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October 15, 1992

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Office of Pollution Prevention and Toxics
Environmental Protection Agency
401 M Street., S.W.
Washington, D.C. 20460
Attn: Section 8(e) Coordinator (CAP Agreement)

Dear Coordinator:

8ECAP-0025

On behalf of the Regulatee and pursuant to Unit II B.1.b. and Unit II C of the 6/28/91CAP Agreement, E.I. Du Pont de Nemours and Co. hereby submits (*in triplicate*) the attached studies. Submission of this information is voluntary and is occasioned by unilateral changes in EPA's standard as to what EPA now considers as reportable information. Regulatee's submission of information is made solely in response to the new EPA §8(e) reporting standards and is not an admission: (1) of TSCA violation or liability; (2) that Regulatee's activities with the study compounds reasonably support a conclusion of substantial health or environmental risk or (3) that the studies themselves reasonably support a conclusion of substantial health or environmental risk.

The "Reporting Guide" creates new TSCA 8(e) reporting criteria which were not previously announced by EPA in its 1978 Statement of Interpretation and Enforcement Policy, 43 Fed Reg 11110 (March 16, 1978). The "Reporting Guide states criteria which expands upon and conflicts with the 1978 Statement of Interpretation. Absent amendment of the Statement of Interpretation, the informal issuance of the "Reporting Guide" raises significant due processes issues and clouds the appropriate reporting standard by which regulated persons can assure TSCA Section 8(e) compliance.

For Regulatee,

Mark H. Christman
Counsel
Legal D-7158
1007 Market Street
Wilmington, DE 19898
(302) 774-6443

3/30/95

ATTACHMENT 1

Submission of information is made under the 6/28/91 CAP Agreement, Unit II. This submission is made voluntarily and is occasioned by recent changes in EPA's TSCA §8(e) reporting standard; such changes made, for the first time in 1991 and 1992 without prior notice and in violation of Regulatee's constitutional due process rights. Regulatee's submission of information under this changed standard is not a waiver of its due process rights; an admission of TSCA violation or liability, or an admission that Regulatee's activities with the study compounds reasonably support a conclusion of substantial risk to health or to the environment. Regulatee has historically relied in good faith upon the 1978 Statement of Interpretation and Enforcement Policy criteria for determining whether study information is reportable under TSCA §8(e), 43 Fed Reg 11110 (March 16, 1978). EPA has not, to date, amended this Statement of Interpretation.

After CAP registration, EPA provided the Regulatee the June 1, 1991 "TSCA Section 8(e) Reporting Guide". This "Guide" has been further amended by EPA, EPA letter, April 10, 1992. EPA has not indicated that the "Reporting Guide" or the April 1992 amendment supersedes the 1978 Statement of Interpretation. The "Reporting Guide" and April 1992 amendment substantively lowers the Statement of Interpretation 's TSCA §8(e) reporting standard[2]. This is particularly troublesome as the "Reporting Guide" states criteria, applied retroactively, which expands upon and conflicts with the Statement of Interpretation.[3] Absent amendment of the Statement of Interpretation, the informal issuance of the "Reporting Guide" and the April 1992 amendment clouds the appropriate standard by which regulated persons must assess information for purposes of TSCA §8(e).

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[2]In sharp contrast to the Agency's 1977 and 1978 actions to soliciting public comment on the proposed and final §8(e) Policy, EPA has unilaterally pronounced §8(e) substantive reporting criteria in the 1991 Section 8(e) Guide without public notice and comment. See 42 Fed Reg 45362 (9/9/77), "Notification of Substantial Risk under Section 8(e): Proposed Guidance".

[3]A comparison of the 1978 Statement of Interpretation and the 1992 "Reporting Guide" is a appended.

Throughout the CAP, EPA has mischaracterized the 1991 guidance as reflecting "longstanding" EPA policy concerning the standards by which toxicity information should be reviewed for purposes of §8(e) compliance. Regulatee recognizes that experience with the 1978 Statement of Interpretation may cause a review of its criteri. Regulatee supports and has no objection to the Agency's amending reporting criteria *provided that* such amendment is not applied to the regulated community in an unfair way. However, with the unilateral announcement of the CAP under the auspices of an OCM enforcement proceeding, EPA has wrought a terrific unfairness since much of the criteria EPA has espoused in the June 1991 Reporting Guide and in the Agency's April 2, 1992 amendment is new criteria which does not.exist in the 1978 Statement of Interpretation and Enforcement Policy.

The following examples of new criteria contained in the "Reporting Guide" that is not contained in the Statement of Interpretation follow:

o even though EPA expressly disclaims each "status report" as being preliminary evaluations that should not be regarded as final EPA policy or intent[4], the "Reporting Guide" gives the "status reports" great weight as "sound and adequate basis" from which to determine mandatory reporting obligations. ("Guide" at page 20).

o the "Reporting Guide" contains a matrix that establishes new numerical reporting "cutoff" concentrations for acute lethality information ("Guide" at p. 31). Neither this matrix nor the cutoff values therein are contained in the Statement of Interpretation. The regulated community was not made aware of these cutoff values prior to issuance of the "Reporting Guide" in June, 1991.

othe "Reporting Guide" states new specific definitional criteria with which the Agency, for the first time, defines as 'distinguishable neurotoxicological effects'; such criteria/guidance not expressed in the 1978 Statement of Interpretation.[5];

othe "Reporting Guide" provides new review/ reporting criteria for irritation and sensitization studies; such criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy.

othe "Reporting Guide" publicizes certain EPA Q/A criteria issued to the Monsanto Co. in 1989 which are not in the Statement of Interpretation; have never been published in the Federal Register or distributed by the EPA to the Regulatee. Such Q/A establishes new reporting criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy .

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[4]The 'status reports' address the significance, if any, of particular information reported to the Agency, rather than stating EPA's interpretation of §8(e) reporting criteria. In the infrequent instances in which the status reports contain discussion of reportability, the analysis is invariably quite limited, without substantial supporting scientific or legal rationale.

[5] *See, e.g,* 10/2/91 letter from Du Pont to EPA regarding the definition of 'serious and prolonged effects' as this term may relate to transient anesthetic effects observed at lethal levels; 10/1/91 letter from the American Petroleum Institute to EPA regarding clarification of the Reporting Guide criteria.

In discharging its responsibilities, an administrative agency must give the regulated community fair and adequate warning to as what constitutes noncompliance for which penalties may be assessed.

> Among the myriad applications of the due process clause is the fundamental principle that statutes and regulations which purport to govern conduct must give an adequate warning of what they command or forbid.... Even a regulation which governs purely economic or commercial activities, if its violation can engender penalties, must be so framed as to provide a constitutionally adequate warning to those whose activities are governed.

Diebold, Inc. v. Marshall, 585 F.2d 1327, 1335-36 (D.C. Cir. 1978). *See also*, Rollins Environemntal Services (NJ) Inc. v. U.S. Environmental Protection Agency, 937 F. 2d 649 (D.C. Cir. 1991).

While neither the are rules, This principle has been applied to hold that agency 'clarification', such as the Statement of Interpretation, the "Reporting Guide" nor the April 1992 amendments will not applied retroactively.

> ...a federal court will not retroactively apply an unforeseeable interpretation of an administrative regulation to the detriment of a regulated party on the theory that the post hoc interpretation asserted by the Agency is generally consistent with the policies underlying the Agency's regulatory program, when the semantic meaning of the regulations, as previously drafted and construed by the appropriate agency, does not support the interpretation which that agency urges upon the court.

Standard Oil Co. v. Federal Energy Administration, 453 F. Supp. 203, 240 (N.D. Ohio 1978), aff'd sub nom. Standard Oil Co. v. Department of Energy, 596 F.2d 1029 (Em. App. 1978):

The 1978 Statement of Interpretation does not provide adequate notice of, and indeed conflicts with, the Agency's current position at §8(e) requires reporting of all 'positive' toxicological findings without regard to an assessment of their relevance to human health. In accordance with the statute, EPA's 1978 Statement of Interpretation requires the regulated community to use scientific judgment to evaluate the significance of toxicological findings and to determining whether they reasonably support a conclusion of a substantial risk. Part V of the Statement of Interpretation urges persons to consider "the fact or probability" of an effect's occurrence. Similarly, the 1978 Statement of Interpretation stresses that an animal study is reportable only when "it contains reliable evidence ascribing the effect to the chemical." 43 Fed Reg. at 11112. Moreover, EPA's Statement of Interpretation defines the substantiality of risk as a function of both the seriousness of the effect and the probability of its occurrence. 43 Fed Reg 11110 (1978). Earlier Agency interpretation also emphasized the "substantial" nature of a §8(e) determination. See 42 Fed Reg 45362, 45363

(1977). [Section 8(e) findings require "extraordinary exposure to a chemical substance...which critically imperil human health or the environment"].

The recently issued "Reporting Guide" and April 1992 Amendment guidance requires reporting beyond and inconsistent with that required by the Statement of Interpretation. Given the statute and the Statement of Interpretation's explicit focus on substantial human or environmental risk, whether a substance poses a "substantial risk" of injury requires the application of scientific judgment to the available data on a case-by-case basis.

If an overall weight-of-evidence analysis indicates that this classification is unwarranted, reporting should be unnecessary under §8(e) because the available data will not "reasonably support the conclusion" that the chemical presents a substantial risk of serious adverse consequences to human health.

Neither the legislative history of §8(e) nor the plain meaning of the statute support EPA's recent lowering of the reporting threshold that TSCA §8(e) was intended to be a sweeping information gathering mechanism. In introducing the new version of the toxic substances legislation, Representative Eckhart included for the record discussion of the specific changes from the version of H. R. 10318 reported by the Consumer Protection and Finance Subcommittee in December 1975. One of these changes was to modify the standard for reporting under §8(e). The standard in the House version was changed from "causes or contributes to an unreasonable risk" to "causes or significantly contributes to a substantial risk". This particular change was one of several made in TSCA §8 to avoid placing an undue burden on the regulated community. The final changes to focus the scope of Section 8(e) were made in the version reported by the Conference Committee.

The word "substantial" means "considerable in importance, value, degree, amount or extent". Therefore, as generally understood, a "substantial risk" is one which will affect a considerable number of people or portion of the environment, will cause serious injury and is based on reasonably sound scientific analysis or data. Support for the interpretation can be found in a similar provision in the Consumer Product Safety Act. Section 15 of the CPSA defines a "substantial product hazard" to be:

> "a product defect which because of the pattern of defect, the number of defective products distributed in commerce, the severity of the risk, or otherwise, creates a substantial risk of injury to the public."

Similarly, EPA has interpreted the word 'substantial' as a quantitative measurement. Thus, a 'substantial risk' is a risk that can be quantified, *See,* 56 Fed Reg 32292, 32297 (7/15/91). Finally, since information pertinent to the exposure of humans or the environment to chemical substances or mixtures may be obtained by EPA through Sections 8(a) and 8(d) regardless of the degree of potential risk, §8(e) has specialized function. Consequently, information subject to §8(e) reporting should be of a type which would lead a reasonable man to conclude that some type action was required immediately to prevent injury to health or the environment.

Attachment

Comparison:

Reporting triggers found in the 1978 "Statement of Interpretation/ Enforcement Policy",43 Fed Reg 11110 (3/16/78) and the June 1991 *Section 8(e) Guide.*

TEST TYPE	1978 POLICY CRITERIA EXIST?	New 1991 GUIDE CRITERIA EXIST?
ACUTE LETHALITY		
Oral	N}	Y}
Dermal	N}	Y}
Inhalation (Vapors)	}[6]	}[7]
aerosol	N}	Y}
dusts/ particles	N}	Y}
SKIN IRRITATION	N	Y[8]
SKIN SENSITIZATION (ANIMALS)	N	Y[9]
EYE IRRITATION	N	Y[10]
SUBCHRONIC (ORAL/DERMAL/INHALATION)	N	Y[11]
REPRODUCTION STUDY	N	Y[12]
DEVELOPMENTAL TOX	Y[13]	Y[14]

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[6]43 Fed Reg at 11114, comment 14:

"This policy statements directs the reporitng of specifiec effects when unknown to the Administrator. Many routine tests are based on a knowledge of toxicity associated with a chemicalL unknown effects occurring during such a range test may have to be reported if they are those of concern tot he Agency and if the information meets the criteria set forth in Parts V and VII."

[7]Guide at pp.22, 29-31.

[8]Guide at pp-34-36.

[9]Guide at pp-34-36.

[10]Guide at pp-34-36.

[11]Guide at pp-22; 36-37.

[12]Guide at pp-22

[13]43 Fed Reg at 11112

"Birth Defects" listed.

[14]Guide at pp-22

NEUROTOXICITY	N	Y[15]
CARCINOGENICITY	Y[16]	Y[17]
MUTAGENICITY		
In Vitro	Y}[18]	Y} [19]
In Vivo	Y}	Y}
ENVIRONMENTAL		
Bioaccumulation	Y}	N
Bioconcentration	Y}[20]	N
Oct/water Part. Coeff.	Y}	N
Acute Fish	N	N
Acute Daphnia	N	N
Subchronic Fish	N	N
Subchronic Daphnia	N	N
Chronic Fish	N	N
AVIAN		
Acute	N	N
Reproductive	N	N
Reprodcutive	N	N

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[15] Guide at pp-23; 33-34.

[16] 43 Fed Reg at 11112
"Cancer" listed

[17] Guide at pp-21.

[18] 43 Fed Reg at 11112; 11115 at Comment 15
"Mutagenicity" listed/ *in vivo* vs *invitro* discussed; discussion of "Ames test".

[19] Guide at pp-23.

[20] 43 Fed Reg at 11112; 11115 at Comment 16.

CAS # 108-45-2
Chem: m-Phenylenediamine
Title: Toxicity of meta-phenylenediamine
Date: 7/27/56
Summary of Effects: Moderately toxic

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TOXICITY OF meta-PHENYLENEDIAMINE

Medical Research Project MR-312

Report No. 32-56

m-Phenylenediamine has been reported in the literature (1-4) to be moderately toxic on an acute basis and slightly less toxic than p-phenylenediamine. Von Oettingen (4) reported the Minimum Fatal Dose (MFD) by oral administration to cats and rabbits to be 300 mg/kg; by subcutaneous administration, the MFD was 200 mg/kg for rabbits, 80 mg/kg for rats, and 100 mg/kg for dogs.

The Organic Chemicals Department requested that Haskell Laboratory investigate this compound in order to determine the cumulative toxicity potential and to ascertain whether the chemical might be absorbed through the skin or cause a skin allergy. In the tests described below, acute and subacute oral toxicity have been studied using rats, acute skin absorption studies have been made with rabbits, and skin tests have been carried out with guinea pigs. The sample supplied by Jackson Laboratory was given Haskell No. 1532.

ACUTE ORAL TOXICITY

The Approximate Lethal Dose (ALD) of m-phenylenediamine for male albino rats was found to be 450 mg/kg of body weight when the material was administered by stomach tube as a 25 per cent suspension in peanut oil. Animals receiving lethal doses in the range 450 to 2250 mg/kg showed reduced activity and evidence of discomfort within 15 minutes after treatment. Within an hour, the urine was deep yellow in color and increased in volume. Dyspnea was also observed. Death usually occurred within 24 hours. Rats receiving sublethal doses in the range 130 to 300 mg/kg showed transient discomfort and reduced activity as well as failure to gain weight normally during the first week after treatment. They also voided abnormally yellow urine.

Gross and microscopic pathological examination of the animals which received lethal doses revealed pleural effusion, pulmonary congestion and edema, hemorrhagic areas in the squamous portion of the stomach, and marked disintegration of the kidney tubular epithelium. Animals receiving sublethal doses down to 130 mg/kg, when sacrificed on the ninth or tenth day after treatment, showed no pathology other than foci of nephrosis. Animals receiving doses below 130 mg/kg showed no pathological changes.

SUBACUTE ORAL TOXICITY

Each of six rats received by stomach tube 90 mg/kg (1/5 ALD) daily, five days a week, for a total of ten treatments. The material was given as a 3 per cent suspension in peanut oil. All survived. Slight decrease in activity and slight depression of growth rate were noted during the treatment

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period. Three rats were sacrificed four hours after the tenth treatment, and three were sacrificed ten days later. One of the rats sacrificed the day of the tenth treatment showed evidence of minimal nephrosis on micropathological examination. None of the others showed any recognizable pathologic changes.

SKIN ABSORPTION TOXICITY

A 40 per cent solution of m-phenylenediamine in 50 per cent aqueous ethanol was applied to the shaved skin of rabbits and the treated area was covered for 24 hours with moistureproof cellophane and gauze to prevent accidental ingestion. The doses of m-phenylenediamine were 1000, 1500, and 2250 mg/kg of body weight, and the Approximate Lethal Dose (ALD) proved to be 1500 mg/kg. Death occurred within 24 hours. The rabbit receiving the 1500 mg/kg dose was found to have pleural effusion and massive pulmonary edema. Bladder urine appeared black in color, but a test for blood in the urine was negative. The rabbit receiving 2250 mg/kg showed evidence of moderate postmortem change. Although the lungs were congested this animal did not show massive pulmonary edema or pleural effusion. The rabbit receiving the 1000 mg/kg dose was sacrificed the tenth day after treatment and showed no pathology attributable to the test chemical.

PRIMARY SKIN IRRITATION AND SENSITIZATION

Application of a 35 per cent aqueous solution of m-phenylenediamine to intact skin of male albino guinea pigs or of a 25 per cent aqueous solution to lightly abraded skin, produced no more than a mild erythema. Retesting of the skin following nine sensitizing treatments and a two-week rest period elicited intense erythematous reactions indicative of skin sensitization.

The guinea pigs, having been sensitized to m-phenylenediamine, also showed evidence of sensitization when challenged with o-phenylenediamine or p-phenylenediamine.

CONCLUSIONS

m-Phenylenediamine can be classified as moderately toxic on the basis of the Approximate Lethal Dose (ALD) of 450 mg/kg. Pleural effusion, pulmonary edema, irritation of the stomach, and nephrosis were the main pathologic findings.

The ten-day subacute oral test did not reveal marked cumulative toxicity. The possibility of secondary anemia as a result of chronic exposure (as with p-phenylenediamine) cannot be excluded since the experiments covered too brief a time span to decide this point.

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Like p-phenylenediamine, the meta-isomer can be absorbed through the skin and produce systemic effects. meta-Phenylenediamine also resembles the para-isomer in being a potent skin sensitizer.

HASKELL LABORATORY FOR TOXICOLOGY
AND INDUSTRIAL MEDICINE

Report by: John A. Zapp, Jr.
Director

JAZ:ecd
Report No. 32-56
7/27/56

Triage of 8(e) Submissions

Date sent to triage: 2/5/96

NON-CAP CAP

Submission number: 12326A

TSCA Inventory: Y N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX SBTOX SEN w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX	CTOX	EPI	RTOX	GTOX
STOX/ONCO	CTOX/ONCO	IMMUNO	CYTO	NEUR

Other (FATE, EXPO, MET, etc.): _____

Notes:

THIS IS THE ORIGINAL 8(e) SUBMISSION; PLEASE REFILE AFTER TRIAGE DATABASE ENTRY

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[illegible] DATE: [illegible] OTS DATE: 10/27/92 CSRAD DATE: 02/20/93

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0001 NO FAX REQUESTED
0002 INFO REQUESTED (TSCA)
0003 INFO REQUESTED (VOL. ACTIONS)
0004 INFO REQUESTED (REPORTING RATIONALE)
[illegible]
0006 REFER TO CHEMICAL SCREENING
0008 CAP NOTICE

VOLUNTARY ACTIONS
0001 NO ACTION REPORTED
0002 STUDIES PLANNED/IN PROGRESS
0003 NOTIFICATION OF WORKER [illegible]
0004 LABELING CHANGES
0005 PROCESS/HANDLING CHANGES
0006 APPLICATION DISCONTINUED
0007 PRODUCTION DISCONTINUED
0008 CONFIDENTIAL

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CHEMICAL NAME

CAS#
103-95-2

INFORMATION TYPE	P F C	INFORMATION TYPE	P F C	INFORMATION TYPE	P F C	INFORMATION TYPE	P F C
ONCO (HUMAN)	01 02 04	0016 EPIDEM	01 02 04			0041 BIOSURV (ANIMAL)	01 02 04
ONCO (ANIMAL)	01 02 04	0017 HUMAN EXPOS (FOOD CONTAM)	01 02 04			0042 BIOSURV (HUMAN)	01 02 04
CELL TRANS (IN VITRO)	01 02 04	0018 HUMAN EXPOS (ACCIDENTAL)	01 02 04			0043 CHEM/PHYS PROP	01 02 04
MUTA (IN VITRO)	01 02 04	0019 HUMAN EXPOS (MONITORING)	01 02 04			0044 CLASTO (IN VITRO)	01 02 04
MUTA (IN VIVO)	01 02 04	0020 DOSIMETRY	01 02 04			0045 CLASTO (ANIMAL)	01 02 04
REPROTOXICITY (HUMAN)	01 02 04	0021 ETHYLOXOTHYLATE	01 02 04			0046 CLASTO (HUMAN)	01 02 04
REPROTOXICITY (ANIMAL)	01 02 04	0022 SOLVENT/PRODUCT CONTAM	01 02 04			0047 DNA DAMAGE/REPAIR	01 02 04
NEURO (HUMAN)	01 02 04	0023 REPORTING DELAY	01 02 04			0048 PROD USE/PROC	01 02 04
NEURO (ANIMAL)	01 02 04	0024 PROD COMPOSITION ID	01 02 04			0051 MSDS	01 02 04
ACUTE TOX. (HUMAN)	01 02 04	0025 REPORTING RATIONALE	01 02 04			0099 OTHER	01 02 04
GEN. TOX. (HUMAN)	01 02 04	0026 CONFIDENTIAL	01 02 04				
ACUTE TOX. (ANIMAL)	01 02 04	0027 ADDRO (HUMAN)	01 02 04				
SUB ACUTE TOX (ANIMAL)	01 02 04	0028 ADDRO (ANIMAL)	01 02 04				
SUB CHRONIC TOX (ANIMAL)	01 02 04	0029 METABPHARMACO (ANIMAL)	01 02 04				
0015 CHRONIC TOX (ANIMAL)	01 02 04	0030 METABPHARMACO (HUMAN)	01 02 04				

[illegible]	TOX CHI INVENTORY	[illegible] REVIEW	SPECIES	TOXICOLOGICAL CONCERNS	USE:	PRODUCTION:
	YES	YES (DROP/REFER)	RBT	LOW Dermal Irritation, Subacute Oral Toxicity		
CAS SR	NO	NO (CONTINUE)	RAT	MED Acute Oral Toxicity, Acute Dermal Toxicity		
	IN TI AMIN	REFER	DOG	HIGH Dermal Sensitization		
			GP			

[illegible] ID

#12326A
H

Dermal sensitization is of high concern based on intense erythematous reactions in guinea pigs.

M

Acute oral toxicity is of medium concern based on an approximate lethal dose of 450 mg/kg in male rats. Animals receiving lethal doses in the range of 450-2250 mg/kg, and in sublethal doses in the range of 130-300 mg/kg, showed clinical signs of hypoactivity and discomfort. Necropsy revealed abnormalities in the lungs, stomach and kidneys in the decedents, and foci of nephrosis in survivors at doses ≥130 mg/kg.

M

Acute dermal toxicity is of medium concern based on an approximate lethal dose of 1500 mg/kg in rabbits. Mortality and corresponding doses were 0/1 (1000) and 1/1 (1500, 2250). Pleural effusion, massive pulmonary edema, and black urine in the bladder were observed at 1500 mg/kg.

L

Dermal irritation is of low concern based on mild erythema in guinea pigs.

L

Subacute oral toxicity is of low concern based on no mortality (0/6) in rats exposed by gavage to 90 mg/kg daily, 5 days/week for 2 weeks. Clinical signs included hypoactivity and slight depression of growth rate. Minimal nephrosis was observed in 1/6 at necropsy.