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

1. 一般情報
GENERAL INFOMATION
1.01 物質情報
SUBSTANCE INFOMATION

CAS番号	111-42-2	111-42-2
物質名(日本語名)	ジエタノールアミン	
物質名(英名)		2,2'-iminodiethanol
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	C4 H11 N O2	C4 H11 N O2
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 INFOMATION

機関名	OECD/HPVプログラム(SIAM24)により収集された情報 (http://cs3-hq.oecd.org/scripts/hpv/)	OECD/HPV Program, SIDS Dossier, assessed at SIAM 24-APR-2007 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:英国	Sponsor Country: United Kingdom

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 INFOMATION

物質のタイプ	有機物	organic
物質の色・におい・形状等の情報	色:無色から黄色 臭い:感知できる臭い	Colour : colourless to yellow Odour : perceptible
物理的状態(20℃、1013hPa)	固体	solid
純度(重量/重量%)	>= 99.3 - % w/w	>= 99.3 - % w/w
出典	(2)	(2)
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	一般工業での製造比率: トリエタノールアミン 37%; モノエタノールアミン 32%; ジエタノールアミン 31%. [R3]	General industry production ratios are: Triethanolamine 37%; Monoethanolamine 32%; Diethanolamine 31%. [R3]
報告年		
出典	(4)	(4)
備考	Source : R3: CHEMICAL PROFILE: ETHANOLAMINE, 1984	Source : R3: CHEMICAL PROFILE: ETHANOLAMINE, 1984

1.6 用途情報
USE PATTERN

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	(11)	(11)
備考	英文参照	Production of: Technical emulsions, boot polish, cleaning agents

主な用途情報	用途タイプ:使用 カテゴリ:吸収剤や吸着剤	Type of use : use Category : Absorbents and adsorbents
工業的用途		
用途分類		
出典	(1) (2)	(1) (2)
備考	ガス集塵機の吸着剤	Gas scrubber absorption aid

1.7 環境および人への暴露情報
SOURCES OF EXPOSURE

1.8 追加情報
ADDITIONAL INFOMATION

2. 物理化学的性状
PHYSICAL CHEMICAL DATA
2.1 融点
MELTING POINT

試験物質名	1.1 - 1.4に規定	as prescribed by 1.1 - 1.4
CAS番号		
純度等		
注釈	キースタディ	key study
方法	BASF standard	BASF standard
GLP	いいえ	no
試験を行った年	1985	1985
試験条件		
結果		
融点: ℃	27.4 ° C	27.4 ° C
分解: ℃		
昇華: ℃		
	DEAの融点 (w/o 水): +27.40 ° C	melting point of DEA (w/o water): +27.40 ° C
結論		
注釈	様々なDEA水溶液の融点: w DEA + (1-w) H2O t/° C 1 +27.40 +/- 0.05 0.98 +27.04 +/- 0.05 0.90 +2.33 +/- 0.1 0.50 -25.7 +/- 0.1 0.30 -9.3 +/- 0.1 0.20 -4.9 +/- 0.1 0.10 -2.5 +/- 0.1 w = DEA 部分	melting point of various aqueous solutions of DEA: w DEA + (1-w) H2O t/° C 1 +27.40 +/- 0.05 0.98 +27.04 +/- 0.05 0.90 +2.33 +/- 0.1 0.50 -25.7 +/- 0.1 0.30 -9.3 +/- 0.1 0.20 -4.9 +/- 0.1 0.10 -2.5 +/- 0.1 w = DEA portion
信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions
信頼性の判断根拠	実験データ、基本情報あり	Experimentally derived data, basic data given
出典	(27) (28) (29)	(27) (28) (29)
引用文献		
備考	フラグ : 化学品安全性データセット、SIDSエンドポイントに重要な試験、キースタディ	Flag : Material Safety Dataset, Critical study for SIDS endpoint, key study

試験物質名	2,2'-イミノジエタノール、純品	2,2'-iminodiethanol, pure
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	2003	2003
試験条件		
結果		
融点: ℃	27.8 - 28 ° C	27.8 - 28 ° C
分解: ℃		
昇華: ℃		
結論		
注釈		
信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions
信頼性の判断根拠	ピアレビューされたデータベース	Peer-reviewed database
出典	(30)	(30)
引用文献		
備考		

2.2 沸点
BOILING POINT

試験物質名	2,2'-イミノジエタノール、純品	2,2'-iminodiethanol, pure
CAS番号		
純度等		
注釈		
方法	その他	other
GLP	データなし	no data
試験を行った年	2003	2003
試験条件		
結果		
沸点: ℃	268 - 271 ° C	268 - 271 ° C
圧力	1013 hPa	1013 hPa
分解: ℃		
結論		
注釈	公開されている値の範囲 (n=18): 温度 圧力 (° C) (hPa) 129 15.9 134 4.0 142 19.9 144 - 145 8.0 154 - 158 13.3 167 - 169 19.9 217 - 218 199.9 268 - 271 996.9 - 1013 キースタディ	Range of published values (n=18): Temperature Pressure (° C) (hPa) 129 15.9 134 4.0 142 19.9 144 - 145 8.0 154 - 158 13.3 167 - 169 19.9 217 - 218 199.9 268 - 271 996.9 - 1013 key study

信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions
信頼性の判断根拠	ピアレビューされたデータベース	Peer-reviewed database
出典	(30)	(30)
引用文献		
備考	フラグ：化学品安全性データセット、SIDSエンドポイントに重要な試験、キースタディ	Flag : Material Safety Dataset, Critical study for SIDS endpoint, key study

試験物質名	ジエタノールアミン、純品	Diethanolamine, pure
CAS番号		
純度等		
注釈		
方法	DIN 51007による	following DIN 51007
GLP	いいえ	no
試験を行った年		
試験条件		
結果		
沸点： ℃	>= 270 ° C	>= 270 ° C
圧力	1013 hPa	1013 hPa
分解： ℃	はい	yes
	オンセット-温度 (=分解開始温度): 270 ° C 最大ピーク温度 (=最大分解点): 365 ° C 放出されたエネルギー: >390 J/g	onset-temperature (=decomposition starting point): 270 ° C maximum peak temperature (=max. decomposition): 365 ° C released energy: >390 J/g
結論		
注釈		
信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions
信頼性の判断根拠	基本情報あり	basic data given
出典	(40)	(40)
引用文献		
備考		

2.3 密度（比重）
DENSITY（RELATIVE DENSITY）

試験物質名	2,2'-イミノジエタノール、純度 > 99.9 %	2,2'-iminodiethanol, purity > 99.9 %
CAS番号		
純度等		
注釈		
方法	BASF standard	BASF standard
GLP	いいえ	no
試験を行った年	1985	1985
試験条件		
結果	1.0953 g/cm³	1.0953 g/cm³
タイプ	密度	density
温度(℃)	23.8 ° C	23.8 ° C
注釈	温度 (° C) 密度Density (g/cm³) 測定値 計算値 23.8 1.0953 1.095 30 1.0910 1.0913 40 1.0851 1.084 50 1.0784 1.0785 60 1.0721 1.0719 70 1.0648 1.0653 80 1.0585 1.0585 100 1.0446 1.0445 120 1.0305 1.0300 130 1.0222 1.0226 140 1.10152 1.0151 160 0.9997 0.9997 キースタディ	Temperature (° C) Density (g/cm³) measured calculated 23.8 1.0953 1.095 30 1.0910 1.0913 40 1.0851 1.0849 50 1.0784 1.0785 60 1.0721 1.0719 70 1.0648 1.0653 80 1.0585 1.0585 100 1.0446 1.0445 120 1.0305 1.0300 130 1.0222 1.0226 140 1.10152 1.0151 160 0.9997 0.9997 key study
信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions
信頼性の判断根拠	科学的に受容可能、実験データ、基本データあり	scientifically acceptable, experimental data, basic data given
出典	(29)	(29)
引用文献		
備考	フラグ：化学品安全性データセット、SIDSエンドポイントに重要な試験、キースタディ	Flag : Material Safety Dataset, Critical study for SIDS endpoint, key study

試験物質名	2,2'-イミノジエタノール、純品	2,2'-iminodiethanol, pure
CAS番号		
純度等		
注釈		
方法	その他	other
GLP	データなし	no data
試験を行った年	2003	2003
試験条件		
結果	1.055 - 1.106 g/cm³	1.055 - 1.106 g/cm³
タイプ	密度	density
温度(℃)		
注釈	公開されている値の範囲 (n=10): 密度 (g/cm³) 温度 (° C) 1.055 - 1.106 10 - 80	Range of published values (n=10): Density (g/cm³) Temperature (° C) 1.055 - 1.106 10 - 80
信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions

信頼性の判断根拠	ピアレビューされたデータベース	Peer-reviewed database
出典	(30)	(30)
引用文献		
備考		

2.4 蒸気圧
VAPOUR PRESSURE

試験物質名	2,2'-イミノジエタノール、純品	2,2'-iminodiethanol, pure
CAS番号		
純度等		
注釈		
方法	その他(測定)	other (measured)
GLP	データなし	no data
試験を行った年	2006	2006
試験条件		
結果		
蒸気圧	.0028 hPa	.0028 hPa
温度: ℃	25 ° C	25 ° C
分解: ℃		
結論		
注釈	キースタディ	key study
信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions
信頼性の判断根拠	信頼できるデータベース	Reliable database
出典	(33)	(33)
引用文献		
備考	フラグ:化学品安全性データセット、SIDSエンドポイントに重要な試験、キースタディ	Flag : Material Safety Dataset, Critical study for SIDS endpoint, key study

試験物質名	2,2'-イミノジエタノール、純品	2,2'-iminodiethanol, pure
CAS番号		
純度等		
注釈		
方法	その他(測定)	other (measured)
GLP	いいえ	no
試験を行った年		
試験条件		
結果		
蒸気圧	.0002 hPa	.0002 hPa
温度: ℃	20 ° C	20 ° C
分解: ℃		
結論		
注釈		
信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions
信頼性の判断根拠	ピアレビューされたデータベース	Peer-reviewed database
出典	(43)	(43)
引用文献		
備考		

2.5 分配係数(log Kow)
PARTITION COEFFICIENT

試験物質名	2,2'-イミノジエタノール、純品	2,2'-iminodiethanol, pure
CAS番号		
純度等		
注釈	オクタノール/水分配係数	Partition coefficient : octanol-water
方法	OECD ガイドライン 107 "分配係数 (n-オクタノール/水), フラスコ振とう法"	OECD Guide-line 107 "Partition Coefficient (n-octanol/water), Flaskshaking Method"
GLP	いいえ	no
試験を行った年	1991	1991
試験条件	pH : = 7.2	pH value : = 7.2
結果		
Log Kow	-2.18	-2.18
温度: ℃	25 ° C	25 ° C
結論	試料の秤量 (A) (B) Pow log Pow 1. 0.0128 1.856 0.0069 -2.16 2. 0.0220 3.504 0.0063 -2.20 (A = DEA濃度 (g/l): オクタノール相; B = DEA濃度 (g/l): 緩衝液相; Pow = A/B)	Weighted samples (A) (B) Pow log Pow 1. 0.0128 1.856 0.0069 -2.16 2. 0.0220 3.504 0.0063 -2.20 (A = DEA conc. (g/l): octanol-phase; B = DEA conc. (g/l): puffer-phase; Pow = A/B)
注釈	英文参照	According to literature (Rekker RF, The hydrophobic fragmental constant, Elsevier, 1977) log Pow = -1.43 for not buffered mixture. pKa-value = 8.99 according to titrimetric determination. key study
信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions
信頼性の判断根拠	良く記載されたガイドライン試験、一般に認められている科学的原則に合致	guideline study, well documented, meets generally accepted scientific principles
出典	(46)	(46)
引用文献		
備考	フラグ:化学品安全性データセット、SIDSエンドポイントに重要な試験、キースタディ	Flag : Material Safety Dataset, Critical study for SIDS endpoint, key study

試験物質名	2,2'-イミノジエタノール、純品	2,2'-iminodiethanol, pure
CAS番号		
純度等		
注釈	オクタノール/水分配係数	Partition coefficient : octanol-water
方法	英文参照	Increment method according to the method of Rekker with the computer program from CompuDrug Ltd.
GLP		
試験を行った年		
試験条件		
結果		
Log Kow	-1.767	-1.767
温度: ℃		
結論		
注釈	Log Pow 計算値: -1.767 Log Pow 測定値: -1.43	Log Pow calculated: -1.767 Log Pow measured: -1.43
信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions
信頼性の判断根拠	科学的に受け入れられる方法	Scientifically acceptable method
出典	(47)	(47)
引用文献		
備考		

2.6.1 水溶解性(解離定数を含む)

WATER SOLUBILITY & DISSOCIATION CONSTANT

試験物質名	2,2'-イミノジエタノール、純品	2,2'-iminodiethanol, pure
CAS番号		
純度等		
注釈	水溶解度	Solubility in : Water
方法	その他	other
GLP	データなし	no data
試験を行った年	2005	2005
試験条件		
結果		
水溶解度		
温度: ℃		
pH		
pH測定時の物質濃度		
結論	混和	miscible
注釈	キースタディ	key study
信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions
信頼性の判断根拠	信頼できるハンドブック	Reliable handbook
出典	(34)	(34)
引用文献		
備考	フラグ:化学品安全性データセット、SIDSエンドポイントに重要な試験、キースタディ	Flag : Material Safety Dataset, Critical study for SIDS endpoint, key study
解離定数		
試験物質		
同一性		
方法		
温度: ℃		
GLP		
試験条件		
試験を行った年	1980	1980
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		

試験物質名	その他の試験物質	other TS
CAS番号		
純度等		
注釈	水溶解度	Solubility in : Water
方法	その他	other
GLP	いいえ	no
試験を行った年		
試験条件		
結果		
水溶解度	1E6 mg/l	1E6 mg/l
温度: ℃	20 ° C	20 ° C
pH		
pH測定時の物質濃度		
結論		
注釈	データベース中の水溶解度の実験値: reference: DOW Chemical Company, 1980	Experimental Water solubility database match: reference: DOW Chemical Company, 1980
信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions
信頼性の判断根拠	信頼できるデータベース	Reliable database
出典	(33)	(33)
引用文献		
備考		
解離定数		
試験物質		
同一性		
方法		

温度:　℃		
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		

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		
温度:　℃		
pH		
pH測定時の物質濃度		
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		
解離定数		
試験物質	2,2'-イミノジエタノール、純品	2,2'-iminodiethanol, pure
同一性		
方法	その他	other
温度:　℃		
GLP	いいえ	no
試験条件		
試験を行った年	2006	2006
結果	pKa　温度 (° C) 9.55　0 8.92　23 8.632　35	pKa　temperature (° C) 9.55　0 8.92　23 8.632　35
結論	酸-塩基 定数 : pka 8.92	Acid-base constant : pka 8.92
注釈	pKa データベースとの一致: SPARC v3.1, 2007年1月リリース. 元文献: IUPAC/Perrin 122, 4060 キースタディ	pKa database match: SPARC v3.1, January 2007 release. Original reference: IUPAC/Perrin 122, 4060 key study
信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions
信頼性の判断根拠	信頼できるデータベース	Reliable database
出典	(33)	(33)
引用文献		
備考	フラグ:化学品安全性データセット、SIDSエンドポイントに重要な試験、キースタディ	Flag : Material Safety Dataset, Critical study for SIDS endpoint, key study

2.6.2 表面張力
SURFACE TENSION

試験物質名	その他の試験物質	other TS
CAS番号		
純度等	> 99.9 %	> 99.9 %
注釈	試験タイプ : Plate法	Test type : Plate method
方法	BASF 標準試験法	BASF standard test method
GLP	いいえ	no
試験を行った年	1985	1985
試験条件		
結果		
表面張力	47.7　mN/m	47.7　mN/m
温度:　℃	23.8 ° C	23.8 ° C
濃度:　mg/L	100 vol%	100 vol%
結論		
注釈	温度　表面張力 (° C)　(mN/m) 23.8　47.7 30　47.4 50　46.2 70　44.7 100　42.3 130　39.7	Temperature Surface tension (° C)　(mN/m) 23.8　47.7 30　47.4 50　46.2 70　44.7 100　42.3 130　39.7
信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions
信頼性の判断根拠	基本データあり	basic data given
出典	(29)	(29)
引用文献		
備考		

試験物質名	2,2'-イミノジエタノール、純品	2,2'-iminodiethanol, pure
CAS番号		
純度等		
注釈	試験タイプ：その他	Test type : other
方法	その他	other
GLP	データなし	no data
試験を行った年	2003	2003
試験条件		
結果		
表面張力	45.15 - 48.71 mN/m	45.15 - 48.71 mN/m
温度： ℃		
濃度： mg/L	100 vol%	100 vol%
結論		
注釈	公開されている値の範囲 (n=1): 表面張力 温度 (mN/m) (° C) 45.15 - 48.71 30 - 70	Range of published values (n=1): Surface tension Temperature (mN/m) (° C) 45.15 - 48.71 30 - 70
信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions
信頼性の判断根拠	ピアレビューされたデータベース	Peer-reviewed database
出典	(30)	(30)
引用文献		
備考		

2.7 引火点（液体）
FLASH POINT(LIQUIDS)

試験物質名	2,2'-イミノジエタノール、純品	2,2'-iminodiethanol, pure
CAS番号		
純度等		
注釈		
方法	その他	other
GLP	データなし	no data
試験を行った年	2006	2006
試験条件		
結果		
引火点： ℃	134 ° C	134 ° C
試験のタイプ	開放式	open cup
結論		
注釈		
信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions
信頼性の判断根拠	ピアレビューされたデータベース	Peer-reviewed database
出典	(51) (52)	(51) (52)
引用文献		
備考		

試験物質名	2,2'-イミノジエタノール、純度: >99.9%	2,2'-iminodiethanol, purity: >99.9%
CAS番号		
純度等		
注釈		
方法	その他	other
GLP	いいえ	no
試験を行った年	2006	2006
試験条件		
結果		
引火点： ℃	134 ° C	134 ° C
試験のタイプ	開放式	open cup
結論		
注釈		
信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions
信頼性の判断根拠	権威ある2次情報源	authoritative secondary source
出典	(39)	(39)
引用文献		
備考		

2.8 自己燃焼性 （固体／気体）
AUTO FLAMMABILITY(SOLIDS/GASES)

試験物質名	2,2'-イミノジエタノール、純品	2,2'-iminodiethanol, pure
CAS番号		
純度等		
注釈		
方法	その他	other
GLP	データなし	no data
試験を行った年	2005	2005
試験条件		
結果		
自動発火点： ℃	335 ° C	335 ° C
圧力		
結論		
注釈		
信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions
信頼性の判断根拠	権威あるデータベース	authoritative data base
出典	(35)	(35)
引用文献		
備考		

試験物質名	2,2'-イミノジエタノール、純品	2,2'-iminodiethanol, pure
CAS番号		
純度等		
注釈		
方法	その他	other
GLP	いいえ	no
試験を行った年	2005	2005
試験条件		
結果		
自動発火点: ℃	365 ° C	365 ° C
圧力		
結論		
注釈		
信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions
信頼性の判断根拠	ハンドブック	handbook
出典	(34)	(34)
引用文献		
備考		

2.9 引火性
FLAMMABILITY

試験物質名	2,2'-イミノジエタノール、純品	2,2'-iminodiethanol, pure
CAS番号		
純度等		
注釈		
方法	その他	other
GLP	いいえ	no
試験を行った年	1998	1998
試験条件		
結果		
固体の場合	自然発火性でない、引火性ガスを発生しない	not pyrophoric, does not develop readily inflammable gases
引火性が高い		
気体の場合		
水との接触		
結論		
注釈	この物質は引火特性を示す化学構造を持たない。この記述は国連の試験とクライテリアマニュアルの附属書6にある推奨事項に合致する。	substance has no chemical groups indicating flammable properties. This statement agrees with the recommendations of appendix 6 in the Manual of Tests and criteria of the United Nations.
信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions
信頼性の判断根拠	専門家判断	Expert judgement
出典	(55)	(55)
引用文献		
備考		

試験物質名	2,2'-イミノジエタノール、純品	2,2'-iminodiethanol, pure
CAS番号		
純度等		
注釈		
方法	その他	other
GLP	データなし	no data
試験を行った年	1977	1977
試験条件		
結果		
固体の場合	自然発火性でない、引火性ガスを発生しない	not pyrophoric, does not develop readily inflammable gases
引火性が高い		
気体の場合		
水との接触		
結論		
注釈	加熱しないと着火しない、水と反応しない	must be preheated before ignition will occur, does not react with water
信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions
信頼性の判断根拠	ピアレビューされたデータベース	Peer-reviewed database
出典	(54)	(54)
引用文献		
備考		

2.10 爆発性
EXPLOSIVE PROPERTIES

試験物質名	2,2'-イミノジエタノール、純品	2,2'-iminodiethanol, pure
CAS番号		
純度等		
注釈		
方法	その他	other
GLP	いいえ	no
試験を行った年	1998	1998
試験条件		
結果		
火により爆発		
m-ジニトロベンゼンより摩擦に敏感		
m-ジニトロベンゼンより衝撃に敏感		
爆発性ない		
その他		

結論	爆発性で無い	not explosive
注釈	英文参照	substance (CAS No. 111-42-2) has no chemical groups indicating explosive properties. This statement agrees with the recommendations of appendix 6 in the Manual of Tests and criteria of the United Nations.
信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions
信頼性の判断根拠	専門家判断	Expert judgement
出典	(56)	(56)
引用文献		
備考		

2.11 酸化性
OXIDISING PROPERTIES

試験物質名	2,2'-イミノジエタノール、純品	2,2'-iminodiethanol, pure
CAS番号		
純度等		
注釈		
方法	その他	other
GLP	いいえ	no
試験を行った年	1998	1998
試験条件		
結果		
最大燃焼速度が参照混合物と同等かそれより高い		
予備試験で激しい反応		
非酸化性		
その他		
結論	酸化特性なし	no oxidizing properties
注釈	英文参照	The substance (CAS No. 111-42-2) has no chemical groups indicating oxidizing properties. This statement agrees with the recommendations of appendix 6 in the Manual of Tests and criteria of the United Nations
信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions
信頼性の判断根拠	専門家判断	Expert judgement
出典	(56)	(56)
引用文献		
備考		

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 INFOMATION

試験物質名	2,2'-イミノジエタノール、純品	2,2'-iminodiethanol, pure
CAS番号		
純度等		
注釈	粒度分布	GRANULOMETRY
方法	その他	other
GLP	いいえ	no
試験を行った年		
試験条件		
結果	この物質は固まりではなく粒状で販売・使用されている。	substance is marketed or used in a non solid or granular form
結論		
注釈		
信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions
信頼性の判断根拠	専門家判断	expert judgement
出典		
引用文献		
備考		

試験物質名	2,2'-イミノジエタノール、純度: >99.9%	2,2'-iminodiethanol, purity: >99.9%
CAS番号		
純度等		
注釈	試験タイプ:その他	Test type : other
方法	英文参照	Ubbelohde viscosimeter (BASF standard test method)
GLP	いいえ	no
試験を行った年		
試験条件		
結果	- mm2/s (static)	- mm2/s (static)
結論		
注釈	温度 粘度 (° C) (mm2/s, static) 30 357.2 50 93.35 70 33.4 110 7.41 150 2.69 キースタディ	Temperature Viscosity (° C) (mm2/s, static) 30 357.2 50 93.35 70 33.4 110 7.41 150 2.69 key study
信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions
信頼性の判断根拠	科学的に受け入れられる試験、基本データあり	Scientifically acceptable study, basic data given
出典		
引用文献	(29)	(29)
備考	フラグ:化学品安全性データセット、SIDSエンドポイントに重要な試験、キースタディ	Flag : Material Safety Dataset, Critical study for SIDS endpoint, key study

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	1.1 - 1.4で規定	as prescribed by 1.1 - 1.4
CAS番号		
純度等		
注釈		
方法	AOP (v1.91)による計算	(calculated): AOP (v1.91)
タイプ	大気	air
GLP		
試験を行った年	2006	2006
光源と波長(nm)		
太陽光強度に基づいた相対強度	太陽光強度に基づく	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(°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)	OH	OH
増感剤濃度	1500000 molecule/cm³	1500000 molecule/cm³
速度定数	.0000000000926898 cm³/(molecule*sec)	.0000000000926898 cm³/(molecule*sec)
半減期t1/2	0.1 日間	.1 day(s)
分解生成物		
結論	半減期:約2.4時間(0.1日)	half-life (t1/2): about 2.4 h (0.1 d).
注釈	仮定データ: 1日12時間、1.5E6 OH/cm3 データは非荷電分子を参照.	Assumed data: 12-h day, 1.5E6 OH/cm3 Data refer to the uncharged molecule.
信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions
信頼性の判断根拠	科学的に受け入れられる方法	Scientifically acceptable method
出典		
引用文献	(33)	(33)
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

3.1.2. 水中安定性(加水分解性)
STABILITY IN WATER

試験物質名	2,2´-イミノジエタノール (DEA)	2,2´-iminodiethanol (DEA)
CAS番号		
純度等		
注釈	タイプ : 非生物学的	Type : abiotic
方法		
GLP		
試験を行った年		
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		
半減期		
分解生成物		
結論		
注釈	英文参照	At environmental pH conditions (pH 7-9) hydrolysis is not expected to be a relevant degradation process due to the structure of the molecule.
信頼性スコア	(4) 信頼性を評価できない	(4) not assignable
信頼性の判断根拠	専門家判断 (BASF製造工場の工場長の記載)	Expert Judgement (statement of factory manager of BASF production site)
出典		
引用文献	(65)	(65)
備考		

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	その他	other
GLP		
試験を行った年		
試験条件		
試験期間		
結果		
試験のタイプ		
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)		
	土壌吸着係数 (Koc)値の4は log Kow 値 −1.43に基づき算出された。この Koc値と DEAが水に完全に溶解する事からこの化合物は土壌中の移動性が非常に高く、水中の浮遊粒子や底質に吸着する事はない。	A soil adsorption coefficient (Koc) of 4 was estimated based on a log Kow of −1.43. This Koc value and the complete solubility of DEA in water suggests that this compound would be extremely mobile in soil and would not adsorb appreciably to suspended solids and sediments in water.
分解生成物		
時間ごとの消失率		
結論		
注釈		
信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions
信頼性の判断根拠	信頼できるハンドブックと、科学的に信頼できる文献に基づく推定	Reliable handbook and estimation according to scientifically valid literature
出典		
引用文献	(32) (66) (67)	(32) (66) (67)
備考		

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

試験物質名		
CAS番号		
純度等		
注釈		
方法		
測定タイプ(地点)	バックグラウンド濃度	background concentration
媒体	表層水	surface water
結果		
結論		
注釈	DEA は日本の環境省が1978年に行った表層水21試料の調査においては、検出されなかった (検出下限: 0.3 − 0.34 μg/l)	DEA was not detected in a study carried out in 1978 by the Japanese Department of Environmental Health in any of the 21 samples taken from surface water (limit of determination: 0.3 − 0.34 μg/l)
信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions
信頼性の判断根拠	科学的に受容可能な試験	Scientifically acceptable study
出典		
引用文献	(68)	(68)
備考		

3.3. 移動と分配
TRONSPORT 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	タイプ:吸着	Type : adsorption
方法	PCKOCWIN (v1.66)による計算	calculated: PCKOCWIN (v1.66)
	実施年:2006	Year : 2006
結果		
媒体	水-底質	water − sediment
	データは非荷電分子を想定	Data refer to the uncharged molecule.
環境分布予測と媒体中濃度 (levelII/III)		
結論	log Koc = 0 (Koc = 1)	log Koc = 0 (Koc = 1)
注釈	大気 : % (Fugacity Model Level I) 水 : % (Fugacity Model Level I) 土壌 : % (Fugacity Model Level I) 生物相 : % (Fugacity Model Level II/III) 土壌 : % (Fugacity Model Level II/III)	Air : % (Fugacity Model Level I) Water : % (Fugacity Model Level I) Soil : % (Fugacity Model Level I) Biota : % (Fugacity Model Level II/III) Soil : % (Fugacity Model Level II/III)
信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions
信頼性の判断根拠	科学的に受容可能な方法	Scientific acceptable method
出典		
引用文献	(33)	(33)
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

試験物質名		
CAS番号		
純度等		
注釈		
媒体	大気 -生物相 − 底質 -土壌 -水	air − biota − sediment(s) − soil − water
	実施年:2003	Year : 2003
方法	Mackay, Level I による計算	Calculation according Mackay, Level I
試験条件		

結果	長時間経過後、この物質は以下のコンパートメントに分配される: - 水: 99.99 % - 土壌: 5.2E-5 % - 底質: 5.3E-5 % - 大気: 0.001 % データは非荷電分子を想定	Over time the substance will distribute into the following compartments: - water: 99.99 % - soil: 5.2E-5 % - sediment: 5.3E-5 % - air: 0.001 % Data refer to the uncharged molecule.
結論		
注釈	英文参照	Physico-chemical properties: --- - molecular mass: 105.14 g/mol (1) - data temperature: 25 ° C (1) - log Kow: -2.18 (2) - water-solubility: 1E6 g/m3 (1) - Henry´s law constant: 3.98E-6 Pa*m3/mol - vapour pressure: 0.037 Pa (1) - melting point: 28 ° C (3) reference: (1) EPIWIN v3.12; (2) BASF AG (1991). Department of Analytical Chemistry. Report J. No. 90P03095.02, 18 Mar 1991, unpublished. (3) BASF AG (1985). Department of Analytics, Die Bestimmung von spezifischen Waermekapazitaeten und Erstarrungspunkten von Di-Ethanolamin (DEA) und verschiedenen Gemischen mit Wasser, Report 126131, 23 November 1985, unpublished.
	英文参照	Environmental properties: --- - volume (m^3) / density (kg/m^3) / org. C (g/g) / fish lipid (g/g) air 6.0E+09 / 1.185 water 7.0E+06 / 1000 soil 45000 / 1500 / 0.02 sediment 21000 / 1300 / 0.05 susp. sed. 35 / 1500 / 0.167 fish 7 / 1000 / 0.05 aerosol 0.12 / 1500
信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions
信頼性の判断根拠	科学的に受容可能な方法	Scientific acceptable method
出典		
引用文献	(73)	(73)
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

3.4 好気性生分解性
AEROBIC BIODEGRADATION

試験物質名	ジエタノールアミン：純度: 98%	Diethanolamine:purity: 98%
CAS番号		
純度等	不純物: モノエタノールアミン: <1% トリエタノールアミン: <1%	impurities: monoethanolamine: <1% triethanolamine: <1%
注釈	タイプ：好気性	Type : aerobic
方法	OECD ガイドライン 301 F "易分解性: Manometric Respirometry 試験"	OECD Guide-line 301 F "Ready Biodegradability: Manometric Respirometry Test"
培養期間		
植種源	activated sludge, domestic, non-adapted	活性汚泥、家庭排水、順化なし
GLP	はい	yes
試験を行った年	1992	1992
試験条件	- 試験装置: Sapromat respirometer - 植種源: 家庭排水の処理施設由来の活性汚泥 - 試験物質濃度: 100 mg/l - 総容量: 250 ml - 試験期間: 28 days - 対照物質: アニリン: 100 mg/l	- Test device: Sapromat respirometer - inoculum: activated sludge from a laboratory sewage treatment plant with domestic sewage - test item concentration: 100 mg/l - total volume: 250 ml - test duration: 28 days - control substance: aniline: 100 mg/l
試験物質濃度	100 mg/l 試験物質として	100 mg/l related to Test substance
汚泥濃度		
培養温度 ℃		
対照物質および濃度(mg/L)	アニリン	Aniline
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	28日後で 93 (±) %	93 (±) % 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	対照: (アニリン, 初期試験物質濃度: 100 mg/l) 99 % DOC-消失 (28 days) (注釈: 信頼できる BOD-値は技術的な問題から利用不可) - 阻害コントロール: (アニリン + 試験物質 = 1:1 (各 100 mg/l)) 93 % BOD/ThOD (28日間; 硝化を考慮) - 生物学的消失コントロール: (試験物質: 100 mg/l; w 塩化水銀が微生物分解を阻害; w/o 植種) 10.4 % BOD/ThOD (28 日後; 硝化を考慮)	Reference: (aniline, initial test item concentration: 100 mg/l) 99 % DOC-elimination (28 days) (remark: reliable BOD-values not available due to technical failure) - inhibition control: (aniline + test substance = 1:1 (each 100 mg/l)) 93 % BOD/ThOD (28 days; nitrification has been considered) - abiotic elimination control: (test substance: 100 mg/l; w mercury chloride to avoid microbial degradation; w/o inoculum) 10.4 % BOD/ThOD (28 days; nitrification has been considered)
	- test substance: time TS1 TS2 TS3 TS4 TS5 TS6 (days) (% BOD/ThOD) 3 3.6 3.2 0.9 0.5 0.0 2.3 5 8.2 15.9 1.8 2.3 0.0 3.1 6 50.3 23.6 4.1 42.1 1.4 5.0 7 62.1 57.1 45.8 50.7 42.1 40.8 14 93.8 83.4 74.8 77.5 68.9 79.7 21 102.4 92.4 85.6 83.4 75.7 87.0 28 107.4 100.1 92.4 87.0 80.2 91.5 (TS1-6 = replicates)	- test substance: time TS1 TS2 TS3 TS4 TS5 TS6 (days) (% BOD/ThOD) 3 3.6 3.2 0.9 0.5 0.0 2.3 5 8.2 15.9 1.8 2.3 0.0 3.1 6 50.3 23.6 4.1 42.1 1.4 5.0 7 62.1 57.1 45.8 50.7 42.1 40.8 14 93.8 83.4 74.8 77.5 68.9 79.7 21 102.4 92.4 85.6 83.4 75.7 87.0 28 107.4 100.1 92.4 87.0 80.2 91.5 (TS1-6 = replicates)
結論	易分解性	readily biodegradable
注釈		
信頼性スコア	(1) 制限無く信頼性あり	(1) valid without restriction
信頼性の判断根拠	ガイドライン試験	Guideline study
出典		
引用文献	(74)	(74)
備考		

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		
GLP	いいえ	no
試験を行った年	1974	1974
試験条件		
結果		
濃度		
結果 mgO_2/L		
BOD/COD比		
その他	理論的: TOD = 2.13 g/g COD = 1.52 g/g NOD = 0.61 g/g 分析による: Reflux COD = 94.7% recovery Rapid COD = 76.6% recovery TKN = 82.7% recovery 非順化植種による値: BOD5 = 0.03 g/g BOD 5/COD = 0.02 順化植種による値: BOD 5 = 0.984 g/g BOD 5/COD = 0.68	Theoretical: TOD = 2.13 g/g COD = 1.52 g/g NOD = 0.61 g/g Analytical: Reflux COD = 94.7% recovery Rapid COD = 76.6% recovery TKN = 82.7% recovery values refer to non-acclimated inoculum: BOD5 = 0.03 g/g BOD 5/COD = 0.02 values refer to acclimated inoculum: BOD 5 = 0.984 g/g BOD 5/COD = 0.68
結論		
注釈		
信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions
信頼性の判断根拠	基礎データあり	Basic data given
出典		
引用文献	(96)	(96)
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	計算: BCF (v2.15)	calculated: BCF (v2.15)
生物種		
暴露期間 (日)		
曝露濃度		
排泄期間		
GLP		
試験を行った年	2006	2006
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)	3.16	3.16
取込／排泄定数		
排泄時間		
代謝物		
その他の観察		
結論	推定 Log BCF = 0.5 (BCF = 3.162). データは非荷電分子を想定	Estimated Log BCF = 0.5 (BCF = 3.162). Data refer to the uncharged molecule
注釈	BCF推定に用いた式: Log BCF = 0.5 (log Kow <1より補正係数は使用していない) 2つの異なる log Kow値がBCF推定に用いられた: a) −2.18 (*) b) −1.43 (#) references: (*) BASF AG (1991), Department of Analytical Chemistry, report J. No. 90P03095.02, 18 Mar 1991 (unpublished). (#) Hansch C and Leo A (1979). Substituent constants for correlation analysis in chemistry and biology. Pomona College, Appendix II, page 188, John Wiley and Sons, New York, USA.	Equation used to make BCF estimate: Log BCF = 0.5 (correction factors not used for log Kow <1) Two different log Kow values have been used by BCF estimate: a) −2.18 (*) b) −1.43 (#) references: (*) BASF AG (1991), Department of Analytical Chemistry, report J. No. 90P03095.02, 18 Mar 1991 (unpublished). (#) Hansch C and Leo A (1979). Substituent constants for correlation analysis in chemistry and biology. Pomona College, Appendix II, page 188, John Wiley and Sons, New York, USA.
信頼性スコア	(2) 制限つきで信頼性あり	(2) valid with restrictions
信頼性の判断根拠	科学的に受容可能な方法	Scientifically acceptable method
出典		
引用文献	(98)	(98)
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	ジエタノールアミン:分析用試薬	Diethanolamine; purity: reagent grade
同一性		
方法	その他: ASTM-Standard E 729-80 (Standard Practice for Conducting Acute Toxicity Tests with Fishes, Macroinvertebrates, and Amphibians)に従った	other: according to ASTM-Standard E 729-80 (Standard Practice for Conducting Acute Toxicity Tests with Fishes, Macroinvertebrates, and Amphibians)
GLP	はい	yes
試験を行った年	1982	1982
魚種、系統、供給者	*Pimephales promelas* (魚類, 淡水)	*Pimephales promelas* (Fish, fresh water)
エンドポイント		
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	※英文参照	LC50 values were calculated by the moving average method of Thompson (1947) or by employing a binomial procedure according to Steel & Torrie, 1960.
試験条件		
試験魚の月齢、体長、体重	※英文参照	Test organism: fathead minnow (Pimephales promelas Rafinesque) - fry: 10 - 15 days old - juveniles: 30 - 35 days old - subadults: 60 - 100 days old Length: - fry: 9 - 10 mm - juveniles: 13.3 - 17.5 mm - subadults: 3.8 - 33.3 Weight: - fry: 5.2 - 15 mg - juveniles: 35 - 99 mg - subadults: 196 - 663 mg
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	※英文参照	Test water: - laboratory water from upper Saginaw Bay of Lake Huron - carbon-filtered and UV-irradiated; - pH 7.6 - 8.3 - hardness: 96 - 125 mg/l as CaCo3 - conductivity: 135 - 215 µmhos/cm
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	※英文参照	Test vessels: - round glass vessels (beakers) - final test volumes: 10 l (juvenile and subadults), 3.5 l (fry) - aeration: gentle - one test vessel per treatment - No. of fish per test vessel: 10 (juveniles and subadults) / 20 (fry) - feeding: none during the test - temperature: 22 +/- 1 ° C (fry, juvenile, subadults)
暴露期間	96時間	96 hour(s)
試験方式	止水	static
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		
実測濃度		
生物学的影響観察		
累積死亡率の表		
統計的結果		
注釈	LC50 (mg/l, with 95 % 信頼限界): 24時間 48時間 72時間 96時間 稚魚: 1580 (1470-1700) 1550 (1440-1660) 1560 (1430-1720) 1480 (1360-1630) 幼魚: 1710 (1530-1960) 1640 (1460-1860) 1640 (1460-1860) 1550 (1300-1990) 成魚: 1790 (1600-2070) 1480 (1300-1720) 1440 (1260-1670) 1370 (1200-1580) 96時間 LC50値の幾何平均: 1460 (1200-1990) 最大、最小LC50値の比 (96時間): 1.1	LC50 (mg/l, with 95 % confidence limits): 24 h 48 h 72 h 96 h Fry: 1580 (1470-1700) 1550 (1440-1660) 1560 (1430-1720) 1480 (1360-1630) Juvenile: 1710 (1530-1960) 1640 (1460-1860) 1640 (1460-1860) 1550 (1300-1990) Subadults: 1790 (1600-2070) 1480 (1300-1720) 1440 (1260-1670) 1370 (1200-1580) Geometric mean of the 96 h LC50 values: 1460 (1200-1990) Ratio of high to low LC50 (96 h values): 1.1

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)	LC50： 1370 mg/l	LC50： 1370 mg/l
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	※英文参照	GLP study comparable to current guidelines with acceptable restrictions (eg. stability and test item concentrations not confirmed; no detailed information on tested concentration range)
出典		
引用文献	(99) (100)	(99) (100)
備考	※英文参照	Dissolved oxygen: - fry: 7.0 - 10.6 mg/l - juveniles: 6.8 - 9.8 mg/l - subadults: 6.4 - 9.6 mg/l pH-value: - fry: 8.0 - 10.2 - juveniles: 8.9 - 10.3 - subadults: 8.9 - 10.5 - aeration: none (only if necessary) - illumination: 860 - 1180 lux - light/dark rhythm: 16/8 h Measurements/observations: - mortality after 24, 48, 72, and 96 h - dissolved oxygen, pH, and temperature: daily
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	ジエタノールアミン、純度記載無し(入手源：Sigma)	Diethanolamine, purity not stated (source: Sigma)
同一性		
方法	OECDガイドライン202	OECD Guide-line 202
GLP	データ無し	no data
試験を行った年		
生物種、系統、供給者	*Daphnia magna* (甲殻類)	*Daphnia magna* (Crustacea)
エンドポイント		
試験物質の分析の有無	無し	no data
試験物質の分析方法		
結果の統計解析手法	※英文参照	Statistics: - NOEC values were analyzed by ANOVA followed by Dunnett's multiple comparison - EC50 values were calculated by probit analysis
試験条件		
試験生物の起源、前処理、繁殖方法	※英文参照	Test organism: - Daphnia magna, clone A - feed during culture: Chlorella vulgaris
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	70mLポリスチレンフラスコ 試験液量：25mL	70 ml polysterene flasks test volume: 25 ml
暴露期間	72時間	72 h
試験方式	止水	static
連数、1連当たりの試験生物数	生物数/容器: 10 連数: 2連で3回繰返し	No. of animals per vessel: 10 replicates: all experiments were performed at least 3 times and at least in duplicate concentrations
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	20 ° C	20 ° C
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	遊泳阻害: 24時間 48時間 72時間 EC50 (mmol/l) 2.78 1.63 0.73 EC50 (mg/l) 292 171 77	Immobilization: 24 h 48 h 72 h EC50 (mmol/l) 2.78 1.63 0.73 EC50 (mg/l) 292 171 77
累積遊泳阻害数の表		
注釈		
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： 171 mg/l	EC50： 171 mg/l
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	※英文参照	Scientifically acceptable study following a guideline, but without detailed documentation of the test design
出典		
引用文献	(112)	(112)

備考	※英文参照	Observations: - immobility after 24, 48, and 72 h
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	ジエタノールアミン、少なくとも分析用試薬（入手源：Eastman Kodak）	Diethanolamine, at least reagent grade (source: Eastman Kodak)
同一性		
方法	※英文参照	Selenastrum capricornutum Printz algal assay bottle test, US EPA 600/9-78-018 (1978)
GLP	はい	yes
試験を行った年	1982	1982
生物種、系統、供給者	その他の藻類: *Pseudokirchneriella subcapitata* （以前の学名：*Selenastrum capricornutum*）	other algae: Pseudokirchneriella subcapitata (formerly Selenastrum capricornutum)
エンドポイント	その他：細胞数	other: cell count
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	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	※英文参照	Statistics ---------- Raw cell count and total cell volume (TCV) were entered in a computer and corrected for dilution factor. The mean cell volume (MCV) was calculated as follows: MCV = TCV/cell count The cell counts, TCV and MCV at 96 h were compared using a t-test. The 96-h EC50 values for growth inhibition were calculated using Finney's probit method or Thompson's method of moving averages.
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		
参照物質での感受性試験結果		
希釈水源	※英文参照	particle free water from deionized steam-condensate, filtered (0.22 µm)
培地の化学的性質	藻類アッセイ培地（AAM）	algal assay medium (AAM)
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	125mL三角フラスコ 試験液量：50mL	125 ml Erlenmeyer flasks Test volume: 50 ml
暴露期間	14日間（本試験No.1）/4日間（本試験No.2）	14 d (definitive test No. 1) / 4 d (definitive test No. 2)
試験方式		
連数	3連/濃度及び対照群	3 per concentration and 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 ° C
照明の状態	※英文参照	cool white fluorescent light, 400 +/- 80 fc
平均測定濃度の計算方法		
結果		
設定濃度	0 (対照群), 0.98, 1.64, 2.77, 4.34, 7.56, 12.6 mg/l	0 (control), 0.98, 1.64, 2.77, 4.34, 7.56, and 12.6 mg/l
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	EC50 値 (95 %信頼限界)(mg/l) ---------- 総細胞量: 96時間 168時間 試験 1: 3.6 (2.4 - 5.9) 3.9 (2.6 - 6.3) 試験 2: 3.3 (1.8 - 5.4) 細胞数: 96時間 試験 1: 2.3 (1.5 - 3.3) 試験 2: 2.1 (0.9 - 3.5)	EC50 values with 95 % confidence limits (mg/l) ---------- Total cell volume: 96 h 168 h Test 1: 3.6 (2.4 - 5.9) 3.9 (2.6 - 6.3) Test 2: 3.3 (1.8 - 5.4) Cell count: 96 h Test 1: 2.3 (1.5 - 3.3) Test 2: 2.1 (0.9 - 3.5)
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）	EC50 : 2.1mg/l	EC50 : 2.1mg/l
結果（NOEC）		
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	※英文参照	Scientifically acceptable study on GLP conditions with acceptable restrictions (e.g. test concentrations were not confirmed by chemical analysis)
出典		
引用文献	(120) (121)	(120) (121)
備考	※英文参照	Measurements ---------- - algal growth: calculated from cell counts and total cell volume (TCV) using a Coulter Counter (samples were counted in triplicate); measurements on days 1, 2, 3, 4, 7, 11, and 14
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

試験物質	ジエタノールアミン(CAS 111-42-2)、純度99.75%	Diethanolamine (CAS 111-42-2), purity 99.75 %
同一性		
方法	その他:ドラフト EEC-ガイドライン XI/681/86 "Prolonged toxicity study with Daphnia magna: Effects on reproduction"	other: draft EEC-guideline XI/681/86 "Prolonged toxicity study with Daphnia magna: Effects on reproduction"
方法	※英文参照	Semi-static test covering also the following guidelines: - OECD-Guideline for testing of chemicals, No. 202 (1981): Daphnia, Acute Immobilisation Test and Reproduction Test - German Industrial Standard DIN 38 412 (draft): Reproduction test with Daphnia magna - EPA-660/3-75-009 (1975): Methods for acute toxicity tests with Fish, Macroinvertebrates and Amphibians
GLP	はい	yes
試験を行った年	1992	1992
試験生物種	*Daphnia magna* (甲殻類)	*Daphnia magna* (Crustacea)
試験物質の分析の有無	有り	yes
試験物質の分析方法	※英文参照	Samples for chemical analysis were taken once each week. For each concentration chosen for analysis (control, 25, 50, 100 mg/l) the freshly prepared test solutions and the corresponding 48 h or 72 h old test solutions were analyzed.
エンドポイント	繁殖率	reproduction rate
結果の統計解析手法	※英文参照	For statistical evaluation of LOEC and NOEC, Duncan's multiple range test was applied.
試験条件		
助剤使用の有無		
助剤の種類、濃度、助剤対照区の有無		
試験温度	19.2 - 21.3 ° C	19.2 - 21.3 ° C
pH		
硬度		
試験生物の情報	※英文参照	test organisms: Daphnia magna STRAUS - age of the animals at start of the test: 2 - 24 h (starting with the 3rd breed of parent animals) feeding: daily with live green algae
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	※英文参照	test and culture medium: aerated synthetic fresh water (M4 medium) according to ISO 10706; total hardness: 2.70 +/- 0.50 mmol/l; molar ratio Ca/Mg: about 4/1; pH 8.0 +/- 0.5; conductivity: 600 - 700 µS/cm
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		
暴露期間	21日間	21 day(s)
暴露容器	試験容器:100mlガラスビーカー(ガラス蓋付き) 試験液量:50ml	test vessels: 100 ml glass-beakers with glass cover test volume: 50 ml
連数、1連当たりの試験生物数	親動物数/容器:1 親動物数/濃度及び対照群:10(10連)	No. of parent animals per vessel: 1 No. of parent animals per concentration and control: 10 (10 replicates)
照明	※英文参照	artificial light, wavelength 400 - 700 nm with about 5 - 6 µE/(m²xs)
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		
平均測定濃度の計算方法		
結果		
設定濃度	0.19, 0.39, 0.78, 1.56, 3.13, 6.25, 12.5, 25, 50, 及び 100 mg/l	0.19, 0.39, 0.78, 1.56, 3.13, 6.25, 12.5, 25, 50, and 100 mg/l
実測濃度	最大及び最小分析濃度と設定濃度の比較 (%): ミジンコ無し / ミジンコ有り 新 (0時間) / 古 (48時間) / 古 (48時間) 96.8 - 107.6 / 95.6 - 100.4 / 93.2 - 98.2 すべての値が > 80 %であったため、結果は設定濃度で示した。	Analytically measured relative minimum and maximum concentrations compared to nominal concentrations (%): Without daphnids / With daphnids fresh (0 h) / aged (48 h) / aged (48 h) 96.8 - 107.6 / 95.6 - 100.4 / 93.2 - 98.2 Since all values were > 80 %, results are given with respect to the nominal concentrations.
実測濃度の詳細		

累積遊泳阻害数	生物学的結果: 濃度 SP* AB** DY*** RP**** (mg/l) (%) (n) (n) (n) 0 90 0.1 0.0 206.6 0.19 100 0.1 0.0 198.0 0.39 100 0.8 0.0 196.4 0.78 100 0.2 0.0 192.6 1.56 90 0.6 0.0 176.9 3.13 90 0.3 0.0 161.0 6.25 80 0.8 1.3 127.6 12.5 0 – – – 25 0 – – – 50 0 – – – 100 0 – – – *SP = 21日後の親の生存率 **AB = 21日後の親当りの堕胎卵数 ***DY = 21日後の生存親当りの死亡産仔数 ****RP = 21日後の生存親当りの生存産仔数(繁殖)	Biological results: Concentration SP* AB** DY*** RP**** (mg/l) (%) (n) (n) (n) 0 90 0.1 0.0 206.6 0.19 100 0.1 0.0 198.0 0.39 100 0.8 0.0 196.4 0.78 100 0.2 0.0 192.6 1.56 90 0.6 0.0 176.9 3.13 90 0.3 0.0 161.0 6.25 80 0.8 1.3 127.6 12.5 0 – – – 25 0 – – – 50 0 – – – 100 0 – – – *SP = percentage of surviving parent animals after 21 days **AB = mean number of aborted subitance eggs per surviving parent animal after 21 days ***DY = mean number of dead young per surviving parent animal after 21 days ****RP = mean number of living young per surviving parent animal after 21 days (reproduction)
累積産仔数		
対照区における反応は妥当か		
生理的影響		
試験の妥当性		
注釈	pH: 7.8 – 9.5 溶存酸素: 8.0 – 9.8 mg/l	pH: 7.8 – 9.5 dissolved oxygen: 8.0 – 9.8 mg/l
結論		
結果(EC50)	LC0 (親動物) : = 3.13mg/l	LC0 (parents) : = 3.13mg/l
結果(NOEC、LOEC)	NOEC : = .78 mg/l LOEC : = 1.56 mg/l	NOEC : = .78 mg/l LOEC : = 1.56 mg/l
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	最近の国際的ガイドラインに匹敵するGLP試験	GLP study comparable to current international guidelines
出典		
引用文献	(137)	(137)
備考	試験はすべての妥当性基準を満たしているので本試験は妥当である。	The test fulfilled all validity criteria and is therefore valid.
備考	※英文参照	Observations/measurements –––––––––––––––––––––––– – mortality and reproduction: daily – temperature: continuously in a separate vessel close to the test vessels – oxygen content and pH: at the start and the end of the study as well as at each change of the test solution in the 48–h or 72–h aged solution in one parallel of each concentration
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

4-6 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	1.1～1.4で規定	as prescribed by 1.1 – 1.4
CAS番号		
純度等		
注釈	供給源： プロトタイプ調製品の成分は調整法の詳細と共にCFTAにより供給された。 遊離DEAを0.28%含むトリエタノールアミンはDow Chemical Co., Midland, MI.から入手した。 遊離DEAを2.79%含むラウラミドDEA及び遊離DEAを11.90%含むコカミドDEAはMona Industries Inc., Paterson, NJ.から入手した。 遊離DEAはバッチのアルカリ番号から決定した。 ジエタノールアミンはSigma Chemical Co., Poole, UK.から入手した。2-[14C]-DEA (32.2 mCi/mmol; 放射化学純度 >98.9%)はResearch Triangle Institute, Research Triangle Park, NCから入手した。	Source: The ingredients for the prototype formulations together with details of formulation preparation were supplied by CTFA. Triethanolamine containing 0.28% free DEA was obtained from Dow Chemical Co., Midland, MI. Lauramide DEA containing 2.79% free DEA and cocamide DEA containing 11.90% free DEA were obtained from Mona Industries Inc., Paterson, NJ. Free DEA was determined from the batch alkali number. Diethanolamine was obtained from Sigma Chemical Co., Poole, UK. 2-[14C]-DEA (32.2 mCi/mmol; >98.9% radiochemical purity) was obtained from Research Triangle Institute, Research Triangle Park, NC
注釈	3H-水 (0.09 mCi/mmol) はAmersham Life Science, UK.から入手した。 シンチレーション液 (HiSafe 3) 及び組織溶解剤(Opti-Solve) はEG&G Wallac, Milton Keynes, UKから入手した。 サンプルはWallac 1409 カウンターで分析した。 テープのストリッピングはScotch 810 Magic (3M) 又は D-Squame Tape (CuDerm, Dallas)を用いて行った。	3H-water (0.09 mCi/mmol) from Amersham Life Science, UK. Scintillation fluid (HiSafe 3) and tissue solubilizer (Opti-Solve) were from EG&G Wallac, Milton Keynes, UK Samples were analyzed on a Wallac 1409 counter. Tape-stripping was carried out using Scotch 810 Magic (3M) or D-Squame Tape (CuDerm, Dallas)
方法		
方法／ガイドライン	その他	other
試験形態	In vitro 吸収	In vitro Absorption
GLP適合	いいえ	no
試験をおこなった年	2005	2005
方法の概略	※英文参照	METHOD FOLLOWED: The in vitro human skin distribution and permeation of DEA from model formulations (applied as finite doses in regimens designed to mimic "in use" conditions) was determined. DEA was present at known concentrations, as an impurity of the additive triethanolamine (0.4% DEA), or as an impurity/constituent of lauramide DEA (5.0% DEA) and cocamide DEA (19.6% DEA), in the representative model formulations. Comparison was made with permeation of DEA from simple aqueous solutions under infinite dose conditions. The possibility that exogenous DEA may be metabolically incorporated into epidermal phospholipids or sphingolipids was also investigated.
方法の概略	※英文参照	Test condition : Preparation of prototype formulations and application vehicles: Five rinse-off formulations (A-E), a leave-on emulsion (F) and a simple aqueous solution were prepared (Table I). Formulations A-D were variations of prototype shampoo formulations containing alternative surfactants (sodium lauryl sulphate; sodium laureth sulphate) and alternate DEA condensates (cocamide; lauramide). Formulation E was a prototype bubble-bath. Formulation F was a prototype moisturizing cream. Representative semi-permanent (G) and oxidative (H) hair dye formulations containing DEA and lauramide DEA were also prepared (Table 2). Target levels of free DEA were attained by the inclusion of additional DEA as either 14C-DEA or a combination of 14C_DEA and unlabeled DEA. In order to ensure content uniformity of radiolabel, five samples of known weight or volume were taken from each application vehicle, solubilized in scintillation fluid and the radiolabel content measured. All formulations were determined as acceptable.

方法の概略	※英文参照	Skin preparation: Human female abdominal and breast skin from several donors was obtained following cosmetic reduction surgery. Fresh and frozen skin, tissue was divided upon receipt with half being evaluated within 3 h of excision and half being stored at 20 ° C for at least 1 week before use. Experiments were all initiated within 3 h of skin excision or skin was immediately frozen at −20° C and thawed just prior to use. For the fresh versus frozen skin comparisons (vehicle F and aqueous solution), at least 12 replicate full thickness skin membranes were prepared. For experiments using vehicles A–E, G and H at least 12 replicate heat-separated (60° C for 50 s) epidermal membranes were prepared from a minimum of four donors for each vehicle but heat separation process could not be used in the experiments that required maintenance of metabolic activity. Skin thickness was not explicitly measured but epidermal membranes are in the region of 100 μm thick and full thickness skin is approximately 1 mm.
方法の概略	※英文参照	Diffusion cells: Franz-type glass diffusion cells (area ca. 1 cm2 and receptor volume ca.3 ml) were used. Contact surfaces were lightly greased with Dow Corning High Vacuum Grease. Full thickness or epidermal membranes were placed on the lower halves of the cells, the stratum corneum facing the donor chamber. The upper halves of the cells were added and the assembly clamped together. The cells were immersed in a constant temperature water bath at 37.0 ° C throughout the experiment, skin surface temperature was maintained at 32.0 ° C. Receptor chamber contents were continuously agitated by PTFE-coated magnetic followers driven by submersible magnetic stirrers. The receptor chambers of the cells used for all the fresh/frozen skin comparisons (simple aqueous solutions and vehicle F) were filled with HEPES buffered Hank's Balanced Salt Solution (pH 7.4). For the remaining experiments the receptor phase was phosphate buffered saline (pH 7.4). The integrity of each membrane was assessed by determining the permeation of H2O over 20 min immediately prior to application of the test vehicles. Skin samples showing water permeation rates greater than 2.0 mg/cm2/h were discarded.
方法の概略	※英文参照	Application of prototype formulations and skin permeation procedure: Target doses were all accurately measured and applied to skin surfaces at time zero. Two hundred μl/cm2 of the aqueous solution were used for the fresh/frozen skin comparisons, target doses of the representative formulations were diluted where appropriate and applied in amounts that modeled in use consumer application. 100 μl/cm2 of 1:10 aqueous dilutions of formulations A–D, 100 μl/cm² of a 1:300 aqueous dilution of formulation E were dosed. The emulsion formulation (formulation F) was dosed at 5 mg/cm2 and for the hair dye formulations 100 mg/cm2 of formulation G and 100 mg/cm2 of a 1:1 dilution with H2O2 of formulation H were applied. The amount of 14C-DEA applied to the skin ranged from 0.015 μCi/cm2 (for the leave-on emulsion formulation) to 6.98 μCi/cm2 (for the simple aqueous solution). For formulations A–E, vehicles were applied by volume using a digital pipette. For formulations G and H the exact weight of vehicle applied was recorded. For formulation F the applied amount was spread evenly over the stratum corneum surface using a round-ended glass rod and the exact weight applied recorded.

方法の概略	※英文参照	The donor surfaces of cells were rinsed six successive times over 2-3 min with 1 ml of distilled water and the rinsate assayed by liquid scintillation counting (LSC). Formulation E was removed from the donor surface 30 min after application, by blotting with sterile filter paper and the removed material assayed by LSC. Two hundred µl samples were taken from each receptor chamber, at appropriate time intervals, and assayed by LSC. Liquid removed was replaced with fresh, temperature equilibrated, receptor medium. Radioactivity remaining on the skin surface and the diffusion cell donor cap was determined before the skin samples were tape-stripped to provide stratum corneum distribution of labelled material. The remaining tissue (epidermis or epidermis plus dermis) was then solubilized in OptiSolve and assayed by LSC. No binding to the filter paper supports was observed.
動物種		human
試験動物:系統		
性別		
細胞株		
年齢		
体重		
試験動物数		3
曝露経路		
溶媒(賦刑剤)		
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	プロトタイプのシャンプー調製品A及びB (蒸留水で1:10に希釈): DEAの浸透を24時間 (調製品B)又は48時間 (調製品A)にわたりモニターした。 調製品A (24時間及び48時間で約 18 ng/cm2 [適用量の約0.019%]) 及び調製品B (24時間で約 25 ng/cm2 [適用量の約 O.025%])の両方に対して浸透性は極めて低かった。 浸透は初期の時点で最高値となり、約8時間までにプラトーになった。10分間の洗浄法により、調製品A及びBに対しそれぞれ適用量の92.3%及び99.5%が回収された。	Prototype shampoo formulations A and B (1:10 dilution in distilled water.): Permeation of DEA was monitored over 24 h (formulation B) or 48 h (formulation A). Permeation was very low for both formulations A (ca. 18 ng/cm2 [ca. O.019% of the applied dose] at 24 hand 48 h,) and formulation B (ca. 25 ng/cm2 [ca. O.025% of the applied dose] at 24 h). Permeation was highest over the early time points and reached a plateau by about 8 h. The 10 min wash procedure removed 92.3% and 99.5% of the applied dose for formulations A and B, respectively.
試験結果	皮膚中の物質の総量は調製品Aに対しては適用量の約0.06% (テープストリップには 0.026%、残存表皮中には0.037%)、調製品Bに対しては適用量の約0.08% (テープストリップに0.052%、残存表皮中に0.026%)と極めて低かった。 プロトタイプのシャンプー調製品C及びD (蒸留水で1:10に希釈): 媒体は適用10分後に皮膚表面から洗浄された。 浸透は両調製品に対して低かった(調製品Cに対しては24時間で8.5 ng/cm2 [適用量の0.034%]及び調製品Dに対しては24時間で2.7 ng/cm2 [適用量の0.011%])。	The total amount of material in the skin was very low at ca. 0.06% of the applied dose (0.026% in the tape-strips and 0.037% in the remaining epidermis) for formulation A and ca. 0.08% of the applied dose (0.052% in the tape-strips and 0.026% in the remaining epidermis) for formulation B. Prototype shampoo formulations C and D (1:10 dilution in distilled water): Vehicles were rinsed from the skin surface 10 min following application. Permeation was very low for both formulations (8.5 ng/cm2) [0.034% of the applied dose] at 24 h for formulation C and 2.7 ng/cm2 [0.011% of the applied dose] at 24 h for formulation D).
試験結果	DEAの適用量のうち大部分 (調製品Cに対して 92.1% 及び調製品Dに対して 91.6%)が適用10分後に皮膚から洗浄された。24時間で皮膚に検出された物質の総量は調製品Cに対しては適用量の約0.04% (テープ片に0.021%及び残存表皮中に0.016%)、また調製品Dに対しては適用量の約 0.04% (テープ片に 0.023%、残存表皮に0.017%)で極めて低かった。 プロトタイプのバブルーバス調製品E (蒸留水で1:30に希釈): 滅菌したろ紙で拭き取ることにより適用30分後に媒体を除去した。調製品EからのDEAの浸透を24時間にわたりモニターした。 累積の浸透率は極めて低かった (24時間で 4.2 ng/cm2 [適用量の0.51%]。適用30分後に皮膚から除去されたDEAの適用量の量は合計77.9%であった。	A large amount of the applied dose of DEA (92.1% for formulation C and 91.6% for formulation D) was rinsed from the skin 1O min following application. The total amount of material found in the skin at 24 h was very low at ca. 0.04% of the applied dose (0.021% in the tape-strips and 0.016% in the remaining epidermis) for formulation C and ca. 0.04% of the applied dose (0.023% in the tape strips and 0.017% in the remaining epidermis) for formulation D. Prototype bubble-bath formulation E (1:300 dilution in distilled water): The vehicle was removed from the skin surface 30 min following application by blotting with sterile filter paper. Permeation of DEA from formulation E was monitored over 24 h. Cumulative permeation, in mass, was very low (4.2 ng/cm2 at 24 h [0.51% of the applied dose). The amount of the applied dose of DEA that was removed from the skin 30 min following application totaled 77.9%.

試験結果	24時間で皮膚に検出された物質の総量は適用量の約1.9%であった(テープ片に 1.31%、残存表皮に 0.61%)。 放射能の全体の回収率 (適用量の83.7%)は調製品A-Dで得られた回収率より低かった。 調製品Eは除去前30分間に皮膚と接触して残存していたが、調製品A-Dは適用10分後に除去した。 プロトタイプの調製品F (乳化状態のままにした調製品、DEA0.4%を含むトリエタノールアミン2.0%を含む): 調製品は約 5.0 mg/cm2 の用量で適用し、試験期間を通して残存している調製品を皮膚と接触させ48時間にわたり浸透率をモニターした。累積の浸透率は極めて低く (48時間で新鮮な皮膚で計 2.3 ng/cm2、凍結した皮膚では1.7 ng/cm2)、新鮮及び凍結皮膚でそれぞれ適用量の0.61%及び0.46%であった。	The total amount of material found in the skin at 24 h was ca. 1.9% of the applied dose (1.31% in the tape-strips and 0.61% in the remaining epidermis). The overall recovery of radiolabel (83.7% applied dose) was lower than those obtained for formulations A-D. Formulation E remained in contact with the skin for a period of 30 min prior to removal whereas formulations A-D were removed 10 min after application. Prototype formulation F (leave-on emulsion formulation, contained 2.0% triethanolamine which contained 0.4% DEA): The formulation was applied at a dose of ca. 5.0 mg/cm2 and permeation monitored over 48 h, the formulation remaining in contact with the skin throughout the test period. Cumulative permeation was very low (a total of 2.3 ng/cm2 permeating fresh skin and 1.7 ng/cm2 permeating frozen skin at 48 h), which represented 0.61% and 0.46% of the applied dose in fresh and frozen skin, respectively.
試験結果	調製品Fは実験期間 (48時間)を通して皮膚との接触を維持したが、この媒体に対する標識の回収率の全体的な収支は調製品A-Dで得られた値と類似していた。 プロトタイプの染毛剤の調製品G (直接に適用)、展開剤と1:1で希釈後適用した調製品H: 調製品は適用30分後に皮膚表面から洗浄した。 浸透率は極めて低かった(24時間で調製品Gに対しては約 48 ng/cm2 [適用量の0.063%]、調製品Hに対しては約 28 ng/cm2 [適用量の0.024%])。 浸透率は初期の時点で最高値を示し、6～12時間でプラトーに達した。30分間の洗浄により調製品G及びHに対して、それぞれ適用量の100.8%及び101.0%が除去された。皮膚の物質の総量は媒体Gに対しては適用量の約0.03% (テープ片で 0.018%、残存表皮で 0.012%)、媒体Hに対しては適用量の約0.06% (テープ片で0.038%、残存表皮で0.023%) で極めて低かった。	Although formulation F remained in contact with the skin throughout the experimental period (48 h), the overall mass balance recoveries of label for this vehicle were similar to those obtained for formulations A-D. Prototype hair dye formulation G (applied directly), formulation H applied following 1:1 dilution with developer: The formulations were rinsed from the skin surface 30 min following application. Permeation was very low (a total of ca. 48 ng/cm2 [0.063% of the applied dose] for formulation G and ca. 28 ng/cm2 [0.024% of the applied dose] for formulation H permeating at 24 h). Permeation was highest over the early time points and reached a plateau between 6 and 12 h. The 30 min wash procedure removed 100.8% and 101.0% of the applied dose for formulations G and H, respectively. The total amount of material in the skin was very low at ca. 0.03% of the applied dose (0.018% in the tape-strips and 0.012% in the remaining epidermis) for vehicle G and ca. 0.06% of the applied dose (0.038% in the tape strips and 0.023% in the remaining epidermis) for vehicle H.
試験結果	単一の液体媒体中に不定の用量としてのDEAの適用、新鮮及び凍結皮膚: 凍結皮膚に対する累積24時間値 (8.67 μg/cm²)は新鮮皮膚のそれ(1.73 μg/cm2)よりも約5倍高く、浸透率には明らかな差がみられた。 凍結皮膚を通しての浸透率は全ての時点で新鮮皮膚を通してのそれより一貫して高い値であった (2時間: 新鮮 0.012 μg/cm2対 凍結 0.022 μg/ cm2; 4時間: 新鮮 0.034 μg/cm2 対 凍結 0.132 μg/cm2; 6時間: 新鮮 0.105 μg/cm2 対 凍結 0.358 μg/cm2; 8時間: 新鮮 0.214 μg/cm2 対 凍結 0.717 μg/cm2;12時間: 新鮮 0.523 μg/cm2 対 凍結 1.888 μg/cm2)。 24時間での累積浸透率の値は新鮮皮膚で適用量の0.086%、凍結皮膚で適用量の0.433%を示した。	Application of DEA in a simple aqueous vehicle as an infinite dose, fresh and frozen skin: There was a clear difference in permeation, the cumulative 24 h value for frozen skin (8.67 μg/cm²) being approximately 5-fold higher than in fresh skin (1.73 μg/cm2). Permeation through frozen skin was consistently higher than that through fresh skin at all time points (2 h: fresh 0.012 μg/cm2versus frozen 0.022 μg/ cm2; 4 h: fresh 0.034 μg/cm2 versus frozen 0.132 μg/cm2; 6 h: fresh 0.105 μg/cm2 versus frozen 0.358 μg/cm2; 8 h: fresh 0.214 μg/cm2 versus frozen 0.717 μg/cm2;12 h: fresh 0.523 μg/cm2 versus frozen 1.888 μg/cm2). The cumulative permeation values at 24 h represented 0.086% of the applied dose for fresh skin and 0.433% of the applied dose for frozen skin.
試験結果	分布のデータから皮膚上及び皮膚内に残存しているDEAの量は同様であることが示された。24時間では適用量の大部分 (約95%)が皮膚表面から回収された (ドナー細胞の洗浄液プラス2枚の角質層のテープ片)。 皮膚 (残存している角質層、生きている表皮及び真皮)から回収したDEAの量は新鮮及び凍結皮膚でそれぞれ適用量の1.14%及び1.68% (22.8 mg/cm2 及び33.7 μg/cm2 に相当) となった。放射能の回収率は良好で、新鮮及び凍結皮膚でそれぞれ計96.3%及び97.4%であった。 2名のドナーからの新鮮皮膚 (n=12)を用いての24時間浸透試験の終わりに皮膚表面に残っている放射能を測定した。 2名のドナーの間には浸透率にやや差があり、ドナー232に対する累積24時間値(8.13 μg/cm2)はドナー235に対するそれ(1.34 μg/cm2)より約6倍高い値を示した。ドナー232は腹部の皮膚で、ドナー235は胸部の皮膚であった。	Distribution data demonstrated that the amount of DEA remaining on and in the skin were similar. The majority of the applied dose (ca. 95%) was recovered from the skin surface (donor cell rinse plus two stratum corneum tapestrips) at 24 h. The amount of DEA recovered from the skin (remaining stratum corneum, viable epidermis and dermis) totaled 1.14% and 1.68% of the applied dose (equivalent to 22.8 mg/cm2 and 33.7 μg/cm2) for fresh and frozen skin respectively. Recovery of label was good and totaled 96.3% and 97.4% of the applied dose for fresh and frozen skin respectively. At the end of a 24 h permeation run using fresh skin from two donors (n = 12), radioactivity remaining on the skin surface was determined. There was some difference in permeation between the two donors, the cumulative 24 h value for donor 232 (8.13 μg/cm2) being approximately 6-fold higher than that for donor 235 (1.34 μg/cm2). Donor 232 was abdominal skin whereas Donor 235 was breast skin.

試験結果

24時間での累積浸透率の値はドナー232では適用量の0.405%、ドナー235では適用量の0.067% (両方のドナーを合わせると0.236%)を示した。

適用量の大部分 (約92%)が皮膚表面から回収された。角質層のテープ片から回収されたDEAの量は1.57%に達した。両ドナーからのテープ片のプロフィルから、24時間までにDEAが角質層を通して均一に分布したことが示された。

放射能の全体の回収率は良好で、適用量の95.7%を占めた。表皮及び真皮組織の水及び有機抽出物中に回収された物質の分布はDEAの大部分 (98.3%)が水抽出物中で回収されることを示した。

詳細は以下の表に示した:

The cumulative permeation values at 24 h represented 0.405% of the applied dose for donor 232 and 0.067% of the applied dose for donor 235 (0.236% for both donors combined).

The majority of the applied dose (ca. 92%) was recovered from the skin surface. The amount of DEA recovered from the stratum corneum tape-strips totaled 1.57%. The tape-strip profiles for both donors indicated that by 24 h the DEA had been evenly distributed throughout the stratum corneum.

Overall recovery of label was good and totalled 95.7% of the applied dose. Distribution of recovered material in the aqueous and organic extracts of the epidermal and dermal tissue indicated that the majority (98.3%) of DEA was recovered in the aqueous extract.

Details are provided in the tables below:

試験結果

調製品A及びBの希釈水溶液中に適用後のDEAに対する分布データ (平均値、n = 12)

% 適用量	A	B
10 分洗浄液	92.28	99.49
表面の洗浄液	0.05	0.056
SC テープ片 1-2	0.005	0.014
SC テープ片 3-5	0.008	0.019
SC テープ片 6-10	0.008	0.009
SC テープ片 11-15	0.005	0.010
残存表皮	0.37	0.026
浸透率	0.019	0.025
総回収率	92.41	99.66

ng/cm²	A	B
10 分間洗浄液	90,740	97,420
表面の洗浄液	49	55
SC テープ片 1-2	5.8	15.1
SC テープ片 3-5	9.0	20.8
SC テープ片 6-10	9.5	10.9
SC テープ片 11-15	5.2	10.9
残存表皮	37	26
浸透率	18	25
総回収率	–	–

Distribution data for DEA following application in aqueous dilutions of formulations A and B (mean, n = 12)

% applied dose	A	B
10 min rinse	92.28	99.49
Surface rinse	0.05	0.056
SC tape strips 1-2	0.005	0.014
SC tape strips 3-5	0.008	0.019
SC tape strips 6-10	0.008	0.009
SC tape strips 11-15	0.005	0.010
Remaining epidermis	0.37	0.026
Permeated	0.019	0.025
Total recovery	92.41	99.66

ng/cm²	A	B
10 min rinse	90,740	97,420
Surface rinse	49	55
SC tape strips 1-2	5.8	15.1
SC tape strips 3-5	9.0	20.8
SC tape strips 6-10	9.5	10.9
SC tape strips 11-15	5.2	10.9
Remaining epidermis	37	26
Permeated	18	25
Total recovery	–	–

試験結果

調製品C及びDの希釈水溶液適用後のDEAの24時間分布データ (平均値、n = 12)

% 適用量	C	D
10 分間洗浄液	92.08	91.63
表面の洗浄液	0.016	0.034
SC テープ片 1-2	0.003	0.010
SC テープ片 3-5	0.005	0.010
SC テープ片 6-10	0.009	0.003
SC テープ片 11-15	0.004	0.000
残存表皮	0.016	0.017
浸透率	0.034	0.011
総回収率	92.17	91.71

ng/cm²	C	D
10 分間洗浄液	23,050	22,990
表面の洗浄液	4	9
SC テープ片 1-2	1.0	3.2
SC テープ片 3-5	1.6	3.0
SC テープ片 6-10	2.7	1.1
SC テープ片 11-15	1.3	0.1
残存表皮	3.9	4.2
浸透率	8.5	2.7
総回収率	–	–

24 h distribution data for DEA following application in aqueous dilutions of formulations C and D (mean, n = 12)

% applied dose	C	D
10 min rinse	92.08	91.63
Surface rinse	0.016	0.034
SC tape strips 1-2	0.003	0.010
SC tape strips 3-5	0.005	0.010
SC tape strips 6-10	0.009	0.003
SC tape strips 11-15	0.004	0.000
Remaining epidermis	0.016	0.017
Permeated	0.034	0.011
Total recovery	92.17	91.71

ng/cm²	C	D
10 min rinse	23,050	22,990
Surface rinse	4	9
SC tape strips 1-2	1.0	3.2
SC tape strips 3-5	1.6	3.0
SC tape strips 6-10	2.7	1.1
SC tape strips 11-15	1.3	0.1
Remaining epidermis	3.9	4.2
Permeated	8.5	2.7
Total recovery	–	–

試験結果

調製品Eの希釈水溶液適用後のDEAの24時間分布データ (平均値、n=12)

部位	%	ng/cm²
30分間表面洗浄液	77.91	649
24時間表面洗浄液	3.33	28
SC テープ片 1-2	0.420	3.9
SC テープ片 3-5	0.450	4.1
SC テープ片 6-10	0.283	2.6
SC テープ片 11-15	0.160	1.5
残存表皮	0.6140	5.1
浸透率	0.508	4.2
総回収率	83.70	–

調製品Fの希釈水溶液適用後のDEAの48時間分布データ (平均値、n=12)

新鮮皮膚	%	ng/cm²
48時間表面洗浄液	79.42	311
SC テープ片 1-2	0.882	3.1
SC テープ片 3-5	1.197	4.4
SC テープ片 6-10	2.775	10.8
SC テープ片 11-15	2.067	8.1
残存表皮	3.852	15.0
真皮	0.877	3.4
浸透率	0.605	2.3
総回収率	94.90	–

24 h distribution data for DEA following application in aqueous dilution of formulation E (mean, n=12)

Site	%	ng/cm²
30 min surface blot	77.91	649
24 h surface rinse	3.33	28
SC tape strips 1-2	0.420	3.9
SC tape strips 3-5	0.450	4.1
SC tape strips 6-10	0.283	2.6
SC tape strips 11-15	0.160	1.5
Remaining epidermis	0.6140	5.1
Permeated	0.508	4.2
Total recovery	83.70	–

48 h distribution data for DEA following application in formulation F (mean, n = 12)

Fresh skin	%	ng/cm²
48 h surface rinse	79.42	311
SC tape strips 1-2	0.882	3.1
SC tape strips 3-5	1.197	4.4
SC tape strips 6-10	2.775	10.8
SC tape strips 11-15	2.067	8.1
Remaining epidermis	3.852	15.0
Dermis	0.877	3.4
Permeated	0.605	2.3
Total recovery	94.90	–

試験結果	凍結皮膚 % ng/cm² 48時間表面洗浄液 77.80 296 SC テープ片 1-2 0.741 2.8 SC テープ片 3-5 1.057 4.0 SC テープ片 6-10 2.742 10.2 SC テープ片 11-15 2.018 7.6 残存表皮 6.165 22.9 真皮 0.534 2.0 浸透率 0.456 1.7 総回収率 95.20 -	Frozen skin % ng/cm² 48 h surface rinse 77.80 296 SC tape strips 1-2 0.741 2.8 SC tape strips 3-5 1.057 4.0 SC tape strips 6-10 2.742 10.2 SC tape strips 11-15 2.018 7.6 Remaining epidermis 6.165 22.9 Dermis 0.534 2.0 Permeated 0.456 1.7 Total recovery 95.20 -
試験結果	媒体G及びHの適用後のDEAの24時間分布データ (平均値、n = 12) % 適用量 G H 30分洗浄液 100.8 100.99 表面洗浄液 0.184 0.190 SC テープ片 1-2 0.0041 0.0132 SC テープ片 3-5 0.0055 0.0119 SC テープ片 6-10 0.0057 0.0084 SC テープ片 11-15 0.0028 0.0044 残存表皮 0.012 0.023 浸透率 0.063 0.024 総回収率 101.08 101.27 ng/cm² G H 30分洗浄液 75,120 125,200 表面洗浄液 115 238 SC テープ片 1-2 3.0 15.6 SC テープ片 3-5 10.0 14.3 SC テープ片 6-10 4.1 10.1 SC テープ片 11-15 2.1 5.5 残存表皮 8.8 28.5 浸透率 47.9 28.2 総回収率 - -	24 h distribution data for DEA following application in vehicle G and H (mean, n = 12) % applied dose G H 30 min rinse 100.8 100.99 Surface rinse 0.184 0.190 SC tape strips 1-2 0.0041 0.0132 SC tape strips 3-5 0.0055 0.0119 SC tape strips 6-10 0.0057 0.0084 SC tape strips 11-15 0.0028 0.0044 Remaining epidermis 0.012 0.023 Permeated 0.063 0.024 Total recovery 101.08 101.27 ng/cm² G H 30 min rinse 75,120 125,200 Surface rinse 115 238 SC tape strips 1-2 3.0 15.6 SC tape strips 3-5 10.0 14.3 SC tape strips 6-10 4.1 10.1 SC tape strips 11-15 2.1 5.5 Remaining epidermis 8.8 28.5 Permeated 47.9 28.2 Total recovery - -
結論		
結論	結論: 典型的な調製品の範囲に対する皮膚透過のデータが使用条件下で得られた。プロトタイプの化粧品製剤を表し、DEAの代表的なレベルを含有する7種のリンスオフ製剤 (A-E、G及びH)、乳化液 (F)が準備された。 14C-DEA又は14C-DEAと非標識DEAの組合わせのいずれかによりDEAを包含するjことによりDEAの標的レベルが達成された。 浸透率は使用条件下では適用した全ての媒体で極めて低かった (24時間で1-48 ng/cm2 の範囲)。	Conclusion : Skin penetration data were generated for a range of typical formulations under in-use conditions. Seven rinse-off formulations (A-E, G and H), a leave-on emulsion (F), representing prototype cosmetic formulations and containing representative levels of DEA were prepared. Target levels of DEA were attained by inclusion of DEA as either 14C-DEA or a combination of 14C-DEA and unlabeled DEA. Permeation was very low from all vehicles applied under in-use conditions (range 1-48 ng/cm2 over 24 h).
結論	水溶液中に不定の用量で適用した場合、24時間でのDEA浸透率は新鮮な皮膚を通した場合よりも凍結した皮膚を通した場合の方が高い値を示した。 乳化液のままの製剤では浸透率は新鮮及び凍結皮膚の両方とも同様で、極めて低かった。 新鮮なヒトの皮膚に水溶液を適用し、表皮と真皮組織の水及び有機抽出を行った後のDEAの回収率はDEAの大部分 (>98%)が水抽出物中にあることを示し、DEAが遊離の状態で脂質の画分と関連していないことを示唆した。	When applied as an infinite dose in aqueous solution DEA permeation at 24 h was greater through frozen than through fresh skin. From the leave-on formulation, permeation was similar and very low for both fresh and frozen skin. Recovery of DEA after application of the aqueous solution to fresh human skin and subsequent aqueous and organic extraction of the epidermal and dermal tissue indicated that the majority (>98%) of DEA was in the aqueous extract, suggesting that DEA was in the free state and not associated with the lipid fraction.
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	一般に許容できる科学的基準を満たし、文章化が良好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)	(138)	(138)
備考		

試験物質名	他のTS	other TS
CAS番号		
純度等		
注釈	DEAの皮膚投与担体。Research Triangle Institute (Research Triangle, NC, USA) で合成された14C-DEA (比放射能: 32.2 mCi/mmol; 306.3 µCi/mg)。放射化学的及び化学的純度は >99 %であった。 投与媒体: 水乳化液中に添加した油	DEA skin dosing vehicle. 14C-DEA (specific activity: 32.2 mCi/mmol; 306.3 µCi/mg), synthesized by Research Triangle Institute (Research Triangle, NC, USA); radiochemical and chemical purity was >99 %. Dosing vehicle: spiked oil - in water emulsion.
方法		
方法／ガイドライン	その他: in vitro 皮膚浸透スクリーニング	other: dermal penetration screening in vitro
試験形態	In vitro 吸収	In vitro Absorption
GLP適合	いいえ	no
試験をおこなった年		
方法の概略	※英文参照	METHOD FOLLOWED: In vitro dermal absorption study using skin from Fuzzy rat. GLP: No data

方法の概略	※英文参照	Test condition : ADMINISTRATION / EXPOSURE 14C-DEA (approximately 0.5 µCi or 2.mg/cm²) was applied to the skin in each diffusion cell at 3 mg/cm2. TEST SYSTEM: Fresh dorsal skin (hair removed) from female Fuzzy rats (Harlan Sprague Dawley) was used immediately for absorption studies. Skin was gently washed with a 10% soap solution. A split-thickness layer of rat (200-330 µm) skin was prepared using a dermatome. Skin discs were mounted with the epidermal side up in flow through diffusion cells (0.64 cm2, exposed skin). The skin surface temperature was maintained at 32° C. The skin was perfused with HEPES buffered Hanks' balanced salt solution (HHBSS),pH 7.4 at a flow rate of 1.5 ml/h for the duration of the absorption studies.
方法の概略	※英文参照	DEA dosing vehicle was applied to the epidermal surface of the skin for 24 hr and then removed (washed 3 times with 0.3 ml of a 10% soap solution). Receptor fluid fractions were collected for 6, 12, 18, and 24 h time points. Some studies were continued for 72hr to determine the fate of DEA remaining in the skin after 24 hr. Skin discs, were taped stripped 10-times to determine the amount of 14C-DEA remaining in the stratum corneum versus the viable epidermis/dermis at the end of the study. The viable epidermis/dermis was digested (Scintigest®). Radioactivity in each sample was measured by liquid scintillation counting. DEA absorption studies were done with an oil-in-water emulsion in three fuzzy rats (n=3). Each study was done with at least 3-4 replicates (i.e., 3-4 diffusion cells) per experiment. The data from the replicates were averaged to obtain the mean and SD for that experiment. Comparison of absorption values were made by the Student's t-test or ANOVA where appropriate.
動物種	ラット	rat
試験動物:系統		
性別		
細胞株		
年齢		
体重		
試験動物数		
曝露経路		
溶媒(賦刑剤)		
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	ラットの皮膚では24時間にわたり吸収された投与量の割合は1.4 +/- 0.5 (平均値、SD)で皮膚には約4%が残っていた。 24時間で角質層及び生存表皮/真皮にはそれぞれ適用量の1.9 +/- 0.8% 及び 1.9 +/- 0.5%が残留していた。 DEAの皮膚レベルは72時間追跡しても変化しなかった。 著者らによれば、これらの研究から24時間で皮膚にみられたDEAのうち、皮膚を通して拡散し、レセプター液に吸収されるものは殆どないことが示された。	In rat skin the percentage of applied dose absorbed over 24 h was 1.4 +/- 0.5 (mean, SD) with approximately 4% remaining in the skin. At 24 h there was 1.9 +/- 0.8% and 1.9 +/- 0.5% of the applied dose remaining in the stratum corneum and viable epidermis/dermis, respectively. Skin levels of DEA did not change when followed for 72 h. According to the authors, these studies indicated that little of the DEA that was found in the skin at 24 h diffused through the skin to be absorbed into the receptor fluid.
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	基礎的なデータが得られた。	Basic data supplied
出典		
引用文献(元文献)	(139)	(139)
備考		

試験物質名	他のTS	other TS
CAS番号		
純度等		
注釈	ジエタノールアミン: 供給源: Dow Chemical Co., Freeport TX, USA 純度: 99.3% 14C-ジエタノールアミン: 供給源: Wizard Laboratories, Davis, CA, USA 放射化学純度: 97.4% 比放射能: 15 mCi/mmol	DIETHANOLAMINE: Source: Dow Chemical Co., Freeport TX, USA Purity: 99.3% 14C-DIETHANOLAMINE: Source: Wizard Laboratories, Davis, CA, USA Radiochemical purity: 97.4% Specific activity: 15 mCi/mmol
方法		
方法/ガイドライン	その他 静注後のラットにおけるファーマコキネティクス	other Pharmacokinetics in rats following intravenous injection
試験形態	In vivo トキシコキネティクス	In vivo Toxicokinetics
GLP適合	いいえ	no

試験をおこなった年	2001	2001
方法の概略	※英文参照	Test condition : TEST ORGANISMS: - Species/Strain: female Sprague-Dawley rats, supplied Charles River Laboratory, Kingston, NY,USA - Acclimatization: at least 7 days - Age at study start: 11 weeks - Body weight at start: 247 - 271 g - Number of animals: 5 per group - Housing: individually ADMINISTRATION / EXPOSURE Prior to exposure, the rats were anesthetized and an indwelling cannula was implanted and recovered for 48 h. - Dose level: 10 and 100 mg/kg bw 14C-DEA - Dosing volume: 2 ml/kg bw - Vehicle: sterile saline
方法の概略	※英文参照	SPECIMEN COLLECTION: All urine and feces voided during the study were collected in dry-ice cooled traps. The traps were changed at 12-h intervals post-dosing for 96 h at which time the animals were anesthetized and euthanized. Urine and feces were stored at -80 C until analyzed. Samples of blood (about 0.15 m1) were collected via the indwelling cannula at 5, 10, 15, 30 min and 1, 2, 4, 6, 12, 24, 36, 48, 60, 72 and 84 h post-dosing. At 96 h post-dosing, rats were anesthetized with methoxyflurane and sacrificed by exsanguination via cardiac puncture. Blood, liver, kidneys, heart, brain, stomach and samples of perirenal fat and skin were collected and the remaining carcass skinned. Metabolism cages were washed with a solution of acetone and water and the volume measured.
方法の概略	※英文参照	Radioactivity in the plasma samples and in aliquots (approx. 1 m1) of urine and cage washings were determined by liquid scintillation spectroscopy (LSC) in a Beckman LS3801 scintillation counter model using Aquasol liquid scintillation cocktail (Packard Co., Meriden, CT, USA). The blood cells (primarily erythrocytes; RBC), perirenal fat (approx. 0.2 g), skin samples (approx. 0.2 g), and approximately 300-µ1 aliquots of the homogenates of feces, liver, kidneys, heart, brain, stomach and carcass were solubilized with Soluene-350® tissue solubilizer (Packard Co.) and counted by LSC using Hionic Fluor liquid scintillation cocktail (Packard Co.).
方法の概略	※英文参照	Analysis of blood samples: Blood samples (approximately 0.05-0.9 g) were mixed immediately with the internal standard solution (0.3-1.0 ml, D8-DEA in 2.5 N KOH) and either derivatized immediately or frozen until derivatization could be performed. Extracts were analyzed using a Hewlett Packard (HP) 5890 GC/5970A MSD system equipped with a HP 7673A autosampler (Hewlett Packard, Palo Alto, CA, USA). Samples were quantitated using matrix standards, which were prepared by fortifying control rat blood with known quantities of DEA. Analysis of urine samples Aliquots of the 0-12, 36-48, 60-72 and 84-96 h pooled urine samples were analyzed for DEA. Aliquots of urine (0.15-0.3 ml) were combined with 0.3 ml internal standard solution (D8-DEA in 2.5 N KOH) and 30 µl PFBCI and then vortexed for 20 min at room temperature. Samples were extracted and analyzed using the GC/MS system.
動物種	ラット	rat
試験動物:系統		
性別		
細胞株		
年齢		
体重		
試験動物数	10匹	10
曝露経路		i.v.
溶媒(賦刑剤)		physiol. Saline
投与量	10 及び 100 mg/kg 体重	10 and 100 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	投与した放射能の平均回収率は10及び100 mg/kgの両用量レベルに対して95-96%であった。投与後96時間で、10及び100 mg/kgの用量レベルで、投与した放射能の回収率の平均はそれぞれ約69及び57%であった。この放射能の大部分は屍体と関連していた（10及び100 mg/kgの用量レベルでそれぞれ35及び28%）。 肝臓及び腎臓が投与量に対して次に大きい割合を占めた。両投与レベルで投与量の約5%が皮膚と関連し、脳、脂肪、心臓及び胃はいずれの用量でも投与量の1%未満であった。 腎臓は両用量レベルで放射能の最高濃度を含有しており、次いで肝臓が腎臓よりもやや低濃度で続いた。腎臓及び肝臓で検出された放射能の濃度は測定した他の全ての組織で検出された濃度よりも約5-20倍高かった。	The mean recoveries of administered radioactivity were 95-96% for both the 10 and 100 mg/ kg dose levels. At 96 h post-dosing, an average of approximately 69 and 57% of the radioactivity administered was recovered in the tissues for the 10 and 100 mg/kg dose levels, respectively. The majority of this radioactivity was associated with the carcass (35 and 28% for the 10 and 100 mg/kg dose levels, respectively). The liver and the kidneys accounted for the next highest percentage of the administered dose. About 5% of the administered dose was associated with the skin at both dose levels and less than 1% of the administered dose was associated with brain, fat, heart and stomach at either dose level. The kidneys contained the highest concentrations of radioactivity at both dose levels, followed by the livers, slightly lower concentrations than found in the kidneys. The concentrations of radioactivity found in the kidneys and liver were approximately 5- to 20-fold higher than the concentrations found in all other tissues measured.
試験結果	放射能の主な排泄経路は尿を介してであり、10及び100 mg/kgの用量レベルで、それぞれ投与量の平均約25及び36%が96時間後までに尿中に排泄された。放射能の尿中排泄は高用量では速やかで、投与量の約23%が投与後最初の12時間で回収された。10 mg/kgの用量レベルでは投与した放射能の僅かに8.5%が最初の12時間で排泄された。10 mg/kgの用量レベルと比べて100 mg/kg の用量レベル投与後には尿を介したより速い放射能の排泄がみられた。 初期に速い尿排泄相がみられ、投与後96時間を通して尿を介した放射能の遅い排泄が続いた。初期の尿排泄の半減期は10及び100 mg/kg の用量でそれぞれ3.5及び2.4時間であった。 両用量レベルで血漿中14C-DEA由来放射能のピーク濃度が投与後5分でみられ、血漿からの放射能の消失は2つの指数関数的に生じた。	The major route of excretion of radioactivity was via the urine with an average of about 25 and 36% of the administered dose excreted in the urine by 96 h post dosing for the 10 and 100 mg/kg dose levels, respectively. Urinary excretion of radioactivity was rapid at the high dose level with approximately 23% of the administered dose recovered in the first 12 h post-dosing. At the 10 mg/kg dose level, only 8.5% of the administered radioactivity was excreted in the first 12 h post-dosing. There was a faster elimination of radioactivity via the urine following the 100 mg/kg dose level when compared to the 10 mg/kg dose level. A rapid initial urinary elimination phase was observed, followed by slow elimination of radioactivity via the urine through 96 h post-dosing. The initial urinary elimination half-lives were estimated to be 3.5 and 2.4 h for the 10 and 100 mg/kg doses, respectively. The peak concentrations of plasma 14C-DEA-derived radioactivity at both dose levels were found at 5 min post-dosing and elimination of the radioactivity from the plasma occurred in a bi-exponential manner.
試験結果	赤血球中の放射能濃度は投与後6時間まで血漿中濃度の約2倍高い値を示したが、両用量レベルで赤血球の14C-DEA由来放射能のピーク濃度も投与後5分でみられた。 両用量レベルで赤血球中の放射能の濃度は最初は速やかに低下したが、投与後6-12時間以降RBCは徐々に放射能を蓄積した。血漿及びRBC中の放射能の濃度は投与後の全ての時間で投与量にほぼ比例した。血漿中の14C及び血中のDEAの濃度はともに2つの指数関数的に減少し、2コンパートメントの薬物動態モデルで記述された。 血漿からの放射能のクリアランスは低用量では約50 ml/h/kgであると算出され、高用量ではほぼ2倍の93 ml/h/kgに増加した。低及び高用量群ともに動物を安楽死させた投与後96時間では血漿中の放射能は検出可能レベルに留まっていた。	The peak concentrations of RBC 14C-DEA-derived radioactivity at both dose levels were also found at 5 min post-dosing, although the concentrations of radioactivity in the RBC were approximately 2-fold higher than plasma concentrations through 6 h post-dosing. At both dose levels, the concentrations of radioactivity in the RBC initially declined rapidly, but starting at 6-12 h post-dosing the RBC gradually accumulated radioactivity. The concentration of radioactivity in both plasma and RBC was roughly proportional across dose levels at all times post-dosing. The concentrations of both 14C in plasma and DEA in blood decreased in a bi-exponential manner and were well described by a two-compartment pharmacokinetic model. Clearance of radioactivity from plasma was calculated to be approximately 50 ml/h/kg at the low dose, increasing almost 2-fold to approximately 93 ml/h/kg at the high dose. Radioactivity remained detectable at 96 h post-dosing in the plasma of both the low and high dose groups, at which time the animals were euthanized.
試験結果	血漿濃度曲線下面積（AUC)は投与量に比例しなかった。用量が10倍増加したのに対し、用量群間で血漿中AUCは5倍に増加した。低用量に対するα（初期)相の半減期の約10分が高用量のc-消失相ではでは約16分にわずかに増加する。14C排泄のβ-消失（終末)相は約4時間後には明らかに緩徐になった。B-消失の終末半減期は低用量では270時間と推定され、高用量では113時間に早まった。 DEAの血液からのクリアランスは低用量では約84 ml/h/kgで、高用量では約242 ml/h/kgとほぼ3倍に増加した。血中DEAのAUCは用量には比例しなかった。用量が10倍増加したのに対し、血漿AUCは用量間で3.5倍の増加であった。	The plasma area under curves (AUC) were not proportional to dose. A 5-fold increase in plasma AUC across the dose groups contrasted with the 10-fold increase in dose. Half-lives of approximately 10 min for the alpha-elimination (initial) phase for the low dose increases slightly to approximately 16 min for the high dose c -elimination phase. A slower beta-elimination (terminal) phase of 14C elimination became apparent after approximately 4 h. The terminal half-life of beta-elimination was estimated as 270 h for the low dose and faster at 113 h for the high dose. The clearance of DEA from blood was calculated to be approximately 84 ml/h/kg at the low dose, increasing almost threefold to approximately 242 ml/h/kg at the high dose. The blood-DEA AUCs were not proportional to dose. A 3.5-fold increase in plasma AUC across the dose groups contrasted with the 10-fold increase in dose.

試験結果	血中DEAに対しては、低用量では α -消失相の半減期約6分が高用量では約35分に増加した。14C排泄の緩徐な β -消失相は約4時間後に明瞭になった。 DEAの尿中濃度は10 mg/kgの用量レベルでは、0-12、36-48、60-72及び84-96時間の採取時間間隔でそれぞれ、18.9、6.35、1.92 及び 2.14 μg/gであった。100 mg/kgの用量レベルでは、投与量の増加に比べて尿中排泄量の比例しない増加が投与後0-12時間でみられ、DEAの尿中濃度は10 mg/kgと比べて40倍高い測定値を示した。100 mg/kg用量レベルではその後の時間間隔でDEAの尿中濃度は36-48、60-72、及び84-96時間の採取間隔でそれぞれ、43.2、18.8 及び19.9 pg/gと測定値を示し、低用量レベルでみられた尿中濃度にほぼ比例した。プールした尿サンプル中の放射能濃度に基づいて、10及び100 mg/kgの両方で尿中に排泄されたDEAは分析した間隔で48-83%の範囲で尿中放射能の大分を占めた。	For blood DEA, half-lives of approximately 6 min for the alpha-elimination phase for the low dose increased to approximately 35 min for the high dose. A slower beta-elimination phase of 14C elimination became apparent after approximately 4 h. The urinary concentrations of DEA were 18.9, 6.35, 1.92 and 2.14 μg/g for the 0-12, 36-48, 60-72 and 84-96 h collection intervals, respectively, at the 10 mg/kg dose level. A disproportionate increase in the urinary excretion of DEA relative to the increase in dose was observed at 0-12 h post dosing for the 100 mg/kg dose level where the urinary concentrations of DEA were determined 40-fold higher than at 10 mg/kg. At subsequent intervals at the 100 mg/kg dose level, the urinary concentrations of DEA were determined to be 43.2, 18.8 and 19.9 pg/g for the 36-48, 60-72 and 84-96 h collection intervals, respectively, which were roughly proportionate to the urinary concentrations found at the lower dose level. Based an the concentration of radioactivity in the pooled urine samples the DEA excreted in the urine at both 10 and 100 mg/kg comprised a majority of the urinary radioactivity ranging from 49 to 83% at the intervals analyzed.
試験結果	C-DEAの静注後に回収された放射能の分布 mg/kg 体重　10#　100# 尿及びケージ 洗浄液　25.05+3.35　36.27+1.18 糞　1.17+0.19　1.50+0.43 最後のケージ 洗浄水　0.56+0.36　0.34+024 組織　69.72+2.93　56.72+1.65 脳　0.41+0.06　0.38+0.01 屍体　34.55+4.29　28.24+1.37 脂肪　0.04+0.02　0.02+0.02 心臓　0.23+0.05　0.21+0.03 腎臓　7.18+1.14　4.87+0.80 肝臓　20.89+2.77　17.14+2.10 胃　0.80+0.12　10.67+0.08 皮膚　5.12+0.63　5.18+0.65 総 回収率　96.00+3.41　94.83+0.92 # %、値は5匹のラットの 平均値 ± SD を表す	Distribution of radioactivity recovered after iv administration of 'C-DEA mg/kg bw　10#　100# Urine and cage rinse　25.05+3.35　36.27+1.18 Feces　1.17+0.19　1.50+0.43 Final cage wash　0.56+0.36　0.34+024 Tissues　69.72+2.93　56.72+1.65 Brain　0.41+0.06　0.38+0.01 Carcass　34.55+4.29　28.24+1.37 Fat　0.04+0.02　0.02+0.02 Heart　0.23+0.05　0.21+0.03 Kidneys　7.18+1.14　4.87+0.80 Liver　20.89+2.77　17.14+2.10 Stomach　0.80+0.12　10.67+0.08 Skin　5.12+0.63　5.18+0.65 Total recovery　96.00+3.41　94.83+0.92 # %, values represent mean ± SD for 5 rats.
試験結果	14C-DEA静注後の尿中に排泄された放射能 時間 0(h)　% 投与放射能 10 mg/kg　100 mg/kg 0-12　8.50±0.77　23.09+1.68 12-24　3.16±0.58　2.69+0.61 24-36　1.27+0.74　0.85±0.14 36-48　2.77±0.90　2.4±0.44 48-60　2.45+1.11　1.6+0.38 60-72　2.61+0.91　2.12+0.43 72-84　1.81+0.31　1.41+0.42 84-96　2.48+0.88　2.12±0.16 25.05±3.35　36.27±1.18 値はラット5匹の 平均値 ± SD を表す	Radioactivity excreted in the urine after iv administration of 14C-DEA Time (h)　% Administration radioactivity 10 mg/kg　100 mg/kg 0-12　8.50±0.77　23.09+1.68 12-24　3.16±0.58　2.69+0.61 24-36　1.27+0.74　0.85±0.14 36-48　2.77±0.90　2.4±0.44 48-60　2.45+1.11　1.6+0.38 60-72　2.61+0.91　2.12+0.43 72-84　1.81+0.31　1.41+0.42 84-96　2.48+0.88　2.12±0.16 25.05±3.35　36.27±1.18 Values represent mean ± SD for 5 rats.
結論		
結論	結論: 肝臓、腎臓、心臓、脳、胃、腎周囲脂肪、及び皮膚を含む組織が投与96時間後に採取された。組織は低用量では投与した放射能の69%、高用量では57%を含んでいた。 屍体で最大割合 (35%、低用量; 28%、高用量)が検出された。検査した組織では肝臓 (21%、高用量; 17%、低用量)及び腎臓 (7%、高用量; 5%、低用量)に最高レベルが残留した。 赤血球も投与後6から96時間の間に放射能を徐々に蓄積する傾向を示した。	Conclusion : Tissues, including liver, kidneys, heart, brain, stomach, perirenal fat, and skin, were collected at 96 hours after administration. The tissues contained 69% of the administered radioactivity at the low dose and 57% at the high dose. The largest portion (35%, low dose; 28%, high dose) was detected in the carcass. In the tissues examined, the highest levels were retained in liver (21%, high dose; 17%, low dose) and kidneys (7%, high dose; 5%, low dose). Red blood cells also showed a tendency for a gradual accumulation of radioactivity between 6 and 96 hours after administration.
結論	投与した放射能の約25% (低用量)及び36% (高用量)が尿中に親化合物として排泄された。 DEAの血液からのクリアランスの計算値は低用量に対しては84 ml/h/kg体重、高用量に対しては242 ml/h/kg体重であった。著者らはDEAの分布及び消失の用量依存性は100 mg/kg体重の高レベルで生体内蓄積過程の飽和を示しているようであると結論した。	About 25% (low dose) and 36% (high dose) of the administered radioactivity was excreted in the urine as the parent compound. The calculated clearance of DEA from blood was 84 ml/h per kilogram bw. for the low dose and 242 ml/h per kg bw for the high dose. The authors concluded that the dose dependency of the distribution and elimination of DEA likely represented a saturation of the processes of bioaccumulation at the higher dose level of 100 mg/kg bw.
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	基本的な科学的原理を満たしている文書化が良好な試験	Well-documented study which meets basic scientific principles
出典		
引用文献(元文献)	(140)	(140)
備考		

A. 急性経口毒性
ACUTE ORAL TOXICITY

試験物質名	データなし	no data
CAS番号		
純度等		
注釈		
方法		
方法／ガイドライン	その他: Smyth et al., 1969 に準じた。	other: according to Smyth et al., 1969
GLP適合	いいえ	no
試験を行った年	1969	1969
試験系(種／系統)	ラット	rat
	Wistar	Wistar
性別(雄:M、雌:F)	雌	female
投与量		
各用量群(性別)の動物数		
溶媒(担体)		
投与経路		
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	英文参照	TEST ORGANISMS: - Species/Strain: female albino rats (Wistar derived) - Body weight (initial): 90 - 120 g - Housing: 5/cage ADMINISTRATION / EXPOSURE - Application: oral by gavage without dilution to groups of 5 non-fasted rats by stainless steel tube, at dose levels differing by a geometric factor of 2.0 - Animal number: 5 per group, - Post dose observation period: 2 weeks
結論		
LD50値又はLC50値	LD50= 約 780 - mg/kg bw	LD50= ca. 780 - mg/kg bw
雌雄のLD50値又はLC50値の違い等		
注釈	LD50は 0.71 ml/kg bwと報告されており、密度 1.096 g/cm3をベースに 780 mg/kg bwに相当する。	LD50 cited as 0.71 ml/kg bw, corresponding to about 780 mg/kg bw based on the density of 1.096 g/cm³ Method described in Smyth et al., 1969.
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	基本的な科学的原理を満たす試験	Study meets basic scientific principles
出典		
引用文献(元文献)	(146) (147)	(146) (147)
備考		

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	供給源: BASF AG、ドイツ、物質番号 No. XV/306、名前:ジエタノールアミン(固体)	Source: BASF AG, Germany, substance-No. XV/306, name: Diethanolamine (solid)
方法		
方法／ガイドライン	その他: 予備的な基本設定試験	other: preliminary base set testing
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		
各用量群(性別)の動物数		
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	METHOD FOLLOWED: approximate median lethal dose determination (ALD50) GLP: No
その他の試験条件	英文参照	TEST ORGANISMS: - Species/Strain: Rat ADMINISTRATION / EXPOSURE - Application: 2 - 20% aqueous preparation by gavage - Post dose observation period: 7 days
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	臨床症状: 呼吸困難、旋回を含む非特異的な急性毒性症状。 剖検所見: 胃腸管の刺激症状、胸水症 潜在的な標的臓器: なし LD50(雌雄合わせて): 約 1600 mg/kg bw LD50 雌: 1100 mg/kg/bw LD50 雄: 2500 mg/kg bw	CLINICAL SIGNS: Unspecific signs of acute intoxication in form of dyspnea, tumbling NECROPSY FINDINGS: Signs of irritation on gastro-intestinal tract, hydrothorax POTENTIAL TARGET ORGANS: None LD50 (combined): approximately 1600 mg/kg bw LD50 females: 1100 mg/kg bw LD50 males: 2500 mg/kg bw
結論		
LD50値又はLC50値	LD50= 約 1600 - mg/kg bw	LD50= ca. 1600 - 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	基本的な科学原理を満たす試験	Study meets basic scientific principles
出典		
引用文献(元文献)	(148)	(148)
備考		

試験物質名	データなし	no data
CAS番号		
純度等		
注釈		
方法		
方法／ガイドライン	その他	other:
GLP適合	なし	no
試験を行った年	1969	1969
試験系(種／系統)	ラット	rat
	Wistar	Wistar
性別(雄:M、雌:F)	雌	female
投与量		
各用量群(性別)の動物数		
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 ORGANISMS: - Species/Strain: female albino rats (Wistar derived) - Body weight (initial): 90 - 120 g - Housing: 5/cage ADMINISTRATION / EXPOSURE - Application: oral by gavage without dilution to groups of 5 non-fasted rats by stainless steel tube, at dose levels differing by a geometric factor of 2.0 - Animal number: 5 per group, - Post dose observation period: 2 weeks
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		
LD50値又はLC50値	LD50= 878 - mg/kg bw	LD50= 878 - mg/kg bw
雌雄のLD50値又はLC50値の違い等		
注釈	LD50の中央値として0.80 ml/kg bwと引用されており、密度1.096 g/cm3をベースとして 878 mg/kg bw に相当する。	Cited as median LD50 of 0.80 ml/kg bw, corresponding to about 878 mg/kg bw based on the density of 1.096 g/cm^3
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	試験は基本的な科学原理を満足する。	Study meets basic scientific principles
出典		
引用文献(元文献)	(147)	(147)
備考		

試験物質名	データなし	no data
CAS番号		
純度等		
注釈		
方法		
方法／ガイドライン	その他:	other:
GLP適合	いいえ	no
試験を行った年	1941	1941
試験系(種／系統)	ラット	rat
	Wistar	Wistar
性別(雄:M、雌:F)	雄	male
投与量		
各用量群(性別)の動物数		
溶媒(担体)	水	water
投与経路		
観察期間(日)		

その他の試験条件	英文参照	TEST ORGANISMS: - Species/Strain: male albino rats (Wistar derived) - Body weight (initial): 90 – 120 g - Housing: 5/cage ADMINISTRATION / EXPOSURE - Application: oral by gavage as a 20% aqueous solution to fasted rats - Animal number: 10 per group, - Post dose observation period: 2 weeks
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		
LD50値又はLC50値	LD50= 12760 – mg/kg bw	LD50= 12760 – mg/kg bw
雌雄のLD50値又はLC50値の違い等		
注釈	LD50 12760 mg/kg (95%信頼限界: 11610–13020 mg/kg bw)	LD50 12760 mg/kg (95% confidence limit: 11610–13020 mg/kg bw)
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	試験は基本的な科学原理を満足する。	Study meets basic scientific principles
出典		
引用文献(元文献)	(153)	(153)
備考		

B. 急性吸入毒性
ACUTE INHALATION 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	供給源: Aldrich Chemical Co., USA 物理性状: 液体 純度: 98%	Source: Aldrich Chemical Co., USA Physical form: liquid Purity: 98%
注釈		
方法		
方法／ガイドライン	その他: 急性吸入スクリーニング	other: acute inhalation screening
GLP適合	いいえ	no
試験を行った年	1971	1971
試験系(種／系統)	ラット	rat
	Sprague–Dawley	Sprague–Dawley
性別(雄:M、雌:F)	雄	male
投与量	30 – 768 ppm	30 – 768 ppm
各用量群(性別)の動物数		
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 ORGANISMS: - Species/Strain: adult male Sprague–Dawley rats, supplied by Spartan Research Animals, Haslett, MI, USA - Body weight at supply: 200 – 225 g - Body weight at study start: 220 – 465 g - Acclimatization: at least 3 days ADMINISTRATION / EXPOSURE DEA was neutralized with HCl to pH 7.4 prior to administration. Rats were restrained throughout the exposures which lasted 2 to 4 hours. Diethanolamine aerosol was generated from unheated compound at average concentrations ranging from 30 to 768 ppm. For 30 minutes before and during the entire exposure, heart rate, electrocardiogram (ECG), respiration rate, systolic blood pressure, and body temperature were continuously monitored. The chamber atmosphere was periodically sampled using a Greenburg–Smith impinger and concentration was determined by the colorimetric method of Miller (1967).
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	動物は暴露中に心拍数の減少、呼吸数の減少 (30–270 ppm)または増加 (769 ppm)、収縮期血圧の増加または減少を示した。血圧の持続的な増加は768 ppmのみでみられた。全例とも暴露に対し生存し、その後は正常に見えた。	During each exposure, animals exhibited a decrease in heart rate, decreased (30–270 ppm) or increased (768 ppm) respiration rate and increased or decreased systolic blood pressure. A sustained increase in blood pressure was observed only at 768 ppm. All rats survived exposures and appeared normal thereafter.
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	試験は基本的な科学原理を満足する。	Study meets basic scientific principles
出典		
引用文献(元文献)	(149)	(149)
備考		

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	供給源： Aldrich Chemical Co., USA 物理性状： 液体 純度： 98%	Source: Aldrich Chemical Co., USA Physical form: liquid Purity: 98%
注釈		
方法		
方法／ガイドライン	その他： 急性吸入スクリーニング	other: acute inhalation screening
GLP適合	いいえ	no
試験を行った年	1971	1971
試験系（種／系統）	ラット	rat
	Sprague-Dawley	Sprague-Dawley
性別（雄：M、雌：F）	雄	male
投与量	1471 及び 1476 ppm	1471 and 1476 ppm
各用量群（性別）の動物数		
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 ORGANISMS: - Species/Strain: adult male Sprague-Dawley rats, supplied by Spartan Research Animals, Haslett, MI, USA - Body weight at supply: 200 - 225 g - Body weight at study start: 220 - 465 g - Acclimatization: at least 3 days ADMINISTRATION / EXPOSURE DEA was neutralized with HCl to pH 7.4 prior to administration. Two groups of 4 rats were exposed for 80 and 105 minutes to DEA aerosol and vapor generated from heated compound (110 ° C) at an average concentration of 1471 and 1476 ppm, respectively. Animals were housed as a group in a stainless steel cage during exposure and physiologic measurements were performed at intervals before and after exposure.
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	暴露後に5/8匹が死亡した。暴露終了後4時間以内に4/5が死亡した。 死亡前に主にみられた毒性症状は嗜眠、非協調運動、蒼白、及びラ音及び喘ぎにより特徴づけられる不規則で緩除な呼吸であった。 急性致死量に対する生理反応には大きな変動幅が示されたが、特徴的な所見は以下の3つであった。 -心拍数は初期に減少し、その後死亡前に顕著に増加 -呼吸数の減少とインピーダンスの増加により特徴づけられる明瞭な呼吸抑制 -収縮期血圧の増加 ECGの変化が認められた。 肉眼病理所見には肺のうっ血、肝臓及び脾臓のうっ血、腎臓の退色、肥大、及び胸腺の点状出血が含まれた。 主な病理組織学的変化は肺の浮腫であった。	5/8 animals died following exposure; 4/5 dying within 4 hours after the termination of the exposure. The predominant toxicological signs preceding death were lethargy, incoordination, pallor, and irregular slow respiration characterized by rales and gasping. Although there was considerable variation in the physiologic responses to acute lethal levels three characteristic findings were evident: - an initial depression of heart rate followed by a marked increase prior to death - marked respiratory distress characterized by decreased respiration rate and increased impedance - increased systolic pressure. Alterations in the ECG were noted. Gross pathological findings consisted of congestion of lungs, congestion of liver and spleen, pale, enlarged kidneys, and petechial hemorrhages of the thymus. The predominant histopathological finding was pulmonary edema.
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	試験は基本的な科学原理を満足する。	Study meets basic scientific principles
出典		
引用文献（元文献）	(149) (158)	(149) (158)
備考		

C. 急性経皮毒性
ACUTE DERMAL TOXICITY

D. 急性毒性（その他の投与経路）
ACUTE TOXICITY、OTHER ROUTES

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	その他： 急性毒性スクリーニング	other: acute toxicity screening
GLP適合	いいえ	no
試験を行った年	1972	1972
試験系（種／系統）	マウス	mouse
	Swiss Webster	Swiss Webster
性別（雄：M、雌：F）	データなし	no data

投与量		
各用量群(性別)の動物数	動物数 : 50匹	Number of animals : 50
溶媒(担体)	水	water
投与経路	腹腔内	i.p.
観察期間(日)		
その他の試験条件	英文参照	METHOD FOLLOWED: Acute toxicity screening. LD50 was estimated according to Litchfield and Wilcoxon, 1949. GLP: No
その他の試験条件	英文参照	TEST ORGANISMS: - Species/Strain: Swiss Webster mice, supplier: Pel Freeze Farms, USA - body weight: 18 - 25 g -Number of animals: 10 per treatment group ADMINISTRATION / EXPOSURE - Application: Mice were fasted over night. A solution ((273 mg/ml) in water was prepared and dose levels ranging from 1.1 - 5.0 g/kg bw were intraperitoneally injected. The solution were adjusted to pH 7.3. EXAMINATIONS: - Necropsy, histopathology and electron microscopy were performed.
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	LD50は2.3 g/kg bw (2.1 - 2.5 g/kg bw)であった。 その用量レベルでは鎮静、運動失調、正向反射消失、チアノーゼをきたし死亡した。動物は投与後15分-24時間後に死亡した。 LD50値では広範な空胞化及び脂肪滴を含む顕著な肝臓の変化が投与4時間後に観察された。24時間までに肝細胞内の空砲は消失し、脂肪滴は数が減少した。	LD50 was 2.3 g/kg bw (2.1 - 2.5 g/kg bw). The dose levels induced sedation, ataxia, loss of rightening, cyanosis followed by death. The animals died within 15 min - 24 h after administration. At the LD50 marked liver changes, including extensive vacuolization and fat droplets, were observed 4 h after dosing. By 24 h, no vacuoles were visible in hepatocytes and fatty droplets were reduced in number.
結論		
毒性値	LD50= 2300 - mg/kg bw	LD50= 2300 - 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	試験は基本的な科学原理を満足する。	Study which meets basic scientific principles
出典		
引用文献(元文献)	(162)	(162)
備考		

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	供給源: BASF AG、ドイツ、物質番号 XV 306、名前:ジエタノールアミン (固体)	Source: BASF AG, Germany, substance-No. XV 306, name: Diethanolamine (solid)
方法		
方法／ガイドライン	その他:予備的な基本設定試験	other: preliminary base set testing
GLP適合	いいえ	no
試験を行った年	1966	1966
試験系(種／系統)	マウス	mouse
性別(雄:M、雌:F)		
投与量		
各用量群(性別)の動物数		
溶媒(担体)		
投与経路	腹腔内	i.p.
観察期間(日)		
その他の試験条件	英文参照	METHOD FOLLOWED: approximate median lethal dose determination (ALD50) GLP: No
その他の試験条件	英文参照	TEST ORGANISMS: - Species/Strain: Mouse ADMINISTRATION / EXPOSURE - Application: 2 - 20% aqueous preparation, intraperitoneally - Post dose observation period: 7 days
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	臨床症状: 異常な姿勢、呼吸困難、痙攣からなる非特異的な急性毒性症状。 剖検所見: 腸の癒着 潜在的な標的臓器:なし LD50: 約 400 mg/kg bw (2% > 400 mg/kg bw; 8% < 400 mg/kg bw)	CLINICAL SIGNS: Unspecific signs of acute intoxication in form of abnormal position, dyspnea, tremors, convulsions NECROPSY FINDINGS: Intestinal adhesions POTENTIAL TARGET ORGANS: None LD50: approximately 400 mg/kg bw (2% > 400 mg/kg bw; 8% < 400 mg/kg bw)
結論		
毒性値	LD50= 約 400 - mg/kg bw	LD50= ca. 400 - 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	試験は基本的な科学原理を満足する	Study meets basic scientific principles
出典		
引用文献(元文献)	(148)	(148)
備考		

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	その他: 急性組織損傷のスクリーニング	other: screening on acute tissue damage
GLP適合	いいえ	no
試験を行った年	1971	1971
試験系(種／系統)	ラット	rat
性別(雄:M、雌:F)		
投与量		
各用量群(性別)の動物数		
溶媒(担体)		
投与経路	腹腔内	i.p
観察期間(日)		
その他の試験条件	英文参照	METHOD FOLLOWED: Screening for tissue damage after single i.p. injection in rats. GLP: No
その他の試験条件	英文参照	TEST ORGANISMS: - Species/Strain: male Sprague-Dawley rats - Body weight: 225 - 300 g - Number of animals: 6 control animals, 3 per sacrifice group ADMINISTRATION / EXPOSURE - Application: DEA neutralized with HCL (28.4%) was injected at 100 and 500 mg/kg calculated as free base to groups of six rats. Rats were fasted after dosing and were sacrificed 4 or 24 h later. The control group received water. EXAMINATIONS: Enzyme activities (LDH and ASL (GOT)) were determined and histopathology and electron microscopy were carried out.
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	雄SDラットへの中和したジエタノールアミンの100又は500 mg/kgの用量での単回腹腔内注射により、投与後4及び24時間に肝細胞における細胞質の空胞化、好塩基性変化及びミトコンドリア膨潤、並びに腎尿細管上皮の壊死及び細胞質の空胞化を生じた。 血清酵素活性の増加 (LDH及びASL(GOT))は500 mg/kg のみで観察された。	Single i.p. injections of neutralized diethanolamine to male Sprague-Dawley rats, at doses of 100 or 500 mg/kg, produced cytoplasmic vacuolization, basophilia, and mitochondrial swelling in hepatocytes, and necrosis and cytoplasmic vacuolization of the renal tubular epithelium at 4 and 24 hr after dosing. Increased serum enzyme activities (LDH and ASL (GOT)) could only be observed at 500 mg/kg.
結論		
毒性値		
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	基本的な科学原理を満たす試験	Study which meets basic scientific principles
出典		
引用文献(元文献)	(149) (163)	(149) (163)
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	1.1～1.4で規定	as prescribed by 1.1 - 1.4
CAS番号		
純度等		
注釈	供給源 : BASF AG、ドイツ、物質番号 XVII/144 (純品)、XVII/146 (工業品)	Source: BASF AG, Germany, substance-No. XVII/144 (pure), XVII/146 (technical)
pH		
方法		
方法／ガイドライン	その他: BASG-試験 (パッチテスト)	other: BASF-Test (Patch-Test)
GLP適合	いいえ	no
試験を行った年	1967	1967
試験系(種／系統)	ウサギ	rabbit

性別(雄:M、雌:F)		
投与量		
各用量群(性別)の動物数		
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	METHOD FOLLOWED: BASF test for skin irritation GLP: No
その他の試験条件	英文参照	TEST ANIMALS: Albino rabbits ADMINISTRATION/EXPOSURE - Preparation of test substance: neat (unchanged) - Area of exposure: shorn back of rabbits or ear - Duration of exposure: shorn back: 1, 5, 15 min., 20 h ear: 20 h
統計学的処理		
結果		
一次刺激スコア		
皮膚反応等		
その他	平均スコア: 純品 (XVII/144) 1 min 5 min 15 min 20 h 剃毛した背 Er(+) Er(+) Er(+) Er++/Ed++ N+/S++ 耳 − − − Er+/C(+) 工業品 (XVII/146) 1 min 5 min 15 min 20 h 剃毛した背 Er(+) Er(+) Er(+) Er++/Ed+ N+/S++ 耳 − − − Er+/N++ Er= 紅斑, Ed= 浮腫, S=剥離, N=壊死, C=痂皮 (+)=軽度, += 中等度, ++= 顕著	AVERAGE SCORE: Pure (XVII/144) 1 min 5 min 15 min 20 h Shorn back Er(+) Er(+) Er(+) Er++/Ed++ N+/S++ Ear − − − Er+/C(+) Technical (XVII/146) 1 min 5 min 15 min 20 h Shorn back Er(+) Er(+) Er(+) Er++/Ed+ N+/S++ Ear − − − Er+/N++ Er= erythema, Ed= edema, S=scaling, N=necrosis, C=crust (+)=slight, += moderate, ++= distinct
結論		
皮膚刺激性	刺激性あり	irritating
皮膚腐食性		
注釈	結論 : Ⅰ-15分後に軽度の皮膚刺激。 20時間後に顕著な刺激。 皮膚刺激に関しては純品と工業品とに有意な差はみられなかった。	Conclusion : Slight skin irritation after 1 - 15 min. Distinct irritation after 20 h There was no reliable difference between the pure and the technical product in respect to skin irritation
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	基本的なデータが与えられている。	Basic data provided
出典		
引用文献(元文献)	(167)	(167)
備考		

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	Merckにより供給されたDEA、純度:98%	DEA supplied by Merck, purity: 98%
注釈		
pH		
方法		
方法／ガイドライン	その他:フランスのガイドライン ("l'arrete du 5 avril 1971")に準じた	other: according to French guidelines ("l'arrete du 5 avril 1971")
GLP適合	いいえ	no
試験を行った年	1982	1982
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 暴露 : 閉塞	Concentration : undiluted Exposure : Occlusive
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	Draize test according to French standard methods, of l'arrete du 5 April 1971
その他の試験条件	英文参照	Test species/strain: Albino New Zealand Rabbit - 3 rabbits for intact, 3 rabbits for abraded skin (supplier: Evic Ceba, France) - body weight: 2.5 - 2.8 kg - housing: individual in cages DEA was applied undiluted and not neutralized. Animals with both intact and abraded skin The animals were observed for 72 hours. The PII (primary irritation index) was scored on a grade ranged between 1 - 8.
統計学的処理		
結果		
一次刺激スコア	PDII : 2.6	PDII : 2.6
皮膚反応等		

その他	試験結果: 8点中2.6のスコアを有する中等度の刺激影響。全てのウサギで中等度の刺激がみられた。傷をつけたウサギの方が無傷のウサギよりも重篤な刺激を示した。72時間後には紅斑は増加し、浮腫は低下する傾向がみられた。	Test results: Moderate irritant effect with a score 2.6 out of 8. Moderate irritation observed in all rabbits, those abraded exhibiting much greater irritation than those none abraded. Tendency to increased erythema and reduced edema after 72 hours.
結論		
皮膚刺激性	刺激性あり	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	基本的なデータが与えられている。	Basic information supplied
出典		
引用文献(元文献)	(168)	(168)
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	1.1～1.4で規定	as prescribed by 1.1 - 1.4
CAS番号		
純度等		
注釈	供給源 : BASF AG、ドイツ、物質番号 XVII/144 (純品)、XVII/146 (工業品)	Source: BASF AG, Germany, substance-No. XVII/144 (pure), XVII/146 (technical)
方法		
方法／ガイドライン	その他: BASF 試験	other: BASF-Test
試験のタイプ		
GLP適合	いいえ	no
試験を行った年	1967	1967
試験系(種／系統)	ウサギ	rabbit
性別(雄:M、雌:F)		
投与量		
各用量群(性別)の動物数		
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	METHOD FOLLOWED: BASF test for eye irritation GLP: No
その他の試験条件	英文参照	TEST ANIMALS: Albino rabbits ADMINISTRATION/EXPOSURE - Preparation of test substance: Test substance was used as delivered. - Amount of substance instilled: 0.1 ml (1 drop) - Post exposure period: 8 days EXAMINATIONS - Examination time points: 24 h, 48 h, 72 h
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	純品 (XVII/144) 0.1 ml (1滴) 表面の腐食、明瞭な角膜混濁 (グレード: ++)、結膜の出血、明瞭な結膜の発赤、明瞭な浮腫、結膜の鱗化 工業品 (XVII/146) 0.1 ml (1滴) 表面の腐食、明瞭な角膜混濁 (グレード: ++)、結膜の出血、明瞭な結膜の発赤、明瞭な浮腫、結膜の鱗化	Pure (XVII/144) 0.1 ml (1 drop) Superficial corrosion, distinct corneal opacity (grade: ++), conjunctival bleeding, distinct conjunctival redding, distinct edema, conjunctival scale Technical (XVII/146) 0.1 ml (1 drop) Superficial corrosion, distinct corneal opacity (grade: ++), conjunctival bleeding, distinct conjunctival redding, distinct edema, conjunctival scale
結論		
眼刺激性	刺激性あり	irritating
眼腐食性		
注釈	結論 : 重度の刺激症状 眼刺激に関して純品と工業品との間には差はなかった。	Conclusion : Severe signs of irritation There was no difference between the pure and the technical product in respect to eye irritation
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	基本的なデータが与えられている	Basic data provided
出典		
引用文献(元文献)	(167)	(167)
備考		

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	Merckにより供給されたDEA、純度:98%	DEA supplied by Merck, purity: 98%
注釈		
方法		
方法／ガイドライン	その他:フランスのガイドライン ("l'arrete du 5 avril 1971")に準じた。 OECD405と比較可能なDraize法 (French standards, 16 April 1973)	other: according to French guidelines ("l'arrete du 16 avril 1973") Draize (French standards, 16 April 1973) comparable to OECD 405.
試験のタイプ		
GLP適合	いいえ	no
試験を行った年	1982	1982
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 :3匹	Number of animals : 3
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 species/strain: Albino New Zealand Rabbit - 3 rabbits (supplier: Evic Ceba, France) - body weight: 2.5 - 2.8 kg - housing: individual in cages DEA was applied undiluted and not neutralized. 100 mg initial dose, measurements given up to seven days after application. Scores calculated using Draize scoring system ranging from 0 - 110.
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	時間 (h) スコア/ 110 24 >=50 48 56 72 52 96 45 168 41 角膜、虹彩及び結膜に強度の刺激が観察され、7日間の観察期間に軽度に低下した。	Time (h) Score / 110 24 >=50 48 56 72 52 96 45 168 41 Strong irritation observed at cornea, iris and conjunctiva which reduced slightly over the 7 day observation period.
結論		
眼刺激性	刺激性あり	irritating
眼腐食性		
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	基本的な情報が与えられている	Basic information supplied
出典		
引用文献(元文献)	(168)	(168)
備考		

5-4 皮膚感作
SKIN SENSITISATION

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	供給源: BASF AG、ドイツ、液体、無色、バッチ:917、純度: 99.5%、安定性は約1年間保証されている	Source: BASF AG, Germany, liquid, colorless, batch: 917, purity: 99.5, stability guaranteed for about 1 year
注釈		
方法		
方法/ガイドライン	その他: OECD 406 (1981), EEC 84/448 (1984)	other: OECD 406 (1981), EEC 84/448 (1984)
試験のタイプ	モルモットマキシマイゼーション試験	Guinea pig maximization test
GLP適合	はい	yes
試験を行った年	1990	1990
試験系(種/系統)	モルモット	guinea pig
性別(雄:M、雌:F)		
投与量		
各用量群(性別)の動物数	動物数 : 40匹	Number of animals : 40
溶媒(担体)	生理食塩液	physiol. Saline
投与経路		
観察期間(日)		
その他の試験条件	英文参照	METHOD FOLLOWED: OECD guideline 406, (adopted 12 May 1981) Directive 84/449, EEC B.6 (March 1984) Magnusson B and Kligman AM (1969) The identification of contact allergens by animal assays. The guinea pig maximization test, J. Invest Dermatol., 52, 268-276

その他の試験条件	英文参照	TEST ANIMALS: - Strain: Himalayan spotted - Source: BRL, Fuellingsdorf, Switzerland - Sex: females - Weight at study initiation: 324 - 342 g (mean) - Number of animals: 40 - Controls: Yes ADMINISTRATION/EXPOSURE 10 animals were used for the control 1, 10 animals were used for the control 2, 20 females for the test group, 2 females for the intracutaneous pretest and 4 females for the epicutaneous pretest. PREPARATION OF TEST MATERIAL: The test substance was placed in to a glass beaker and a weight/weight dilution was prepared with physiological saline immediately prior to each application PRETEST: For the identification of irritant test substance concentration suitable for the induction phase, intradermal injections (0.1 ml/site) were made into the clipped flank of 2 animals at concentrations of 1%, 3% and 5% dissolved in physiological saline. The dermal reactions were assessed 24 hours later. For epidermal applications patches of filter paper (2 cm x 2 cm) were saturated with the undiluted test substance (100%) and with preparations in physiological saline of 25%, 50%, 75%% and were applied occlusively to the clipped and shaved skin of 4 animals. The dressings were removed after 24 hours and investigated for erythema and edema and re-investigated after 48 hours.
その他の試験条件	英文参照	MAIN STUDY: Induction by intradermal injection: An area of 6 cm x 8 cm of the dorsal skin was clipped and 3 pairs of intradermal injection (0.1 ml/site) were made at the border of a 4 cm x 6 cm area of the clipped region as follows: Test groups: 1 Freund's complete adjuvant 50:50 (FCA) with bi-distilled water 2 Test substance diluted to 5% with physiological saline 3 Test substance at 5% in physiological saline emulsified in a 50:50 physiological saline ethanol: (FCA/ saline) Control group: 1 Freund's complete adjuvant 50:50 (FCA) with bi-distilled water 2 Vehicle used in (2) for test group 3 Freund's complete adjuvant 50:50 (FCA) with bi-distilled water Induction by epidermal application: One week after injections, the scapular region was clipped and shaved free. 2 cm x 4 cm patch of filter paper was saturated with the test substance (75% in physiological saline) and placed over the injection sites. The patch was covered occlusively. The dressings were left in place for 48 hours. The control group animals were treated accordingly. Reaction sites were assessed for erythema and edema immediately, 24 and 48 hours after removal of the dressings. Challenge: The animals of test group and control group 1 were challenged 2 weeks after epidermal induction. Hair was clipped, shaved on the left and right flank. Two patches (2 cm x 2 cm) of filter paper were saturated with a) non-irritant concentration (25%) and b) with the vehicle only and applied to the (a) left flank and (b) right flank using the same method as for the epidermal application. The dressings were removed approximately 24 h later. The sites were assessed for erythema and edema immediately, 24 h and 48 h after removal of the dressing. The animals of control group 2 remained untreated.
その他の試験条件	英文参照	ADDITIONAL EXAMINATION: - mortality/viability: daily - body weights: at start of acclimatization, application and termination - Signs (local/systemic): daily SKIN EXAMINATIONS The following parameters were recorded: Erythema (E) 0 to 4 numerical scores Edema (O) 0 to 4 numerical scores Diameter (D) mm The reactions were scored according to the following numerical grading system according to Draize: Erythema and eschar formation: 0 No erythema 1 Very slight erythema (barely perceptible) 2 Well-defined erythema 3 Moderate to severe erythema 4 Severe erythema (beet redness) to slight eschar formation (injuries in depth) Edema formation: 0 No edema 1 Very slight edema (barely perceptible) 2 Slight edema (edges of area well-defined by definite raising) 3 Moderate edema (raised approximately 1 mm) 4 Severe edema (raised more than 1 mm and extending beyond the area of exposure)

その他の試験条件	英文参照	INTERPRETATION OF RESULTS: Based upon percentage of animals sensitized, one to five grades of allergen potency can be assigned: Sensitization rate Grade Classification 0-8% I Non-allergic/weak 9-28% II Mild 29-64% III Moderate 65-80% IV Strong 81-100% V Extreme Approval of sensitivity: The sensitivity of the test animals was confirmed at regular intervals (2times/year) using formaldehyde solution as positive control.
統計学的処理		
結果		
試験結果	予備試験結果: 予備試験の反応に基づいて、本試験の皮内注射には5%の濃度が選択された。 経皮適用に関しての予備試験の反応に基づいて、誘導に選択された濃度は75%、惹起に選択された濃度は25%とした。 本試験の結果: 死亡例または毒性症状は生じなかった。 対照群: 生理食塩水で処置した場合も25%ジエタノールアミンで処置した場合も1回目の惹起後に明瞭な皮膚の陽性反応は示されなかった。 試験群: 25%ジエタノールアミンで処置した場合、24時間の判定時に2/20 (10%) のみに紅斑がみられ、48時間の判定時には1/20 (5%)に低下した。これ以上の所見は認められなかった。 惹起後の皮膚反応は以下の通りである。	RESULTS OF PRETEST: Based on the reactions of the pre-test, the concentration of 5% was selected for intradermal injection for the main study Based on the reactions of the pre-test with regards to epidermal application, the concentration selected for the induction was 75% and for the challenge procedure was 25%. RESULTS OF MAIN TEST No mortalities or toxic signs occurred. Control group: No positive skin reactions were evident after 1st challenge neither with when treated with physiological saline nor with 25% Diethanolamine. Test group: Only 2/20 (10%) showed erythema findings at 24 h readings, declining to 1/20 (5%) at 48 h reading when treated with 25% Diethanolamine. No further finding were noted. The skin reactions after challenge were as follows:
試験結果	24 h 48 h 対照群 75% 塗布 DEA で 誘導中 0/10 0/10 生理食塩水 0/10 0/10 試験群 25% DEA 2/20 1/20 生理食塩水 0/20 0/20	24 h 48 h Control group 75% epidermal DEA during induction 0/10 0/10 Phys. Saline 0/10 0/10 Test group 25% DEA 2/20 1/20 Phys. saline 0/20 0/20
その他		
結論		
感作性	感作性なし	not sensitizing
注釈	分類 : 感作性なし	Classification : not sensitizing
	結論 : 一般的な評価基準に従い、モルモットマイキマイゼーション試験では試験物質の皮膚感作性のポテンシャルは認められなかった。	Conclusion : According to the general assessment criteria, no skin sensitizing potential of the test substance was noted in the Guinea pig maximization test.
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のガイドライン試験	GLP Guideline study
出典		
引用文献(元文献)	(174)	(174)
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	1.1 - 1.4の記載どおり	as prescribed by 1.1 - 1.4
CAS番号		
純度等	純度: >99%	Purity: >99%
注釈		
方法		
方法/ガイドライン	OECD408と同等	other: comparable to OECD 408
GLP適合	はい	yes
試験を行った年		1992
試験系(種/系統)	rat/Fischer 344	rat/Fischer 344
性別(雄:M、雌:F)	雌雄	male/female
投与量	320, 630, 1250, 2500, 5000 ppm (males) 160, 320, 630, 1250, 2500 ppm (females)	320, 630, 1250, 2500, 5000 ppm (males) 160, 320, 630, 1250, 2500 ppm (females)
各用量群(性別)の動物数		
溶媒(担体)		
投与経路	飲水	drinking water
対照群に対する処理	処理なし	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)	13週間	13 weeks
投与頻度	毎日	daily
回復期間(日)		
試験条件		
統計学的処理		

結果		
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)		
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		
剖検所見(発生率、重篤度)		
臓器重量		
病理組織学的所見(発生率、重篤度)		
実際に摂取された量		
用量反応性		
注釈		
結論		
NOAEL (NOEL)		
LOAEL (LOEL)	320 ppm (雄)、160 ppm (雌)	320 ppm (雄)、160 ppm (雌)
NOAEL/LOAELの推定根拠		
雌雄のNOAEL(LOAEL)の違い等		
注釈	ラットの雄に0、320、630、1250、2500、5000 ppm、雌に0、160、320、630、1250、2500 ppmの濃度で13 週間飲水投与した。最高用量群の雄に死亡がみられた。最高用量群の生存動物に体重増加抑制がみられた。全て投与群に小球性貧血がみられた。また、重篤な腎症、尿細管壊死、石灰化の発生率の増加を示した。雄の2500 ppm群以上に精巣精細管の変性と精子の運動性の低下と精子数の減少がみられた。雌雄の高用量群 (雄の2500と5000 ppm、雌の1250と2500 ppm).に脳と脊髄の脱髄が観察された。	Rats received 0, 320, 630, 1250, 2500, and 5000 ppm (males) or 0, 160, 320, 630, 1250, and 2500 ppm (females) in drinking water for 13 weeks. Deaths occurred in 2/10 male rats in the top dose group. Surviving animals in the higher concentration groups exhibited depressed weight gains. The animals developed a dose-dependently a microcytic anemia form the lowest dose level onwards. They showed also an increased incidences or severity of nephropathy, tubular necrosis, and mineralization. Degeneration of the seminiferous tubules of the testis was noted in dosed males and sperm motility and count were decreased at and above 2500 ppm. Demyelination in the brain and spinal cord was observed in male and female rats at the two highest dose level (2500+5000 ppm in males; 1250+2500 ppm in females).
信頼性	(1) valid without restriction	(1) valid without restriction
信頼性の判断根拠	Acceptable, well-documented study which meets scientific principles	Acceptable, well-documented study which meets scientific principles
出典		
引用文献(元文献)	(187) (188) (189) (190)	(187) (188) (189) (190)
備考		

試験物質名	1.1 - 1.4の記載どおり	as prescribed by 1.1 - 1.4
CAS番号		
純度等	純度: >99%	Purity: >99%
注釈		
方法		
方法／ガイドライン	OECD408と同等	other: comparable to OECD 408
GLP適合	はい	yes
試験を行った年	1992	1992
試験系(種／系統)	rat/Fischer 344	rat/Fischer 344
性別(雄:M、雌:F)	雌雄	male/female
投与量	630, 1250, 2500, 5000, or 10000 ppm	630, 1250, 2500, 5000, or 10000 ppm
各用量群(性別)の動物数		
溶媒(担体)		
投与経路	飲水	drinking water
対照群に対する処理	処理なし	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)	14日間	14 days
投与頻度	毎日	daily
回復期間(日)		
試験条件		
統計学的処理		
結果		
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)		
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		
剖検所見(発生率、重篤度)		
臓器重量		
病理組織学的所見(発生率、重篤度)		
実際に摂取された量		
用量反応性		
注釈		
結論		
NOAEL (NOEL)		
LOAEL (LOEL)	630 ppm	630 ppm
NOAEL/LOAELの推定根拠		
雌雄のNOAEL(LOAEL)の違い等		

注釈	ラットに0, 630, 1250, 2500, 5000, 10000 ppm の濃度で2 週間飲水投与した結果、10000 ppm群の雄2匹及び5000 ppm以上の群の雌の全数が死亡した。最高用量群の生存動物に体重増加抑制がみられ、全て投与群に小球性貧血がみられた。雌雄のラットに腎臓重量が増加し、尿細管上皮の壊死と腎臓の機能の低下がみられた。また雄に精巣精細管の変性がみられた。	The administration of the test substance for 2 week via the drinking water at concentrations of 0, 630, 1250, 2500, 5000, or 10000 ppm led to increased mortality as all female rats in the 2 highest dose groups and 2 males in the 10000 ppm group died. Surviving animals in the higher concentration groups exhibited depressed weight gains. A microcytic anemia was noted in all treatment groups. Male and female rats had increased kidney weights, renal tubular cell necrosis, and decreased renal function. Degeneration of the seminiferous tubules of the testis was noted in dosed males.
信頼性	(1) valid without restriction	(1) valid without restriction
信頼性の判断根拠	Acceptable, well-documented study which meets scientific principles	Acceptable, well-documented study which meets scientific principles
出典		
引用文献(元文献)	(189) (190)	(189) (190)
備考		

試験物質名	1.1 - 1.4の記載どおり	as prescribed by 1.1 - 1.4
CAS番号		
純度等	純度: >99%	Purity: >99%
注釈		
方法		
方法／ガイドライン	OECD408と同等	other: comparable to OECD 408
GLP適合	はい	yes
試験を行った年		1992
試験系(種／系統)	mouse/B6C3F1	mouse/B6C3F1
性別(雄:M、雌:F)	雌雄	male/female
投与量	630, 1250, 2500, 5000, 10000 ppm	630, 1250, 2500, 5000, 10000 ppm
各用量群(性別)の動物数		
溶媒(担体)		
投与経路	飲水	drinking water
対照群に対する処理	処理なし	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)	13 weeks	13 weeks
投与頻度		
回復期間(日)		
試験条件		
統計学的処理		
結果		
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)		
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		
剖検所見(発生率、重篤度)		
臓器重量		
病理組織学的所見(発生率、重篤度)		
実際に摂取された量		
用量反応性		
注釈		
結論		
NOAEL (NOEL)		
LOAEL (LOEL)	630 ppm	630 ppm
NOAEL/LOAELの推定根拠		
雌雄のNOAEL(LOAEL)の違い等		
注釈	マウスに0、630、1250、2500、5000、10000 ppmの濃度で13 週間飲水投与した。2500 ppm以上の群に死亡がみられた。最高用量群の生存動物に体重増加抑制がみられた。雄に腎症と尿細管壊死がみられ、雌雄ともに心筋細胞、肝細胞壊死の変性、顎下唾液腺の細胞診の変化がみられた。全ての投与群に肝細胞の変化がみられた。はまた、マウスのすべての投与群で認められた。この結果から、LOAEL を630 ppm (雄で104 mg/kg/day、雌で142 mg/kg/day) とする。	Mice received 0, 630, 1250, 2500, 5000 and 10000 ppm in drinking water for 13 weeks. Deaths of occurred in the 3 highest dose groups. Surviving animals in the higher concentration groups exhibited depressed weight gains. Nephropathy and tubular necrosis were observed in males, and degeneration of cardiac myocytes, and hepatocellular necrosis were recorded in males and females. In addition, cytologic alteration in the submandibular salivary gland was noted in male and female mice. Hepatocellular alteration also was noted in all dosed groups of mice. Finally, the most sensitive parameters were the increased liver weight with associated morphological findings in the liver at all dose levels and a No Observed Adverse Effect Level (NOAEL) was not achieved for this effect. Consequently, the Lowest Observed Adverse Effect Level (LOAEL) 630 ppm (corresponding to 104 mg/kg bw in male mice or 142 mg/kg bw in female mice).
信頼性	(1) valid without restriction	(1) valid without restriction
信頼性の判断根拠	Acceptable, well-documented study which meets scientific principles	Acceptable, well-documented study which meets scientific principles
出典		
引用文献(元文献)	(197) (198) (189) (199) (190)	(197) (198) (189) (199) (190)
備考		

試験物質名	1.1 - 1.4の記載どおり	as prescribed by 1.1 - 1.4
CAS番号		
純度等	純度: >99%	Purity: >99%
注釈		
方法		
方法／ガイドライン	OECD408と同等	other: comparable to OECD 408
GLP適合	はい	yes
試験を行った年		1992
試験系（種／系統）	mouse/B6C3F1	mouse/B6C3F1
性別（雄：M、雌：F）	雌雄	male/female
投与量	630, 1250, 2500, 5000, 10000 ppm	630, 1250, 2500, 5000, 10000 ppm
各用量群（性別）の動物数		
溶媒（担体）		
投与経路	飲水	drinking water
対照群に対する処理	処理なし	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）	2週間	2 weeks
投与頻度		
回復期間（日）		
試験条件		
統計学的処理		
結果		
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）		
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		
剖検所見（発生率、重篤度）		
臓器重量		
病理組織学的所見（発生率、重篤度）		
実際に摂取された量		
用量反応性		
注釈		
結論		
NOAEL (NOEL)	630 ppm	630 ppm
LOAEL (LOEL)		
NOAEL/LOAELの推定根拠		
雌雄のNOAEL(LOAEL)の違い等		
注釈	マウスに0、630、1250、2500、5000、10000 ppmの濃度で2 週間飲水投与した結果、5000 ppm以上の群の雌及び10000 ppm群の雄で体重減少がみられた。、1250 ppm以上の群の雌雄に肝臓重量の増加がみられ、最高用量群に雌雄で肝細胞の腫脹などの変性が認められた。	The administration of the test substance for 2 week via the drinking water at concentrations of 0, 630, 1250, 2500, 5000, or 10000 ppm led dose-dependently to body weights reductions in males at 10000 ppm and in females from 5000 ppm onwards. There were increases in liver weight in males and females at and above 1250 ppm. In the liver cytologic alterations and necrosis of individual hepatocytes were observed in the highest dose group.
信頼性	(1) valid without restriction	(1) valid without restriction
信頼性の判断根拠	Acceptable, well-documented study which meets scientific principles	Acceptable, well-documented study which meets scientific principles
出典		
引用文献（元文献）	(189)	(189)
備考		

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	2,2'-イミノジエタノール	2,2'-iminodiethanol
CAS番号	111-42-2	111-42-2
純度等	純度：>= 99.3 - % w/w	Purity：>= 99.3 - % w/w
注釈	入手源：記述されていない。 バッチ：17584 純度：99.7%	Source: not stated, batch: 17584, purity: 99.7%
方法		
方法／ガイドライン	エームス試験	Ames test
	他	other
GLP適合	情報無し	no data
試験を行った年	1980年	1980
細胞株又は検定菌	Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538	Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538
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 : 125, 250, 500, 1000, 2000, 4000 µg/plate. SYSTEM OF TESTING Salmonella typhimurium TA1535, TA1537, TA1538, TA98 and TA100 were obtained from Professor B.N. Ames, University of California CULTURE MEDIUM For detecting revertants of the Salmonella tester strains, ready-poured petri plates containing 25 ml of a minimal agar medium based on Vogel and Bonner (1956), were obtained from either Difco Laboratories, West Molesey, Surrey or Gibco Europe Ltd., Paisley, Scotland. PLATE INCORPORATION ASSAY The method used was basically that described by Ames et al. (1975), using S9 microsomal fraction obtained from a rat liver homogenate from rats pre-treated with Aroclor 1254. 0.1 ml of a dilution (1 : 20 000) of an overnight bacterial culture was added to 2 ml top agar, together with 20µl test compound to give final amounts of 125, 250, 500, 1000, 2000 and 4000 µg/plate and 0.5 ml S9 mix (+S9) or 0.5 ml pH 7.4 phosphate buffer (- S9). In the mutation assays control plates were set up with the solvent alone and with a known positive control compounds (ethyl methanesulphonate, methyl methanesulphonate, cyclophosphamide).
試験条件	原文参照	PRE-INCUBATION ASSAY The method used was that described by Brooks and Dean (1981). Bacteria (0.5 ml) and S9 mix or pH 7.4 phosphate buffer (2.5 ml) were incubated at 37° C with the test solution (0.1 ml) or solvent for 30 rain before incorporation of 0.5 ml of this pre-incubation mixture into 2 ml of top agar. All assays were carried out at least in triplicate (i.e. 3 plates per data point). All tests were carried out in quadruplicate. Two replicate assays were carried out on different days in order to confirm the reproducibility of the results. SPOT TEST The method used was that described by Ames et al. (1975). 20 µl of test compound was added to a 1-cm diameter sterile filter disc before adding to the centre of the seeded plate. The plates were then incubated at 37° C in sealed gas jars before the revertant colonies were counted.
試験条件	原文参照	TREAT AND PLATE METHOD Overnight broth cultures were washed and resuspended in phosphate buffer pH 7.0. The suspension was then distributed in 2-ml volumes into universal containers and 20 µl test compound solution was added (- S9). For studies incorporation microsomal activation (+ S9), 0.5 ml S9 mix was added to each 2-ml bacterial suspension culture together with 25 µl test compound solution. All cultures were then incubated at 37° C for 1 h before 0.1-ml volumes were seeded onto minimal agar plates with the appropriate amino acid supplement. Appropriate dilutions were plated onto nutrient agar to determine the numbers of survivors. The plates were then incubated at 37° C before the colonies were counted. Solvent: Water
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	個々の結果は示されていない。	Individual results were not supplied.
結論		
遺伝子突然変異	陰性	negative
注釈	被験物質は選択された条件下ではAmes試験で変異原性がなかた。	The test substance was not mutagenic in the Ames test under the conditions chosen.
信頼性	(2)制限付きで有効	(2) valid with restrictions
信頼性の判断根拠	基本的な原理に合致する受容可能な十分記載された試験	Acceptable, well-documented study which meets basic scientific principles
出典	OECD SIDS Dataset, 2008	OECD SIDS Dataset, 2008
引用文献（元文献）	Dean, B.J., Brooks, T.M., Hodson-Walker, G., Hutson, D.H. (1985) Genetic toxicology testing of 41 industrial chemicals. Mutat. Res., 153, 57-77	Dean, B.J., Brooks, T.M., Hodson-Walker, G., Hutson, D.H. (1985) Genetic toxicology testing of 41 industrial chemicals. Mutat. Res., 153, 57-77
備考		

試験物質名	2,2'-イミノジエタノール	2,2'-iminodiethanol
CAS番号	111-42-2	111-42-2
純度等	純度 : >= 99.3 - % w/w	Purity : >= 99.3 - % w/w
注釈	入手源：記述されていない。 バッチ：17584 純度：99.7%	Source: not stated, batch: 17584, purity: 99.7%
方法		
方法／ガイドライン	大腸菌の復帰突然変異試験	Escherichia coli reverse mutation assay
	他	other
GLP適合	非適合	no
試験を行った年	1980年	1980
細胞株又は検定菌	Escherichia coli WP2 and WP2uvrA	Escherichia coli WP2 and WP2uvrA
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 : 125, 250, 500, 1000, 2000, 4000 µg/plate. SYSTEM OF TESTING Escherichia coli WP 2 and WP 2 uvrA, described by Professor B.A. Bridges (1972), were obtained from Dr. M.H.L. Green, University of Sussex. PLATE INCORPORATION ASSAY The method used was basically that described by Ames et al. (1975), using S9 microsomal fraction obtained from a rat liver homogenate from rats pre-treated with Aroclor 1254. 0.1 ml of a dilution (1 : 20 000) of an overnight bacterial culture was added to 2 ml top agar, together with 20µl test compound to give final amounts of 125, 250, 500, 1000, 2000 and 4000 µg/plate and 0.5 ml S9 mix (+S9) or 0.5 ml pH 7.4 phosphate buffer (- S9). In the mutation assays control plates were set up with the solvent alone and with a known positive Control compounds (ethyl methanesulphonate, methyl methanesulphonate, cyclophosphamide).
試験条件	原文参照	PRE-INCUBATION ASSAY The method used was that described by Brooks and Dean (1981). Bacteria (0.5 ml) and S9 mix or pH 7.4 phosphate buffer (2.5 ml) were incubated at 37° C with the test solution (0.1 ml) or solvent for 30 rain before incorporation of 0.5 ml of this pre-incubation mixture into 2 ml of top agar. All assays were carried out at least in triplicate (i.e. 3 plates per data point). All tests were carded out in quadruplicate. Two replicate assays were carried out on different days in order to confirm the reproducibility of the results. SPOT TEST The method used was that described by Ames et al. (1975). 20 µl of test compound was added to a 1-cm diameter sterile filter disc before adding to the centre of the seeded plate. The plates were then incubated at 37° C in sealed gas jars before the revertant colonies were counted.
試験条件	原文参照	TREAT AND PLATE METHOD Overnight broth cultures were washed and resuspended in phosphate buffer pH 7.0. The suspension was then distributed in 2-ml volumes into universal containers and 20 µl test compound solution was added (- S9). For studies incorporation microsomal activation (+ S9), 0.5 ml S9 mix was added to each 2-ml bacterial suspension culture together with 25 µl test compound solution. All cultures were then incubated at 37° C for 1 h before 0.1-ml volumes were seeded onto minimal agar plates with the appropriate amino acid supplement. Appropriate dilutions were plated onto nutrient agar to determine the numbers of survivors. The plates were then incubated at 37° C before the colonies were counted. Solvent: Water
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	個々の結果は示されていない。	Individual results were not supplied.
結論		
遺伝子突然変異	陰性	negative
注釈	被験物質は選択された条件下で変異原性がなかった。	The test substance was not mutagenic under the conditions chosen.
信頼性	(2)制限付きで有効	(2) valid with restrictions
信頼性の判断根拠	基本的な原理に合致する受容可能な十分記載された試験	Acceptable, well-documented study which meets basic scientific principles
出典	OECD SIDS Dataset, 2008	OECD SIDS Dataset, 2008
引用文献（元文献）	Dean, B.J., Brooks, T.M., Hodson-Walker, G., Hutson, D.H. (1985) Genetic toxicology testing of 41 industrial chemicals. Mutat. Res., 153, 57-77	Dean, B.J., Brooks, T.M., Hodson-Walker, G., Hutson, D.H. (1985) Genetic toxicology testing of 41 industrial chemicals. Mutat. Res., 153, 57-77
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	2,2'-イミノジエタノール	2,2'-iminodiethanol
CAS番号	111-42-2	111-42-2
純度等	純度 : >= 99.3 - % w/w	Purity : >= 99.3 - % w/w
注釈	入手源：記述されていない。 バッチ：17584 純度：99.7%	Source: not stated, batch: 17584, purity: 99.7%
方法		
方法／ガイドライン	Saccharomyces cerevisiaeを用いる分裂組み換え	Mitotic recombination in Saccharomyces cerevisiae
	他	other
GLP適合	情報無し	no data
試験を行った年	1980年	1980
細胞株又は検定菌	Saccharomyces cerevisiae JD1	Saccharomyces cerevisiae JD1
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 - 5000 µg/ml. SYSTEM OF TESTING Saccharomyces cerevisiae JD1, heteroallelic at the histidine-4 and tryptophan-5 loci, was obtained from Dr. J.M. Parry, University College of Swansea (Davies, et al., 1975) Mitotic gene conversion may be scored by supplementing yeast minimal medium with histidine to score tryptophan prototrophs and with tryptophan to score histidine prototrophs. CULTURE MEDIIUM The yeast complete (YEPD) and yeast minimal (YM) media have been described by Davies et al. (1975). TREATMENT OF STATIONARY PHASE CELLS Yeast cells were grown to stationary phase in YEPD broth, washed and suspended in pH 7.0 phosphate buffer solution at a concentration of 20 X 106 cells/ml. This suspension was then divided into 1.9-ml amounts in 30-ml universal containers and test compound was added (-S9). For the experiments with metabolic activation (+ S9) 0.5 ml of S9 mix was added. The cultures were incubated, with shaking, at 30° C for the required time. Aliquots were then spread onto YM plates supplemented with either histidine or tryptophan to determine the number of prototrophs at each locus, and dilutions were spread onto YEPD plates to determine cell viability.
試験条件	原文参照	TREATMENT OF LOG PHASE CELLS Yeast cells were grown to log-phase, washed, and resuspended in 2/5 strength YEPD broth at a concentration of 10 × 106 cells/ml. This suspension was then divided into 1.9-ml amounts in 30-ml universal containers and 0.1 ml of test compound solution was added (-S9). For the experiments with metabolic activation (+ S9) 0.1 ml of test compound was added to 1.6 ml of yeast cell suspension, together with 0.3 ml of S9 mix. The cultures were incubated, with shaking, at 30° C for 18 h. Aliquots were then plated as for stationary phase cells. The S9 fraction used in these assays were prepared from the livers of Aroclor-induced rats according to Ames et al. (1975). Solvent: Water
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		
結論		
遺伝子突然変異	陰性	negative
注釈	被験物質は選択された条件下で変異原性がなかった。	The test substance was not mutagenic under the conditions chosen.
信頼性	(2)制限付きで有効	(2) valid with restrictions
信頼性の判断根拠	基本的な原理に合致する受容可能な十分記載された試験	Acceptable, well-documented study which meets basic scientific principles
出典	OECD SIDS Dataset, 2008	OECD SIDS Dataset, 2008
引用文献（元文献）	Dean, B.J., Brooks, T.M., Hodson-Walker, G., Hutson, D.H. (1985) Genetic toxicology testing of 41 industrial chemicals. Mutat. Res., 153, 57-77	Dean, B.J., Brooks, T.M., Hodson-Walker, G., Hutson, D.H. (1985) Genetic toxicology testing of 41 industrial chemicals. Mutat. Res., 153, 57-77
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	2,2'-イミノジエタノール	2,2'-iminodiethanol
CAS番号	111-42-2	111-42-2
純度等		
注釈	入手源: Kodak Laboratory and Specialty Chemicals (Rochester, NY), バッチ: A16, clear, colorless, purity: >99% (TLC/GC) 同定、純度、安定性分析はMidwest Research Institute (Kansas City, MO)の分析化学研究室にて実施。	Source: Kodak Laboratory and Specialty Chemicals (Rochester, NY), batch: A16, clear, colorless, purity: >99% (TLC/GC) Identity, purity, and stability analyses were conducted by the analytical chemistry laboratory, Midwest Research Institute (Kansas City, MO)
方法		
方法／ガイドライン	エームス試験	Ames test
	他：Haworth et al., Environ. Mutagen. 5 (suppl.1), 3-142 (1983)に従う。	other: according to Haworth et al., Environ. Mutagen. 5 (suppl.1), 3-142 (1983)
GLP適合	情報無し	no data
試験を行った年	1983年	1983
細胞株又は検定菌	Salmonella typhimurium strains TA98, 100, 1535, 1537	Salmonella typhimurium strains TA98, 100, 1535, 1537
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 : 33, 100, 333, 1000, 3333 µg/plate. SYSTEM OF TESTING Salmonella typhimurium tester strains TA98, TA100, TA1535, and TA1537 either in buffer or S9 mix (metabolic activation enzymes and cofactors from Aroclor 1254-induced male Sprague-Dawley rat or Syrian hamster liver) for 20 minutes at 37 ° C. Top agar supplemented with L-histidine and d-biotin was added, and the contents of the tubes were mixed and poured onto the surfaces of minimal glucose agar plates. Histidine-independent mutant colonies arising on these plates were counted following incubation for 2 days at 37° C. Each trial consisted of triplicate plates of concurrent positive and negative controls and five doses of diethanolamine. The high dose was limited by toxicity; 3333 µg/plate was selected as the high dose. All trials were repeated. In this assay, a positive response is defined as a reproducible, dose-related increase in histidine-independent (revertant) colonies in any one strain/activation combination. An equivocal response is defined as an increase in revertants that is not dose related, is not reproducible, or is not of sufficient magnitude to support a determination of mutagenicity. A negative response is obtained when no increase in revertant colonies is observed following chemical treatment. There is no minimum percentage or fold increase required for a chemical to be judged positive or weakly positive. -Solvent: Distilled water -Positive controls: In the absence of metabolic activation: sodium azide (TA100 and TA1535), 9-aminoacridine (TA1537), 4-nitro-o-phenylenediamine (TA98). In the presence of metabolic activation with all strains: 2-aminoanthracene.
結果		
細胞毒性		
代謝活性ありの場合	5000 µg/plate	5000 µg/plate
代謝活性なしの場合	5000 µg/plate	5000 µg/plate
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	µg/plate -S9 +S9 10% hamster +S9 10% rat TA100 T1 T2 T1 T2 T1 T2 0 131 124 206 198 173 163 33 143 127 211 189 203 172 100 132 130 211 194 219 160 333 141 125 239 198 216 180 1,000 144 121 233 178 228 153 3333 122 119 208 180 203 167 Neg Neg Neg Neg Equi Neg PC 527 365 808 651 442 365 TA 1535 0 8 8 10 10 12 12 33 11 8 15 11 14 12 100 5 6 17 13 11 9 333 9 9 14 10 19 11 1000 8 8 18 13 15 12 3333 9 7 19 11 17 12 Neg Neg Neg Neg Neg Neg PC 380 227 40 33 30 25
注釈	原文参照	µg/plate -S9 +S9 10% hamster +S9 10% rat TA1357 0 9 8 10 8 11 9 33 7 4 10 7 14 8 100 6 5 8 6 12 8 333 4 3 9 7 14 5 1000 8 5 12 7 10 7 3333 6 7 12 6 8 7 Neg Neg Neg Neg Neg Neg PC 380 119 59 65 33 25 TA98 0 17 16 24 35 20 30 33 14 14 21 37 27 41 100 17 18 18 38 22 36 333 17 16 17 25 24 41 1000 11 20 19 33 21 45 3333 15 18 20 33 20 31 Neg Neg Neg Neg Neg Neg PC 600 190 812 677 303 322 PC = positive control (see test condition)
結論		
遺伝子突然変異	陰性	negative
注釈	被験物質は選択された条件下ではAmes試験で変異原性がなかた。	The test substance was not mutagenic in the Ames test under the conditions chosen.
信頼性	(1)制限なしに有効	(1) valid without restriction
信頼性の判断根拠	基本的な原理に合致する受容可能な十分記載された試験	Acceptable, well-documented study which meets basic scientific principles
出典	OECD SIDS Dataset, 2008	OECD SIDS Dataset, 2008

引用文献(元文献)	・Haworth, S., Lawlor, T., Mortelmans, K., Speck, W., and Zeiger, E. (1983). Salmonella mutagenicity test results for 250 chemicals. Environ. Mutagen. 5 (Suppl. 1), 3-142. ・National Toxicology Program (1992). Toxicity Studies of Diethanolamine (CAS No. 111-42-2) Administered Topically and in Drinking Water to F344/N Rats and B6C3F1 Mice (Tech. Rep. Ser. No. 20; NIH Publication No. 92-3343), Department of Health and Human Services, Research Triangle Park, NC. ・National Toxicology Program (1999) Toxicology and Carcinogenesis Studies of Diethanolamine (CAS No. 111-42-2) in F344/N Rats and B6C3F1 Mice (Dermal Studies) (Tech. Rep. Ser. No. 478; NIH Publ. No. 99-3968), Research Triangle, NC.	・Haworth, S., Lawlor, T., Mortelmans, K., Speck, W., and Zeiger, E. (1983). Salmonella mutagenicity test results for 250 chemicals. Environ. Mutagen. 5 (Suppl. 1), 3-142. ・National Toxicology Program (1992). Toxicity Studies of Diethanolamine (CAS No. 111-42-2) Administered Topically and in Drinking Water to F344/N Rats and B6C3F1 Mice (Tech. Rep. Ser. No. 20; NIH Publication No. 92-3343), Department of Health and Human Services, Research Triangle Park, NC. ・National Toxicology Program (1999) Toxicology and Carcinogenesis Studies of Diethanolamine (CAS No. 111-42-2) in F344/N Rats and B6C3F1 Mice (Dermal Studies) (Tech. Rep. Ser. No. 478; NIH Publ. No. 99-3968), Research Triangle, NC.
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	2,2'-イミノジエタノール	2,2'-iminodiethanol
CAS番号	111-42-2	111-42-2
純度等	純度: >99% (GC)	Purity: >99% (GC)
注釈	入手源：Kodak Laboratory and Specialty Chemicals (Rochester, NY, USA) 物理的形体：液体、無色、青黄色 バッチ：記載無し 保存：室温、遮光	Source: Kodak Laboratory and Specialty Chemicals (Rochester, NY, USA) Physical form: liquid, colorless to pale yellowish Batch: not stated Storage: room temperature, protected from light
方法		
方法／ガイドライン	マウスリンフォーマ試験	Mouse lymphoma assay
	他：OECD476と比較可能	other: comparable to OECD 476
GLP適合	適合	Yes
試験を行った年	1992年	1992
細胞株又は検定菌	L5178Y mouse lymphoma cells	L5178Y mouse lymphoma cells
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 : 25, 50, 100, 200, 300, 400, 600 µg/ml. METHOD FOLLOWED: Method comparable to OECD 476, performed at Litton Bionetics according to the method of Myhr, B., Bowers, L., and Caspary, W.J. (1985). Assays for the induction of gene mutations at the thymidine kinase locus in L5178Y mouse lymphoma cells in culture. In Progress in Mutation Research: Evaluation of Short-term Tests for Carcinogens; Report of the International Programme on Chemical Safety's Collaborative Study on In vitro Assays (J. Ashby, F.J. de Serres, M. Draper, M. Ishidate, Jr., B.H. Margolin, B.E. Matter, and M.D. Shelby, Eds.), Vol. 5, pp. 555-568. Elsevier Science Publishers, Amsterdam. STATISTICAL METHODS: All data were evaluated statistically for trend and peak responses.
試験条件	原文参照	SYSTEM OF TESTING - Species/cell type: L5178Y mouse lymphoma cells were maintained at 37° C as suspension cultures in supplemented Fischer's medium; normal cycling time was approximately 10 hours. To reduce the number of spontaneously occurring cells resistant to trifluorothymidine (TFT), subcultures were exposed to medium containing thymidine, hypoxanthine, methotrexate, and glycine for 1 day; to medium containing thymidine, hypoxanthine, and glycine for 1 day; and to normal medium for 3 to 5 days. For cloning, the horse serum content was increased and Noble agar was added. TEST PROCEDURE All treatment levels within an experiment, including concurrent positive and solvent controls, were triplicated. Treated cultures contained 6 × 10xE6 cells in 10 ml medium. This volume included the S9 fraction in those experiments performed with metabolic activation. Incubation with diethanolamine continued for 4 hours, at which time the medium plus diethanolamine was removed and the cells were resuspended in fresh medium and incubated for an additional 2 days to express the mutant phenotype. Cell density was monitored so that log phase growth was maintained. After the 48-hour expression period, cells
試験条件	原文参照	were plated in medium and soft agar supplemented with TFT for selection of TFT-resistant cells, and cells were plated in non-selective medium and soft agar to determine cloning efficiency. Plates were incubated at 37° C in 5% CO for 10 to 12 days. The test was initially performed without S9. - Metabolic activation system: Freshly prepared S9 from the livers of Aroclor 1254-induced male Fischer 344 rats - Tested concentration: -S9: 25, 50, 100, 200, 300, 400, 600 µg/ml +S9: 25, 50, 100, 200, 300, 400, 600 µg/ml - Controls: Methyl Methanesulfonate: 2.5 µg/ml +S9, 5 µg/ml -S9 Ethanol: solvent control
結果		
細胞毒性		
代謝活性ありの場合	400 µg/ml	400 µg/ml
代謝活性なしの場合	400 µg/ml	400 µg/ml
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	Trial 1: −S9: induction of trifluorothymidine resistance in mouse lymphoma L5178Y cells μg/ml CE (%) RTG (%) MC MF Ethanol 92 91 66 24 75 80 51 23 96 108 65 23 113 121 84 25 MMS 55 27 578 352 5 48 42 582 403 48 28 472 329 DEA 25 53 57 39 24 75 70 54 24 85 91 49 19 50 93 90 44 16 66 92 33 17 98 85 47 16 100 70 68 48 23 80 62 46 19 68 66 53 26 200 66 35 59 30 75 42 50 22 61 43 31 17 300 47 12 47 33 70 14 46 22 lethal MMS=methyl Methanesulfonate, CE=cloning efficiency, RTG=total relative growth, MC=mutant count, MF=mutant fraction
注釈	原文参照	Trial 2: −S9: induction of trifluorothymidine resistance in mouse lymphoma L5178Y cells μg/ml CE (%) RTG (%) MC MF Ethanol 95 109 81 28 111 102 80 24 114 117 34 10 75 73 37 16 MMS 69 57 277 134 5 56 49 390 233 59 55 448 252 DEA 50 89 91 66 25 109 86 87 27 100 108 83 28 100 98 96 115 39 105 100 127 40 110 102 102 31 150 110 98 108 33 108 58 91 28 93 96 87 31
注釈	原文参照	200 117 104 93 26 118 89 93 26 89 99 88 33 300 96 78 74 26 85 64 67 26 116 59 81 23 400 98 51 59 20 87 38 78 30 93 38 65 23 600 Lethal Lethal Lethal MMS=methyl Methanesulfonate, CE=cloning efficiency, RTG=total relative growth, MC=mutant count, MF=mutant fraction
注釈	原文参照	Trial 1: +S9: induction of trifluorothymidine resistance in mouse lymphoma L5178Y cells μg/ml CE (%) RTG (%) MC MF Ethanol 80 111 103 43 81 114 102 42 76 92 117 52 62 83 105 56 MMS 58 21 710 412 2.5 47 20 622 438 50 52 621 413 DEA 25 58 109 94 54 55 75 82 50 70 106 96 46 50 65 90 131 67 91 120 122 45 66 93 97 49 100 64 91 104 54 80 114 130 54 74 108 120 54 200 49 96 72 49 76 93 130 57 60 94 99 55

		300 56 86 94 56 70 99 92 44 73 90 101 46 400 63 67 106 56 80 83 115 48 53 72 54 34 600 lethal lethal lethal MMS=methyl Methanesulfonate, CE=cloning efficiency, RTG=total relative growth, MC=mutant count, MF=mutant fraction
注釈	原文参照	Trial 2: +S9: induction of trifluorothymidine resistance in mouse lymphoma L5178Y cells µg/ml CE (%) RTG (%) MC MF Ethanol 76 96 120 53 85 117 68 27 68 95 92 45 72 91 83 38 MMS 2.5 60 63 651 363 74 61 716 323 62 68 482 260 DEA 100 57 83 60 35 68 67 63 31 200 72 62 66 31 62 69 72 39 81 78 72 30 300 72 37 77 36 67 13 71 35 67 27 75 37 400 lethal lethal lethal MMS=methyl Methanesulfonate, CE=cloning efficiency, RTG=total relative growth, MC=mutant count, MF=mutant fraction
結論		
遺伝子突然変異	陰性	negative
注釈	被験物質は選択された試験条件下でマウスリンフォーマ試験で変異原性を示さなかった。 試験系の感受性は、陽性対照物質が期待される陽性反応を示したことから、証明された。	The test substance was shown to be not mutagenic in the mouse lymphoma assay under the chosen test condition. The sensitivity of the test system was verified since the positive control substance showed the expected positive reactions.
信頼性	(1)制限なしに有効	(1) valid without restriction
信頼性の判断根拠	基本的な原理に合致する受容可能な十分記載された試験	Acceptable, well-documented study which meets basic scientific principles
出典	OECD SIDS Dataset, 2008	OECD SIDS Dataset, 2008
引用文献(元文献)	・Myhr BC, Bowers LR, Caspary WJ (1986) Results from the testing of coded chemicals in the L5178Y TK+/- mouse lymphoma mutagenesis assay, Environ. Mutagen., 7(Suppl 3), 58 (154, abstract). ・National Toxicology Program (1992) Toxicity Studies of Diethanolamine (CAS No. 111-42-2) Administered Topically and in Drinking Water to F344/N Rats and B6C3F1 Mice (Tech. Rep. Ser. No. 20; NIH Publication No. 92-3343), Department of Health and Human Services, Research Triangle Park, NC. ・National Toxicology Program (1999) Toxicology and Carcinogenesis Studies of Diethanolamine (CAS No. 111-42-2) in F344/N Rats and B6C3F1 Mice (Dermal Studies) (Tech. Rep. Ser. No. 478; NIH Publ. No. 99-3968), Research Triangle, NC.	・Myhr BC, Bowers LR, Caspary WJ (1986) Results from the testing of coded chemicals in the L5178Y TK+/- mouse lymphoma mutagenesis assay, Environ. Mutagen., 7(Suppl 3), 58 (154, abstract). ・National Toxicology Program (1992) Toxicity Studies of Diethanolamine (CAS No. 111-42-2) Administered Topically and in Drinking Water to F344/N Rats and B6C3F1 Mice (Tech. Rep. Ser. No. 20; NIH Publication No. 92-3343), Department of Health and Human Services, Research Triangle Park, NC. ・National Toxicology Program (1999) Toxicology and Carcinogenesis Studies of Diethanolamine (CAS No. 111-42-2) in F344/N Rats and B6C3F1 Mice (Dermal Studies) (Tech. Rep. Ser. No. 478; NIH Publ. No. 99-3968), Research Triangle, NC.
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

B. 染色体異常
CHROMOSOMAL ABBERATION

試験物質名	2,2'-イミノジエタノール	2,2'-iminodiethanol
CAS番号	111-42-2	111-42-2
純度等	純度 : >= 99.3 - % w/w	Purity : >= 99.3 - % w/w
注釈	入手源：記述されていない。 バッチ：17584 純度：99.7%	Source: not stated, batch: 17584, purity: 99.7%
方法		
方法／ガイドライン	染色体異常試験、 他：Dean, B.J. and Hodson-Walker, G.: Mutation Research 64, 329-337に従う。	Cytogenetic assay, other: according to Dean, B.J. and Hodson-Walker, G.: Mutation Research 64, 329-337
GLP適合	情報無し	no data
試験を行った年	1980年	1980
細胞株	ラット肝細胞株RL1及びRL4	Rat liver cell lines RL1 and RL4
代謝活性化(S9)の有無	無し	without

試験条件	原文参照	Test concentration : 0.125, 0.25, 0.5 of GI50 (50% growth inhibition). SYSTEM OF TESTING The rat-liver cell lines, RL 1 and RL 4, are both epithelial-type cell lines derived in the test laboratory following the procedure described by Williams et al. (1971). RL x was initiated in 1973 from a 10-day old Carworth Farm E rat and RL 4 was derived from a 10-day old Wistar rat in 1978 (Dean and Hodson-Walker, 1979). CULTURE MEDIUM Stock cultures were maintained and assays were performed using Minimal Essential Medium (Wellcome Reagents Ltd., Beckenham, Kent) supplemented with 10% foetal calf serum (Flow Laboratories Ltd., Irvine, Scotland) and 1% non-essential amino acids (Flow Laboratories Ltd.). CYTOTOXICITY ASSAY Monolayer cultures of rat-liver cells were prepared in multi-well tissue culture trays. The cultures were incubated at 37° C for 24 h to commence active growth before treatment with the test compounds. After 24 h exposure the cell monolayers were stained and the growth inhibition effects noted. The concentrations selected for the chromosome assay were 0.5, 0.25 and 0.125 of the GI50 (50% growth inhibition). CHROMOSOME ASSAY Cultured rat-liver cells were grown on microscope slides contained in petri dishes. Treatment was for a 24-h period and positive control slides were included. Colcemid was added 2 h before exposure was complete. The slides were then subject to hypotonic treatment followed by fixation and staining as in Method A. The chromosome preparations were randomly coded and 100 cells from each culture were analysed microscopically. Solvent: Water
結果		
細胞毒性		
代謝活性ありの場合		
代謝活性なしの場合		
染色体異常		
代謝活性ありの場合		
代謝活性なしの場合		
注釈		
結論		
染色体異常	陰性	negative
注釈	被験物質は選択された条件下で変異原性がなかった。	The test substance was not mutagenic under the conditions chosen.
信頼性	(2)制限付きで有効	(2) valid with restrictions
信頼性の判断根拠	基本的な原理に合致する受容可能な十分記載された試験	Acceptable, well-documented study which meets basic scientific principles
出典	OECD SIDS Dataset, 2008	OECD SIDS Dataset, 2008
引用文献(元文献)	Dean, B.J., Brooks, T.M., Hodson-Walker, G., Hutson, D.H. (1985) Genetic toxicology testing of 41 industrial chemicals. Mutat. Res., 153, 57-77	Dean, B.J., Brooks, T.M., Hodson-Walker, G., Hutson, D.H. (1985) Genetic toxicology testing of 41 industrial chemicals. Mutat. Res., 153, 57-77
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	情報無し	no data
CAS番号		
純度等		
注釈		
方法		
方法／ガイドライン	染色体異常試験、 他 : OECD473と比較可能	Cytogenetic assay, other: comparable to OECD 473
GLP適合	情報無し	no data
試験を行った年	1989年	1989
細胞株	チャイニーズハムスター卵巣(CHO)細胞	Chinese hamster ovary (CHO) cells
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 : (-S9): 101, 505, 2010 µg/ml; (+S9): 303, 1010, 3010 µg/ml. METHOD FOLLOWED: Method comparable to OECD 473 STATISTICAL METHODS: Analyses were conducted on both the dose response curve and individual dose points.
試験条件	原文参照	SYSTEM OF TESTING - Species/cell type: Cultured Chinese hamster ovary (CHO) cells TEST PROCEDURE A single flask per dose was used. - Without S9: CHO cells were incubated in McCoy's 5A medium with diethanolamine for 8 hours; Colcemid was added and incubation continued for 2.5 hours at 37° C. The cells were then harvested by mitotic shake-off, fixed, and stained with Giemsa. - With S9: CHO cells were treated with diethanolamine and S9 for 2 hours, after which the treatment medium was removed and the cells were incubated for 10 hours in fresh medium, with Colcemid present for the final 2 to 3 hours. Cells were harvested in the same manner as for the treatment without S9. The harvest time for the Abs test was based on the cell cycle information obtained in the SCE test.

試験条件	原文参照	Cells were selected for scoring on the basis of good morphology and completeness of karyotype (21 ± 2 chromosomes). All slides were scored blind and those from a single test were read by the same person. 100 metaphase cells were scored at each dose level. Classes of aberrations included simple (breaks and terminal deletions), complex (rearrangements and translocations), and other (pulverized cells, despiralized chromosomes, and cells containing 10 or more aberrations). - tested concentrations: -S9: 101, 505, 2010 µg/ml +S9: 303, 1010, 3010 µg/ml - Metabolic activation system: Aroclor 1254-induced male Sprague-Dawley rat liver S9 and cofactor mix. - Controls: Mitomycin C: 5 µg/ml: -S9 Cyclophosphamide: 50 µg/ml: +S9 McCoy's 5A medium: solvent control
結果		
細胞毒性		
代謝活性ありの場合	3010 µg/ml (+S9)	3010 µg/ml (+S9)
代謝活性なしの場合		
染色体異常		
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	Harvest: 10.5 h cells No.Abs Abs/cell %Cells+Abs - S9 µg/ml Medium 100 1 0.01 1.0 Mitomycin C 5 100 33 0.33 24.0 DEA 101 100 1 0.01 1.0 505 100 0 0.0 0.0 2010 100 1 0.02 2.0 Harvest: 12 h + S9 µg/ml Medium 100 3 0.03 2.0 Cyclophosphamide 50 100 55 0.55 34.0 DEA 303 100 1 0.01 1.0 1010 100 2 0.01 2.0 3010 100 8 0.08 7.0
結論		
染色体異常	陰性	negative
注釈	被験物質はCHO細胞で染色体異常を誘発しなかった。すなわち、選択された試験条件下で変異原性の能力を示さなかった。 試験系の感受性は、陽性対照物質が期待される陽性反応を示したことから証明された。	The test substance did not induce chromosomal aberrations in CHO cell und thus, showed no mutagenic potential under the chosen test condition. The sensitivity of the test system was verified since the positive control substances showed the expected positive reactions.
信頼性	(2)制限付きで有効	(2) valid with restrictions
信頼性の判断根拠	基本的な原理に合致する受容可能な十分記載された試験	Acceptable, well-documented study which meets basic scientific principles
出典	OECD SIDS Dataset, 2008	OECD SIDS Dataset, 2008
引用文献(元文献)	Loveday KS, Lug MH, Resnick MA, Anderson BE, Zeiger E (1989). Chromosome aberration and sister chromatid exchange tests in Chinese hamster ovary cells in vitro. II. Results with 20 chemicals, Environ. Mol. Mutagen., 13, 60-94, in: National Toxicology Program (1999) Toxicology and Carcinogenesis Studies of Diethanolamine (CAS No. 111-42-2) in F344/N Rats and B6C3F1 Mice (Dermal Studies) (Tech. Rep. Ser. No. 478; NIH Publ. No. 99-3968), Research Triangle, NC	Loveday KS, Lug MH, Resnick MA, Anderson BE, Zeiger E (1989). Chromosome aberration and sister chromatid exchange tests in Chinese hamster ovary cells in vitro. II. Results with 20 chemicals, Environ. Mol. Mutagen., 13, 60-94, in: National Toxicology Program (1999) Toxicology and Carcinogenesis Studies of Diethanolamine (CAS No. 111-42-2) in F344/N Rats and B6C3F1 Mice (Dermal Studies) (Tech. Rep. Ser. No. 478; NIH Publ. No. 99-3968), Research Triangle, NC
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	情報無し	no data
CAS番号		
純度等		
注釈		
方法		
方法／ガイドライン	姉妹染色分体交換試験、 他法：OECD479と比較可能	Sister chromatid exchange assay, other: comparable to OECD 479
GLP適合	情報無し	no data
試験を行った年	1989年	1989
細胞株	チャイニーズハムスター卵巣(CHO)細胞	Chinese hamster ovary (CHO) cells
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 : 150, 500, 1500 µg/ml. METHOD FOLLOWED: Method comparable to OECD 479 STATISTICAL METHODS: Statistical analyses were conducted on the slopes of the dose-response curves and the individual dose points.

試験条件	原文参照	SYSTEM OF TESTING - Species/cell type: Cultured Chinese hamster ovary (CHO) cells TEST PROCEDURE A single flask per dose was used. - Without S9: CHO cells were incubated for 26 hours with diethanolamine in supplemented McCoy's 5A medium. Bromodeoxyuridine (BrdU) was added 2 hours after culture initiation at 37° C. After 26 hours, the medium containing diethanolamine was removed and replaced with fresh medium plus BrdU and Colcemid, and incubation was continued for 2.5 hours. Cells were then harvested by mitotic shake-off, fixed, and stained with Hoechst 33258 and Giemsa. - With S9: CHO cells were incubated with diethanolamine, serum-free medium, and S9 for 2 hours. The medium was then removed and replaced with medium containing serum and BrdU and no diethanolamine. Incubation proceeded for an additional 25.5 hours, with Colcemid present for the final 2 hours.
試験条件	原文参照	All slides were scored blind and those from a single test were read by the same person. Fifty second-division metaphase cells were scored for frequency of SCEs/cell from each dose level. - tested concentrations: 150, 500, 1500 µg/ml (+/- S9) - Metabolic activation system: Aroclor 1254-induced male Sprague-Dawley rat liver S9 and cofactor mix. - Positive control: Mitomycin C: 0.002 and 0.010 µg/ml: -S9 Cyclophosphamide: 0.5 and 2.5 µg/ml: +S9 - Negative control: McCoy's 5A medium (solvent)
結果		
細胞毒性		
代謝活性ありの場合	1500 µg/ml	1500 µg/ml
代謝活性なしの場合	1500 µg/ml	1500 µg/ml
姉妹染色分体交換		
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	Induction of sister chromatid exchanges in Chinese hamster ovary cells cells No. SCE SCE/chromosome SCE/cells - S9 µg/ml Medium 50 465 0.44 9.3 Mitomycin C 0.002 50 727 0.69 14.5 0.010 10 319 1.54 31.9 DEA 150 50 459 0.43 9.2 500 50 487 0.46 9.7 1500 50 469 0.45 9.4
注釈	原文参照	+ S9 µg/ml Medium 50 518 0.51 10.4 Cyclophosphamide 0.5 50 1053 1.03 21.1 2.5 10 592 2.94 59.2 DEA 50 150 50 505 0.49 10.1 500 50 539 0.53 10.8 1500 565 0.56 11.3
結論		
姉妹染色分体交換	陰性	negative
注釈	被験物質はCHO細胞でSCEを誘発しなかった。従って、選択された試験条件下で、変異原性の能力は示さなかった。 試験系は、陽性対照物質が期待された陽性反応を示したため、その感受性があることが証明された。	The test substance did not induce sister chromatid exchanges in CHO cell and thus, showed no mutagenic potential under the chosen test condition. The sensitivity of the test system was verified since the positive control substances showed the expected positive reactions.
信頼性	(2)制限付きで有効	(2) valid with restrictions
信頼性の判断根拠	基本的な原理に合致する受容可能な十分記載された試験	Acceptable, well-documented study which meets basic scientific principles
出典	OECD SIDS Dataset, 2008	OECD SIDS Dataset, 2008

引用文献(元文献)	Loveday KS, Lug MH, Resnick MA, Anderson BE, Zeiger E (1989). Chromosome aberration and sister chromatid exchange tests in Chinese hamster ovary cells in vitro. II. Results with 20 chemicals, Environ. Mol. Mutagen., 13, 60-94, in: National Toxicology Program (1999) Toxicology and Carcinogenesis Studies of Diethanolamine (CAS No. 111-42-2) in F344/N Rats and B6C3F1 Mice (Dermal Studies) (Tech. Rep. Ser. No. 478; NIH Publ. No. 99-3968), Research Triangle, NC	Loveday KS, Lug MH, Resnick MA, Anderson BE, Zeiger E (1989). Chromosome aberration and sister chromatid exchange tests in Chinese hamster ovary cells in vitro. II. Results with 20 chemicals, Environ. Mol. Mutagen., 13, 60-94, in: National Toxicology Program (1999) Toxicology and Carcinogenesis Studies of Diethanolamine (CAS No. 111-42-2) in F344/N Rats and B6C3F1 Mice (Dermal Studies) (Tech. Rep. Ser. No. 478; NIH Publ. No. 99-3968), Research Triangle, NC
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

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

試験物質名	2,2'-イミノジエタノール	2,2'-iminodiethanol
CAS番号	111-42-2	111-42-2
純度等	純度: >99% (GC)	Purity: >99% (GC)
注釈	入手源:Kodak Laboratory and Specialty Chemicals (Rochester, NY, USA) 物理的形体:液体、無色～青黄色	Source: Kodak Laboratory and Specialty Chemicals (Rochester, NY, USA) Physical form: liquid, colorless to pale yellowish Batch: not stated Storage: room temperature, protected from light
方法		
方法／ガイドライン	他:末梢血リンパ球の小核試験	other: Micronucleus assay on peripheral blood lymphocytes
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	1992年	1992
試験系(種／系統)	マウス	mouse
	B6C3F1	B6C3F1
性別(雄:M、雌:F)	雌雄	male/female
投与量	0, 80, 160, 320, 630, 1250 mg/kg bw	0, 80, 160, 320, 630, 1250 mg/kg bw
投与経路	経皮	dermal
試験期間	13週間	13 weeks
試験条件	原文参照	METHOD FOLLOWED: At the end of the 13 week toxicity study in mice with dermal application peripheral blood samples were obtained from male and female mice and examined for the occurrence of micronuclei GLP: Yes STATISTICAL METHODS: Log transformation of NCE data, testing for normality by the Shapiro-Wilk test, and testing for heterogeneity of variance by Cochran's test. The frequency of micronucleated cells among NCEs was analyzed by analysis of variance with the SAS GLM procedure. The NCE data for each dosed group were compared with the concurrent solvent control group by Student's t-test.
試験条件	原文参照	TEST ORGANISMS: - Species/Strain: Mice, B6C3F1 supplied by Taconic Farms, Germantown, NY, USA - Acclimatization: 12-13 days - Age at study start: about 5-6 weeks - Number of animals: 10 males and 10 females per dose group - Housing: Animals were housed individually ADMINISTRATION / EXPOSURE Solutions of diethanolamine were prepared in 95% ethanol (USP grade). Dose solutions were stored no longer than 20 days at room temperature, protected from light. Results of analyses of dose formulations by gas chromatography before and after administration to animals were within 10% of theoretical values. 10 animals per sex were administered diethanolamine in 95% ethanol once per day, except for weekends and holidays, at concentrations of 0, 37.5, 75, 150, 300, and 600 mg/ml (corresponding to 0, 80, 160, 320, 630, or 1250 mg/kg bw) for 13 weeks (65 exposures). MOUSE PERIPHERAL BLOOD MICRONUCLEUS Smears were prepared from peripheral blood samples obtained by cardiac puncture of dosed and control animals at the termination of the 13-week study. Smears were immediately prepared and fixed in absolute methanol. The methanol-fixed slides were stained with Hoechst 33258/pyronin Y (MacGregor et al., 1983) and coded. Slides were scanned to determine the frequency of micronuclei in 10,000 normochromatic erythrocytes (NCEs) in up to 10 male and 10 female mice per dose group. - Dose levels: 0, 80, 160, 320, 630, 1250 mg/kg bw Positive control: Three male mice were treated with urethane (0.2%) in drinking water, these animals were not part of the main 13 week study.
統計学的処理		
結果		
性別及び投与量別の結果	陰性	negative
遺伝毒性効果		
NOAEL (NOEL)		
LOAEL (LOEL)		
統計的結果		

注釈	原文参照	Frequency of micronuclei in peripheral blood erythrocytes of mice exposed dermally to DEA for 13 weeks mg/kg N MN-NCE/1000 NCE % PCE Males 0 10 1.37 1.82 80 10 1.37 1.67 160 9 1.44 1.72 320 9 1.10 1.72 630 10 1.07 1.51 1250 8 0.81 1.51 Females 0 10 0.82 1.52 80 10 0.79 1.61 160 10 0.80 1.56 320 10 0.73 1.27 630 10 0.72 1.25 1250 5 0.71 0.95 Urethane 3 18.7 No data MN = micronuclei; MN-NCE micronuclei per normochromatic erythrocytes, PCE = polychromatic erythrocytes
結論		
*in vivo*遺伝毒性	陰性	negative
注釈	被験物質はマウスに13週間1250 mg/kg bw以下の用量で経皮投与した場合、マウスの末梢血赤血球に小核を誘発しなかった。 試験系の感受性は、陽性対照物質が期待される陽性反応を示したことから証明された。	The test substance did not induce micronuclei in peripheral blood erythrocytes of mice exposed dermally to concentrations of up to 1250 mg/kg bw for 13 weeks. The sensitivity of the test system was verified since the positive control substance showed the expected positive reactions.
信頼性	(1)制限なしに有効	(1) valid without restrictions
信頼性の判断根拠	受容可能な科学的原理に合致する十分な記載の試験	Acceptable, well-documented study which meets scientific principles
出典	OECD SIDS Dataset, 2008	OECD SIDS Dataset, 2008
引用文献(元文献)	・National Toxicology Program (1992) Toxicity Studies of Diethanolamine (CAS No. 111-42-2) Administered Topically and in Drinking Water to F344/N Rats and B6C3F1 Mice (Tech. Rep. Ser. No. 20; NIH Publication No. 92-3343), Department of Health and Human Services, Research Triangle Park, NC. ・Witt KL, Knapton A, Wehr CM, Hook GJ, Mirsalis J, Shelby MD, MacGregor JT (2000) Micronucleated erythrocyte frequency in peripheral blood of B6C3F1 mice from short-term, prechronic and chronic studies of the NTP carcinogenesis bioassay program, Environmental Molecular Mutagenesis, 36, 163-194.	・National Toxicology Program (1992) Toxicity Studies of Diethanolamine (CAS No. 111-42-2) Administered Topically and in Drinking Water to F344/N Rats and B6C3F1 Mice (Tech. Rep. Ser. No. 20; NIH Publication No. 92-3343), Department of Health and Human Services, Research Triangle Park, NC. ・Witt KL, Knapton A, Wehr CM, Hook GJ, Mirsalis J, Shelby MD, MacGregor JT (2000) Micronucleated erythrocyte frequency in peripheral blood of B6C3F1 mice from short-term, prechronic and chronic studies of the NTP carcinogenesis bioassay program, Environmental Molecular Mutagenesis, 36, 163-194.
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	2,2'-イミノジエタノール	2,2'-iminodiethanol
CAS番号	111-42-2	111-42-2
純度等	純度: 99.7%	Purity: 99.7%
注釈	入手源: Shell Chemicals, Carrington, UK ﾊﾞｯﾁ: 17584	Source: Shell Chemicals, Carrington, UK Batch: 17584
方法		
方法／ガイドライン		
試験のタイプ	他 : アルカリ溶出試験	other: alkaline elution assay
GLP適合	適合	Yes
試験を行った年	1982年	1982
試験系(種／系統)	ラット	rat
	Wistar	Wistar
性別(雄 : M、雌 : F)	雌雄	male/female
投与量	910 mg/ kg bw	910 mg/ kg bw
投与経路	経口(特定されていない)	oral unspecified
試験期間	6時間	6 h
試験条件	原文参照	METHOD FOLLOWED: Study on the effect of DEA on the integrity of rat liver DNA in vivo by alkaline elution assay. GLP: Yes
試験条件	原文参照	TEST ORGANISMS: - Species/Strain: male and female Wistar rats, supplied by Shell Toxicology Laboratory, Tunstall, UK - Body weight: males: 340 - 470 g, females: 200 - 250 g ADMINISTRATION / EXPOSURE DEA was administered as an aqueous solution (40%) in distilled water. - Dose level: 910 mg/kg bw - Control group: distilled water - Positive control: methyl methane sulphonate: 300 - 350 mg/kg bw - Exposure time: 6 h LIVER PREPARATION AND TREATMENT: Partial hepatectomy was performed. The liver DNA was labelled with [3H]- thymidine during peak restorative DNA synthesis (18 - 36 h). Animals treated in this way were used for experiments after a minimum recovery of 2 weeks, when the liver had returned to its quiescent state. A 2 g sample of liver was placed in a small beaker and the tissue was gently squashed and the resultant cell suspension was centrifuged to sediment large pieces of liver. Each of the eluant fraction was blended with 4 ml of scintillation cocktail and the radioactivity was determined in a LKB Rackbeta liquid scintillation spectrometer.

統計学的処理		
結果		
性別及び投与量別の結果	陰性	negative
遺伝毒性効果		
NOAEL (NOEL)		
LOAEL (LOEL)		
統計的結果		
注釈	原文参照	Alkaline elution profiles of rat liver DNA, derived from animals receiving a single oral dose of 910 mg/kg bw showed no detectable DNA single-strand damage after exposure time of 6 h under the experimental condition. The sensitivity of the test system was demonstrated since the positive control methyl methansulphonate induced single-strand DNA damage.
結論		
*in vivo*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	受容可能な科学的原理に合致する十分な記載の試験	Acceptable, well-documented study which meets scientific principles
出典	OECD SIDS Dataset, 2008	OECD SIDS Dataset, 2008
引用文献(元文献)	TSCATS, OTS 0520408, Doc. I. D. 86-890000970, 8DS, Studies of effects of Diethanolamine in the integrity of rat liver DNA in vivo with attachment, cover sheets and letter, Shell Chemical Company, 09 June 1989	TSCATS, OTS 0520408, Doc. I. D. 86-890000970, 8DS, Studies of effects of Diethanolamine in the integrity of rat liver DNA in vivo with attachment, cover sheets and letter, Shell Chemical Company, 09 June 1989
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	1.1～1.4で規定	as prescribed by 1.1 - 1.4
CAS番号		
純度等	ジエタノールアミン 供給源: Kodak Laboratory and Specialty Chemicals (Rochester, NY, USA) 物理的形状: 液体、無色から淡黄色 バッチ: A16 純度: >99% (GC) 保管: 室温、遮光 エタノール: 供給源: Aaper Alcohol and Chemical Company (Shelbyville, KY, USA) 物理的形状: 液体、無色 純度: 98.7 - 101.3%	DIETHANOLAMINE: Source: Kodak Laboratory and Specialty Chemicals (Rochester, NY, USA) Physical form: liquid, colorless to pale yellowish Batch: A16 Purity: >99% (GC) Storage: room temperature, protected from light ETHANOL: Source: Aaper Alcohol and Chemical Company (Shelbyville, KY, USA) Physical form: liquid, colorless Purity: 98.7 - 101.3%
注釈		
方法		
方法／ガイドライン	その他: OECD 451相当	other: comparable to OECD 451
試験のタイプ		
GLP適合	はい	yes
試験を行った年	1992	1992
試験系(種／系統)	ラット	rat
	Fischer 344	Fischer 344
性別(雄:M、雌:F)	雌雄	male/female
投与量	0、16、32、64 mg/kg 体重 (雄) 又は 0、8、16、32 mg/kg 体重 (雌)	0, 16, 32, 64 mg/kg bw (males) or 0, 8, 16, 32 mg/kg bw (females)
各用量群(性別)の動物数		
溶媒(担体)		
投与経路	経皮	dermal
処理頻度	1日1回、5回/週	once daily, 5x/week
対照群と処理	あり、溶媒対照	yes, concurrent vehicle
試験条件	暴露期間: 103週間 暴露後の期間: なし	Exposure period : 103 weeks Post exposure period : none
試験条件	※英文参照	METHOD FOLLOWED: Carcinogenicity study with dermal application. Design and extent of examinations comparable to OECD 451. GLP: Yes
試験条件	※英文参照	Test condition : TEST ORGANISMS: - Species/Strain: Rats, F344/N supplied by Taconic Farms, Germantown, NY, USA - Acclimatization: 11 days - Age at study start: about 6 weeks - Number of animals: 50 males and 50 females per dose group - Housing: Rats were housed individually ADMINISTRATION / EXPOSURE The dose formulations were prepared every 3 weeks by mixing diethanolamine with 95 % ethanol to give the desired concentration. The dose formulations were stored at room temperature, protected from light, in amber glass bottles for up to 28 days. Stability studies of a 0.5 mg/ml formulation were performed by the analytical chemistry laboratory using gas chromatography. The formulation had only small losses of diethanolamine when stored at room temperature, protected from light, for up to 28 days; it was stable for 3 hours when stored open to air and light.

試験条件	※英文参照	Periodic analyses of the dose formulations of diethanolamine were conducted at the study laboratory using gas chromatography. Dose formulations were analyzed approximately every 9 weeks. All dose formulations and animal room samples for rats and mice were within 10% of the target concentrations Groups of 50 male rats were administered dermal doses of 0, 16, 32, or 64 mg/kg bw application of 0, 27.5, 55, or 110 mg/ml ethanol solutions, 5 days per week for 103 weeks. Groups of 50 female rats were administered dermal doses of 0, 8, 16, or 32 mg/kg by the application of 0, 13.8, 27.5, or 55 mg/ml solutions, 5 days per week for 103 weeks. Dose volumes were adjusted to provide the appropriate mg/kg dose based on group mean body weights. CLINICAL OBSERVATIONS AND FREQUENCY: -Body weight: weekly through week 13 and monthly thereafter -Mortality and clinical findings: 2x/day including moribundity but clinical findings recorded: monthly
試験条件	※英文参照	PATHOLOGY Complete necropsy and microscopic examination were performed on all animals. At necropsy, all organs and tissues were examined for grossly visible lesions, and all major tissues were fixed and preserved in 10% neutral buffered formalin, processed and trimmed, embedded in paraffin, sectioned to a thickness of 5 to 6 µm, and stained with hematoxylin and eosin for microscopic examination. For all paired organs (e.g., adrenal gland, kidney, ovary), samples from each organ were examined.
試験条件	※英文参照	Histopathology: Gross lesions, tissue masses, adrenal gland, bone with marrow, brain, clitoral gland, esophagus, gallbladder (mice), heart with aorta, large intestine (cecum, colon, and rectum), small intestine (duodenum, jejunum, and ileum), kidney, liver, lung, lymph nodes (mandibular and mesenteric), mammary gland (except male mice), nose, ovary, pancreas, parathyroid gland, pituitary gland, preputial gland, prostate gland, salivary gland, skin (site of application), spleen, stomach (forestomach and glandular), testis with epididymis and seminal vesicle, thymus, thyroid gland, trachea, urinary bladder, uterus.
統計学的処理	※英文参照	STATISTICAL METHODS: Survival Analyses The probability of survival was estimated by the product-limit procedure of Kaplan and Meier (1958. Statistical analyses for possible dose-related effects on survival used Cox's (1972) method for testing two groups for equality and Tarone's (1975) life table test to identify dose-related trends. All reported P values for the survival analyses are two sided. Analysis of Neoplasm and Non-neoplastic Lesion Incidences The Poly-k test (Bailer and Portier, 1988; Portier and Bailer, 1989; Piegorsch and Bailer, 1997) was used to assess neoplasm and non-neoplastic lesion prevalence. This test is a survival-adjusted quantal-response procedure that modifies the Cochran-Armitage linear trend test to take survival differences into account. Tests of significance included pairwise comparisons of each dosed group with controls and a test for an overall dose-related trend. Continuity-corrected tests were used in the analysis of lesion incidence, and reported P values are one sided.
統計学的処理	※英文参照	Analysis of Continuous Variables Average severity values were analyzed for significance with the Mann-Whitney U test (Hollander and Wolfe, 1973).
結果		
体重、体重増加量	8週から89週にかけて、64 mg/kg群の雄の平均体重は媒体対照群の体重より低値であった。 97週以降、32 mg/kgの雌の平均体重は媒体対照群のそれより低値であった。	Mean body weights of 64 mg/kg males were less than those of the vehicle controls from week 8 to week 89. Mean body weights of 32 mg/kg females were less than those of the vehicle control group after week 97.
	体重増加量 mg/kg 体重 0 16 32 64 雄 g g (%)* g (%) g (%) 1-13 週 242 244(101) 238(98) 230(95) 14-52週 398 396(99) 384(96) 370(93) 53-104週 446 440(99) 433(97) 413(93) mg/kg 体重 0 8 16 32 雌 1-13 週 154 154(100) 152(99) 151(98) 14-52週 217 219(101) 214(99) 213(98) 53-104週 285 285(100) 281(99) 273(96) * = 対照群の %	Body weight gain mg/kg bw 0 16 32 64 Males g g (%)* g (%) g (%) Week 1-13 242 244(101) 238(98) 230(95) Week 14-52 398 396(99) 384(96) 370(93) Week 53-104 446 440(99) 433(97) 413(93) mg/kg bw 0 8 16 32 Females 0 Week 1-13 154 154(100) 152(99) 151(98) Week 14-52 217 219(101) 214(99) 213(98) Week 53-104 285 285(100) 281(99) 273(96) * = % of control
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）	投与による唯一の臨床症状は適用部位皮膚の刺激であった。この影響は用量相関性があった（雄：媒体対照、0/50；16 mg/kg、1/50；32 mg/kg、0/50；64 mg/kg、4/50；雌：媒体対照、2/50；8 mg/kg、2/50；16 mg/kg、2/50；32 mg/kg、8/50）。	The only clinical finding attributed to administration was irritation of the skin at the site of application. This effect was dose related (males: vehicle control, 0/50; 16 mg/kg, 1/50; 32 mg/kg, 0/50; 64 mg/kg, 4/50; females: vehicle control, 2/50; 8 mg/kg, 2/50; 16 mg/kg, 2/50; 32 mg/kg, 8/50).

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	生存率: 投与した雌雄のラットの生存率は溶媒対照群のそれと同様であった。	Survival Survival of dosed male and female rats was similar to that of the vehicle control groups
	ラットの生存率 mg/kg 体重 0 16 32 64 雄 開始時の例数 50 50 50 50 瀕死例 31 31 25 22 自然死亡例 5 9 4 6 終了時の 例数 14 10 21 22 平均生存期間 (日) 651 648 678 655 mg/kg 体重 0 8 16 32 雌 開始時の例数 50 50 50 50 瀕死例 11 16 12 13 自然死亡例 14 5 9 13 終了時の 例数 25 29 29 24 平均生存期間 (日) 669 689 679 665	Survival of Rats mg/kg bw 0 16 32 64 Males No at start 50 50 50 50 Moribund 31 31 25 22 Natural deaths 5 9 4 6 No. at termina- tion 14 10 21 22 Mean survival (days) 651 648 678 655 mg/kg bw 0 8 16 32 Females No at start 50 50 50 50 Moribund 11 16 12 13 Natural deaths 14 5 9 13 No. at termina- tion 25 29 29 24 Mean survival (days) 669 689 679 665
剖検所見(発生率、重篤度)		
臓器重量		
病理組織学的所見(発生率、重篤度)	病理所見: 皮膚: 投与群には生物学的に有意な頻度の皮膚又は皮下の腫瘍は生じなかった。投与した雌雄ラットの表皮には適用部位にごく軽度ないし軽度の非腫瘍性病変がみられた。最も共通した影響の一つは表皮の肥厚又はアカントーシスであった。64 mg/kgの雄ではアカントーシスの頻度は媒体対照群よりも有意に高かった。皮膚表面上にケラチンの増量がみられる過角化は雄よりも処置した雌でより多くみられた。この病変の程度はごく軽度であった。雄の32及び64 mg/kg群及び雌の投与全群の過角化の頻度は媒体対照群のそれよりも有意に高かった。血清と表皮の細胞片の局所における蓄積からなる滲出液が雄の64 mg/kg群及び雌の全投与群では頻度が有意に増加した。	PATHOLOGY: Skin: No biologically significant incidences of skin or subcutaneous neoplasms occurred in the dosed groups. Minimal to mild non-neoplastic lesions occurred at the site of application in the epidermis of dosed male and female rats. One of the most common effects was thickening of the epidermis, or acanthosis. In 64 mg/kg males, the incidence of acanthosis was significantly greater than that in the vehicle control group. Hyperkeratosis, consisting of an increased amount of keratin on the surface of the skin, was more common in treated females than in males. This lesion was of minimal severity. The incidences of hyperkeratosis in the 32 and 64 mg/kg male groups and in all dosed female groups significantly exceeded those in the vehicle control groups. Exudate, consisting of focal accumulations of serum and cellular debris on the epidermal surface, occurred at significantly increased incidences in 64 mg/kg males and in all dosed female groups
病理組織学的所見(発生率、重篤度)	腎臓: 投与した雌群の腎症の頻度 (媒体対照、40/50; 8 mg/kg、47/50; 16 mg/kg、48/50; 32 mg/kg、48/50)及び程度 (1.2、1.5、1.9、2.7) は媒体対照のそれよりも有意に大きかった。しかし、投与した雄ラットの腎症の頻度も程度も媒体対照のそれらとは有意差はなかった。ごく軽度の腎症は小さい塩基性の上皮細胞を有する数個の散在性の尿細管からなった。より重度の腎症は間質の線維症及びネフロンの損失を包含した。等級の程度は腎臓の関与の程度並びに線維症及び尿細管/ネフロンの損失の量に基づいた。64 mg/kgの雄ラット1例は単一の腎尿細管癌を有していた。	Kidney: The incidences (vehicle control, 40/50; 8 mg/kg, 47/50; 16 mg/kg, 48/50; 32 mg/kg, 48/50) and severities (1.2, 1.5, 1.9, 2.7) of nephropathy in dosed female groups were significantly greater than those in the vehicle controls; however, neither the incidences nor the severities of nephropathy in dosed male rats were significantly different from those in the vehicle controls. Minimal nephropathy consisted of a few scattered tubules with small, basophilic epithelial cells. More severe nephropathy included interstitial fibrosis and loss of nephrons. The severity grades were based on extent of kidney involvement as well as the amount of fibrosis and tubule/nephron loss. One 64 mg/kg male rat had a single renal tubule carcinoma.
病理組織学的所見(発生率、重篤度)	肝臓: ジエタノールアミン暴露と関連した肝臓における腫瘍性応答はみられなかった。好塩基性巣の頻度は投与群の雌雄全群で有意に減少した (雄: 媒体対照、15/50; 16 mg/kg、5/50; 32 mg/kg、1/50; 64 mg/kg、2/50; 雌: 40/50、31/50、20/50、7/50)。好酸性巣の頻度は投与した雄では媒体対照よりもごく軽度に低下し(4/50, 2/50, 2/50, 2/50)、混合細胞巣の頻度は投与した雌で若干変動した(0/50, 3/50, 6/50, 1/50)。 乳腺: 32 mg/kgの雌では線維腺腫の頻度が媒体対照群の頻度と比べて有意に減少した (14/50, 8/50, 9/49, 5/50)。線維腺腫の頻度は陰性の傾向を生じた。全投与群の頻度は歴史的対照値の範囲よりも小さかった。	Liver: There was no neoplastic response in the liver associated with diethanolamine exposure. The incidences of basophilic foci were significantly decreased in all dosed groups of males and females (males: vehicle control, 15/50; 16 mg/kg, 5/50; 32 mg/kg, 1/50; 64 mg/kg, 2/50; females: 40/50, 31/50, 20/50, 7/50). The incidences of eosinophilic foci in dosed males were marginally less than that in the vehicle controls (4/50, 2/50, 2/50, 2/50), and the incidences of mixed cell foci in dosed females were somewhat variable (0/50, 3/50, 6/50, 1/50). Mammary Gland: The incidence of fibroadenoma in 32 mg/kg females was significantly decreased compared to the vehicle control incidence (14/50, 8/50, 9/49, 5/50). Incidences of fibroadenoma occurred with a negative trend. The incidences in all dosed groups were less than the historical control range.

病理組織学的所見（発生率、重篤度）	2年間経皮的に処置したラットにおける適用部位での皮膚の非腫瘍性病変の頻度： mg/kg 体重 0 16 32 64 雄 N 50 50 50 50 真皮 潰瘍 0 0 0 2(1.0)# 表皮 アカントーシス 0 2(10) 4(1.0) 10**(1.1) 滲出液 0 3(1.0) 2(1.0) 7*(1.0) 過角化 0 3(1.0) 5*(1.0) 11**(1.0) mg/kg 体重 0 8 16 32 雌 N 50 50 50 50 真皮 潰瘍 2(2.0) 1(1.0) 1(3.0) 1(3.0) 表皮 アカントーシス 1(2.0) 1(1.0) 4(1.0) 6(1.2) 滲出液 1(1.0) 7*(1.0) 7*(1.0) 7*(1.0) 過角化 3(1.0) 13*(1.0) 23**(1.9) 23**(1.9) # 平均の程度； * p<= 0.05; ** p<= 0.01	Incidences of non-neoplastic lesions of the skin at the application site in rats treated dermally for 2 years: mg/kg bw 0 16 32 64 Males N 50 50 50 50 Dermis Ulcer 0 0 0 2(1.0)# Epidermis Acanthosis 0 2(10) 4(1.0) 10**(1.1) Exudate 0 3(1.0) 2(1.0) 7*(1.0) Hyperkeratosis 0 3(1.0) 5*(1.0) 11**(1.0) mg/kg bw 0 8 16 32 Females N 50 50 50 50 Dermis Ulcer 2(2.0) 1(1.0) 1(3.0) 1(3.0) Epidermis Acanthosis 1(2.0) 1(1.0) 4(1.0) 6(1.2) Exudate 1(1.0) 7*(1.0) 7*(1.0) 7*(1.0) Hyperkeratosis 3(1.0) 13*(1.0) 23**(1.9) 23**(1.9) # average severity; * p<= 0.05; ** p<= 0.01
実際に摂取された量		
腫瘍発生までの時間		
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	結論： 雌雄各50匹のFischer 344/N ラットの群に95%エタノール中でDEAを週あたり5日間で2年間経皮適用により投与した。雄には0、16、32又は64 mg/kg体重を、雌には0、8、16又は32 mg/kg体重を投与した。投与した雌雄の群の生存率は対応する媒体対照群の値と同様であった。雄の高用量群の平均体重は8週以降媒体対照群のそれよりも低値を示し、雌の高用量群の平均体重は97週以降媒体対照のそれより低値を示した。 DEA投与に起因する唯一の臨床症状は適用部位皮膚の刺激であった。	Conclusion : Groups of 50 male and 50 female Fischer 344/N rats were administered DEA in 95% ethanol by dermal application on five days per week for two years. Males received 0, 16, 32 or 64 mg/kg bw and females 0, 8, 16 or 32 mg/kg bw. Survival rates for dosed male and female groups were similar to those of corresponding vehicle control groups. The mean body weight of the high-dose male group was lower than that of the vehicle controls from week 8 and the mean body weight of the high-dose female group was lower than that of the vehicle controls from week 97. The only clinical finding attributed to DEA administration was irritation of the skin at the site of application.
注釈	ごく軽度ないし軽度の非腫瘍性病変が適用部位で投与した雌雄のラットの表皮に生じた。雄の64 mg/kg群でのアカントーシスの頻度、雄の32及び64 mg/kg群及び雌の投与全群での過角化の頻度、及び雄の64 mg/kg群及び雌の投与全群での滲出液の頻度は対照群の各頻度よりも増加した。 腎症の頻度及び程度は雌の投与群では媒体対照群に比べて有意に増加した。 処置群では媒体対照群と比べて腫瘍の頻度の増加はみられなかった。	Minimal to mild non-neoplastic lesions occurred at the site of application in the epidermis of dosed male and female rats. The incidence of acanthosis in 64 mg/kg males, the incidences of hyperkeratosis in 32 and 64 mg/kg males and in all dosed female groups, and the incidences of exudate in 64 mg/kg males and in all dosed female groups were greater than those in the controls. The incidences and severities of nephropathy were significantly increased in dosed female rats compared to the vehicle controls. There were no increases in tumor incidences in treated groups compared with the vehicle controls.
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	許容でき、科学的基準を満たす文章化の良好な試験	Acceptable, well-documented study which meets scientific principles
出典		
引用文献（元文献）	(210)	(210)
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

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	ジエタノールアミン 供給源：Kodak Laboratory and Specialty Chemicals (Rochester, NY, USA) 物理的形状：液体、無色から淡黄色 バッチ：A16 純度：>99% (GC) 保管：室温、遮光 エタノール： 供給源：Aaper Alcohol and Chemical Company (Shelbyville, KY, USA) 物理的形状：液体、無色 純度：98.7 - 101.3%	DIETHANOLAMINE: Source: Kodak Laboratory and Specialty Chemicals (Rochester, NY, USA) Physical form: liquid, colorless to pale yellowish Batch: A16 Purity: >99% (GC) Storage: room temperature, protected from light ETHANOL: Source: Aaper Alcohol and Chemical Company (Shelbyville, KY, USA) Physical form: liquid, colorless Purity: 98.7 - 101.3%
注釈		
方法		
方法／ガイドライン	その他：OECD 451相当	other: comparable to OECD 451
試験のタイプ		
GLP適合	はい	yes
試験を行った年	1999	1999
試験系（種／系統）	マウス B6C3F1	mouse B6C3F1
性別（雄：M、雌：F）	雌雄	male/female
投与量	40、80、160 mg/kg 体重	40, 80, 160 mg/kg bw
各用量群（性別）の動物数		
溶媒（担体）		

投与経路	経皮	dermal
処理頻度	1日1回、5回/週	once daily, 5x/week
対照群と処理	あり、媒体対照	yes, concurrent vehicle
試験条件	暴露期間：103週間 暴露後の期間：なし	Exposure period : 103 weeks Post exposure period : none
試験条件	※英文参照	METHOD FOLLOWED: Carcinogenicity study with dermal application. Design and extent of examinations comparable to OECD 451. GLP: Yes
試験条件	※英文参照	Test condition : TEST ORGANISMS: - Species/Strain: Mice, B6C3F1 supplied by Taconic Farms, Germantown, NY, USA - Acclimatization: 13 days - Age at study start: about 6 weeks - Number of animals: 50 males and 50 females per dose group - Housing: Mice were housed individually ADMINISTRATION / EXPOSURE The dose formulations were prepared every 3 weeks by mixing diethanolamine with 95 % ethanol to give the desired concentration. The dose formulations were stored at room temperature, protected from light, in amber glass bottles for up to 28 days
試験条件	※英文参照	Stability studies of a 0.5 mg/ml formulation were performed by the analytical chemistry laboratory using gas chromatography. The formulation had only small losses of diethanolamine when stored at room temperature, protected from light, for up to 28 days; it was stable for 3 hours when stored open to air and light. Periodic analyses of the dose formulations of diethanolamine were conducted at the study laboratory using gas chromatography. Dose formulations were analyzed approximately every 9 weeks. All dose formulations and animal room samples for mice and mice were within 10% of the target concentrations Groups of 50 male and 50 female mice were administered dermal doses of 0, 40, 80 and 160 mg/kg bw application of 0, 22.5, 45 and 90 mg/ml ethanol solutions, 5 days per week for 103 weeks. Dose volumes were adjusted to provide the appropriate mg/kg dose based on group mean body weights.
		CLINICAL OBSERVATIONS AND FREQUENCY: -Body weight: weekly through week 13 and monthly thereafter -Mortality and clinical findings: 2x/day including moribundity but clinical findings recorded: monthly PATHOLOGY Complete necropsy and microscopic examination were performed on all animals. At necropsy, all organs and tissues were examined for grossly visible lesions, and all major tissues were fixed and preserved in 10% neutral buffered formalin, processed and trimmed, embedded in paraffin, sectioned to a thickness of 5 to 6 µm, and stained with hematoxylin and eosin for microscopic examination. For all paired organs (e.g., adrenal gland, kidney, ovary), samples from each organ were examined.
試験条件	※英文参照	Histopathology: Gross lesions, tissue masses, adrenal gland, bone with marrow, brain, clitoral gland, esophagus, gallbladder (mice), heart with aorta, large intestine (cecum, colon, and rectum), small intestine (duodenum, jejunum, and ileum), kidney, liver, lung, lymph nodes (mandibular and mesenteric), mammary gland (except male mice), nose, ovary, pancreas, parathyroid gland, pituitary gland, preputial gland, prostate gland, salivary gland, skin (site of application), spleen, stomach (forestomach and glandular), testis with epididymis and seminal vesicle, thymus, thyroid gland, trachea, urinary bladder, uterus.
統計学的処理	※英文参照	STATISTICAL METHODS: Survival Analyses The probability of survival was estimated by the product-limit procedure of Kaplan and Meier (1958. Statistical analyses for possible dose-related effects on survival used Cox's (1972) method for testing two groups for equality and Tarone's (1975) life table test to identify dose-related trends. All reported P values for the survival analyses are two sided. Analysis of Neoplasm and Non-neoplastic Lesion Incidences The Poly-k test (Bailer and Portier, 1988; Portier and Bailer, 1989; Piegorsch and Bailer, 1997) was used to assess neoplasm and non-neoplastic lesion prevalence. This test is a survival-adjusted quantal-response procedure that modifies the Cochran-Armitage linear trend test to take survival differences into account. Tests of significance included pairwise comparisons of each dosed group with controls and a test for an overall dose-related trend. Continuity-corrected tests were used in the analysis of lesion incidence, and reported P values are one sided.

統計学的処理	※英文参照	Analysis of Continuous Variables Average severity values were analyzed for significance with the Mann-Whitney U test (Hollander and Wolfe, 1973).
結果		
体重、体重増加量	体重及び臨床所見 雄の80及び160 mg/kg群の平均体重はそれぞれ88週及び77週以降に媒体対照群の値より低値を示した。 雌の40及び80 mg/kg群の平均体重は73週以降、媒体対照群の値よりも低値を示した。160 mg/kg群の雌の平均体重は53週以降、媒体対照群の値よりも低かった。	Body Weights and Clinical Findings Mean body weights of 80 and 160 mg/kg males were less than those of the vehicle controls after weeks 88 and 77, respectively. Mean body weights of 40 and 80 mg/kg females were less than those of vehicle controls after week 73; mean body weights of 160 mg/kg females were less than those of the vehicle controls after week 53.
体重、体重増加量	体重増加量 mg/kg bw 0 40 80 160 雄 g g(%)# g(%) g(%) 週 1-13 28.7 28.9(99) 28.6 (100) 8.5 (99) 週 14-52 43.0 42.7(99) 42.4 (99) 41.4 (96) 週 53-104 50.4 50.5(100) 48.5 (96) 45.1 (89) 雌 週 1-13 24.8 24.9(100) 25.1(101) 25.3 (102) 週 14-52 39.3 39.56(101) 39.5(101) 38.1 (97) 週 53-104 52.8 48.2(91) 45.1(85) 39.9 (76) # = 対照群の %	Body weight gain mg/kg bw 0 40 80 160 Males g g(%)# g(%) g(%) Week 1-13 28.7 28.9(99) 28.6 (100) 8.5 (99) Week 14-52 43.0 42.7(99) 42.4 (99) 41.4 (96) Week 53-104 50.4 50.5(100) 48.5 (96) 45.1 (89) Females Week 1-13 24.8 24.9(100) 25.1(101) 25.3 (102) Week 14-52 39.3 39.56(101) 39.5(101) 38.1 (97) Week 53-104 52.8 48.2(91) 45.1(85) 39.9 (76) # = % of control
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)		
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	生存率 生存率は雄の投与群及び媒体対照群では同様であった。雌の投与群の生存率は媒体対照群のそれより有意に低値で、用量の増加につれて有意に減少した。	Survival Survival was similar in dosed male groups and vehicle controls. Survival of dosed female groups was significantly lower than that of the vehicle control group and decreased significantly with increasing dose.
死亡数(率)、死亡時間	マウスの生存率 mg/kg 体重 0 40 80 160 雄 開始時の例数 50 50 50 50 瀕死例 3 1 6 10 自然死亡例 7 6 10 9 試験終了時の 例数 40 43 34 30 平均生存期間 (日) 701 717 699 687 雌 開始時の例数 50 50 50 50 瀕死例 4 8 9 13 自然死亡例 2 9 8 14 試験終了時の 例数 44 33 33 23 平均生存期間 (日) 720 669 695 691	Survival of Mice mg/kg bw 0 40 80 160 Males No at start 50 50 50 50 Moribund 3 1 6 10 Natural deaths 7 6 10 9 No. at termination 40 43 34 30 Mean survival (days) 701 717 699 687 Females No at start 50 50 50 50 Moribund 4 8 9 13 Natural deaths 2 9 8 14 No. at termination 44 33 33 23 Mean survival (days) 720 669 695 691
剖検所見(発生率、重篤度)		
臓器重量		
病理組織学的所見(発生率、重篤度)	病理所見: 肝臓、腎臓、甲状腺、皮膚及び唾液腺の腫瘍及び非腫瘍性病変の頻度における生物学的に重要な変化は以下に記述される: 肝臓: 投与した雄マウスの全群において肝細胞腺腫、及び肝細胞の腺腫又はがん(組合わせ)の頻度は媒体対照群の頻度よりも有意に増加した。雄の80及び160 mg/kg群では肝細胞がん及び肝芽細胞種の頻度も媒体対照群に比し有意に増加した。雌マウスの投与群では肝細胞腫瘍の頻度が媒体対照群の頻度よりも有意に高かった。雄及び雌の全投与群では肝細胞腫瘍の頻度が歴史的対照の範囲を超えた。	PATHOLOGY: The biologically noteworthy changes in the incidences of neoplasms and/or non-neoplastic lesions of the liver, kidney, thyroid gland, skin, and salivary gland are described below: Liver: The incidences of hepatocellular adenoma and of hepatocellular adenoma or carcinoma (combined) in all dosed groups of male mice were significantly greater than those in the vehicle control group. The incidences of hepatocellular carcinoma and hepatoblastoma in 80 and 160 mg/kg males were also significantly increased compared to the vehicle controls. In dosed groups of female mice, the incidences of hepatocellular neoplasms were significantly greater than those in the vehicle control group. The incidences of hepatocellular neoplasms in all dosed groups of males and females exceeded the historical control ranges.

病理組織学的所見（発生率、重篤度）	これらの肝臓腫瘍の顕微鏡的な外観はB6C3F1マウスで通常見られる典型的なものであった。腺腫からがんには形態的な連続性があり、区別は困難であった。がんはしばしば直径が1cm以上あったが、腺腫は一般に小さく分離していた。腺腫及びがんはともに正常な肝の実質を示し、いずれも正常な肝臓の葉構造を構成していなかった。肺の転移がんが肝細胞がん又は肝芽細胞種を有するマウスでみられた（雄：3/50, 4/50, 9/50, 7/50；雌：0/50, 3/50, 6/50, 1/50）。 肝芽腫はしばしば肝細胞がん内で発生し、濃染に好塩基性の紡錘形の細胞の束からなる境界が明瞭で限局性の部分で特徴づけられた。	The microscopic appearance of these liver neoplasms was typical of that usually observed in B6C3F 1 mice. There was a morphologic continuum from adenoma to carcinoma, with less differentiation. Carcinomas were often a centimeter or more in diameter, whereas adenomas were generally smaller and more discrete. Both adenomas and carcinomas displaced normal liver parenchyma and neither contained the normal liver lobular architecture. Lung metastases were seen in mice with hepatocellular carcinomas or hepatoblastomas (males: 3/50, 4/50, 9/50, 7/50; females: 0/50, 3/50, 6/50, 1/50). Hepatoblastomas often originated within hepatocellular carcinomas and were characterized by well- demarcated, focal areas composed of bundles of deeply basophilic spindle-shaped cells.
病理組織学的所見（発生率、重篤度）	処置群の動物における腫瘍の大きさと多様性は媒体対照群と比べてかなり大きかった。 非腫瘍性病変は投与した雌雄全群のマウスの肝臓のみでみられ、軽度ないし中等度の小葉中心性肝細胞肥大により特徴づけられた細胞質の変化及び3つ以上の小さい核を持つびまん性の肝細胞により特徴づけられた合胞体性変化からなった。	The size and multiplicity of neoplasms in treated animals was considerably greater than in the vehicle controls. Non-neoplastic lesions were seen only in the liver of all dosed male and female mice and consisted of cytoplasmic alteration, characterized by mild to moderate enlargement of centrilobular hepatocytes, and syncytial alteration, characterized by scattered hepatocytes with three or more small nuclei.
病理組織学的所見（発生率、重篤度）	肝臓の腫瘍の頻度 mg/kg 0 40 80 160 雄 N 50 50 50 50 肝細胞腺腫（複数を含む） 31/50(65%) 42/50(86.5%) 49/50(98%) 5/50(93.5%) 肝細胞がん（複数を含む） 12/50(25.1%) 17/50(34.9%) 33/50(66.9%) 4/50(72.3%) 肝細胞の腺腫又はがん（複数を含む） 39/50（79%) 47/50(95.3%) 50/50(100%) 49/50(99.9%) 肝芽腫 0/50(0%) 2/50(4.2%) 8/50(17.5%) 5/50(11.3%) 雌 N 50 50 50 50 肝細胞腺腫（複数を含む） 32/50(66.1%) 50/50 100%) 48/50(96.4%) 8/50(96.4%) 肝細胞がん（複数を含む） 5/50(10.4%) 19/50(43.4%) 38/50(77.9%) 42/50(84.9%) 肝細胞の腺腫又はがん（複数を含む） 33/50(68.2%) 50/50(100%) 50/50(100%) 50/50(100%) 肝芽腫 0/50(0%) 2/50 (4%) 1/50 (2%) 1/50 (2%)	Incidences of Neoplasms of the liver: mg/kg 0 40 80 160 Male N 50 50 50 50 Hepatocellular Adenoma (includes multiple) 31/50(65%) 42/50(86.5%) 49/50(98%) 5/50(93.5%) Hepatocellular Carcinoma (includes multiple) 12/50(25.1%) 17/50(34.9%) 33/50(66.9%) 4/50(72.3%) Hepatocellular Adenoma or Carcinoma (includes multiple) 39/50 (79%) 47/50(95.3%) 50/50(100%) 49/50(99.9%) Hepatoblastoma 0/50(0%) 2/50(4.2%) 8/50(17.5%) 5/50(11.3%) Female N 50 50 50 50 Hepatocellular Adenoma (includes multiple) 32/50(66.1%) 50/50 100%) 48/50(96.4%) 8/50(96.4%) Hepatocellular Carcinoma (includes multip1e) 5/50(10.4%) 19/50(43.4%) 38/50(77.9%) 42/50(84.9%) Hepatocellular Adenoma or Carcinoma (includes multiple) 33/50(68.2%) 50/50(100%) 50/50(100%) 50/50(100%) Hepatoblastoma 0/50(0%) 2/50 (4%) 1/50 (2%) 1/50 (2%)
病理組織学的所見（発生率、重篤度）	腎臓： 雄では腎尿細管の腺腫の頻度が陽性の傾向を示し生じたが、がん及び過形成の頻度はこのパターンにあてはまらなかった。雄マウスでは腺腫またはがん（組合わせ）の頻度は歴史的対照の範囲を超えた。 単一及び段階的な切片の組合わせによる解析では、雄マウスでは腎尿細管の過形成及び腎尿細管の腺腫の頻度は用量に相関した増加が示された。40 mg/kg群では2つ、80 mg/kg群では4つ、160 mg/kg群では1つの追加の腺腫がみられた。過形成の追加の頻度は全群でみられ、160 mg/kg群では単一及び段階的切片（組合わせの）頻度は媒体対照群と比べ有意に増加した。腺腫は限局性で圧縮性の塊で尿細管の直径の大きさは約5以上であった。がんは形態的には同様であったが、比較的大きく、しばしば細胞の破片及び/又は石灰化を示した。腎尿細管の腫瘍は皮質及び/又は外側の髄質に局在した。	Kidney: The incidences of renal tubule adenoma in males occurred with a positive trend; however, the incidences of carcinoma and hyperplasia did not follow this pattern. The incidences of adenoma or carcinoma (combined) in male mice exceeded the historical control range. The combined analysis of single and step sections indicated a dose-related increase in the incidences of renal tubule hyperplasia and renal tubule adenoma in male mice. Two additional adenomas were found in the 40 mg/kg group, four in the 80 mg/kg group, and one in the 160 mg/kg group. Additional incidences of hyperplasia were found in all groups, and the single and step-section (combined) incidence in the 160 mg/kg group was significantly greater than that in the vehicle control group. Adenomas were focal compressive masses approximately the size of five tubule diameters or greater. Carcinomas were similar morphologically but were relatively large and often showed cellular debris and/or mineralization. Renal tubule neoplasms were located in the cortex and/or outer medulla.
病理組織学的所見（発生率、重篤度）	腎尿細管腫瘍の頻度 mg/kg 0 40 80 160 雄 N 50 50 50 50 腎尿細管腺腫（複数を含む） 1/50(2.2%) 4/50(8.3%) 6/50(13.1%) 6/50(13.3 %) 腎尿細管がん（複数を含む） 2/50(4%) 1/50(2%) 0/50(0%) 2/50(4%) 腎尿細管の腺腫又はがん（複数を含む） 3/50(6.6%) 5/50(10.4%) 6/50(13.1 %) 8/50(17.8%) 雌 N 50 50 50 50 腎尿細管腺腫（複数を含む） Overall rate 1/50(2.2%) 6/50(12.5%) 8/50(17.5%) 7/50(15.5%) 腎尿細管がん（複数を含む） 2/50(4%) 1/50(2%) 0/50(0%) 2/50(4%) 腎尿細管の腺腫又はがん（複数を含む） 3/50(6.6%) 7/50(14.5%) 8/50 (17.5%) 9/50(20%)	Incidences of Renal Tubule Neoplasms mg/kg 0 40 80 160 Males N 50 50 50 50 Renal Tubule Adenoma (includes multiple) 1/50(2.2%) 4/50(8.3%) 6/50(13.1%) 6/50(13.3 %) Renal Tubule Carcinoma (includes multiple) 2/50(4%) 1/50(2%) 0/50(0%) 2/50(4%) Renal Tubule Adenoma or Carcinoma (includes multiple) 3/50(6.6%) 5/50(10.4%) 6/50(13.1 %) 8/50(17.8%) Females N 50 50 50 50 Renal Tubule Adenoma (includes multiple) Overall rate 1/50(2.2%) 6/50(12.5%) 8/50(17.5%) 7/50(15.5%) Renal Tubule Carcinoma (includes multip1e) 2/50(4%) 1/50(2%) 0/50(0%) 2/50(4%) Renal Tubule Adenoma or Carcinoma (includes multiple) 3/50(6.6%) 7/50(14.5%) 8/50 (17.5%) 9/50(20%)

病理組織学的所見（発生率、重篤度）	甲状腺： 濾胞細胞の過形成の頻度が全群で有意に増加した(雄：媒体対照、18/50；40 mg/kg、22/49；80 mg/kg、30/50；160 mg/kg、42/50；雌：18/50、28/50、32/50、39/49)。この病変はある場合には乳頭突起をを形成することもある増加した数の上皮細胞により配列された甲状腺濾胞の限局的な部分からなった。甲状腺細胞の過形成に対する重篤度のグレード(雄：1.6、1.5、1.6、2.2；雌：1.9、2.0、1.7、1.9）は病変の大きさを基にした。甲状腺の濾胞細胞の腺腫の頻度（雄：4/50、5/50、4/50、2/50；雌：4/50、9/50、5/50、3/49)は媒体対照群と比べて増加しなかった。また、甲状腺の濾胞細胞がんは本試験では観察されなかった。	Thyroid Gland: Incidences of follicular cell hyperplasia were significantly increased in dosed groups (males: vehicle control, 18/50; 40 mg/kg, 22/49; 80 mg/kg, 30/50; 160 mg/kg, 42/50; females: 18/50, 28/50, 32/50, 39/49). This lesion consisted of focal areas of thyroid gland follicles lined by increased numbers of epithelial cells, which in some instances formed papillary projections. The severity grade for follicular cell hyperplasia (males: 1.6, 1.5, 1.6, 2.2; females: 1.9, 2.0, 1.7, 1.9) was based on the size of the lesion. Incidences of thyroid gland follicular cell adenomas were not increased relative to vehicle controls (males: 4/50, 5/50, 4/50, 2/50; females: 4/50, 9/50, 5/50, 3/49), and no thyroid gland follicular cell carcinomas were detected in this study.
病理組織学的所見（発生率、重篤度）	皮膚（適用部位）： 過角化、アカントーシス、及び滲出物が適用部位の皮膚における処置に関連した変化であった。雌の40 mg/kg群を除く全投与群で過角化の頻度が媒体対照群よりも有意に増加した（表15)。過角化はごく軽度ないし軽度で表面の増加したケラチンからなった。アカントーシス及び滲出物は投与した数匹の動物でみられた。アカントーシスは表皮の厚みの増加からなった。滲出物は細胞の破片と表皮の表面上の炎症細胞の混合物であり、通常肥厚したケラチン層と混ざった。 唾液腺： 80及び160 mg/kg群の雄マウスでは細胞質の変化と名づけられた分泌管に沿って並ぶ細胞の正常な粒度を失った例数の有意な増加が示された（1/50、2/50、8/50、23/50)。この変化の生物学的な意義は不明である。	Skin (Site of Application): Hyperkeratosis, acanthosis, and exudate were treatment-related changes in the skin at the site of application. The incidences of hyperkeratosis in all dosed groups except 40 mg/kg females were significantly greater than those in the vehicle control groups (Table 15). Hyperkeratosis was of minimal to mild severity and consisted of increased keratin on the surface. Acanthosis and exudate were observed in a few dosed mice. Acanthosis consisted of increased thickness of the epidermis. Exudate was a mixture of cellular debris and inflammatory cells on the surface of the epidermis, usually mixed with the thickened keratin layer. Salivary Gland: A significant number of 80 and 160 mg/kg male mice showed a loss of the normal granularity of the cells lining the secretory ducts, which was termed cytoplasmic alteration (1/50, 2/50, 8/50, 23/50). The biologic significance of this change is unknown
病理組織学的所見（発生率、重篤度）	2年間経皮的に処置したマウスにおける適用部位皮膚の非腫瘍性病変の頻度： mg/kg bw 0 40 80 160 雄 N 50 50 50 50 表皮 アカントーシス 0 0 2(2.0) 4(1.8) 滲出物 0 0 0 3(1.3) 過角化 0 13**(1.0) 10*(1.0) 17**(1.1) 雌 N 50 50 50 50 表皮 アカントーシス 0 2(2.0) 1(1.0) 2(2.0) 滲出物 0 1(4.0) 1(1.0) 3(1.7) 過角化 1 3(2.0) 8*(1.0) 16**(1.0) # 平均の程度；* p<= 0.05; ** p<= 0.01	Incidences of non-neoplastic lesions of the skin at the application site in mice treated dermally for 2 years: mg/kg bw 0 40 80 160 Males N 50 50 50 50 Epidermis Acanthosis 0 0 2(2.0) 4(1.8) Exudate 0 0 0 3(1.3) Hyperkeratosis 0 13**(1.0) 10*(1.0) 17**(1.1) Females N 50 50 50 50 Epidermis Acanthosis 0 2(2.0) 1(1.0) 2(2.0) Exudate 0 1(4.0) 1(1.0) 3(1.7) Hyperkeratosis 1 3(2.0) 8*(1.0) 16**(1.0) # average severity; * p<= 0.05; ** p<= 0.01
実際に摂取された量		
腫瘍発生までの時間		
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	陽性	positive
注釈	結論： 雌雄各50匹のB6C3F1マウスの群に週あたり5日間で2年間経皮適用により、95%エタノール中で0、40、80又は160 mg/kg体重のDEAを投与した。 投与した雄マウスの生存率は媒体対照群のそれと同様であったが、投与した雌マウスの生存率は低下した（対照群、低、中及び高用量群でそれぞれ44/50、33/50、33/50 及び 23/50)。 雄の中及び高用量群の平均体重はそれぞれ88週及び77週以降、媒体対照群の平均体重より低下した。雌の低及び中用量群の平均体重は73週以降、媒体対照群の値より低値を示したが、雌の高用量群の平均体重は53週から媒体対照群と比べて低下した。	Conclusion : Groups of 50 male and 50 female B6C3F1 mice ere administered 0, 40, 80 or 160 mg/kg bw DEA in 95% ethanol by dermal application on five days per week for two years. Survival of dosed male mice was similar to that of the vehicle control group, but survival of dosed female mice was reduced (44/50, 33/50, 33/50 and 23/50 for the control, low-, mid- and high-dose groups, respectively). The mean body weights of the mid- and high-dose males were lower than those of the vehicle controls after weeks 88 and 77, respectively. The mean body weights of the low- and mid-dose females were lower than those of the vehicle controls from week 73, but those of the high-dose females were reduced compared with the vehicle controls from week 53.
注釈	雄マウスでは全ての投与群において肝細胞の腺腫、肝細胞の腺腫及びがん（組合わせ)の頻度が媒体対照群の頻度よりも有意に増加した。また、中及び高用量群では肝芽腫の頻度が媒体対照群と比べ有意に増加した。 雌マウスでは肝細胞の腫瘍の頻度が媒体対照群の頻度よりも有意に高値を示した。 雄では腎尿細管の腺腫の頻度が陽性の傾向を示し生じたが、がん及び過形成の頻度はこのパターンを示さなかった。腎臓の段階切片による拡張した評価により、全投与群に追加の腺腫及び過形成が示された。単一切片と段階切片を組合わせた解析により、雄マウスでは腎尿細管過形成、及び腎尿細管の腺腫又はがん（組合わせ)の頻度の用量に相関した増加及び腎尿細管の頻度の増加が示された。	In male mice, the incidences of hepatocellular adenoma and of hepatocellular adenoma and carcinoma (combined) in all dosed groups were significantly greater than those in the vehicle control group. In addition, the incidences of hepatoblastoma in the mid- and high-dose groups were significantly increased compared with the vehicle control. In the female mice, the incidences of hepatocellular neoplasms were significantly higher than those in the vehicle control group. The incidences of renal tubule adenoma in males occurred with a positive trend; however, the incidences of carcinoma and hyperplasia did not follow this pattern. An extended evaluation of kidney step sections revealed additional adenomas and hyperplasias in all dosed groups. The combined analysis of single and step sections indicated a dose-related increase in the incidences of renal tubule hyperplasia and renal tubule adenoma or carcinoma (combined), and an increase in the incidences of renal tubule adenoma in male mice.

注釈	甲状腺濾胞細胞の過形成の頻度は媒体対照群と比べて投与した雌雄のマウスでは増加した。 過角化、アカントーシス及び滲出物が適用部位皮膚における処置に関連した変化であった。過角化の頻度は雌の40 mg/kg群を除く全ての投与群において、媒体対照群の頻度よりも有意に大きかった。	Incidences of thyroid gland follicular cell hyperplasia were increased in dosed male and female mice compared to vehicle controls. Hyperkeratosis, acanthosis, and exudate were treatment-related changes in the skin at the site of application. The incidences of hyperkeratosis were significantly greater than those in the vehicle control groups in all dosed groups except 40 mg/kg females.
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	許容でき、科学的基準を満たす文章化の良好な試験	Acceptable, well-documented study which meets scientific principles
出典		
引用文献(元文献)	(210)	(210)
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	1.1～1.4で規定	as prescribed by 1.1 - 1.4
CAS番号		
純度等	供給源: BASF AG バッチ: コンテナーB 810からの試料929 物理的状態/外観: 液体/無色 純度: >98.7% 均一性: 均一 安定性: 保管条件下での安定性が再解析により確認された。 保管条件: 室温、遮光、N2下で無酸素	Source: BASF AG Batch: sample 929 from container B 810 Physical state/appearance: Liquid / colorless Purity: >98.7% Homogeneity: homogeneous Stability: The stability under storage conditions was confirmed by reanalysis Storage conditions: Room temperature, without light and oxygen under N2
注釈		
方法		
方法／ガイドライン	OECDガイドライン414「催奇形性」	OECD Guide-line 414 "Teratogenicity"
GLP適合	はい	yes
試験を行った年	1993	1993
試験系(種／系統)	ラット	rat
	Wistar	Wistar
性別(雄:M、雌:F)	雌	female
投与量	0.01、0.05、0.2 mg/l (頭鼻部暴露)	0.01, 0.05, 0.2 mg/l (head nose exposure)
各用量群(性別)の動物数		
投与経路	吸入	inhalation
試験期間	20日間	20 days
交配前暴露期間		
試験条件	暴露期間: 妊娠6-15日 処置頻度: 6時間/日 対照群: あり、媒体対照	Exposure period : gestation day 6 - 15 Frequency of treatm. : 6h/day Control group : yes, concurrent vehicle
試験条件	※英文参照	METHOD FOLLOWED: - OECD guidelines for Testing of Chemicals, Section 4; Health Effects, Paris 1981, Method 414 GLP: In accordance with the OECD Principles of Good Laboratory Practice (Paris, 1981) and the GLP provision of the German Chemicals act (Chemikaliengesetz, Bundesgesetzblatt 1994, Part I, 22 March 1990)
試験条件	※英文参照	ANALYTICAL METHODS: - Monitoring of the inhalation atmosphere: Vacuum compressed air pump (Millipore) Sampling equipment with probe (Millipore), 7 mm diameter, filter MN 85/90 Bf, 1.25 m/s sampling velocity, hourly sampling frequency Gravimetrical determination of concentration by means of balance (Mettler AE 249) - Particle size analysis: EACD 50% MMAD Geometric standard deviation (GSD) Total dust Respirable dust
試験条件	※英文参照	Test condition : TEST ORGANISMS - Strain: Sexually mature Wistar rats (SPF-Wistar/Chhb:THOM) supplied by Dr. K. Thomae, Biberach, Germany - Number: 25 females per group - Age at start of the study: 68 - 70 days - Weight at start of the study: 214 g (mean) ADMINISTRATION / EXPOSURE: Pregnant female Wistar rats were exposed to an aerosol of Diethanolamine (DEA) in head/nose exposure systems for 6 h/day on day 6 through day 15 post coitum. A control group was exposed under similar conditions to clean air only. Concentrations: 0; 0.01; 0.05; 0.2 mg/l The test substance was supplied to a two-component atomizer at a constant rate by means of a metric pump. An aerosol was generated by means of compressed air and passed into the inhalation system.

試験条件	※英文参照	- Generator system The aerosol was generated using a diaphragm metering pump Prominent (CfG). a two-component atomizer mod. 970 (Schlick) and a glass cyclone separator (BASF). The head-nose exposure technique was preferably selected for this inhalation study to minimize fur contamination of the animals with the test substance, which cannot be avoided during whole-body exposure. The aerosol was passed into an aerodynamic exposure apparatus (INA 60, volume V = 90 1, BASF Aktiengesellschaft). The apparatus consists of a cylindrical inhalation chamber of stainless steel sheeting and cone-shaped outlets and inlets. The rats were restrained in exposure tubes (glass tubes). Their snouts projected into the inhalation chamber and thus they inhaled the aerosol. The apparatus was also connected to an exhaust air system. A slight positive pressure was maintained by adjusting the air flow of the exhaust air system. This ensured that the aerosol in the breathing zones of the animals was not diluted by laboratory air.
試験条件	※英文参照	In order to accustom the animals to the exposure conditions they were exposed to supply air in head nose only exposure systems under comparable flow conditions before the exposure period (preflow period). Then all test groups were exposed for 6 hours on each workday over a time period of 10 consecutive days (gestation days 6 – 15). The animals did not have access to water or feed during the exposure. Measurement of the operation conditions (air flows, relative humidity, temperature and pressure conditions) of the exposure systems The amounts of test substance set at the metering pumps were recorded once daily. The supply air and exhaust air flows were adjusted by means of flowmeters (Rotameter) for all test groups and recorded, as a rule, 1 time/exposure. The relative humidity was checked and recorded with a humidity measuring probe (Ultrakust) at least once per exposure day. The generator parameters temperature and compressed air were also recorded by means of this system. MATING PROCEDURES: After acclimatization and adaptation 1 – 4 female rats were mated with 1 male overnight. Day 0 post coitum was defined by detection of sperm in the vaginal smears. The animals were assigned to tests groups by randomization
試験条件	※英文参照	PARAMETERS ASSESSED DURING STUDY: - Mortality and clinical finding: once/workday during pre-flow; at least 3times on exposure days, - Body weight gain: On days 0, 3, 6, 9, 12, 15, 18 and 20; the body weight change was calculated - Corrected body weight gain (net maternal body weight change): Parameter calculated after terminal sacrifice (terminal body weight on day 20 p.c. minus weight of unopened uterus minus body weight on day 6 p.c.) - Examination of uterine content: Gravid uterine weight, number of corpora lutea, number and distribution of implantation sites as live fetuses, dead implantations in form of early and late resorptions and dead fetuses, calculation of conception rate, pre- and postimplantation loss - Examination of fetuses after dissection from uterus: litter size, fetal weight, sex ratio, grossly visible/external/soft tissue/skeletal abnormalities. Fetal viability, condition of placenta, umbical cords, fetal membranes and fluids were examined. Individual placental weights were recorded. Approximately one half of the fetuses were placed in ethyl alcohol; the other was placed in Bouin's solution for fixation and further evaluation
試験条件	※英文参照	- Soft tissue examination: according to the method of Barrow and Taylor (1969) - Skeletal examination: Stained according to the modified method of Dawson et al., 1926 followed by examination under stereomicroscope. - Evaluation criteria: Modified according to Muentefering, 1978 and Neubert, 1978 and classified in: - Malformation - Variation - Retardation - Unclassified observation

統計学的処理	※英文参照	STATISTICAL METHODS: - Dunnett's Test: body weight, body weight change, corrected body weight gain (net maternal body weight change), weight of the uterus before it was opened, weight of fetuses, weight of placentae, corpora lutea, implantations, pre and postimplantation losses, resorptions and live fetuses. - Fisher's Exact Test: conception rate, mortality (of the dams) and all fetal findings.
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	- 濃度: 設定値 実測値 MMAD % エアロゾル 0.01 mg/l 10.0 mg/m³ <1.2 µm 100% 0.05 mg/l 50.2 mg/m³ 0.4 µm 98% 0.2 mg/l 202 mg/m³ 0.6 µm 98%	- Concentrations: Target Measured MMAD % aerosol 0.01 mg/l 10.0 mg/m³ <1.2 µm 100% 0.05 mg/l 50.2 mg/m³ 0.4 µm 98% 0.2 mg/l 202 mg/m³ 0.6 µm 98%
注釈	用量レベルごとの母動物毒性影響: -母動物の死亡率、体重、補正体重増加量、剖検所見、子宮重量、生殖データ: 死亡例なし、あるいは投与に関連した所見なし -臨床症状: 暴露前の期間中、全動物は臨床症状及び所見を何ら示さなかったが、暴露期間中に最高濃度群 (0.2 mg/l)の8例が妊娠14日の暴露後に膣からの血液様分泌を示した。	MATERNAL TOXIC EFFECTS BY DOSE LEVEL: - Mortalities, body weight, corrected body weight gain, necropsy findings, uterus weight, reproduction data of the dams: No deaths or treatment related finding - Clinical findings: During the preflow period the animals of all showed no clinical signs and findings but during the exposure period eight animals of the highest concentration group (0.2 mg/l) showed bloody discharge from the vagina on day 14 p.c. after exposure
注釈	胎児の検査: -性比: いずれの群にも影響なし。 -胎盤重量: いずれの群にも影響なし。 -胎児重量: いずれの群にも影響なし。 -胎児の外表、軟組織及び骨格の観察: 物質に関連した唯一の所見は高用量群で痕跡の頸肋骨を呈した胎児の発現頻度の増加であった。0.2 mg/l ではの胎児ではこの所見が高頻度であったため、骨格変異の頻度が統計的に有意に増加した。 胎児の外表、軟組織及び/又は骨格の観察所見に関して、対照群と物質処置群との間の他の全ての差異は生物学的な関連性がない、及び/又は歴史的対照データとほぼ同程度であるとみなされた。	EXAMINATION OF FETUSES: - Sex distribution: Not affected in any group. - Placenta weights: Not affected in any group. - Weight of fetuses Not affected in any group. - External, soft tissue and skeletal fetal observations: The only substance-related finding was the increased occurrence of high dose fetuses with rudimentary cervical rib(s). Due to the high frequency of this finding in the 0.2 mg/l fetuses, the incidence of skeletal variations was statistically significantly increased. All other differences between the control group and the substance-treated groups concerning fetal external, soft tissue and/or skeletal observations were without biological relevance and/or appeared to about the same extent as in the historical control data.

注釈	母動物、腹、胎児のデータ − Wistarラットにおける出生前発生毒性(吸入)試験 mg/m³ 0 10 50 200 N 25 25 25 25 妊娠動物 21 21 23 23 死亡例 0 0 0 0 BWG 妊娠6-15日、g 71 71 77 70 妊娠6日からの NWC、g 38 43 39 41 妊娠子宮、 g 71 68 76 67 黄体数 (平均値) 14.5 15.3 15.2 14.6 着床数 (平均値) 13.2 13.2 13.9 12.5 着床後損失 胚数 5.5 10.0 4.9 10.2 吸収胚数 (平均値) 0.8 1.4 0.7 1.3 生存胎児数 (平均値) 12.5 11.8 13.2 11.2 胎盤重量、 g 0.44 0.44 0.43 0.43 胎児終了、g (雄/雌) 4.0/3.8 4.0/3.8 4.0/3.8 4.1/3.9 0/0 1/1 0/0 0/0 総外表変異 (胎児/腹) 0/0 0/0 0/0 0/0 総軟組織奇形 (胎児/腹) 1/1 2/2 2/2 0/0 総軟組織変異 (胎児/腹) 20/9 20/15 25/16 16/10 総骨格奇形 (胎児/腹) 5/5 5/4 7/6 5/5 総骨格変異 (胎児/腹) 59/19 58/20 69/22 78/22* BWG = 体重増加量、NWC = 正味の体重変化、 * p<0.05 **p<0.01	Maternal, litter, fetal data − prenatal developmental toxicity (inhalation) study in Wistar rats mg/m³ 0 10 50 200 N 25 25 25 25 Pregnant 21 21 23 23 Mortality 0 0 0 0 BWG GD 6-15, g 71 71 77 70 NWC from GD 6, g 38 43 39 41 Gravid uterus, g 71 68 76 67 Corpora lutea (mean) 14.5 15.3 15.2 14.6 Implantation (mean) 13.2 13.2 13.9 12.5 Post implanta- ion loss 5.5 10.0 4.9 10.2 Resorption (mean) 0.8 1.4 0.7 1.3 Live fetuses (mean) 12.5 11.8 13.2 11.2 Placental weight, g 0.44 0.44 0.43 0.43 Fetal weight, g (males/females) 4.0/3.8 4.0/3.8 4.0/3.8 4.1/3.9 0/0 1/1 0/0 0/0 Total external variations (fetus/litter) 0/0 0/0 0/0 0/0 Total soft tissue malformations (fetus/litter) 1/1 2/2 2/2 0/0 Total soft tissue variations (fetus/litter) 20/9 20/15 25/16 16/10 Total skeletal malformations (fetus/litter) 5/5 5/4 7/6 5/5 Total skeletal variations (fetus/litter) 59/19 58/20 69/22 78/22* BWG = body weight gain, NWC = net body weight change, * p<0.05 **p<0.01
結論		
Pに対するNOAEL (NOEL)又はLOAEL (LOEL)	NOAEL 母動物毒性 : = .05 − mg/l	NOAEL maternal tox. : = .05 − mg/l
F1に対するNOAEL (NOEL)又はLOAEL (LOEL)	NOAEL 催奇形性 : = .05 − mg/l	NOAEL teratogen. : = .05 − mg/l
F2に対するNOAEL (NOEL)又はLOAEL (LOEL)		
注釈	結論: 0、0.01、0.05、0.2 mg/l (0、10、50、200 mg/m³)の濃度で 6時間/日で交配後6-15日までジエタノールアミンのエアロゾルを頭部/鼻部暴露システムにより妊娠雌Wistarラットに暴露した結果、最高濃度(0.2 mg/l)で母動物毒性の兆候を生じた。 母動物毒性は交配後14日に21匹の妊娠ラットのうち8例に有害な臨床症状 (膣出血)により示された。この用量レベルでは骨格変異 (主に頸肋骨)を有する胎児の顕著な増数も記録されたが、物質に関連した催奇形性影響はいずれの胎児にも検出されなかった。このように、出生前の発生毒性の徴候が母動物の毒性濃度で生じた。	Conclusion : The exposure of pregnant female Wistar to an aerosol of Diethanolamine in a head/nose exposure systems for 6 h/day on day 6 through day 15 post coitum at concentrations of 0; 0.01; 0.05; 0.2 mg/l (0; 10, 50, 200 mg/m³) led to signs of maternal toxicity at the highest concentration (0.2 mg/l). Maternal toxicity was substantiated by adverse clinical symptoms (vaginal hemorrhages) in 8 of the 21 pregnant rats on day 14 p.c. At this dose level a markedly increased number of fetuses with skeletal variations (mainly cervical rib(s)) were also recorded but substance-related teratogenic effects were not detected in any fetus. Thus, signs of prenatal developmental toxicity did only occur at a maternal toxic concentration.
注釈	低又は中濃度 (0.01又は0.05 mg/l)では母動物又は胎児に有害影響はみられなかった。 母動物毒性及び出生前発生毒性に対するNOAECは0.05 mg/l (50 mg/m³)であり、催奇形性に対するNOAECは >0.2 mg/l (200 mg/m³)であった。	There were no adverse effects on dams or fetuses at the low or mid concentrations (0.01 or 0.05 mg/l). The NOAEC for maternal and prenatal developmental toxicity was 0.05 mg/l (50 mg/m³), the NOAEC for teratogenicity was >0.2 mg/l (200 mg/m³).
注釈	注釈: 本試験は別の記載として報告した用量範囲設定試験と組合せて考察されるべきである。 BASF AG, Product Safety, Range-finding study on the prenatal inhalation toxicity of Diethanolamine in pregnant rats, BASF Project No. 11R0233/90011, Experimental Toxicology and Ecology, BASF AG, Ludwigshafen, Germany, unpublished report, 20 August 1991	Remark : This study has to be considered in combination with the range-finding study reported as a separate entry: BASF AG, Product Safety, Range-finding study on the prenatal inhalation toxicity of Diethanolamine in pregnant rats, BASF Project No. 11R0233/90011, Experimental Toxicology and Ecology, BASF AG, Ludwigshafen, Germany, unpublished report, 20 August 1991
信頼性	(1) 制限付きで信頼性あり	(1) valid without restriction
信頼性の判断根拠	GLPのガイドライン試験	GLP guideline study
出典		
引用文献(元文献)	(215)	(215)
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

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	供給源: BASF AG バッチ: コンテナーB 810からの試料929 物理的状態/外観: 液体/無色 純度: >98.7% 均一性: 均一 安定性: 保管条件下での安定性が再解析により確認された。 保管条件: 室温、遮光、N2下で無酸素	Source: BASF AG Batch: sample 929 from container B 810 Physical state/appearance: Liquid / colorless Purity: >98.7% Homogeneity: homogeneous Stability: The stability under storage conditions was confirmed by reanalysis Storage conditions: Room temperature, without light and oxygen under N2
注釈		
方法		
方法／ガイドライン	その他: 用量範囲設定試験	other: range-finding study
GLP適合	はい	yes
試験を行った年	1991	1991
試験系(種／系統)	ラット Wistar	rat Wistar
性別(雄:M、雌:F)		
投与量	0、0.1、0.2、0.4 mg/l (測定された分析値: 0、0.11、0.21、0.40 mg/l、頭部鼻部暴露)	0; 0.1; 0.2; 0.4 mg/l (analytical determined: 0; 0.11; 0.21; 0.40 mg/l, head nose exposure)
各用量群(性別)の動物数		
投与経路	吸入	inhalation
試験期間	20日間	20 days
交配前暴露期間		
試験条件	暴露期間: 妊娠6-15日 処置頻度: 6時間/日 対照群: あり、媒体対照	Exposure period : gestation days 6 – 15 Frequency of treatm. : 6h/day Control group : yes, concurrent vehicle
試験条件	※英文参照	METHOD FOLLOWED: Not applicable because range-finding study GLP: In accordance with the OECD Principles of Good Laboratory Practice (Paris, 1981). ANALYTICAL METHODS: - Monitoring of the inhalation atmosphere: Vacuum compressed air pump (Millipore) Sampling equipment with probe (Millipore), 7 mm diameter, filter MN 85/90 Bf, 1.25 m/s sampling velocity, hourly sampling frequency Gravimetrical determination of concentration by means of balance (Mettler AE 249) - Particle size analysis: EACD 50% MMAD Geometric standard deviation (GSD) Total dust Respirable dust
試験条件	※英文参照	Test condition : TEST ORGANISMS Strain: Sexually mature Wistar rats (SPF-Wistar/Chhb:THOM) supplied by Dr. K. Thomae, Biberach, Germany Number: 10 females per group ADMINISTRATION / EXPOSURE: Pregnant female Wistar rats were exposed to an aerosol of Diethanolamine (DEA) in a head/nose exposure systems for 6 h/day on day 6 through day 15 post coitum. A control group was exposed under similar conditions to clean air only. Concentrations: Target: 0; 0.1; 0.2; 0.4 mg/l (analytical determined: 0; 0.11; 0.21; 0.40 mg/l) The test substance was supplied to a two-component atomizer at a constant rate by means of a metric pump. An aerosol was generated by means of compressed air and passed into the inhalation system.
試験条件	※英文参照	MATING PROCEDURES: After acclimatization and adaptation 1 – 4 female rats were mated with 1 male overnight. Day 0 post coitum was defined by detection of sperm in the vaginal smears. The animals were assigned to tests groups by randomization. PARAMETERS ASSESSED DURING STUDY: Mortality, clinical signs and findings, body weight/body weight gain, corrected body weight, necropsy finding of the dams, reproduction data of the dam, uterus weight, weight of fetus, weight of placenta, external examination of the fetus, clinical pathology and hematology in the dams
統計学的処理		
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	- 濃度: 設定値　実測値　MMAD (GSD) 0.1 mg/l,　0.11 mg/l　0.6 µm (4.5) 0.2 mg/l　0.21 mg/l　0.1.2 µm (3.6) 0.4 mg/l　0.40 mg/l　0.0.6 µm (4.5) - 死亡率、臨床症状、体重: 死亡例はなく、処置に関連した所見もなし。	- Concentrations: Target　Measured　MMAD (GSD) 0.1 mg/l,　0.11 mg/l　0.6 µm (4.5) 0.2 mg/l　0.21 mg/l　0.1.2 µm (3.6) 0.4 mg/l　0.40 mg/l　0.0.6 µm (4.5) - Mortalities, clinical findings, body weight: No deaths nor treatment related finding
注釈	用量レベルごとの毒性影響: 0.4 mg/l 試験群 肝臓絶対及び相対重量の増加 ナトリウム及びクレアチニンの血清中濃度の増加 コレステロール及びトリグリセリドの血清中濃度の減少 0.2 mg/l 試験群 肝臓相対重量の増加 ナトリウム及びクレアチニンの血清中濃度の増加 コレステロール及びトリグリセリドの血清中濃度の減少 0.1 mg/l 試験群 処置に関連した影響なし	TOXIC EFFECTS BY DOSE LEVEL: Test group 0.4 mg/l absolute and relative liver weight increased increase in sodium and creatinine serum concentrations decrease in cholesterol and triglycerides serum concentrations Test group 0.2 mg/l relative liver weight increased increase in sodium and creatinine serum concentrations decrease in cholesterol and triglycerides serum concentrations Test group 0.1 mg/l No treatment related effects.
結論		
Pに対するNOAEL (NOEL)又はLOAEL (LOEL)		
F1に対するNOAEL (NOEL)又はLOAEL (LOEL)		
F2に対するNOAEL (NOEL)又はLOAEL (LOEL)		
注釈	結論: 0、0.1、0.2、0.4 mg/l の濃度で 6時間/日で交配後6-15日までジエタノールアミンのエアロゾルを頭部/鼻部暴露システムにより妊娠雌Wistarラットに暴露した結果、0.4 mg/lで肝臓毒性影響の明らかな兆候 (絶対及び相対肝臓重量の増加、コレステロール及びトリグリセリドの血清中濃度の減少、トランスアミナーゼASTの増加)が生じた。0.2 mg/lでは肝臓相対重量がなお増加し、コレステロール及びトリグリセリドは減少した。 これらの所見は母動物毒性の明らかな兆候と考えられた。	Conclusion : The exposure of pregnant female Wistar to an aerosol of Diethanolamine in a head/nose exposure systems for 6 h/day on day 6 through day 15 post coitum at concentrations of 0; 0.1; 0.2; 0.4 mg/l led at 0.4 mg/l to a marked indication of hepatotoxic effects (increase of absolute and relative liver weights, decrease in cholesterol and triglyceride serum concentration, increase in transaminase AST). At 0.2 mg/l relative liver weight was still increased and cholesterol and triglycerides decreased. These findings were considered as clear indications for maternal toxicity.
注釈	注釈: 本試験は別に記載した本試験と組合わせることでのみ有効である。 BASF AG, Product Safety, Study of the prenatal inhalation toxicity of Diethanolamine in rats after inhalation, BASF Project No. 31R0233/90010, Experimental Toxicology and Ecology, BASF AG, Ludwigshafen, Germany, unpublished report, 08 July 1993	Remark : This study is only valid in combination with the main study reported as a separate entry: BASF AG, Product Safety, Study of the prenatal inhalation toxicity of Diethanolamine in rats after inhalation, BASF Project No. 31R0233/90010, Experimental Toxicology and Ecology, BASF AG, Ludwigshafen, Germany, unpublished report, 08 July 1993
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	用量範囲設定試験で許容でき、基礎的な科学原理を満たす文書化の良好な試験報告である。	Range-finding study, acceptable, well-documented study report which meets basic scientific principles
出典		
引用文献(元文献)	(216)	(216)
備考		

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	供給源: Aldrich Chemical Company, USA バッチ: 02216PG 純度: >=98% 均一性: 均一 安定性: 保管条件下での安定性が再分析により確認された。	Source: Aldrich Chemical Company, USA Batch: 02216PG Purity: >=98% Homogeneity: homogeneous Stability: The stability under storage conditions was confirmed by reanalysis
注釈		
方法		
方法／ガイドライン	その他: 出生前、出生後の発生毒性スクリーニング	other: pre-, postnatal developmental toxicity screening
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	rat
	Sprague-Dawley	Sprague-Dawley
性別(雄:M、雌:F)	雌	female
投与量	0、50、125、200、250、300 mg/kg 体重/日	0, 50, 125, 200, 250, 300 mg/kg bw/day
各用量群(性別)の動物数		
投与経路	強制経口	gavage
試験期間	40日間	40 days
交配前暴露期間		
試験条件	暴露期間: 妊娠6日-生後19日 処置頻度: 毎日 対照群: あり、媒体対照	Exposure period : gestation day 6 - postnatal day 19 Frequency of treatm. : daily Control group : yes, concurrent vehicle
試験条件	※英文参照	METHOD FOLLOWED: No guideline for this screening study available. Postnatal developmental study of rat pups after maternal exposure from gestation day 6 - 19. GLP: No information supplied ANALYTICAL METHODS: The identity was analyzed by infrared spectroscopy (IR). The purity of the neat substance was analyzed by gas chromatography (GC) coupled with flame ionization detection (FID) The stability of the of the aqueous preparations and concentration control analysis was performed by GC
試験条件	※英文参照	Test condition : TEST ORGANISMS Strain: Sexually mature, timed-mated Sprague-Dawley rats (Crl:CD (SD)BR VAF/Plus) supplied by Charles river, Raleigh, USA Number: 12 females per group Weight at study initiation (confirmed mating): 221 - 275 g ADMINISTRATION / EXPOSURE: - Duration of test/exposure: from implantation to two days prior to expected day of parturition (day 6 to day 19 post coitum) - Treatment: oral (gavage) - Control group and treatment: gavage of 5 ml/kg bw distilled water - Vehicle: Distilled (Pico) water - Test substance preparation: Formulation in distilled water, pH adjusted by hydrochloric acid, stored in sealed, amber glass bottles at room temperature for a period of proven stability - Concentration in the vehicle: 0, 10 - 60 mg/ml - Application volume: 5 ml/kg bw - Dose levels: 0, 50, 125, 250, 300 mg/kg bw - Analysis: check of stability and concentration control by GC.
試験条件	※英文参照	MATING PROCEDURES: After 10 day quarantine, individual breeding pairs were mated overnight. The morning of sperm detection was designated gestation day 0. The animals were assigned to tests groups by randomization. PARAMETERS ASSESSED DURING STUDY: Maternal evaluations: For confirmed-mated females, body weight (g) was recorded on the mornings of GD and 6-20. For dams with litters, maternal body weight was recorded on the mornings of PND 0, 4, 7, 14, and 21, and immediately after termination on PND 21. Females were observed for clinical condition at least once daily on GD 0-5 (before dosing) and on GD 20 through termination. On GD 6-19, females were observed daily for clinical condition and signs of toxicity at dosing and ~ 1-2 hr after each dose administration. On GD 20, and on PND 0, 4, 7, 14, and 21 females were observed for clinical condition at weighing (in-life), and also at scheduled termination on PND 21.
		Feed and water consumption were monitored on GD 0, 6, 9, 12, 15, 18, and 20 for all timed-mated females, as well as PND 0, 4, 7, 14, and 21 for dams with litters. Beginning on GD 20, timed-mated females were checked twice daily (morning and afternoon) for evidence of littering. The day on which each litter was found was designated as PND ° for that litter. Timed mated females were terminated if they failed to deliver a litter by GD 24. Uteri presenting no visible implantation sites were stained with ammonium sulfide 00%) to visualize any implantation sites that might have undergone very early resorption (Salewski, 1964). At such time as a dam had no surviving pups, the dam was terminated and visible uterine implantation sites were counted. On PND 21, all remaining maternal females and pups were terminated by C02 asphyxiation. The body, liver, and paired kidneys of each timed-mated female were weighed. Thoracic and abdominal cavities were examined. Visible uterine implantation sites were counted.

試験条件	※英文参照	Pup Evaluations: Naturally delivered litters were evaluated for clinical signs, litter size, pup sex and individual pup body weight on PND 0, 4, 7, 14, and 21. Pups were examined for external malformations or variations on PND 0. On PND 7, each litter was culled to a maximum size of eight pups, except that one litter at 250 mg/kg/ day was inadvertently culled to nine pups. Ideally, four pups of each sex were retained in each litter, but smaller litters or litters with unbalanced sex ratios were also retained in the study. Pups were subjected to gross necropsy on PND 7 (culling) or PND 21 (scheduled
統計学的処理	※英文参照	Statistics Statistical procedures were based on SAS software (Version 6.12; SAS Institute, Inc., Cary, NC), the alpha level was 0.05. Nonparametric tests applied to continuous variables included the Kruskal–Wallis one–way analysis of variance by ranks for among–group differences and, if significant ($p < 0.05$), the Mann– Whitney U–test for pairwise comparisons to the vehicle control group. A one–tailed Mann–Whitney U–test was used for all parameters, except that maternal and pup body weight parameters, and maternal feed and water consumption were examined using a two–tailed test.
統計学的処理	※英文参照	Jonckheere's test for k–independent samples was used to identify significant dose–response trends. Nominal scale measures were analyzed by Chi–Square test for independence for differences among treatment groups and by the Cochran–Armitage test for linear trend on proportions. When Chi–Square test showed significant ($p < 0.05$) differences among groups, then a one–tailed Fisher's exact probability test, with appropriate adjustments for multiple comparisons, was used for pairwise comparisons between control and DEA treated groups. A probit analysis was used to determine the maternal LD10 in this study.
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	試験物質の分析 試験物質調製液の室温での安定性が証明された。 濃度管理の分析は設定濃度の97.8–101.2%を示した。	TEST SUBSTANCE ANALYSIS. The stability of the test substance preparation at room temperatures was demonstrated. The concentration control analyses showed 97.8 – 101.2% of the nominal concentrations.

注釈	母動物の毒性影響 妊娠は1群当たり11-12匹の雌で確認された。 最高用量 (300 mg/kg体重)では妊娠11日に雌2匹が瀕死のために屠殺された。この過度の毒性のために同じ群の残りの雌全例は計画屠殺の前に安楽死させ、更なる結果のまとめからは除外した。 対照群、50及び125 mg/kg体重群の雌各12匹並びに200 mg/kg体重群の雌11匹は生存児を分娩し、PND21の計画屠殺まで生存した。 200 mg/kg体重では雌1匹が妊娠22日に瀕死状態で屠殺したが、この雌は15匹の同腹児を分娩しようとしたが、全児が剖検で子宮内で死亡発見された。 250 mg/kg体重では雌1匹が妊娠15日に死亡発見され、他1匹が妊娠21日に瀕死状態で屠殺され、子宮内には12匹の死亡児を有していた。250 mg/kg体重群の残りの雌では、5匹が生存児を分娩し、PND21の計画屠殺まで生存し、1匹は分娩したが全児死亡 (PND 0)、3匹が妊娠24日の子宮検査で完全に吸収された腹を有し、1匹は妊娠しなかった。	MATERNAL TOXIC EFFECTS: Pregnancy was confirmed in 11- 12 females per group At the highest dose (300 mg/kg bw), two females were terminated in extremis on GD 11. Due to this excessive toxicity, all remaining females in that group were humanely terminated before scheduled necropsy and excluded from further summary of results. Twelve females each from the control, 50 and 125 mg/kg bw groups, as well as 11 females from the 200 mg/kg bw group delivered a live litter and survived until scheduled necropsy on PND 21. At 200 mg/kg bw, one female was terminated in extremis on GD 22 while attempting to deliver a litter of 15 pups, all of which were found dead in utero at necropsy. At 250 mg/kg bw, one female was found dead on GD 15 and another was terminated in extremis on GD 21 with 12 dead pups in utero. Among the remaining females in the 250 mg/kg bw group, five delivered live litters and survived to scheduled termination on PND 21, one delivered a litter in which all pups were dead (PND 0), three had completely resorbed litters at uterine examination on CD 24, and one was not pregnant.
注釈	プロビット解析により母動物のLD10は218 mg/kg/日と算出された。 200 mg/kg体重以上では投与期間中最も頻繁に認められた臨床症状は体重減少、立毛、及び嗜眠であった。 哺育中、125、200及び250 mg/kg体重群では投与に関連した臨床症状は立毛の頻度の明らかな増加に限定されたが、PND5日以降投与に関連した臨床症状は観察されなかった。 母動物の体重低下が200 mg/kg体重以上で認められた。250 mg/kg/日では母動物の体重は妊娠12-20日の間に有意に減少し、PND4には6%低下した。投与期間 (GD 6-20)及び妊娠期間 (GD 0-20)の間、母動物の体重変化は200及び250 mg/kg体重で有意に低下した。 投与期間中、母動物の相対的な摂餌量は200及び250 mg/kg体重では妊娠6-9日、9-12日、及び12-15日に減少した。250 mg/kg/日では摂餌量はPND0-4日にも一過性に減少した。	Probit analysis yielded a calculated maternal LD10 of 218 mg/kg/day. At >= 200 mg/kg bw, the clinical signs noted most frequently during the treatment period were weight loss, piloerection, and lethargy. During lactation, treatment-related clinical signs were limited to an apparent increase in the incidence of piloerection in the 125, 200, and 250 mg/kg bw groups but no treatment-related clinical signs were observed after PND 5.thereafter. Reduced maternal body weight was notable at >=200mg/kg bw. At 250 mg/kg/ day, maternal body weight was significantly decreased during GD 12 - 20 and 6% reduction on PND 4. For the treatment (GD 6-20) and gestational periods (G 0-20), maternal body weight change was significantly reduced at 200 and 250 mg/kg bw. During treatment, maternal relative feed intake was decreased at 200 and 25 0mg/kg bw from GD 6-9, 9-12, and 12-15. At 250 mg/kg/ day, feed intake was also transiently decreased from PND 0-4.
注釈	母動物の相対的な摂水量は125及び250 mg/kg体重で妊娠9-12日に低下した。 投与期間を通した平均値では、母動物の相対的な摂餌量は200 mg/kg体重異常で減少したが、相対的な摂水量は影響を受けなかった。 対照群の母動物は妊娠21又は22日に分娩したが、DEA暴露群の母動物は妊娠22又は23日に分娩した。 計画屠殺時 (PND21)に、母動物の体重及び肝臓重量には影響はみられなかった。母動物の腎臓重量は増加する傾向を示し、腎臓絶対重量は125、200、及び250 mg/kg体重で有意に上昇した。	Maternal relative water intake was reduced from GD 9-12 at 125 and 250 mg/kg bw. Averaged across the treatment period, maternal relative feed intake was reduced at >= 200 mg/kg bw and relative water intake was not affected. Dams in the control group delivered on GD 21 or 22, whereas dams in DEA-exposed groups delivered on GD 22 or 23. At scheduled necropsy (PND 21), maternal body weight and liver weight were unaffected. Maternal kidney weight showed an increasing trend, and absolute kidney weight was significantly elevated at 125, 200, and 250 mg/kg bw.
注釈	母動物のデータ mg/kg 体重/日 0 50 125 200 250 N 12 12 12 12 12 死亡例、n 0 0 0 1 2 妊娠動物数 12 12 12 12 11 生存腹数 12 12 12 11 5 腹を有する例数 PND 0 12 12 12 11 6 PND 4-21 12 12 12 11 5 PND 21のN 12 12 12 11 5 PND 21の体重, g 308 318 310 327 325 肝臓重量 g 17.38 17.69 18.23 17.17 17.82 % 肝臓重量 5.65 5.57 5.89 5.22 5.48 腎臓重量、g 2.64 2.77 2.91* 3.01* 3.10* % 腎臓重量 0.86 0.87 0.94 0.92 0.95 * p < 0.05, ** p <0.01	Maternal data mg/kg bw/day 0 50 125 200 250 N 12 12 12 12 12 died, n 0 0 0 1 2 pregnant 12 12 12 12 11 live litters 12 12 12 11 5 N with litters PND 0 12 12 12 11 6 PND 4-21 12 12 12 11 5 N on PND 21 12 12 12 11 5 BW PND 21, g 308 318 310 327 325 liver weight g 17.38 17.69 18.23 17.17 17.82 % liver weight 5.65 5.57 5.89 5.22 5.48 kidney weight,g 2.64 2.77 2.91* 3.01* 3.10* % kidney weight 0.86 0.87 0.94 0.92 0.95 * p < 0.05, ** p <0.01

注釈	腹のデータ mg/kg体重/日 0 50 125 200 250 母動物数 12 12 12 12 12 妊娠動物数 12 12 12 12 11 生存腹数 12 12 12 11 5 妊娠日期間 21.9 22.2 22.3 22.3 22.2 着床数./腹 14.25 13.75 14.33 14.42 14.91 着床後胚. 損失 % 2.48 5.83 3.41 17.31** 50.9** 死亡児 PND 0 1 5 PND 1 PND 4 1 3 4 8 PND 14 2 1 2 PND 0-21 1 1 10 5 11 % 死亡例/腹 PND 0-4 0.6 0.6 1.8* 2.8* 13.4** PND 7-14 0.0 0.0 2.1 1.1 5.0 * p < 0.05, ** p <0.01	Litter data mg/kg bw/day 0 50 125 200 250 dams 12 12 12 12 12 pregnant 12 12 12 12 11 live litters 12 12 12 11 5 Gestation d 21.9 22.2 22.3 22.3 22.2 Implant./litter 14.25 13.75 14.33 14.42 14.91 Postimplant. loss % 2.48 5.83 3.41 17.31** 50.9** Dead pups PND 0 1 5 PND 1 PND 4 1 3 4 8 PND 14 2 1 2 PND 0-21 1 1 10 5 11 % mortality/litter PND 0-4 0.6 0.6 1.8* 2.8* 13.4** PND 7-14 0.0 0.0 2.1 1.1 5.0 * p < 0.05, ** p <0.01
注釈	発生毒性影響: 着床後胚損失は200及び250 mg/kg体重群では対照群より有意に高く、対照群から250 mg/kg体重群で母動物当たりの着床部位数の2、6、3、17、及び51%であった。250 mg/kg体重/日では雌9匹のうち4匹 (44%)が100%の着床後胚損失を示した。 暴露は生後0日の腹当たりの平均生存児数に対しては減少傾向を示して関連性があった。50-250 mg/kg体重で、腹当たりの平均生存児数は対照群の平均値の91、97、85、及び55%であったが、生存腹当たりの平均生存児数は群間で統計的に有意な差を示さなかった。 生存率、平均同腹生存児数は誕生時には投与群間でほぼ同じであった。	DEVELOPMENTAL TOXIC EFFECTS: Postimplantation loss was significantly higher than controls in the 200 and 250 mg/kg bw groups and for 2, 6, 3, 17, and 51% of implantation sites/dam in the control – 250 mg/kg bw group. At 250 mg/kg bw day, four of nine (44%) females had 100% postimplantation loss. Exposure was associated with a decreasing trend for the average number of live pups per litter on PND 0; at 50 – 250 mg/kg bw, the mean number of live pups per litter was 91, 97, 85, and 55% of the control group mean but the average number of live pups/live litter showed no statistically significant difference among groups. Survival, average live litter size was comparable across treatment groups at the beginning of the postnatal period.
注釈	生存腹当たりの生存児数には生後4及び7日で有意な減少傾向が認められたが、間引き (生後7日)後には生後14又は21日の生存腹当たりの生存児数に群間での差はなかった。 生後0-4日で生後の死亡率は対照群から250 mg/kg体重にかけて、それぞれ腹当たりの児数%で0、0.6、1.8、2.8及び13.4%で、125 mg/kg体重以上で統計的に有意であった。 雄と雌児の比率には生物学的関連性を示す差はみられなかった。 児体重は50 mg/kg体重では影響がなかったが、125 mg/kg/日では生後14日に腹当たりの平均児体重に7-8%の増加がみられた。200 mg/kg体重では雌児の体重が生後0及び4日で8%、生後21日には10%の有意な減少を示した。同用量では雄児の体重は生後21日に11%有意に低下した。250 mg/kg体重では腹当たりの雌児の体重は生後0、4、7日には16-17%、生後21日には10%有意に低下し、腹当たりの雄児の体重は生後0日に11%、生後4日に15%及び生後21日に14%、有意に低下した。	Significant decreasing trends for the number of live pups/live litter were noted on PND 4 and 7 but after culling (PND 7), there were no differences among groups for the number of live pups/live litter on PND 14 or 21. From PND 0-4, postnatal mortality occurred in 0, 0.6, 1.8, 2.8, and 13.4% of pups /litter in the control – 250 mg/kg bw, respectively, being statistically significant at >= 125 mg/kg bw. There was no biological relevant difference in the proportion of male and female pups. Pup body weight was not affected at 50 mg/kg bw, at 125mg/kg/day, there was a 7-8% increase in average pup body weight/litter on PND 14. At 200 mg/kg bw, female pup body weight was significantly reduced by 8% on PND 0 and 4 and by 10% on PND 21. At the same dose, male pup body weight was significantly reduced by 11% on PND 21. At 250 mg/kg bw, female pup body weight/litter was significantly reduced by 16-17% on PND 0, 4, 7, and by 10% on PND 21 and male pup body weight/litter was significantly reduced by 11% on PND 0, 15% on PND 4 and 14% on PND 21
注釈	脱毛 (200 mg/kg体重)及び先に述べた生後の死亡の頻度には用量相関のない増加がみられた。 250 mg/kg/日では5匹の死亡児に水尿管及び/又は水腎症がみられたが、これらの所見はこの種/系統にはありふれたものである。生後に死亡した大部分の児動物では胃内に乳汁がみられず、哺育拒否が示唆された。 生後7日 (間引き)及び生後21日 (試験終了時)の計画剖検では、形態学的所見は尿管拡張が1匹 (生後7日、200 mg/kg/日)及び片側性の水腎症が1匹 (生後21日、50 mg/kg/日)にみられたのみであった。	There was a non-dose-related increase in the incidence of alopecia (200 mg/kg bw) and the previously noted incidence of postnatal deaths. At 250 mg/kg/ day, five dead pups displayed hydroureter and/or hydronephrosis but these findings are common to this species/strain. For most pups that died postnatally, there was no milk found in the stomach, indicating unsuccessful nursing. At scheduled necropsy on PND 7 (culling) and PND 21 (study termination), morphological findings were limited to one pup with distended ureter (PND 7, 200 mg/ kg/ day) and one with unilateral hydronephrosis (PND 21, 50 mg/kg/ day).
注釈	児の体重増加量 (平均値) mg/kg体重/日 0 50 125 200 250 生存腹数 12 12 12 11 5 PND 0 6.1 6.34 6.33 5.65 5.25* PND 4 9.72 10.17 9.96 8.81* 8.15* PND 7 13.86 14.71 14.54 12.74 11.99* PND 14 33.1 33.88 35.53 30.72 30.18 PND 21 53.8 55.26 55.96 48.02* 47.46* * p < 0.05, ** p <0.01	Pup body weight gain (mean) mg/kg bw/day 0 50 125 200 250 Live litter 12 12 12 11 5 PND 0 6.1 6.34 6.33 5.65 5.25* PND 4 9.72 10.17 9.96 8.81* 8.15* PND 7 13.86 14.71 14.54 12.74 11.99* PND 14 33.1 33.88 35.53 30.72 30.18 PND 21 53.8 55.26 55.96 48.02* 47.46* * p < 0.05, ** p <0.01
結論		
Pに対するNOAEL (NOEL)又はLOAEL (LOEL)	NOAEL母動物毒性 : = 50 - mg/kg体重	NOAEL maternal tox. : = 50 - mg/kg bw
F1に対するNOAEL (NOEL)又はLOAEL (LOEL)		
F2に対するNOAEL (NOEL)又はLOAEL (LOEL)		

注釈	時間交配した妊娠ラットに妊娠6-19日にかけて0、50、125、200、250、300 mg/kg体重の用量レベルのDEAを投与した結果、200及び250 mg/kg体重では母動物に疾病例及び死亡例を生じ、300 mg/kg体重では過度の毒性のために雌全例を早期に屠殺せざるを得なかった。本試験条件下での母動物の推定LD10は218 mg/kg体重であった。 母動物の摂水量は妊娠早期には一過性に影響を受けた（125及び250 mg/kg体重)が、妊娠12日以降全測定期間にわたり対照群と同程度であった。母動物の腎臓絶対重量は生後21日に増加し（125 mg/kg体重以上)、暴露休止後約3週までDEA誘発毒性が持続することが示唆された。母動物の体重及び体重変化量の低下並びに摂餌量の低下が200 mg/kg体重以上で認められた。50 mg/kg体重への暴露は投与期間中又は投与期間後に何ら有意な母動物毒性を示さなかった。	Conclusion : Treatment of time-mated pregnant rats with DEA dose levels of 0, 50, 125, 200, 250, 300 mg/kg bw from gestation day 6 - 19 led to maternal morbidity or mortality occurred at 200 and 250 mg/bw and all females at 300 mg/kg bw had to be terminated early due to excessive toxicity. The estimated maternal LD10 under the conditions of this study was 218 mg/kg bw. Maternal water intake was transiently affected during early gestation (125 and 250 mg/kg bw) but was comparable to controls for all measurement periods after GD 12. Maternal absolute kidney weight was increased on PND 21 (>= 125 mg/kg bw) indicating persistence of DEA-induced toxicity for up to about 3 weeks after cessation of exposure. Reduced maternal body weight and weight change, as well as reduced feed intake, were noted at >= 200 mg/kg bw. Exposure to 50 mg/kg bw was not associated with any significant maternal toxicity during or after the treatment period.
注釈	発生毒性は特に200 mg/kg体重以上で生後0日に着床後死亡率の増加の形でみられ、生後早期（生後0-4日)の死亡率は125 mg/kg体重以上で増加した。児体重は200 mg/kg体重以上で低下し、雌では雄よりも影響が大きかった。対照群の重量の%として表した場合、児体重の減少率は生後早期の間に最も顕著であった。統計的に有意な差は哺育期間終了時にも明瞭であった。 結果として、母動物毒性及び発生毒性に対するNOAELは50 mg/kg体重であった。このように、発生毒性の徴候が母動物の毒性用量のみで生じた。	Developmental toxicity was observed specifically in form of an increase in postimplantation mortality at >= 200 mg/kg bw on PND 0, and early postnatal mortality (PND 0-4) was increased at >= 125 mg/kg bw. Pup body weight was reduced at >= 200 mg/kg bw, with females more affected than males. When expressed as a percentage of control weight, pup body weight reductions were most pronounced during the early postnatal period. Statistically significant differences were also evident at the end of the lactational period. Consequently, the NOAEL for maternal and developmental toxicity was 50 mg/kg bw. Thus, signs of developmental toxicity did only occur at maternal toxic dose levels.
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	基本的な科学原理を満たしている文書化の良好な文献で、評価に受け入れられる。	Well-documented publication which meets basic scientific principles, acceptable for assessment
出典		
引用文献(元文献)	(217) (218)	(217) (218)
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

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	供給源: Radian Corp., Austin, TX, USA	Source: Radian Corp., Austin, TX, USA
方法		
方法／ガイドライン	Chernoff-Kavlokの催奇形性スクリーニング試験	Chernoff-Kavlok teratogenicity screening test
GLP適合	はい	yes
試験を行った年	1987	1987
試験系(種／系統)	マウス	mouse
	CD-1	CD-1
性別(雄:M、雌:F)	雌	female
投与量	200、380、720、1370、2605 mg/kg 体重	200, 380, 720, 1370, 2605 mg/kg bw
各用量群(性別)の動物数		
投与経路	強制経口	gavage
試験期間	17日間	17 days
交配前暴露期間		
試験条件	暴露期間: 妊娠6-15日 処置頻度: 毎日 対照群: なし	Exposure period : gestation days 6 - 15 Frequency of treatm. : daily Control group : no
試験条件	※英文参照	METHOD FOLLOWED: Screening of National Toxicology Program (NTP) priority compounds for the potential to cause adverse reproductive effects using the post-natal mouse screening test (Chernoff and Kavlock, 1982, 1983) GLP: Yes ANALYTICAL METHODS: Stability and concentration control analysis were performed by means of GC/FID.
試験条件	※英文参照	Test condition : TEST ORGANISMS - Strain: primigravida female CD-1 mice, supplier: Charles River Breeding Laboratories, Kingston, NY, USA - Number: 4 females per group - Acclimatization: 5 days - Age at supply: 6 - 8 weeks - Housing: individual, polycarbonate shoe box cages ADMINISTRATION / EXPOSURE: - Treatment: the test substance was admixed in distilled water and was applied orally by gavage on 10 consecutive days - Application volume: 10 ml/kg bw - Dose levels: 200, 380, 720, 1370, 2605 mg/kg bw

試験条件	※英文参照	PARAMETERS ASSESSED DURING STUDY: - clinical signs including mortality: twice daily - body weights: at randomization, on days 6 - 15 through gestation, and on day 17. TERMINATION: All surviving mice were sacrificed by carbon dioxide asphyxiation following the collection of terminal body weights. On gestation day 17, all surviving mice were sacrificed and uteri were examined. Each female was classified as pregnant or non-pregnant. Pregnant mice were noted as having live fetuses or no live fetuses.
統計学的処理	※英文参照	Statistical Analysis An overall test for homogeneity of variance (Bartlett's test) and F-test were performed Probit analysis of mortality and morbidity data generated in Phase II of the range finding study was used to determine the predicted LD10 for the Phase III. Random weights analysis of variance (ANOVA Survival: Fisher's exact test (one-tail) Weight gains: Mann-Whitney U-Test (2-tail Proportion of viable litters: Fisher's exact test (one-tail) Survival of pups: Chi-Square test (one-tail) The Mann-Whitney U-test (2-tail) was used to compare each group to the concurrent control: Number live pups/litter (day 0, day 3); Length of gestation; Average wt. pup (day 0, day 3); average wt. gain/litter (day 3-day 0).
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	- 体重のデータ: mg/kg bw 200 380 720 1370* 2605* BWC Day 1-10 15.4 14.3 14.3 0 0 Day 10-12 6.1 6.9 6.4 * 投与後7日に全例が死亡した - 死亡率及び妊娠状態: mg/kg bw 200 380 720 1370* 2605* 投与した動物数 4 4 4 4 4 死亡発見された動物 1* 0 3 4 4 硫化アンモニウム陽性 - - 3 3 3 硫化アンモニウム陰性 1 - - 1 1 屠殺した動物 3 4 1 0 0 生存児動物 2 2 1 - - 硫化アンモニウム陽性 - - - - - 硫化アンモニウム陰性 1 2 - - - * 誤投与により死亡した	- Body weight data: mg/kg bw 200 380 720 1370* 2605* BWC Day 1-10 15.4 14.3 14.3 0 0 Day 10-12 6.1 6.9 6.4 * all animals died on post-treatment day 7 - Mortality and pregnancy status: mg/kg bw 200 380 720 1370* 2605* Number of animals treated 4 4 4 4 4 Animals found dead 1* 0 3 4 4 Ammonium Sulfide positive - - 3 3 3 Ammonium Sulfide negative 1 - - 1 1 Animals Sacrificed 3 4 1 0 0 Live Pups 2 2 1 - - Ammonium sulfide positive - - - - - Ammonium sulfide negative 1 2 - - - * died due to gavage error

注釈	-臨床所見: 200 mg/kg体重: 全動物で被毛粗剛。投与7日の投与直後に1匹が死亡して発見された。この死亡例は投与のショックにより生じたように思われた。 380 mg/kg体重: この用量レベルでは全動物が被毛粗剛を示した。 720 mg/kg体重: 被毛粗剛、不活発な行動、斜視、及び円背姿勢。 投与3日の午後の観察中に1匹が死亡しているのが発見された。2匹が午前の観察中に死亡発見された。1匹が投与7日、1匹が投与8日目であった。 1370 mg/kg体重: 被毛粗剛、不活発な行動、円背姿勢、血液様の膣分泌物、努力呼吸、斜視、不安定歩行、及び低体重の動物。3匹が午前の観察中に死亡発見され、2匹が投与7日、1匹が投与8日目であった。1匹が投与9日の午後の観察中に死亡発見された。 2605 mg/kg体重: 被毛粗剛、円背姿勢、疲憊、努力呼吸、血液様の膣分泌物、及び眼及び四肢の退色。この用量レベルで全例が投与5日に死亡発見された。	- Clinical findings: 200 mg/kg bw: Rough hair coat in all animals. One animal was found dead immediately after dosing on treatment day 7; this death appeared to be caused by dosing trauma. 380 mg/kg bw: All animals at this dose level exhibited a rough hair coat. 720 mg/kg bw: Rough hair coat, languid behavior, squinted eyes, and hunched posture. One animal was found dead during the afternoon observation on treatment day 3. Two animals were found dead during the morning observation; one on treatment day 7 and one an treatment day 8. 1370 mg/kg bw: Rough hair coat, languid behavior, hunched posture, bloody vaginal discharge, labored breathing, squinted eyes, unsteady gait, and animals underweight. Three animals were found dead during the morning observations, two on treatment day 7 and one on treatment day 8. One animal was found dead during the afternoon observation on treatment day 9. 2605 mg/kg bw: Rough hair coat, hunched posture, prostrate, labored breathing, bloody vaginal discharge, and pale eyes and extremities. All animals at this dose level were found dead on treatment day 5.
結論		
Pに対するNOAEL (NOEL)又はLOAEL (LOEL)		
F1に対するNOAEL (NOEL)又はLOAEL (LOEL)		
F2に対するNOAEL (NOEL)又はLOAEL (LOEL)		
注釈	注釈: フェーズⅠ及びⅡの試験の死亡率のデータを組合わせたプロビット解析によりフェーズⅢ生殖試験の推奨用量 (LD10)はジエタノールアミンの450 mg/kg体重であった。	Remark : Based on the probit analysis of combined mortality data from the Phase I and II tests, the recommended doses for the Phase III reproductive study (LD10) were 450 mg/kg bw for diethanolamine.
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	基本的な科学原理を満たしている許容できる文書化の良好な試験	Acceptable, well-documented study which meets basic scientific principles
出典		
引用文献(元文献)		
備考	(200) (201)	(200) (201)

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	供給源: Radian Corp., Austin, TX, USA	Source: Radian Corp., Austin, TX, USA
方法		
方法／ガイドライン	Chernoff-Kavlokの催奇形性スクリーニング試験	Chernoff-Kavlok teratogenicity screening test
GLP適合	はい	yes
試験を行った年	1987	1987
試験系(種／系統)	マウス	mouse
	CD-1	CD-1
性別(雄:M、雌:F)	雌	female
投与量	450 mg/kg体重	450 mg/kg bw
各用量群(性別)の動物数		
投与経路	強制経口	gavage
試験期間	24日間	24 days
交配前暴露期間		
試験条件	暴露期間: 妊娠6-15日 処置頻度: 毎日 対照群: あり、媒体対照	Exposure period : gestation days 6 - 15 Frequency of treatm. : daily Control group : yes, concurrent vehicle
試験条件	※英文参照	METHOD FOLLOWED: Screening of National Toxicology Program (NTP) priority compounds for the potential to cause adverse reproductive effects using the post-natal mouse screening test (Chernoff and Kavlock, 1982, 1983) GLP: Yes ANALYTICAL METHODS: Stability and concentration control analysis were performed by means of GC/FID.

試験条件	※英文参照	Test condition : TEST ORGANISMS - Strain: primigravida female CD-1 mice, supplier: Charles River Breeding Laboratories, Kingston, NY, USA - Number: 50 females per group - Acclimatization: 5 days - Age at supply: 6 - 8 weeks - Housing: individual, polycarbonate shoe box cages ADMINISTRATION / EXPOSURE: - Treatment: the test substance was admixed in distilled water and was applied orally by gavage on 10 consecutive days - Application volume: 10 ml/kg bw - Dose levels: 0, 450 mg/kg bw - Control group: distilled water at 10 ml/kg bw PARAMETERS ASSESSED DURING STUDY: - clinical signs including mortality: twice daily - body weights: at randomization, on days 6 - 15 through gestation, on day 17, day 0 and 3 post partum
試験条件	※英文参照	TERMINATION: Litter box bedding was not changed from gestation day 17 throughout the post partum observation period. Beginning on day 18 of gestation and continuing until all litters were delivered, females were observed twice daily for evidence of labor and delivery of litters. The day of delivery was recorded to the nearest half day. The time, date, and gestation day were recorded when labor, fetuses, or other evidence of delivery was observed. After delivery was complete, the dam was removed and weighed then placed temporarily in a holding container. The pups were removed from the cage and the nesting material was probed for dead fetuses and parts of cannibalized fetuses. The number of live and dead pups, and the weight of all live pups were recorded. The live pups of a litter were weighed together to give a litter weight, and the average litter weight was calculated. The live pups were then returned to the nesting box and the dam was returned last. Dead fetuses were discarded.
試験条件	※英文参照	Any female that did not show signs of delivering a litter by gestation day 22 was sacrificed and the uterus examined for evidence of pregnancy. If there was no gross evidence of pregnancy, the uterus was placed in a 10 percent ammonium sulfide solution to make early implantation sites visible. Based on the presence of early implantation sites, the female was classified as having been either pregnant or never pregnant. Following the observations made on day a post partum, females and litters were not disturbed until post partum Day 3. At that time the maternal body weight and the number of live and dead neonatal mice, and the total litter weight of live pups were recorded. Females and litters were than sacrificed and discarded.
統計学的処理	※英文参照	Statistical Analysis An overall test for homogeneity of variance (Bartlett's test) and F-test were performed Probit analysis of mortality and morbidity data generated in Phase II of the range finding study was used to determine the predicted LD10 for the Phase III. Random weights analysis of variance (ANOVA Survival: Fisher's exact test (one-tail) Weight gains: Mann-Whitney U-Test (2-tail Proportion of viable litters: Fisher's exact test (one-tail) Survival of pups: Chi-Square test (one-tail) The Mann-Whitney U-test (2-tail) was used to compare each group to the concurrent control: Number live pups/litter (day 0, day 3); Length of gestation; Average wt. pup (day 0, day 3); average wt. gain/litter (day 3-day 0).
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	-死亡率及び生存率: 投与期間中及び投与後の期間中に死亡例は生じなかった。 -臨床観察: 投与に関連した臨床症状がみられた。 -母動物の体重: 母動物の体重は分娩後0日には軽度に増加したが、分娩後3日には軽度に減少した。	- Mortality and survival: No animal died during the application period during pots treatment. - Clinical observation: There were treatment-related clinical sign. - Maternal body weight: The dams body weight was slightly increased on post partum day 0 but slightly decreased on post partum day 3.
注釈	-生殖指標及び腹のデータ 生殖指標及び0日の平均生存同腹児数は影響を受けなかったが、3日目の平均生存同腹児数は低下し、児の生後死亡率の増加が示唆された。 -妊娠期間: 妊娠期間には僅かな増加がみられた (18.5日に対し、対照群は18.2日)。 -児の重量のデータ: 生後0日には対照群と差はなかったが、平均体重及び体重増加量は生後3日に低下した。	- Reproductive index and litter data: The reproductive index and the average number of live litters on day 0 were not affected but the average number of live litters on day 3 was reduced as an indication of increased postnatal pup mortality. - Duration of gestation: There was a slight increase in the duration of gestation (18.5 days vs. 18.2 days in controls). - Pup weight data: There was no difference from control on post natal day 0 but mean body weight and body weight gain were reduced on PND 3.
結論		
Pに対するNOAEL (NOEL)又はLOAEL (LOEL)		
F1に対するNOAEL (NOEL)又はLOAEL (LOEL)		
F2に対するNOAEL (NOEL)又はLOAEL (LOEL)		
注釈	結論 : 450 mg/kg体重で妊娠6-15日に投与したジエタノールアミンは母動物の死亡率、同腹児数及び児動物の生時重量には影響を示さなかったが、同腹生存児数、児の生存率及び児の重量増加量を減少させた。Hardin (Hardin, 1987)のランキングシステムを用いると、最大スコアは22で母動物の死亡率が低いため以下のスコアを差し引くべきである:生存腹 (0); 同腹児数 (2); 児の生存率% (0); 児の生時体重 (1); 及び児の増体重 (0)。従って、ジエタノールアミンのスコアは19となり、通常の発生毒性試験で試験を行うべき優先順位は高いことが示される。 ジエタノールアミンは Chernoff/Kavlock予備的発生毒性試験で陽性と判定された。	Conclusion : Diethanolamine applied on gestation days 6 - 15 at 450 mg/kg bw had no effect on maternal mortality, on litter size and on birth weight of the pups, but did decrease the number of viable litters, the percent survival of the pups and the weight gained by the pups. Using the ranking system of Hardin (Hardin, 1987) with a maximum score of 22 and for low maternal mortality the following scores should be subtracted: viable litters (0); litter size (2); percent survival of the pups (0); birth weight of the pups (1); and weight gained by the pups (0). Therefore, the score for diethanolamine was 19 which represent high priority for testing in a conventional developmental toxicity test. Diethanolamine was judged positive in the Chernoff/Kavlock preliminary developmental toxicity test.
注釈	注釈 : このスクリーニングの結果は通常の発生毒性試験(York et al. 1988)のための化学物質の順番をランクするためのスコアリングシステムと組合わせて用いた。潜在的な発生毒性の5つの指標が母動物の死亡率によって変化する各時点の値に割り当てられた。これらの指標は最低1匹以上の生存児を持つ腹を生じた妊娠生存動物の割合、同腹児数及び生時児重量の平均値、及び児の生存率及び3日間の増体重の平均値であった。このスクアリング手法により、DEAに対しては更なる試験が必要との高い優先順位が得られた。	Remark : The results from this screen were used in conjunction with a scoring system to numerically rank the chemicals for conventional developmental toxicity testing (York et al. 1988). Five indices of potential developmental toxicity were assigned point values that varied according to maternal mortality. These indices were the proportion of pregnant survivors that produced a litter of at least one live-born pup, average litter size and pup weight at birth, and average pup survival and weight gain to 3 d. This scoring method produced a high priority classification for further testing for DEA.
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	基本的な科学原理を満たしている許容できる文書化の良好な試験	Acceptable, well-documented study which meets basic scientific principles
出典		
引用文献(元文献)	(200) (201) (219)	(200) (201) (219)
備考		

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	供給源: Union Carbide Corp., North Seadrift, TX, USA 純度: >= 99.4%	Source: Union Carbide Corp., North Seadrift, TX, USA Purity: >= 99.4%
注釈		
方法		
方法／ガイドライン	その他: OECD 414相当	other: comparable to OECD 414
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 Crj: CD(SD)	rat Crj: CD(SD)
性別(雄:M、雌:F)	雌	female
投与量	150、380 (500)、1500 mg/kg体重	150, 380 (500), 1500 mg/kg bw
各用量群(性別)の動物数		
投与経路	経皮	dermal
試験期間		
交配前暴露期間		
試験条件	暴露期間: 妊娠6-15日 処置頻度: 6時間/日 対照群: あり、媒体対照	Exposure period : gestation day 6 -15 Frequency of treatm. : 6 h/day Control group : yes, concurrent vehicle

試験条件	※英文参照	METHOD FOLLOWED: Prenatal developmental toxicity study with dermal application in rats, comparable to OECD 414 GLP: No data ANALYTICAL METHODS: Concentration and homogeneity of the DEA dosing solutions were verified using a Hewlett-Packard 5880A gas chromatograph equipped with a flame ionization detector.
試験条件	※英文参照	Test condition : TEST ORGANISMS - Strain: Sexually mature, CD rats, supplier: Charles River Laboratories, Portage, MI, USA - Number: 25 females per group - Acclimatization: 2 weeks - Weight at mating: 209 – 251 g - Housing: individual, stainless-steel wire-mesh cages
試験条件	※英文参照	ADMINISTRATION / EXPOSURE: - Duration of test/exposure: from implantation through gestation day 15 - Treatment: Dermal: Diluted DEA or water (control) was administered daily directly to the backs (clipped free of hair). To apply DEA, the entire treatment site was covered initially with half of the calculated dosing volume and then the remainder of the dosing volume was applied. The dosing site was covered by sterilized gauze and then further occluded with polyvinyl film attached to a specially designed Lycra-Spandex jacket with Velcro closures. Approximately 6 h after dosing, the jacket and gauze were removed, and the dosing site was wiped gently with gauze dampened with warm water and blotted dry. - Control group and treatment: 4 ml/kg bw water - Vehicle: deionized water (Milli-Q) - Application volume: 4 ml/kg bw - Dose levels: 0, 150, 500, 1500 mg/kg bw (nominal): Due to a preparation error the mid dose had to be reduced to 380 mg/kg bw.
試験条件	※英文参照	MATING PROCEDURES: Virgin female rats were mated overnight with male rats (one female:one male). Evidence of vaginal or dropped copulation plugs was considered a sign of successful mating and the day on which such evidence was found was designated GD 0.
試験条件	※英文参照	PARAMETERS ASSESSED DURING STUDY: - Throughout the study, animals were observed daily for clinical signs indicative of altered health status. Animals were observed twice daily for evidence of skin irritation and clinical signs during the dosing period and once daily during the post-treatment period. Skin reactions were scored according to standards outlined by the Federal Hazardous Substances Act (16 CFR, Part 1500). - Maternal body weights were collected on GD 0, 6 (prior to the onset of dosing), 9, 12, 15, 18, 21 - Food consumption was measured at 3-day intervals from GD 0-21, - Prior to necropsy on GD 21 maternal blood samples were collected and evaluated for a variety of hematological parameters which included hematocrit, leukocyte, differential leukocyte, erythrocyte and platelet counts, mean corpuscular volume (MCV), hemoglobin, mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC). To collect these samples, rat dams were lightly anesthetized using methoxyflurane, and blood was obtained by orbital sinus puncture. - After blood collection, rat dams were sacrificed by carbon dioxide asphyxiation.
試験条件	※英文参照	- Maternal liver, kidney, and gravid uterine weights were collected. Ovarian corpora lutea were counted. Uterine horns were examined for the number and location of all live and dead fetuses, as well as resorption and Implantation sites. - All live fetuses were weighed and examined externally for variations and malformations, including cleft palate. Rat fetuses were examined externally for sex determination and approximately 50% of live rat fetuses in each litter were examined for thoracic and abdominal visceral abnormalities by a modification of the Staples' method (1974). In order to evaluate craniofacial structures, the heads of these fetuses were removed, placed in Bouin's fixative, and then sectioned according to methods modified from Wilson (1965). Approximately 50% of live rat fetuses (intact fetuses not used for Bouin's examination) were processed for skeletal staining with Alizarin Red S (Crary, 1962; Peltzer and Schardein, 1966) and were examined for skeletal malformations and variations. When classifying fetal alterations as "variations" or "malformations," the definitions outlined by the Middle Atlantic Reproduction and Teratology Society (MARTA, 1997) were applied.

統計学的処理	※英文参照	Statistical Analysis Continuous variables were compared for homogeneity of variance using Levene's test for equal variances (Levene, 1960). A parametric or nonparametric analysis of variance (ANOVA) was performed , f parametric ANOVA analyses were significant, pooled T-tests were used for pairwise comparisons. If results from a nonparametric ANOVA were significant, separate variance T tests for pairwise comparisons were performed. Data from nongravid females and females delivering early were not included in the statistical analyses. Nonparametric data were statistically evaluated using the Kruskal-Wallis test, followed by the Mann Whitney U test. Incidence data were compared using the Fisher's exact test (Sokal and Rohlf, 1969), with the exception of frequency data for fetal malformations and variations, statistical analyses were performed using BMDP Statistical Software (Dixon, 1990). For all statistical tests, the critical level of significance was set a priori at a = 0.05 (two-tailed).
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	-濃度: DEAの濃度は設定値の100.7～101.7%の範囲であった。	- Concentrations: DEA concentrations ranged from 100.7 to 101.7% of target.
注釈	用量レベルごとの母動物の毒性影響: -体重のデータ: 1500 mg/kg体重の母動物は投与期間の最後及び投与後の期間(妊娠15-21日)に体重増加量の有意な低下を示した。これは妊娠子宮重量で補正した場合に4.5%の体重の減少に対応した。異なる時点で体重増加量に有意差が示されたが、試験期間全体 (妊娠0-21日)にわたり用量群間で体重増加量に有意な差はなかった。150及び380(500) mg/kg/日ではいずれの時間間隔での母親の体重増加量にも投与に関連した減少はみられなかった。 -摂餌量:　無影響 -臨床症状: 380 (500)及び1500 mg/kg体重では皮膚刺激の徴候がみられ、頻度及び程度は用量依存的であった。高用量ではこの状態が投与後の期間まで持続した。150 mg/kg体重では皮膚刺激への有意な影響はみられなかった。対照群の動物には皮膚刺激はみられなかった。	MATERNAL TOXIC EFFECTS BY DOSE LEVEL: - Body weight data: Dams at 1500 mg/kg bw showed significant declines in body weight gains at the end of the dosing period and during the post-dosing period (GD 15-21). This corresponded with a 4.5% decrease in body weight, when corrected for gravid uterine weight. Despite significant differences in body weight gain at discrete time points, there was no significant difference in body weight gains across dose groups over the entire duration of the study (GD 0-21). At 150 and 380 (500) mg/kg/day, there were no treatment-related declines in maternal weight gain at any time interval. - Food consumption: no effect - Clinical signs: At 380 (500) and 1500 mg/kg bw signs of skin irritation, which were dose-dependent in incidence and severity). At the high dose, this condition persisted into the post-treatment period. No significant effects on skin irritation were observed at 150 mg/kg bw. No skin irritation was observed in control animals.
注釈	終了時の母動物の検査: -母動物の生殖データ: DEAの投与は試験したいずれの投与レベルにおいても、妊娠率、黄体数、着床数、同腹児数、死亡胎児数、胎児体重、胎児の性比、又は妊娠子宮重量に影響を生じなかった。 -血液検査: DEAは全ての濃度でヘマトクリット、MCV、MCH、ヘモグロビン濃度、及び赤血球数を含む赤血球パラメータを軽度に減少させた。DEAの最高用量レベルは白血球数及びリンパ球数の増加を生じたが、血小板数を減少させた。全投与群の試験動物で赤血球形態のプロフィルにおける変化 (異型赤血球増加、赤血球大小不同、多染性)が観察された。 -臓器重量: 腎臓の絶対及び相対重量の用量依存的な増加380 (500)及び1500 mg/kg/日で示された。肝臓重量は絶対及び相対重量のいずれも有意な変化はみられなかった。	EXAMINATION OF THE DAMS AT TERMINATION: - Reproduction data of dams: DEA administration had no effect on pregnancy rate, corpora lutea number, implantation number, litter size, resorption rate, number of dead fetuses, fetal body weight, fetal sex ratio, or gravid uterine weight at any of the dose levels tested. - Hematology: DEA slightly decreased red blood cell parameters, including hematocrit, MCV, MCH, hemoglobin concentration, and erythrocyte number at all concentrations. The highest dose level of DEA produced increased numbers of leukocytes and lymphocytes, but decreased platelet numbers. Changes in the profile of red cell morphology (poikilocytosis, anisocytosis, polychromasia) were observed in treated animals from all dose groups. - Organ weights: Dose dependent increases in both absolute and relative kidney weights at the 380 (500) and 1500 mg/kg/day dose levels. No significant changes in absolute or relative liver weights were observed.

注釈	胎児の検査: ラットの胎児には外表、内臓、又は骨格の奇形又は変異の全体的な頻度への影響はみられなかった。全体の頻度に差はなかったが、1500 mg/kg体重群の腹は6つの特異的な骨格変化の頻度の有意な増加を示した。これらの変化は主に骨化遅延からなった。「全ての近接した後肢の指の未骨化」の頻度の上昇は「いくつかの近接した後肢の指の骨化不全」の腹の頻度における有意な逆の減少と対応した。1500 mg/kg体重群では「いくつかの前肢の中手骨の骨化不全」を示した腹の頻度の増加もみられた。150又は380 (500) mg/kg体重ではいずれの発生パラメータにも影響はみられなかった。	EXAMINATION OF FETUSES: No effect on the overall incidence of external, visceral, or skeletal malformations or variations observed in rat fetuses. Although there was no difference in the overall incidence, litters from the 1500 mg/kg bw group had significantly increased incidences of six specific skeletal alterations. These alterations consisted primarily of delays in ossification. An elevated incidence of "all proximal hindlimb phalanges unossified corresponded with significant reciprocal reductions in litter frequency for "some proximal hindlimb phalanges poorly ossified." There was also an increase in the litter incidence of "some forelimb metacarpals poorly ossified" in the 1500 mg/kg bw group. There was no effect on any of there developmental parameters at 150 or 380 (500) mg/kg bw.
注釈	母動物、腹、胎児のデータ - CDラットにおける出生前発生毒性 (経皮)試験 mg/kg体重 0 150 380(500) 1500 例数 25 25 25 25 妊娠動物 23 24 25 22 死亡例 0 0 0 0 BWG 妊娠6-15、g 49 51 50 45 補正 BW、g 307 308 308 294 皮膚刺激 0 0 1 10 RBC 6.22 6.01 5.95 5.69** HGB 11.7 11.1 11.0* 10.3** HCT 34.2 32.4* 32.2* 30.1** MCV 55.1 54.0* 54.2* 53.1** MCH 18.7 18.3* 18:4 18.0** 腎臓絶対重量、 g 1.96 2.01 2.13** 2.24** % 腎臓重量 0.64 0.65 0.69** 0.77** 妊娠子宮重量、 g 116 119 114 118 黄体数 (平均値) 18.8 17.1 17.5 17.4 着床数 (平均値) 16.2 16.3 15.6 16.1 % 吸収胚 5.4 5.4 4.6 4.2 生存胎児数 (平均値) 15.3 15.4 14.8 15.4 胎児重量、g 5.4 5.5 5.5 5.4	Maternal, litter, fetal data - prenatal developmental toxicity (dermal) study in CD rats mg/kg bw 0 150 380(500) 1500 N 25 25 25 25 Pregnant 23 24 25 22 Mortality 0 0 0 0 BWG GD 6-15, g 49 51 50 45 Corrected BW, g 307 308 308 294 Skin irritation 0 0 1 10 RBC 6.22 6.01 5.95 5.69** HGB 11.7 11.1 11.0* 10.3** HCT 34.2 32.4* 32.2* 30.1** MCV 55.1 54.0* 54.2* 53.1** MCH 18.7 18.3* 18:4 18.0** Kidney weight absolute, g 1.96 2.01 2.13** 2.24** % kidney weight 0.64 0.65 0.69** 0.77** Gravid uterus, g 116 119 114 118 Corpora lutea (mean) 18.8 17.1 17.5 17.4 Implantation (mean) 16.2 16.3 15.6 16.1 % Resorption 5.4 5.4 4.6 4.2 Live fetuses (mean) 15.3 15.4 14.8 15.4 Fetal weight, g 5.4 5.5 5.5 5.4
注釈	総外表奇形 (胎児/腹) 0/0 0/0 0/0 0/0 総外表変異 (胎児/腹) 50/21 57/22 61/22 47/19 総軟組織奇形 (胎児/腹) 5/4 3/3 9/7 10/8 総軟組織変異 (胎児/腹) 95/22 97/24 110/25 114/20 総骨格奇形 (胎児/腹) 1/1 0/0 0/0 0/0 総骨格変異 (胎児/腹) 171/23 179/24 180/25 163/22 胎児 (腹)の数として表された鍵となる骨格変異の頻度: 中心頸椎 (No.5)の骨化不全:: 25(13) 35(16) 26(14) 38(19)* 中心胸椎 (No.10)の骨化不全: 1(1) 1(1) 6(5) 7(7)* 頭頂骨の骨化減少: 7(3) 5(4) 10(6) 44(13)** 全ての近接した指骨 (後肢)の骨化不全: 71(17) 84(19) 104(23) 105(22)* いくつかの中手骨 (前肢)の骨化不全: 0(0) 0(0) 2(2) 4(4)* BWG = 体重増加量、* p<0.05 **p<0.01	Total external malformations (fetus/litter) 0/0 0/0 0/0 0/0 Total external variations (fetus/litter) 50/21 57/22 61/22 47/19 Total soft tissue malformations (fetus/litter) 5/4 3/3 9/7 10/8 Total soft tissue variations (fetus/litter) 95/22 97/24 110/25 114/20 Total skeletal malformations (fetus/litter) 1/1 0/0 0/0 0/0 Total skeletal variations (fetus/litter) 171/23 179/24 180/25 163/22 Incidences for key skeletal variations expressed as No. of fetus (litter): Cervical centrum (No.5) poorly ossified: 25(13) 35(16) 26(14) 38(19)* Thoracic centrum (No.10) poorly ossified: 1(1) 1(1) 6(5) 7(7)* Parietal, reduced ossification: 7(3) 5(4) 10(6) 44(13)** all proximal phalanges (hindlimb) poorly ossified: 71(17) 84(19) 104(23) 105(22)* some metacarpals (forelimb) poorly ossified: 0(0) 0(0) 2(2) 4(4)* BWG = body weight gain, * p<0.05 **p<0.01
結論		
Pに対するNOAEL (NOEL)又はLOAEL (LOEL)	LOAEL 母動物毒性 : = 150 - mg/kg体重	LOAEL Maternal Toxicity : = 150 - mg/kg bw
F1に対するNOAEL (NOEL)又はLOAEL (LOEL)	NOAEL 催奇形性 : > 1500 - mg/kg体重	NOAEL teratogen. : > 1500 - mg/kg bw
F2に対するNOAEL (NOEL)又はLOAEL (LOEL)		
注釈	結論 : DEAが妊娠6-15日に0、150、500及び1500 mg/kg体重の濃度で妊娠CDラットに投与された。 500及び1500 mg/kg体重で、それぞれ中等度及び重度の皮膚刺激が生じた。1500 mg/kg体重では母親の体重増加量は減少した。腎臓の絶対及び相対重量は500及び1500 mg/kg体重で増加した。貧血、異常な赤血球の形態 (異型赤血球増加、赤血球大小不同、多染性)及び血小板数の減少を含む血液学的な影響が全投与群で観察された。1500 mg/kg体重群はリンパ球及び総白血球数の増加も示した。	Conclusion : DEA was administered to pregnant CD rats from gestation day 6 through day 15 at concentration of 0, 150, 500 and 1500 mg/kg bw. At 500 and 1500 mg/kg bw moderate and severe skin irritation was caused, respectively. Maternal body weight gain was decreased in the 1500 mg/kg bw. Absolute and relative kidney weights were increased at 500 and 1500 mg/kg bw. Hematological effects including anemia, abnormal red cell morphology (poikilocytosis, anisocytosis, polychromasia), and decreased platelet count were observed in all treatment groups. The 1500 mg/kg bw group also had increased lymphocytes and total leukocytes.

注釈	胎児には体重又は外表、内臓、又は骨格の奇形/異常の頻度への投与による影響はなかった。中心軸の骨格及び遠位の付属骨を含む6つの骨格変異の頻度の増加が1500 mg/kg体重群の腹にみられた。骨格変異は頭頂骨、中心頸椎#5、及び中心胸椎#10の骨化不全、全ての近接した後肢の指骨及びいくつかの前肢の中手骨、及び癒合した肋骨の骨化の欠如を含んでいた。	In the fetuses, there were no effects of treatment on body weight or on incidence of external, visceral, or skeletal malformations/abnormalities. Increased incidences of six skeletal variations involving the axial skeleton and distal appendages were observed in litters from the 1500 mg/kg bw group. The skeletal variations included poor ossification in the parietal bones, cervical centrum #5, and thoracic centrum #10, lack of ossification in all proximal hindlimb phalanges and some forelimb metacarpals, and callused ribs.
注釈	従って、母動物毒性に対するLOAELは150 mg/kg体重であり、一方、出生前発生毒性に対するNOAELは500 mg/kg体重群での投与の矛盾のため380 mg/kg体重に調整された。催奇形性に対するNOAELは > 1500 mg/kg体重であった。このように、出生前の発生毒性の兆候が明らかに母動物毒性用量レベルでのみ生じた。	Consequently, the LOAEL for maternal toxicity was 150 mg/kg bw, while the NOAEL for prenatal developmental toxicity was adjusted to 380 mg/kg bw due to dosing discrepancy at the 500 mg/kg bw group. The NOAEL for teratogenicity was >1500 mg/kg bw. Thus, signs of prenatal developmental toxicity did only occur at clearly maternal toxic dose levels.
注釈	注釈 : 様々な用量群におけるラットは妊娠12-15日にはDEAの総量を投与されなかった。期待された用量の恐らく10-24%不足した量が投与され、最大の差異は500 mg/kg体重投与群で妊娠13日にみられた。投与量の最大限の不足 (24%)を考慮すると、500 mg/kg体重投与群はDEAに対する途中の暴露量はこの期間中は(150及び1500 mg/kg/日群と比較して)約380 mg/kg体重のなお投与されていた。従って、用量反応相関性は維持された。	Remark : Rats in various dose groups did not receive the total volume of DEA during dosing on GD 12-15. There was a possible 10-24% deficit in the expected doses delivered with the greatest difference seen in the 500 mg/kg bw dose group on GD 13. Assuming the maximum deficit in dose delivery (24%), the 500 mg/kg bw dose group still received an intermediate exposure to DEA about 380 mg/kg bw (relative to the 150 and 1500 mg/kg/day group) during this period; therefore, dose-response relationships were maintained.
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	基本的な科学原理を満たしている許容できる文書化の良好な試験	Acceptable, well-documented study which meets basic scientific principles
出典		
引用文献(元文献)	(220) (221) (222)	(220) (221) (222)
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

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	供給源: Union Carbide Corp., North Seadrift, TX, USA 純度: >= 99.4%	Source: Union Carbide Corp., North Seadrift, TX, USA Purity: >= 99.4%
注釈		
方法		
方法／ガイドライン	その他: OECD 414相当	other: comparable to OECD 414
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)	ウサギ ニュージーランド白色	rabbit New Zealand white
性別(雄:M、雌:F)	雌	female
投与量	35、100、350 mg/kg体重	35, 100, 350 mg/kg bw
各用量群(性別)の動物数		
投与経路	経皮	dermal
試験期間		
交配前暴露期間		
試験条件	暴露期間: 妊娠6-18日 処置頻度: 6時間/日 対照群: あり、媒体対照	Exposure period : gestation days 6 - 18 Frequency of treatm. : 6 h /day Control group : yes, concurrent vehicle
試験条件	※英文参照	METHOD FOLLOWED: Prenatal developmental toxicity study with dermal application in rabbits, comparable to OECD 414 GLP: No data ANALYTICAL METHODS: Concentration and homogeneity of the DEA dosing solutions were verified using a Hewlett-Packard 5880A gas chromatograph equipped with a flame ionization detector.
試験条件	※英文参照	Test condition : TEST ORGANISMS Hazleton Research Products, Inc., Denver, PA, USA - Number: 15 females per group - Acclimatization: 2 weeks - Weight at mating: 2959 - 4414 g - Housing: individual, stainless-steel wire-mesh cages

試験条件	※英文参照	ADMINISTRATION / EXPOSURE: - Duration of test/exposure: from implantation through gestation day 18 - Treatment: Dermal: Diluted DEA or water (control) was administered daily directly to the backs (clipped free of hair). To apply DEA, the entire treatment site was covered initially with half of the calculated dosing volume and then the remainder of the dosing volume was applied. The dosing site was covered by sterilized gauze and then further occluded with polyvinyl film attached to a specially designed Lycra-Spandex jacket with Velcro closures. Approximately 6 h after dosing, the jacket and gauze were removed, and the dosing site was wiped gently with gauze dampened with warm water and blotted dry. Several females had mating bites or scratches within the designated treatment area. These lesions were noted at the onset of the study. Whenever possible, direct application of test compound to these lesions was avoided, but complete avoidance of these areas was impossible due to their location and the occlusion techniques used. - Control group and treatment: 2 ml/kg bw water - Vehicle: deionized water (Milli-Q) - Application volume: 2 ml/kg bw - Dose levels: 0, 35, 100, 350 mg/kg bw (nominal)
試験条件	※英文参照	MATING PROCEDURES: Virgin female rabbits were mated overnight with male rabbits (1 female:2 males). The day of coitus was designated GD 0. PARAMETERS ASSESSED DURING STUDY: - Throughout the study, animals were observed daily for clinical signs indicative of altered health status. Animals were observed twice daily for evidence of skin irritation and clinical signs during the dosing period and once daily during the post-treatment period. Skin reactions were scored according to standards outlined by the Federal Hazardous Substances Act (16 CFR, Part 1500). - Maternal body weights were collected on GD 0, 6 (prior to the onset of dosing), 9, 12, 15, 24, 29. - Food consumption: daily - Prior to necropsy on GD 29 maternal blood samples were collected and evaluated for a variety of hematological parameters which included hematocrit, leukocyte, differential leukocyte, erythrocyte and platelet counts, mean corpuscular volume (MCV), hemoglobin, mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC). Blood was obtained from an ear artery.
試験条件	※英文参照	- After blood collection, rabbit dams were euthanized after blood collection by lethal injection of sodium pentobarbital into the marginal ear vein. - Maternal liver, kidney, and gravid uterine weights were collected. Ovarian corpora lutea were counted. Uterine horns were examined for the number and location of all live and dead fetuses, as well as resorption and Implantation sites. - All live fetuses were weighed and examined externally for variations and malformations, including cleft palate. The fetuses in each litter were examined internally for determination of gender and for thoracic and abdominal visceral abnormalities. Heads from approximately one-half of the live rabbit fetuses were fixed in Bouin's solution and evaluated by cranial serial sectioning for craniofacial structures (Van Julsingha and Bennet, 1977). All live rabbit fetuses (50% intact, 50% decapitated) were processed for skeletal staining with Alizarin Red S (Crary, 1962; Peltzer and Schardein, 1966) and were examined for skeletal malformations and variations. When classifying fetal alterations as "variations" or "malformations," the definitions outlined by the Middle Atlantic Reproduction and Teratology Society (MARTA, 1997) were applied.
統計学的処理	※英文参照	Statistical Analysis Continuous variables were compared for homogeneity of variance using Levene's test for equal variances (Levene, 1960). A parametric or nonparametric analysis of variance (ANOVA) was performed , f parametric ANOVA analyses were significant, pooled T-tests were used for pairwise comparisons. If results from a nonparametric ANOVA were significant, separate variance T tests for pairwise comparisons were performed. Data from nongravid females and females delivering early were not included in the statistical analyses. Nonparametric data were statistically evaluated using the Kruskal-Wallis test, followed by the Mann Whitney U test. Incidence data were compared using the Fisher's exact test (Sokal and Rohlf, 1969), with the exception of frequency data for fetal malformations and variations, statistical analyses were performed using BMDP Statistical Software (Dixon, 1990). For all statistical tests, the critical level of significance was set a priori at a = 0.05 (two-tailed).
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	-濃度: DEAの濃度は設定値の94.4-98.2%の範囲であった。	- Concentrations: DEA concentrations ranged from 94.4 to 98.2% of target.
注釈	用量レベルごとの母動物毒性影響: -体重のデータ: 投与期間中、100及び350 mg/kg体重投与群では妊娠期の体重増加量が全体的に減少した。最高用量では体重増加量は投与後の期間に減少した。 -摂餌量: 投与期間の妊娠17及び18日、及び投与後の4日間、350 mg/kg体重群で摂餌量は低下した。 -臨床症状: DEAの投与期間及びその後の回復期間ともに350 mg/kg体重では皮膚の傷害及び刺激が観察された。35又は100 mg/kg/日を投与したウサギでは皮膚の刺激又は傷害の頻度に感知可能な変化はなかった。ミリQ水対照群には皮膚刺激はみられなかった。	MATERNAL TOXIC EFFECTS BY DOSE LEVEL: - Body weight data: There was an overall decrease in gestational body weight gains in the 100 and 350 mg/kg bw dose groups during the treatment period. At the highest dose, weight gain was decreased during the post-treatment period. - Food consumption: On GD 17 and 18 of the treatment period and for 4 days subsequent to treatment, food consumption was reduced in the 350 mg/kg bw group. - Clinical signs: Skin lesions and irritation were observed in the 350 mg/kg bw group during both the DEA treatment period and the subsequent recovery period. There were no perceptible changes in skin irritation or lesion frequency in rabbits administered 35 or 100 mg/kg/day. Skin irritation was not observed in the Milli-Q water control group.
注釈	終了時の母動物の検査: -母動物の生殖データ: 生殖パラメータには有意な影響はみられなかった。350 mg/kg体重群の母動物1匹が妊娠14-15日以降摂餌量が激減し、妊娠27日に流産した。この動物は剖検で腎臓の色調の変化及び肝臓の全葉の網目状模様を示した。100 mg/kg/日群の母動物1匹は早期吸収を示した胎児の着床部位が1箇所しか有していなかった。 -血液検査: 試験したDEA投与量のいずれにおいても血液パラメータに有意な変化はみられなかった。 -肉眼病理検査及び臓器重量: 高用量では処置した母ウサギの50%が腎臓の色調の変化を示したのに対し、対照群のウサギでは17%であった。統計的に有意ではないが、肝臓の絶対及び相対重量、及び腎臓の相対重量の増加がみられた。	EXAMINATION OF THE DAMS AT TERMINATION: - Reproduction data of dams: There were no significant effects on reproductive parameters. One dam from the 350 mg/kg bw group aborted her litter on GD 27, an outcome which followed a sharp decline in food consumption beginning on GD 14-15. At necropsy, this animal had color changes in the kidneys and a reticular pattern in all hepatic lobes. One dam from the 100 mg/kg/day group had a single implantation site with a fetus that had undergone early resorption. - Hematology: There were no significant changes in hematological parameters at any of the DEA doses tested. - Gross pathology and organ weights: At the high dose, 50% of treated rabbit dams exhibited color changes in the kidneys compared with 17% in control rabbits. Although not statistically significant, absolute and relative liver weights and relative kidney weights were increased.
注釈	胎児の検査: ウサギの胎児には外表、内臓、又は骨格の奇形又は変異の全体的な頻度に影響はなかった。350 mg/kg体重群では奇形により多い多様性がみられたが、これらの奇形 (卵形のレンズ、総動脈幹、心室中核欠損、横隔膜ヘルニア、No.8の過剰腰椎、No.8の両側性過剰腰椎弓、尾節No.2での骨島、及び胸骨分節の二重重複、奇形及び癒合)の多くは同一の胎児で生じていた。さらに、高用量DEA群の奇形の全体的な頻度 (胎児の4.5%、腹の30.8%)は対照群の動物の頻度 (胎児の6.7%、腹の25.0%)と同程度であった。観察された53種の異なる胎児の骨格変異のうち、頭頂骨の骨化不全のみが350 mg/kg/日投与群で統計的に増加した。しかし、頭部の骨化遅延には一貫した用量依存的なプロフィルはみられなかった。	EXAMINATION OF FETUSES: No effect on the overall incidence of external, visceral, or skeletal malformations or variations observed in rabbit fetuses. Although there was a greater variety of malformations in the 350 mg/kg bw group, many of these malformations (ovoid lenses; common truncus; ventricular septal defect; herniated diaphragm; extra lumbar centrum No. 8; extra bilateral lumbar arch No. 8; bone island at caudal segment No. 2; and duplicated, misshaped, and fused sternebrae) occurred in the same fetus. Furthermore, the overall incidence of malformations in the high dose DEA group (4.5% of fetuses, 30.8% of litters) was similar to the incidence seen in control animals (6.7% of fetuses, 25.0% of litters). Of the 53 different fetal skeletal variations observed, only the occurrence of poorly ossified interparietal was statistically increased in the 350 mg/kg/day dose group. However, a consistent, dose-dependent profile of delayed ossification in the head region was not observed.

注釈	母動物、腹、胎児のデータ － ニュージランド白色ウサギにおける出生前発生毒性（経皮）試験 mg/kg体重 0 35 100 350 N 15 15 15 15 妊娠動物 12 14 14 14 死亡例 0 0 0 0 BWG 妊娠6-18, g 59 98 12 -5.6 FC 妊娠6-18, g 164 175 160 152 皮膚刺激 0 0 0 10 妊娠子宮重量、 g 528 562 513 542 黄体数 （平均値） 9.6 9.8 9.1 9.5 着床数 （平均値） 8.0 8.7 8.0 9.1 % 吸収胚 16.7 7.1 21.4 23.1 生存胎児数 （平均値） 7.5 8.6 7.7 8.5 胎児重量、g 44 44 43 40	Maternal, litter, fetal data - prenatal developmental toxicity (dermal) study in New Zealand White rabbits mg/kg bw 0 35 100 350 N 15 15 15 15 Pregnant 12 14 14 14 Mortality 0 0 0 0 BWG GD 6-18, g 59 98 12 -5.6 FC GD 6-18, g 164 175 160 152 Skin irritation 0 0 0 10 Gravid uterus, g 528 562 513 542 Corpora lutea (mean) 9.6 9.8 9.1 9.5 Implantation (mean) 8.0 8.7 8.0 9.1 % Resorption 16.7 7.1 21.4 23.1 Live fetuses (mean) 7.5 8.6 7.7 8.5 Fetal weight, g 44 44 43 40
注釈	総外表奇形（胎児/腹） 1/1 0/0 0/0 1/1 総外表変異（胎児/腹） 0/0 0/0 0/0 0/0 総軟組織奇形（胎児/腹） 4/1 9/4 5/3 2/2 総軟組織変異（胎児/腹） 19/12 30/9 28/10 35/13 総骨格奇形（胎児/腹） 1/1 1/1 2/2 3/3 総骨格変異（胎児/腹） 90/12 120/14 108/13 111/13 BWG = 体重増加量、FC = 摂餌量、* p<0.05 **p<0.01	Total external malformations (fetus/litter) 1/1 0/0 0/0 1/1 Total external variations (fetus/litter) 0/0 0/0 0/0 0/0 Total soft tissue malformations (fetus/litter) 4/1 9/4 5/3 2/2 Total soft tissue variations (fetus/litter) 19/12 30/9 28/10 35/13 Total skeletal malformations (fetus/litter) 1/1 1/1 2/2 3/3 Total skeletal variations (fetus/litter) 90/12 120/14 108/13 111/13 BWG = body weight gain, FC = food consumption, * p<0.05 **p<0.01
結論		
Pに対するNOAEL (NOEL)又はLOAEL (LOEL)	NOAEL 母動物毒性 : = 35 - mg/kg 体重	NOAEL maternal tox. : = 35 - mg/kg bw
F1に対するNOAEL (NOEL)又はLOAEL (LOEL)	NOAEL 催奇形性 : > 350 - mg/kg 体重	NOAEL teratogen. : > 350 - mg/kg bw
F2に対するNOAEL (NOEL)又はLOAEL (LOEL)		
注釈	結論 : DEAを0、35、100及び350 mg/kg体重の濃度で妊娠6-18日までニュージーランド白色妊娠ウサギに投与した。 350 mg/kg体重での母親ウサギは顕著な皮膚刺激、摂餌量低下、及び腎臓の色調変化のいくつかの症状を示したが、血液学的な変化は示さなかった。体重増加量は100 mg/kg体重で低下した。 妊娠パラメータには障害はみられなかった。	Conclusion : DEA was administered to pregnant New Zealand White rabbits from gestation day 6 through day 18 at concentration of 0, 35, 100 and 350 mg/kg bw. Rabbit dams at 350 mg/kg bw showed several signs of marked skin irritation, reduced food consumption, and color changes in the kidneys but no hematological changes. Body weight gain was reduced at 100 mg/kg bw. There was no impairment of gestational parameters.
注釈	発生毒性の証拠はいずれの用量レベルでも観察されず、特に、外表、内臓又は骨格の異常の頻度には明らかな影響はみられなかった。 従って、母動物毒性に対するNOAELは35 mg/kg体重で、催奇形性を含めた出生前発生毒性に対するNOAELは >350 mg/kg体重であった。	No evidence of developmental toxicity was observed at any dose level, especially, there were no apparent effects of treatment on the incidences of external, visceral, or skeletal abnormalities. Consequently, the NOAEL for maternal toxicity was 35 mg/kg bw, the NOAEL for prenatal developmental toxicity including teratogenicity was >350 mg/kg bw.
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	基本的な科学原理を満たしている許容できる文書化の良好な試験	Acceptable, well-documented study which meets basic scientific principles
出典		
引用文献（元文献）	(220) (221)	(220) (221)
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

試験物質名		
CAS番号		
純度等		
注釈		
方法		
方法／ガイドライン	タイプ : 生化学又は細胞の相互作用	Type : Biochemical or cellular interactions
GLP適合		
試験を行った年		
試験条件	※英文参照	Test condition : TEST ORGANISMS: - Species/Strain: male Sherman or Wistar rats ADMINISTRATION / EXPOSURE - Application: Male rats received DEA either by single gavage or by repeated dietary application for 7 or 12 days. The phospholipids of the liver (PL) were examined by means of P32-labelling. - Application route: oral (gavage) or diet - Dose levels: 100 mg/kg bw (oral, gavage) or 5000 ppm (diet)
結果		

結果	結果 : Wistar又はShermanラットをジエタノールアミンで処置すると肝臓のリン脂質の生成増加を生じた。これらの異常なリン脂質は天然の類似体よりも遅い速度で代謝され、投与期間の延長により肝臓に蓄積した。 DEAの大量単回投与により肝臓のリン脂質 (コリン及び非コリン)の生成が増加した。しかし、DEAを餌に単独で混ぜてより長期間ラットに与えた場合には非コリン含有リン脂質の顕著な増加とともにコリン含有リン脂質の生成の減少がみられた。DEAは脂質のリン酸化を促進することが示された。	Result : Treatment of Wistar or Sherman rats with diethanolamine caused increased formation of hepatic phospholipids. These atypical phospholipids are metabolized at a slower rate than their natural analogs, and prolonged administration results in their accumulation in liver. A single large dose of DEA produced an increase in the formation of liver phospholipids (choline and noncholine). However, when DEA was fed alone in the diet to rats for longer periods of time, a decrease in the formation of choline-containing phospholipids was observed with a marked increase in the noncholine-containing phospholipids. DEA was shown to stimulate lipid phosphorylation.
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	基本的な科学原理を満たしている試験	Study which meets basic scientific principles
出典		
引用文献(元文献)	(248)	(248)
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	タイプ : 生化学又は細胞の相互作用	Type : Biochemical or cellular interactions
GLP適合		
試験を行った年		
試験条件		
結果		
結果	注釈 : 肝臓組織におけるホスファチジルコリン及び-エタノールアミンのin vitro合成の阻害の Ki=3mM (315.5 mg/l)以上であった。リン脂質への取込みは、Km=11.6mM (1219 mg/l) 及び Vmax=21nmol(2.21ug)/mg 蛋白/60 分 であった。	Remark : Inhibition of in vitro synthesis of phosphatidylcholine and -ethanolamine in liver tissues from Ki=3mM (315.5 mg/l) onwards. Incorporation in phospholipids at Km=11.6mM (1219 mg/l) and Vmax=21nmol(2.21ug)/mg protein/60 min.
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	許容でき、基本的な科学原理を満たしている試験	Acceptable, study which meets basic scientific principles
出典		
引用文献(元文献)	(249)	(249)
備考		

試験物質名		
CAS番号		
純度等	ジエタノールアミン 供給源: J. T. Baker Chemical Company, USA 純度: 供給された通りで使用	Diethanolamine Source: J. T. Baker Chemical Company, USA Purity: used as supplied
注釈		
方法		
方法／ガイドライン	タイプ : 生化学又は細胞の相互作用	Type : Biochemical or cellular interactions
GLP適合		
試験を行った年		
試験条件	※英文参照	Method : METHOD FOLLOWED: In vitro and in vivo investigations for effects on hepatic and renal mitochondrial functions and structures in male Sprague-Dawley rats GLP: No STATISTICAL METHODS: Analysis of variance and Student's t-test
試験条件	※英文参照	Test condition : ADMINISTRATION / EXPOSURE / EAXAMINATIONS: Hepatic mitochondria were isolated according to the method of Barbee et al., 1974. The respiratory rate, acceptor control ratio and ADP/O for hepatic mitochondria were determined using a Model 53 oxygen electrode system. Outer membrane permeability was examined according to Wattiaux-DeConnock and Wattiaux, 1971 by investigating cytochrome c. Inner membrane permeability was examined according to the method of Byard et al., 1975 by assaying oxygen consumption using NADH. Examination of in vitro and in vivo effects on hepatic mitochondria: Doses: in vitro: 5mM in vivo: acute: 490 mg/kg bw Protein measurement: The protein content was investigated according to the method of Lowry et al., 1951
結果		

結果	結果 ： In vitro： 5 mMのDEAは肝ミトコンドリアの機能を変化しなかった。 急性投与： 490 mg/kg体重の単回経口投与ではミトコンドリアの機能への影響は生じなかった。	Result : In vitro: 5 mM DEA did not alter hepatic mitochondrial function. Acute treatment: Single oral administration of 490 mg/kg bw had no effect on mitochondrial function.
結論		
結論	結論 ： DEAを 3 mg/mlで24時間単回経口投与したが、ミトコンドリアの機能に変化はなく、ミトコンドリアをin vitroでDEAと処置しても影響を示さなかった。	Conclusion : Single oral ingestion of DEA for 24 hr at 3 mg/ml resulted in no alteration of mitochondrial function and in vitro treatment of mitochondria with DEA was without effect.
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	許容でき、基本的な科学原理を満たしている文書化の良好な試験	Acceptable, well-documented study which meets basic scientific principles
出典		
引用文献(元文献)	(184) (185) (186)	(184) (185) (186)
備考		

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	供給源: BASF AG, Ludwigshafen, Germany から入手したジエタノールアミン	Source: Diethanolamine from BASF AG, Ludwigshafen, Germany
製造／加工／使用情報		
研究デザイン	経験のタイプ ： その他：金属加工液でのヒトパッチテストの結果	Type of experience : other: Human patch testing results with metal working fluids
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	注釈： 刺激性及びアレルギー性接触皮膚炎の両方を生じる13種の良く用いられる水をベースにした金属加工液 (MWF)の成分が選択され、現在又は過去にMWFへの職業暴露を受けた233名の皮膚炎患者を対象に5つのセンターでパッチテストが行われた。 174名のパッチテストを受けた皮膚炎患者のうち1名のみ (すなわち、06%)がワセリン中2%のDEA調製品を用いた誘発刺激で陽性反応を示した。	Remark : 13 frequently used water based metal working fluids (MWF) components which may cause both irritant and allergic contact dermatitis, were selected and patch tested in 5 centres on 233 dermatitis patients with present or past occupational exposure to MWF. Only one person out of 174 (i. e. 0.6%) patch tested dermatitis patients showed a positive skin reaction towards the challenge with a 2% DEA preparation in vaseline.
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	基本的な科学原理を満足する文書化の良好な試験	Well-documented study which meets basic scientific principles
出典		
引用文献(元文献)	(224)	(224)
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 ： ヒトー疫学	Type of experience : Human – Epidemiology
仮説検証		
データ収集方法	※英文参照	Method : Historical cohort: UAW/GM, 1941–1985 Population: >45,000 workers from 3 auto-part manufacturing facilities (Plants I, II, and III) employed at least 3 years from 1920–1985. Vital status obtained through Social Security Administration and National Death Index; cause of death ascertained from UA W records and death certificates (>10,000 deaths). Exposure: Metalworking fluids (straight oil, soluble, and synthetic); use of synthetic fluids expanded in mid 1970s.
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	注釈: ヒトのがんとDEAへの特異的な暴露との相関性について報告した研究はない。にもかかわらず、エタノールアミンは1950年代以来ある種の金属加工液に共通して添加され、金属加工液（切断液としても知られる)に暴露された作業者で発がん性を評価した多くの研究例がある。 結果: 特殊な金属加工液に対して影響は示されなかった。	Remark : No studies have been reported on the relationship between human cancer and exposure specifically to DEA. Nevertheless, ethanolamines commonly have been added to certain types of metalworking fluids since the 1950s, and numerous studies have evaluated cancer in workers exposed to metalworking fluids (also known as cutting fluids). Result : No effects given for specific types of metalworking fluids.
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	基本的な科学原理を満足する文書化の良好な試験	Well-documented study which meets basic scientific principles
出典		
引用文献(元文献)	(225)	(225)
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：ヒトー疫学	Type of experience : Human – Epidemiology
仮説検証		
データ収集方法	※英文参照	Method : Historical cohort: Extended follow-up of UAW/GM cohort of Eisen et al. 1992 (10 years longer). 1940–1994 Population: >45000 workers from 3 auto-part manufacturing facilities (Plants I, II, and III) employed at least 3 years from 1920–1985. Vital status obtained through Social Security Administration and National Death Index; cause of death ascertained from UA W records and death certificates (>10,000 deaths). Extended follow-up includes> 1.5 million person-years and> 15000 deaths. Exposure: In mid 1970s, use of water-based fluids expanded, and polyaromatic hydrocarbons in straight oils were reduced. Semisynthetic and soluble fluids were combined. A type of fluid was assigned to each plant, department, and job-specific exposure category based on historical records. Cumulative exposure (mg/m3) were calculated for each person.
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	結果: 累積暴露の解析:それぞれのがん (Poisson　回帰)及び暴露の階層に対するRR。 溶解液での研磨: 食道がん*、喉頭がん**、皮膚及び脳のがん*に対してRR (1.5–2.6)の上昇がみられた。 合成液: 食道がん*、肝臓がん*及び前立腺がんに対してRR (1.3–2.6)の上昇がみられた。 *複数の暴露カテゴリーで有意な関係がみられた、 **傾向検定	Result : Cumulative exposure analyses: RR for each cancer (Poisson regression) and exposure stratum. Grinding with soluble fluids: Elevated RRs (1.5–2.6) observed for esophageal*, laryngeal**, skin, and brain* cancer. Synthetic fluids: Elevated RRs (1.3–2.6) observed for esophageal*, liver*, and prostate cancer. *Significant associations observed in some exposure categories. **Test for trend
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	基本的な科学原理を満足する文書化の良好な試験	Well-documented study which meets basic scientific principles
出典		
引用文献(元文献)	(226)	(226)
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	BASF AG (2006). Product Details DIETHANOLAMINE PURE, 01 Dec 2006.
2	BASF AG (2006). Safety data sheet according to 91/155/EEC, Diethanolamine pure, revised 04 Dec 2006.
3	BASF AG (2007). Unpublished info on purity and impurities. 11 Jan 2007.
4	HSDB database (through 2006/09). Available online via TOXNET at http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB.
5	GESTIS (2006). Database (Gefahrstoffinformationssystem der gewerblichen Berufsgenossenschaften). Available online at http://biade.itrust.de/biade/lpext.dll?f=templates&fn=main-h.htm, request of 01 Dec 2006.
6	Akzo Nobel (2007). Info on composition, 11 Jan 2007, unpublished.
7	SASOL (2007). Info on composition, 11 Jan 2007, unpublished.
8	BASF AG (2006). Info on ethanolamines world production capacity, 28 Nov 2006, unpublished.
9	BASF AG (2007). Info on number of production sites; internal note, 22 Jun 2007, unpublished.
10	Commission Directive 2004/73/EC, 29 April 2004 (29th adaption to the technical progress of 67/548/EEC).
11	RÖMPP Online (2006). Georg Thieme Verlag, status 01 Dec 2006.
12	Ullmann´s Encyclopedia of Industrial Chemistry (2006). Ethanolamines and Propanolamines, release 2006, 7th edition. http://www.mrw.interscience.wiley.com/emrw/9783527306732/ueic/article/a10_001/current/pdf.
13	Commission of the European Communities (CEC, 1997). Classification and labelling of dangerous substances under Directive 67/548/EEC. 2,2'-iminobisethanol, report prepared by Austria, 18 Aug 1997.
14	SPIN (2006). Substances in Preparations in Nordic Countries. Data base information, available online at http://www.spin2000.net/spin.html.
15	WILEY-VCH Verlag GmbH, Weinheim, Germany (2007). List of MAK- and BAT-values 2007 (Notification 43), 2007.
16	ACGIH (1991-1992).
17	Umweltbundesamt Berlin (2006). Catalogue of Substances Hazardous to Water, 20 Sep 2006.
18	National Chemical Inventories, NCI (2006). 2006 Issue 1.
19	Ariel WebInsight® 4.1 (2006). Chemical Database, November 2006 Update.
20	TRI (2007). Toxics Release Inventory of the U.S.EPA. DEA environmental release data for USA in 2004 as stated by the Canadian (Env) Competent Authority in the Collated Comments, compiled on 18 Mar 2007.
21	(NPRI, 2007)
22	ACC (2006). Letter of the Alkanolamines Panel of the American Chemistry Council to the U.S. EPA Office of Pollution, Prevention and Toxics, 24 Aug 2006, unpublished.
23	BASF AG (2006). Internal note, German Emission Register, 22 Dec 2006, unpublished.
24	INEOS Oxide (2007). Info on emissions to air and to water, 11 Jan 2007, unpublished.
25	INEOS Oxide (2007). Info on production sites, 01 Feb 2007, unpublished.
26	BASF AG (2006). Internal note on emission via wwtp, 28 Nov 2006, unpublished.
27	BASF AG (1985). Department of Analytics, Die Bestimmung von spezifischen Waermekapazitaeten und Erstarrungspunkten von Di-Ethanolamin (DEA) und verschiedenen Gemischen mit Wasser, Report 126131, 23 November 1985, unpublished.
28	BASF AG (1985). Order No. 126131, 23 Nov 1985, unpublished.
29	BASF AG (1985). Physical-chemical constants, report BRU 85.213, 11 Dec 1985, unpublished.
30	Beilstein Database. Copyright 1988-2003 Beilstein Institut zur Foerderung der Chemischen Wissenschaften. CrossFire Beilstein, licensed by MDL Information Systems GmbH, update: 23 Oct 2003.
31	Chemische Werke Huels AG (1969). Diethanolamin rein (DEA pure), Handbook, Marl, Germany, January 1969
32	DOW Chemical (1988). The Alkanolamines Handbook. Form No. 11-1159-88R-SAI. The DOW Chemical Company, Midland, MI, USA.
33	BASF AG (2006). Department of Product Safety, data assessment, EPIWIN (v3.12), 28 Aug 2006, unpublished.
34	Hommel G (ed.) (2005). Handbuch der gefährlichen Güter (Handbook of Dangerous Goods), 2005. Springer-Verlag Berlin Heidelberg, data sheet No. 72.

35	GESTIS (2005). Database (Gefahrstoffinformationssystem der gewerblichen Berufsgenossenschaften. Available online at http://biade.itrust.de/biade/lpext.dll?f=templates&fn=main-h .tm, request of 17 Oct 2006.
36	BASF AG (undated); Alkanolamine, Physikalische Eigenschaften, Handbook
37	Roempp (2005). Handbook, Document RD-09-00256, 29 April 2005
38	Chemsafe Dechema (2005). Database
39	IPCS (1999), International Programme on Chemical Safety, ICSC: 0618, Prepared in the context of cooperation between the International Programme on Chemical Safety and the Commission of the European Communities © IPCS, CEC 1999
40	BASF AG (1998). SIK-No. 98/0952, Dynamic Scanning Calorimetry, 19 Jun 1998, unpublished.
41	BASF AG (1985). Sicherheitstechnische Kenndaten, SIK-No. 85/0710, 28 Aug 1985, unpublished.
42	BASF AG (undated) Alkanolamine, Physikalische Eigenschaften, Handbook
43	Wilson; IECHAD; Ind. Eng. Chem.; 27; 1935; 867, 870. cited in Beilstein Database. Copyright 1988-2003 Beilstein Institut zur Foerderung der Chemischen Wissenschaften. CrossFire Beilstein, licensed by MDL Information Systems GmbH, update: 23 Oct 2003.
44	Lyman WJ, Reehl WF, and Rosenblatt DH (1990). Handbook of Chemical Property Estimation Methods. McGraw-Hill Book Company, NY, USA.
45	BASF AG (1993). Department of Analytical Chemistry. Report BRU 93.209, 19 Jan 1993, unpublished.
46	BASF AG (1991). Department of Analytical Chemistry. Report J. No. 90P03095.02, 18 Mar 1991, unpublished.
47	GBCh (1995). BUA-Stoffberichte 158 und 159, Diethanolamin (No. 158), Triethanolamin (No. 159), Beratergremium fuer umweltrelevante Altstoffe, Frankfurt, Germany
48	Hansch C and Leo A (1979). Substituent Constants for Correlation Analysis in Chemistry and Biology. Pomona College, Appendix II, page 188, John Wiley and Sons, New York, USA.
49	SRC; Hansch C, Leo AJ; Medchem Project Issue no. 26 Claremont, CA: Pomona College (1985); Lyman WJ et al; Handbook of Chemical Property Estimation Methods NY: McGraw-Hill p. 5-5 (1982). cited in HSDB 21 Sep 2006
50	Lide, D.R. (ed). CRC Handbook of Chemistry and Physics. 72nd ed. Boca Raton, FL: CRC Press, 1991-1992., p. 3-214. cited in HSDB 21 Sep 2006
51	ILO (2007). International Labour Organisation. Diethanolamine. International Occupational Safety and Health Information Centre (CIS). Retrieved from www.ilo.org/public/english/protection/safework/cis/products/icsc/dtasht/_icsc06/icsc0618.htm, request dated 26 Mar 2007.
52	Toxic and Hazardous Industrial Chemicals Safety Manual. Tokyo, Japan: The International Technical Information Institute (1988)., p. 172, cited by HSDB 21 Sep 2006.
53	ITII. Toxic and Hazardous Industrial Chemicals Safety Manual. Tokyo, Japan: The International Technical Information Institute, 1988., p. 172. cited in HSDB, 21 Sep 2006
54	Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997., p. 325-36, cited by HSDB 21 Sep 2006.
55	BASF AG (1998). Test Laboratory for Safety Engineering, internal note, 01 Sep 1998 (unpublished).
56	BASF AG (1998). Test Laboratory for Safety Engineering, internal notice, 01 Sep 1998 (unpublished).
57	BASF AG (2006). Department of Product Safety, SPARC-calculations, 01 Dec 2006, unpublished.
58	Davis JW and Carpenter CL (1997). Environmental assessment of alkanolamines. Rev. Environ. Contam. Toxicol. 149, 87-137.
59	BASF AG (2006). Department of Product Safety, SPARC-calculations, 29 Aug 2006, unpublished.
60	BASF AG (1985). Depertment of Analysis, Die Bestimmung von spezifischen Waermekapazitaeten und Erstarrungspunkten von Di-Ethanolamin (DEA) und verschiedenen Gemischen mit Wasser, Report 126131, 23 November 1985, unpublished.
61	BASF AG (2006). Technical Development, Waermeleitfaehigkeit von Diethanolamin, Report 186.0086.1, 14 February 1986, unpublished.
62	Lewis GE (1992). Determination of pH of aqueous alkanolamines. In: Davis & Carpenter (1997). Environmental assessment of alkanolamines. Rev. Environ. Contam. Toxicol. 149, 87-137.
63	BASF AG (2006). Department of Product Safety, data assessment, AOP (v1.91), 31 Aug 2006, unpublished.
64	Atkinson R (1987). A structure activity relationship for the estimate of rate constants for the gas phase reaction of OH radicals with organic compounds. Intern. J. Chem. Kinet. 19, 799-828.

65	BASF AG (2006). Expert judgement on stability of DEA in water, 28 Dec 2006, unpublished.
66	Lyman WJ, Reehl WF, and Rosenblatt DH (1982). Handbook of Chemical Property Estimation Methods. McGraw-Hill Book Company, NY, USA.
67	Swann RL, Laskowski DA, McCall PJ, Vander Kuy K, and Dishburger (1983). A rapid method for the estimation of the environmental parameters octanol/water partition coefficient, soil sorption constant, water to air ratio, and water solubility. Res. Rev. 85, 17-28.
68	Anonymous (1985). Chemicals in the environment. Report on Environmental Survey and Wildlife Monitoring in F. Y. 1982 and 1983. Office of Health Science, Department of Environmental Health, Environment Agency, Japan, March 1985.
69	Bouyoucos SA and Melcher RG (1986). Collection of ethanolamines in air and determination by mobile phase ion chromatography. American Ind. Hygiene Assoc. J. 47, 185-188.
70	Pietsch J, Sacher F, Schmidt W, and Brauch HJ (2001). Polar nitrogen compounds and their behaviour in the drinking water treatment process. Wat. Res. 35, 3537-3544.
71	Headley JV, Peru KM, and Dickson LC (1999). Ion-exchange electrospray ionization liquid chromatography mass spectrometry and tandem mass spectrometry of alkanolamines in wetland vegetation exposed to sour-gas contaminated groundwater. Rapid Commun. Mass Spectrom. 13, 730-736.
72	Hine J and Mookerjee PK (1975). The intrinsic hydrophilic character of organic compounds. Correlations in terms of structural contributions. J. Org. Chem. 40, 292-298.
73	BASF AG (2006). Department of Product Safety. Mackay Level I calculation, 22 Dec 2006, unpublished.
74	BASF AG (1992). Department of Ecology. Prüfung der biologischen Abbaubarkeit von Diethanolamin rein im manometrisch-respiratorischen Test (Sapromat). 1/91/1168/26/2, 20 May 1992, unpublished.
75	BASF AG (1993). Department of Ecology. Prüfung der biologischen Abbaubarkeit von Diethanolamin im DOC-Abnahme (Die-Away) Test, 93/1316/21/1, 11 Nov 1993, unpublished.
76	BASF AG (1993). Department of Ecology. Prüfung der biologischen Abbaubarkeit von Diethanolamin im DOC-Abnahme (Die-Away) Test, 93/1316/21/2, 11 Nov 1993, unpublished.
77	BASF AG (1993). Department of Ecology. Prüfung der biologischen Abbaubarkeit von Diethanolamin im modifiziertem OECD-Screening Test, 93/1316/20/1, 11 Nov 1993, unpublished.
78	BASF AG (1993). Department of Ecology. Prüfung der biologischen Abbaubarkeit von Diethanolamin im modifiziertem OECD-Screening Test, 93/1316/20/2, 11 Nov 1993, unpublished.
79	BASF AG (1993). Department of Ecology. Prüfung der biologischen Abbaubarkeit von Diethanolamin im modifiziertem OECD-Screening Test, 93/1316/20/3, 11 Nov 1993, unpublished.
80	Chemische Werke Hüls AG (1979). Biologischer Abbau im statischen Test nach Zahn-Wellens, 21 Mar 1979, unpublished.
81	Mills EJ and Stack VT (1953). Biological Oxidation of Synthetic Organic Chemicals. In: Proceedings of the 8th Industrial Waste Conf., 83, 492-517.
82	Mills EJ and Stack VT (1955). Acclimation of microorganisms for the oxidation of pure organic chemicals. In: Proceedings of the 9th Industrial Waste Conf., Eng. Bull. of Purdue Univ., Ext. Ser. 9, 449-464.
83	Bridié AL, Wolff CJM, and Winter M (1979). BOD and COD of some petrochemicals. Water Research 13, 627-630.
84	Pitter P (1976). Determination of biological degradability of organic substances. Water Research 10, 231-235.
85	Gannon JE, Adams MC, and Bennett EO (1978). Microbial degradation of diethanolamine and related compounds. Microbios 23, 7-18.
86	Boethling RS and Alexander M (1979). Microbial degradation of organic compounds at trace levels. Environ. Sci. Technol. 13, 989-991.
87	Yordy JR and Alexander MJ (1981). Formation of N-Nitrosodiethanolamine in lake water and sewage. J. Environ. Qual. 10, 266-270.
88	Gerike P and Fischer WK (1979). A correlation study of biodegradability determinations with various chemicals in various tests. Ecotoxicol. Environ. Safety 3, 159-173.
89	Gerike P and Fischer WK (1981). A correlation study of biodegradability determinations with various chemicals in various tests. II. Additional results and conclusion, Ecotoxicol. Environ. Safety 5, 45-55.

90	CITI (1992). Biodegradtion and Bioaccumulation Data of Existing Chemicals based on the CSCL Japan, compiled under the Supervision of Chemical Products Safety Division. Basic Industries Bureau MITI, CR-No 2-302, 2-46.
91	National Institute of Technology and evaluation (2006). Biodegradation and Bioconcentration of Existing Chemical Substances under the Chemical Substances Control Law. Online inquiry 30 Aug 2006. (http://www.safe.nite.go.jp/data/hazkizon/pk_e_kizon_data_re slt.home_data).
92	Sasaki S (1978). The scientific aspects of the chemical substances control law in Japan. In: Hutzinger et al. (eds), Aquatic pollutants: transformation and biological effects, Pergamon Press, Oxford, 283-298.
93	Price KS, Waggy GT, and Conway RA (1974). Brine shrimp bioassay and seawater BOD of petrochemicals. J. Water Pollut. Contr. Fed. 46(1), 63-77.
94	Kondo M, Nishihara T, Shimamoto T, Koshikawa T, Ilo T, Sawamura R, and Tanaka K (1988). Biodegradation test of chemicals by cultivation method. Eisei Kagaku 34, 188-195.
95	Knapp JS, Jenkey ND, and Townsley CC (1996). The anaerobic biodegradation of diethanolamine by a nitrate reducing bacterium. Biodegradation 7, 183-189.
96	NAPM (1974). Environmental effect of photoprocessing chemicals, Volume I and II. National Association of Photographic Manufacturers, Inc., Harrison, New York, USA.
97	Lamb CB and Jenkins GF (1952). B.O.D. of synthetic organic chemicals. In: Bloodgood (ed.), Proceedings of the 8th Industrial Waste Conference, Engineering Bulletin. Purdue University, West Lafayette, IN, USA, 326-339.
98	BASF AG (2006). Department of Product Safety, data assessment, BCFWIN (v2.15), 31 Aug 2006, unpublished.
99	Dow Chemical (1982). Environmental Science Research Laboratory. A study to assess the influence of age on the response of fathead minnows in static acute toxicity tests. Dow Chemical Company, 09 April 1982, TSCATS, EPA OTS 0517180, Doc.ID 86-870002091.
100	Mayes MA, Alexander HC, and Dill DC (1983). Study to assess the influence of age on the response of fathead minnows in static acute toxicity tests. Bull. Environ. Contam. Toxicol. 31, 139-147.
101	Ewell WS, Gorsuch JW, Kringle RO, Robillard KA, and Spiegel RC (1986). Simultaneous evaluation of the acute effects of chemicals on seven aquatic species. Environ. Toxicol. Chem. 5, 831-840.
102	Heitmuller PT, Hollister TA, and Parrish PR (1981). Acute toxicity of 54 industrial chemical to sheepshead minnow (Cyprinodon variegatus). Bull. Environm. Contam. Toxicol. 27, 596-604.
103	Wallen IE, Greer WC, and Lasater R (1957). Toxicity to Gambusia affinis of certain chemicals in turbid waters. Sewage Ind. Wastes 29(6), 695-711.
104	TSCATS (1989). Toxicity data submitted by Ciba Geigy Corporation. OTS 0520601, Doc. ID 86-890000562, 13 Jun 1989.
105	TSCATS (1989). Toxicity data submitted by Ciba Geigy Corporation. OTS 0520612, Doc. ID 86-890000573, 13 Jun 1989.
106	TSCATS (1989). Toxicity data submitted by Ciba Geigy Corporation. OTS 0520613, Doc. ID 86-890000574, 13 Jun 1989.
107	TSCATS (1989). Toxicity data submitted by Ciba Geigy Corporation. OTS 0521258, Doc. ID 86-890000560, 13 Jun 1989.
108	Juhnke I and Lüdemann (1978). Ergebnisse der Untersuchung von 200 chemischen Verbindungen auf akute Fischtoxizität mit dem Goldorfentest. Z. f. Wasser- und Abwasserforsch. 11, 161-164.
109	TSCATS (1987). Acute fish toxicity data submitted by Dow Chemical on 11 Jul 1978. OTS 0517164, Doc.ID 86-870002075, 04 Sep 1987.
110	Turnbull H, DeMann JG, and Weston RF (1954). Toxicity of various refinery materials to fresh water fish. Ind. Eng. Chem. 46, 324-333.
111	Bridié AL, Wolff CJM, and Winter M (1979). The acute toxicity of some petrochemicals to goldfish. Water Research 13, 623-626.
112	Zurita JL, Repetto G, Jos A, del Paso A, Salguero M, López-Artiguez M, Olano D, Cameán A (2005). Ecotoxicological evaluation of diethanolamine using a battery of microbiotests. Toxicol. in Vitro 19, 879-886.
113	LeBlanc GA (1980). Acute toxicity of priority pollutants to water flea (Daphnia magna). Bull. Environ. Contam. Toxicol. 24, 684-691.
114	Cowgill UM, Takahashi IT, and Applegath SL (1985). A comparison of the effect of four benchmark chemicals on Daphnia magna and Ceriodaphnia Dubia-affinis tested at two different temperatures. Environ. Toxicol. Chem. 4, 415-422.
115	Bringmann G and Kühn R (1982). Ergebnisse der Schadwirkung wassergefährender Stoffe gegen Daphnia magna in einem weiterentwickelten standardisierten Testverfahren. Z. Wasser Abwasser Forsch. 15(1), 1-6.

116	Bringmann G and Kühn R (1977). Befunde der Schadwirkung wassergefährender Stoffe gegen Daphnia magna. Z.f. Wasser- und Abwasser Forschung 10(5), 161-166.
117	ECT Oekotoxikologie GmbH (2006). Statistical evaluation of a quantal response with ToxRatPro (v.2.09). Daphnia magna, Test A - NAPM, 1974 - Run #VIIID1, 24-Nov-2006, unpublished.
118	ECT Oekotoxikologie GmbH (2006). Statistical evaluation of a quantal response with ToxRatPro (v.2.09). Daphnia magna, Test B - NAPM, 1974 - Run #IVD3, 24-Nov-2006, unpublished.
119	ECT Oekotoxikologie GmbH (2006). Statistical evaluation of a quantal response with ToxRatPro (v.2.09). Daphnia magna, Test C - NAPM, 1974 - Run #IIID5, 24-Nov-2006, unpublished.
120	Cowgill UM, Milazzo DP, and Landenberger BD (1989). Toxicity to nine benchmark chemicals on Skeletonema costatum, a marine diatom. Environ. Toxicol. Chem. 8, 451-455.
121	Dow Chemical (1982). Environmental Science Research Laboratory. The toxicity of chemicals to the freshwater green alga Selenastrum capricornutum PRINTZ. Dow Chemical Company, 07 April 1982, TSCATS, OTS 0520294, Doc. ID 86-8900011548.
122	BASF AG (1992). Department of Ecology. Diethanolamine: algae growth inhibition test with S. subspicatus, neutralized test conditions. Project No. 92/1444/60/scr2, 09 Jul 1992, unpublished.
123	BASF AG (1992). Department of Ecology. Diethanolamine: algae growth inhibition test with S. subspicatus, non-neutralized test conditions. Project No. 92/1444/60/scr1, 09 Jul 1992, unpublished.
124	BASF AG (1992). Department of Ecology. Diethanolamine: algae growth inhibition test with A. bibraianus, neutralized test conditions. Project No. 92/1444/60/scr3, 09 Jul 1992, unpublished.
125	BASF AG (1992). Department of Ecology. Diethanolamine: algae growth inhibition test with A. bibraianus, non-neutralized test conditions. Project No. 92/1444/60/scr4, 09 Jul 1992, unpublished.
126	Bringmann G and Kühn R (1977). Grenzwerte der Schadwirkung wassergefährdender Stoffe gegen Blaualgen (Microcystis aeurginosa) und Grünalgen (Scenedesmus quadricauda) im Zellvermehrungshemmtest. Vom Wasser 50, 45-60.
127	Bringmann G and Kühn R (1978). Testing of substances for their toxicity threshold: Model organisms Microcystis (Diplocystis) aeruginosa and Scenedesmus quadricauda, Mitt. Internat. Verein Limnol. 21, 275-284.
128	Bringmann G and Kühn R (1977). Grenzwerte der Schadwirkung wassergefährdender Stoffe gegen Bakterien (Pseudomonas putida) und Grünalgen (Scenedesmus quadricauda) im Zellvermehrungshemmtest. Zeitschrift für Wasser- und Abwasserforschung 10 (No. 3/4), 87-98.
129	Bringmann G and Kühn R (1980). Comparison of the toxicity thresholds of water pollutants to bacteria, algae, and protozoa in the cell multiplication inhibition test. Water Research 14, 231-241.
130	Bringmann G, Kühn R, and Winter A (1980). Bestimmung der biologischen Schadwirkung wassergefährdender Stoffe gegen Protozoen. III. Saprozoische Flagellaten. Zeitschrift für Wasser- und Abwasserforschung 13 (No. 5), 170-173.
131	Bringmann G (1978). Bestimmung der biologischen Schadwirkung wassergefährdender Stoffe gegen Protozoen. I. Bakterienfressende Flagellaten. Zeitschrift für Wasser- und Abwasserforschung 11 (No. 6), 210-215.
132	Hockenbury MR and Grady CPL (1977). Inhibition of nitrification effects of selected organic compounds. J. WPCF 49, 768-777.
133	Bringmann G (1973). Bestimmung der biologischen Schadwirkung wassergefährdender Stoffe aus der Hemmung der Glucose Assimilation des Bakteriums Pseudomonas fluorescens. Gesundheits Ingenieur 94, 366-369.
134	Bringmann G and Kühn R (1980). Bestimmung der biologischen Schadwirkung wassergefährdender Stoffe gegen Protozoen. II. Bakterienfressende Ciliaten. Zeitschrift für Wasser- und Abwasserforschung 13 (No. 1), 26-31.
135	Jennings VLK, Rayner-Brandes MH, and Bird DJ (2001). Assessing chemical toxicity with bioluminescent photobacterium (Vibrio fischeri): A comparison of three commercial systems. Wat. Res. 35, 3448-3456.
136	BASF AG (1992). Department of Ecology. Prüfbericht über einen Atmungshemmtest mit Belebtschlamm (Kurzzeitatmungstest). 1/91/1168/08/1, 1992, unpublished.
137	BASF AG (1992). Department of Ecology. Chronic toxicity of diethanolamine to Daphnia magna Straus. Project No. 92/1444/51/1 (study report in German), 28 Aug 1992, unpublished.
138	Brain KR, Walters KA, Green DM, Brain S, Loretz LJ, Sharma RK, Dressler WE (2005) Percutaneous penetration of Diethanolamin through human skin in vitro: Application from cosmetic vehicles, Food Chem. Toxicol., 43, 681-690

139	Yourick JJ, Marks A, Lochhead RY, Bronaugh RL (undated) Diethanolamine (DEA) in vitro dermal absorption in Fuzzy rat skin, unpublished manuscript (submitted for publication)
140	Mendrala AL, Waechter JM, Bormett GA, Bartels MJ, Stott WT (2001) The pharmacokinetics of diethanolamine in Sprague-Dawley rats following intravenous administration, Food and Chemical Toxicology, 39, 931-939
141	Kraeling MEK, Yourick JJ, Bronaugh RL (2004) In vitro skin penetration of diethanolamine, Food Chem. Toxicol., 42, 1553 - 1561
142	Sun JD, Beskitt JL, Tallant MJ (1996) In vitro skin penetration of monoethanolamine and diethanolamine using excised skin from rats, mice, rabbits, and humans, J. Toxicol. Cut. Ocular. Toxicol., 15, 131-146
143	Mathews JM, Gamer CR, Matthews RB (1995) Metabolism, bioaccumulation, and incorporation of diethanolamine into phospholipids, Chem. Res. Toxicol., 18, 625-633, in: Report on Carcinogens (2002) Background document Diethanolamine, prepared by: Technology Planning and Management Corporation, Durham, NC, USA, Contract Number N01-ES-85421 for US Department of Health and Human Services, Public Health Service, National Toxicology Program, Research Triangle Park, NC, USA, 22 March 2002
144	Mathews JM, Gamer CR, Black SL, Matthews RB (1997) Diethanolamine absorption, metabolism and disposition in rat and mouse following oral, intravenous and dermal administration, Xenobiotica, 27, 733-746
145	Sidorov KK, Gorban GM, Tikhonova GP (1968). Comparative toxicological characteristics of some regenerable absorbens of carbon dioxide, translated from Kosmicheskaya Biologiya i Meditsina, 2 44-49 (original article submitted 25 September 1967)
146	Smyth HF, Weil CS, West JS, Carpenter CP (1970) An exploration of joint toxic action II. Equitoxic versus equivolume mixtures, Toxicol. Appl. Pharmacol., 17, 498-503
147	Smyth HF, Weil CS, West JS, Carpenter CP (1969) An exploration of joint toxic action: Twenty-seven industrial chemicals intubated in rats in all possible pairs, Toxicol. Appl. Pharmacol., 14, 340-347
148	BASF AG, Product Safety, Gewerbetoxikologische Vorprüfung, Substanz-Nr. XV 306, Diethanolamin (fest) [Occupational toxicity preliminary base set testing, substance-No. XV/306, Diethanolamine (solid)], unpublished report, 17 February 1966
149	Foster GV (1971) Studies of the acute and subacute toxicologic responses to Diethanolamine in the rat, Dissertation, University of Michigan, USA
150	ACGIH: Documentation of TLV Values (1986)
151	BIBRA International Ltd., Toxicity profile, Diethanolamine, 1993
152	Cosmetic Ingredient Review (CIR) Expert Panel (1983) Final report on the safety assessment of triethanolamine, diethanolamine, and monoethanolamine, Cosmetic Fragrance Ingredient Review, J. Am. Coll. Toxicol., 2, 183-235
153	Smyth HF, Seaton J, Fischer L (1941) The single dose toxicity of some glycols and derivatives, J. Ind. Hyg. Toxicol., 23, 259-268
154	Smyth HF, Carpenter CP, Weil CS (1951) Range-finding toxicology data: List IV, A.M.A. Arch. Ind. Hyg. Occup. Med., 4, 119-122
155	TSCATS, OTS 0516742, Doc. ID 86-890000205, 8DS, Health and safety studies for Diethanolamine with cover letter, Eastman Kodak Company, 08 May 1989
156	Anonymous (1968), Ethanolamines, Amer. Ind. Hyg. Assoc. J., 29, 312-315
157	Korsrud GO, Grice HG, Goodman TK, Knippel JE, McLaughlan JM (1973) Sensitivity of several serum enzymes for the detection of thioacetamide-, dimethylnitrosamine-, and diethanolamine-induced liver damage in rats, Toxicol. Appl. Pharmacol., 26, 299-313
158	Hartung R, Rigas LK, Cornish HH (1970) Acute and chronic toxicity of diethanolamine (abstract), Toxicol. Appl. Pharmacol., 17, 308 (abstract)
159	Union Carbide Chemicals Division Booklet F-41175A: Ethanolamines, Union Carbide Corporation, New York, NY, USA, 1966, in: DFG (Deutsche Forschungsgemeinschaft): Arbeitsmedizinisch-toxikologische Begruendung von MAK-Werten, VCH, Weinheim, 1981
160	Union Carbide Chemicals Division Booklet F-41175A: Ethanolamines, Union Carbide Corporation, New York, NY, USA, 1966, in: Anonymous (1968), Ethanolamines, Amer. Ind. Hyg. Assoc. J., 29, 312-315
161	CTFA (1973). Submission of data by CTFA. (2-5-57). Acute rabbit percutaneous toxicity (TEA), in: Cosmetic Ingredient Review (CIR) Expert Panel (1983) Final report on the safety assessment of triethanolamine, diethanolamine, and monoethanolamine, Cosmetic Fragrance Ingredient Review, J. Am. Coll. Toxicol., 2, 183-235
162	Blum K, Huizenga CG, Ryback RS, Johnson DK, Geller I (1972) Toxicity of diethanolamine in mice; Toxicol. appl. Pharmacol., 22, 175-185
163	Grice HC, Barth ML, Cornish HH, Foster GV, Gray RH (1971) Correlation between serum enzymes, isozyme patterns and histologically detectable organ damage, Food Cosmet. Toxicol., 9, 847-855
164	Koch R (1954) Zur Toxikologie verschiedener Theophyllinverbindungen und - derivate sowie einiger Lösungsvermittler, Arzneimittelforschung 4, 649-654

165	Sato M, Tamura T, Sato S (1964) Pharmacological contributions to Vitamin B preparations commonly used in the oral area Part III. Relationship between toxicities of pyridoxal-5-phosphate, sodium bisulfite and Diethanolamine and flavin-adenine-dinucleotide together with actions of pyridoxal and pyridoxine on the rat intestinal canal, J. Nihon Univ. School Dent. Tokyo, 6, 149-155
166	BASF AG, Product Safety, Bericht über die orientierende Prüfung der Hautreizwirkung von Mono-, Di- und Triethanolamin, Substanz-Nr. V/77, Diethanolamin [Report on the orientating testing of skin irritation of mnon-, di- and triethanolamin substance-No. V/77, Diethanolamin], unpublished report, 24 April 1956
167	BASF AG, Product Safety, Bericht über die Prüfung der akuten Haut- und Schleimhautreizwirkung von Mono-, Di- und Triethanolamin, Substanz-Nr. XVII/144 (rein), XVII/146 (technisch), Diethanolamin [Report on the testing of skin and mucous membrane (eye) irritation of mnon-, di- and triethanolamin substance-No. XVII/144 (pure), XVII/146 (technical), Diethanolamin], unpublished report, 28 August 1967
168	Dutertre-Catella H, Lich NP, Huyen VN, Truhaut R (1982) Etude comparative de l'agressivit é cutanée et oculaire des éthanolamines (mono, di, tri et poly), Arch. Mal. Prof., 43, 455-460
169	Hinglais H (1947) Méthode de mesure des effets d'irritation et de nécrose produits par les dé rivés chimiques sur la peau et sur les muqueises, Produits Pharmaceutiques, 2, 445-449 (1947)
170	CTFA (1944), Submission of data by CTFA (2-5-26), CIR safety data test summary, primary skin irritation of Diethanolamine, in: Cosmetic Ingredient Review (CIR) Expert Panel (1983) Final report on the safety assessment of triethanolamine, diethanolamine, and monoethanolamine, Cosmetic Fragrance Ingredient Review, J. Am. Coll. Toxicol., 2, 183-235
171	CTFA (1979), Submission of data by CTFA (2-5-24), CIR safety data test summary, primary skin and eye irritation of Diethanolamine, in: Cosmetic Ingredient Review (CIR) Expert Panel (1983) Final report on the safety assessment of triethanolamine, diethanolamine, and monoethanolamine, Cosmetic Fragrance Ingredient Review, J. Am. Coll. Toxicol., 2, 183-235
172	Grant WM (1962) Toxicology of the Eye, Charles C. Thomas Publisher, Springfield, IL, USA, in: DFG (Deutsche Forschungsgemeinschaft): Arbeitsmedizinisch-toxikologische Begruendung von MAK-Werten, VCH, Weinheim, 1981
173	Carpenter CP, Smyth HF (1946) Chemical burns of the rabbit cornea, Am. J. Ophthalmol., 29, 1363-1372
174	RCC, Contact hypersensitivity to Diethanolamin, rein in albino Guinea pigs, Maximization test, RCC Project 264903, RCC, Itingen, Switzerland, unpublished report, 04 October 1990 (Propertity of BG Chemie)
175	Kimber I, Basketter DA, Butler M, Gamer A, Garrigue JL, Gerberick GF, Newsome C, Steiling W, Vohr HW (2003) Classificattion of contact allergens to potency: Proposals, Food Chemical Toxicol., 41, 1799-1809
176	CTFA (1981) Submission of data by CTFA. Sensitisation study on products Triethanolamine (TEA) products No. 76 and 78 and diethanolamine (DEA) product No. 80. Cosmetic, Tioletry and Fragrance Association, unpublished study, in: Cosmetic Ingredient Review (CIR) Expert Panel (1983) Final report on the safety assessment of triethanolamine, diethanolamine, and monoethanolamine, Cosmetic Fragrance Ingredient Review, J. Am. Coll. Toxicol., 2, 183-235
177	HTR (July 7th 1981) Submission of data by CTFA (2-5-63). Repeated insult patch test 81-0242-74, CTFA, unpublished study, in: Cosmetic Ingredient Review (CIR) Expert Panel (1983) Final report on the safety assessment of triethanolamine, diethanolamine, and monoethanolamine, Cosmetic Fragrance Ingredient Review, J. Am. Coll. Toxicol., 2, 183-235
178	HTR (March 31 1980) Submission of data by CTFA (2-5-7). The appraisal of the contact sensitising potential of 4 (4) materials by means of the maximisation study, Ivy Research protocol No. 4308/01, CTFA, unpublished study, in: Cosmetic Ingredient Review (CIR) Expert Panel (1983) Final report on the safety assessment of triethanolamine, diethanolamine, and monoethanolamine, Cosmetic Fragrance Ingredient Review, J. Am. Coll. Toxicol., 2, 183-235
179	Kharchenko TF, Ivanova TP (1980) Gig.Tr.Prof.Zabol. 7, 63-64, in: BG Chemie (Berufsgenossenschaft der chemischen Industrie, 1990): Toxikologische Bewertung - Diethanolamin, Nr. 158, Ausgabe 05/90, Heidelberg, Germany
180	Knaak JB, Leung HW, Stott WT, Busch J, Bilsky J (1997) Toxicology of mono-, di-, and triethanolamine, Rev. Environ. Contam. Toxicol., 149, 1-86

181	BASF AG, Product Safety, Report - Study on the inhalation toxicity including neurotoxicological examination of Diethanolamn as a liquid aerosol in rats, 14-day test, BASF Project No. 36I0233/90009, BG No. 158, Experimental Toxicology and Ecology, BASF AG, Ludwigshafen, Germany, unpublished report, 25 February 1993
182	BASF AG, Product Safety, Diethanolamine - Subchronic inhalation toxicity and neurotoxicity study in Wistar rats, 90-day liquid aerosol exposure, BASF Project No. 50I0075/93011, BG No. 158, Experimental Toxicology and Ecology, BASF AG, Ludwigshafen, Germany, unpublished report, 19 August 1996
183	BASF AG, Product Safety, Diethanolamine - Subchronic inhalation toxicity study in Wistar rats, liquid aerosol/vapor exposure, study focus on irritation of upper respiratory tract, BASF Project No. 51I0299/99125, Experimental Toxicology and Ecology, BASF AG, Ludwigshafen, Germany, unpublished report, 02 April 2002
184	Barbee SJ, Hartung R (1976) Subacute toxicity of Diethanolamine: Alteration of mitochondrial function, Tox. Appl. Pharm., 37, 122 (abstract)
185	Barbee SJ, Hartung R (1979) Diethanolamine-induced alteration of hepatic mitochondrial function and structure, Toxicol. Appl. Pharmacol., 47, 431-440
186	Barbee SJ, Hartung R (1979) The effect of diethanolamine on hepatic and renal phospholipid metabolism in the rat, Toxicol. Appl. Pharmacol., 47, 421-430
187	Hejtmancik, M. et al. "The prechronic dosed water study of Diethanolamine (CAS 111-42-2) in Fischer F344 rats, the US National Toxicology Programme report of September 23rd, 1988 prepared by Batelle, Columbus, Ohio
188	Melnick RL, Mahler J, Bucher JR, Thompson M, Hejtmancik M, Ryan MJ, Mezza LE (1994) Toxicity of diethanolamine. 1. Drinking water and topical application exposures in F344 rats, J. Appl. Toxicol., 14, 1-9
189	National Toxicology Program (1992) Toxicity Studies of Diethanolamine (CAS No. 111-42-2) Administered Topically and in Drinking Water to F344/N Rats and B6C3F1 Mice (Tech. Rep. Ser. No. 20; NIH Publication No. 92-3343), Department of Health and Human Services, Research Triangle Park, NC
190	TSCAT OTS0537119, Doc I.D. 88-920001656, 8ECP, Letter submitting studies on Diethanolamine in rats and mice, 07.04.1992, Dow Chemical Corporation
191	Gulf South Research Institute (GSRI), Subchronic test of Diethanolamine (C55174) in B6C3F1 mice and Fischer 344 rats, submitted to Tracor Jitco Inc., Rockvilly, USA, Subcontract Nr. 76-36-106002, GSRI Project No. 410-798, 09 May 1980
192	Hejtmancik, M. et al.: Prechronic Dermal study of Diethanolamine (CAS 111-42-2) in Fischer F344 rats, Final NTP Report of August 1988, prepared by Batelle, Columbus, Ohio
193	TSCAT OTS0520184, Doc I.D. 86-890001041, 8D, The prechronic dermal study of Diethanolamine in Fischer 344 rats with cover letter, 14.07.1989, Union Carbide
194	TSCAT OTS0537090, Doc I.D. 88-920001193, 8ECP, 28.02.1992, Shell Oil Co, 90 day dermal toxicity study in rats of simulated cutting fluid containing para tertiary butyl benzoic ester with cover letter
195	Melnick R, Hejtmancik M, Mezza L, Ryan M, Persing RL, Peters A (1988) Comparative effects of triethanolamine (TEA) and diethanolamine (DEA) in shortterm dermal studies, Toxicologist, 8, 505 (abstract)
196	Burdock GA, Masten LW (1979) Dietanolamine induced changes in the neonatal rat, Toxicol. Appl. Pharmacol., 48, A30 (abstract)
197	Hejtmancik, M. et al.: Prechronic Dosed water study of Diethanolamine (CAS 111-42-2) in B6C3F1 mice, NTP report of October 1988, prepared by Batelle, Columbus, Ohio
198	Melnick RL, Mahler J, Bucher JR, Hejtmancik M, Singer A, Persing RL(1994) Toxicity of diethanolamine. 2. Drinking water and topical application exposures in B6C3F1 mice. J. Appl. Toxicol., 14, 11-19
199	TSCAT OTS0520186, Doc I.D. 86-890001043, 8D, The prechronic dosed water study of Diethanolamine in B6C3F1 mice with cover letter, 14.07.1989, Union Carbide
200	Environmental Health Research and Testing, Inc. (EHRT, 1987) Screening of priority chemicals for reproductive hazards. Monoethanolamine, diethanolamine and triethanolamine, ETOX-85-1002, prepared for National Institute for Occupational safety and Health (NIOSH), PB98-139067, 14 April 1987
201	TSCATS, OTS0526003, Doc. ID. 86-900000423, 8DS, Screening of priority chemicals for reproductive hazards, Final report: Monoethanolamine, Diethanolamine, Triethanolamine with cover letter, Union Carbide Corporation, 24 April 1990
202	Lehman-McKeeman LD, Gamsky EA, Hicks SM, Vassallo JD, Mar M-H, Zeisel SH (2002). Diethanolamine induces hepatic choline deficiency in mice, Toxicol. Sci., 67, 38-45
203	Annau E, Manginelli A (1950) Alkaline phosphatase activity and nuclear changes in the liver induced by diethanolamine, Nature, 166, 816-817
204	Burnett C, Goldenthal EI, Harris SB, Wazeter FX, Strausburg J, Kapp R, Voelker R (1976) Teratology and percutaneous toxicity studies on hair dyes, J. Toxicol. Environ.Healthm, 1, 1027-1040

205	Dean, B.J., Brooks, T.M., Hodson-Walker, G., Hutson, D.H. (1985) Genetic toxicology testing of 41 industrial chemicals. Mutat. Res., 153, 57-77
206	Hedenstedt A (1978) Mutagenicity screening of industrial chemicals: seven aliphatic amines and one amide tested in the Salmonella/microsomal assay, Mutat. Res., 53, 198-199 (abstract)
207	Loveday KS, Lug MH, Resnick MA, Anderson BE, Zeiger E (1989). Chromosome aberration and sister chromatid exchange tests in Chinese hamster ovary cells in vitro. II. Results with 20 chemicals, Environ. Mol. Mutagen., 13, 60-94, in: National Toxicology Program (1999) Toxicology and Carcinogenesis Studies of Diethanolamine (CAS No. 111-42-2) in F344/N Rats and B6C3F1 Mice (Dermal Studies) (Tech. Rep. Ser. No. 478; NIH Publ. No. 99-3968), Research Triangle, NC
208	Haworth, S., Lawlor, T., Mortelmans, K., Speck, W., and Zeiger, E. (1983). Salmonella mutagenicity test results for 250 chemicals. Environ. Mutagen. 5 (Suppl. 1), 3-142
209	National Toxicology Program (1992). Toxicity Studies of Diethanolamine (CAS No. 111-42-2) Administered Topically and in Drinking Water to F344/N Rats and B6C3F1 Mice (Tech. Rep. Ser. No. 20; NIH Publication No. 92-3343), Department of Health and Human Services, Research Triangle Park, NC
210	National Toxicology Program (1999) Toxicology and Carcinogenesis Studies of Diethanolamine (CAS No. 111-42-2) in F344/N Rats and B6C3F1 Mice (Dermal Studies) (Tech. Rep. Ser. No. 478; NIH Publ. No. 99-3968), Research Triangle, NC
211	Myhr BC, Bowers LR, Caspary WJ (1986) Results from the testing of coded chemicals in the L5178Y TK+/- mouse lymphoma mutagenesis assay, Environ. Mutagen., 7(Suppl 3), 58 (154, abstract)
212	Duerksen-Hughes PJ, Yang J, Ozcan O (1999) p53 induction as a genotoxic test for twenty-five chemicals undergoing in vivo carcionogenicity testing, Environ. Health Perspectives, 107, 805-812
213	Witt KL, Knapton A, Wehr CM, Hook GJ, Mirsalis J, Shelby MD, MacGregor JT (2000) Micronucleated erythrocyte frequency in peripheral blood of B6C3F1 mice from short-term, prechronic and chronic studies of the NTP carcinogenesis bioassay program, Environmental Molecular Mutagenesis, 36, 163-194
214	TSCATS, OTS 0520408, Doc. I. D. 86-890000970, 8DS, Studies of effects of Diethanolamine in the integrity of rat liver DNA in vivo with attachment, cover sheets and letter, Shell Chemical Company, 09 June 1989
215	BASF AG, Product Safety, Study of the prenatal inhalation toxicity of Diethanolamine in rats after inhalation, BASF Project No. 31R0233/90010, Experimental Toxicology and Ecology, BASF AG, Ludwigshafen, Germany, unpublished report, 08 July 1993
216	BASF AG, Product Safety, Range-finding study on the prenatal inhalation toxicity of Diethanolamin in pregnant rats, BASF Project No. 11R0233/90011, Experimental Toxicology and Ecology, BASF AG, Ludwigshafen, Germany, unpublished report, 20 August 1991
217	Price CJ (1999). Developmental toxicity screen for diethanolamine (CAS No. 111-42-2) administered by gavage to Sprague-Dawley (CD®) rats on gestational days 6 through 19: Evaluation of dams and pups through postnatal day 21. Research Triangle Park NC, USA: Research Triangle Institute, 1999; NTP Study No: TER-96-001 (available from National Technical Information Service, Springfield VA, USA; rep no PB2001-103718)
218	Price CJ, Marr MC, Myers CM, Jahnke GD (2005) Postnatal developmental of rat pups after maternal exposure to Diethanolamine, Birth Defects Res. (Part B), 74, 243-254
219	York RG, Barnwell PL, Pierrera M, Schuler RL, Hardin BD (1988) Evaluation of twelve chemicals in a preliminary developmental toxicity test, Teratology, 37, 503-504
220	Marty MS, Neeper-Bradley TL, Neptun DA, Carney EW (1999) Developmental toxicity of diethanolamine applied cutaneously to CD rats and New Zealand White rabbits, Regul. Toxicol. Pharmacol., 30, 169-181
221	Neeper-Bradley TL (1992) Developmental toxicity evaluation of diethanolamine applied cutaneously to CD rats and New Zealand white rabbits. Project 54-563, Union Carbide Bushy Run Research Center, Export, PA. in: Knaak JB, Leung HW, Stott WT, Busch J, Bilsky J (1997) Toxicology of mono-, di-, and triethanolamine, Rev. Environ. Contam. Toxicol., 149, 1-86
222	TSCATS, OTS 0533705, Doc. I. D. 88-920000004, 8ES, Initial submission from Chemical Manufactures Association to US EPA submitting preliminary findings from an developmental toxicity study in rats on Diethanolamine with attachment, Chemical Manufacturers Assoc., 03 October 1991
223	Craciunescu CN, Wu R, Zeisel SH (2006) Diethanolamine alters neurogenesis and induces apoptosis in fetal mouse hippocampus, FASEB J., 20, 1635-1640
224	Geier J, Lessmann H, Frosch PJ, Pirker C, Koch P, Aschoff R, Richter G, Becker D, Eckert C, Uter W, Schnuch A, Fuchs T (2003) Patch testing with components of water-based metalworking fluids, Contact Dermatitis, 49, 85-90

225	Eisen EA, Tolbert PE, Monson RR, Smith TJ (1992) Mortality studies of machining fluid exposure in the automobile industry I: a standardized mortality ratio analysis, Am. J. Ind. Med. 22, 809-824
226	Eisen EA, Bardin J, Gore R, Woskie SR, Hallock MF, Monson RR (2001) Exposure-response models based on extended follow-up of a cohort mortality study in the automobile industry, Scand. J. Work Environ. Health., 27, 240-249
227	Tolbert PE, Eisen EA, Pothier LJ, Monson RR, Hallock MF, Ssmith TJ (1992) Mortality studies of machining-fluid exposure in the automobile industry. II. Risks associated with specific fluid types, Scand. J. Work Environ. Health., 18, 351-360
228	Eisen EA, Tolbert PE, Hallock MF, Monson RR, Smith TJ, Woskie SR (1994) Mortality studies of machining fluid exposure in the automobile industry III: a case-control study of larynx cancer, Am. J. Ind. Med. 26, 185-202
229	Schroeder JC, Tolbert PE, Eisen EA, Monson RR, Hallock MF, Smith TJ, Woskie SR, Hammond SK, Milton DK (1997) Mortality studies of machining fluid exposure in the automobile industry IV: a case-control study of lung cancer, Am. J. Ind. Med. 31, 525-533
230	Bardin JA, Eisen EA, Tolbert PE, Hallock MF, Hammond SK, Woskie SR, Smith TJ, Monson RR (1997) Mortality studies of machining fluid exposure in the automobile industry V: a case-control study of pancreatic cancer, Am. J. Ind. Med., 32, 240-247
231	Sullivan PA, Eisen EA, Woskie SR, Kriebel D, Wegman DH, Hallock MF, Hammond SK, Tolbert PE, Smith TJ, Monson RR (1998) Mortality studies of metalworking fluid exposure in the automobile industry: VI. A casecontrol study of esophageal cancer, Am. J. Ind. Med. 34, 36-48
232	Jaervholm B, Lavenius B (1987) Mortality and cancer morbidity in workers exposed to cutting fluids, Arch., Environ. Health., 42, 361-366
233	Park RM, Wegman DH, Silverstein MA, Maizlish NA, Mirer FE (1988) Causes of death among workers in a bearing manufacturing plant, Am. J. Ind. Med., 13, 569-580
234	Silverstein MR, Park R, Marmor M, Maizlish N, Mirer F (1988) Mortality among bearing plant workers exposed to metalworking fluids and abrasives, J. Occup. Med., 30, 706-714
235	Park RM, Mirer FE (1996) A survey of mortality at two automotive engine manufacturing plants, Am. J. Ind. Med., 30, 664-673
236	Park RM (2001) Mortality at an automotive engine foundry and machining complex, J. Occup. Environ. Med. 43, 483-493
237	BASF AG (2006). Workplace Exposure of Diethanolamine (CAS 111-42-2). Internal information, 13 Dec 2006, unpublished.
238	DFG (Deutsche Forschungsgemeinschaft). Arbeitsmedizinisch-toxikologische Begruendung von MAK-Werten, VCH, Weinheim, 2001.
239	Geier J, Lessmann H, Dickel H, Frosch P, Koch P, Becker D, Jappe U, Aberer W, Schnuch A, Uter W (2004a) Patch test results with metalworking fluid series of the German Contact Dermatitis Research Group (DKG), Contact Dermatitis, 51, 118-130
240	Geier J, Uter W, Lessmann H, Frosch P (2004b) Patch testing with metalworking fluids from patient's workplace, Contact Dermatitis, 51, 172-179
241	Geier J, Lessmann H, Schnuch A, Uter W (2004c) Contact sensitizations in metalworkres with occupational dermatitis exposed to water-based metal working fluids: Results of the research project "FaSt", Int. Arch. Occup. Environ. Health, 77, 543-551
242	Blum A, Lischka G (1997) Allergic contact dermatitis from mono-, di-, and triethanolamine, Contact dermatitis, 36, 166
243	Bruze M, Hradil E, Eriksohn IL, Gruvberger B, Wildstroem L (1995) Occupational allergic contact dermatitis from alkanolamineborates in metalworking fluids, Contact Dermatitis, 32, 24-27
244	Heydorn S, Menne T, Johansen JD (2003) Fragrance allergy and hand eczema - a review, Contact Dermatitis, 48, 59-66
245	Leikauf GD (2002) Hazardous air pollutants and asthma, Environ. Health Perspect., 110, Suppl 4, 505-526
246	Piipari R, Tuppurainen M, Tuomi T, Maentylae L, Henriks-Eckerman ML, Keskinen H, Nordman H (1998) Diethanolamine-induced occupational asthma, a case report, Clin. Exp. Allergy, 28, 358-362
247	Piipari R, Tuppurainen M, Tuomi T, Maentylae L, Kiskinen H (1996) Diethanolamine-induced occupational asthma, Allergy, 51, Suppl., P129, 84
248	Artom C, Cornatzer WE, Crowder M (1949) The action of an analogue of ethanolamine (diethanolamine) on the formation of liver phospholipids, J. biol. Chem., 180, 495-503
249	Barbee SJ, Hartung R (1978) Tox. Appl. Pharm. 45, 314-315 (abstract)
250	Artom C, Lofland HB, Oates JA (1958) In vivo incorporation of diethanolamine into liver lipids, J. Biol. Chem., 233, 833-837
251	Hruban Z, Swift H, Slesers A (1965) Effect of triparanol and diethanolamine on the fine structure of hepatocytes and pancreatic acinar cells, Lab. Invest., 14, 1652-1672

252	Lehman-McKeeman LD, Gamsky EA (2000) Choline supplementation inhibits diethanolamine-induced morphological transformation in Syrian hamster embryo cells: evidence for a carcinogenic mechanism, Toxicol Sci, 55, 303-10
253	Dierickx P J (1989) Cytotoxicity testing of 114 compounds by determination of protein content in Hep G2 cell cultures, Toxicol. in Vitro, 3, 189-193
254	Preussmann, R, B. Spiegelhalder, Eisenbrand, Würtele, G, Hofmann I (1981) Urinary excretion of N-nitrosodiethanolamine in rats following its epicutaneous and intratracheal administration and its formation in vivo following skin application of diet hanol amine, Cancer Lett., 13, 227-231
255	Report on Carcinogens (2002) Background document Diethanolamine, prepared by: Technology Planning and Management Corporation, Durham, NC, USA, Contract Number N01-ES-85421 for US Department of Health and Human Services, Public Health Service, National Toxicology Program, Research Triangle Park, NC, USA, 22 March 2002
256	Sundlof SF, Mayhew IG (1983) A neuroparalytic syndrome associated with an oral flea repellant containing diethanolamine, Vet. Hum. Toxicol., 25, 247-249
257	Munoz ER, Mazar Barnett B (2003) Chromosome malsegregation induced by the rodent carcinogens acetamide, pyridine and diethanolamine in Drosophila melanogaster females, Mutat Res., 539, 137-144
258	Hayashi S-M, Ton VT, Hong H-HL, Irwin RD, Haseman JK, Devereux TR, Sills RC (2003) Genetic alterations in the Catnb gene but not the H-ras gene in hepatocellular neoplasms and hepatoblastomas of B6C3F1 mice following exposure to diethanolamine for 2 years, Chemico-Biological Interactions, 146, 251-261
259	Munson AE, White KL, McCay JA (1992). Immunotoxicity of diethanolamine in female Fischer 344 rats. Report to National Toxicology Program. Richmond VA, USA: Virginia Commonwealth University, Medical College of Virginia, Immunotoxicology Program
260	Munson AE, White KL, McCay JA (1992). Immunotoxicity of diethanolamine in female B6C3F1 mice. Report to National Toxicology Program. Richmond VA, USA: Virginia Commonwealth University, Medical College of Virginia, Immunotoxicology Program
261	Bachman AN, Kamendulis LM, Goodmann JI (2005) Diethanolamine (DEA) and Phenobarbital (PB) produce an altered pattern of methylation in GC-rich regions in B6C3F1 mouse hepatocytes similar to that resulting from choline deficiency (CD), unpublished manuscript (submitted to be published), 31 October 2005
262	Kamendulis LM (2002) Examination of epigenetic mechanisms of Diethanolamine carcinogenesis: Species comparison studies, Depertament of Pharmacology and Toxicology, Indiana University, Medical Science 1021, Indianapolis, Indiana, USA, unpublished study, 03 December 2002
263	Kamendulis LM (2006) personal communication on the methodology and quality of investigated human hepatocytes, 26 September 2006, unpublished
264	Kamendulis LM and Klaunig JE (2005) Species differences in the induction of hepatocellular DNA synthesis by Diethanolamnin, unpublished manuscript (submitted to be published)
265	Kamendulis LM, Smith DJ, Jiao Z, Klaunig JE (2003) Species differences in the induction of hepatocellular DNA synthesis by Diethanolamine, The Toxicologist, (abstract), 11155, 238
266	Kamendulis LM, Smith DJ, Klaunig JE (2002) Role of choline depletion in Diethanolamine induced DNA synthesis in mouse hepatocytes, The Toxicologist, 66 (abstract), 1507, 308
267	BASF AG, Product Safety, Diethanolamine - S-phase response study in liver and kidney of male B6C3F1 mice, dermal administration for 1, 4 and 13 weeks, BASF Project No. 99C0299/99041, Experimental Toxicology and Ecology, BASF AG, Ludwigshafen, Germany, unpublished report, 16 November 2001
268	Mellert W, Bahnemann R (2001) Diethanolamine (DEA) - Sustained increase in cell proliferation is restricted to target cells in liver and kidneys, The Toxicologist, 60, abstract 1365, 287
269	Mellert W, Kaufmann W, Rossbacher R, van Ravenzwaay B (2004). Investigations on cell proliferation in B6C3F1 mouse by diethanolamine. Food Chem. Toxicol. 42, 127-134
270	BASF AG, Product Safety, Diethanolamine - S-phase response study in liver and kidney of male B6C3F1 mice, dermal administration for 1 week and recovery period of 3 weeks, BASF Project No. 99C0299/99123, Experimental Toxicology and Ecology, BASF AG, Ludwigshafen, Germany, unpublished report, 23 October 2002
271	BASF AG, Product Safety, Diethanolamine - S-phase response in liver and kidney of male B6C3F1 mice, dermal administration for 1 and 13 weeks, BASF Project No. 99C0299/99134, Experimental Toxicology and Ecology, BASF AG, Ludwigshafen, Germany, unpublished report, 15 November 2002

272	BASF AG, Product Safety, Diethanolamine - S-phase response in liver and kidney of male B6C3F1 mice, dermal administration for 1 and 4 weeks with and without choline supplementation in the diet, BASF Project No. 99C0299/99148, Experimental Toxicology and Ecology, BASF AG, Ludwigshafen, Germany, unpublished report, 04 February 2003
273	Fiserova-Bergerova V, Pierce JT, Droz PO (1990) Dermal absorption potential of industrial chemicals: Criteria for skin notation, Am. J. Ind. Med. 17, 617-635
274	Allen DG, Pearse G, Haseman JK, Maronpot RR (2004) Prediction of rodent carcinogenesis: An evaluation of prechronic liver lesions as forecasts of liver tumors in NTP carcinogenicity studies, Toxicologic Pathology, 32, 393-401
275	Rosenkranz HS, Ennever FK, Dimayuga, Klopman G (1990) Significant differences in the structural basis of the induction of sister chromatid exchanges and chromosomal aberrations in Chinese Hamster ovary cells, Environ. Molecular Mutagenesis, 16, 149-177
276	Thompson KL, Rosenzweig BA, Tsong Y, Sistare FD (2000) Evaluation of in vitro reporter gene induction assay for use in a rapid pre-screen for compound selection to test specifity in the Tg.AC mouse short-term carcinogenicity assay, Toxicological science, 57, 43-53
277	Leung HW, Kamendulis LM, Stott WT (2005) Review of the carcinogenic activity of Diethanolamine and evidence of choline deficiency as a plausible mode of action, Regul. Toxicol. Pharmacol. 43, 260-271 (2005)
278	IARC (2000) Some Industrial Chemicals, IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Vol. 77. World Health Organization, Lyon, France
279	McElroy NR, Thompson ED, Jurs PC (2003) Classification of diverse organic compounds that induce chromosomal aberrations in Chinese hamster cells, J. Chem. Inf. Comput. Sci, 43, 2111-2119
280	Balbaa M, Abdel-Hady N, El-Rashidy F, Awad L, El-Ashry E-SH, Schmidt RR (1999) Inhibition of some hepatic lysosomal glycosidases by ethanolamines and phenyl 6-deoxy-6-(morpholin-4-yl)-ß-D-glucopyranoside, Carbohydr. Res., 317, 100-109
281	Inoue K, Sunakawa T, Okamoto K, Tanaka Y (1982) Mutagenicity tests and in vitro transformation assays on triethanolamine, Mutat. Res. 101, 305-313, in: Report on Carcinogens (2002) Background document Diethanolamine, prepared by: Technology Planning and Management Corporation, Durham, NC, USA, Contract Number N01-ES-85421 for US Department of Health and Human Services, Public Health Service, National Toxicology Program, Research Triangle Park, NC, USA, 22 March 2002
282	Kerckaert GA, Brauninger R, LeBoeuf RA, Isfort RJ (1996) Use of Syrian hamster embryo cell transformation assay for carcinogenicity prediction of chemicals currently being tested by the National Toxicology Program in rodent bioassays, Environ. Health Perspect., 104 (Suppl. 5), 1075-1084
283	TSCAT OTS0572566, New Doc I.D. 86950000260, 8D, 24 hour clonal transformation assay using Syrian Golden Hamster (SHE) cells on Diethanolamine as test substance R0430.01 with cover letter, Procter & Gamble, 18 August 1995
284	TSCAT OTS0572568, New Doc I.D. 86950000262, 8D, Letter from Proctor & Gamble to US EPA: 7 day low dose clonal transformation assay on Diethanolamine (R0430.01) with attachments, Proctor & Gamble, 18 August 1995
285	Pritchard JB, French JE, Davis BJ, Haseman JK (2003) The role of transgenic mouse models in carcinogen identification, Environm. Health Perspect., 111, 444-454
286	Spalding IW, French JE, Stasiewicz S, Furedi-Machacek M, Conner F, Tice RR, Tennant RW (2000) Responses of transgenic mouse lines p53+/- and Tg.AC to agents tested in conventional carcinogenicity bioassays, Toxicol. Sci., 53, 213-223
287	American Chemistry Council (2001) Potential mechanisms of tumorigenic action of diethanolamine in mice, Toxicology & Environmental Research and Consulting, The Dow Chemical Company, Midland, MI, USA, report, 23 March 2001
288	Stott WT, Bartels MJ, Brzak KA, Mar M, Markham DA, Thornton CM, Zeisel SH (2000) Potential mechanisms of tumorigenic action of diethanolamine in mice, Toxicol. Lett., 114, 67-75
289	Beard RR, Noe JT (1981) 3168-3169: in Pattys Industrial Hygiene and Toxicology, 3.Ed.
290	BG Chemie (Berufsgenossenschaft der chemischen Industrie, 1990): Toxikologische Bewertung - Diethanolamin, Nr. 158, Ausgabe 05/90, Heidelberg, Germany
291	DFG (Deutsche Forschungsgemeinschaft): Arbeitsmedizinisch-toxikologische Begruendung von MAK-Werten, VCH, Weinheim, 2007
292	Patty FA (1962) Industrial Hygiene and Toxicology, 2nd. Edition, Interscience Publishers, 2066
293	Ullmanns Encyclopedia of Industrial Chemistry Vol.A10, 1-22 (1987)