone marrow were prepared for the microscopic examination of chromosomes. Fifty cells per animal were scored for chromatid aberrations, chromosome aberrations and abnormal cells, with the exception of female controls where 35, 43, 19 and 25 cells were scored and one female in the 5 ppm group where only 2 cells were scored. |
| 統計学的処理 | | |
| 結果 | | |
| 性別及び投与量別の結果 | | |
| 遺伝毒性効果 | 陰性 | negative |
| NOAEL (NOEL) | | |
| LOAEL (LOEL) | | |
| 統計的結果 | | |
| 注釈 | HEAの暴露の結果、骨髄に染色体の変化は認められなかった。 | No bone marrow cytogenetic alterations were found as a result of exposure to HEA. |
| 結論 | | |
| <i>in vivo</i> 遺伝毒性 | 陰性 | negative |
| 注釈 | | |
| 信頼性 | (2)制限付きで有効 | (2) valid with restrictions |
| 信頼性の判断根拠 | | |
| 出典 | OECD SIDS Dossier, 2005 | OECD SIDS Dossier, 2005 |
| 引用文献(元文献) | Rampy L.W. Kociba, R.J., Balmer, M.F., Keyes, D.G., Schuetz, J.D. and Yakel, H.O. (1978) Results of a Two-Year Inhalation Toxicity Study of Hydroxyethyl Acrylate in Rats. Toxicol. Appl. Pharmacol., 45: 310. | Rampy L.W. Kociba, R.J., Balmer, M.F., Keyes, D.G., Schuetz, J.D. and Yakel, H.O. (1978) Results of a Two-Year Inhalation Toxicity Study of Hydroxyethyl Acrylate in Rats. Toxicol. Appl. Pharmacol., 45: 310. |
| 備考 | フラグ: SIDSエンドポイントの重要な試験 | Flag : Critical study for SIDS endpoint |

5-8 発がん性
CARCINOGENICITY

| | | |
|--------------|--|--|
| 試験物質名 | 他のTS: 96% HEA | other TS: 96% HEA |
| CAS番号 | | |
| 純度等 | 供給源: Texas Division of The Dow Chemical Company 純度: 96.3% 蒸気相クロマトグラフィによるアクリル酸2-ヒドロキシエチル | SOURCE: Texas Division of The Dow Chemical Company PURITY: 96.3% 2-hydroxyethyl acrylate by vapor phase chromatography |
| 注釈 | 不純物: アクリル酸 0.91% 水 0.06% エチレンオキシド 0.43% 酢酸ヒドロキシエチル 0.82% メタクリル酸ヒドロキシエチル 0.1% ジアクリル酸エチレン 0.11% ニトロアクリル酸ジエチレングリコール 1.11% ジアクリル酸の2-ヒドロキシエチルエステル 0.19% メチルエチルヒドロキノン (ppm) 475 一般名: アクリル酸2-ヒドロキシエチル ロット番号: TB-08153 最初の分析から14ヵ月後の再分析で試験物質が安定であることが示された。 | IMPURITIES: Acrylic acid 0.91% Water 0.06% Ethylene oxide 0.43% Hydroxyethyl acetate 0.82% Hydroxyethyl methacrylate 0.1% Ethylene diacrylate 0.11% Diethylene glycol nitroacrylate 1.11% 2-Hydroxyethyl ester of diacrylic acid 0.19% methyl ethyl hydroquinone (ppm) 475 COMMON NAME: 2-hydroxyethyl acrylate LOT NUMBER: TB-08153 Reanalysis 14 months from the initial analysis showed the test material to be stable. |
| 方法 | | |
| 方法/ガイドライン | その他 | other |
| 試験のタイプ | | |
| GLP適合 | いいえ | no |
| 試験を行った年 | 1979 | 1979 |
| 試験系(種/系統) | ラット Sprague-Dawley | rat Sprague-Dawley |
| 性別(雄:M、雌:F) | 雄/雌 | male/female |
| 投与量 | 0 ppm、0.5 ppm (2.4 mg/m ³)、及び 5.0 ppm (24 mg/m ³) | 0 ppm, 0.5 ppm (2.4 mg/cubic meter), and 5.0 ppm (24 mg/cubic meter) |
| 各用量群(性別)の動物数 | | |
| 溶媒(担体) | | |
| 投与経路 | 吸入 | inhalation |
| 処理頻度 | 6時間/日、5日/週 | 6 hours/day; 5 days/week |
| 対照群と処理 | あり | yes |

| | | |
|--------|--------------------------------------|---|
| 試験条件 | 暴露期間：18ヶ月間 暴露後の期間：5ヶ月間（雄）、6ヶ月間（雌） | Exposure period：18 months Post exposure period：5 months (male); 6 months (females) |
| 試験条件 | ※英文参照 | <p>TEST ORGANISMS: Age: not specified Weight at study initiation: Male group means ranging from 287–300 g; Female group means ranging from 217–224 g Number of animals: 99 or 100 animals/sex/exposure level</p> <p>ADMINISTRATION/EXPOSURE: Duration of test/exposure: 18 months Type of exposure: Whole body Post exposure period: Males: 5 months, Females: 6 months Vehicle: none/not applicable Target Exposure Concentrations: 0, 0.5 and 5 ppm vapor Actual Analytical Mean +/- S.D. Exposure Concentrations: 0, 0.56 +/- 0.39 ppm, 3.66 +/- 1.65 ppm.</p> |
| 試験条件 | ※英文参照 | <p>CLINICAL OBSERVATIONS AND FREQUENCY: Body weights: All animals weighed on the following study days: 0,5,7,12,19,26,33,40,54,68,96,131,159,194,223,251,286,314,342,377,405,433,468,496,532,552,585,620,648,675,702,723</p> <p>Clinical signs: animals examined at “frequent intervals” for mortality/morbidity</p> <p>Hematology: 12 months, 5 rats/sex/exposure level; and at end of 5 or 6 month post-exposure period, 10 rats/sex/exposure level. Packed cell volume, erythrocyte count, hemoglobin concentration, total and differential leukocyte count.</p> <p>Cytogenetic evaluation: 12 months, 4 rats/sex/exposure level; chromosomal aberrations, breaks</p> <p>Clinical Chemistry: 12 months, 5 rats/sex/exposure level, Blood urea nitrogen, alkaline phosphatase, glutamic pyruvic transaminase</p> <p>Urinalysis: 12 months, 5 rats/sex/exposure level; and at end of 5- or 6-month post-exposure period, 10 rats/sex/exposure level. Specific gravity, pH, glucose, protein, ketones, bilirubin and blood.</p> |
| 試験条件 | ※英文参照 | <p>ORGANS EXAMINED AT NECROPSY: Macroscopic: At 12-month interim sacrifice: all organs, weight of brain, heart, liver, kidneys, testes, 5 rats/sex/exposure level. At terminal sacrifice: all organs, all surviving animals. The weights of brain, heart, liver, kidneys, testes were recorded at the terminal sacrifice for 9–19 animals per sex/exposure level.</p> |
| 試験条件 | ※英文参照 | <p>Microscopic: Control and 5 ppm, at interim and terminal sacrifice: brain, heart, liver kidneys, testes, lungs, thoracic and/or mesenteric lymph nodes, salivary glands, pancreas, adrenals, spleen, thymus, aorta, skeletal muscle, small intestine, large intestine, thyroid gland, trachea, spinal cord, peripheral nerve, pituitary gland, epididymides, urinary bladder, accessory sex glands, adipose tissue, ovaries, uterus, nasal turbinates, and any gross lesion suggestive of a pathologic process or with tumor formation.</p> <p>At 0.5 ppm terminal sacrifice lungs, livers, kidneys, lymph nodes tracheas and grossly visible lesions from all surviving animals; at interim sacrifice grossly visible lesions or tissues where lesions seen at 5 ppm.</p> <p>Rats dying or culled during the course of the study, complete necropsy and microscopic exam as described above (except when autolysis precluded evaluation) and the presence and absence of neoplasms recorded.</p> |
| 統計学的処理 | ※英文参照 | <p>STATISTICAL METHODS: Hematology, clinical chemistries, body weights, absolute and relative organ weights were analyzed using analysis of variance and Dunnett’s Test. Cumulative mortality data were analyzed using Fisher’s Exact Probability Test. In both cases, p values of less than 0.05 considered statistically significant.</p> |

| | | |
|------------------------|--|--|
| 統計学的処理 | ※英文参照 | Gross and microscopic pathology data were analyzed using Fisher's Exact Probability Test ($p<0.05$) as follows: Gross necropsy: the total collated data from each of the high and low exposure groups were compared with the data of the control group. Each sex was compared separately. Microscopic observations: the incidence of lesions in tissue for each sex from highest exposure group (5 ppm) was compared with the data from controls. At the terminal sacrifice, data from the lower exposure group (0.5 ppm) were analyzed statistically when the number of tissues examined was similar to the controls. The incidence rate for each type of neoplasm was compared separately for each sex between the high exposure group and controls. For the lower exposure (0.5 ppm), statistical evaluation was conducted for neoplasms in those organs upon which microscopic exam was conducted to the degree comparable to the controls and highest exposure group (liver, kidney, lung and lymph nodes and subcutaneous masses/nodules). |
| 統計学的処理 | ※英文参照 | To examine the possibility that neoplasms appeared earlier in treated vs. control rats the following parameters were compared for 6 month time periods using Fisher's Exact Probability Test and the Mantel-Haenzel Test with $p<0.05$: 1) Total number of rats bearing tumors, 2) Number of rats with benign tumors, 3) Number of rats with malignant neoplasms, and 4) Number of rats bearing subcutaneous masses/nodules. |
| 結果 | | |
| 体重、体重増加量 | 体重：統計的に有意な体重の減少が12ヶ月で0.5及び5.0 ppmの雄ラットでみられたが、最終屠殺時にはみられなかった(表3及び4)。12ヶ月での体重の差は濃度依存的ではなかった。0.5 ppm群は5 ppm群よりも体重の平均値は低値を示した。 | BODY WEIGHTS: A statistically significant decrease in body weights was observed for male rats at 0.5 and 5.0 ppm at 12 months but not at terminal sacrifice (Tables 3 and 4). The difference in body weight at 12 months was not concentration dependent; the 0.5 ppm group having a lower mean weight than the 5 ppm group. |
| 摂餌量、飲水量 | 摂餌/摂水量：データは得られていない。 | FOOD/WATER CONSUMPTION: No data collected |
| 臨床所見(重篤度、所見の発現時期と持続時間) | 臨床症状：5 ppmに暴露したラットの被毛は特徴的な黄色の汚染を呈し、慢性ネズミ肺炎の頻度及び重篤度の増加を示した。 | CLINICAL SIGNS: The haircoat of rats exposed to 5 ppm had a characteristic yellow staining as well as an increased incidence and severity of chronic murine pneumonia. These effects were not observed in rats exposed to 0.5 ppm |
| 眼科学的所見(発生率、重篤度) | 眼科学的検査：剖検時に検眼鏡を用いて眼の表面を拡大し、眼の内側も検査したが、投与に関連した影響はみられなかった。 | OPHTHALMIC EXAMINATION: No treatment-related effect observed at necropsy using a glass microscope slide on the surface of the eye for magnification and examination of the interior of the eye. |
| 血液学的所見(発生率、重篤度) | 血液検査：中間屠殺時に雄ラットには統計的な差はみられなかった。5 ppmの雌は平均ヘモグロビン濃度の統計的に有意な上昇及び統計的に低値の白血球数を示した。最終屠殺時には5 ppmに暴露した雄ラットで白血球数の増加がみられた以外に対照群との統計的な差はなかった。 | HEMATOLOGY: At the interim sacrifice, no statistical differences were observed for male rats. Females at 5 ppm had statistically significant elevation of the mean hemoglobin concentration and statistically lower total leukocyte count. At the terminal sacrifice, there were no statistical differences from controls with the exception of a increase in red blood cell count in male rats exposed to 5 ppm. |
| 血液生化学的所見(発生率、重篤度) | 臨床化学：血中尿素窒素、又は血清GPT及びAPには中間又は最終屠殺時のいずれも対照群と暴露群の間で有意な差はなかった。 | CLINICAL CHEMISTRY: There were no significant differences between control and exposed groups in regard to blood urea nitrogen, or SGPT and AP activities either at the interim or terminal sacrifice. |
| 尿検査所見(発生率、重篤度) | 尿検査：中間又は最終屠殺のいずれでも投与に関連した影響はみられなかった。 | URINALYSIS: No treatment-related effects were observed at either the interim or terminal sacrifice. |
| 死亡数(率)、死亡時間 | 死亡率及び死亡までの時間：5 ppmのHEAに暴露した雄ラットの累積死亡率は試験16ヶ月目のみ対照群と比べ統計的に増加した。これは最初にこの群に生じ、その後他の暴露群及び対照群に広がったネズミ慢性肺炎の発症と一致していた。暴露した雌の死亡率は5 ppmの17ヶ月目及び0.5 ppmの15ヶ月目の統計的な増加を除けば対照群と同程度であった。累積死亡率のデータは全体的には暴露群と対照群との間で顕著な差はなく、5 ppmに暴露したラットにおけるネズミ慢性肺炎の発症に関連した初期の死亡率増加を除外すれば投与に関連した影響はないことが示された。 | MORTALITY AND TIME TO DEATH: The cumulative mortality for male rats exposed to 5 ppm HEA was statistically increased from controls in the 16th month of the study only. This correlated with the onset of chronic murine pneumonia which initially affected this group and subsequently spread to the other exposure and control groups. Mortality of exposed females was comparable to controls except for a statistical increase in the 17th month at 5 ppm and in the 15th month at 0.5 ppm. Overall the cumulative mortality data were not markedly different between exposed and control groups indicating an absence of a treatment-related effect with the possible exception of the initial increased mortality associated with the onset of chronic murine pneumonia in rats exposed to 5 ppm (Tables 1 & 2). |

死亡数(率)、死亡時間

| Table 1 | | | |
|--|---------------------------|-------------------------|---------------------------|
| CUMULATIVE PERCENT MORTALITY FOR MALE RATS EXPOSED TO VAPORS OF 2-HYDROXYETHYL ACRYLATE 5 DAYS/WEEK FOR 18 MONTHS FOLLOWED BY A 5 MONTH OBSERVATION PERIOD | | | |
| Months on Study | Exposure Level | | |
| | Control No. Dead (% Dead) | 5 PPM No. Dead (% Dead) | 0.5 PPM No. Dead (% Dead) |
| No. Rats Alive on Day 0 ^a | 91 | 91 | 91 |
| 1 | 0 (0) | 0 (0) | 1 (1) |
| 2 | 1 (1) | 0 (0) | 2 (2) |
| 3 | 1 (1) | 0 (0) | 2 (2) |
| 4 | 1 (1) | 1 (1) | 3 (3) |
| 5 | 1 (1) | 1 (1) | 5 (5) |
| 6 | 1 (1) | 1 (1) | 5 (5) |
| 7 | 2 (2) | 1 (1) | 6 (7) |
| 8 | 2 (2) | 1 (1) | 7 (8) |
| 9 | 2 (2) | 1 (1) | 7 (8) |
| 10 | 2 (2) | 1 (1) | 8* (9) |
| 11 | 3 (3) | 1 (1) | 8 (9) |
| 12 | 4 (4) | 2 (2) | 8 (9) |
| 13 | 5 (5) | 5 (5) | 9 (10) |
| 14 | 7 (8) | 7 (8) | 9 (10) |
| 15 | 8 (9) | 11 (12) | 10 (11) |
| 16 | 8 (9) | 28* (31) | 13 (14) |
| 17 | 37 (41) | 42 (46) | 24* (26) |
| 18 | 53 (58) | 44 (48) | 44 (48) |
| 19 | 57 (63) | 48 (53) | 54 (59) |
| 20 | 66 (73) | 49* (54) | 64 (70) |
| 21 | 70 (77) | 56* (62) | 71 (78) |
| 22 | 74 (81) | 60* (66) | 80 (88) |
| 23 | 77 (85) | 70 (77) | 82 (90) |
| Beginning of 24 | 77 (85) | 72 (79) | 82 (90) |
| Terminal Kill | 14 | 19 | 9 |
| 12 Month Interim Kill | 5 | 5 | 5 |
| 12 Month Kill for Cytogenetics | 4 | 4 | 4 |
| Total Rats In Study | 100 | 100 | 100 |

^aExcludes those rats used in interim kill (5/sex/dose), and used for cytogenetic examination (4/sex/dose).

* Statistically different from control data when analyzed using Fisher's Exact Probability test, p<0.05.

| Table 1 | | | |
|--|---------------------------|-------------------------|---------------------------|
| CUMULATIVE PERCENT MORTALITY FOR MALE RATS EXPOSED TO VAPORS OF 2-HYDROXYETHYL ACRYLATE 5 DAYS/WEEK FOR 18 MONTHS FOLLOWED BY A 5 MONTH OBSERVATION PERIOD | | | |
| Months on Study | Exposure Level | | |
| | Control No. Dead (% Dead) | 5 PPM No. Dead (% Dead) | 0.5 PPM No. Dead (% Dead) |
| No. Rats Alive on Day 0 ^a | 91 | 91 | 91 |
| 1 | 0 (0) | 0 (0) | 1 (1) |
| 2 | 1 (1) | 0 (0) | 2 (2) |
| 3 | 1 (1) | 0 (0) | 2 (2) |
| 4 | 1 (1) | 1 (1) | 3 (3) |
| 5 | 1 (1) | 1 (1) | 5 (5) |
| 6 | 1 (1) | 1 (1) | 5 (5) |
| 7 | 2 (2) | 1 (1) | 6 (7) |
| 8 | 2 (2) | 1 (1) | 7 (8) |
| 9 | 2 (2) | 1 (1) | 7 (8) |
| 10 | 2 (2) | 1 (1) | 8* (9) |
| 11 | 3 (3) | 1 (1) | 8 (9) |
| 12 | 4 (4) | 2 (2) | 8 (9) |
| 13 | 5 (5) | 5 (5) | 9 (10) |
| 14 | 7 (8) | 7 (8) | 9 (10) |
| 15 | 8 (9) | 11 (12) | 10 (11) |
| 16 | 8 (9) | 28* (31) | 13 (14) |
| 17 | 37 (41) | 42 (46) | 24* (26) |
| 18 | 53 (58) | 44 (48) | 44 (48) |
| 19 | 57 (63) | 48 (53) | 54 (59) |
| 20 | 66 (73) | 49* (54) | 64 (70) |
| 21 | 70 (77) | 56* (62) | 71 (78) |
| 22 | 74 (81) | 60* (66) | 80 (88) |
| 23 | 77 (85) | 70 (77) | 82 (90) |
| Beginning of 24 | 77 (85) | 72 (79) | 82 (90) |
| Terminal Kill | 14 | 19 | 9 |
| 12 Month Interim Kill | 5 | 5 | 5 |
| 12 Month Kill for Cytogenetics | 4 | 4 | 4 |
| Total Rats In Study | 100 | 100 | 100 |

^aExcludes those rats used in interim kill (5/sex/dose), and used for cytogenetic examination (4/sex/dose).

* Statistically different from control data when analyzed using Fisher's Exact Probability test, p<0.05.

死亡数(率)、死亡時間

| Table 2 | | | |
|--|---------------------------|-------------------------|---------------------------|
| CUMULATIVE PERCENT MORTALITY FOR FEMALE RATS EXPOSED TO VAPORS OF 2-HYDROXYETHYL ACRYLATE 5 DAYS/WEEK FOR 18 MONTHS FOLLOWED BY A 5 MONTH OBSERVATION PERIOD | | | |
| Months on Study | Exposure Level | | |
| | Control No. Dead (% Dead) | 5 PPM No. Dead (% Dead) | 0.5 PPM No. Dead (% Dead) |
| No. Rats Alive on Day 0 ^a | 91 | 91 | 91 |
| 1 | 0 (0) | 0 (0) | 1 (1) |
| 2 | 0 (0) | 0 (0) | 1 (1) |
| 3 | 0 (0) | 0 (0) | 1 (1) |
| 4 | 0 (0) | 0 (0) | 1 (1) |
| 5 | 0 (0) | 0 (0) | 1 (1) |
| 6 | 0 (0) | 0 (0) | 1 (1) |
| 7 | 0 (0) | 0 (0) | 1 (1) |
| 8 | 2 (2) | 1 (1) | 1 (1) |
| 9 | 3 (3) | 3 (3) | 2 (2) |
| 10 | 3 (3) | 4 (4) | 3 (3) |
| 11 | 4 (4) | 4 (4) | 5 (5) |
| 12 | 4 (4) | 5 (5) | 7 (8) |
| 13 | 4 (4) | 8 (9) | 9 (10) |
| 14 | 5 (5) | 9 (10) | 12 (13) |
| 15 | 5 (5) | 10 (11) | 13* (14) |
| 16 | 5 (5) | 16 (18) | 16 (18) |
| 17 | 16 (18) | 28* (31) | 21 (23) |
| 18 | 23 (25) | 36 (37) | 27 (30) |
| 19 | 28 (31) | 39 (43) | 35 (39) |
| 20 | 37 (41) | 42 (46) | 41 (44) |
| 21 | 43 (47) | 46 (51) | 46 (51) |
| 22 | 53 (58) | 56 (62) | 59 (66) |
| 23 | 62 (68) | 61 (67) | 65 (72) |
| 24 | 70 (77) | 64 (70) | 70 (78) |
| Terminal Kill | 21 | 27 | 20 |
| 12 Month Interim Kill | 5 | 5 | 5 |
| 12 Month Kill for Cytogenetics | 4 | 4 | 4 |
| Total Rats In Study | 100 | 100 | 99 |

^aExcludes those rats used in interim kill (5/sex/dose), and used for cytogenetic examination (4/sex/dose).

* Statistically different from control data when analyzed using Fisher's Exact Probability test, p<0.05.

| Table 2 | | | |
|--|---------------------------|-------------------------|---------------------------|
| CUMULATIVE PERCENT MORTALITY FOR FEMALE RATS EXPOSED TO VAPORS OF 2-HYDROXYETHYL ACRYLATE 5 DAYS/WEEK FOR 18 MONTHS FOLLOWED BY A 5 MONTH OBSERVATION PERIOD | | | |
| Months on Study | Exposure Level | | |
| | Control No. Dead (% Dead) | 5 PPM No. Dead (% Dead) | 0.5 PPM No. Dead (% Dead) |
| No. Rats Alive on Day 0 ^a | 91 | 91 | 91 |
| 1 | 0 (0) | 0 (0) | 1 (1) |
| 2 | 0 (0) | 0 (0) | 1 (1) |
| 3 | 0 (0) | 0 (0) | 1 (1) |
| 4 | 0 (0) | 0 (0) | 1 (1) |
| 5 | 0 (0) | 0 (0) | 1 (1) |
| 6 | 0 (0) | 0 (0) | 1 (1) |
| 7 | 0 (0) | 0 (0) | 1 (1) |
| 8 | 2 (2) | 1 (1) | 1 (1) |
| 9 | 3 (3) | 3 (3) | 2 (2) |
| 10 | 3 (3) | 4 (4) | 3 (3) |
| 11 | 4 (4) | 4 (4) | 5 (5) |
| 12 | 4 (4) | 5 (5) | 7 (8) |
| 13 | 4 (4) | 8 (9) | 9 (10) |
| 14 | 5 (5) | 9 (10) | 12 (13) |
| 15 | 5 (5) | 10 (11) | 13* (14) |
| 16 | 5 (5) | 16 (18) | 16 (18) |
| 17 | 16 (18) | 28* (31) | 21 (23) |
| 18 | 23 (25) | 36 (37) | 27 (30) |
| 19 | 28 (31) | 39 (43) | 35 (39) |
| 20 | 37 (41) | 42 (46) | 41 (44) |
| 21 | 43 (47) | 46 (51) | 46 (51) |
| 22 | 53 (58) | 56 (62) | 59 (66) |
| 23 | 62 (68) | 61 (67) | 65 (72) |
| 24 | 70 (77) | 64 (70) | 70 (78) |
| Terminal Kill | 21 | 27 | 20 |
| 12 Month Interim Kill | 5 | 5 | 5 |
| 12 Month Kill for Cytogenetics | 4 | 4 | 4 |
| Total Rats In Study | 100 | 100 | 99 |

^aExcludes those rats used in interim kill (5/sex/dose), and used for cytogenetic examination (4/sex/dose).

* Statistically different from control data when analyzed using Fisher's Exact Probability test, p<0.05.

剖検所見(発生率、重篤度)

肉眼病理検査: 5 ppm のHEAに暴露した雌雄両方のラットでは暴露後の試験期間を通して持続した被毛の明瞭に視認できる黄色汚染を示す動物数が統計的に有意に増加した。黄色汚染は被毛とHEA蒸気の接触による結果と判断されたが、0.5 ppmのHEAに暴露したラットではみられなかった。マイコプラズマ種により生じたネズミ慢性肺炎が肺の硬変及び気管支系に沿った粘液膿性の炎症により証拠づけられたように全群に観察された。これはしばしば膿瘍形成、胸膜炎、心膜炎、鼻炎及び/又は気管炎を含んでいた。ネズミ慢性肺炎の二次的な影響として生じた多くの肉眼ないし顕微鏡的に確認可能な病変の頻度の増加が5 ppmのHEAに暴露した雌雄両方のラットで観察された。

GROSS PATHOLOGY: A statistically significant number of both male and female rats exposed to 5 ppm HEA had a distinctive grossly visible yellow staining of the haircoat that persisted into the post-exposure portion of the study. The yellow staining was judged to be a result of the contact of the HEA vapor with the haircoat and was not observed in rats exposed to 0.5 ppm HEA. Chronic murine pneumonia caused by Mycoplasma sp. was observed in all groups as evidenced by pulmonary consolidation and mucopurulent inflammation along the tracheobronchial system. This sometimes included abscess formation, pleuritis, pericarditis, rhinitis and/or tracheitis. An increase in the incidence of numerous gross or microscopically visible lesions occurring as part of or secondary to the chronic murine pneumonia was observed in both male and female rats exposed to 5 ppm HEA.

剖検所見(発生率、重篤度)

5又は0.5 ppmのHEAに暴露した群では全部で3つの肉眼的に明らかな皮下の腫瘍を有する雌ラットの頻度に増加がみられた。しかし、これは1、2、4又は5個の皮下の腫瘍を有しないいずれの暴露群の雌ラットにもあてはまらなかった。

An increase was observed in the incidence of female rats having a total of 3 grossly-visible subcutaneous masses in the groups exposed to 5 or 0.5 ppm HEA. However, this was not the case with female rats of either exposure group that had 1,2,4, or 5 subcutaneous masses.

| | | |
|-------------------|---|--|
| 臓器重量 | 臓器重量：中間屠殺時に絶対臓器重量には統計的に有意な差はなかった。0.5 ppmに暴露した雄での脳及び精巣相対重量は対照群と比較して有意に増加し、最終体重における統計的に有意な減少による二次的なものであった。12ヶ月間HEAに暴露した雌では絶対重量も相対重量も対照群の臓器重量と比べ有意な差はなく、雌では体重への影響がないことと一致していた。 | ORGAN WEIGHTS: At the interim sacrifice, there were no statistically significant differences in absolute organ weights; the relative brain and testes weight for males exposed to 0.5 ppm were significantly increased relative to controls secondary to a statistically significant decrease in the terminal body weights. There were no significant differences from either absolute or relative control organ weights for females exposed to HEA for twelve months, consistent with the absence of an effect on body weight in females. |
| 臓器重量 | 最終屠殺時には0.5 ppmの雄での脳絶対重量の減少及び5 ppmに暴露した雌での心臓絶対重量の減少以外に、HEAに暴露したラットでは体重、又は絶対又は相対器官重量において対照群と統計的に有意な差はなかった。これらの所見は相対重量には変化がないことから毒性学的な意義はないと考えられた。また、雌では1匹の動物からの”異常に低い”心臓重量の値が一つ含まれたことも差には影響を与えた。 中間及び最終屠殺時の平均臓器重量のデータはそれぞれ表3及び4に示した。 | At the terminal sacrifice, there were no statistically significant differences from controls in body weight, or the absolute or relative organ weights for HEA exposed rats with the exception of a decrease in the absolute weight of the brain for males at 0.5 ppm and of the heart for females exposed to 5 ppm. These observations were considered of no toxicologic significance in view of no change in the relative weight. In addition for the females, the inclusion of one “inordinately low” heart weight from one animal also had impact on the differences. Mean organ weight data for interim and terminal sacrifices are shown in Tables 3 and 4, respectively. |
| 病理組織学的所見(発生率、重篤度) | 病理組織学的検査：ネズミ慢性肺炎に関連した呼吸器の病変において、対照群とHEAを暴露したラットの間で統計的な差がみられた。特に5 ppmでは慢性ネズミ肺炎に関連した病変の頻度及び重篤度の増加がみられた。 | HISTOPATHOLOGY: Statistical differences between control and HEA exposed rats in the respiratory tract lesions related to chronic murine pneumonia were observed. Specifically, at 5 ppm, an increase in the incidence and severity of the lesions associated with chronic murine pneumonia was observed. |
| 病理組織学的所見(発生率、重篤度) | リンパ細網系：5及び0.5 ppmの雌では慢性ネズミ肺炎の二次的な変化として、胸部リンパ節の水腫、炎症及び反応性リンパ過形成の頻度の統計的な増加がみられた。0.5 ppmの雌では腸間膜リンパ節の水腫の頻度の増加も存在した。 | Lymphoreticular System: Statistical increases in the incidence of edema, inflammation and reactive lymphoid hyperplasia of the thoracic lymph nodes in females at 5 and 0.5 ppm, secondary to chronic murine pneumonia were observed; an increased incidence of edema in mesenteric lymph nodes was also present in females at 0.5 ppm. |
| 病理組織学的所見(発生率、重篤度) | 肝臓：最終屠殺時に5 ppmに暴露した雄では腫大した肝細胞の限局性の領域及び単核球細胞の局所の凝集に対照群と比べて統計的に有意な増加がみられた。5 ppmのHEAに暴露した雌ラットでは限局性の胆管増殖の頻度にも対照群と比べて統計的に有意な増加がみられた。 | Liver: At the terminal sacrifice a statistically significant increase as compared to controls was observed in the focal areas of swollen hepatocytes and focal aggregates of mononuclear cells in males exposed to 5 ppm. A statistically significant increase as compared to controls in the incidence of focal bile duct proliferation in female rats exposed to 5 ppm HEA was also observed. |
| 病理組織学的所見(発生率、重篤度) | 雌の生殖器官：最終屠殺時のみ、5 ppmに暴露した雌ラットの子宮の炎症の頻度に統計的に有意な増加がみられた(表5)。頻度のデータは試験報告書の付表に示されている。雌の生殖器官の病理組織学的所見には他には統計的に有意な差は検出されなかった。特に、HEAを暴露したラットの卵巣には投与に関連したと考えられる病理組織学的な影響はみられなかった。また、中間屠殺時に5 ppmのHEA暴露での12ヶ月後に直ちに評価した5匹の動物の雌の生殖器官には投与に関連した病理組織学的な影響は認められなかった。 | Female reproductive organs: At the terminal sacrifice only, a statistically significant increase in the incidence of inflammation of the uterus of female rats exposed to 5 ppm was observed (Table 5). Incidence data are shown in the attached table from the study report (HEA histopath uterus.pdf). No other statistically significant differences for histopathologic observations of the female reproductive organs were found. Specifically, there were no histopathological effects in the ovaries of HEA exposed rats that were considered treatment-related. In addition, at the interim sacrifice, no treatment-related histopathological effects were noted in female reproductive organs of five animals evaluated immediately after 12 months of HEA exposure at 5 ppm. |
| 病理組織学的所見(発生率、重篤度) | 雄の生殖器官：最終屠殺時のみ、5 ppmに暴露した雄ラットの精巣に血管チャンネルのフィブリノイド変性(この系統のラットでは加齢性病変としてみられる腸間膜動脈周囲炎症候群の局所的な血管の特徴)の統計的に有意な頻度の増加がみられた(対照群では8/14例、または57%、5 ppm 群では17/19例、又は89%)(表6A)。この系統の対照群の加齢ラットにおいてこの研究所で行われた試験で共通してみられたこの病変は70年代半ばから後期にその使用中に試験で観察された頻度(7つの慢性毒性/発がん性試験からの歴史的対照値は37-85%の範囲であった)と同様であった。腸間膜血管の動脈周囲炎も対照群とHEA暴露ラットに共通していた(表6B)。雄の生殖器官の病理組織学的所見にはこの他には統計的に有意な差はみられなかった。特に、精巣における精子形成、雄の副生殖腺における形態及び分泌内容物に投与群と対照群で差はなかった。また、中間屠殺時には5 ppmで2-HEAに12ヶ月暴露直後に評価した5匹の動物の雄の生殖器官には投与に関連した病理組織学的な影響はみられなかった。 | Male reproductive organs: At the terminal sacrifice only, there was a statistically significant increase in the incidence of fibrinoid degeneration of the vascular channels (local vascular manifestation of mesenteric periarteritis syndrome observed as age-related lesion in this rat strain) in the testes of male rats exposed to 5 ppm (8/14 or 57% in controls; 17/19 or 89% in the 5 ppm group) (Table 6A). The laboratory conducting this study commonly observed this lesion in control aging rats of this strain at similar incidence as was observed in this study during its use in the mid to late '70s (historical control values from seven chronic toxicity/oncogenicity studies ranged from 37 to 85%). Periarthritis of the mesenteric blood vessels was also common in the control and HEA exposed rats (Table 6B). No other statistically significant differences were found in the histopathologic observations of the male reproductive organs. Specifically, there was no difference between treated and control groups in spermatogenesis in the testes or in the morphology and secretory content of the male accessory sex glands. In addition, at the interim sacrifice, no treatment-related histopathological effects were noted in male reproductive organs of five animals evaluated immediately after 12 months of 2-HEA exposure at 5 ppm. |

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|--|--|--|--------|--|--|--|--|--|--|--|--|-------------|---|---|-----|--|---------------------------------------|----|----|----|--|-------------------------|-----|-----|-----|--|---------------------------------|--|--|--|--|------------------|--|--|--|--|---|----------|----------|--------|--|---|---------|---------|--------|--|---|---------|-----------------------|--------|--|---------------------------------------|---------|---------|--------|--|---------------------------------------|---------|---------|--------|--|--|---------|---------|--------|--|---|---------|----------------------|--------|--|---|---------|-----------------------|--------|--|--|----------|----------|--------|--|---|---------|---------|--------|--|--|---------|---------|--------|--|--|---------|---------|-------|--|--|----------|----------|-------|--|----------------------------------|---------|----------|--------|--|---|--|--|--|--|--|--|--|--|--|--|----------|--|--|--|--|---|--|--|--|--|--|---|---|-----|--|---------------------------------------|----|----|-----|--|---------------------------------------|-----|-----|-----|--|-------------------------|-----|-----|-----|--|---------------------------------|--|--|--|--|---|---------|----------|-------|--|---|----------|----------|--------|--|---|---------|---------|--------|--|---------------------------|---------|-----------------------|--------|--|---------------------------------------|---------|---------|--------|--|---------------------------------------|---------|---------|--------|--|---|---------|---------|--------|--|---------------------------------------|---------|----------------------|--------|--|---|----------|-----------------------|--------|--|---|---------|---------|--------|--|--|---------|---------|--------|--|--|---------|---------|--------|--|--|---------|---------|-------|--|---|----------|----------|-------|--|---|---------|----------|--------|--|--|--|--|--|--|--|--|--|--|--|---|--|--|--|--|
| 病理組織学的所見(発生率、重篤度) | 胃：5 ppmのHEAに暴露した雄ラットでは胃小窩の顕微鏡で確認できる拡張の頻度の増加がみられた。 心血管系：5 ppmに暴露した雌ラットでは心血管の顕微鏡的に確認可能な変性の頻度の増加がみられた(表7)。 | Stomach: An increase in the incidence of microscopically visible dilatation of gastric pits in male rats exposed to 5 ppm HEA was observed. Cardiovascular system: An increase in the incidence of microscopically visible degeneration of myocardial blood vessels in female rats exposed to 5 ppm was observed (Table 7). | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 病理組織学的所見(発生率、重篤度) | その他：細胞遺伝学的評価 - 骨髄：HEA暴露に関連した変化の徴候は細胞遺伝学的評価では観察されなかった。 | OTHER: CYTOGENETIC EVALUATION – Bone Marrow: There were no indications of alterations related to HEA exposure that were observed in the cytogenetic evaluation. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 病理組織学的所見(発生率、重篤度) | <table><tr><td colspan="5">Table 5</td></tr><tr><td colspan="5">MICROSCOPIC OBSERVATIONS ON FEMALE RATS EXPOSED TO VAPORS OF 2-HYDROXYETHYL ACRYLATE (Terminal Kill After Month 24)</td></tr><tr><td>Dose in ppm</td><td>0</td><td>5</td><td>0.5</td><td></td></tr><tr><td>Number of rats per group^a</td><td>21</td><td>27</td><td>20</td><td></td></tr><tr><td>Number of rats in study</td><td>100</td><td>100</td><td>99</td><td></td></tr><tr><td colspan="5">REPRODUCTIVE SYSTEM (Continued)</td></tr><tr><td colspan="5">UTERUS</td></tr><tr><td>Multiple areas of cystic endometrial hyperplasia</td><td>14/21/21</td><td>20/27/27</td><td>1/3/20</td><td></td></tr><tr><td>Sclerosing carcinoma of uterus with metastasis to lungs</td><td>0/21/21</td><td>0/27/27</td><td>1/3/20</td><td></td></tr><tr><td>Uterine inflammation</td><td>2/21/21</td><td>11/27/27^b</td><td>1/3/20</td><td></td></tr><tr><td>Adenomatous polyp formation in uterus</td><td>4/21/21</td><td>9/27/27</td><td>0/3/20</td><td></td></tr><tr><td>Squamous keratinization of uterus</td><td>0/21/21</td><td>1/27/27</td><td>0/3/20</td><td></td></tr><tr><td>Fibrotic polyp of uterus</td><td>0/21/21</td><td>0/27/27</td><td>1/3/20</td><td></td></tr><tr><td>Neutogenous pigment within uterus</td><td>2/21/21</td><td>6/27/27</td><td>1/3/20</td><td></td></tr><tr><td>Cyst formation within endometrium</td><td>3/21/21</td><td>8/27/27</td><td>0/3/20</td><td></td></tr><tr><td>Uterine polyp formation</td><td>1/21/21</td><td>0/27/27</td><td>0/3/20</td><td></td></tr><tr><td>Adenocarcinoma of uterus</td><td>1/21/21</td><td>1/27/27</td><td>0/3/20</td><td></td></tr><tr><td>Abscess of uterus</td><td>1/21/21</td><td>2/27/27</td><td>0/3/20</td><td></td></tr><tr><td colspan="5">GASTROINTESTINAL SYSTEM</td></tr><tr><td colspan="5">Stomach</td></tr><tr><td>Dilatation of gastric pits</td><td>7/21/21</td><td>11/27/27</td><td>0/1/20</td><td></td></tr><tr><td colspan="5">Data listed as number of observations/total number of tissues, organs, or masses examined microscopically/number of animals examined grossly.</td></tr><tr><td colspan="5">^aMicroscopic examination of all major organs limited to control and top dose group. Liver, kidney, lungs, nasal turbinates, thoracic lymph nodes, and all lesions grossly suggestive of tumor formation were examined from the low dose group.</td></tr><tr><td colspan="5">^bStatistically different from control by the Fisher Exact Probability Test, p<0.05.</td></tr></table> | Table 5 | | | | | MICROSCOPIC OBSERVATIONS ON FEMALE RATS EXPOSED TO VAPORS OF 2-HYDROXYETHYL ACRYLATE (Terminal Kill After Month 24) | | | | | Dose in ppm | 0 | 5 | 0.5 | | Number of rats per group ^a | 21 | 27 | 20 | | Number of rats in study | 100 | 100 | 99 | | REPRODUCTIVE SYSTEM (Continued) | | | | | UTERUS | | | | | Multiple areas of cystic endometrial hyperplasia | 14/21/21 | 20/27/27 | 1/3/20 | | Sclerosing carcinoma of uterus with metastasis to lungs | 0/21/21 | 0/27/27 | 1/3/20 | | Uterine inflammation | 2/21/21 | 11/27/27 ^b | 1/3/20 | | Adenomatous polyp formation in uterus | 4/21/21 | 9/27/27 | 0/3/20 | | Squamous keratinization of uterus | 0/21/21 | 1/27/27 | 0/3/20 | | Fibrotic polyp of uterus | 0/21/21 | 0/27/27 | 1/3/20 | | Neutogenous pigment within uterus | 2/21/21 | 6/27/27 | 1/3/20 | | Cyst formation within endometrium | 3/21/21 | 8/27/27 | 0/3/20 | | Uterine polyp formation | 1/21/21 | 0/27/27 | 0/3/20 | | Adenocarcinoma of uterus | 1/21/21 | 1/27/27 | 0/3/20 | | Abscess of uterus | 1/21/21 | 2/27/27 | 0/3/20 | | GASTROINTESTINAL SYSTEM | | | | | Stomach | | | | | Dilatation of gastric pits | 7/21/21 | 11/27/27 | 0/1/20 | | Data listed as number of observations/total number of tissues, organs, or masses examined microscopically/number of animals examined grossly. | | | | | ^a Microscopic examination of all major organs limited to control and top dose group. 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| MICROSCOPIC OBSERVATIONS ON FEMALE RATS EXPOSED TO VAPORS OF 2-HYDROXYETHYL ACRYLATE (Terminal Kill After Month 24) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Dose in ppm | 0 | 5 | 0.5 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Number of rats per group ^a | 21 | 27 | 20 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Number of rats in study | 100 | 100 | 99 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| REPRODUCTIVE SYSTEM (Continued) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| UTERUS | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple areas of cystic endometrial hyperplasia | 14/21/21 | 20/27/27 | 1/3/20 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Sclerosing carcinoma of uterus with metastasis to lungs | 0/21/21 | 0/27/27 | 1/3/20 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Uterine inflammation | 2/21/21 | 11/27/27 ^b | 1/3/20 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adenomatous polyp formation in uterus | 4/21/21 | 9/27/27 | 0/3/20 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Squamous keratinization of uterus | 0/21/21 | 1/27/27 | 0/3/20 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Fibrotic polyp of uterus | 0/21/21 | 0/27/27 | 1/3/20 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Neutogenous pigment within uterus | 2/21/21 | 6/27/27 | 1/3/20 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Cyst formation within endometrium | 3/21/21 | 8/27/27 | 0/3/20 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Uterine polyp formation | 1/21/21 | 0/27/27 | 0/3/20 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adenocarcinoma of uterus | 1/21/21 | 1/27/27 | 0/3/20 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Abscess of uterus | 1/21/21 | 2/27/27 | 0/3/20 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| GASTROINTESTINAL SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Stomach | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Dilatation of gastric pits | 7/21/21 | 11/27/27 | 0/1/20 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Data listed as number of observations/total number of tissues, organs, or masses examined microscopically/number of animals examined grossly. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| ^a Microscopic examination of all major organs limited to control and top dose group. Liver, kidney, lungs, nasal turbinates, thoracic lymph nodes, and all lesions grossly suggestive of tumor formation were examined from the low dose group. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| ^b Statistically different from control by the Fisher Exact Probability Test, p<0.05. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Table 6 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| MICROSCOPIC OBSERVATIONS ON FEMALE RATS EXPOSED TO VAPORS OF 2-HYDROXYETHYL ACRYLATE (Terminal Kill After Month 24) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Dose in ppm | 0 | 5 | 0.5 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Number of rats per group ^a | 21 | 27 | 20 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Number of rats in study | 100 | 100 | 99 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| REPRODUCTIVE SYSTEM (Continued) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| UTERUS | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple areas of cystic endometrial hyperplasia | 14/21/21 | 20/27/27 | 1/3/20 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Sclerosing carcinoma of uterus with metastasis to lungs | 0/21/21 | 0/27/27 | 1/3/20 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Uterine inflammation | 2/21/21 | 11/27/27 ^b | 1/3/20 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adenomatous polyp formation in uterus | 4/21/21 | 9/27/27 | 0/3/20 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Squamous keratinization of uterus | 0/21/21 | 1/27/27 | 0/3/20 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Fibrotic polyp of uterus | 0/21/21 | 0/27/27 | 1/3/20 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Neutogenous pigment within uterus | 2/21/21 | 6/27/27 | 1/3/20 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Cyst formation within endometrium | 3/21/21 | 8/27/27 | 0/3/20 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Uterine polyp formation | 1/21/21 | 0/27/27 | 0/3/20 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adenocarcinoma of uterus | 1/21/21 | 1/27/27 | 0/3/20 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Abscess of uterus | 1/21/21 | 2/27/27 | 0/3/20 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| GASTROINTESTINAL SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Stomach | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Dilatation of gastric pits | 7/21/21 | 11/27/27 | 0/1/20 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Data listed as number of observations/total number of tissues, organs, or masses examined microscopically/number of animals examined grossly. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| ^a Microscopic examination of all major organs limited to control and top dose group. Liver, kidney, lungs, nasal turbinates, thoracic lymph nodes, and all lesions grossly suggestive of tumor formation were examined from the low dose group. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| ^b Statistically different from control by the Fisher Exact Probability Test, p<0.05. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 病理組織学的所見(発生率、重篤度) | <table><tr><td colspan="5">Table 5A</td></tr><tr><td colspan="5">MICROSCOPIC OBSERVATIONS ON MALE RATS EXPOSED TO VAPORS OF 2-HYDROXYETHYL ACRYLATE (Terminal Kill During Month 24)</td></tr><tr><td>Dose in ppm</td><td>0</td><td>5</td><td>0.5</td><td></td></tr><tr><td>Number of rats per group^a</td><td>14</td><td>19</td><td>9</td><td></td></tr><tr><td>Number of rats in study</td><td>100</td><td>100</td><td>100</td><td></td></tr><tr><td colspan="5">URINARY SYSTEM (Continued)</td></tr><tr><td colspan="5">Progenital Tract</td></tr><tr><td>Diffuse hyperplasia of urinary bladder mucosa</td><td>2/14/14</td><td>0/19/19</td><td>0/9/9</td><td></td></tr><tr><td>Organized plug within lumen of urinary bladder</td><td>3/14/14</td><td>1/19/19</td><td>0/9/9</td><td></td></tr><tr><td colspan="5">REPRODUCTIVE SYSTEM</td></tr><tr><td colspan="5">Testis</td></tr><tr><td>Decreased spermatogenesis, one testis</td><td>1/14/14</td><td>0/19/19</td><td>0/9/9</td><td></td></tr><tr><td>Decreased spermatogenesis, both testes</td><td>2/14/14</td><td>1/19/19</td><td>0/9/9</td><td></td></tr><tr><td>Focal atrophy of seminiferous tubules</td><td>9/14/14</td><td>7/19/19^b</td><td>0/9/9</td><td></td></tr><tr><td>Vascular fibroid degeneration in the testes</td><td>8/14/14</td><td>17/19/19^b</td><td>0/9/9</td><td></td></tr><tr><td>Focal interstitial fibrosis of testicle</td><td>3/14/14</td><td>5/19/19</td><td>0/9/9</td><td></td></tr><tr><td>Interstitial cell tumor of testicle</td><td>1/14/14</td><td>2/19/19</td><td>0/9/9</td><td></td></tr><tr><td>Diffuse testicular atrophy</td><td>1/14/14</td><td>2/19/19</td><td>0/9/9</td><td></td></tr><tr><td colspan="5">Accessory Sex Glands</td></tr><tr><td>Decreased secretory content of accessory sex glands</td><td>11/14/14</td><td>10/19/19</td><td>0/9/9</td><td></td></tr><tr><td>Atrophy of accessory sex glands</td><td>2/14/14</td><td>5/19/19</td><td>0/9/9</td><td></td></tr><tr><td colspan="5">Data listed as number of observations/total number of tissues, organs, or masses examined microscopically/number of animals examined grossly.</td></tr><tr><td colspan="5">^aMicroscopic examination of all major organs limited to control and top dose group. Liver, kidney, lungs, nasal turbinates, thoracic lymph nodes, and all lesions grossly suggestive of tumor formation were examined from the low dose group.</td></tr><tr><td colspan="5">^bStatistically different from control by the Fisher Exact Probability test, p<0.05.</td></tr></table> | Table 5A | | | | | MICROSCOPIC OBSERVATIONS ON MALE RATS EXPOSED TO VAPORS OF 2-HYDROXYETHYL ACRYLATE (Terminal Kill During Month 24) | | | | | Dose in ppm | 0 | 5 | 0.5 | | Number of rats per group ^a | 14 | 19 | 9 | | Number of rats in study | 100 | 100 | 100 | | URINARY SYSTEM (Continued) | | | | | Progenital Tract | | | | | Diffuse hyperplasia of urinary bladder mucosa | 2/14/14 | 0/19/19 | 0/9/9 | | Organized plug within lumen of urinary bladder | 3/14/14 | 1/19/19 | 0/9/9 | | REPRODUCTIVE SYSTEM | | | | | Testis | | | | | Decreased spermatogenesis, one testis | 1/14/14 | 0/19/19 | 0/9/9 | | Decreased spermatogenesis, both testes | 2/14/14 | 1/19/19 | 0/9/9 | | Focal atrophy of seminiferous tubules | 9/14/14 | 7/19/19 ^b | 0/9/9 | | Vascular fibroid degeneration in the testes | 8/14/14 | 17/19/19 ^b | 0/9/9 | | Focal interstitial fibrosis of testicle | 3/14/14 | 5/19/19 | 0/9/9 | | Interstitial cell tumor of testicle | 1/14/14 | 2/19/19 | 0/9/9 | | Diffuse testicular atrophy | 1/14/14 | 2/19/19 | 0/9/9 | | Accessory Sex Glands | | | | | Decreased secretory content of accessory sex glands | 11/14/14 | 10/19/19 | 0/9/9 | | Atrophy of accessory sex glands | 2/14/14 | 5/19/19 | 0/9/9 | | Data listed as number of observations/total number of tissues, organs, or masses examined microscopically/number of animals examined grossly. | | | | | ^a Microscopic examination of all major organs limited to control and top dose group. 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| MICROSCOPIC OBSERVATIONS ON MALE RATS EXPOSED TO VAPORS OF 2-HYDROXYETHYL ACRYLATE (Terminal Kill During Month 24) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Dose in ppm | 0 | 5 | 0.5 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Number of rats per group ^a | 14 | 19 | 9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Number of rats in study | 100 | 100 | 100 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| URINARY SYSTEM (Continued) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Progenital Tract | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Diffuse hyperplasia of urinary bladder mucosa | 2/14/14 | 0/19/19 | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Organized plug within lumen of urinary bladder | 3/14/14 | 1/19/19 | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| REPRODUCTIVE SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Testis | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Decreased spermatogenesis, one testis | 1/14/14 | 0/19/19 | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Decreased spermatogenesis, both testes | 2/14/14 | 1/19/19 | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Focal atrophy of seminiferous tubules | 9/14/14 | 7/19/19 ^b | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Vascular fibroid degeneration in the testes | 8/14/14 | 17/19/19 ^b | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Focal interstitial fibrosis of testicle | 3/14/14 | 5/19/19 | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Interstitial cell tumor of testicle | 1/14/14 | 2/19/19 | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Diffuse testicular atrophy | 1/14/14 | 2/19/19 | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Accessory Sex Glands | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Decreased secretory content of accessory sex glands | 11/14/14 | 10/19/19 | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Atrophy of accessory sex glands | 2/14/14 | 5/19/19 | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Data listed as number of observations/total number of tissues, organs, or masses examined microscopically/number of animals examined grossly. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| ^a Microscopic examination of all major organs limited to control and top dose group. Liver, kidney, lungs, nasal turbinates, thoracic lymph nodes, and all lesions grossly suggestive of tumor formation were examined from the low dose group. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| ^b Statistically different from control by the Fisher Exact Probability test, p<0.05. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Table 6A | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| MICROSCOPIC OBSERVATIONS ON MALE RATS EXPOSED TO VAPORS OF 2-HYDROXYETHYL ACRYLATE (Terminal Kill During Month 24) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Dose in ppm | 0 | 5 | 0.5 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Number of rats per group ^a | 14 | 19 | 9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Number of rats in study | 100 | 100 | 100 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| URINARY SYSTEM (Continued) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Progenital Tract | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Diffuse hyperplasia of urinary bladder mucosa | 2/14/14 | 0/19/19 | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Organized plug within lumen of urinary bladder | 3/14/14 | 1/19/19 | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| REPRODUCTIVE SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Testis | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Decreased spermatogenesis, one testis | 1/14/14 | 0/19/19 | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Decreased spermatogenesis, both testes | 2/14/14 | 1/19/19 | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Focal atrophy of seminiferous tubules | 9/14/14 | 7/19/19 ^b | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Vascular fibroid degeneration in the testes | 8/14/14 | 17/19/19 ^b | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Focal interstitial fibrosis of testicle | 3/14/14 | 5/19/19 | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Interstitial cell tumor of testicle | 1/14/14 | 2/19/19 | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Diffuse testicular atrophy | 1/14/14 | 2/19/19 | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Accessory Sex Glands | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Decreased secretory content of accessory sex glands | 11/14/14 | 10/19/19 | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Atrophy of accessory sex glands | 2/14/14 | 5/19/19 | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Data listed as number of observations/total number of tissues, organs, or masses examined microscopically/number of animals examined grossly. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| ^a Microscopic examination of all major organs limited to control and top dose group. Liver, kidney, lungs, nasal turbinates, thoracic lymph nodes, and all lesions grossly suggestive of tumor formation were examined from the low dose group. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| ^b Statistically different from control by the Fisher Exact Probability test, p<0.05. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 病理組織学的所見(発生率、重篤度) | <table><tr><td colspan="5">Table 5B</td></tr><tr><td colspan="5">MICROSCOPIC OBSERVATIONS ON MALE RATS EXPOSED TO VAPORS OF 2-HYDROXYETHYL ACRYLATE (Terminal Kill During Month 24)</td></tr><tr><td>Dose in ppm</td><td>0</td><td>5</td><td>0.5</td><td></td></tr><tr><td>Number of rats per group^a</td><td>14</td><td>19</td><td>9</td><td></td></tr><tr><td>Number of rats in study</td><td>100</td><td>100</td><td>100</td><td></td></tr><tr><td colspan="5">CARDIOVASCULAR SYSTEM</td></tr><tr><td colspan="5">Heart</td></tr><tr><td>Focal myocardial degeneration and inflammation - slight</td><td>8/14/14</td><td>11/19/19</td><td>0/9/9</td><td></td></tr><tr><td>Focal myocardial degeneration and inflammation - moderate</td><td>3/14/14</td><td>5/19/19</td><td>0/9/9</td><td></td></tr><tr><td>Focal myocardial degeneration and inflammation - pronounced</td><td>1/14/14</td><td>0/19/19</td><td>0/9/9</td><td></td></tr><tr><td>Myocardial mineralization</td><td>1/14/14</td><td>0/19/19</td><td>0/9/9</td><td></td></tr><tr><td colspan="5">Aorta</td></tr><tr><td>Aortic mural mineralization</td><td>0/14/14</td><td>4/19/19</td><td>1/8/9</td><td></td></tr><tr><td>Thickening of endothelial lining of aorta</td><td>2/14/14</td><td>3/19/19</td><td>0/8/9</td><td></td></tr><tr><td colspan="5">Blood Vessels</td></tr><tr><td>Degeneration of myocardial blood vessels</td><td>10/14/14</td><td>14/19/19</td><td>0/9/9</td><td></td></tr><tr><td>Periarteritis and sclerosis of mesenteric blood vessels</td><td>6/14/14</td><td>7/19/19</td><td>2/2/9</td><td></td></tr><tr><td>Thrombosis and hematoma formation associated with mesenteric periarteritis</td><td>1/14/14</td><td>0/19/19</td><td>1/2/9</td><td></td></tr><tr><td>Mineralization of selected blood vessels</td><td>1/14/14</td><td>2/19/19</td><td>0/2/9</td><td></td></tr><tr><td>Wall thickening and thickening of mesenteric blood vessels</td><td>2/14/14</td><td>6/19/19</td><td>0/2/9</td><td></td></tr><tr><td>Congestion of myocardial vessels</td><td>1/14/14</td><td>0/19/19</td><td>0/9/9</td><td></td></tr><tr><td colspan="5">Data listed as number of observations/total number of tissues, organs, or masses examined microscopically/number of animals examined grossly.</td></tr><tr><td colspan="5">^aMicroscopic examination of all major organs limited to control and top dose group. 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| MICROSCOPIC OBSERVATIONS ON MALE RATS EXPOSED TO VAPORS OF 2-HYDROXYETHYL ACRYLATE (Terminal Kill During Month 24) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Dose in ppm | 0 | 5 | 0.5 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Number of rats per group ^a | 14 | 19 | 9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Number of rats in study | 100 | 100 | 100 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| CARDIOVASCULAR SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Heart | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Focal myocardial degeneration and inflammation - slight | 8/14/14 | 11/19/19 | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Focal myocardial degeneration and inflammation - moderate | 3/14/14 | 5/19/19 | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Focal myocardial degeneration and inflammation - pronounced | 1/14/14 | 0/19/19 | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Myocardial mineralization | 1/14/14 | 0/19/19 | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Aorta | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Aortic mural mineralization | 0/14/14 | 4/19/19 | 1/8/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Thickening of endothelial lining of aorta | 2/14/14 | 3/19/19 | 0/8/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Blood Vessels | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Degeneration of myocardial blood vessels | 10/14/14 | 14/19/19 | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Periarteritis and sclerosis of mesenteric blood vessels | 6/14/14 | 7/19/19 | 2/2/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Thrombosis and hematoma formation associated with mesenteric periarteritis | 1/14/14 | 0/19/19 | 1/2/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mineralization of selected blood vessels | 1/14/14 | 2/19/19 | 0/2/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Wall thickening and thickening of mesenteric blood vessels | 2/14/14 | 6/19/19 | 0/2/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Congestion of myocardial vessels | 1/14/14 | 0/19/19 | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Data listed as number of observations/total number of tissues, organs, or masses examined microscopically/number of animals examined grossly. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| ^a Microscopic examination of all major organs limited to control and top dose group. Liver, kidney, lungs, nasal turbinates, thoracic lymph nodes, and all lesions grossly suggestive of tumor formation were examined from the low dose group. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Table 6B | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| MICROSCOPIC OBSERVATIONS ON MALE RATS EXPOSED TO VAPORS OF 2-HYDROXYETHYL ACRYLATE (Terminal Kill During Month 24) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Dose in ppm | 0 | 5 | 0.5 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Number of rats per group ^a | 14 | 19 | 9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Number of rats in study | 100 | 100 | 100 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| CARDIOVASCULAR SYSTEM | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Heart | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Focal myocardial degeneration and inflammation - slight | 8/14/14 | 11/19/19 | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Focal myocardial degeneration and inflammation - moderate | 3/14/14 | 5/19/19 | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Focal myocardial degeneration and inflammation - pronounced | 1/14/14 | 0/19/19 | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Myocardial mineralization | 1/14/14 | 0/19/19 | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Aorta | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Aortic mural mineralization | 0/14/14 | 4/19/19 | 1/8/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Thickening of endothelial lining of aorta | 2/14/14 | 3/19/19 | 0/8/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Blood Vessels | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Degeneration of myocardial blood vessels | 10/14/14 | 14/19/19 | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Periarteritis and sclerosis of mesenteric blood vessels | 6/14/14 | 7/19/19 | 2/2/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Thrombosis and hematoma formation associated with mesenteric periarteritis | 1/14/14 | 0/19/19 | 1/2/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mineralization of selected blood vessels | 1/14/14 | 2/19/19 | 0/2/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Wall thickening and thickening of mesenteric blood vessels | 2/14/14 | 6/19/19 | 0/2/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Congestion of myocardial vessels | 1/14/14 | 0/19/19 | 0/9/9 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Data listed as number of observations/total number of tissues, organs, or masses examined microscopically/number of animals examined grossly. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| ^a Microscopic examination of all major organs limited to control and top dose group. Liver, kidney, lungs, nasal turbinates, thoracic lymph nodes, and all lesions grossly suggestive of tumor formation were examined from the low dose group. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

| 病理組織学的所見(発生率、重篤度) | <div>Table 7</div> <div>MICROSCOPIC OBSERVATIONS ON FEMALE RATS EXPOSED TO VAPORS OF 2-HYDROXYETHYL ACRYLATE (Terminal Kill After Month 24)</div> <table><tr><th>Dose in ppm</th><th>0</th><th>5</th><th>0.5</th></tr><tr><td>Number of rats per group^a</td><td>21</td><td>27</td><td>20</td></tr><tr><td>Number of rats in study</td><td>100</td><td>100</td><td>99</td></tr></table> <div>CARDIOVASCULAR SYSTEM</div> <div>Heart</div> <div>Focal myocardial degeneration and inflammation - slight</div> <div>Focal pericarditis</div> <div>7/21/21</div> <div>12/27/27</div> <div>0/1/20</div> <div>0/21/21</div> <div>1/27/27</div> <div>0/1/20</div> <div>Aorta</div> <div>Aortic mural mineralization</div> <div>Thickening of endothelial lining of aorta</div> <div>1/19/21</div> <div>1/27/27</div> <div>0/16/20</div> <div>3/19/21</div> <div>7/27/27</div> <div>2/16/20</div> <div>Blood Vessels</div> <div>Degeneration of myocardial blood vessels</div> <div>Periarteritis and sclerosis of mesenteric blood vessels</div> <div>Mineralization of selected blood vessels</div> <div>Fibrosis around blood vessel in thoracic adipose tissue</div> <div>1/21/21</div> <div>11/27/27^b</div> <div>0/1/20</div> <div>4/21/21</div> <div>1/27/27</div> <div>0/1/20</div> <div>1/21/21</div> <div>0/27/27</div> <div>0/20/20</div> <div>1/21/21</div> <div>0/27/27</div> <div>0/16/20</div> | Dose in ppm | 0 | 5 | 0.5 | Number of rats per group ^a | 21 | 27 | 20 | Number of rats in study | 100 | 100 | 99 |
|---------------------------------------|--|-------------|-----|---|-----|---------------------------------------|----|----|----|-------------------------|-----|-----|----|
| Dose in ppm | 0 | 5 | 0.5 | | | | | | | | | | |
| Number of rats per group ^a | 21 | 27 | 20 | | | | | | | | | | |
| Number of rats in study | 100 | 100 | 99 | | | | | | | | | | |

Data listed as number of observations/total number of tissues, organs, or masses examined microscopically/
number of animals examined grossly.

^aMicroscopic examination of all major organs limited to control and top dose group. Liver, kidney, lungs, nasal turbinates, thoracic lymph nodes, and all lesions grossly suggestive of tumor formation were examined from the low dose group.

^bStatistically different from control by the Fisher Exact Probability Test, p<0.05.

 Table 7 MICROSCOPIC OBSERVATIONS ON FEMALE RATS EXPOSED TO VAPORS OF 2-HYDROXYETHYL ACRYLATE (Terminal Kill After Month 24) | Dose in ppm | 0 | 5 | 0.5 | |---------------------------------------|-----|-----|-----| | Number of rats per group ^a | 21 | 27 | 20 | | Number of rats in study | 100 | 100 | 99 | CARDIOVASCULAR SYSTEM Heart Focal myocardial degeneration and inflammation - slight Focal pericarditis 7/21/21 12/27/27 0/1/20 0/21/21 1/27/27 0/1/20 Aorta Aortic mural mineralization Thickening of endothelial lining of aorta 1/19/21 1/27/27 0/16/20 3/19/21 7/27/27 2/16/20 Blood Vessels Degeneration of myocardial blood vessels Periarteritis and sclerosis of mesenteric blood vessels Mineralization of selected blood vessels Fibrosis around blood vessel in thoracic adipose tissue 1/21/21 11/27/27^b 0/1/20 4/21/21 2/27/27 0/1/20 1/21/21 0/27/27 0/20/20 1/21/21 0/27/27 0/16/20 Data listed as number of observations/total number of tissues, organs, or masses examined microscopically/ number of animals examined grossly. ^aMicroscopic examination of all major organs limited to control and top dose group. Liver, kidney, lungs, nasal turbinates, thoracic lymph nodes, and all lesions grossly suggestive of tumor formation were examined from the low dose group. ^bStatistically different from control by the Fisher Exact Probability Test, p<0.05. || 実際に摂取された量 | | |
| 腫瘍発生までの時間 | 腫瘍までの時間：統計解析では対照群と比べて良性腫瘍、悪性腫瘍又は全ての型の腫瘍を持つHEA暴露ラットの頻度の増加は示されず、一時的な腫瘍の発生率も対照群と比べて差はなかった。 | TIME TO TUMORS: Statistical analyses revealed no increases in the incidence of HEA exposed rats bearing benign neoplasms, malignant neoplasms or all types of neoplasms as compared to controls nor were there differences as compared to controls in the temporal occurrence of neoplasms. |
| 用量反応性 | | |
| 統計的結果 | | |
| 注釈 | | |
| 結論 | | |
| 実験動物における発がん性の有無 | 陰性 | negative |
| 注釈 | 注釈： 5 ppm に暴露した雄ラットの精巣の血管網のフィブリノイド変性の頻度の統計的に有意な増加はこの系統のラット (Sprague-Dawley, Spartan 亜系統)での加齢性病変としてみられる腸間膜動脈周囲炎の局所の血管の特徴であることが知られていた。この系統の対照群の加齢ラットにおいてこの研究所で行われた試験で共通してみられたこの病変は70年代半ばから後期にその使用中に試験で観察された頻度 (7つの慢性毒性/発がん性試験からの歴史的対照値は37-85%の範囲であった)と同様であった。 | Remark： The statistically significant increase in the incidence of fibrinoid degeneration of the vascular channels in the testes of male rats exposed to 5 ppm was known to be a local vascular manifestation of mesenteric periarteritis syndrome observed as age-related lesion in this rat strain (Sprague-Dawley, Spartan substrain). The laboratory conducting this study commonly observed this lesion in control aging rats of this strain at similar incidence as was observed in this study during it's period of use in the mid to late '70s (the incidence in historical controls in this period ranged from approximately 37 to 85% for seven chronic toxicity/oncogenicity studies) |
| 注釈 | 多発動脈炎 (多発性動脈炎又は結節性動脈周囲炎)はラットの血管の最も顕著な炎症性病変である。病因は不明で、頻度は系統とコロニーにより変動する (Mitsumori, K. (1990) Chapter 29 in Pathology of the Fischer Rat. Eds: Boorman et al., Academic Press, Inc. p 477)。雄ラットの共通部位は精巣の動脈であり、精索の動脈にも少ないがある(Burek, J.D. (1978) Pathology of the Aging Rat. CRC Press p. 87)。Carlton and Engelhardt (Polyarteritis, In: Cardiovascular and Musculoskeletal Systems Eds: Jones, T.C., Mohr, U. and Hunt, R.D., Springer-Verlag, 1991, p 71) もこの病変が精巣動脈に存在することを示している。 | Polyarteritis (polyarteritis or periarteritis nodosa) is the most conspicuous inflammatory lesion of the blood vessels of rats. The etiology is unknown and the incidence varies among strains and colonies (Mitsumori, K. (1990) Chapter 29 in Pathology of the Fischer Rat. Eds: Boorman et al., Academic Press, Inc. p 477). A common site in male rats are the arteries of the testicle and to a lesser extent the arteries of the spermatic cord (Burek, J.D. (1978) Pathology of the Aging Rat, CRC Press p. 87). Carlton and Engelhardt (Polyarteritis, In: Cardiovascular and Musculoskeletal Systems Eds: Jones, T.C., Mohr, U. and Hunt, R.D., Springer-Verlag, 1991, p 71) also indicate that this lesion can be present in spermatic arteries. |
| 注釈 | 結論： 本試験結果は2-HEAのラットによる慢性吸入は5 ppmで最初限度の毒性 (被毛の汚染及び慢性ネズミ肺炎の頻度及び重篤度の増加)のみ生じた。最終屠殺時に5 ppm群における雌ラットは対照群の動物と比べて子宮の炎症の頻度増加を示した。しかしながら、この他には卵巣を含めて雌の生殖器官の病理組織学的所見には統計的に有意な差はみられなかった。5 ppmに暴露した雄の動物の病理組織学的なデータの評価はこの系統のラットでは加齢性病変として観察される腸間膜動脈周囲炎の局所の血管の特徴をである精巣の血管網のフィブリノイド変性の頻度の増加を示した。この影響は対照群のラットにも存在した。 | Conclusion： The results of this study indicate that chronic inhalation of 2-HEA by rats produced only a minimal degree of toxicity at 5 ppm (haircoat staining and increased incidence and severity of chronic murine pneumonia). Female rats in the 5 ppm group at the terminal sacrifice showed an increased incidence of uterine inflammation as compared to the control animals. However, no other statistically significant differences for histopathological observations of the female reproductive organs were found, including the ovaries. An evaluation of the histopathological data from the male animals exposed to 5 ppm indicated an increased incidence of fibrinoid degeneration in the vascular channels of the testes which was a local vascular manifestation of mesenteric periarteritis syndrome observed as age-related lesion in this rat strain. This effect was also present in the control rats. |

| | | |
|-----------|---|--|
| 注釈 | 試験の病理担当者及び主任の著者による雌雄の生殖器官における病理組織学的所見の最近の総説の中で、精巣のフィブリノイド変性は物質に特異的なHEAの毒性影響であるとは考えがたく、子宮の影響は2-HEAの生殖毒性の可能性を示唆するものとは考えられなかった。すなわち、NOAELは0.5 ppmであり、本試験では2-HEAはいずれの暴露群においても生殖毒性の可能性も発がん性を示すという証拠もなかった。 以下に上記の結果の節にあげた表を示す。 | In a recent review of the histopathological findings in male and female reproductive organs by the study pathologist and principal author, the fibrinoid degeneration in the testes was not considered to be a substance-specific toxic effect of HEA and the effects in the uterus were not considered indicative of a reproductive toxicity potential for 2-HEA. In summary, the NOAEL was 0.5 ppm and there was no evidence in this study that 2-HEA has the potential for reproductive toxicity or an oncogenic effect in either of the exposure groups. Following are the tables referenced in the Results section, above. |
| 信頼性 | (2) 制限付きで信頼性あり | (2) valid with restrictions |
| 信頼性の判断根拠 | 一般的に受入れられる科学的基準に合致し、良好に文書化され、評価に受入れられる。 試験開始時の群当たりの動物数は慢性毒性/発がん性の現行ガイドラインで規定された数の2倍であった。 | Meets generally accepted scientific standards, well-documented and acceptable for assessment. The number of animals per group at the start of the study was twice the number specified in current guidelines for chronic toxicity/carcinogenicity studies. |
| 出典 | | |
| 引用文献(元文献) | (105) | (105) |
| 備考 | フラグ : SIDSエンドポイントにとって重要な試験 | Flag : Critical study for SIDS endpoint |

5-9 生殖・発生毒性(受胎能と発生毒性を含む)
REPRODUCTIVE TOXICITY(Including Fertility and Development Toxicity)

A. 受胎能
FERTILITY

B. 発生毒性
DEVELOPMENTAL TOXICITY

| | | |
|--------------|---|---|
| 試験物質名 | 他のTS | other TS |
| CAS番号 | | |
| 純度等 | 試験物質はガスクロマトグラフィーで純度が95.8%と報告されており、Rohm (ドイツ)から入手した。 | The test material was received from Rohm (Germany) with a reported purity of 95.8% by gas chromatography. |
| 注釈 | | |
| 方法 | | |
| 方法/ガイドライン | その他: 僅かな逸脱を含むが、OPPTS 870.3700 と一致 | other: consistent with OPPTS 870.3700 with minor exceptions |
| GLP適合 | データなし | no data |
| 試験を行った年 | 1999 | 1999 |
| 試験系(種/系統) | ラット Sprague-Dawley | rat Sprague-Dawley |
| 性別(雄:M、雌:F) | 雌 | female |
| 投与量 | 1、5 又は 10 ppm | 1, 5 or 10 ppm |
| 各用量群(性別)の動物数 | | |
| 投与経路 | 吸入 | inhalation |
| 試験期間 | 21日間 | 21 days |
| 交配前暴露期間 | | |
| 試験条件 | 暴露期間 : 6時間/日 処理頻度 : 妊娠6-20日 対照群 : あり、無処置対照群 | Exposure period : 6 hours/day Frequency of treatm. : during days 6 to 20 of gestation Control group : yes, concurrent no treatment |
| 試験条件 | ※英文参照 | TEST ORGANISMS -Age: Young, nulliparous females -Weight at study initiation: 200-220g -Number of animals: groups of 20-29 bred female rats (19-22 pregnant) ADMINISTRATION/EXPOSURE -Route: inhalation -Concentrations: The analytical concentrations were 1.1+/-0.1, 5.0+/-0.6 and 10.6+/-1.4 for the 1, 5 and 10 ppm groups as measured by gas chromatography. Control animals were exposed concurrently to filtered room air in an adjacent chamber with characteristics identical to those of the treatment groups. |

| | | |
|------------------------|-------|---|
| 試験条件 | ※英文参照 | -Exposures: Exposures were conducted in 200-L glass/stainless-steel inhalation chambers with dynamic and adjustable laminar air flow (6-20m ³ /hour). 2-hydroxyethyl acrylate was delivered with an infusion pump, a constant rate of liquid chemical from the top of a heated glass column filled with glass beads. Compressed air heated by a glass heater was introduced at the bottom of the glass column in a countercurrent fashion to the liquid flow. Concentrations were monitored continuously with a gas chromatograph equipped with a flame ionization detector and an automatic gas-sampling valve. In addition, exposure levels were determined once during each 6-hour exposure period by collecting atmosphere samples through glass tubes packed with activated charcoal. Samples were then desorbed with dichloromethane and analyzed by gas chromatography. |
| 試験条件 | ※英文参照 | SATELLITE GROUPS AND REASONS THEY WERE ADDED: none MATING PROCEDURES: Females were housed overnight with adult males (one male:two or three females) from the same strain and supplier. The day that vaginal smears were found to be sperm-positive was considered day 0 of gestation. |
| 試験条件 | ※英文参照 | PARAMETERS ASSESSED DURING STUDY: -Body weight/body weight gain: Maternal body weights were recorded on GD 0, 6, 13 and 21. -Food consumption: Food consumption was recorded on GD 0-6, 6-13, and 13-21. -Clinical observations performed and frequency: Parent: no data Fetus: no data -Examination of uterine content: Uteri were removed and weighed, and the number of implantation sites, resorptions, and dead and live fetuses were recorded. Uteri which had no visible implantation sites were stained with ammonium sulfide to detect very early resorptions. |
| 試験条件 | ※英文参照 | -Examination of fetuses: Live fetuses were weighed, sexed, and examined for external anomalies including those of the oral cavity. Half of the live fetuses from each litter were preserved in Bouin's solution and examined for internal soft tissue changes. The other half were fixed in ethanol, eviscerated, and then processed for skeletal staining with alizarin red S for subsequent skeletal examination. -Organs examined at necropsy: Parent: none Fetus: see results table |
| 統計学的処理 | ※英文参照 | STATISTICAL METHODS: Data were presented as mean +/- SD. The number of implantation sites and live fetuses and the various body weights were analyzed by one-way analysis of variance (ANOVA), followed by Dunnett's test if differences were found. The percentages of non-live implants and resorptions and the proportions of fetuses with alterations in each litter were evaluated by using the Kruskal-Wallis test, followed by the Dixon-Massey test where appropriate. Rates of pregnancy, fetal sex ratio, and percentage of litters with malformations or external, visceral, or skeletal variations were analyzed by using Fisher's test. Where applicable, least-squares analysis was carried out. For all statistical tests, the level of significance was set a priori at alpha=0.05. |
| 結果 | | |
| 死亡数(率)、死亡時間 | | |
| 用量あたり妊娠数 | | |
| 流産数 | | |
| 早期/後期吸収数 | | |
| 着床数 | | |
| 黄体数 | | |
| 妊娠期間(妊娠0日から起算) | | |
| 体重、体重増加量 | | |
| 摂餌量、飲水量 | | |
| 臨床所見(重篤度、所見の発現時期と持続時間) | | |
| 血液学的所見(発生率、重篤度) | | |
| 血液生化学的所見(発生率、重篤度) | | |
| 剖検所見(発生率、重篤度) | | |
| 臓器重量(総子宮量への影響) | | |
| 病理組織学的所見(発生率、重篤度) | | |
| 同腹仔数及び体重 | | |
| 生存数(生存胎仔数及び胎仔数) | | |
| 性比 | | |

| | | |
|-----------------------|--|--|
| 生存率(生後4日目生存仔数/総分娩仔数) | | |
| 生後発育 | | |
| 分娩後生存率 | | |
| 肉眼的異常(外表観察、内臓標本、骨格標本) | | |
| 実際に投与された量 | | |
| 用量反応性 | | |
| 統計的結果 | | |
| 注釈 | 用量レベルごとの母動物の毒性影響: - 死亡率及び死亡日: なし - 体重/体重増加量: 母動物の体重増加量は妊娠6-21日に減少し、10 ppmのHEAに暴露した動物では妊娠6-13日に対照群より統計的に減少したとして検出された。また、絶対重量増加[(21日の体重)-(妊娠子宮重量)-(6日の体重)]の減少が10 ppmで統計的に確認された。 | MATERNAL TOXIC EFFECTS BY DOSE LEVEL: -Mortality and day of death: none -Body weight/body weight gain: Maternal body weight gain was decreased through GD 6-21 and statistically identified as decreased from controls on GD 6-13 for animals exposed to 10 ppm HEA. In addition, decreases in absolute weight gain [(Day 21 body weight)-(gravid uterus weight)-(Day 6 body weight)] was statistically identified at 10 ppm. |
| 注釈 | 実験 母動物 体重BW 妊娠中の体重増加量(g) 絶対濃度 数 妊娠6日 6-13 13-21 6-21 重量増加(g) 0 21 262±18 29±9 105±15 134±17 34±15 1 19 261±16 23±13 113±34 135±36 31±6 5 22 264±18 25±6 109±20 134±21 29±14 10 21 263±21 22±7* 98±15 120±19 15±14** *** 対照群(0 ppm)の値と統計的に有意差あり、それぞれp<0.05、及びp<0.01 | Exp. No. of BW BW gain (g) on GD Absolute Conc. Dams GD 6 6-13 13-21 6-21 wt gain(g) 0 21 262±18 29±9 105±15 134±17 34±15 1 19 261±16 23±13 113±34 135±36 31±6 5 22 264±18 25±6 109±20 134±21 29±14 10 21 263±21 22±7* 98±15 120±19 15±14** *** Significant differences from control (0 ppm) value, p<0.05, and p<0.01, respectively |
| 注釈 | - 摂餌量: 10 ppmでは全暴露期間(妊娠6-21日)に対して、軽度であるが統計的に有意な摂餌量の減少がみられた。 実験 母動物 妊娠中の摂餌量 (g/母動物/日) 濃度 数 0-6 6-13 13-21 6-21 0 21 24±2 22±2 28±2 25±2 1 19 23±2 22±2 28±3 25±2 5 22 23±2 22±2 28±2 25±2 10 21 24±2 20±2** 25±2** 23±2** ** 対照群(0 ppm)の値と有意差あり、p<0.01. | -Food consumption: A slight but statistically significant decrease in food consumption was seen at 10 ppm for the entire exposure period (GD 6-21). Exp No. of Food Consumption (g/dam/day) on GD Conc. Dams 0-6 6-13 13-21 6-21 0 21 24±2 22±2 28±2 25±2 1 19 23±2 22±2 28±3 25±2 5 22 23±2 22±2 28±2 25±2 10 21 24±2 20±2** 25±2** 23±2** ** Significant difference from control (0 ppm) value, p<0.01. |
| 注釈 | -着床及び吸収胚: 着床数及び生存胎児数、非生存着床胚及び吸収胚の頻度には有意な変化はみられなかった。 着床した腹 実験 雌の 腹の 着床 % 濃度 数 数 部位 非生存 吸収部位 0 23 21 14.71±2.53 10.93±13.99 10.93±13.99 1 23 19 15.00±3.27 8.93±22.70 8.93±22.70 5 23 22 14.91±2.62 7.63±11.02 7.63±11.02 10 22 21 15.33±1.53 6.52±6.73 6.52±6.73 | -Implantations and resorptions: There were no significant changes in the numbers of implantations and live fetuses, incidence of non-live implants and resorptions. Litters with implants Exp. No. of No. of No. of sites/litter % of non-live % of resorptions Conc. females litters sites/litter implants/litter sites/litter 0 23 21 14.71±2.53 10.93±13.99 10.93±13.99 1 23 19 15.00±3.27 8.93±22.70 8.93±22.70 5 23 22 14.91±2.62 7.63±11.02 7.63±11.02 10 22 21 15.33±1.53 6.52±6.73 6.52±6.73 |
| 注釈 | 胎児のデータ: -胎児体重: 群間で胎児の体重には有意な変化はなかった。 生存胎児を有する腹 実験 腹の 生存 平均の胎児体重(g)/腹 濃度 数 数 全体 雄 雌 0 21 13.05±2.91 5.68±0.32 5.83±0.41 5.55±0.31 1 18 14.61±2.79 5.71±0.27 5.85±0.27 5.52±0.31 5 22 13.82±2.94 5.69±0.32 5.84±0.34 5.50±0.31 10 21 14.33±1.80 5.54±0.25 5.64±0.28 5.43±0.25 | FETAL DATA: -Fetal body weights: There were no significant changes in the fetal body weights across groups. Litters with Live Fetuses Exp. No. of fetuses/ Average Fetal Body Weight (g)/litter Conc. litters litter All Males Females 0 21 13.05±2.91 5.68±0.32 5.83±0.41 5.55±0.31 1 18 14.61±2.79 5.71±0.27 5.85±0.27 5.52±0.31 5 22 13.82±2.94 5.69±0.32 5.84±0.34 5.50±0.31 10 21 14.33±1.80 5.54±0.25 5.64±0.28 5.43±0.25 |
| 注釈 | 生存胎児を有する腹 胎児の性比 実験 腹の 性比 濃度 数 雄:雌 0 21 0.93 1 18 1.31 5 22 1.19 10 21 1.06 | Litters with live fetuses Fetal sex ratio Exp. No. of Ratio Conc. litters M:F 0 21 0.93 1 18 1.31 5 22 1.19 10 21 1.06 |

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|--|---|----------------|--------------|----------|---|-------|---------|----------|----------|----------|----------|--------------------|----------|----------|----------|-----------|-------------------|-------------|-------------|-------------|-------------|--|-------------|----------------|--------------|--|---|------------|----------|----------|----------|----------|-----------------------------|----------|----------|----------|----------|---------------------------------------|-------------|-------------|-------------|-------------|--|----------|----------|----------|-------------|--|---------------|----------------|---|---|
| 注釈 | <p>-胎児の奇形：観察された唯一の奇形は1ppmでの片側性の小眼症であった。外表、内臓、又は骨格の変異の頻度に有意な変化はなかった。T</p> <p>胎児における奇形及び変異の頻度 (a)</p> <p>検査した胎児の総数(腹数)</p> <table><tr><td>実験濃度</td><td>0</td><td>1</td><td>5</td><td>10</td></tr><tr><td>外表</td><td>274 (21)</td><td>263 (18)</td><td>304 (22)</td><td>301 (21)</td></tr><tr><td>内臓</td><td>137 (21)</td><td>132 (18)</td><td>152 (22)</td><td>150 (21)</td></tr><tr><td>骨格</td><td>137 (21)</td><td>131 (18)</td><td>152 (22)</td><td>151 (21)</td></tr></table> | 実験濃度 | 0 | 1 | 5 | 10 | 外表 | 274 (21) | 263 (18) | 304 (22) | 301 (21) | 内臓 | 137 (21) | 132 (18) | 152 (22) | 150 (21) | 骨格 | 137 (21) | 131 (18) | 152 (22) | 151 (21) | <p>-Fetal malformations: The only malformation observed was a unilateral microphthalmia at 1 ppm. There were no significant changes in the incidence of external, visceral, or skeletal variations.</p> <p>Incidence of Malformations and Variations in Fetuses (a)</p> <p>Total No. fetuses (litters) examined</p> <table><tr><td>Exp. Conc.</td><td>0</td><td>1</td><td>5</td><td>10</td></tr><tr><td>External</td><td>274 (21)</td><td>263 (18)</td><td>304 (22)</td><td>301 (21)</td></tr><tr><td>Visceral</td><td>137 (21)</td><td>132 (18)</td><td>152 (22)</td><td>150 (21)</td></tr><tr><td>Skeletal</td><td>137 (21)</td><td>131 (18)</td><td>152 (22)</td><td>151 (21)</td></tr></table> | Exp. Conc. | 0 | 1 | 5 | 10 | External | 274 (21) | 263 (18) | 304 (22) | 301 (21) | Visceral | 137 (21) | 132 (18) | 152 (22) | 150 (21) | Skeletal | 137 (21) | 131 (18) | 152 (22) | 151 (21) | | | | | | | | | | |
| 実験濃度 | 0 | 1 | 5 | 10 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 外表 | 274 (21) | 263 (18) | 304 (22) | 301 (21) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 内臓 | 137 (21) | 132 (18) | 152 (22) | 150 (21) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 骨格 | 137 (21) | 131 (18) | 152 (22) | 151 (21) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Exp. Conc. | 0 | 1 | 5 | 10 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| External | 274 (21) | 263 (18) | 304 (22) | 301 (21) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Visceral | 137 (21) | 132 (18) | 152 (22) | 150 (21) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Skeletal | 137 (21) | 131 (18) | 152 (22) | 151 (21) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 注釈 | <p>奇形(b)</p> <table><tr><td>実験濃度</td><td>0</td><td>1</td><td>5</td><td>10</td></tr><tr><td>小眼(片側性)</td><td>0</td><td>1 (1)</td><td>0</td><td>0</td></tr><tr><td>いずれかの奇形を有する胎児数 (%)</td><td>0</td><td>1 (0.4)</td><td>0</td><td>0</td></tr><tr><td>いずれかの奇形を有する腹数 (%)</td><td>0</td><td>1 (5.5)</td><td>0</td><td>0</td></tr><tr><td>いずれかの奇形を有する胎児の平均 %/腹</td><td>0</td><td>0.40+/-1.68(c)</td><td>0</td><td>0</td></tr></table> | 実験濃度 | 0 | 1 | 5 | 10 | 小眼(片側性) | 0 | 1 (1) | 0 | 0 | いずれかの奇形を有する胎児数 (%) | 0 | 1 (0.4) | 0 | 0 | いずれかの奇形を有する腹数 (%) | 0 | 1 (5.5) | 0 | 0 | いずれかの奇形を有する胎児の平均 %/腹 | 0 | 0.40+/-1.68(c) | 0 | 0 | <p>Malformations(b)</p> <table><tr><td>Exp. Conc.</td><td>0</td><td>1</td><td>5</td><td>10</td></tr><tr><td>Microphthalmia (unilateral)</td><td>0</td><td>1 (1)</td><td>0</td><td>0</td></tr><tr><td>No. (%)fetuses with any malformations</td><td>0</td><td>1 (0.4)</td><td>0</td><td>0</td></tr><tr><td>No. (%) litters with any malformations</td><td>0</td><td>1 (5.5)</td><td>0</td><td>0</td></tr><tr><td>Mean % fetuses with any malformations/litter</td><td>0</td><td>0.40+/-1.68(c)</td><td>0</td><td>0</td></tr></table> | Exp. Conc. | 0 | 1 | 5 | 10 | Microphthalmia (unilateral) | 0 | 1 (1) | 0 | 0 | No. (%)fetuses with any malformations | 0 | 1 (0.4) | 0 | 0 | No. (%) litters with any malformations | 0 | 1 (5.5) | 0 | 0 | Mean % fetuses with any malformations/litter | 0 | 0.40+/-1.68(c) | 0 | 0 |
| 実験濃度 | 0 | 1 | 5 | 10 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 小眼(片側性) | 0 | 1 (1) | 0 | 0 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| いずれかの奇形を有する胎児数 (%) | 0 | 1 (0.4) | 0 | 0 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| いずれかの奇形を有する腹数 (%) | 0 | 1 (5.5) | 0 | 0 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| いずれかの奇形を有する胎児の平均 %/腹 | 0 | 0.40+/-1.68(c) | 0 | 0 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Exp. Conc. | 0 | 1 | 5 | 10 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Microphthalmia (unilateral) | 0 | 1 (1) | 0 | 0 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| No. (%)fetuses with any malformations | 0 | 1 (0.4) | 0 | 0 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| No. (%) litters with any malformations | 0 | 1 (5.5) | 0 | 0 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mean % fetuses with any malformations/litter | 0 | 0.40+/-1.68(c) | 0 | 0 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 注釈 | <p>外表の変異</p> <p>口蓋 (粘膜皺の奇形)</p> <table><tr><td>0</td><td>1 (1)</td><td>0</td><td>0</td></tr></table> <p>こぶ状の肢 (片側性)</p> <table><tr><td>1 (1)</td><td>0</td><td>1 (1)</td><td>2 (2)</td></tr></table> <p>外表奇形を有する胎児の数 (%)</p> <table><tr><td>1 (0.4)</td><td>1 (0.4)</td><td>1 (0.3)</td><td>2 (0.7)</td></tr></table> <p>外表の変異を有する胎児の数 (%)</p> <table><tr><td>1 (4.8)</td><td>1 (5.6)</td><td>1 (4.5)</td><td>2 (9.5)</td></tr></table> <p>外表の変異を有する胎児の平均 %/腹</p> <table><tr><td>0.37+/-1.68</td><td>0.40+/-1.68</td><td>0.28+/-1.33</td><td>0.62+/-1.97</td></tr></table> | 0 | 1 (1) | 0 | 0 | 1 (1) | 0 | 1 (1) | 2 (2) | 1 (0.4) | 1 (0.4) | 1 (0.3) | 2 (0.7) | 1 (4.8) | 1 (5.6) | 1 (4.5) | 2 (9.5) | 0.37+/-1.68 | 0.40+/-1.68 | 0.28+/-1.33 | 0.62+/-1.97 | <p>External variations</p> <p>Palate (rugae mishappen)</p> <table><tr><td>0</td><td>1 (1)</td><td>0</td><td>0</td></tr></table> <p>Club foot (unilateral)</p> <table><tr><td>1 (1)</td><td>0</td><td>1 (1)</td><td>2 (2)</td></tr></table> <p># (%) fetuses with external variations</p> <table><tr><td>1 (0.4)</td><td>1 (0.4)</td><td>1 (0.3)</td><td>2 (0.7)</td></tr></table> <p># (%) litters with external variations</p> <table><tr><td>1 (4.8)</td><td>1 (5.6)</td><td>1 (4.5)</td><td>2 (9.5)</td></tr></table> <p>Mean % fetuses with external variations/litter</p> <table><tr><td>0.37+/-1.68</td><td>0.40+/-1.68</td><td>0.28+/-1.33</td><td>0.62+/-1.97</td></tr></table> | 0 | 1 (1) | 0 | 0 | 1 (1) | 0 | 1 (1) | 2 (2) | 1 (0.4) | 1 (0.4) | 1 (0.3) | 2 (0.7) | 1 (4.8) | 1 (5.6) | 1 (4.5) | 2 (9.5) | 0.37+/-1.68 | 0.40+/-1.68 | 0.28+/-1.33 | 0.62+/-1.97 | | | | | | | | | | |
| 0 | 1 (1) | 0 | 0 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 1 (1) | 0 | 1 (1) | 2 (2) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 1 (0.4) | 1 (0.4) | 1 (0.3) | 2 (0.7) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 1 (4.8) | 1 (5.6) | 1 (4.5) | 2 (9.5) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 0.37+/-1.68 | 0.40+/-1.68 | 0.28+/-1.33 | 0.62+/-1.97 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 0 | 1 (1) | 0 | 0 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 1 (1) | 0 | 1 (1) | 2 (2) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 1 (0.4) | 1 (0.4) | 1 (0.3) | 2 (0.7) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 1 (4.8) | 1 (5.6) | 1 (4.5) | 2 (9.5) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 0.37+/-1.68 | 0.40+/-1.68 | 0.28+/-1.33 | 0.62+/-1.97 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 注釈 | <p>内臓の変異</p> <p>腎盂拡張</p> <table><tr><td>0</td><td>0</td><td>2 (2)</td><td>0</td></tr></table> <p>水尿管 (片側性)</p> <table><tr><td>0</td><td>0</td><td>2 (2)</td><td>0</td></tr></table> <p>尿管拡張</p> <table><tr><td>5 (3)</td><td>7 (5)</td><td>19 (8)</td><td>15 (6)</td></tr></table> <p>内臓の変異を有する胎児の数 (%)</p> <table><tr><td>5 (3.6)</td><td>7 (5.3)</td><td>19 (12.5)</td><td>15 (10.0)</td></tr></table> <p>内臓の変異を有する腹の数 (%)</p> <table><tr><td>3 (14.3)</td><td>5 (27.8)</td><td>8 (36.4)</td><td>6 (28.6)</td></tr></table> <p>腹当たりの内臓変異を有する胎児の平均 %</p> <table><tr><td>3.26+/-9.12</td><td>5.16+/-9.33</td><td>12.21+/-19.56</td><td>9.48+/-19.22</td></tr></table> | 0 | 0 | 2 (2) | 0 | 0 | 0 | 2 (2) | 0 | 5 (3) | 7 (5) | 19 (8) | 15 (6) | 5 (3.6) | 7 (5.3) | 19 (12.5) | 15 (10.0) | 3 (14.3) | 5 (27.8) | 8 (36.4) | 6 (28.6) | 3.26+/-9.12 | 5.16+/-9.33 | 12.21+/-19.56 | 9.48+/-19.22 | <p>Visceral variations</p> <p>Dilated renal pelvis</p> <table><tr><td>0</td><td>0</td><td>2 (2)</td><td>0</td></tr></table> <p>Hydroureter (unilateral)</p> <table><tr><td>0</td><td>0</td><td>2 (2)</td><td>0</td></tr></table> <p>Distended ureter</p> <table><tr><td>5 (3)</td><td>7 (5)</td><td>19 (8)</td><td>15 (6)</td></tr></table> <p># (%) fetuses with visceral variations</p> <table><tr><td>5 (3.6)</td><td>7 (5.3)</td><td>19 (12.5)</td><td>15 (10.0)</td></tr></table> <p># of litters with visceral variations</p> <table><tr><td>3 (14.3)</td><td>5 (27.8)</td><td>8 (36.4)</td><td>6 (28.6)</td></tr></table> <p>Mean % fetuses with visceral variations per litter</p> <table><tr><td>3.26+/-9.12</td><td>5.16+/-9.33</td><td>12.21+/-19.56</td><td>9.48+/-19.22</td></tr></table> | 0 | 0 | 2 (2) | 0 | 0 | 0 | 2 (2) | 0 | 5 (3) | 7 (5) | 19 (8) | 15 (6) | 5 (3.6) | 7 (5.3) | 19 (12.5) | 15 (10.0) | 3 (14.3) | 5 (27.8) | 8 (36.4) | 6 (28.6) | 3.26+/-9.12 | 5.16+/-9.33 | 12.21+/-19.56 | 9.48+/-19.22 | | |
| 0 | 0 | 2 (2) | 0 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 0 | 0 | 2 (2) | 0 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 5 (3) | 7 (5) | 19 (8) | 15 (6) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 5 (3.6) | 7 (5.3) | 19 (12.5) | 15 (10.0) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 3 (14.3) | 5 (27.8) | 8 (36.4) | 6 (28.6) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 3.26+/-9.12 | 5.16+/-9.33 | 12.21+/-19.56 | 9.48+/-19.22 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 0 | 0 | 2 (2) | 0 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 0 | 0 | 2 (2) | 0 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 5 (3) | 7 (5) | 19 (8) | 15 (6) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 5 (3.6) | 7 (5.3) | 19 (12.5) | 15 (10.0) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 3 (14.3) | 5 (27.8) | 8 (36.4) | 6 (28.6) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 3.26+/-9.12 | 5.16+/-9.33 | 12.21+/-19.56 | 9.48+/-19.22 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 注釈 | <p>骨格の変異</p> <p>頭蓋骨</p> <p>頭頂骨、骨化不全、軽度</p> <table><tr><td>0</td><td>0</td><td>1 (1)</td><td>0</td></tr></table> <p>舌骨、骨化不全</p> <table><tr><td>0</td><td>0</td><td>0</td><td>2 (2)</td></tr></table> <p>第5胸骨、骨化不全又は未骨化 (d)</p> <table><tr><td>12 (8)</td><td>4 (3)</td><td>5 (4)</td><td>3 (3)</td></tr></table> <p>肋骨</p> <p>頸肋骨、痕跡</p> <table><tr><td>1 (1)</td><td>2 (2)</td><td>0</td><td>0</td></tr></table> <p>第14肋骨、過剰</p> <table><tr><td>7 (4)</td><td>6 (3)</td><td>16 (7)</td><td>6 (5)</td></tr></table> <p>第13肋骨、短縮</p> <table><tr><td>0</td><td>1 (1)</td><td>0</td><td>1 (1)</td></tr></table> | 0 | 0 | 1 (1) | 0 | 0 | 0 | 0 | 2 (2) | 12 (8) | 4 (3) | 5 (4) | 3 (3) | 1 (1) | 2 (2) | 0 | 0 | 7 (4) | 6 (3) | 16 (7) | 6 (5) | 0 | 1 (1) | 0 | 1 (1) | <p>Skeletal variations</p> <p>Skull</p> <p>Parietals, incomplete ossification, slight</p> <table><tr><td>0</td><td>0</td><td>1 (1)</td><td>0</td></tr></table> <p>Hyoid, incomplete ossification</p> <table><tr><td>0</td><td>0</td><td>0</td><td>2 (2)</td></tr></table> <p>5th sternbra, incomplete ossification or unossified (d)</p> <table><tr><td>12 (8)</td><td>4 (3)</td><td>5 (4)</td><td>3 (3)</td></tr></table> <p>Rib(s)</p> <p>Cervical, rudimentary</p> <table><tr><td>1 (1)</td><td>2 (2)</td><td>0</td><td>0</td></tr></table> <p>14th, supernumerary</p> <table><tr><td>7 (4)</td><td>6 (3)</td><td>16 (7)</td><td>6 (5)</td></tr></table> <p>13th, short</p> <table><tr><td>0</td><td>1 (1)</td><td>0</td><td>1 (1)</td></tr></table> | 0 | 0 | 1 (1) | 0 | 0 | 0 | 0 | 2 (2) | 12 (8) | 4 (3) | 5 (4) | 3 (3) | 1 (1) | 2 (2) | 0 | 0 | 7 (4) | 6 (3) | 16 (7) | 6 (5) | 0 | 1 (1) | 0 | 1 (1) | | |
| 0 | 0 | 1 (1) | 0 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 0 | 0 | 0 | 2 (2) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 12 (8) | 4 (3) | 5 (4) | 3 (3) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 1 (1) | 2 (2) | 0 | 0 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 7 (4) | 6 (3) | 16 (7) | 6 (5) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 0 | 1 (1) | 0 | 1 (1) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 0 | 0 | 1 (1) | 0 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 0 | 0 | 0 | 2 (2) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 12 (8) | 4 (3) | 5 (4) | 3 (3) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 1 (1) | 2 (2) | 0 | 0 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 7 (4) | 6 (3) | 16 (7) | 6 (5) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 0 | 1 (1) | 0 | 1 (1) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

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|--------------------------------------|---|--|
| 注釈 | <p>胸椎及び/又は腰椎中心、骨化不全 (1箇所から3箇所) 10 (6) 12 (8) 18 (11) 12 (10) 骨格変異を有する胎児の数 (%) 28 (20.4) 23 (17.6) 38 (25.0) 22 (14.6) 骨格変異を有する腹の数 (%) 11 (52.4) 12 (66.7) 16 (72.7) 13 (61.9) 骨格変異を有する胎児の平均 % / 腹 19.37±22.58 18.77±19.53 25.05±25.55 14.76±13.58 いずれかの変異を有する胎児の数 (%) 34 (12.4) 31 (11.8) 57 (18.7) 39 (13.0) いずれかの変異を有する腹の数 (%) 13 (61.9) 13 (72.2) 17 (77.3) 16 (76.2) いずれかの変異を有する胎児の平均 % / 腹 11.60±12.10 12.49±12.85 18.49±15.00 13.02±12.79 (a) 個別の異常の頻度は胎児数 (腹の数)として表されている。 生存胎児のみが検査された。1匹の胎児は個別の異常を掲載 する際には1回以上示されている。 (b) 1 ppm群の胎児1匹は小眼と口蓋の贅の奇形を有してい た。 (c) 平均値 +/-SD (d) 未骨化: アリザリン赤染色で陰性</p> | <p>Thoracic and/or lumbar vertebral centra. incomplete ossification (one to three) 10 (6) 12 (8) 18 (11) 12 (10) # (%) fetuses with skeletal variations 28 (20.4) 23 (17.6) 38 (25.0) 22 (14.6) # (%) litters with skeletal variations 11 (52.4) 12 (66.7) 16 (72.7) 13 (61.9) Mean % fetuses with skeletal variations /litter 19.37±22.58 18.77±19.53 25.05±25.55 14.76±13.58 # (%) fetuses with any variations 34 (12.4) 31 (11.8) 57 (18.7) 39 (13.0) # (%) litters with any variations 13 (61.9) 13 (72.2) 17 (77.3) 16 (76.2) Mean % fetuses with any variations /litter 11.60±12.10 12.49±12.85 18.49±15.00 13.02±12.79 (a) The incidence of individual defect is presented as number of fetuses (number of litters). Only live fetuses were examined. A single fetus may be represented more than once in listing individual defects. (b) One fetus in the 1 ppm group had mcrophthalmia and misshappen palate ruggae. (c) Mean +/-SD (d) Unossified: alizarin red S negative</p> |
| 結論 | | |
| PIに対するNOAEL (NOEL)又は LOAEL (LOEL) | NOAEL 母動物毒性 : = 5 ppm | NOAEL maternal tox. : = 5 ppm |
| F1に対するNOAEL (NOEL)又は LOAEL (LOEL) | NOAEL 催奇形性 : = 10 ppm | NOAEL teratogen. : = 10 ppm |
| F2に対するNOAEL (NOEL)又は LOAEL (LOEL) | | |
| 注釈 | 結果: 陰性 | Result : negative |
| 注釈 | <p>結論 : 10 ppmのHEAへの暴露は明瞭な母動物毒性を生じた。これは 暴露中の体重変化の一過性減少、絶対重量増加量、及び摂餌 量の連続的な減少により証拠づけられた。HEAの5 ppmに暴露 した動物では母動物毒性の影響はなかった。母動物毒性のある 程度の証拠があったが、有害な発生影響は認められなかつ た。従って、発生毒性に対するNOAELはHEAの >= 10 ppmで あった。</p> | <p>Conclusion : Exposure to 10 ppm HEA caused overt maternal toxicity. This was evidenced by a transient decrease in body weight changes, a decrease in absolute weight gain and a continuous reduction of food consumption during exposure. There were no effects in maternal toxicity in animals exposed to 5 ppm HEA. The NOAEL for maternal toxicity was 5 ppm. Although there were some evidence of maternal toxicity, no adverse developmental effects were noted. Therefore, the NOAEL for developmental toxicity was >= 10 ppm for HEA</p> |
| 信頼性 | (2) 制限付きで信頼性あり | (2) valid with restrictions |
| 信頼性の判断根拠 | 一般的に受入れられる科学的基準に合致し、良好に文書化さ れ、評価に受入れられる。 | Meets generally accepted scientific standards, well- documented and acceptable for assessment. |
| 出典 | | |
| 引用文献(元文献) | (106) | (106) |
| 備考 | フラグ : SIDSエンドポイントにとって重要な試験 | Flag : Critical study for SIDS endpoint |

5-10その他関連情報
OTHER RELEVANT INFOMATION

5-11 ヒト暴露の経験
EXPEIENCE WITH HUMAN EXPOSURE

| | | |
|-------------|---------------------|---|
| 試験物質名 | | |
| CAS番号 | | |
| 純度等 | | |
| 注釈 | | |
| 製造/加工/使用情報 | | |
| 研究デザイン | 経験のタイプ : ヒト - 医療データ | Type of experience : Human - Medical Data |
| 仮説検証 | | |
| データ収集方法 | | |
| 被験者の説明 | | |
| 暴露期間 | | |
| 測定又は評価曝露データ | | |
| 結果 | | |
| 統計的結果 | | |
| 発病頻度 | | |
| 相関 | | |
| 分布 | | |
| 研究提供者等 | | |

| | | |
|-----------|---|--|
| 注釈 | <p>結果：(メタ)アクリル酸に対するパッチテストの15年間試験 1993年1月から1998年3月までの(約14,000例)接触性皮膚炎調査部門の全パッチテスト記録の後ろ向き評価が行われた。パッチテスト及びスコアリングは2日間の閉塞によるScanporテープ上のFinnチャンバーを用いて患者の背中で行った。2-HEAは0.5%濃度で適用した。2及び4日に反応を評価した。</p> <p>GLP - データなし 試験した2-HEAは陽性。試験した250名の患者のうち、24名でアレルギー症状 (9.6%)。</p> | <p>Result : A 15-Year Study of Patch Testing to (Meth)Acrylates A retrospective appraisal of all patch test records from the Contact Dermatitis Investigation Unit from between January 1983 and March 1998 (approximately 14,000 records) was conducted. Patch testing and scoring were performed on the back of patients using Finn Chambers on Scanpor tape, with an occlusion time of 2 days. 2-HEA was applied at a 0.5% concentration. Reactions were assessed at 2 and 4 days.</p> <p>GLP- no data 2-HEA tested positive, 24 allergic/250 patients tested (9.6%).</p> |
| 結論 | | |
| 結論 | | |
| 注釈 | | |
| 信頼性 | (2) 制限付きで信頼性あり | (2) valid with restrictions |
| 信頼性の判断根拠 | | |
| 出典 | | |
| 引用文献(元文献) | (107) | (107) |
| 備考 | | |

| | | |
|-------------|--|---|
| 試験物質名 | | |
| CAS番号 | | |
| 純度等 | | |
| 注釈 | | |
| 製造／加工／使用情報 | | |
| 研究デザイン | 経験のタイプ：ヒト - 医療データ | Type of experience : Human - Medical Data |
| 仮説検証 | | |
| データ収集方法 | | |
| 被験者の説明 | | |
| 暴露期間 | | |
| 測定又は評価曝露データ | | |
| 結果 | | |
| 統計的結果 | | |
| 発病頻度 | | |
| 相関 | | |
| 分布 | | |
| 研究提供者等 | | |
| 注釈 | <p>結果：</p> <p>FIOH で1975-1995年にアクリル酸化合物により生じたアレルギー</p> <p>1990年代にアクリル酸化合物に暴露された履歴を持つ124名の患者が通常のパッチ試験法によりパッチテストを受けた。2-HEAは0.1-0.5% (w/w)の範囲で投与された。</p> <p>一人の化粧品の専門家が感光性接着剤で装飾した爪で職業的に感作された。感光性接着剤を施した爪に使用した爪のゲルはGC/MS分析に基づき、アクリル酸メチル0.3%、アクリル酸ヒドロキシエチル2%、アクリル酸トリプロピレングリコール0.3%及びジアクリル酸トリプロピレングリコール8%を含んでいた。これらの成分がそれぞれパッチテストされた。</p> <p>GLP- データなし 23名の患者が少なくとも1つの陽性パッチテスト反応を示した (Kanerva L., Estlander T., Jolanki R. and Tarvainen K. Statistics on allergic patch test reactions caused by acrylate compounds, including data on ethyl methacrylate. Am J Contact Dermatitis 1995;6:1-4.)。2-HEAは頻繁に陽性を示した3つのアクリル酸化合物の一つで、124名の患者のうち14名で陽性であった。</p> <p>感光性接着剤処理した爪に用いた爪用ゲルのアクリル酸ヒドロキシエチルの成分はワセリン中0.32%の濃度で投与した場合に2+のパッチテストスコアを示した。</p> | <p>Result :</p> <p>Allergy Caused by Acrylate Compounds at the FIOH 1975-1995</p> <p>In the 1990's, 124 patients with a history of exposure to acrylate compounds were patch tested with conventional patch test techniques. 2-HEA was administered at a range of 0.1-0.5% (w/w).</p> <p>A cosmetologist became occupationally sensitized from photobonded sculptured nails. The nail gel used for the photobonded nails contained 0.3% methyl acrylate, 2% hydroxyethyl acrylate, 0.3% tripropylene glycol acrylate and 8% tripropylene glycol diacrylate based on GC/MS analysis. Each of these components was patch tested.</p> <p>GLP- no data Twenty-three patients showed at least one positive patch test reaction (Kanerva L., Estlander T., Jolanki R. and Tarvainen K. Statistics on allergic patch test reactions caused by acrylate compounds, including data on ethyl methacrylate. Am J Contact Dermatitis 1995;6:1-4.) 2-HEA was one of three acrylate compounds most often positive and tested positive in 14 of 124 patients.</p> <p>The hydroxyethyl acrylate component of the nail gel used for the photobonded nails resulted in a patch test score of 2+ when administered at a concentration of 0.32% in pet.</p> |
| 結論 | | |
| 結論 | | |
| 注釈 | | |
| 信頼性 | (2) 制限付きで信頼性あり | (2) valid with restrictions |
| 信頼性の判断根拠 | | |
| 出典 | | |
| 引用文献(元文献) | (108) | (108) |
| 備考 | | |

| | | |
|------------|-------------------|---|
| 試験物質名 | | |
| CAS番号 | | |
| 純度等 | | |
| 注釈 | | |
| 製造／加工／使用情報 | | |
| 研究デザイン | 経験のタイプ：ヒト - 医療データ | Type of experience : Human - Medical Data |
| 仮説検証 | | |
| データ収集方法 | | |
| 被験者の説明 | | |
| 暴露期間 | | |

| | | |
|-------------|---|---|
| 測定又は評価曝露データ | | |
| 結果 | | |
| 統計的結果 | | |
| 発病頻度 | | |
| 相関 | | |
| 分布 | | |
| 研究提供者等 | | |
| 注釈 | <p>結果：(メタ)アクリル酸への暴露の履歴を持つ合計275名の患者での1985-1995年の間の(メタ)アクリル酸のシリーズによる10年間パッチ試験が0.1-0.5%の2-HEAを用いてパッチ試験が行われた。パッチテスト及び採点法は以前に述べた[1]Estlander, T. (1990). Occupational skin disease in Finland. Observations made during 1974-1988 at the Institute of Occupational Health, Helsinki. Acta Dermato-venerologica 1990: (suppl 155): 1-85 and 2)Jolanki R. (1991). Occupational skin disease from epoxy compounds. Acta Dermato-venerologica 1991: (suppl 159):1-80]ように、1ないし2日、背中に閉塞適して行った。</p> <p>GLP- データなし</p> <p>試験したアクリル酸のうち、2-HEAが最も頻度高くアレルギー性のパッチテスト反応を誘発した。試験した132人の患者のうち、16名の患者、又は12.1%がアレルギー反応を示した。</p> | <p>Result : 10 Years of Patch Testing with the (Meth)Acrylate Series During 1985-1995, a total of 275 patients with a history of exposure to (meth)acrylates were patch tested with 0.1-0.5% 2-HEA. Patch testing and scoring were performed on the back with an occlusion time of 1 or 2 days as previously described [1]Estlander, T. (1990). Occupational skin disease in Finland. Observations made during 1974-1988 at the Institute of Occupational Health, Helsinki. Acta Dermato-venerologica 1990: (suppl 155): 1-85 and 2)Jolanki R. (1991). Occupational skin disease from epoxy compounds. Acta Dermato-venerologica 1991: (suppl 159):1-80].</p> <p>GLP- no data</p> <p>Of the acrylates tested, 2-HEA most often provoked an allergic patch test reaction. Sixteen patients had an allergic reaction out of 132 patients tested or 12.1%.</p> |
| 結論 | | |
| 結論 | | |
| 注釈 | | |
| 信頼性 | (2) 制限付きで信頼性あり | (2) valid with restrictions |
| 信頼性の判断根拠 | | |
| 出典 | | |
| 引用文献(元文献) | (109) | (109) |
| 備考 | | |

6 参考文献(以下に欄を追加の上、一文献について一行にて一覧を記載)

| 文献番号(半角数字: 自動的に半角になります) | 詳細(OECD方式での記入をお願いします。下の記入例参照。) |
|-------------------------|---|
| 1 | All synonyms from the Hazardous Substances Data Bank (HSDB) |
| 2 | Lacson, J.G., Lochner, U. and Toki, G. Acrylic Acid and Esters Chemical Economics Handbook Marketing Research Report, August, 2004. SRI Consulting. |
| 3 | Rapport Insake Grenswarde 2-Hydroxyethylacrylaat Gezondheidskundig Advies Van De Werkgroep Van Deskundigen Ter Vaststelling Van De MAC-Waarden Directoraat-Generaal Van De Arbeid, RA13/87 |
| 4 | TRGS 900 und 905 von 4/1995 |
| 5 | DFG (Deutsche Forschungsgemeinschaft); MAK- und BAT-Werte-Liste 1997; Senatskommission zur Prüfung gesundheitsschädlicher Arbeitsstoffe (Mitteilung 33); VCH Verlagsgesellschaft mbH, Weinheim (1997); ISBN: 3-527-27576-2 |
| 6 | SZW; De Nationale MAC-lijst 1995; P 145, De Haag (1995); ISBN 90-399-0819-2 |
| 7 | Arbejdstilsynet, At-anvisning Nr. 3.1.0.2, Direktoratet for Arbejdstilsynet, Kobenhavn (1996) |
| 8 | AFS (Arbetsarkyddsstyrelsens Forfattningssamling), Hygieniska Gransvarden, AFS 1996: 2, Stockholm (1996); ISBN: 91-7930-306-4 |
| 9 | BASF AG, Sicherheitsdatenblatt Hydroxyethylacrylat (15.09.1995) |
| 10 | DIMDI Deutsches Institut fuer Medizinische Dokumentation und Information (09.07.1993); File: HSDB Hazardous Substances Data Bank (Last-update 30.04.1993); source: SRC |
| 11 | Rohm GmbH, product information FA 201, 2-Hydroxyethyl acrylate (July 1997) |
| 12 | R. L. Rowley, W. V. Wilding, J. L. Oscarson, Y. Yang, N. A. Zundel, T. E. Daubert, R. P. Danner, DIPPR® Data Compilation of Pure Chemicals Properties, Design Institute for Physical Properties, AIChE, New York, NY (2004). Data from Hazardous Chemicals Data Book, Noyes Data Corporation Park Ridge, New Jersey (1980). |
| 13 | Dow Product Stewardship Manual (October 2002). |
| 14 | Hazardous Chemicals Data Book, Noyes Data Corporation, Park Ridge, New Jersey (1980). Accepted experimental value cited in: R. L. Rowley, W. V. Wilding, J. L. Oscarson, Y. Yang, N. A. Zundel, T. E. Daubert, R. P. Danner, DIPPR® Data Compilation of Pure Chemicals Properties, Design Institute for Physical Properties, AIChE, New York, NY (2004). |
| 15 | Safety Data Sheet, Dow Europe S.A., Rev. 2/95 |
| 16 | Dow Product Stewardship Manual (October, 2002) |
| 17 | Othmer, D.F., Yu, E., "Correlating Vapor Pressures and Vapor Volumes," Ind. Eng. Chem., 60, 22 (1968). Experimental Data cited in: R. L. Rowley, W. V. Wilding, J. L. Oscarson, Y. Yang, N. A. Zundel, T. E. Daubert, R. P. Danner, DIPPR® Data Compilation of Pure Chemicals Properties, Design Institute for Physical Properties, AIChE, New York, NY (2004). |
| 18 | Dow Product Stewardship Manual (October, 2002) Castille, M.J. (1981) Vapor Pressure Data Hydroxyethyl Acrylat (HEA) and Hydroxypropyl Acrylate (HPA) by a Microcalorimetric Technique. Unpublished report of The Dow Chemical Company. |
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