FOREWORD INTRODUCTION

11-Aminoundecanoic Acid

CAS N°: 2432-99-7

SIDS Initial Assessment Report

For

SIAM 15

Boston, Massachusetts, 22 - 25 October 2002

1. Chemical Name:	11-aminoundecanoic acid
2. CAS Number:	2432-99-7
3. Sponsor Country:	France National SIDS Contact Point in Sponsor Country: Mme Laurence Musset Ministère de l'Environnement et de l'Aménagement du Territoire 20, avenue de Ségur 75302 Paris 07 SP France
4. Shared Partnership with:	
5. Roles/Responsibilities of the Partners:	
• Name of industry sponsor /consortium	
• Process used	
6. Sponsorship History	
• How was the chemical or category brought into the OECD HPV Chemicals Programme ?	
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SIDS INITIAL ASSESSMENT PROFILE

CAS No.	2432-99-7
Chemical Name	11-aminoundecanoic acid
Structural Formula	$HO_2C—(CH_2)10—NH_2$

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Limited information indicated that 11-aminoundecanoic acid is rapidly and extensively absorbed by rats after an oral administration, distributed in the body and rapidly excreted mainly via urine.

The acute toxicity of 11-aminoundecanoic acid is negligible: oral LD_{50} in rats >14700 mg/kg, and dermal LD_0 in rats >2000 mg/kg.

11-aminoundecanoic acid induced no skin irritation and only a slight transient eye irritation in rabbits and did not induce positive response in a skin sensitisation assay in Guinea pigs performed according to the Magnusson and Kligman method.

A NOAEL of 5000 ppm in rats (equivalent to 472 mg/kg bw/d for males and 507 mg/kg bw/d for females) and 9000 ppm in mice was established based on a 4-week and a 13-week dietary toxicity study, respectively. At higher concentrations (up to 21000 ppm) administered for up to 13 weeks to rats and/or mice, 11-aminoundecanoic acid has produced histopathological lesions in the kidney in both species.

In vitro, 11-aminoundecanoic acid did not induce gene mutations on bacteria (Ames test), chromosomal aberrations on CHO cells and gene mutations on L5178Y cells. A slight increase of Sister Chromatid Exchanges (SCEs) has been observed in CHO cells. However, the results of *in vivo* assays override the SCEs increase: 11-aminoundecanoic acid was not genotoxic in a Drosophila recessive lethal test, an *in vivo/in vitro* DNA-repair test on rat hepatocytes and a micronucleus test in mice. In addition, in a DNA-binding study with 11-aminoundecanoic acid, using male and female F-344 rats, no indication of DNA alkylation was found in liver, kidneys or bladder. The overall interpretation of the results provided by *in vitro* and *in vivo* assays is that 11-aminoundecanoic acid is not mutagenic. 11-aminoundecanoic acid was tested for carcinogenicity in mice and rats by administration in the diet at 7500 and 15000 ppm. Increased incidence of transitional-cell carcinomas of the urinary bladder and neoplastic nodules of the liver were observed in male rats. Epithelial hyperplasia of the urinary bladder and renal pelvis were observed in male and female rats. No clear evidence for an increased incidence of treatment-related tumours was seen in mice. The carcinogenic effect observed in animals, involved only male rats treated with very high doses of 11-aminoundecanoic acid, and no clear evidence was found in female rats and in male and female mice. Consequently, the excess of malignant tumours of the urinary tract found in male rats are believed to have occurred through a non-genotoxic mechanism and to be associated with the non-neoplastic local tissue damages which were induced when the dose of 11-aminoundecanoic acid reached a sufficiently high level. IARC categorised 11-aminoundecanoic acid as "non classifiable as to its carcinogenicity to humans" (Category 3), due to the limited evidence provided by the animal data and the absence of epidemiological data (IARC, 1986).

No standard fertility studies are available. However, no effects on the reproductive organs (testes, seminal vesicles, and prostate for male or ovaries and uterus for female) were observed in good quality 90-day and 2-year studies in rats and mice where 11-aminoundecanoic acid was administered in feed at doses up to 21000 and 15000 ppm, respectively. Developmental toxicity studies have been carried out in the rat; 11-aminoundecanoic acid did not produce embryotoxicity or fetotoxicity up to the dose-level of 18000 ppm, with the exception of a slight retardation of growth/skeletal development at dose-levels of 6000 ppm and particularly 18000 ppm (dose-level at which a slight reduction in fetal body weight was also noted). The No Adverse Effect Level for maternal toxicity and embryo-fetal development was established at 6000 ppm (i.e. 520 mg/kg/day). Based on the lack of toxicity on the reproductive organs of male and female rats and mice and the absence of embryo-toxicity and fetotoxicity in pregnant rats, 11-aminoundecanoic acid is unlikely to present reproductive toxicity.

Environment

A pKa (amine) of 11.15 and a pKa (carboxylate) of 4.55 have been determined for 11-aminoundecanoic acid. Therefore, at relevant environmental pH (6-8), the substance will be mainly in zwitterion form. The solubility of 11-aminoundecanoic is pH dependent. At 25°C and pH>=4, the solubility is at maximum 3.2 g/l, a typical value of 0.8 g/l having been measured at environmental pH. At pH <4, the solubility of 11-aminoundecanoic increases with decreasing pH (> 20 g/l below pH 3).

Due to the relatively high solubility (0.8 - 2 g/l), the low octanol-water partition coefficient (log Kow = - 0.16) and the low volatility (2.07 10^{-7} Pa at 25°C) of 11-aminoundecanoic acid, the substance will mainly be present in the aqueous phase. In water it is not expected to hydrolyse. It is readily biodegradable. It is not likely to bioaccumulate. Due to its ionised form, adsorption to soil or sediment with capacity of ion exchange may occur. In the atmosphere, 11-aminoundecanoic acid is rapidly photodegraded by reaction with hydroxyl radicals with an atmospheric average half-life of 4.3 h.

11-aminoundecanoic acid is slightly toxic to aquatic organisms, algae being the most sensitive species with a 72h EbC50 of 23 mg/l. (fish: 96 h LC50 > 833 mg/l; daphnid: 48 h EC50 > 355 mg/l). A PNEC of 45 µg/l may be derived from the NOEC of 4.5 mg/l available on algae applying a safety factor of 100.

Exposure

There is only one producer of 11-aminoundecanoic acid in the world. The production plant is located in the South of France. The annual production capacity is approximately 22,000 tonnes.

11-aminoundecanoic acid is exclusively used as a monomer for the production of polyamides 11 at three different sites; located in Europe (2 sites) and in the US (1 site). Polyamides 11 are used in a number of applications including automotive and aeronautics industries, offshore sector, sport sector, medical and food contact material sector.

The substance is produced and used in closed system. Emissions of 11-aminoundecanoic acid to the environment may occur mainly from production. Aqueous effluents are treated in a waste treatment plant where 11-aminoundecanoic acid is expected to degrade to a large extent due to its ready biodegradability. There are no aqueous streams from the processing of the substance.

There is a potential for professional exposure mainly through inhalation of particles. Personnel protection equipment (mask, gloves and safety glasses) is used during production, handling and use of the substance.

There are no direct consumer uses of 11-aminoundecanoic acid. Food contact materials made of 11-aminoundecanoic acid contain low residual levels of 11-aminoundecanoic acid (< 100 ppm) and are subject to very strict regulations (EU specific migration limit = 0.05 mg/kg food). Therefore, consumer exposure to 11-aminoundecanoic acid is not expected.

RECOMMENDATION

The chemical is currently of low priority for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

The chemical is currently of low priority for further work because of its low hazard potential.

SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substance

CAS Number:	2432-99-7
IUPAC Name:	11-aminoundecanoic acid
Molecular Formula:	$C_{11}H_{23}NO_2$
Structural Formula:	$HO_2C—(CH_2)10—NH_2$
EINECS n°:	219-417-6
Molecular Weight:	201.31
Synonyms:	Aminoundecanoic acid, ω-aminoundecanoic acid, 11-aminoundecylic acid, Undecanoic acid, 11-amino-

1.2 Purity/Impurities/Additives

Purity : > 99.5 %,

Impurities : iron < 12 ppm, calcium < 100 ppm

1.3 Physico-Chemical properties

Form:	white crystalline solid
Bulk density:	550 kg/m^3 at 20°C
Boiling Point:	480.11°C (calculated EPIWIN)
Vapor Pressure	2.07 10^{-7} Pa at 25° C (estimated EPIWIN)
Melting Point:	184°C
Solubility in Water:	pH dependent
	Maximum 3,2g/l at 25°C and pH >= 4 :
	800mg/l at 25°C and pH between 6 and 8
	> 20g/l from pH 3
Density (bulk):	500kg/m3 (at 20°C)
l pKa (amine):	11.15 (at 16°C)
pKa (COOH group):	4.55 (at 16°C)
log Kow:	-0.16 (calculated EPIWIN)
log Koc:	2.45 (calculated)
Flammability:	Not flammable
Odor:	None
Convertion factor:	mg/m^3 = 8.24 ppm (25°C and 760 mmHg)

2 GENERAL INFORMATION ON EXPOSURE

11-Aminoundecanoic acid is produced and used in closed systems. Emissions of the substance to the environment may occur mainly from production. Aqueous effluents are treated in a waste treatment plant where 11-aminoundecanoic acid is expected to degrade to a large extent due to its readily biodegradability. There are no aqueous streams from the processing of the substance.

2.1 Production Volumes and Use Pattern

The substance is produced and used in closed systems. Emissions of 11-aminoundecanoic acid to the environment may occur mainly from production. Aqueous effluents are treated in a waste treatment plant where 11-aminoundecanoic acid is expected to degrade at a large extend due to its readily biodegradability. There are no aqueous streams from the processing of the substance.

In the production of 11-aminoundecanoic acid, castor oil is transesterified with methanol to produce glycerol and methyl ricinoleate. A pyrolitic process converts methyl ricinoleate to methyl 10-undecylenate and heptaldehyde. Methyl 10-undecylenate is hydrolysed, and the resultant acid is treated with hydrogen bromide in the presence of peroxides to yield 11-bromoundecanoic acid. This compound is then converted to 11-aminoundecanoic acid.

ATOFINA is the only producer of 11-aminoundecanoic acid in the world. The production plant is located at Marseille Saint Menet (France). The manufacturing capacity is 22000 tons/year in Europe.

11-aminoundecanoic acid is used exclusively as a monomer for the manufacture of polyamide 11 polymers at three different sites located in Europe (2 sites) and the USA (1 site).

Polyamides 11 are used in wide-ranging applications: oil drilling pipes, brake lines for cars and heavy good vehicles (HGV), electrical cable and optical fibre sheating, medical syringues, food packaging film, sport shoe soles etc. Polyamides 11 are also used for powder anticorrosion coatings which are resistant to wear and impact.

2.2 Environmental Exposure and Fate

2.2.1 Fate in Waste Water Treatment Plants

Based on the SIMPLETREAT model and its ready biodegradability, 11-aminoundecanoic acid is expected to degrade to a large extent in sewage treatment plants. Based on the SIMPLETREAT model, the distribution in a waste water treatment plant is estimated to be:

Air: 0%

Water: 9%

Sludge: 0%

Degraded: 91%

2.2.2 Distribution in Air, Water and Soil

A theoretical distribution of 11-aminoundecanoic acid has been calculated at 20° C using the fugacity model level 1 of Mackay with a vapor pressure of 2.07E-7 Pa and a solubility of 2.0 g/l. Approximately 99.99 % of 11-aminoundecanoic acid released into the environment will enter the water, 0.0.732E-6 % the air compartment, 0.01 % the soils and 0.01 % the sediments.

2.2.3 Abiotic and Biotic Degradation in Air, Water and Soil

2.2.3.1 Atmospheric degradation.

The calculated rate constant of the reaction with OH radicals using the AOP version 1.89 from Syracuse corp. is 44.4 10^{-12} cm^3 $molecule^{-1}$ sec^{-1}.

This corresponds to an atmospheric average 1/2 life of 4.3 hour on the basis of an average concentration of the OH radical of 10^6 molecules/cm^3.

2.2.3.2 Hydrolysis

Based on the structure of the substance, it is not expected to hydrolyse.

2.2.3.3 Biodegradation

11-aminoundecanoic acid is readily biodegradable (77% after 19 days in the OECD 301 B assay) using non-adapted inoculum (ELF ATOCHEM, 1994).

2.2.4 Bioaccumulation

There are no experimental data available for logKow. QSAR methods have been used to calculate the partition coefficient of 11-aminoundecanoic acid. A log K_{ow} of - 0.16 has been estimated using the EPIWIN program.

To evaluate the accuracy of the predicted values versus measured values, EPIWIN was used to estimate the logKow of other aminoacids. The predicted values were compared with the available measured values of these substances. Only very few measured values were found in the literature.

The results are given in the following table :

Substances	CAS n°	logKow Estimated	logKow measured	References
6-aminohexanoic acid	60-32-2	-2.62	-2.95	SRC, Kowin (2002)
8-aminooctanoic acid	1002-57-9	-1.64	-2.55	SRC, Kowin (2002)

The above results support the low bioaccumulation potential of aminoacids. 11-Aminoundecanoic acid is therefore not expected to bioaccumulate.

2.3 Human Exposure

2.3.1 Occupational Exposure

Occupational exposure to 11-aminoundecanoic acid may occur mainly by inhalation of particles.

No specific occupational exposure limits have been determined for 11-aminoundecanoic acid. To recognize the adverse effects of exposure to non toxic particle matter, a TLV-TWA of 10 mg/m^3 for inhalable particle and a TLV-TWA of 3 mg/m^3 for respirable particles have been established by ACGIH (2001).

An occupational exposure survey was conducted in Atofina's production plant of Marseille-Saint Menet. In 1994, inhalable particles were monitored one time at 2 working places and in the ambient air:

Activity	8-hour TWA (mg/m^3)
Operator in charge of the packaging in big bags (Personal monitoring)	11.62
Driver of fork-lift trucks (Personal monitoring)	2.52
Ambient air close to the bag-filling machine (Static sampling)	8.8

Corrective measures were applied to reduce the exposure of the operator in charge of packaging. New big bags were used for packaging instead of recycled big bags, which were at the origin of the release of a large amount of inhalable particles.

Following this corrective measure, the 8-hour TWA at the packaging working area was reduced to 0.90 mg/m^3 (mean of 2 measurements), in a new measurement campaign performed in 1995. Inhalable particles were assumed to be reduced in the same proportion for the driver of fork-lift trucks and in the ambient air close to the bag filling machine.

Moreover, personnel protection equipment (mask, gloves and safety glasses) are used during production, handling and use of the substance

No information is available from sites using the substance.

2.3.2 Consumer Exposure

There are no direct consumer uses of 11-aminoundecanoic acid. Food contact materials made of polyamide 11 contain low residual levels of 11-aminoundecanoic acid (<100 ppm) and are subject to very strict regulations (EU specific migration limit = 0.05 mg/kg food). Therefore, consumer exposure to 11-aminoundecanoic acid is not expected

2.3.3 Indirect exposure via the environment

Based on its low partition coefficient (logKow = - 0.16), 11-aminoundecanoic acid is not expected to bioaccumulate.

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Toxicokinetics, Metabolism and Distribution

Within 24 hours of the oral administration of 1 mCi of 11-^{14}C-aminoundecanoic acid with a specific activity of 14.22 mCi/mmol to male and female F344 rats, approximately 80% of radioactivity was excreted in urine in the form of metabolites and minor amounts of $^{14}C0_2$ were produced by metabolism of 11-^{14}C-aminoundecanoic acid (Atochem, 1988).

3.1.2 Acute Toxicity

11-Aminoundecanoic acid is of relatively low acute toxicity to mammals. Single lethal dosages of 11-aminoundecanoic acid to laboratory animals (table 3.1.2) range from > 14.7 to 21.5 g/kg (LD_{50}) for oral exposure (NTP, 1982; reliability 2) and greater than 2.0 g/kg (LD_0) for dermal exposure (Ato-Chimie, 1978a; reliability 2).

The studies indicated in the table 3.1.2 are equivalent to OECD guideline studies.

Table 3.1.2 Summary of acute oral and dermal toxicity data.

Species	Result	Reference	Reliability
ORAL			
Rat (male)	$LD_0 > 21.5$ g/kg	NTP, 1982	2
Rat (female)	$14.7 < LD_{50} < 21.5$ g/kg	NTP, 1982	2
Rat (male & female)	$LD_{50} > 15$ g/kg	Ato-Chimie, 1978a	2
DERMAL			
Rat (male & female) 24-hour exposure	$LD_0 > 2$ g/kg	Ato-Chimie, 1978a	2

Conclusion

The acute toxicity of 11-aminoundecanoic acid is negligible: oral LD_{50} in rats are >14700 mg/kg, and dermal LD_0 in rats are >2000 mg/kg.

3.1.3 Irritation

Skin Irritation

11-Aminoundecanoic acid is not irritant after a 24-hour occlusive application on the rabbit skin (Ato-Chimie, 1978b; reliability 2)

Eye Irritation

11-Aminoundecanoic acid induced a slight transient irritation when instillated in the rabbit eye (Ato-Chimie, 1978b, reliability, 2).

3.1.4 Sensitisation

11-Aminoundecanoic acid was not sensitizer in Guinea pigs in a test performed according to the maximization method of Magnusson and Kligman (Elf Atochem, 1999; reliability 1).

3.1.5 Repeated Dose Toxicity

Two 90-day oral range-finding studies in rats and mice, preliminary to chronic/carcinogenicity studies have been performed by the US National Toxicology Program (NTP, 1982). Although these range-finding studies were of good quality and well reported (at least for the histopatological examination), they did not cover all the parameters recommended by the OECD guidelines (hematological, clinical biochemistry, urine analysis and FOB were not performed and daily intake, clinical signs, food consumption, and organ weights were not reported) and did not allow to establish a precise NOAEL. Accordingly, to determine a NOAEL and to fill the SIDS requirements,

a new sub-acute oral toxicity was performed with rats according to OECD guideline #407 and GLP (Atofina, 2001a).

In this sub-acute oral toxicity study (Atofina, 2001a ; reliability 1), 11-aminoundecanoic acid was given by dietary admixture to groups of 6 males and 6 females Sprague-Dawley rats for 4 weeks at the concentrations of 1250, 5000 and 20000 ppm, corresponding to 118, 472 and 1644 mg/kg/day in males and 129, 507 and 1828 mg/kg/day in females. 11-Aminoundecanoic acid was well-tolerated at the lowest dose-levels. At 5000 ppm, the only adverse effect was a slight decrease in body weight gain (not statistically significant) correlated with lower food consumption noted among treated males. At 20000 ppm, moderate decrease in body weight gain and food consumption were noted among the treated males and females. At clinical pathology, lower values for red blood cell parameters, and APTT, higher fibrinogen, and urea levels in both sexes were noted. Decreased liver enzyme activities and increased triglyceride levels were noted in males. Treatment-related lesions were observed in the kidneys of both sexes. Consequently, 5000 ppm (472 mg/kg/day for the males and 507 mg/kg/day for the females) was established as the No Observed Adverse Effect Level (NOAEL).

In the two range-finding toxicity studies preliminary to chronic/carcinogenicity studies performed by the US National Toxicology Program (1982; reliability 2), diets containing 0; 9,000; 12,000; 15,000; 18,000; 20,000 (mice) or 21,000 ppm (rats) 11-aminoundecanoic acid were given for 13 weeks to groups of 12 male and 12 female F 344 rats and to groups of 10 male and 10 female B6C3F1 mice. Animals were checked for mortality and signs of morbidity twice a day. Each animal was given a weekly clinical examination, including palpation for tissue masses or swelling. Body weight and feed consumption data were collected weekly. At the end of the 91-day study, survivors were killed with carbon dioxide, necropsies were performed and a full range of organs[1] were examined histopathologically for control and high-dose groups. Histopathologic examination for all other dosed groups was limited to the kidneys and liver, except for male and female rats (kidneys, liver, lungs, and heart) and male and female mice (no histological examination) administered 12,000 ppm.

One of the 12 female rats fed with the 18,000 ppm diet died at day 9. Mean body weight gain in male rats fed with diets containing 18,000 or 21,000 ppm 11-aminoundecanoic acid was depressed 13 % and 14 %, respectively. Multifocal tubular mineralization of the kidneys was noted in 70 % - 100 % of all groups of female rats administered 11-aminoundecanoic acid. The severity of the mineralization was dose related. Transitional-cell hyperplasia was found in the kidneys of 1/10 male rat fed 21,000 ppm, in 6/10 females fed 21,000 ppm, and in 2/9 females fed 18,000 ppm 11-aminoundecanoic acid. Hyperplasia of the renal pelvis were seen in 2/9 females fed 18,000 ppm and in 1/10 male and 6/10 females fed 21,000 ppm.

Deaths occurred in 2/10 male and 2/10 female mice administered 15,000 ppm, 4/10 males and 2/10 females receiving 18,000 ppm, and 3/10 males receiving 20,000 ppm. The cause of death of animals dying during the study was not determined. Mean body weight gain was depressed 20 % in male mice receiving 15,000 ppm, but only 10 % in male mice receiving 18,000 or 20,000 ppm. Mean body weight gain was depressed by more than 10 % in female mice fed diets containing 18,000 - 20,000 ppm 11-aminoundecanoic acid. Focal mineralization of the kidney was noted in males that received 15,000 - 20,000 ppm and in females that received 15,000 - 18,000 ppm, particularly in those mice that died.

[1] Organs examined histopatologicaly included: gross lesions, tissue masses, abnormal lymph nodes, skin, mandibular lymph nodes, mammary gland, salivary gland, thigh muscle, sciatic nerve, bone marrow, costochondral junction (rib), thymus, larynx, trachea, lungs and bronchi, heart, thyroid, parathyroid, esophagus, stomach, duodenum, jejunum, ileum, colon, mesenteric lymph nodes, liver, gallbladder (mice), pancreas, spleen, kidneys, adrenals, bladder, seminal vesicles/prostate/ testes or ovaries/uterus, nasal cavity, brain pituitary, and spinal cord.

A no adverse effect level of 9000 ppm in mice and lower than 9000 ppm in rats were established in that 90-day sub-chronic study.

The studies are summarized in the table 3.1.5

Table 3.1.5 Summary of repeated dose oral toxicity data.

	ATOFINA, 2001a	NTP, 1982	NTP, 1982
Guideline	OECD # 407, 1995	US NTP range-finding study	US NTP range-finding study
GLP	Yes	No data	No data
Reliability	1	2	2
Protocol			
Species	Sprague-Dawley rats	F344 rats	B6C3F1 mice
Number of animals	6/sex/group	12/sex/group	10/sex/group
Route of administration	Oral feed	Oral feed	Oral feed
Dose levels	0, 1250, 5000 & 20000 ppm	0, 9000, 12000, 15000, 18000 & 21000 ppm	0, 9000, 12000, 15000, 18000 & 20000 ppm
Exposure period	4 weeks	13 weeks	13 weeks
Post-exposure period	None	None	None
Results			
Daily intake	118/129, 472/507 and 1644/1828 mg/kg bw/d for male/female, respectively	Not reported	Not reported
Mortality	None	18000 ppm: 1/12 ♀ on day 9	15000 ppm: 2/10 ♂ and 2/10 ♀ 18000 ppm: 4/10 ♂and 2/10 ♀ 20000 ppm: 3/10 ♂
Clinical signs	None	Not reported	Not reported
Functional observation battery	No effect	Not done	Not done
Body weight	↓ at 20000 ppm ♂♀	♂: ↓ at 18000 and 21000 ppm	15,000 ppm: ↓ 20 % in ♂ 18000 and 20000 ppm: ↓ 10 % in ♂ and 13 & 25% in ♀
Food consumption	↓ at 20000 ppm ♂♀	Not reported	Not reported
Haematology[1]	20000 ppm ♂♀: ↓ Hb, PCV & APTT, ↑ fibrinogen. ♂: ↓ MCV & MCH	Not done	Not done
Blood chemistry[2]	20000 ppm ♂: ↓ P; AP & ALAT, ↑ urea & TG ♀: ↑ urea	Not done	Not done
Urinalysis	No effect	Not done	Not done

[1] Hb, hemoglobin concentration; PCV, packed cell volume; MCV, mean cell volume; MCH, mean cell hemoblobin; APTT activated partial thromboplasmin time.

[2] P, inorganic phosphorus; AP, alkaline phosphatase, ALAT, alanine aminotransferase, TG, triglycerides.

Organ weights	♂♀: ↑ kidney weight at 5000 (ns) & 20000 ppm ($p<0.01$)	Not reported	Not reported
Histopathology	Kidney (20000 ppm): ♂♀: cortical tubular dilatation ♀: lesions of the renal papilla	Kidney: . Multifocal tubular mineralization in 70-100% of all ♀ groups (the severity was dose related). . Transitional-cell hyperplasia in 1/10 ♂ (21,000 ppm), 6/10 ♀ (21,000 ppm), and 2/9 ♀ (18,000 ppm). . Hyperplasias of the renal pelvis in 2/9 ♀ (18,000 ppm) and 1/10 ♂ and 6/10 ♀ (21,000 ppm).	Kidney: . Focal mineralization in ♂ (15,000 - 20,000 ppm) & ♀ (15,000 - 18,000 ppm, particulary in those mice that died).
NOAEL[3]	5000 ppm, 472 mg/kg bw/d for ♂ and 507 mg/kg bw/d for ♀	< 9000 ppm (about 900 mg/kg bw/d)	9000 ppm[4] (about 1800 mg/kg bw/d)

Conclusion

A NOAEL of 5000 ppm in rats (equivalent to 472 mg/kg bw/d for males and 507 mg/kg bw/d for females) and 9000 ppm in mice was established based on a 4-week and a 13-week dietary toxicity study, respectively. At higher concentrations (up to 21000 ppm) administered for up to 13 weeks to rats and/or mice, 11-aminoundecanoic acid has produced histopathological lesions in the kidney in both species.

3.1.6 Mutagenicity

In 1986, based on the results of a sex-linked recessive mutation assay (Yoon et al., 1985) and an unscheduled DNA synthesis assay in hepatocytes of rats treated *in vivo* (Mirsalis et al., 1983), IARC concluded that the degree of evidence in short-term tests for genetic activity was inadequate. Since this date, 11-aminoundecanoic acid has been tested extensively *in vitro* in mammalian and non-mammalian cells and *in vivo* in rodents.

In vitro Studies

11-Aminoundecanoic acid did not show a genotoxic potential in reverse gene mutation assays in *Salmonella typhimurium* and *Escherichia coli*, in a chromosome aberrations test on CHO cells and in a gene mutations test on L5178 Y tk+/tk- cells. A slight increase of sister chromatid exchanges (SCE) in CHO cells has been observed in the absence of metabolic activation.

The studies indicated in the table 3.1.6.1 are equivalent to OECD guideline studies.

[3] NOAEL, no-observed adverse effect level.

[4] The histological examination was not performed on the 12000 ppm dose level.

Table 3.1.6.1 Summary of *in vitro* genotoxicity data.

Test system	Results	References	Reliability
Salmonella typhimurium TA100, TA1535, TA1537, TA98 Up to 10 mg/plate +/- S9	Negative	Mortelmans et al., 1986	2
Salmonella typhimurium TA100, TA1535, TA1538, TA1537, TA98 Up to 1 mg/plate +/- S9	Negative	Ato-Chimie, 1982	2
Salmonella typhimurium TA100, TA1535, TA1538, TA1537, TA98 Up to 5 mg/plate +/- S9	Negative	TORAY, 1982	2
Escherichia coli WP2 uvrA Up to 5 mg/plate +/- S9	Negative	TORAY, 1982	2
Gene mutation in L5178Y tk+/tk- Mouse Lymphoma cells. Up to 320 µg/ml +/- S9	Negative	Mc Gregor et al., 1988	2
Chromosome aberrations in CHO cells. Up to 1 mg/ml +/- S9	Negative	Galloway et al., 1987	2
Sister chromatid exchanges in CHO cells Up to 1 mg/ml +/- S9	Ambiguous – S9 Negative + S9	Galloway et al, 1987	2

In vivo Studies

11-Aminoundecanoic acid has not shown a genotoxic potential in a Drosophila recessive lethal test (Yoon et al., 1985; reliability 2), an *in vivo/in vitro* DNA-repair test on rat hepatocytes (Mirsalis et al., 1989; reliability 2) and a micronucleus test in mice (Shelby et al, 1993; reliability 2).

In a DNA-binding study with labelled 11-aminoundecanoic acid using male and female F-344 rats, liver, kidneys and urinary bladder have been examined both for association of radioactivity with DNA and for DNA alkylation (i.e., formation of altered radioactive nucleosides in DNA). There was minor incorporation of 11-aminoundecanoic acid derived radioactivity into the physiological DNA nucleosides (in the liver higher than in kidneys, in males higher than in females). This could not be observed in DNA from the urinary bladder, but from this organ only low amounts of DNA were isolated due to the limited mass of tissue available. Upon chromatography (HPLC) of hydrolysates from DNA (isolated from livers and kidneys) no significant radioactive peaks were observed besides those of the physiological nucleosides; therefore, there was no indication of DNA alkylation by 11-aminoundecanoic acid or a metabolite thereof. On this basis, this DNA-binding study was considered as being negative (Atochem, 1987; reliability 2).

The studies indicated in the table 3.1.6.2 are equivalent to OECD guideline studies.

Table 3.1.6.2 Summary of *in vivo* genotoxicity data.

Test system	**Test conditions**	Results	References	Reliability
Micronucleus assay in mouse bone marrow	3 daily i.p. injection up to 500 mg/kg	Negative	Shelby et al., 1993	2
Drosophila melanogaster SLRL assay	Single injection at 1000 ppm	Negative	Yoon et al., 1985	2
Ex vivo uncheduled DNA synthesis assay in rat hepatocytes	Single oral administration up to 1000 mg/kg	Negative	Mirsalis et al., 1989	2
DNA binding assay in liver, kidneys and bladder of rats	Single oral administration at 1 mCi/rat	Negative	Atochem, 1987	2

Conclusion

The overall interpretation of the results provided by *in vitro* and *in vivo* assays is that 11-aminoundecanoic acid is not mutagenic. The slight increase in SCE observed *in vitro* is overridden by the negative *in vivo* assays. Morever, no DNA binding was observed in the target organs identified in the carcinogenicity study with rats.

3.1.7 Carcinogenicity

The carcinogenic potential of 11-aminoundecanoic acid has been evaluated in two cancer bioassays in rats and mice (NTP, 1982; reliability 2).

Rat study

Groups of 50 male and 50 female Fischer 344/N rats, six weeks of age, were fed a diet containing 7500 or 15000 ppm 11-aminoundecanoic acid for 104 weeks. An equal number of untreated rats served as controls. Survival was 78 % of control, 74 % of low-dose and 60 % of high-dose males and 76 % of control, 64 % of low-dose and 84 % of high-dose females. All surviving animals were killed after 109 weeks. A treatment-related increase in the incidence of transitional-cell carcinoma of the urinary bladder was observed in males only: in 0/48 control, 0/48 low-dose and 7/49 ($p < 0.01$) high-dose animals; there were also 1/49 transitional-cell papilloma of the urinary bladder and 1/50 transitional-cell carcinoma of the kidney in the high-dose group. Dose-related transitional-cell hyperplasia of the urinary bladder and renal pelvis was observed in males and females. An increased incidence of calculi of the urinary bladder was seen in males in the high-dose group (1/48 (2 %) control, 1/48 (2 %) low-dose and 5/49 (10 %) high-dose animals) only in animals that did not develop a transitional-cell carcinoma. Two of 50 high-dose females had transitonal-cell carcinomas of the kidney, and no calculi were observed in these animals. Treatment-related neoplastic nodules of the liver were also observed in males: in 1/50 controls; 9/50 ($p < 0.01$) low-dose and 8/50 ($p < 0.01$) high-dose animals; in addition, 1/50 low-dose and 2/50 high-dose animals had hepato-cellular carninomas.

Comments on neoplastic nodules of the liver in Fischer 344 male rats:

These tumours are benign tumours very common in this specific strain and sex. From one bioassay to another, the background incidences within the control groups are highly fluctuant, from 0 to 20.8% (Lang, 1990). The observed incidences in the NTP bioassay remain within the overall historical variations. The higher incidence in the 11-aminoundecanoic acid treated rats compared with the control group in the same bioassay can be interpreted as a random distribution, especially because there is no dose-related effect (same rate at 7500 and 15,000 ppm) because no similar effect was seen in female rats which are also prone to develop such tumors (control: 4/50; low dose: 5/50; high dose: 6/50).

Consequently, the actual biological significance of the observed elevation of such benign neoplastic nodules in the liver is very unclear.

Comments on transition-cell carcinoma of the urinary bladder:

Firstly, these malignant tumours occurred only in the higher dose group. This may be interpreted as an effect submitted to a dose threshold. The threshold would be localized between 7500 and 15,000 ppm of 11-aminoundecanoic acid in the diet for a two year treatment.

Secondly, all the animals bearing transition-cell carcinoma had hyperplasia of the urinary bladder epithelium. Such non neoplastic lesions of the urinary tract were pre-existing to the tumours since they were observed already at an earlier stage with the same doses of 11-aminoundecanoic acid (as found, e.g in the 90-day prechronic study of the same NTP bioassay). Such hyperplasia of the epithelium may be linked to the mineralization process that occurred in the urinary tract of rodents repeatedly treated with high dose levels of 11-aminoundecanoic acid. These non-neoplastic lesions of the urinary organs may create specific conditions where an accelerated regeneration of the epithelial cells and the associate cells is continuously present during nearly the whole life of the treated animals.

This specific cell situation can be associated with a high elevation of the chances that some of the cells may proceed to a malignant stage.

Although the mechanism for development of these tumors is unknown, it can be hypothesized that the transition-cell carcinoma found in male Fischer 344 rats were an indirect consequence of the non-neoplastic local effect induced by 11-aminoundecanoic acid when very high dose levels are repeatedly ingested by the rats, exceeding the threshold level of 7500 ppm in the diet, every day during almost their whole life.

Mouse study

Groups of 50 male and 50 female B6C3F1 mice, six weeks of age, were fed a diet containing 7500 or 15000 mg/kg (ppm) 11-aminoundecanoic acid for 103 weeks. An equal number of untreated mice served as controls. Survival was 74 % of control, 68 % of low-dose and 36 % of high-dose males, and 85 % of control, 76 % of low-dose and 51 % of high-dose females. All surviving animals were killed after 108-109 weeks. Increases in the incidence of malignant lymphomas occurred in male mice only: in 2/50 control, 9/50 ($p < 0.05$) low-dose, and 4/50 (ns) high-dose animals.

Comments on malignant lymphomas in male mice:

The increase of malignant lymphomas in male mice was statistically significant only at the low dose but not at the high dose. In most of the affected mice, two or more organs were involved in the neoplastic process. Malignant lymphomas were among the most common tumours. The background incidence was reported to be up to 17.9% for male control mice (Lang, 1989; Tamano et al., 1988) and 2 to 20% (mean 8.3%) in control B6C3F1 mice from 2-year carcinogenicity studies carried out by NTP (Haseman et al., 1998). The observed incidences in the NTP bioassay remain within the overall historical variations.

Conclusion

11-Aminoundecanoic acid was tested for carcinogenicity in mice and rats by administration in the diet at 7500 and 15000 ppm. An increased incidence of transitional-cell carcinomas of the urinary bladder and neoplastic nodules of the liver were observed in male rats. Epithelial hyperplasia of the urinary bladder and renal pelvis were observed in male and female rats. No clear evidence for an increased incidence of treatment-related tumours was seen in mice. The overall interpretation of the

results provided by a battery of *in vitro* and *in vivo* short term genotoxicity test is that 11-aminoundecanoic acid has no genotoxic potential. Consequently, the excess of malignant tumours of the urinary tract found in male rats are believed to have occurred through a non-genotoxic mechanism and to be associated with the hyperplasia which were induced when the dose of 11-aminoundecanoic acid reached a sufficiently high level. IARC categorized 11-aminoundecanoic acid as "non classifiable as to its carcinogenicity to humans" (Category 3), due to the limited evidence provided by the animal data and the absence of epidemiological data (IARC, 1986).

3.1.8 Toxicity for Reproduction

No standard fertility studies are available. However, according to the SIDS manual, when a 90-day repeated dose study is available and is sufficiently documented with respect to studying effects on reproductive organs, and a developmental study is available, the requirements for the reproduction toxicity endpoint are satisfied.

Effects on Fertility

No effects on the reproductive organs (testes, seminal vesicles, prostate or ovaries and uterus) were observed in good quality 90-day and 2-year studies (see sections 3.1.3 and 3.1.5) in rats and mice where 11-aminoundecanoic acid was administered in feed at doses up to 21000 and 15000 ppm, respectively (NTP, 1982, reliability 2).

Developmental Toxicity

In developmental toxicity study performed according to the OECD guideline #414 and GLP, 11-aminoundecanoic acid was administered daily to pregnant Sprague-Dawley female rats by dietary admixture at the constant concentrations of 2000, 6000 and 18000 ppm from day 2 to day 19 post-coitum (equivalent to a daily intake of 172, 520 and 1394 mg/kg bw/day, respectively). 11-Aminoundecanoic acid was well tolerated at 2000 and 6000 ppm. As a consequence of poor appetite, possibly due to the unpalatability of the dietary admixture at 18000 ppm, lower food consumption (-19% compared to control group, $p<0.01$), maternal body weight gain (-44% compared to control group, $p<0.01$) and fetal body weight (3.81 g versus 4.07 in control group, $p<0.05$) were recorded. The incidence of skeletal variations was slightly higher in the 6000 and 18000 ppm treated groups than in the control group. The difference in the incidence of affected fetuses and litters, when expressed as % are actually small: 81.7, 89.5, 92.9 and 89.9% at 0, 2000, 6000 and 18000 ppm, respectively. The differences in the overall incidence of variation achieved significance ($p<0.01$) only in the case of the fetuses in the 6000 ppm group. The increases are considered to represent a slight retardation in the growth and do not represent a direct adverse effect. Consequently, the No Adverse Effect Level for maternal toxicity and embryofetal development was established at 6000 ppm (i.e. 520 mg/kg/day) (Atofina, 2001b; reliability 1).

Conclusion

Based on, i) the lack of toxicity on the reproductive organs of male and female rats and mice after a 90-day and a 2-years administration in feed at doses up to 21000 and 15000 ppm, respectively, ii) the absence of embryo-toxicity and foeto-toxicity in pregnant rats up to the dose-level of 18000 ppm (with the exception of a slight retardation of growth/skeletal development at dose-levels of 6000 ppm and particularly 18000 ppm dose-level, at which a slight reduction in fetal body weight was also noted), 11-aminoundecanoic acid is unlikely to present reproductive toxicity, and no additional study is necessary.

3.2 Initial Assessment for Human Health

Limited information indicated that 11-aminoundecanoic acid is rapidly and extensively absorbed by rats after an oral administration, distributed in the body and rapidly excreted mainly via urine.

11-Aminoundecanoic acid is of low acute oral (LD50 > 14700 mg/kg in rats) and dermal (LD0 > 2000 mg/kg in rats) toxicity.

A NOAEL of 5000 ppm in rats (equivalent to 472 mg/kg bw/d for males and 507 mg/kg bw/d for females) and 9000 ppm in mice was established based on a 4-week and a 13-week dietary toxicity study, respectively. At higher concentrations (up to 21000 ppm) administered for up to 13 weeks to rats and/or mice, 11-aminoundecanoic acid have produced histopathological lesions in the kidney in both species.

Regarding genetic toxicity, 11-aminoundecanoic acid when tested *in vitro* did not show a genotoxic potential in Ames tests, a chromosome aberrations test on CHO cells and a gene mutations test on L5178Y cells. A slight increase of SCE in CHO cells hase been observed. However, the results of i*n vivo* assays override the SCEs increase, 11-aminoundecanoic acid was not genotoxic in a Drosophila recessive lethal test, an *in vivo/in vitro* DNA-repair test on rat hepatocytes and a micronucleus test in mice. In addition, in a DNA-binding study with 11-aminoundecanoic acid, using male and female F-344 rats, no indication of DNA alkylation was found in liver, kidneys or bladder. The overall interpretation of the results provided by *in vitro* and *in vivo* assays is that 11-aminoundecanoic acid is not mutagenic.

11-aminoundecanoic acid was tested for carcinogenicity in mice and rats by administration in the diet at 7500 and 15000 ppm. Increased incidence of transitional-cell carcinomas of the urinary bladder and neoplastic nodules of the liver were observed in male rats. Epithelial hyperplasia of the urinary bladder and renal pelvis were observed in male and female rats. No clear evidence for an increased incidence of treatment-related tumours was seen in mice. The carcinogenic effect observed in animals, involved only male rats treated with very high doses of 11-aminoundecanoic acid, and no clear evidence were found in female rats and in male and female mice. Consequently, the excess of malignant tumours of the urinary tract found in male rats are believed to have occured through a non-genotoxic mechanism and to be associated with the non-neoplastic local tissue damages which were induced when the dose of 11-aminoundecanoic acid reached a sufficiently high level. That interpretation is consistent with the IARC evaluation, that categorized 11-aminoundecanoic acid as "non classifiable as to its carcinogenicity to humans" (Category 3), due to the limited evidence provided by the above data and the absence of epidemiological data (IARC, 1986).

No standard reprotoxicity studies are available. However, no effects on the reproductive organs (testes, seminal vesicles, prostate or ovaries and uterus) were observed in good quality 90-day and 2-years studies in rats and mice where 11-aminoundecanoic acid were administered in feed at doses up to 21000 and 15000 ppm, respectively (NTP, 1982, reliability 2).

Developmental toxicity studies have been carried out in the rat; 11-aminoundecanoic acid did not produce embryotoxicity or fetotoxicity up to the dose-level of 18000 ppm, with the exception of a slight retardation of growth/skeletal development at dose-levels of 6000 ppm and particularly 18000 ppm (dose-level at which a slight reduction in fetal body weight was also noted). The No Adverse Effect Level for maternal toxicity and embryofetal development was established at 6000 ppm (i.e. 520 mg/kg/day). According to the SIDS manual, the requirements for the reproduction toxicity endpoint are satisfied.

11-aminoundecanoic acid induced no skin irritation and only a slight transient eye irritation in rabbits and did not induce positive response in a skin sensitization assay in Guinea pigs performed according to the Magnusson and Kligman method.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

11-Aminoundecanoic acid has been shown to be practically not harmful to fish and daphnids and harmful to algae (fish : 96 h LC50 > 833 mg/l; daphnid : 48 h EC50 > 355 mg/l; algae : 72 h EC50 = 23 mg/l)

Acute Toxicity Test Results

Acute toxicity to fish

The study on fish species can be considered valid without restrictions.

Species	Duration	Results	Remarks	References	Reliability
Brachydanio rerio	96 h	LC50 > 833 mg/l	Static, with analysis	Atofina, 2001c	1

Acute toxicity to daphnia

The study on daphnid can be considered to be valid without restrictions.

Species	Duration	Results	Remarks	References	Reliability
Daphnia magna	48 h	EC50 > 350 mg/l	with analysis	Elf Atochem, 1995	1

Acute toxicity to algae

There is one acute toxicity test available for algae, which can be considered as valid without restriction.

Species	Duration	Results	Remarks	References	Reliability
Pseudokirchneriella subcapitata	72 h	ErC50 = 53 mg/l ErC10 = 10 mg/l NOEC = 4.5 mg/l EbC50 = 23 mg/l EbC10 = 5.8 mg/l NOEC = 4.5 mg/l	with analysis	Atofina, 2001d	1

Acute toxicity to micro-organisms

The study followed ISO/DIS 10712 standard and determined a 16 h EC50 of 1.5 mg/l for inhibition of the growth of *Pseudomonas putida*.

Chronic Toxicity Test Results

No data.

PNEC for the aquatic environment

Data are available from short term tests at 3 trophic levels. A safety factor of 1000 should be applied to the lowest EC/LC50 according to the TGD.

Due to the fact that algae seem to be more sensitive that both fish and daphnia (LC50 fish> 833 mg/l, EC50 daphnia > 350mg/l), it is proposed to apply a safety factor of 100 to the algae NOEC.

Based on the *Pseudokirchneriella subcapitata* study, a PNEC of 45 µg/l may therefore be derived.

4.2 Terrestrial Effects

No data

4.3 Initial Assessment for the Environment

Due to the relatively high solubility, low octanol water partition coefficient and low volatility of 11-aminoundecanoic acid, the substance is not expected to adsorb to sediment and will mainly be present in the aqueous phase. The substance is readily biodegradable and not likely to bioaccumulate.

Due to its ionised form, adsorption to soil or sediment with capacity of ion exchange may occur. In the atmosphere, 11-aminoundecanoic acid is rapidly photodegraded by reaction with hydroxyl radicals with an atmospheric average half-life of 4.3 h.

11-aminoundecanoic acid is slightly toxic to aquatic organisms, algae being the most sensitive species with a 72h EbC50 of 23 mg/l. (fish: 96 h LC50 > 833 mg/l; daphnid : 48 h EC50 > 355 mg/l). A PNEC of 45 µg/l may be derived from the EC10 of 4.5 mg/l available on algae applying a safety factor of 100.

5 RECOMMENDATIONS

11-aminoundecanoic acid is currently of low priority for further work because of its low hazard potential.

6 REFERENCES

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I U C L I D

Data Set

Existing Chemical	:	ID: 2432-99-7
CAS No.	:	2432-99-7
EINECS Name	:	11-aminoundecanoic acid
EC No.	:	219-417-6
Molecular Weight	:	201
Molecular Formula	:	C11H23NO2

Producer related part

Company	:	Atofina
Creation date	:	04.01.2001

Substance related part

Company	:	Atofina
Creation date	:	04.01.2001
Status	:	
Memo	:	
Printing date	:	13.08.2004
Revision date	:	
Date of last update	:	13.08.2004
Number of pages	:	101
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

Type	:	manufacturer
Name	:	ATOFINA
Contact person	:	
Date	:	
Street	:	4, cours Michelet - Cedex 42
Town	:	92091 Paris la defense 10
Country	:	France
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

29.01.2002

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

Type	:	manufacturer
Name of plant	:	ATOFINA
Street	:	123, bd de la Millière B.P. 6
Town	:	13367 MARSEILLE
Country	:	France
Phone	:	+33 4 91 24 10 00
Telefax	:	+33 4 91 24 10 04
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

01.02.2002

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

IUPAC Name	:	11-aminoundecanoic acid
Smiles Code	:	O=C(O)CCCCCCCCCCN
Molecular formula	:	C11H23NO2
Molecular weight	:	201.31
Petrol class	:	

29.01.2002

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type : typical for marketed substance
Substance type : organic
Physical status : solid
Purity : > 99.5 % w/w
Colour : white
Odour : None

Remark : Transmittence at 400 nm : 93.7% (Minimum specifications: 92%)
Reliability : The administration of up to 20000 ppm 11-aminoundecanoic acid in the diet of mice for 13 weeks leads to focal mineralisation of the kidneys and body weight depression. The NOAEL was estimated to be 9000 ppm.

11.06.2002

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

Undecanoic acid, 11-amino- ; Aminoundecanoic acid

11.06.2002

1.3 IMPURITIES

Purity : other
CAS-No :
EC-No :
EINECS-Name :
Molecular formula :
Value :

Remark : Ca content : 46 ppm (Maxi 100)
Iron content : 1 ppm (Maxi 12)

11.06.2002

1.4 ADDITIVES

1.5 TOTAL QUANTITY

Quantity : = - 22000 tonnes produced in 2002

Remark : Manufacturing capacity : 22000 tons
Only one site of production.

08.08.2003

1.6.1 LABELLING

Labelling : no labelling required (no dangerous properties)
Specific limits :

11.06.2002

1.6.2 CLASSIFICATION

Classified : no classification required (no dangerous properties)
Class of danger :
R-Phrases :
Specific limits :
1st Concentration :
2nd Concentration :
3rd Concentration :
4th Concentration :
5th Concentration :
6th Concentration :
7th Concentration :
8th Concentration :
1st Classification :
2nd Classification :
3rd Classification :
4th Classification :
5th Classification :
6th Classification :
7th Classification :
8th Classification :

11.06.2002

1.6.3 PACKAGING

1.7 USE PATTERN

1.7.1 DETAILED USE PATTERN

Industry category : 11 Polymers industry
Use category : 33 Intermediates
Extra details on use category : Polymer processing
No extra details necessary
Emission scenario document : not available
Product type/subgroup :
Tonnage for Application :
Year :
Fraction of tonnage for application :
Fraction of chemical in formulation :
Production : :
Formulation : :
Processing : :
Private use :
Recovery :

11.06.2002

1.7.2 METHODS OF MANUFACTURE

Origin of substance : Synthesis
Type : Production

Remark : Aminoundecanoic acid is synthesized through a series of reactions from ricinoleic acid isolated from castor bean oil.

Process description:
- Transesterification of the castor oil with methanol to form methyl ricinoleate.
- Washing with water to recover the glycerine.
- Elimination of methanol and soaps in excess.
- Thermal cracking of the methyl ricinoleate to form heptanal and methyl undecylenate.
- Hydrolysis of the methyl undecylenate to form undecylenic acid (and methanol), methanol is recycled.
- Purification of undecylenic acid by hydrobromic acid to form undecanoic acid, 11-bromo.
- The solvent is evaporated and recycled.
- Reaction between ammonia and undecanoic acid, 11-bromo to form UNDECANOIC ACID, 11-AMINO.
- Purification of the product by dissolution, filtration, crystallization and drying.

08.08.2003

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

Type of limit : TLV (US)
Limit value : 10 mg/m3

Country : USA
Remark : Dust value
11.06.2002 (33)

Type of limit : other
Limit value : 10 mg/m3

Country : FRANCE
Remark : Dust value (VME)
Source : ELF ATOCHEM Paris la defense 10
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
26.01.1995 (32)

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

Source of exposure : Human: exposure by production
Exposure to the : Substance

Remark : Occupational exposure to 11-aminoundecanoic acid may mainly occurs by inhalation of particles.

An occupational exposure survey was conducted in the Atofina's production plant of Marseille-Saint Menet. $
In 1994, inhalable particles were monitored one time at 2 working places and in the ambient air:

Activity	8-hour TWA (mg/m3)
Operator in charge of the packaging in big bags (Personal monitoring)	11.62
Driver of fork-lift trucks (Personal monitoring)	2.52
Ambient air close to the bag-filling machine (static sampling)	8.8

Corrective measures were applied to reduce the exposure of the operator in charge of the packaging. New big bags were used instead of recycled big bags for the packaging.

According to this corrective measure, the 8-hour TWA at this working area was reduced to 0.90 mg/m3, in a new measurement campain performed in 1995 (mean of 2 measurements). Inhalable particles were assumed to be reduced in the same proportion for the driver of fork-lift trucks and in the ambient air close to the bag filling machine.

Moreover, personnel protection equipment (mask, gloves and safety glasses) are used during production, handling and use of the substance.

Source : Atofina, Paris la Défense, France.
08.08.2003 (24) (25)

Source of exposure : Environment: exposure from production

Exposure to the : Substance

Remark : Releases associated to the production process:

- waste water emissions:
11-aminoundecanoic acid is produced and used in closed system. Emissions of the substance to the environment may occur mainly from production. Aqueous effluents are treated in a waste treatment plant on site where 11-aminoundecanoic acid is expected to degrade at a large extend due to its readily biodegradability. DCO is measured daily. There are no aqueous stream from the processing of the substance. After treatment, the waste water are sent to the sewer of the town.

- Atmospheric emissions:
Vents of distillation columns.

Source : Atofina, Paris la Défense, France.
08.08.2003

1.11 ADDITIONAL REMARKS

Remark : Transport information: not regulated.
26.01.1995 (22)

1.12 LAST LITERATURE SEARCH

Type of search : Internal and External
Chapters covered : 3, 4, 5
Date of search : 09.10.2002

Remark : Data bases:
Toxline/Toxlit
Chemlist
CIS
SANSS
TSCATS
Aquire
Biolog
CESAR
Datalog
Envirofate
Ishow
NIOSHTIC SUBSET
Phytotox

Source : ATOFINA, PARIS-LA-DEFENSE, FRANCE.
09.10.2002

1.13 REVIEWS

2.1 MELTING POINT

Value : = 184 °C
Sublimation :
Method : other: no data
Year :
GLP : no data
Test substance :

Remark : This figure corresponds to the value measured by ATOFINA during the processing of the substance
Reliability : (1) valid without restriction
08.08.2003 (11)

2.2 BOILING POINT

Value : ca. 480.1 °C at
Decomposition :
Method : other
Year :
GLP :
Test substance :

Remark : EPIWIN ESTIMATION
480.11 °C (Adapted Stein and Brown Method)
Reliability : (2) valid with restrictions
08.08.2003

Value : ca. 332 °C at
Decomposition : yes
Method : other
Year :
GLP :
Test substance :

Remark : Lydersen method
Reliability : (2) valid with restrictions
reliability 2 because details on the method used are missing
13.08.2004

2.3 DENSITY

Type : bulk density
Value : = 550 kg/m3 at 20 °C
Method : other
Year :
GLP : no data
Test substance : no data

Method : NORME NF T 51-003 (= EN ISO 60).Détermination de la masse volumique apparente des matières susceptibles de s'écouler à travers un entonnoir donné (version française)
Remark : Compressed powder : 770 kg/m3
True value : 1040 kg/m3
Reliability : (1) valid without restriction

08.08.2003 (12)

2.3.1 GRANULOMETRY

Method : other
Year :
GLP : no
Test substance : no data

Remark : 10-70 µm
29.01.2002

2.4 VAPOUR PRESSURE

Value : = .00000000207 hPa at °C
Decomposition :
Method : other (calculated)
Year :
GLP :
Test substance :

Remark : EPIWIN CALCULATION :

Vapor Pressure Estimations (25 deg C):
(Using BP: 480.11 deg C (estimated))
(Using MP: 191.00 deg C (exp database))
VP: 6.04 E-09 Pa (Antoine Method)
VP: 2.07 E-07 Pa (Modified Grain Method)
VP: 5.53 E-07 Pa (Mackay Method)
Selected VP: 2.07E-07 Pa (Modified Grain Method)

Reliability : (2) valid with restrictions
08.08.2003

2.5 PARTITION COEFFICIENT

Partition coefficient : octanol-water
Log pow : = -.16 at °C
pH value :
Method : other (calculated)
Year :
GLP :
Test substance :

Remark : logKow of other aminoacids have been calculated using the EPIWIN program (KowWin v1.66 fragment description).
The results are as follows :

6 aminohexanoic acid (60-32-2):
logKow (estimated) = - 2.62
logKow (experimental) : -2.95

8-aminooctanoic acid (1002-57-9):
logKow (estimated) = -1.64

Experimental logKow = - 2,55
Reliability : (2) valid with restrictions
Accepted calculation method
11.06.2002 (29)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in : Water
Value : = 2 g/l at 20 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
PKa : at 25 °C
Description :
Stable :
Deg. product :
Method : other: no data.
Year :
GLP : no data
Test substance :

Remark : 100 °C 40 g/l
105 90
110 140
115 220
120 310
130 510
140 590
Reliability : (2) valid with restrictions
08.08.2003 (36)

Solubility in : Organic Solvents
Value : at °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
PKa : at 25 °C
Description :
Stable :

Remark : Soluble in cresols and Butanol-1
29.01.2002

Solubility in : Water
Value : = 1 g/l at 30 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
PKa : at 25 °C
Description :
Stable :
Deg. product :
Method :
Year : 1992
GLP : no data

Test substance : no data

29.01.2002 (44)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

Method :
Year : 2000
GLP :
Test substance : no data

Result : Evaluation of the risk of flammability of the substance on hot surfaces. It was shown that the product did not flamme spontaneously up to 360°C, but that it was decomposed at a relatively low temperature of < 240°C.

29.01.2002 (1)

2.9 FLAMMABILITY

Result : non flammable
Method : Directive 92/69/EEC, A.10
Year : 2000
GLP : no data
Test substance : no data

Remark : In an other test (test BAM), it was shown that the minimal temperature of flammability of a cloud of powder of the test substance was approximately 350°C.
Reliability : (1) valid without restriction

08.08.2003 (1)

2.10 EXPLOSIVE PROPERTIES

Result : explosive under influence of a flame
Method : other: no data
Year : 1996
GLP : no data
Test substance :

23.01.2002 (23)

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

Acid-base constant : pka = 11.15; pka(COOH) = 4.55

Reliability : (2) valid with restrictions
08.08.2003 (16)

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

Memo : Critical pressure : 20.86 Bar

23.01.2002

Memo : Critical temperature : 500 °C

23.01.2002

Memo : Melting Heat : 63.8 cal/g

23.01.2002

Memo : Specific Heat = 0.432 cal/g/°C (Kopp Method)

23.01.2002

Memo : resistivity (measured) : 10E12 Ohm.m

29.01.2002 (15)

3.1.1 PHOTODEGRADATION

INDIRECT PHOTOLYSIS

Sensitizer	:	OH
Conc. of sensitizer	:	1000000 molecule/cm³
Rate constant	:	= .00000000004437 cm³/(molecule*sec)
Degradation	:	= 50 % after 4.3 hour(s)
Reliability	:	(2) valid with restrictions
Flag	:	Risk Assessment

08.08.2003 (17)

3.1.2 STABILITY IN WATER

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	:	**fugacity model level I**
Media	:	
Air	:	0 % (Fugacity Model Level I)
Water	:	99.99 % (Fugacity Model Level I)
Soil	:	.01 % (Fugacity Model Level I)
Biota	:	% (Fugacity Model Level II/III)
Soil	:	% (Fugacity Model Level II/III)
Method	:	
Year	:	
Method	:	Model used : Nord base

physico-chemical parameters :

Temperature : 20°C
Molecular weight : 201.31
Vapor pression : 0.207E-6
Solubility : 2000 g/m3
Solubility : 9.93 mol/m3
Henry's law constant : 0.2085585E-7 Pa.m3/mol
log octanol/water partition coefficient : -0.16
Organic C-water partition coefficient : 0.28
Air-water partition coefficient : 0.8548812E-11
Soil-water partition coefficient : 0.01
Sediment-water partition coefficient : 0.02
Amount of chemical : 1 mole
Fugacity : 0.2976197e-14 Pa
Total VZ products : 335999223425445

Reliability : (2) valid with restrictions

08.08.2003

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type	:	**aerobic**
Inoculum	:	other: secondary effluent from a biologic treatment plant
Concentration	:	22.5 mg/l related to Test substance related to
Contact time	:	27 day(s)
Degradation	:	= 77 (±) % after 19 day(s)
Result	:	readily biodegradable
Kinetic of testsubst.	:	1 day(s) = 1 % 4 day(s) = 22 % 7 day(s) = 45 % 12 day(s) = 65 % 19 day(s) = 77 %
Control substance	:	Benzoic acid, sodium salt
Kinetic	:	1 day(s) = 34 % 27 day(s) = 90 %
Deg. product	:	
Method	:	OECD Guide-line 301 B "Ready Biodegradability: Modified Sturm Test (CO2 evolution)"
Year	:	1994
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Test condition	:	- Inoculum : 6*104 bacteria/ml medium secondary effluent from a biologic treatment plant of Versailles , France. - Concentration of test chemical 22.5 mg/l of the test substance, corresponding to 15 mg TOC/l - Temperature of incubation °C : 22±2 °C - Dosing procedure : CO2 evolution - Sampling frequency : 0, 1, 4, 7, 12, 15, 19, 22, 26, 27 day - Appropriate controls and blank system used? Yes - Analytical method used to measure biodegradation The CO2 produced is trapped in barium hydroxide and is measured by titration of the residual hydroxide.
Result	:	Fb : blank Ft : test Fc : Reference Substance : Sodium Benzoate Fs : sterile Fi : inhibition

C02 (mg)/day

day	0	1	4	7	12	15	19	22	26	27
Fb1	0	7.0	9.8	7.5	4.7	2.6	7.9	1.9	2.3	0.3
Fb2	0	6.9	8.6	8.3	5.7	2.3	10.8	5.1	7.5	1.2
Mean										
Fb	0	7.0	9.2	7.9	5.2	2.5	9.3	3.5	4.9	0.8
Ftl	0	1.8	20.0	18.5	12.9	9.4	0.6	-0.9	-2.4	-0.7
Ft2	0	-0.8	15.1	19.5	19.3	8.9	2.4	0.8	0.8	0.8
Mean										
Ft	0	0.5	17.5	19.0	16.1	9.1	1.5	-0.1	-0.8	0.1
Fc	0	36.9	67.5	-0.5	0.1	0.3	-0.4	-0.6	-3.4	-0.6
Fi	0	41.4	40.0	56.4	25.0	12.3	5.2	2.4	4.1	-0.3
Fs	0	-1.3	2.0	1.0	1.7	3.1	3.7	0.6	-0.1	0.6

CO2 cumul mg

day	0	1	4	7	12	15	19	22	26	27
Fbt	0.0	7.0	16.8	24.3	29	31.7	39.6	41.5	43.8	44.1
Fb2	0.0	6.9	15.5	23.8	29.5	31.8	42.6	47.6	55.1	56.3
Mean										
Fb	0.0	7.0	16.2	24.0	29.3	31.7	41.1	44.6	49.4	50.2
Ft1	0.0	1.8	21.8	40.3	53.2	62.6	63.2	62.3	59.9	59.2
Ft2	0.0	-0.8	14.3	33.8	53.1	62.0	64.4	65.2	66.1	66.8
Mean										
Ft	0.0	0.5	18.0	37.1	53.2	62.3	63.8	63.7	63.0	63.0
Fc	0.0	36.9	104.4	103.9	104.0	104.2	103.8	103.2	99.8	99.3
Fi	0.0	41.4	81.5	137.9	162.9	175.2	180.3	182.7	186.8	186.5
Fs	0.0	-1.3	0.7	1.7	3.3	6.4	10.1	10.7	10.6	11.1

DEGRADATION (%)

day	0	1	4	7	12	15	19	22	26	27
Ft1	0	2	26	49	65	76	77	76	73	72
Ft2	0	-1	17	41	64	75	78	79	80	81
Mean										
Ft	0	1	22	45	65	76	77	77	76	77
Fc	0	34	95	94	94	95	94	94	91	90
Fi	0	22	42	72	85	91	94	95	97	97
Fs	0	-2	1	2	4	8	12	13	13	13

- 65% degradation in the 10 days window
- No inhibition of inoculum observed

Attached document : courbe Acide amino 11 undécanoïque.bmp
resultats Acide amino 11 undécanoïque.bmp

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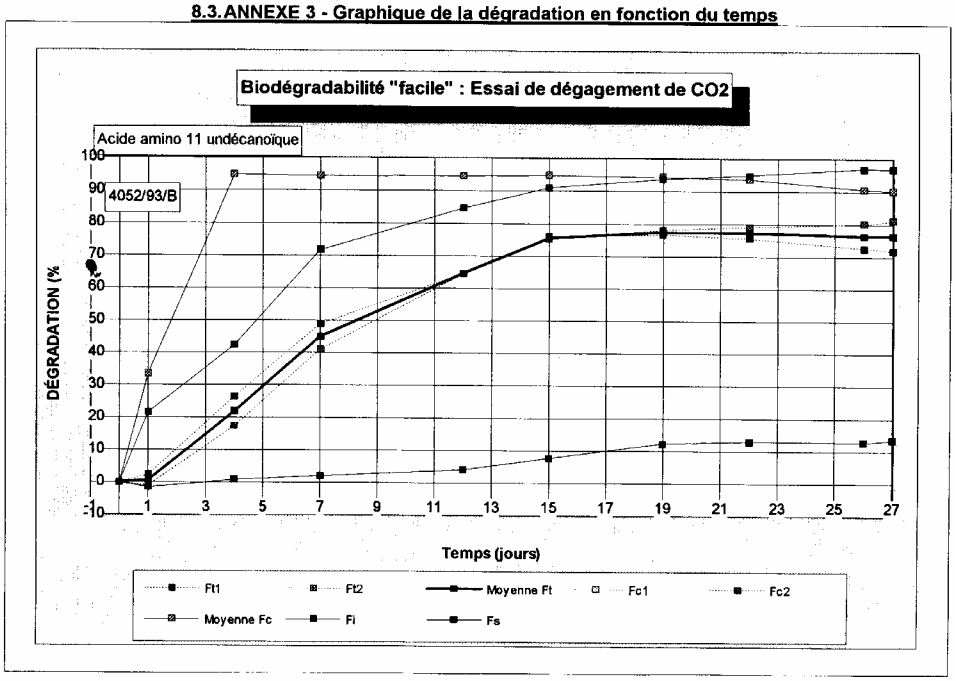
8.3. ANNEXE 3 - Graphique de la dégradation en fonction du temps



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BIODÉGRADABILITÉ FACILE
Essai de dégagement de CO2
92/69/CEE : C.4-C

N° d'étude : 4052/93/B
Substance étudiée : **Acide amino 11 undécanoïque**
Substance de référence : Benzoate de sodium

CO2 (mg) / jour	Jour	0	1	4	7	12	15	19	22	26	27
1,1*(Vba-Vb)	Fb1	0	7.0	9.8	7.5	4.7	2.6	7.9	1.9	2.3	0.3
1,1*(Vba-Vb)	Fb2	0	6.9	8.6	8.3	5.7	2.3	10.8	5.1	7.5	1.2
1,1*(Vba-Vb)	Moyenne Fb	0	7.0	9.2	7.9	5.2	2.5	9.3	3.5	4.9	0.8
1,1*(Vb-Vt)	Ft1	0	1.8	20.0	18.5	12.9	9.4	0.6	-0.9	-2.4	-0.7
1,1*(Vb-Vt)	Ft2	0	-0.8	15.1	19.5	19.3	8.9	2.4	0.8	0.8	0.8
1,1*(Vb-Vt)	Moyenne Ft	0	0.5	17.5	19.0	16.1	9.1	1.5	-0.1	-0.8	0.1
1,1*(Vb-Vc)	Fc1	0	36.9	67.5	-0.5	0.1	0.3	-0.4	-0.6	-3.4	-0.6
1,1*(Vb-Vc)	Fc2	0	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
1,1*(Vb-Vc)	Moyenne Fc	0	36.9	67.5	-0.5	0.1	0.3	-0.4	-0.6	-3.4	-0.6
1,1*(Vb-Vi)	Fi	0	41.4	40.1	56.4	25.0	12.3	5.2	2.4	4.1	-0.3
1,1*(Vbs-Vs)	Fs	0	-1.3	2.0	1.0	1.7	3.1	3.7	0.6	-0.1	0.6

CO2 cumulé (mg)	Jour	0	1	4	7	12	15	19	22	26	27
	Fb1	0.0	7.0	16.8	24.3	29.0	31.7	39.6	41.5	43.8	44.1
	Fb2	0.0	6.9	15.5	23.8	29.5	31.8	42.6	47.6	55.1	56.3
	Moyenne Fb	0.0	7.0	16.2	24.0	29.3	31.7	41.1	44.6	49.4	50.2
	Ft1	0.0	1.8	21.8	40.3	53.2	62.6	63.2	62.3	59.9	59.2
	Ft2	0.0	-0.8	14.3	33.8	53.1	62.0	64.4	65.2	66.1	66.8
	Moyenne Ft	0.0	0.5	18.0	37.1	53.2	62.3	63.8	63.7	63.0	63.0
	Fc1	0.0	36.9	104.4	103.9	104.0	104.2	103.8	103.2	99.8	99.3
	Fc2	0.0	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
	Moyenne Fc	0.0	36.9	104.4	103.9	104.0	104.2	103.8	103.2	99.8	99.3
	Fi	0.0	41.4	81.5	137.9	162.9	175.2	180.3	182.7	186.8	186.5
	Fs	0.0	-1.3	0.7	1.7	3.3	6.4	10.1	10.7	10.6	11.1

DÉGRADATION (%)	Jour	0	1	4	7	12	15	19	22	26	27
	Ft1	0	2	26	49	65	76	77	76	73	72
	Ft2	0	-1	17	41	64	75	78	79	80	81
	Moyenne Ft	0	1	22	45	65	76	77	77	76	77
	Fc1	0	34	95	94	94	95	94	94	91	90
	Fc2	0	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
	Moyenne Fc	0	34	95	94	94	95	94	94	91	90
	Fi	0	22	42	72	85	91	94	95	97	97
	Fs	0	-2	1	2	4	8	12	13	13	13

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Source : ATOFINA, PARIS-LA-DEFENSE, FRANCE.
Reliability : (1) valid without restriction
Flag : Directive 67/548/EEC, Critical study for SIDS endpoint
30.08.2002 (27)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type : **static**
Species : Brachydanio rerio (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
LC50 : > 833 measured/nominal
Limit test :
Analytical monitoring : yes
Method : OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year : 2001
GLP : yes
Test substance : other TS: ATOFINA, 93.7% purity

Method : · Analytical procedures : Liquid chromatography (HLPC), with UV detection

Test condition : - species/Supplier: Danio rerio from HB Developpement Elevage (69490, Saint Forgeux) Fish Hatchery, France.

Test fish :
length between 31 to 35 mm

- Dilution water is prepared in the laboratory using pure water and salts according to C.1 92/69/CEE method.
Final concentrations :
294 mg CaCl2, 2 H2O /l ultrapure water
123.3 mg MgSO4, 7 H2O /l ultrapure water
63.0 mg NaHCO3 /l ultrapure water
5.5 mg KCl /l ultrapure water

- The solutions were individually prepared and directly put in the vessel.
Range of concentrations : from 402 to 833 mg/l

- Exposure vessels: contained 5 l test solution
no. of replicates: 2 rep per concentration and 5 fish per vessel

- Temperature : 22.6 °C +-0.5

- Water chemistry:

Nominal conc. mg/l	0 hours DO %	pH	48 hours DO %	pH	96 hours DO %	pH
833	93	7.43	98	7.73	85	7.78
694	93	7.49	96	7.75	85	7.73
579	97	7.50	98	7.76	90	7.80
482	99	7.44	100	7.75	84	7.73
402	115	7.68	101	7.73	81	7.70
0	123	7.57	105	8.00	85	8.01

Result : - Nominal/measured concentrations:

nominal mg/l	initial	final	% Final/initial
833	799	833	104
694	664	713	107
579	553	NA	
482	464	NA	
402	391	NA	

NA : not analyzed

- Nominal concentrations mg/l	Mortality % 24	48	72	96 h
833	0	0	0	0
694	0	0	0	0
579	0	0	0	0
482	10	10	10	10
402	0	0	0	0
0	0	0	0	0

Sub-lethal effects were noted at the highest concentration.

Reliability : (1) valid without restriction
Flag : Directive 67/548/EEC, Critical study for SIDS endpoint
11.06.2002 (14)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
EC50 : > 350 measured/nominal
EC100 : > 350
EC50, 24h : > 350
Analytical monitoring : yes
Method : OECD Guide-line 202
Year : 1995
GLP : yes
Test substance : no data

Method : · Analytical procedures : Liquid chromatography (HLPC), with UV detection
- Test organisms
Daphnia magna Straus.Breeding colony realized in the laboratory. Organisms are selected by sieving.
< 24h old, laboratory bred.

Test condition : - Before the beginning of test,a stock solution is prepared, by mixing 100 mg of the substance with 1 litre of dilution water.
Concentrations from 0.1 to 100 mg/l are used for preliminary tests.
10 daphnia are exposed to these concentrations for 24, then 48 hours.
The results are used to evaluate the concentrations to be applied for the definitive test.

- Stock solutions preparation : 350 mg/l substance in dilution water
- Temperature range : 19-21°C
- Exposure vessel : 250 ml beakers

- Dilution water is prepared in the laboratory using pure water and salts according to ISO 6341.
25 ml/l of the below solutions , aerated up to oxygen saturated :

11.76 g CaCl2, 2 H2O /l ultrapure water
4.93 g MgSO4, 7 H2O /l ultrapure water
2.59 g NaHCO3 /l ultrapure water
0.23 g KCl /l ultrapure water

- incubation of test flasks in darkness.

- Water chemistry in test :

C mg/l	0	350	
O2 (48h) mg/l	8.4	8.2	
pH (48h)	7.81	7.82	
pH (T0)	7.85		

- Exposure vessel type : 250 ml beakers.
Exposure period : 24 and 48 hours
Analytical monitoring : at t0 and t48 h
· Nominal concentrations : 150, 250 and 350 mg/l
· Measured concentrations :
initial : 139.5 255.4 350.8 mg/l
final : 152.5 258.1 374.4 mg/l
% final/initial : 109.3 101.1 106.7

Result : - 20 daphnia per concentrations.

mg/l subst.	% immo.	(1)	(2)
150	0	10	10
250	0	10	10
350	0	10	10
0 (temoin)	0	10	10

Attached document : 2 Acide amino 11 undecanoïque.bmp
Acide amino 11 undecanoïque.bmp

définitif. Les différentes concentrations de cette gamme sont données dans les annexes 2 et 3.

2 béchers de 10 daphnies âgées de moins de 24 heures sont préparés pour chaque concentration et pour le témoin.

Au bout de 24 heures, les daphnies encore mobiles sont dénombrées, les récipients sont replacés à l'obscurité puis un deuxième dénombrement est réalisé 48 heures après le début de l'essai.

6.3.5. Contrôle de sensibilité du réactif biologique

Périodiquement, et selon le même mode opératoire, la CE_{50} - 24h du dichromate de potassium est déterminée afin de contrôler la sensibilité des organismes. À titre indicatif, les résultats du dernier essai, réalisé le 28/12/94, ont abouti à une CE_{50} - 24 h de 0,91 mg/l.

7. RÉSULTATS

7.1. Essai définitif

Les concentrations réelles (mg/l) d'ACIDE AMINO 11 UNDECANOÏQUE dans l'eau de dilution, mesurées selon la méthode décrite en annexe 4 sont les suivantes :

Concentrations (mg/l)			%
nominales	initiales	finales	final/initial
150	139,5	152,5	109,3
250	255,4	258,1	101,1
350	350,8	374,4	106,7

Les bulletins d'analyses sont joints en annexe 4.

Les résultats obtenus dans l'essai sont rassemblés dans les tableaux en annexe 2 (résultats à 24 heures) et en annexe 3 (résultats à 48 heures).

Aux concentrations nominales de 150, 250 et 350 mg/l aucune toxicité de l'ACIDE AMINO 11 UNDECANOÏQUE vis-à-vis des daphnies n'a été enregistrée. Les CE_{50} - 24h et CE_{50} - 48h sont par conséquent supérieures à 350 mg/l.

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9.3. Annexe 3 : Concentrations utilisées et résultats des calculs à 48 heures

TOXICITÉ AIGUË VIS-À-VIS DES DAPHNIES

Substance d'essai : **Acide amino 11 undécanoïque**
Numéro d'étude : 4052/93/A

Essai définitif, 48 heures

Nombre de daphnies par concentration : 20

		Nombre de daphnies mobiles				
mg/l subst.	% IMMO	Récipient 1	Récipient 2	Récipient 3	Récipient 4	total
150	0	10	10			20
250	0	10	10			20
350	0	10	10			20
	100					0
	100					0
	100					0
	100					0
	100					0
	100					0
	100					0
	100					0
0 (témoin)	0	10	10			20
0 (solvant)	100					0

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Reliability : (1) valid without restriction
Flag : Directive 67/548/EEC, Critical study for SIDS endpoint
28.10.2002 (28)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	**other algae: Pseudokirchneriella subcapitata**
Endpoint	:	other: biomass and growth rate
Exposure period	:	72 hour(s)
Unit	:	mg/l
Limit test	:	
Analytical monitoring	:	yes
Method	:	OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year	:	2001
GLP	:	yes
Test substance	:	other TS: Atofina, 93.7% purity

Method :

Method C3 described in directive 92/69/EEC of the European Commission and in the guideline 201 of the OECD.

Statistical method :
The No Observed Effect Concentration is determined by a statistical procedure : analysis of variance and Dunnett's test.

Test condition :

- Static test
· Test temperature range : 23 ± 1 °C
· Growth/test medium chemistry
Prepared according to § 1.6.1.2 of C.3. method (Annex 5 of 92/69/EEC Directive)
pH 8
· Dilution water source
See above

· Exposure vessel type
120 ml glass bottles completely filled with test solution and stoppered with PTFE bungs and sealed with aluminum caps

· Water chemistry in test

C mg/l nominal	T0 pH	T72h	T0 dissolved O2(mg/l	T72h
0	7.55	7.71	8.1	8.7
150	7.47	7.47	8.6	8.3
90.9	7.47	7.53	8.1	8.2
55.1	7.55	7.50	8.0	8.4
33.4	7.61	7.57	8.1	8.4
20.2	7.65	7.62	8.2	8.6
12.3	7.55	7.72	8.1	8.7
7.4	7.62	7.96	8.1	8.9
4.5	7.63	7.89	8.0	8.5

Measurements were carried out in non inoculated solutions at T0 and ininoculated solutions at T72h

· Stock solutions preparation

Ultrapure water (ultrafiltration, active carbon, ions exchange, 0.22 µm filter)
Stock solution prepared at the beginning of the test, by adding 150 ml of substance in 1 l of dilution water.After about one hour of agitation, the solution was colourless

and homogenate.

· Light levels and quality during exposure
Constantly illuminated between 6000 to 10000 lx.

- Test design
3 replicates at each test concentration
9 concentrations (nominal) : 0, 4.5, 7.4, 12.3, 20.2, 33.4, 55.1, 90.9, 150 mg/l

Result : · Nominal concentrations in mg/l / Measured concentrations in mg/l

Nominal (mg/l)	Initial (mg/l)	Final (mg/l)	Final/Initial %
150	169	152.7 (156.5)	90.4 (92.6)
90.9	96.4	NA	
55.1	52.4	NA	
33.4	32.7	35.4 (33.4)	108.2 (102.1)
20.2	19.7	NA	
12.3	11.5	NA	
7.4	6.4	7.6 (7.4)	118.8 (115.6)
4.5	3.5	NA	

Initial and final concentrations were measured in no inoculated solutions.
Within parenthesis : measured in inoculated series (with algae).

- Values
EbC50, 72h = 23
EbC10, 72h = 5.8
ErC50, 72h = 53
ErC10, 72h = 10

NOECb : 4.5
NOECr : 4.5

- control response satisfactory : yes

- BIOLOGICAL OBSERVATIONS

+Cell density at each flask at each measuring point

Sample C (m/l) nominal	Replicat N°	algal conc. (Cell/ml) T0	T24h	T48h	T72h
0	1	1.0E+04	6.40E+04	2.09E+05	9.30E+05
	2	1.0E+04	6.50E+04	2.31E+05	9.45E+05
	3	1.0E+04	6.10E+04	1.71E+05	9.90E+05
	mean	1.00E+0	6.33E+04	2.04E+05	9.55E+05
4.5	1	1.0E+04	5.40E+04	2.82E+05	9.60E+05
	2	1.0E+04	5.50E+04	2.55E+05	9.70E+05
	3	1.0E+04	5.70E+04	2.44E+05	9.35E+05
	mean	1.00E+04	5.53E+04	2.60E+05	9.55E+05
7.4	1	1.0E+04	6.10E+04	1.90E+05	7.30E+05
	2	1.0E+04	6.30E+04	2.35E+05	6.70E+05
	3	1.0E+04	5.00E+04	2.34E+05	7.20E+05

	mean	1.00E+04	5.80E+04	2.20E+05	7.07E+05
12.3	1	1.0E+04	6.90E+04	1.01E+05	5.40E+05
	2	1.0E+04	6.10E+04	1.51E+05	5.90E+05
	3	1.0E+04	5.70E+04	1.74E+05	5.80E+05
	mean	1.00E+04	6.23E+04	1.42E+05	5.70E+05
20.2	1	1.0E+04	6.10E+04	7.20E+04	2.31E+05
	2	1.0E+04	5.60E+04	8.10E+04	1.36E+05
	3	1.OE+04	4.70E+04	9.80E+04	2.08E+05
	mean	1.00E+04	5.47E+04	8.37E+04	1.92E+05
33.4	1	1.OE+04	6.60E+04	5.20E+04	7.20E+04
	2	1.0E+04	5.60E+04	6.70E+04	7.40E+04
	3	1.OE+04	6.50E+04	5.30E+04	8.10E+04
	mean	1.00E+04	6.23E+04	5.73E+04	7.57E+04
55.1	1	1.0E+04	6.00E+04	5.20E+04	5.90E+04
	2	1.0E+04	5.50E+04	5.70E+04	8.40E+04
	3	1.0E+04	4.20E+04	4.10E+04	7.90E+04
	mean	1.00E+04	5.23E+04	5.00E+04	7.40E+04
90.9	1	1.0E+04	4.50E+04	4.80E+04	7.80E+04
	2	1.0E+04	5.20E+04	4.60E+04	6.60E+04
	3	1.0E+04	5.00E+04	4.80E+04	5.70E+04
	mean	1.00E+04	4.90E+04	4.73E+04	6.70E+04
150	1	1.0E+04	4.90E+04	4.70E+04	2.80E+04
	2	1.0E+04	5.30E+04	3.90E+04	4.20E+04
	3	1.0E+04	4.90E+04	4.10E+04	5.30E+04
	mean	1.00E+04	5.03E+04	4.23E+04	4.10E+04

+Growth curves
See attached file : Amino11-growth algae.bmp

The values of concentrations plotted on the curve are as follows :

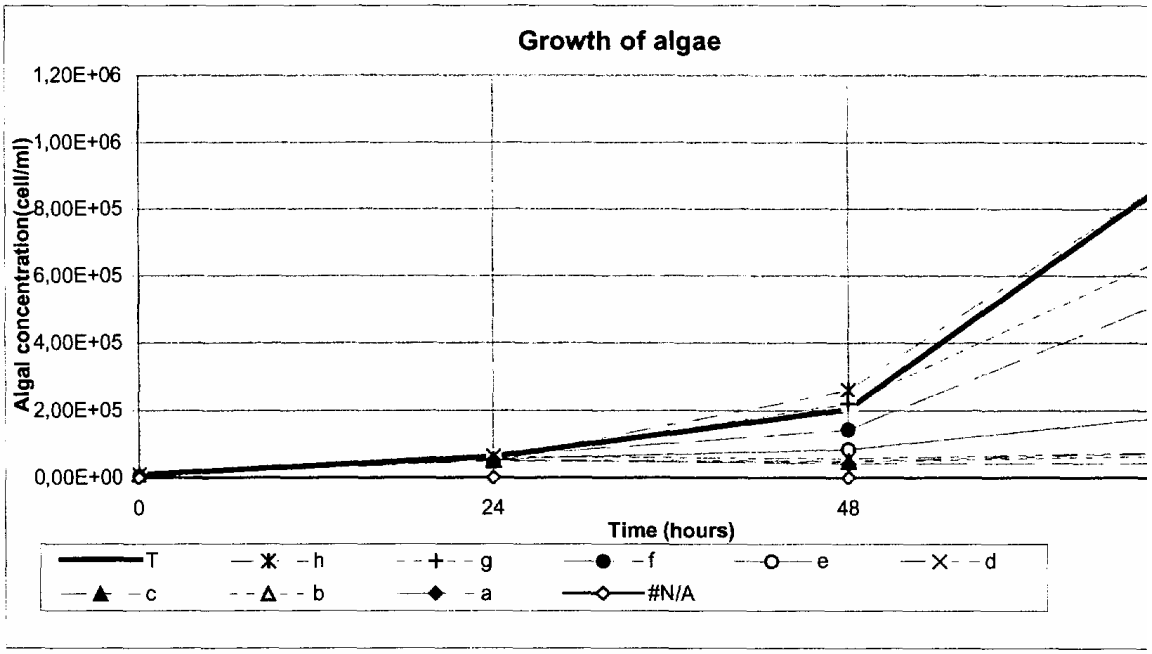
	Nominal Conc.(mg/l)
T	0
h	4.5
g	7.4
f	12.3
e	20.2
d	33.4
c	55.1
b	90.9
a	150

+Percent biomass/growth rate inhibition per concentration

sample	mean Inhibition % integral biomass	growth rate
%vol/GM	AI (%)	INi (%)
0	0.00	0.00
4.5	-6.76	0.00
7.4	15.77	6.61

12.3	35.46	11.32
20.2	70.93	35.23
33.4	81.58	55.61
55.1	84.11	56.10
90.9	85.43	58.28
150	87.75	69.05

Attached document : Amino11-growth algae.bmp



Reliability : (1) valid without restriction
Flag : Directive 67/548/EEC, Critical study for SIDS endpoint
11.06.2002 (13)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type	:	**aquatic**
Species	:	Pseudomonas putida (Bacteria)
Exposure period	:	16 hour(s)
Unit	:	mg/l
EC10	:	= .34
EC50	:	= 1.5
Analytical monitoring	:	no
Method	:	other: ISO/DIS 10712
Year	:	1995
GLP	:	no
Test substance	:	other TS: Atofina, purity not given
Test condition	:	-Stock solution : 100 mg/l - Temperature : 21+-1°C - pH T0 T16h 0 mg/l 7.04 6.94 10 mg/l 6.93 7.15 - Tested Concentrations 0, 1, 2, 5 and 10 mg/l - Reference substance : 3,5-dichlorophenol
Result	:	TS Conc(mg/l) Inhibition (%) 1 29.5 2 69.7 5 89.5 10 93.2
Reliability	:	(1) valid without restriction

08.08.2003 (26)

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

In Vitro/in vivo : In vivo
Type : Excretion
Species : rat
Number of animals
Males : 5
Females : 5
Doses
Males : 1 mCi of 11-14C-aminoundecanoic acid
Females : 1 mCi of 11-14C-aminoundecanoic acid
Vehicle : other: 5% aqueous acetic acid
Route of administration : gavage
Exposure time :
Product type guidance :
Decision on results on acute tox. tests :
Adverse effects on prolonged exposure :
Half-lives : 1st.:
2nd.:
3rd.:
Toxic behaviour :
Deg. product :
Method :
Year :
GLP : no
Test substance : other TS

Test substance : 11-Aminoundecanoic acid-[11-14C], specific activity 14.22 mCi/mmol.

Method : Five male and female F-344 rats were each dosed orally with 1 mCi of 11-14C-aminoundecanoic acid (11-AA) with a specific activity of 14.22 mCi/mmol) which was dissolved in 1 ml of 5% aqueous acetic acid. After application of the substance, the animals were placed separately in closed all-glass
metabolic cages; a continuous airstream was sucked through these cages and was drawn through soda lime (14C02 trapping). Some radioactivity (not quantitated) was found in the soda lime, indicating that minor amounts of 14C02 had been produced by metabolism of 14C-AA.
In the 24 hours following application of the compound, urine and feces were collected.
Total radioactivity in urine and feces collected during 24 h was determined by liquid scintillation counting of aliquots.
Result : Approximately 80% of radioactivity derived from 14C-AA is excreted in form of metabolites in rat urine.
Reliability : (2) valid with restrictions
11.06.2002 (6)

5.1.1 ACUTE ORAL TOXICITY

Type : **LD50**
Value : = 14700 - 21500 mg/kg bw
Species : rat
Strain : Fischer 344
Sex : male/female
Number of animals : 35
Vehicle : other: corn oil

Doses	:	Males: 14,700 and 21,500 mg/kg Female: 6,810, 10,000, 14,700, and 21,500 mg/kg
Method	:	other: equivalent to OECD Guide-line 401
Year	:	1982
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Test substance	:	Purity : 99.13 ± 0.03 wt%
Method	:	Male and female F344 rats were obtained from Frederick Cancer Research Center (Frederick, MD), quarantined, and held for approximately 2 months before the test began. Animals were approximately 11 weeks old when placed on study. Groups of five male F344 rats were administered a single dose of 11-aminoundecanoic acid (14,700 or 21,500 mg/ kg body weight) in corn oil by gavage and groups of five female rats received doses of 6,810, 10,000, 14,700, or 21,500 mg/kg by the same route. All animals were observed for mortality for 14 days. Animals were housed two or three per cage and received water and feed ad libitum during the observation period. Animals were observed for mortality every 30 minutes for the first 8 hours on the day of dosing and then daily for 14 days. Weights were taken on the day of dosing and then on days 7 and 14. Gross necropsies were performed on all animals that died during the study and on those surviving to day 14.
Result	:	Rats were observed for 14 days and, at the end of the 14-day observation period. survival was 100% in females administered 6,810 or 10,000 mg kg and in males administered 14,700 or 21,500 mg kg. Deaths occurred in 1/5 females administered 14.700 mg/kg and in 5/5 females administered 21,500 mg kg; depressions in mean body weight were observed in males and females at these dose.
Conclusion	:	Male : LD0 > 21500 mg/kg Female : 14700 mg/kg < LD50 < 21500 mg/kg
Reliability	:	(2) valid with restrictions
Flag	:	Directive 67/548/EEC, Critical study for SIDS endpoint

28.10.2002 (39)

Type	:	**LD50**
Value	:	>= 15000 mg/kg bw
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	15
Vehicle	:	CMC
Doses	:	15000 mg/kg
Method	:	other: equivalent to OECD Guide-line 401
Year	:	1978
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Test condition	:	- Age : Male : 175 g Female : 150-165 g - Volume administered : 30 ml/kg - Post dose observation period : 14 days
Result	:	- Number of deaths at each dose level :

		Mortality	
Dose level (mg/kg)	Male	Female
15000	0/5	1/10

- Time of death :
15000 mg/kg : 1 female on day 7
- clinical signs : 15000 mg/kg: decrease of spontaneous activity at 6h, increase urine emission on D2.
- Necropsy findings : not reported.

Reliability : (2) valid with restrictions
Flag : Directive 67/548/EEC, Critical study for SIDS endpoint
28.10.2002 (3)

5.1.2 ACUTE INHALATION TOXICITY

5.1.3 ACUTE DERMAL TOXICITY

Type : **LD0**
Value : >= 2000 mg/kg bw
Species : rat
Strain : Sprague-Dawley
Sex : male/female
Number of animals : 10
Vehicle : other: none
Doses : 2000 mg/kg
Method : other: equivalent to OECD Guide-line 402
Year : 1978
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Test condition : - Condition of administration : on scarified skin and under occlusive patch
- Age :
Male : 210 g
Female : 205 g
- Post dose observation period : 14 days

Result : - Number of deaths at each dose level : none
- Time of death : none
- Clinical signs : none
- Necropsy findings : not reported.

Reliability : (2) valid with restrictions
Flag : Directive 67/548/EEC, Critical study for SIDS endpoint
11.06.2002 (18)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species : rabbit
Concentration : undiluted
Exposure : Occlusive
Exposure time : 24 hour(s)
Number of animals : 6

Vehicle	:	other: none
PDII	:	0
Result	:	not irritating
Classification	:	not irritating
Method	:	other: JO RF 21/4/1971
Year	:	1971
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Test condition	:	Rabbit: New Zealand white. Substance tested undiluted, on intact and scarified skin, under occlusive dressing for 24 hours.
Reliability	:	(2) valid with restrictions
Flag	:	Directive 67/548/EEC, Critical study for SIDS endpoint

11.06.2002 (2)

5.2.2 EYE IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Dose	:	100 other: mg
Exposure time	:	
Comment	:	not rinsed
Number of animals	:	6
Vehicle	:	other: none
Result	:	slightly irritating
Classification	:	not irritating
Method	:	other: JO RF of 21/4/1971
Year	:	1971
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	The slight irritation recovered totally after 24 hours.
Reliability	:	(2) valid with restrictions
Flag	:	Directive 67/548/EEC, Critical study for SIDS endpoint

11.06.2002 (2)

5.3 SENSITIZATION

Type	:	**Guinea pig maximization test**
Species	:	guinea pig
Concentration	:	1st: Induction .1 % intracutaneous 2nd: Induction 40 % occlusive epicutaneous 3rd: Challenge 40 % occlusive epicutaneous
Number of animals	:	30
Vehicle	:	other: corn oil
Result	:	not sensitizing
Classification	:	not sensitizing
Method	:	OECD Guide-line 406 "Skin Sensitization"
Year	:	1992
GLP	:	yes
Test substance	:	other TS
Test substance	:	Elf Atochem, batch VRA980303137, conform to specifications.
Method	:	Thirty guinea-pigs were allocated to two groups: a control group 1 (five males and five females) and a treated group 2 (ten males and ten females).

On day 1, intradermal injections of Freund's complete adjuvant mixed with the test substance (treated group) or the vehicle (control group) were performed in the interscapular region.

On day 7, the same region received a topical application of sodium lauryl sulfate in vaseline (10% w/w) in order to induce local irritation.

On day 8, the test substance (treated group) or the vehicle (control group) was applied to the same test site which was then covered by an occlusive dressing for 48 hours.

On day 22, after a rest period of 12 days, all animals of the treated and control groups were challenged by a cutaneous application of the test substance to the right flank. The left flank served as control and received the vehicle only. Test substance and vehicle were maintained under an occlusive dressing for 24 hours.
Skin reactions were evaluated approximately 24 and 48 hours after removal of the dressing.

Test substance concentrations were as follows:

Induction (treated groups)
. intradermal injections: UNDECANOIC ACID, 11-AMINO at the concentration of 0.1% (w/w) in corn oil,
. topical application: UNDECANOIC ACID, 11-AMINO at the concentration of 40% (w/w) in corn oil.

Challenge (all groups)
. topical application: UNDECANOIC ACID, 11-AMINO at the concentration of 40% (w/w) in corn oil.

At the end of the study, animals were killed without examination of internal organs. No skin samples were taken from the challenge application sites.

The sensitivity of the guinea-pigs in laboratory experimental conditions was checked with a positive sensitizer, 2,4-Dinitro Chlorobenzene (DNCB). During the induction period, the reference substance DNCB was applied at the concentrations of 0.1 % (w/w) (day 1) and I % (w/w) (day 8) in corn oil. For the challenge application, the reference substance DNCB was applied at the concentration of 1% (w/w) in corn oil.

Result : No clinical signs and no deaths were noted during the study.
No cutaneous reactions were observed after the challenge application.
The species and strain which were used showed a satisfactory sensitization response in 90% animals treated with DNCB.

Conclusion : According to the maximization method of Magnusson and Kligman, the test substance UNDECANOIC ACID, 11-AMINO does not induce delayed contact hypersensitivity in guinea-pigs.

Reliability : (1) valid without restriction

Flag : Directive 67/548/EEC, Critical study for SIDS endpoint

11.06.2002 (19)

5.4 REPEATED DOSE TOXICITY

Type :

Species : rat

Sex : male/female

Strain : Sprague-Dawley

Route of admin.	:	oral feed
Exposure period	:	28 days
Frequency of treatm.	:	ad libitum
Post exposure period	:	none
Doses	:	1250, 5000 and 20000 ppm
Control group	:	yes, concurrent no treatment
NOAEL	:	= 5000 ppm
LOAEL	:	= 20000 ppm
Method	:	OECD Guide-line 407 "Repeated Dose Oral Toxicity - Rodent: 28-day or 14-d Study"
Year	:	1995
GLP	:	yes
Test substance	:	other TS

Test substance	:	Atofina, batch USA000523365, conform to specifications.
Method	:	A total of 48 (24 males and 24 females) Sprague-Dawley rats were assigned to four groups of six males and six females each: one control group receiving the untreated diet, three treated groups receiving the test substance mixed with the diet at constant concentrations of 1250, 5000 or 20000 ppm for 4 weeks. The animals were checked twice daily for mortality and clinical signs were observed once a day. The neurotoxicity was assessed by a functional observation battery (FOB: including a detailed clinical observation and reactivity to manipulation or to different stimuli) which was performed on all animals before the first day of treatment and then once a week (on the first five animals). Motor activity was recorded for all animals before the first day of treatment and in week 4 (on the first five animals). Body weight was recorded before the beginning of the study and then once a week. Food consumption was recorded once a week. The achieved dosages were calculated. Hematological, blood biochemical and urinary parameters were determined during week 4 on the first five surviving animals of each sex and group. At scheduled sacrifice, a macroscopic post-mortem examination was performed on all animals, designated organs were weighed and preserved. A microscopic examination was carried out for the first five animals on selected organs of the control and high-dose groups. The kidneys of the low and intermediate dose groups were also examined.
Result	:	Achieved dosages The concentrations of 1250, 5000 or 20000 ppm corresponded to achieved dosages of 118, 472 or 1644 mg/kg/day for the males and 129, 507 or 1828 mg/kg/day for the females, demonstrating a satisfactory intake of the test substance. Mortality No mortality occurred during the treatment period. Clinical signs During the study, no clinical signs were observed in any group. Functional observation battery There were no relevant differences in the neurotoxicological parameters as evaluated by the FOB. Body weight and food consumption At 1250 ppm, the body weight gain and food consumption of males and females were similar to that of control group. At 5000 ppm, a slight and transitory decrease (not statiscally significant) in body weight gain in males during weeks 2 and 3 was noted and was not considered as an adverse effect. No differences were noted among treated

females.
At 20000 ppm, a decrease in body weight gain in both males and females was noted during weeks 1, 2 and 3.
These dose-related decreases in body weight gain correlated with lower food consumption values.

Hematology
At 1250 or 5000 ppm, there were no changes in hematological parameters.
At 20000 ppm, decrease in hemoglobin concentration, packed cell volume, mean cell volume and mean cell hemoglobin, decrease in activated partial thromboplastin time and increase in fibrinogen level were noted in males.
Treated females at 20000 ppm showed also a tendency to lower hemoglobin concentration, lower packed cell volume, decreased Activated Partial Thromboplasmin (APTT) values and increased fibrinogen level.
These differences in red blood cell or coagulation parameters observed in the 20000 ppm group were considered to be related to treatment with the test substance.

Blood biochemistry
At 1250 or 5000 ppm, there were no changes in blood biochemical parameters. At 20000 ppm, a decrease in inorganic phosphorus levels, an increase in urea and triglyceride levels and a decrease in alkaline phosphatase or alanine aminotransferase activities were noted in treated males. Increased urea levels were noted among treated females at 20000 ppm. The above-mentioned differences noted in the 20000 ppm group were considered to be the consequence of treatment with the test substance.

Urinalysis
Neither qualitative nor quantitative treatment-related changes were observed in urinary parameters.

Organ weights
There were no relevant differences in organ weights in the 1250 ppm group. At 5000 or 20000 ppm, the absolute and relative kidney weights (expressed as a percentage) were higher when compared to controls, as follows:

Concentration (ppm)	5000	20000
Males	+15 (+21)	+23 (+41**)
Females	+10 (+7)	+52** (+64**)

relative weight in brackets; **: p<0.01

At 20000 ppm, these differences correlated with macroscopic and microscopic findings in the kidneys and were attributed to treatment with the test substance.

Macroscopic post-mortem examination
At 1250 ppm, there were no notable necropsy findings.
At 5000 ppm, grey/green color of the kidneys was observed in 1/6 males.
At 20000 ppm, grey/green color of the kidneys was observed in 3/6 males (associated with enlargement or irregular color in one male); greyish/whitish or yellowish areas were noted in 5/6 females.
These abnormalities observed among the 5000 or 20000 ppm groups correlated with higher kidney weights and were considered to be treatment-related.

Microscopic examination

No relevant microscopic findings were seen in the kidneys of animals from the 1250 or 5000 ppm groups.
At 20000 ppm, lesions of the renal papilla were seen in 5/5 females (e.g. acute inflammatory cells infiltration, hyperplasia of the epithelium, dilatation of collecting ducts) and both sexes showed cortical tubular dilatation.

Conclusion : 11-AMINOUNDECANOIC ACID (batch No. USA000523365), when given by dietary admixture to Sprague-Dawley rats for 4 weeks at the concentrations of 1250, 5000 and 20000 ppm, corresponding to 118, 472 and 1644 mg/kg/day in males and 129, 507 and 1828 mg/kg/day in females, was well-tolerated at the lowest dose-levels.
At 5000 ppm, the only adverse effect was a slight decrease in body weight gain (not statistically significant) correlating with lower food consumption noted among treated males.
At 20000 ppm, moderate decrease in body weight gain and food consumption were noted among treated males and females. At clinical pathology, lower values for red blood cell parameters, and APTT, higher fibrinogen, and urea levels in both sexes were noted. Decreased liver enzyme activities and increased triglyceride levels were noted in males. Treatment-related lesions were observed in the kidneys of both sexes. Consequently, 5000 ppm (472 mg/kg/day for the males and 507 mg/kg/day for the females) was established as the No Observed Adverse Effect Level (NOAEL).

Reliability : (1) valid without restriction
Flag : Directive 67/548/EEC, Critical study for SIDS endpoint
11.06.2002 (7)

Type :
Species : rat
Sex : male/female
Strain : Fischer 344
Route of admin. : oral feed
Exposure period : 14 days
Frequency of treatm. : ad libitum
Post exposure period : none
Doses : 0, 5000, 10000, 15000, 20000 and 30000 ppm
Control group : yes, concurrent no treatment
NOAEL : = 15000 ppm
LOAEL : = 20000 ppm
Method : other: NTP range finding study
Year : 1982
GLP : no data
Test substance : other TS

Test substance : Purity : 99.13 ± 0.03 wt%
Method : Male and female F344 rats were obtained from Frederick Cancer Research Institute, quarantined, and held for approximately 3 months before the study began. Animals were approximately 15 weeks old when placed on study.
Groups of five males and five females were fed diets containing 0, 5,000, 10,000, 15,000, 20,000, or 30,000 ppm 11-aminoundecanoic acid for 2 weeks. Test diets were prepared several days before the start of the study by mixing the test chemical and ground Purina Lab Chow in a Patterson-Kelly Twin Shell Blender. Diets were refrigerated until use.
Animals were housed two or three per cage and received water and feed ad libitum. The rats were observed daily for mortality and were weighed weekly. Gross necropsies were performed on all animals at the end of the 14-day study.

Result : All animals survived to the end of the dosing period. No

compound associated effects were observed in rats fed 0-15,000 ppm, but groups of male and female rats fed 20,000 or 30,000 ppm had depressions in mean body weight gain compared with controls. Daily food consumption data were not collected.

Reliability : (2) valid with restrictions
11.06.2002 (38)

Type	:	
Species	:	rat
Sex	:	male/female
Strain	:	Fischer 344
Route of admin.	:	oral feed
Exposure period	:	91 days
Frequency of treatm.	:	ad libitum
Post exposure period	:	none
Doses	:	0, 9000, 12000, 15000, 18000 and 21000 ppm
Control group	:	yes, concurrent no treatment
NOAEL	:	< 9000 ppm
Method	:	other: NTP range-finding study
Year	:	1982
GLP	:	no data
Test substance	:	other TS

Test substance : Purity : 99.13 ± 0.03 wt%

Method : Animals were checked for mortality and signs of morbidity twice daily. Each animal was given a clinical examination weekly, including palpation for tissue masses or swelling. Body weight and feed consumption data were collected weekly.

At the end of the 91-day study, survivors were killed with carbon dioxide and necropsies were performed. The following specimens were examined for control and high-dose groups: gross lesions, tissue masses, abnormal lymph nodes, skin, mandibular lymph nodes, mammary gland, salivary gland, thigh muscle, sciatic nerve, bone marrow, costochondral junction (rib), thymus, larynx, trachea, lungs and bronchi, heart, thyroid, parathyroid, esophagus, stomach, duodenum, jejunum, ileum, colon, mesenteric lymph nodes, liver, pancreas, spleen, kidneys, adrenals, bladder, seminal vesicles/prostate/ testes or ovaries/uterus, nasal cavity, brain pituitary, and spinal cord. Tissues were preserved in 10 % neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. Histopathologic examination for all other dosed groups was limited to the kidneys and liver, except for male and female rats administered 12,000 ppm. The kidneys, liver, lungs, and heart of animals in the 12,000 ppm groups were examined histo-pathologically.

Test condition : - Test Subjects
Age at study initiation : 5 weeks
No. of animals per sex per dose : 12

Result : - Actual dose received by dose level by sex : not reported.
- Body weight : Mean body weight gain in male rats fed diets containing 18,000 or 21,000 ppm 11-aminoundecanoic acid was depressed 13 % and 14 %, respectively
- Food/water consumption : not reported
- Clinical signs : not reported
- Ophthalmologic examination : not done
- Hematological examination : not done
- Clinical biochemistry examination : not done
- Mortality and time to death : One of 12 female rats fed the 18,000 ppm diet died at day 9
- Gross pathology : not reported

- Organ weight changes : not reported
- Histopathology incidence and severity : Multifocal tubular mineralization of the kidneys was noted in 70 % - 100 % of all groups of female rats administered 11-aminoundecanoic acid. The severity of the mineralization was dose related. Transitional-cell hyperplasia was found in the kidneys of 1/10 males rats fed 21,000 ppm, in 6/10 females fed 21,000 ppm, and in 2/9 females fed 18,000 ppm 11-aminoundecanoic acid. Hyperplasias of the renal pelvis were seen in 2/9 females fed 18,000 ppm and in 1/10 males and 6/10 females fed 21,000 ppm.

Conclusion : The administration of up to 21000 ppm 11-aminoundecanoic acid in the diet of rats for 13 weeks leads to transitional cell hyperplasia in the kidneys in males and females and bodyweight depression in males at 18000 and 21000 ppm. Mineralization of the kidney was observed in all female groups. The NOAEL was lower than 9000 ppm.

Reliability : (2) valid with restrictions

Flag : Directive 67/548/EEC, Critical study for SIDS endpoint

11.06.2002 (38)

Type :
Species : mouse
Sex : male/female
Strain : B6C3F1
Route of admin. : oral feed
Exposure period : 14 days
Frequency of treatm. : ad libitum
Post exposure period : none
Doses : 0, 5000, 10000, 15000, 20000 and 30000 ppm
Control group : yes, concurrent no treatment
NOAEL : = 30000 ppm
LOAEL : > 30000 ppm
Method : other: NTP range-finding study
Year : 1982
GLP : no data
Test substance : other TS

Test substance : Purity : 99.13 ± 0.03 wt%

Method : Male and female B6C3F1 mice were obtained from Frederick Cancer Research Institute, quarantined, and held for approximately 3 months before the study began. Animals were approximately 15 weeks old when placed on study.
Groups of five males and five females were fed diets containing 0, 5,000, 10,000, 15,000, 20,000, or 30,000 ppm 11-aminoundecanoic acid for 2 weeks. Test diets were prepared several days before the start of the study by mixing the test chemical and ground Purina Lab Chow in a Patterson-Kelly Twin Shell Blender. Diets were refrigerated until use.
Animals were housed two or three per cage and received water and feed ad libitum. The mice were observed daily for mortality and were weighed weekly. Gross necropsies were performed on all animals at the end of the 14-day study.

Result : All animals survived to the end of the dosing period. No compound-associated effects were observed in mice at any dose level.

Reliability : (2) valid with restrictions

11.06.2002 (38)

Type :
Species : mouse
Sex : male/female

Strain	:	B6C3F1
Route of admin.	:	oral feed
Exposure period	:	90 days
Frequency of treatm.	:	ad libitum
Post exposure period	:	none
Doses	:	0, 9000, 12000, 15000, 18000 and 20000 ppm
Control group	:	yes, concurrent no treatment
NOAEL	:	= 9000 ppm
Method	:	other: NTP range-finding study
Year	:	1982
GLP	:	no data
Test substance	:	other TS
Test substance	:	Purity : 99.13 ± 0.03 wt%
Method	:	Animals were checked for mortality and signs of morbidity twice daily. Each animal was given a clinical examination weekly, including palpation for tissue masses or swelling. Body weight and feed consumption data were collected weekly. At the end of the 91-day study, survivors were killed with carbon dioxide and necropsies were performed. The following specimens were examined for control and high-dose groups: gross lesions, tissue masses, abnormal lymph nodes, skin, mandibular lymph nodes, mammary gland, salivary gland, thigh muscle, sciatic nerve, bone marrow, costochondral junction (rib), thymus, larynx, trachea, lungs and bronchi, heart, thyroid, parathyroid, esophagus, stomach, duodenum, jejunum, ileum, colon, mesenteric lymph nodes, liver, gallbladder, pancreas, spleen, kidneys, adrenals, bladder, seminal vesicles/prostate/ testes or ovaries/uterus, nasal cavity, brain pituitary, and spinal cord. Tissues were preserved in 10 % neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. Histopathologic examination for all other dosed groups (excepted the 12000 ppm group which was not examined) was limited to the kidneys and liver.
Test condition	:	- Test Subjects Age at study initiation : 5 weeks No. of animals per sex per dose : 10
Result	:	- Actual dose received by dose level by sex : not reported. - Body weight : Mean body weight gain was depressed 20 % in male mice receiving 15,000 ppm, but only 10 % in male mice receiving 18,000 or 20,000 ppm. Mean body weight gain was depressed by more than 10 % in female mice fed diets containing 18,000 - 20,000 ppm 11-aminoundecanoic acid. - Food/water consumption : not reported - Clinical signs : not reported - Ophthalmologic examination : not done - Hematological examination : not done - Clinical biochemistry examination : not done - Mortality and time to death : Deaths occurred in 2/10 male and 2/10 female mice administered 15,000 ppm, 4/10 males and 2/10 females receiving 18,000 ppm, and 3/10 males receiving 20,000 ppm. The cause of death of animals dying during the study was not determined. - Gross pathology incidence and severity : not reported - Organ weight changes : not reported - Histopathology incidence and severity : Focal mineralization of the kidney was noted in males that received 15,000 - 20,000 ppm and in females that received 15,000 - 18,000 ppm, particulary in those mice that died.
Conclusion	:	The administration of up to 20000 ppm 11-aminoundecanoic acid in the diet of mice for 13 weeks leads to focal mineralisation of the kidneys and body weight depression.

The NOAEL was estimated to be 9000 ppm.

Reliability : (2) valid with restrictions
Flag : Directive 67/548/EEC, Critical study for SIDS endpoint
11.06.2002 (38)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : **Salmonella typhimurium reverse mutation assay**
System of testing : Strains TA98, TA100, TA 1535, 1537 and 1538
Test concentration : 0, 50, 100, 250, 500, 750 and 1000 µg/plate
Cycotoxic concentr. : With metabolic activation : > 1000 µg/plate
Without metabolic activation : > 1000 µg/plate
Metabolic activation : with and without
Result : negative
Method : other: equivalent to OECD Guide-line 471
Year : 1982
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Test condition : · Metabolic activation :
- Species : rat
- Quantity : 10% S9
- Induction: Aroclor 1254
· Statistical Methods : none
· Test Design
- Number of replicates : 1
- Positive controls :
Without activation : Ethylmethanesulfonate (TA1535 and TA
100), 9-aminoacridine (TA 1537), nitrofluorene (TA98 and TA1538),
With activation : 2-aminoanthracene (TA98).
- Solvent : distilled water
- Description of follow up repeat study : same conditions than the initial experiment

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
11.06.2002 (4)

Type : **Salmonella typhimurium reverse mutation assay**
System of testing : Strains TA 98, TA100, TA 1535, TA 1537 and TA1538
Test concentration : 10, 50, 100, 500, 1000 and 5000 µg/plate
Cycotoxic concentr. : With metabolic activation : > 5000 µg/plate
Without metabolic activation : > 5000 µg/plate
Metabolic activation : with and without
Result : negative
Method : other: equivalent to OECD Guide-line 471
Year : 1982
GLP : no data
Test substance : other TS

Test substance : Purity : 99.7 wt%
Test condition : · Metabolic activation :
- Species : rat
- Quantity : 10% S9
- Induction: PCB
· Statistical Methods : none
· Test Design

- Number of replicates : 2
- Positive controls :
Without activation : 2-AF (TA98, TA100), ENNG (TA1535), 9-aminoacridine (TA 1537), 2-nitrofluorene (TA1538),
With activation : Benzopyrene (TA 98, TA100, TA1537 and TA 1538), 2-aminoantracene (TA 1535).
- Solvent : DMSO
- Description of follow up repeat study : not reported

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
11.06.2002 (43)

Type : **Salmonella typhimurium reverse mutation assay**
System of testing : Strains TA98, TA100, TA1535 and TA1537
Test concentration : 100, 333, 1000, 3333 and 10000 µg/plate
Cycotoxic concentr. : With metabolic activation : > 10000 µg/plate
Without metabolic activation : > 10000 µg/plate
Metabolic activation : with and without
Result : negative
Method : OECD Guide-line 471
Year : 1986
GLP : no data
Test substance : no data

Test condition : · Metabolic activation : preincubation assay
- Species : rat and hamster
- Quantity : 10% S9
- Induction: Aroclor 1254
· Statistical Methods : none
· Test Design
- Number of replicates : 3
- Positive controls :
Without activation : sodium azide (TA1535 and TA 100), 9-aminoacridine (TA97 and TA 1537), 4-nitro-o-phenylenediamine (TA98),
With activation : 2-aminoanthracene (all strains).
- Solvent : distilled water
- Description of follow up repeat study : same conditions than the initial experiment

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
11.06.2002 (37)

Type : **Escherichia coli reverse mutation assay**
System of testing : Strain WP2 uvrA
Test concentration : 10, 50, 100, 500, 1000 and 5000 µg/plate
Cycotoxic concentr. : With metabolic activation : > 5000 µg/plate
Without metabolic activation : > 5000 µg/plate
Metabolic activation : with and without
Result : negative
Method : other: equivalent to OECD Guide-line 472
Year : 1982
GLP : no data
Test substance : other TS

Test substance : Purity : 99.7 wt%
Test condition : · Metabolic activation :
- Species : rat
- Quantity : 10% S9

- Induction: PCB
· Statistical Methods : none
· Test Design
- Number of replicates : 2
- Positive controls :
Without activation : 2-AF
With activation : 2-aminoantracene
- Solvent : DMSO
- Description of follow up repeat study : not reported

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
11.06.2002 (43)

Type : **Cytogenetic assay**
System of testing : Chinese Hamster ovary (CHO) cells
Test concentration : 100, 333 and 1000 µg/ml without S9; 3.3, 100, 333 and 1000 µg/ml with S9.
Cycotoxic concentr. : With and without metabolic activation : >1000 µg/ml
A precipitate was observed at 1000 µg/ml
Metabolic activation : with and without
Result : negative
Method : other: equivalent to OECD Guide-line 473
Year : 1987
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Test condition : · Metabolic activation :
- Species : rat
- Quantity : 15 µl S9/ml
- Induction : Aroclor 1254
· Statistical Methods : yes
· Test Design
- Number of replicates : 1 culture/experimental point
- Conditions of treatment :
Without S9 : the cultures were incubated with the test or control substances which remainded in the culture medium for 10.5 hours,
With S9 : the test or control substances remainded in a culture medium with S9 for 2 hours. They were then centrifuged, the treatment medium removed, and the cells were then incubated in fresh culture medium for 8.5 additional hours.
- Positive and negative control groups and treatment
Positive controls : mitomycin C (without S9) and cyclophosphamide (with S9).
Negative control : no data
- Number of metaphases analyzed : 100
- Description of follow up repeat study : none
- Criteria for evaluating results (e.g. cell evaluated per dose group) : 100 metaphases per experimental point

Result : - Frequency of aberrant cells (%)

	-S9	+S9
Dose (µg/ml)		
0	3	2
3.3		1
100	4	2
333	4	3
1000	1	3
+ve control	19	28

- Mitotic index (% of control): not reported

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
08.10.2002 (30)

Type : **Mammalian cell gene mutation assay**
System of testing : Mouse lymphoma L5178Y cells; TK+/TK-
Test concentration : Without S9
1st assay: 1.25, 2.5, 5, 10 and 20 µg/ml
2nd assay: 12, 14, 16, 18 and 20 µg/ml
3rd assay: 160, 200, 240, 280 and 320 µg/ml
With S9: 160, 200, 240, 280 and 320 µg/ml
Cycotoxic concentr. : Without S9
1st assay: none
2nd assay: >=14 µg/ml
3rd assay: none
With S9: none
Metabolic activation : with and without
Result : negative
Method : other: equivalent to OECD Guide-line 476
Year : 1988
GLP : no data
Test substance : no data

Test condition : Insolubility prevented testing higher than 320 µg/ml.
The pH of the medium was progressively reduced at concentration of 120 µg/ml and higher.
Result : No mutagenic or toxic response was observed in 3 of 4 experiments without S9. In the experiment that was positive, the chemical induced both toxicity and mutagenic response. However, since these effects were not reproduced in any on the repeat experiments, the chemical was judged not mutagenic in the absence of S9.
Because the 2 experiments with S9 also showed no response, the assay was judged negative.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
17.12.2003 (34)

Type : **Sister chromatid exchange assay**
System of testing : Chinese Hamster ovary (CHO) cells
Test concentration : 500, 750 and 1000 µg/ml
Cycotoxic concentr. : A precipitate was observed at all concentrations
Metabolic activation : with and without
Result : ambiguous
Method : other: equivalent to OECD Guide-line 479
Year : 1987
GLP : no data
Test substance : no data

Result : The number of SCE/cell was not significantly increase with S9 (result negative).
The number of SCE/cell was slightly increase without S9 (result ambiguous); respectively 7.73, 9.57, 12.05, 11.91 and 27.52 in negative control, 500, 750 and 1000 µg/ml and positive control (MMC).
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
08.10.2002 (30)

Type	:	**other: Cell transformation**
System of testing	:	Syrian hamster embryo cells
Test concentration	:	0.6, 1.2, 2.5, 5.0 and 10.0 mM
Cycotoxic concentr.	:	>= 5.0 mM
Metabolic activation	:	without
Result	:	ambiguous
Method	:	other
Year	:	1986
GLP	:	no data
Test substance	:	no data
Remark	:	This test is known to be excessively sensitive. Up to 2.5 mM (ca 0.24 mg/ml) results are clearly negative.
Reliability	:	(3) invalid

11.06.2002 (31)

5.6 GENETIC TOXICITY 'IN VIVO'

Type	:	**Micronucleus assay**
Species	:	mouse
Sex	:	male
Strain	:	B6C3F1
Route of admin.	:	i.p.
Exposure period	:	three daily injection
Doses	:	0, 62.5, 1258, 250 and 500 mg/kg
Result	:	negative
Method	:	other: equivalent to OECD Guide-line 474
Year	:	1993
GLP	:	no data
Test substance	:	no data

Test condition :

- Age at study initiation : 9-14 weeks
- No. of animals per dose : 4-6
- Frequency of treatment : three daily injection
- Sampling times and number of samples : 24 hrs after the third treatment
- Control groups : DMBA or MMS, not specified
- Clinical observations : twice daily
- Organs examined at necropsy (macroscopic and microscopic) : bone marrow
- Criteria for evaluating results (for example, cell types examined, number of cells counted in a mouse micronucleus test) : MN-PCE/2000 PCE and % of PCE among 200 erythrocytes
- Criteria for selection of M.T.D. : mortality ; administration characteristics, or depression in the % of bone marrow PCE

· Statistical methods : The data were analyzed using the Micronucleus Assay Data Management and Statistical software package (version 1.4), which was designed specifically for in vivo micronucleus data [ILS, 1990]. The %PCE data were analyzed by an analysis of variance (ANOVA) test based on pooled data. Pairwise comparisons between each group and the concurrent solvent control group was by an unadjusted one-tailed Pearson chisquared test which incorporated the calculated variance inflation factor for the study.

Result : · Effect on PCE/NCE ratio by dose level :

Dose (mg/kg)	% PCE
0	53.0
62.5	53.2
125	39.1
250	42.1

500	42.3

· Genotoxic effects : negative
· NOEL : > 500 mg/kg
· Remarks field for Results :
- Mortality at each dose level :

Dose (mg/kg)	Mortality
0	0/5
62.5	0/5
125	1/6
250	0/5
500	0/4

- MN-PCE frequency :

Dose (mg/kg)	MN-PCE/1000 PCE
0	2.30 ± 0.37
62.5	2.00 ± 0.35
125	1.90 ± 0.62
250	2.30 ± 0.37
500	2.38 ± 0.24

- clinical signs : not reported
- Body weight changes : not reported
- Food/water consumption changes : not reported

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
11.06.2002 (42)

Type : **Drosophila SLRL test**
Species : Drosophila melanogaster
Sex : male/female
Strain : no data
Route of admin. : other: injection
Exposure period : Single
Doses : 1000 ppm
Result : Negative
Method : other: equivalent to OECD Guide-line 477
Year :
GLP : no data
Test substance : other TS

Test substance : Purity > 99%
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
11.06.2002 (45)

Type : **Unscheduled DNA synthesis**
Species : Rat
Sex : Male
Strain : Fischer 344
Route of admin. : Gavage
Exposure period : Single
Doses : 50, 250 and 1000 mg/kg
Result : Negative
Method : other: equivalent to draft OECD guideline "Unscheduled DNA synthesis test with mammalian liver cells in vivo
Year : 1996
GLP : no data
Test substance : other TS

Test substance : Purity : 99.13 ± 0.03 wt%
Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint
11.06.2002 (35)

Type : **other: DNA-binding**
Species : Rat
Sex : male/female
Strain : Fischer 344
Route of admin. : Gavage
Exposure period : Single
Doses : 1 mCi/rat
Result : Negative
Method : other
Year : 1987
GLP : No
Test substance : other TS

Test substance : 11-Aminoundecanoic acid-[11-14C], specific activity 14.22 mCi/mmol.
Method : Animals and treatment
Five male and female F-344 rats were each dosed orally with 1 mCi of 11-14C-aminoundecanoic acid (11-AA) with a specific activity of 14.22 mCi/mmol) which was dissolved in 1 ml of 5% aqueous acetic acid. After application of the substance, the animals were placed separately in closed all-glass metabolic cages; a continuous airstream was sucked through these cages and was drawn through soda lime (14CO2 trapping). Some radioactivity (not quantitated) was found in the soda lime, indicating that minor amounts of 14C02 had been produced by metabolism of 14C-AA.
In the 24 hours following application of the compound, urine and feces were collected. After these 24 hours, the animals were sacrificed and the liver, kidneys and urinary bladder tissues were removed.

Radioactivity excretion
Total radioactivity in urine and feces collected during 24 h was determined by liquid scintillation counting of aliquots.

Tissue radioactivity
The extracted organs were homogenized. The radioactivity in liver and kidneys was determined by liquid scintillation counting after dissolving aliquots of the crude homogenate with 0.5 ml tissue solubilizer. Bladder tissue homogenates were not controled in this manner because contamination with the highly radioactive urine would have resulted in erroneous radioactivity values.

The 3 organs (liver, kidney, bladder) were individually processed for each individual test animal. This individual processing included preparation of nuclei, DNA isolation, and counting of radioactivity in DNA.

Result : Radioactivity distribution
The excretion of radioactivity derived from 11-AA is slow; only some 10% of the dose was excreted in urine and feces during the first 24 h after dosing (Tab. 1). In addition, minor amounts of radioactivity (not quantitated) were excreted in breath, apparently as 14C02.

Table 1: Total radioactivity (dpm) in urine and feces after 24 hours of a single oral dose of (11-14C)aminoundecanoic acid as determined by liquid scintillation counting of

aliquots (0.1 ml urine/50 µg feces)

F-344 rats, female		F-344 rats, male	
no. urine	feces	no. urine	feces
1 4.92x10e7	3.93x10e5	1 2.01x10e8	1.01x10e8(+)
2(++) 1.29x10e8	3.15x10e7(+)	2 2.55x10e8	7.61x10e7
3 2.20x10e8	1.65x10e8(+)	3 1.32x10e8	1.38x10e6
4 4.93x10e7	1.43x10e6	4 2.90x10e8	2.78x10e7
5 1.64x10e8	1.64x10e8(+)	5 1.89x10e8	5.23x10e5

(+) feces contaminated with urine
(++) female No. 2 received only 1/2 dose

% of radioactivity dose excreted within 24 h (x+S.D.):

	F-344 rats, female	F-344 rats, male
urine:	6.7 ± 4.3	9.6 ± 2.8
feces:	3.3 ± 3.8	1.9 ± 2.0
urine + feces:	9.9 ± 7.2	11.5 ± 4.0

The nature of the metabolites excreted is not known so far. It appears, however, that some (probably minor) portion of the administered compound is degraded and finally enters pathways of intermediary metabolism. The data of radioactivity incorporation into DNA (see below) are supportive of this view.

At the time of sacrifice (i.e., 24 h after dosing) the liver tissue contained significantly less radioactiity (based per gram tissue) than the kidneys (Tab. 2). This may be related to renal excretion of metabolites; however, it may be speculated that significant quantities of 11-AA could be stored in extrahepatic tissues.

Table 2: Radioactivity (dpm/g wet weight) of liver and kidneys, 24 h after dosing (14C)AA.

F-344 rats, female		F-344 rats, male	
no. liver	kidneys	no. liver	kidneys
1 5.4 10e5	3.3 10e6	1 5.24 10e5	4.52 10e6
2(*) 2.24 10e5	1.89 10e6	2 3.84 10e5	4.14 10e6
3 5.0 10e5	3.9 10e6	3 8.16 10e5	5.12 10e6
4 5.68 10e5	3.93 10e6	4 5.16 10e5	4.84 10e6
5 5.0 10e5	3.56 10e6	5 4.52 10e5	2.21 10e6

(*) female No. 2 received only 1/2 dose

After careful isolation and purification (hydroxy-apatite) of DNA from the relevant tissues, no 14C-radio-activity derived from 11-AA was detected in urinary bladder tissue (Tab. 3). However, this may be related to the very low amounts of DNA extracted from this organ. Radioactivity associated with renal DNA was very low, but significant amounts of radioactivity were associated with liver DNA. More radioactivity was associated with hepatic (and renal)

DNA from male, compared to female rats.

Table 3: Radioactivity in DNA. The figures (a) give the dpm, and the amount of DNA (mg) in each counted aliquot (counting time 10 min) of the samples. After pooling the samples of parallel animals (b) again 3 aliquots were formed and counted for radioactivity.

(a) Single animals

	liver		kidneys		bladder	
no.	dpm	µg DNA	dpm	µg DNA	dpm	µg DNA
F-344 rats, female						
1	75	197	8	13.8	8	1.8
2(+)	46	184	4	10.8	4	1
3	64	112	5	11.1	6	1.4
4	42	114	4	9.5	4	1
5	63	98	5	11.6	6	1.9
F-344 rats, male						
1	57	211	11	24.4	7	2.8
2	189	225	13	30.2	9	3.6
3	41	128	8	20	10	3.8
5	35	125	7	17.5	2	1.1

High radioactivity values in DNA from some bladder tissues resulted from small counting samples and a high background (compared with (b)).

(b) pooled organ DNA samples (dpm/mg DNA; 3 aliquots counted (counting time 20 min); x±S.D.)

F-344 rats, female			F-344 rats, male		
liver	kidneys	bladder	liver	kidneys	bladder
210±15	60±14	n.d.	370±45	90±20	n.d.

n.d. = no detectable radioactivity

(+) = female No. 2 received only 1/2 dose; material not included in pooled samples (b)

Examination for DNA alkylation
In order to distinguish between alkylation of DNA (associated with genotoxicity) and incorporation of radioactivity into natural nucleosides, pooled samples of DNA from the organs examined were enzymatically hydrolyzed (to the deoxyribonucleosides) and then subjected to HPLC separation.
It is evident that minor radioactivity counts are associated with the physiological nucleosides (especially dA and dC). Significant radioactivity peaks not coinciding with the physiological nucleosides are not apparent. This means that there was no sign of DNA alkylation by either 11-AA or a (radioactively labelled) metabolite.

Conclusion : DNA-binding with 11-AA (labelled with 14C at carbon-11), using male and female F-344 rats, liver, kidneys and urinary bladder have been examined both for association of radioactivity with DNA and for DNA alkylation (i.e.,

formation of altered radioactive nucleosides in DNA).

There was minor incorporation of 11-AA derived radioactivity into the physiological DNA nucleosides (in liver higher than in kidneys, in males higher than in females). This could not be observed in DNA from urinary bladder, but from this organ only low amounts of DNA were isolated due to the limited mass of tissue available.

Upon chromatography (HPLC) of hydrolysates from DNA (isolated from livers and kidneys) no significant radioactive peaks were observed besides those of the physiological nucleosides; therefore, there was no indication of DNA alkylation by 11-AA or a metabolite thereof .

On this basis, this DNA-binding study as being considered negative.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
09.11.2001 (5) (41)

5.7 CARCINOGENICITY

Species	:	**Rat**
Sex	:	male/female
Strain	:	Fischer 344
Route of admin.	:	oral feed
Exposure period	:	104 weeks
Frequency of treatm.	:	ad libitum
Post exposure period	:	5 weeks
Doses	:	7500 and 15000 ppm
Result	:	Positive
Control group	:	yes, concurrent no treatment
Method	:	other: NTP bioassay
Year	:	1982
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Test substance : Purity : 99.13 ± 0.03 wt%
Method : All animals were observed twice daily for signs of toxicity. Clinical signs were recorded monthly. Body weights and feed consumption by cage were recorded every 2 weeks for the first 13 weeks and monthly thereafter. The mean body weight of each group was calculated by dividing the total weight of all animals in the group by the number of surviving animals in the group. The average feed consumption per animal was calculated by dividing the total feed consumption measured for all cages by the number of surviving animals in the group. Moribund animals and animals that survived to the end of the bioassay were killed using carbon dioxide and necropsied.

Examinations for grossly visible lesions were performed on major tissues or organs. Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. The following were examined microscopically: tissue masses, abnormal lymph noces, skin, mandibular lymph noces, mammary gland, salivary gland, thigh muscle, sciatic nerve, bone marrow, costochondral junction (rib), thymus, larynx, trachea, lungs and bronchi, heart, thyroid, para-thyroid, esophagus, stomach, duodenum, jejunum, ileum, colon,

mesenteric lymph nodes, liver, gallbladder (mice), pancreas, spleen, kidneys, adrenals, bladder, seminal vesicles/ prostate/ testes or ovaries/ uterus, nasal cavity, brain, pituitary, and spinal cord. Special staining techniques were used as necessary.
Necropsies were performed on all animals found dead and on those killed at the end of the study, unless precluded in whole or in part by autolysis or cannibalization. Thus, the number of animals from which particular organs or tissues were examined microscopically varies and is not necessarily equal to the number of animals that were placed on study in each group.

The pathology report and selected slides were evaluated by the NTP Pathology Working Group as described by Ward et al. (1978). The classification of neoplastic nodules was clone according to the recommandations of Squire and Levitt (1975), and the National Academy of Sciences (1980). The diagnoses represent a consensus of contracting pathologists and the NTP Pathology Working Group.

Data on this experiment were recorded in the Carcinogenesis Bioassay Data System (Linhart et al., 1974). The data elements include descriptive information on the chemicals, animals, experimental design, clinical observations, survival, body weight, and individual pathologic results, as recommended by the International Union Against Cancer (Berenblum, 1969).

Test condition : - Test Subjects
Age at study initiation : 5 weeks
No. of animals per sex per dose : 50

Result : - Actual dose received by dose level by sex : not reported.
- Body weight : Throughout the last year of the study, mean body weights of high-dose rats of either sex were lower than those of the controls.
- Food consumption : The average daily feed consumption per rat by low- and high-dose rats was 98% and 88% that of the controls for males and 88% and 86% for females.
- Clinical signs : No compound-related clinical signs were observed.
- Ophthalmologic examination : not done
- Hematological examination : not done
- Clinical biochemistry : not done
- Mortality and time to death : In male rats, 39/50 (78%) of the control group, 37/50 (74%) of the low-dose group, and 30/50 (60%) of the high-dose group lived to the end of the study at 109 weeks. In female rats, 38/50 (76%) of the control group, 32/50 (64%) of the low-dose group, and 42/50 (84%) of the high-dose group lived to the end of the study at 109 weeks. The cause of death of animals dying during the study was not determined.
- Gross pathology : not reported
- Organ weight changes : not reported
- Histopathology :

A variety of tumors was found in control and dosed groups, including leukemias, pituitary chromophobe adenomas, interstitial-cell tumors, pheochromocytomas, mammary fibroadenomas, and lesser incidences of other neoplasms.

Urinary Bladder: Transitional-cell carcinomas of the urinary bladder were observed in a significantly increased incidence (P <0.01) in the high-dose group of male rats (controls, 0/48 0%; low-dose, 0/48, 0%; high-dose, 7/49, 14%). These tumors generally tended to grow toward the lumen of the bladder, often forming papillary processes. These tumors had a large number of anaplastic cells, mitotic activity, and areas of focal necrosis. Invasion of the basement membrane and underlying tissues was often seen in malignant tumors; however, no vascular invasion or metastases were observed. Transitional-cell carcinomas of the urinary bladder were not observed in any of the three female rat groups.

Focal or diffuse hyperplasia of the transitional

epithelium of the urinary bladder was observed with a significantly (P < 0.01) increased incidence in high-dose male rats (controls, 0/48,0%; low-dose, 2/48, 4%; high-dose, 20/49, 41%). These lesions were also observed with increased incidence in dosed female rats (controls, 4/49, 8%; low-dose, 12/47, 26%; high-dose, 9/48, 19%), but only in the low-dose group was this increase statistically significant (P < 0.05).
An increased incidence of calculi of the urinary bladder was seen in males in the high-dose group (controls, 1/48, 2%; low-dose, 1/48, 2%; high-dose, 5/49, 10%). However, these calculi were not found in any of the animals for which transitional-cell carcinomas were seen.
Kidneys: Focal or diffuse hyperplasia of the transitional epithelium of the kidney was observed with significantly (P < 0.01) increased incidence in high-dose male rats (controls, 0/50, 0%; low-dose, 4/50, 8%; high-dose 15/50, 30%) and female rats (controls, 0/49, 0%; low-dose 5/50, 10%; high-dose, 34/50, 68%) administered 11-aminoundecanoic acid. The increased incidence in low-dose female rats was also statistically significant (P < 0.05). None was seen in the controls. Foci of calcification in the renal cortex and medulla, especially at the cortico-medullary junction and tip of the medulla, were common lesions in dosed female rats. Nonneoplastic kidney lesions (e.g., chronic nephropathy), commonly seen in aging rats were observed in all groups.
Liver: Neoplastic nodules occurred with a significantly increased incidence (P<0.01) in dosed male rats (controls, 1/50, 2%; low-dose 9/50, 18%; high-dose, 8/50, 16%). The neoplastic nodules were not life shortening. The slight increase in neoplastic nodules observed in female rats was not statistically significant. Hepatocellular carcinomas were also observed in two high-dose male rats and one long-dose male rat.
Mammary gland: Fibroadenomas showed an increased incidence (P <0.05) in the low-dose male rat group (controls, 0/50, 0%; low-dose, 5/50, 10%; high-dose, 2/50, 4%). The slight increase at the high dose was not statistically significant.
Hematopoietic System: A significantly decreased incidence (P<0.05) of leukemia was observed in male rats administered 11-aminoundecanoic acid (control, 14/ 50, 28%; low-dose, 4/50, 8%; high-dose, 5/50, 10%).
Subcutaneous tissue: A decreasing trend (P <0.05) was seen in neurofibromas of the sub-cutaneous tissue of male rats (control, 3/50, 6%; low-dose, 0/50, 0%; high-dose, 0/50, 0%).

Conclusion : Under the conditions of this bioassay, 11-aminoundecanoic acid was carcinogenic for male F344 rats, inducing neoplastic nodules in the liver and transitional-cell carcinomas in the urinary bladder. The test chemical was not carcinogenic for female F344 rats.

Remark : Comments on neoplastic nodules of the liver in Fischer 344 male rats:
These tumours are benign tumours very common in this specific strain and sex. From one bioassay to another, the background incidences within the control groups are highly fluctuant. The observed incidences in the NTP 11-AMINOUNDECANOIC ACID bioassay remain within the overall historical variations. The higher incidence in the 11-AMINOUNDECANOIC ACID treated rats compared with the control group in the same bioassay can be interpreted as a random distribution, especially because there is no dose-related effect (same rate at 7500 and 15,000 ppm) because no similar effect was seen in female rats which are also prone to developp such tumors (control : 4/50 ; low dose 11-AMINOUNDECANOIC ACID : 5/50 ; high dose 11-AMINOUNDECANOIC ACID : 6/50).
Consequently, the actual biological significance of the observed elevation of such benign neoplastic nodules in the liver is very unclear.

Comments on transition-cell carcinoma of the urinary bladder:

First, these malignant tumours occured only in the higher dose group. This may be interpreted as an effect submitted to a dose threshold. The threshold would be localized between 7500 and 15,000 ppm of 11-AMINOUNDECANOIC ACID in the diet for a two years treatment.

Secondly, all the animals bearing transition-cell carcinoma had hyperplasia of the urinary bladder epithelium. Such non neoplastic lesions of the urinary tract were preexisting to the tumours since they were observed already at earlier stage with the same doses of 11-AMINOUNDECANOIC ACID (as found, e.g in the 90-day prechronic study of the same NTP bioassay). Such (non-neoplastic) hyperplasia of the epithelium may be linked to the mineralization process which occures in the urinary tract of rodents repeatedly treated with high dose levels of 11-AMINOUNDECANOIC ACID. These non-neoplastic lesions of the urinary organs may create specific conditions where an accelerated regeneration of the epithelial cells and the associate cells is continuously present during nearly the whole life of the treated animals.

This specific cell situation can be associated with a high elevation of the chances that some of the cells may proceed to a malignant stage.

Consequently, the transition-cell carcinoma found in male Fischer 344 rats can be interpreted as an indirect consequence of the non-oncogenic local effect induced by 11-AMINOUNDECANOIC ACID when very high dose levels are repeatedly ingested by the rats, exceeding the threshold level of 7500 ppm in the diet, every day during almost their whole life.

This interpretation is strengthen by the general lack of genotoxicity exhibited by 11-AMINOUNDECANOIC ACID in a battery of mutagenicity short term tests. Due to the lack of genotoxic potential of 11-AMINOUNDECANOIC ACID, it is very unlikely that 11-AMINOUNDECANOIC ACID might have produced the transition-cell carcinoma via a direct DNA interaction in these cells.

Reliability : (2) valid with restrictions
11.06.2002 (38)

Species	:	**mouse**
Sex	:	male/female
Strain	:	B6C3F1
Route of admin.	:	oral feed
Exposure period	:	103 weeks
Frequency of treatm.	:	ad libitum
Post exposure period	:	6 weeks
Doses	:	7500 and 15000 ppm
Result	:	ambiguous
Control group	:	yes, concurrent no treatment
Method	:	other: NTP bioassay
Year	:	1982
GLP	:	no data
Test substance	:	other TS

Test substance	:	Purity : 99.13 ± 0.03 wt%
Method	:	All animals were observed twice daily for signs of toxicity. Clinical signs were recorded monthly. Body weights and feed consumption by cage were recorded every 2 weeks for the first 13 weeks and monthly thereafter. The mean body weight of each group was calculated by dividing the total weight of all animals in the group by the number of surviving animals in the group. The average feed consumption per animal was calculated by dividing the total feed consumption measured for all cages by the number of surviving animals in the group. Moribund animals and animals that survived to the

end of the bioassay were killed using carbon dioxide and necropsied.

Examinations for grossly visible lesions were performed on major tissues or organs. Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. The following were examined microscopically: tissue masses, abnormal lymph noces, skin, mandibular lymph noces, mammary gland, salivary gland, thigh muscle, sciatic nerve, bone marrow, costochondral junction (rib), thymus, larynx, trachea, lungs and bronchi, heart, thyroid, para-thyroid, esophagus, stomach, duodenum, jejunum, ileum, colon, mesenteric lymph nodes, liver, gallbladder (mice), pancreas, spleen, kidneys, adrenals, bladder, seminal vesicles/ prostate/ testes or ovaries/ uterus, nasal cavity, brain, pituitary, and spinal cord. Special staining techniques were used as necessary.

Necropsies were performed on all animals found dead and on those killed at the end of the study, unless precluded in whole or in part by autolysis or cannibalization. Thus, the number of animals from which particular organs or tissues were examined microscopically varies and is not necessarily equal to the number of animals that were placed on study in each group.

The pathology report and selected slides were evaluated by the NTP Pathology Working Group as described by Ward et al. (1978). The classification of neoplastic nodules was clone
according to the recommandations of Squire and Levitt (1975), and the National Academy of Sciences (1980). The diagnoses represent a consensus of contracting pathologists and the NTP Pathology Working Group. Data recording and statistical methods: data on this experiment were recorded in the Carcinogenesis Bioassay Data System (Linhart et al., 1974). The data elements include descriptive information on the chemicals, animals, experimental design, clinical observations, survival, body weight, and individual pathologic results, as recommended by the International Union Against Cancer (Berenblum, 1969).

Test condition : - Test Subjects
Age at study initiation : 5 weeks
No. of animals per sex per dose : 50

Result : - Actual dose received by dose level by sex : not reported.
- Body weight : Mean body weights of dosed mice of either sex were lower than those of the controls throughout the study, and the depressions in mean body weight gain were
dose related.
- Food consumption : The average daily feed consumption per mouse by low- and high- dose mice was 110% and 123% that of the controls for males and 110 % and 97% for females.
- Clinical signs : No compound-related clinical signs were observed.
- Ophthalmologic examination : not done.
- Hematological examination : not done.
- Clinical biochemistry : not done.
- Mortality and time to death : In male mice, 37/50 (74%) of the control group, 34/50 (68%) of the low-dose group, and 18/50 (36%) of the high-dose group lived to the end of the study at 109 weeks. In female mice, 42/50 (84%) of the control group, 37/49 (76%) of the low-dose group, and 25/49 (51%) of the high-dose group lived to the end of the study at 109 weeks. The cause of death of animals dying during the study was not determined.
- Gross pathology : not reported
- Organ weight changes : not reported
- Histopathology :
Hematopoietic System: Malignant lymphomas occurred with a significant ($P < 0.05$) increasing trend in male mice (control, 2/50, 4%; low-dose, 9/50,

18%, high-dose, 4/50, 8%). The increase was statistically significant (P<0.05) at the low dose but not at the high dose. In most of the affected mice, two or more organs were involved in the neoplastic process. For female mice, a slight increase in malignant lymphomas was not statistically significant. If the results of the two sexes are combined, then the increasing trend is significant (P<0.05) by a life table analysis but not by an incidental tumor test.
Kidneys: The incidence of mineralization of the kidneys or kidney medulla was significantly (P < 0.01) increased in high-dose male mice (controls, 0/50, 0%; low-dose, 4/50, 8%; high-dose, 11/49, 22%), and in dosed female mice (controls, 0/50, 0%; low-dose, 8/49, 16%; high-dose, 9/49, 18%) fed 11-aminoundecanoic acid.
Liver: Hepatocellular vacuolization was observed with significantly (P < 0.05) increased incidence in high-dose male mice (controls, 2/50, 4%; long-dose, 2/50, 4%; high-dose 10/49, 20%) and in dosed female mice (controls, 0/50 %%; low-dose, 5/49, 10%; high-dose, 6/49,12%) fed 11-aminoundecanoic acid.

Conclusion : Under the conditions of this bioassay, no clear evidence was found for the carcinogenicity of 11-aminoundecanoic acid in B6C3F1 mice of either sex, although the increase in malignant lymphoma in male mice may have been associated with the administration of 11-aminoundecanoic acid.

Reliability : (2) valid with restrictions
11.06.2002 (38)

5.8.1 TOXICITY TO FERTILITY

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	**rat**
Sex	:	female
Strain	:	Sprague-Dawley
Route of admin.	:	oral feed
Exposure period	:	day 2 to day 19 post coitum inclusive
Frequency of treatm.	:	ad libitum
Duration of test	:	sacrifice on day 20 post-coitum
Doses	:	2000, 6000 and 18000 ppm (equivalent to 172, 520 and 1394 mg/kg bw/d)
Control group	:	yes, concurrent no treatment
NOAEL maternal tox.	:	= 6000 ppm
NOAEL teratogen.	:	= 18000 ppm
NOAEL Embryotoxicity	:	= 6000 ppm
other: NOEL Embryotoxicity	:	= 2000 ppm
Method	:	EPA OPPTS 870.3700
Year	:	1998
GLP	:	yes
Test substance	:	other TS

Test substance : Atofina, batch USA000523365, conform to specifications.

Method : Three groups of 24 mated female Sprague-Dawley rats received the test substance, 11-AMINOUNDECANOIC ACID, ad libitum by dietary admixture at constant concentrations of 2000, 6000 or 18000 ppm from day 2 to day 19 post-coitum inclusive. A group of 24 mated female Sprague-Dawley rats received the untreated diet alone under the same experimental conditions and acted as the control group.
Clinical signs (including evidence of abortion) and

mortality were checked daily. Food consumption and body weight were recorded at designated intervals during pregnancy.
On day 20 post-coitum, all females were killed. The fetuses were removed by hysterectomy and the dams examined macroscopically. The following litter parameters were recorded: number of corpora lutea, implantation sites, implant scars, early and late resorptions, dead and live fetuses. All the fetuses were weighed and submitted to an external examination. The sex of each live fetus was determined.
Approximately 50% of the live fetuses in each litter were fixed with Harrisson's fluid and submitted to a detailed soft tissue examination by serial sectioning.
The remaining live fetuses per litter were fixed with ethyl alcohol and then stained with alizarin red S and alcian blue. A detailed examination of the skeleton and cartilage was performed.

Result : Maternal data
. No deaths or treatment-related clinical signs were seen in any group.
. No evidence of abortion was observed in any of the females.
. Lower food consumption (-19%) and body weight gain (-44% for the net BWG) were recorded throughout the treatment period in females given the test substance at a concentration of 18000 ppm. This was not considered to be a direct toxic effect of the test substance but a consequence of a poor appetite possibly due to the unpalatability of the dietary admixture at this high concentration.
. No treatment-related macroscopic post-mortem findings were observed in any female from any group.

Litter data
. The number of corpora lutea and implantation sites per female was similar in all groups.
. The number of resorptions and post-implantation loss per female was similar in all groups.
. No dead fetus was found in any group.
. The mean number of live fetuses was similar in all groups.
The mean body weight of the fetuses was similar in the control, 2000 and 6000 ppm groups. It was slightly lower in fetuses given 18000 ppm (3.81g versus 4.07g in control group), probably as a consequence of the lower maternal body weight gain.

Fetal examination
. There were no external malformations or variations in any treated group.
. There were no treatment-related soft tissue malformations or variations in any treated group.
. There were no skeletal malformations, which could be related to treatment with the test substance at any dose-level.
. The incidence of skeletal variations was very slightly higher in the 6000 and 18000 ppm treated groups than in the control group. The difference in the incidence of affected fetuses and litters, when expressed as % are actually small: 81.7, 89.5, 92.9 and 89.9% at 0, 2000, 6000 and 18000 ppm, respectively. The differences in the overall incidence of variation achieved significance ($p<0.01$) only in the case of the fetuses in the 6000 ppm group. The increases are considered to represent a slight retardation in the growth and do not represent a direct adverse effect.

Conclusion	:	11-AMINOUNDECANOIC ACID administered daily to pregnant Sprague-Dawley female rats by dietary admixture at the constant concentrations of 2000, 6000 and 18000 ppm from day 2 to day 19 post-coitum was well tolerated at 2000 and 6000 ppm. As a consequence of poor appetite, possibly due to the unpalatability of the dietary admixture at this concentration, lower food consumption and body weight gain were recorded at the high concentration of 18000 ppm. Nevertheless, under the conditions of this study, the test substance did not produce embryo-toxicity nor feto-toxicity at any dose-level, with the exception of a slight retardation of growth/skeletal development at dose-levels of 6000 ppm and 18000 ppm (dose-level at which a slight reduction in fetal body weight was also noted). Consequently, the No Effect Level for embryofetal development was established at 2000 ppm (i.e. 172 mg/kg/day); 6000 ppm (i.e. 520 mg/kg/day) can be considered as a No Adverse Effect Level. No teratogenic effect was observed.
Reliability	:	(1) valid without restriction
Flag	:	Directive 67/548/EEC, Critical study for SIDS endpoint
23.10.2003		(9)

Species	:	**rat**
Sex	:	female
Strain	:	Sprague-Dawley
Route of admin.	:	oral feed
Exposure period	:	day 2 to day 19 post coitum inclusive
Frequency of treatm.	:	ad libitum
Duration of test	:	sacrifice on day 20 post-coitum
Doses	:	3000, 10000 and 30000 ppm
Control group	:	yes, concurrent no treatment
NOAEL maternal tox.	:	= 10000 - ppm
Method	:	other: range-finding study
Year	:	2000
GLP	:	no
Test substance	:	other TS

Test substance	:	Atofina, batch USA000523365, conform to specifications.
Method	:	Three groups of 7 mated female Sprague-Dawley rats received the test substance, 11-AMINO UNDECANOIC ACID, ad libitum by dietary admixture at a constant concentration of 3000, 10000 or 30000 ppm from day 2 to day 19 post-coitum inclusive. A group of 7 mated female Sprague-Dawley rats received the untreated diet alone under the same experimental conditions and acted as the control group. Clinical signs (including evidence of resorption or abortion) and mortality were checked daily. Food consumption and body weight were recorded at designated intervals during pregnancy. On day 20 post-coitum, all females were killed. The fetuses were removed by hysterectomy and the dams examined macroscopically. The following litter parameters were recorded: number of corpora lutea, implantation sites, implant scars, early and late resorptions, dead and live fetuses. All the fetuses were weighed, sexed and submitted to an external examination to check for malformations and/or variations. They were then killed and discarded without further investigation.
Result	:	Matemal data

- No deaths or treatment-related clinical signs were seen in any group.
- Neither total resorption nor evidence of abortion was observed.
- Markedly lower food consumption and body weight gain were recorded throughout the treatment period in females given the test substance at the concentration of 30000 ppm. This was not considered as a direct toxic effect of the test substance but as a consequence of a poor appetence of the dietary admixture at this high concentration.
- No treatment-related macroscopic post-mortem finding was observed in treated females except for pallor of kidneys and/or liver in a number of animals of the 30000 ppm group; a relationship to treatment with the test substance remains debatable.

Litter data
- The number of corpora lutea and implantation sites per female was similar in all groups.
- The number of resorptions and the post-implantation loss per female were similar in all groups.
- No dead fetus was found in any group.
- The mean number and body weight of live fetuses were similar in the 3000 and 10000 ppm groups. In the 30000 ppm group, the fetal weight was slightly lower than that recorded in the control group, probably as a consequence of the lower maternal body weight gain.

Fetal examination
- There were no external malformations or variations in any treated group.

Conclusion : 11-AMINO UNDECANOIC ACID administered daily to pregnant Sprague-Dawley female rats by dietary admixture at the constant concentrations of 3000, 10000 and 30000 ppm from day 2 to day 19 post-coitum was well tolerated at 3000 and 10000 ppm. As a consequence of a poor appetence of the dietary admixture, lower food consumption and body weight gain were recorded in the dams at the high concentration of 30000 ppm and this resulted in a slightly lower fetal weight. Nevertheless under the same conditions of this study, the test substance did not produce direct embryo-toxicity or feto-toxicity at any dose-level.

Reliability : (1) valid without restriction
23.10.2003 (8)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

Type	:	other: Reproductive organs toxicity
In vitro/in vivo	:	In vivo
Species	:	rat
Sex	:	male/female
Strain	:	Fischer 344
Route of admin.	:	oral feed
Exposure period	:	91days
Frequency of treatm.	:	ad libitum
Duration of test	:	91 days
Doses	:	0, 9000, 12000, 15000, 18000 and 21000 ppm
Control group	:	yes, concurrent no treatment

Result	:	No histopathological effects on the male and female reproductive organs up to 21000 ppm.
Method	:	other: NTP range-finding study
Year	:	1982
GLP	:	no data
Test substance	:	other TS
Test substance	:	Purity : 99.13 ± 0.03 wt%
Method	:	Animals were checked for mortality and signs of morbidity twice daily. Each animal was given a clinical examination weekly, including palpation for tissue masses or swelling. Body weight and feed consumption data were collected weekly. At the end of the 91-day study, survivors were killed with carbon dioxide and necropsies were performed. The following reproductive organs were examined for control and high-dose groups: seminal vesicles/prostate/ testes or ovaries/uterus. Tissues were preserved in 10 % neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin.
Test condition	:	- Test Subjects Age at study initiation : 5 weeks No. of animals per sex per dose : 10
Result	:	- Actual dose received by dose level by sex : not reported. - Body weight : Mean body weight gain in male rats fed diets containing 18,000 or 21,000 ppm 11-aminoundecanoic acid was depressed 13 % and 14 %, respectively - Food/water consumption : not reported - Clinical signs : not reported - Mortality and time to death : One of 12 female rats fed the 18,000 ppm diet died at day 9 - Gross pathology : not reported - Organ weight changes : not reported - Histopathology : no effect on the male and female reproductive organs.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

11.06.2002 (40)

Type	:	other: Reproductive organs toxicity
In vitro/in vivo	:	In vivo
Species	:	rat
Sex	:	male/female
Strain	:	Fischer 344
Route of admin.	:	oral feed
Exposure period	:	104 weeks
Frequency of treatm.	:	ad libitum
Duration of test	:	109 weeks
Doses	:	7500 and 15000 ppm
Control group	:	yes, concurrent no treatment
Result	:	No histopathological effects on the male and female reproductive organs up to 15000 ppm.
Method	:	other: NTP bioassay
Year	:	1982
GLP	:	no data
Test substance	:	other TS
Test substance	:	Purity : 99.13 ± 0.03 wt%
Method	:	All animals were observed twice daily for signs of toxicity. Clinical signs were recorded monthly. Body weights and feed consumption by cage were recorded every 2 weeks for the first 13 weeks and monthly thereafter. The mean body weight of each group was calculated by dividing the total weight

of all animals in the group by the number of surviving animals in the group. The average feed consumption per animal was calculated by dividing the total feed consumption measured for all cages by the number of surviving animals in the group. Moribund animals and animals that survived to the end of the bioassay were killed using carbon dioxide and necropsied.

Examinations for grossly visible lesions were performed on major tissues or organs. Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. The following reproductive organs were examined microscopically : seminal vesicles, prostate and testes in males or ovaries, vagin and uterus in females.
Estrous cycle length and pattern : not done.
Sperm examination (epididymal or vas sperm, concentration, motility, morphology): not done.

Test condition : - Test Subjects
Age at study initiation : 5 weeks
No. of animals per sex per dose : 50

Result : - Actual dose received by dose level by sex if known : not reported
- Body weight : Throughout the last year of the study, mean body weights of high-dose rats of either sex were lower than those of the controls.
- Food consumption : The average daily feed consumption per rat by low- and high-dose rats was 98% and 88% that of the controls for males and 88% and 86% for females.
- Clinical signs: No compound-related clinical signs were observed.
- Mortality : In male rats, 39/50 (78%) of the control group, 37/50 (74%) of the low-dose group, and 30/50 (60%) of the high-dose group lived to the end of the study at 109 weeks. In female rats, 38/50 (76%) of the control group, 32/50 (64%) of the low-dose group, and 42/50 (84%) of the high-dose group lived to the end of the study at 109 weeks. The cause of death of animals dying during the study was not determined.
- Organ weight changes : not reported
- Histopathology incidence and severity : not histological finding on the reproductive organs

Conclusion : Under the conditions of a 104-week toxicity study, no treatment related effects were observed on the reproductive organs in male and female F344 rats.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
11.06.2002 (40)

Type : other: Reproductive organs toxicity
In vitro/in vivo : In vivo
Species : mouse
Sex : male/female
Strain : B6C3F1
Route of admin. : oral feed
Exposure period : 90 days
Frequency of treatm. : ad libitum
Duration of test : 90 days
Doses : 9000, 12000, 15000, 18000 and 20000 ppm
Control group : yes, concurrent no treatment
Result : No histopathological effects on the male and female reproductive organs up to 20000 ppm.
Method : other: NTP range-finding study
Year : 1982
GLP : no data
Test substance : other TS

Test substance : Purity : 99.13 ± 0.03 wt%

Method	:	Animals were checked for mortality and signs of morbidity twice daily. Each animal was given a clinical examination weekly, including palpation for tissue masses or swelling. Body weight and feed consumption data were collected weekly. At the end of the 91-day study, survivors were killed with carbon dioxide and necropsies were performed. The following reproductive organs were examined for control and high-dose groups: seminal vesicles/prostate/ testes or ovaries/uterus. Tissues were preserved in 10 % neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin.
Test condition	:	- Test Subjects Age at study initiation : 5 weeks No. of animals per sex per dose : 10
Result	:	- Actual dose received by dose level by sex : not reported. - Body weight : Mean body weight gain was depressed 20 % in male mice receiving 15,000 ppm, but only 10 % in male mice receiving 18,000 or 20,000 ppm. Mean body weight gain was depressed by more than 10 % in female mice fed diets containing 18,000 - 20,000 ppm 11-aminoundecanoic acid. - Food/water consumption : not reported - Clinical signs : not reported - Mortality and time to death : Deaths occurred in 2/10 male and 2/10 female mice administered 15,000 ppm, 4/10 males and 2/10 females receiving 18,000 ppm, and 3/10 males receiving 20,000 ppm. The cause of death of animals dying during the study was not determined. - Gross pathology incidence and severity : not reported - Organ weight changes : not reported - Histopathology incidence and severity : no effects on the reproductive organs.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint
11.06.2002		(40)

Type	:	other: Reproductive organs toxicity
In vitro/in vivo	:	In vivo
Species	:	mouse
Sex	:	male/female
Strain	:	B6C3F1
Route of admin.	:	oral feed
Exposure period	:	103 weeks
Frequency of treatm.	:	ad libitum
Duration of test	:	109 weeks
Doses	:	7500 and 15000 ppm
Control group	:	yes, concurrent no treatment
Result	:	No histopathological effects on the male and female reproductive organs up to 15000 ppm.
Method	:	other: NTP bioassay
Year	:	1982
GLP	:	no data
Test substance	:	other TS

Test substance	:	Purity : 99.13 ± 0.03 wt%
Method	:	All animals were observed twice daily for signs of toxicity. Clinical signs were recorded monthly. Body weights and feed consumption by cage were recorded every 2 weeks for the first 13 weeks and monthly thereafter. The mean body weight of each group was calculated by dividing the total weight of all animals in the group by the number of surviving animals in the group. The average feed consumption per animal was calculated by dividing the total feed consumption measured for all cages by the number of surviving

animals in the group. Moribund animals and animals that survived to the end of the bioassay were killed using carbon dioxide and necropsied.

Examinations for grossly visible lesions were performed on major tissues or organs. Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. The following reproductive organs were examined microscopically : seminal vesicles, prostate and testes in males or ovaries, vagin and uterus in females.
Estrous cycle length and pattern (number of days spent in each phase), not done.
Sperm examination (epididymal or vas sperm, concentration, motility, morphology) : not done.

Test condition : - Test Subjects
Age at study initiation : 5 weeks
No. of animals per sex per dose : 50

Result : - Actual dose received by dose level by sex if known : not reported
- Body weight : Mean body weights of dosed mice of either sex were lower than those of the controls throughout the study, and the depressions in mean body weight gain were dose related.
- Food consumption : The average daily feed consumption per mouse by low- and high- dose mice was 110% and 123% that of the controls for males and 110 % and 97% for females.
- Clinical signs : No compound-related clinical signs were observed.
- Mortality : In male mice, 37/50 (74%) of the control group, 34/50 (68%) of the low-dose group, and 18/50 (36%) of the high-dose group lived to the end of the study at 109 weeks. In female mice, 42/50 (84%) of the control group, 37/49 (76%) of the low-dose group, and 25/49 (51%) of the high-dose group lived to the end of the study at 109 weeks. The cause of death of animals dying during the study was not determined.
- Organ weight changes : not reported
- Histopathology incidence and severity : not histological finding on the reproductive organs.

Conclusion : Under the conditions of a 103-week toxicity study, no treatment related effects were observed on the reproductive organs in male and female B6C3F1 mice.

Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint

11.06.2002 (40)

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

Type of experience : other: Occupational exposure survey

Remark : The substance is produced and used in closed system. Personnel protection equipments (mask, gloves and safety glasses) are used during production, handling and use of the substance. Occupational exposure to 11-aminoundecanoic acid may mainly occurs by inhalation of particles.

No specific occupational exposure limits have been determined for 11-aminoundecanoic acid. To recognize the adverse effects of exposure to non toxic particle matter, a TLV-TWA of 10 mg/m3 for inhalable particle and a TLV-TWA of 3 mg/m3 for respirable particles have been established by ACGIH (2001).

An occupational exposure survey was conducted in the Atofina's production plant of Marseille-Saint Menet in 1994 and 1995.
In 1994, inhalable particulates were monitored one time at 2 working places and in the ambient air:

Activity	8-hour TWA (mg/m3)
Operator in charge of the packaging in big bags (Personal monitoring)	11.62
Driver of fork-lift trucks (Personal monitoring)	2.52
Ambient air close to the bag-filling machine (Static sampling)	8.8

Corrective measures were applied to reduce the exposure of the operator in charge of the packaging. New big bags were used for the packaging instead of recycled big bags, which were at the origin of the release of a large amount of inhalable particles.

According to this corrective measure, the 8-hour TWA at the packaging working areas was reduced to 0.90 mg/m3 (mean of 2 measurements), in a new measurement campain performed in 1995. Inhalable particles were assumed to be reduced in the same proportion for the driver of fork-lift trucks and in the ambient air close to the bag filling machine. This assumption was confirmed in subsequent occupational exposure surveys (Personal monitoring) performed in 2000, 2001, 2002 and 2003. All measurements were well below the TLV-TWA of 10 mg/m3 for inhalable particle and the TLV-TWA of 3 mg/m3 for respirable particles

Activity	8-hour TWA (mg/m3)			
	2000	2001	2002	2003
Operator in charge of the packaging in big bags				
Inhalable particle	2.13	-	3.4	0.53
Respirable particle	<0.37	-	<0.18	<0.08
Driver of fork-lift trucks				
Inhalable particle	1.0	0.04	0.91	1.83
Respirable particle	<0.37	0.71	<0.18	<0.08
Tank loading				
Inhalable particle	<0.57	2.72	-	-
Respirable particle	<0.37	0.35	-	-

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5.11 ADDITIONAL REMARKS

6.1 ANALYTICAL METHODS

6.2 DETECTION AND IDENTIFICATION

7.1 FUNCTION

7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED

7.3 ORGANISMS TO BE PROTECTED

7.4 USER

7.5 RESISTANCE

8.1	**METHODS HANDLING AND STORING**
8.2	**FIRE GUIDANCE**
8.3	**EMERGENCY MEASURES**
8.4	**POSSIB. OF RENDERING SUBST. HARMLESS**
8.5	**WASTE MANAGEMENT**
8.6	**SIDE-EFFECTS DETECTION**
8.7	**SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER**
8.8	**REACTIVITY TOWARDS CONTAINER MATERIAL**

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10.1 END POINT SUMMARY

Memo : Acute oral toxicity

Conclusion : 11-Aminoundecanoic acid is of low acute toxicity by oral route:

Species	Result	Reference	Reliability
Male rat	LD0 >21.5 g/kg	NTP, 1982	2
Female rat	LD50 >14.7 g/kg	NTP, 1982	2
Rat (male+female)	LD0 >15.0 g/kg	Ato-Chimie, 1978	2

28.10.2002

Memo : Acute Inhalation toxicity

Remark : 5.1.2
Conclusion : No data available.
11.06.2002

Memo : Acute dermal toxicity

Remark : 5.1.3
Conclusion : 11-aminoundecanoic acid is of low acute toxicity by dermal route. The LD0 is higher than 2000 mg/kg in rats (Ato-Chimie, 1978; reliability 2)
11.06.2002

Memo : Skin irritation

Remark : 5.2.1
Conclusion : 11-aminoundecanoic acid is not irritation after a 24-hour occlusive application on the rabbit skin (Ato-Chimie, 1978; reliability 2)
11.06.2002

Memo : Eye irritation

Remark : 5.2.2
Conclusion : 11-aminoundecanoic acid induced a slight transient irritation when instillated in the rabbit eye (Ato-Chimie, 1978, reliability, 2).
11.06.2002

Memo : Sensitization

Remark : 5.3
Conclusion : 11-aminoundecanoic acid was not sensitizer in Guinea pigs in a test performed according to the maximization method of Magnusson and Kligman (Elf Atochem, 1999; reliability 1).
11.06.2002

Memo : Repeated dose toxicity

Remark : 5.4
Conclusion : Diets containing 0; 9,000; 12,000; 15,000; 18,000; 20,000 (mice) or 21,000 ppm (rats) 11-AMINOUNDECANOIC ACID were fed

for 13 weeks to groups of 12 male and 12 female F 344 rats and to groups of 10 male and 10 female B6C3F1 mice. Animals were checked for mortality and signs of morbidity twice daily. Each animal was given a clinical examination weekly, including palpation for tissue masses or swelling. Body weight and feed consumption data were collected weekly. At the end of the 91-day study, survivors were killed with carbon dioxide and necropsies were performed. The following specimens were examined for control and high-dose groups: gross lesions, tissue masses, abnormal lymph nodes, skin, mandibular lymph nodes, mammary gland, salivary gland, thigh muscle, sciatic nerve, bone marrow, costochondral junction (rib), thymus, larynx, trachea, lungs and bronchi, heart, thyroid, parathyroid, esophagus, stomach, duodenum, jejunum, ileum, colon, mesenteric lymph nodes, liver, gallbladder (mice), pancreas, spleen, kidneys, adrenals, bladder, seminal vesicles/prostate/ testes or ovaries/uterus, nasal cavity, brain pituitary, and spinal cord. Tissues were preserved in 10 % neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. Histopathologic examination for all other dosed groups was limited to the kidneys and liver, except for male and female rats administered 12,000 ppm. The kidneys, liver, lungs, and heart of animals in the 12,000 ppm groups were examined histo-pathologically.
One of 12 female rats fed the 18,000 ppm diet died at day 9. Mean body weight gain in male rats fed diets containing 18,000 or 21,000 ppm 11-AMINOUNDECANOIC ACID was depressed 13 % and 14 %, respectively. Multifocal tubular mineralization of the kidneys was noted in 70 % - 100 % of all groups of female rats administered 11-AMINOUNDECANOIC ACID. The severity of the mineralization was dose related. Transitional-cell hyperplasia was found in the kidneys of 1/10 males rats fed 21,000 ppm, in 6/10 females fed 21,000 ppm, and in 2/9 females fed 18,000 ppm 11-AMINOUNDECANOIC ACID. Hyperplasias of the renal pelvis were seen in 2/9 females fed 18,000 ppm and in 1/10 males and 6/10 females fed 21,000 ppm.
Deaths occurred in 2/10 male and 2/10 female mice administered 15,000 ppm, 4/10 males and 2/10 females receiving 18,000 ppm, and 3/10 males receiving 20,000 ppm. The cause of death of animals dying during the study was not determined. Mean body weight gain was depressed 20 % in male mice receiving 15,000 ppm, but only 10 % in male mice receiving 18,000 or 20,000 ppm. Mean body weight gain was depressed by more than 10 % in female mice fed diets containing 18,000 - 20,000 ppm 11-AMINOUNDECANOIC ACID. Focal mineralization of the kidney was noted in males that received 15,000 - 20,000 ppm and in females that received 15,000 - 18,000 ppm, particulary in those mice that died.
A no adverse effect level of 12,000 ppm in mice and 15,000 ppm in rats were established in that 90-day sub-chronic study (NTP, 1982; reliability 2).

11.06.2002

Memo : Genetic toxicity "in vitro"

Remark : 5.5
Conclusion : 11-AMINOUNDECANOIC ACID has no genotoxic potential in the reverse gene mutation assay in Salmonella typhimurium and

Escherichia coli, the chromosome aberrations test on CHO cells and the gene mutations test on L5178 Y tk+/tk- cells. A slight increase of SCE in CHO cells and transformation test of Syrian hamster embryo cells by adenovirus SA 7 have been observed. The overall interpretation of the results provided by that battery of short term test is that 11-AMINOUNDECANOIC ACID has no genotoxic potential.

Test system	Results	References	Reliab.
Salmonella Typhymurium TA100, TA1535, TA 1537, TA 98	Negative +/- S9	Mortelmans et al., 1986	2
Salmonella Typhymurium TA100, TA1535, TA1538 TA 1537, TA 98	Negative +/- S9	Ato-Chimie, 1982	2
Salmonella Typhymurium TA100, TA1535, TA1538 TA 1537, TA 98	Negative +/- S9	TORAY, 1982	2
Escherichia coli WP2 uvrA,	Negative +/- S9	TORAY, 1982	2
Gene mutation in L5178Y tk+/tk- Mouse Lymphoma cells	Negative +/- S9	Mc Gregor et al., 1988	2
Chromosome aberrations in CHO cells	Negative +/- S9	Galloway et al., 1987	2
Sister chromatid exchanges in CHO cells	ambiguous -S9 Negative +S9	Galloway et al., 1987	2
Transformation of Syrian hamster embryo cells by adenovirus SA7	Positive	Hatch et al., 1986	3

11.06.2002

Memo : Genetic toxicity "in vivo"

Remark : 5.6

Conclusion : 11-AMINOUNDECANOIC ACID has no genotoxic potential in the Drosophila recessive lethal test (Yoon et al., 1985; reliability 2), the in vivo/in vitro DNA-repair test on rat hepatocytes (Mirsalis et al., 1989; reliability 2) and the micronucleus test in mice (Shelby et al, 1993; reliability 2).

In a DNA-binding study with labelled 11-AMINOUNDECANOIC ACID, using male and female F-344 rats, organs liver, kidneys and urinary bladder have been examined both for association of radioactivity with DNA and for DNA alkylation (i.e., formation of altered radioactive nucleosides in DNA). There was minor incorporation of 11-AMINOUNDECANOIC ACID derived radioactivity into the physiological DNA nucleosides

(in liver higher than in kidneys, in males higher than in females). This could not be observed in DNA from urinary bladder, but from this organ only low amounts of DNA were isolated due to the limited mass of tissue available.
Upon chromatography (HPLC) of hydrolysates from DNA (isolated from livers and kidneys) no significant radioactive peaks were observed besides thoses of the physiological nucleosides; therefore, there was no indication of DNA alkylation by 11-AMINOUNDECANOIC ACID or a metabolite thereof. On this basis, this DNA-binding study was considered as being negative (Atochem, 1987; reliability 2).

11.06.2002

Memo : Carcinogenicity

Remark : 5.7

Conclusion : The carcinogenic potential of 11-aminoundecanoic acid has been evaluated in two cancer bioassays in rats and mice (NTP, 1982; reliability 2).

Rat study
Groups of 50 male and 50 female Fischer 344/N rats, six weeks of age, were fed a diet containing 7500 or 15000 mg/kg (ppm) 11-AMINOUNDECANOIC ACID for 104 weeks. An equal number of untreated rats served as controls. Survival was 78 % of control, 74 % of low-dose and 60 % of high-dose males and 76 % of control, 64 % of low-dose and 84 % of high-dose females. All surviving animals were killed at 109 weeks. A treatment-related increase in the incidence of transitional-cell carcinoma of the urinary bladder was observed in males only : in 0/48 control, 0/48 low-dose and 7/49 ($p < 0.01$) high-dose animals ; there were also 1/49 transitional-cell papilloma of the urinary bladder and 1/50 transitional-cell carcinoma of the kidney in the high-dose group. Dose-related transitional-cell hyperplasia of the urinary bladder and renal pelvis was observed in males and females. An increased incidence of calculi of the urinary bladder was seen in males in the high-dose group (1/48 (2 %) control, 1/48 (2 %) low-dose and 5/49 (10 %) high-dose animals) only in animals that did not develop a transitional-cell carcinoma. Two of 50 high-dose females had transitonal-cell carcinomas of the kidney, and no calculi were observed in these animals. Treatment-related neoplastic nodules of the liver were also observed in males : in 1/50 controls ; 9/50 ($p < 0.01$) low-dose and 8/50 ($p < 0.01$) high-dose animals ; in addition, 1/50 low-dose and 2/50 high-dose animals had hepato-cellular carninomas.

Mouse study
Groups of 50 male and 50 female B6C3F1 mice, six weeks of age, were fed a diet containing 7500 or 15000 mg/kg (ppm) 11-AMINOUNDECANOIC ACID for 103 weeks. An equal number of untreated mice served as controls. Survival was 74 % of control, 68 % of low-dose and 36 % of high-dose males, and 85 % of control, 76 % of low-dose and 51 % of high-dose females. All surviving animals were killed at 108-109 weeks. Increases in the incidence of malignant lymphomas occurred in male mice only : in 2/50 control, 9/50 ($p < 0.05$) low-dose, and 4/50 high-dose animals.

The overall interpretation of the results provided by a battery of short term genotoxicity test is that 11-AMINOUNDECANOIC ACID has no genotoxic potential. The carcinogenic effect observed in animals, involved only male rats treated with very high doses of 11-AMINOUNDECANOIC ACID, and no clear evidence were found in female rats and in male and female mice. Consequently, the excess of malignant tumours of the urinary tract found in male rats are believed to have occured through a non-genotoxic mechanism and to be associated with the non-neoplastic local tissue damages which were induced when the dose of 11-AMINOUNDECANOIC ACID reached a sufficiently high level. That interpretation is consistent with IARC evaluation. In 1985, IARC categorized 11-AMINOUNDECANOIC ACID as "non classifiable as to its carcinogenicity to humans" (Category 3), due to the limited evidence provided by the above data.

11.06.2002

Memo : Toxicity to reproduction

Remark : 5.8.1
Conclusion : There is no standard reproductive toxicity study available on 11-aminoundecanoic acid. Nevertheless, in well documented 13-week and 2-year toxicity studies (see sections 5.4 and 5.7), no histological alteration of the male and female reproductive organs was observed in F344 rats and B6C3F1 mice (NTP, 1982; reliability 2).

11.06.2002

Memo : Developmental toxicity/Teratogenicity

Remark : 5.8.2
Conclusion : 11-AMINOUNDECANOIC ACID was administered daily to pregnant Sprague-Dawley female rats by dietary admixture at the constant concentrations of 2000, 6000 and 18000 ppm from day 2 to day 19 post-coitum (equivalent to a daily intake of 172, 520 and 1394 mg/kg bw/day, respectively). It was well tolerated at 2000 and 6000 ppm. As a consequence of poor appetite, possibly due to the unpalatability of the dietary admixture at this concentration, lower food consumption and body weight gain were recorded at the high concentration of 18000 ppm.
Nevertheless, under the conditions of this study, the test substance did not produce embryo-toxicity nor feto-toxicity at any dose-level, with the exception of a slight retardation of growth/skeletal development at dose-levels of 6000 ppm and particularly 18000 ppm (dose-level at which a slight reduction in fetal body weight was also noted). Consequently, the No Adverse Effect Level for maternal toxicity and embryofetal development was established at 6000 ppm (i.e. 520 mg/kg/day) (Atofina, 2001; reliability 1).

11.06.2002

10.2 HAZARD SUMMARY

Memo : Human health

Conclusion : Acute toxicity

11-AMINOUNDECANOIC ACID is of very low acute oral (LD50 > 14700 mg/kg in rats) and dermal (LD0 > 2000 mg/kg in rats) toxicity.

Corrosiveness and irritation
11-AMINOUNDECANOIC ACID induced no skin irritation and only a slight transient eye irritation in rabbits.

Sensitization
11-AMINOUNDECANOIC ACID did not induce positive response in a skin sensitization assay in Guinea pigs performed according to the Magnusson and Kligman method.

Repeated dose toxicity
Very high concentrations (18000-20000 or 21000 ppm) of 11-AMINOUNDECANOIC ACID administered in diet during 13 weeks, have produced transitional-cell hyperplasia in the kidney and tubular mineralization in rats and focal mineralization of the kidney in mice. However concentrations as high as 12000 ppm in mice and 15000 in rats did not produce adverse effect.

Genetic toxicity "in vitro"
11-AMINOUNDECANOIC ACID has no genotoxic potential in the Ames test, the chromosome aberrations test on CHO cells and the gene mutations test on L5178Y cells. A slight increase of SCE in CHO cells and transformation test of Syrian hamster embryo cells by adenovirus SA 7 have been observed.

Genetix toxicity "in vivo"
11-AMINOUNDECANOIC ACID has no genotoxic potential in the Drosophila recessive lethal test, the in vivo/in vitro DNA-repair test on rat hepatocytes and the micronucleus test in mice. In addition, in a DNA-binding study with 11-AMINOUNDECANOIC ACID, using male and female F-344 rats, no indication of DNA alkylation was found in liver, kidneys or bladder.

The overall interpretation of the results provided by that battery of in vitro and in vivo short term test is that 11-AMINOUNDECANOIC ACID has no genotoxic potential.

Carcinogenicity
11-AMINOUNDECANOIC ACID was tested for carcinogenicity in mice and rats by administration in the diet at 7500 and 15000 ppm. Increased incidence of transitional-cell carcinomas of the urinary bladder and neoplastic nodules of the liver were observed in male rats. Transitional-cell carcinomas of the kidney and epithelial hyperplasia of the urinary bladder and renal pelvis were observed in male and female rats. No clear evidence for an increased incidence of treatment-related tumours was seen in mice. The carcinogenic effect observed in animals, involved only male rats treated with very high doses of 11-AMINOUNDECANOIC ACID, and no clear evidence were found in female rats and in male and female mice. Consequently, the excess of malignant tumours of the urinary tract found in male rats are believed to have occured through a non-genotoxic mechanism and to be associated with the non-neoplastic local tissue damages which were induced when the dose of 11-AMINOUNDECANOIC ACID reached a sufficiently high level.

Toxicity to reproduction
No histological alteration of the male and female reproductive organs was observed in 13-week and 2-year toxicity studies in F344 rats and B6C3F1 mice.

Developmental toxicity/Teratogenicity
11-AMINOUNDECANOIC ACID did not produce embryo-toxicity nor feto-toxicity up to the dose-level of 18000 ppm, with the exception of a slight retardation of growth/skeletal development at dose-levels of 6000 ppm and particularly 18000 ppm (dose-level at which a slight reduction in fetal body weight was also noted). The No Adverse Effect Level for maternal toxicity and embryofetal development was established at 6000 ppm (i.e. 520 mg/kg/day).

11.06.2002

10.3 RISK ASSESSMENT