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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:

SECAP-0025

On behalf of the Regulatee and pursuant to Unit II B.1.b. and Unit II C of the 6/28/91 CAP 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,

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Counsel
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Wilmington, DE 19898
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3/29/95

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 standard². 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).

²In 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".

³A comparison of the 1978 Statement of Interpretation and the 1992 "Reporting Guide" is 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 criteria. 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 intent⁴, 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.
- o the "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;
- o the "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.
- o the "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 .

⁴The '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 Environmental 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*.

<u>TEST TYPE</u>	<u>1978 POLICY CRITERIA EXIST?</u>	<u>New 1991 GUIDE CRITERIA EXIST?</u>
ACUTE LETHALITY		
Oral	N}	Y}
Dermal	N}	Y}
Inhalation (Vapors)	N} ⁶	Y} 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

⁶43 Fed Reg at 11114, comment 14:

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

⁷Guide at pp.22, 29-31.

⁸Guide at pp-34-36.

⁹Guide at pp-34-36.

¹⁰Guide at pp-34-36.

¹¹Guide at pp-22; 36-37.

¹²Guide at pp-22

¹³43 Fed Reg at 11112

"Birth Defects" listed.

¹⁴Guide at pp-22

NEUROTOXICITY	N	Y ¹⁵
CARCINOGENICITY	Y ¹⁶	Y ¹⁷
MUTAGENICITY		
<i>In Vitro</i>	Y ¹⁸	Y ¹⁹
<i>In Vivo</i>	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
Reproductive	N	N

¹⁵Guide at pp-23; 33-34.

¹⁶43 Fed Reg at 11112
"Cancer" listed

¹⁷Guide at pp-21.

¹⁸43 Fed Reg at 11112; 11115 at Comment 15

"Mutagenicity" listed/ *in vivo* vs *in vitro* discussed; discussion of "Ames test".

¹⁹Guide at pp-23.

²⁰43 Fed Reg at 11112; 11115 at Comment 16.

CAS# 91-15-6

CHEM: Phthalonitrile

TITLE: The toxicity of phthalonitrile

DATE: 12/12/56

SUMMARY OF EFFECTS: Muscle tremors, convulsions at high doses

8-39

THE TOXICITY OF PHTHALONITRILE

A. J. Fleming, M.D., and F. M. Mitchell

Preliminary tests have been carried out on rats as a rough means of comparing the effects of the compound by oral and skin absorption. A few tests were also made on animals exposed to the substance through inhalation.

Oral Treatments

Forty-nine rats were given single oral doses of a suspension of phthalonitrile in agar, the dosage ranging from 45 to 305 mg/kg. The effect of varying dosage is indicated in the following table:

<u>Dosage range mg/kg</u>	<u>No. of animals in group</u>	<u>No. showing convulsions*</u>	<u>No. died</u>	<u>Time until death</u>	<u>Mortality</u>
40-59	4	2	0		0
110-119	5	1	0		0
120-139	5	3	2	2-1/2 - 4 hours	40%
140-159	5	2	1	5 hours	20%
160-179	3	3	0		0
180-199	8	7	4	3 - 24 hours	50%
200-219	5	3	2	4-1/2 - 7 hours	40%
220-239	5	1	4	4 - 72 hours	80%
240-259	6	2	6	18 or less	100%
260-309	3	0	3	18 or less	100%

* These animals were observed during the daytime only and many of the animals dying at night showed post-mortem evidence of having had convulsions prior to death.

Shortly after oral treatment the animals showed signs of irritation and discomfort. They became restless and the fur was ruffled. Some became weak and unable to stand. With the higher doses muscle tremors, cyanosis and convulsions developed sometimes as early as forty minutes after treatment. At first the convulsions lasted for a few seconds, but became progressively more severe and were of two to three minutes' duration just before death.

An interesting post-mortem finding was the rapidity with which rigor mortis developed, the animals becoming perfectly rigid within one minute after death. The findings at gross autopsy were multiple hemorrhages in the lungs, marked distention of the stomach with food, gas, and a great deal of frothy mucus. The mucosa was smooth and edematous.

The rats that survived the single oral treatment were killed with illuminating gas within seven to sixteen days following treatment and did not exhibit any significant pathology at gross autopsy except the signs of old hemorrhages in the lungs.

Repeated Oral Treatments

Four rats were given daily oral treatments of phthalonitrile in agar, the dosage ranging from 40 to 50 mg/kg. One animal had two convulsions after the first treatment and one after the fourth, fifth and sixth treatments. It died during the night after the sixth treatment. Another animal had a convulsion after the fifth treatment but survived up to thirteen treatments when it was killed for autopsy. The remaining two animals did not have convulsions. One died after the sixth treatment and the other after the thirteenth treatment. This group at autopsy showed the same gross pathology as the single oral treatment animals.

A second group of five rats was given repeated oral treatments of phthalonitrile in agar, the doses ranging from 110-119 mg/kg. Two rats had convulsions and died after the fourth treatment, a third died after the sixth treatment and the remaining two died after the seventh treatment. The pathology in the lung and stomach was the same as in the single oral treatment group and in addition one rat showed multiple pin point hemorrhages in the stomach.

Skin Treatments

A group of ten rats was given daily skin applications of 1 cc of a 5% suspension of phthalonitrile in agar. Care was taken to prevent the animals from ingesting the material. There were no signs of acute toxicity up to nine treatments and five of the animals were killed at this time for autopsy. No gross pathology was noted and there were no skin changes at the site of application.

The remaining five animals began to lose weight and were killed after the thirteenth treatment. In two of the five there were signs of old hemorrhages in the lungs. Fairly marked pitting of the liver was present in three animals and a fourth showed extensive mottling of the liver. There was no sign of injury to the skin at the site of application.

Another group of six rats was given daily skin applications of 1 cc of a 5% suspension of phthalonitrile in olive oil. These animals lost 9% of their initial weight in the first five days of treatment and were still losing weight after ten treatments. No significant pathology was noted except for a slight pitting of the livers of two animals and a slight mottling in the liver of a third. There were no signs of injury to the skin.

Inhalation of Phthalonitrile

Phthalonitrile was heated to the fusion point in a closed container and air passed over the substance at a rate of six liters per minute into a bell jar in which two rats were placed. The rats were left in the bell jar for one hour on two successive days. Inhalation of the phthalonitrile gave rise to irritation of the nose and eyes and the animals attempted to keep the vapor off their fur. They appeared sleepy in from ten to thirty minutes but did not become narcotized or comatose. At the end of forty minutes a slight cyanosis was noted. Both animals were killed after the second treatment and showed small hemorrhages in the lungs. No other gross pathology was noted.

Summary and Conclusions

Phthalonitrile when given orally to rats produces gastric irritation, muscle tremors, convulsions and death. Doses of 120-139 mg/kg produced death.

in from two and one-half hours to three days after a single treatment. Single doses of about 200 mg/kg produced death in 80% of the animals. Repeated oral treatments of doses as low as 40-59 mg/kg produced convulsions and death in two out of four animals.

No deaths resulted in animals treated with skin applications of phthalonitrile but when applied in olive oil the substance upsets the metabolism of the animals enough to interfere with nutrition and possibly to damage such tissues as the liver. The substance appears to be less toxic when applied in an agar suspension than in an olive oil suspension.

Phthalonitrile vapors are irritating to the eyes and mucous membranes and if inhaled in sufficient quantity may give rise to small hemorrhages in the lungs.

While it appears that the hazard from phthalonitrile is much less pronounced with skin exposure than by ingestion, it is evident that workmen exposed to this compound should be under close medical supervision, particularly for signs of pulmonary and gastrointestinal upsets and for changes in the circulation indicative of upsets in the physiological balance of the circulation.

S/Florence M. Mitchell

S/ Allan J. Fleming, M.D.

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12-12-56

Triage of 8(e) Submissions

Date sent to triage: 2/5/96

NON-CAP

Submission number: 12329A

TSCA Inventory: Y N D

CAP
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.): _____

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CHEMICAL TRACKING DATABASE ENTRY FORM

REPORTS DATA
 NUMBER # 1111 SEQ. # 1

TYPE (INT/SUPP/FLWP)

SUBMITTER NAME ...

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NO. DATE: ... OTH DATE: ...

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REPORTING RATIONALE: FLWP DATA
 0101 NO ACTION REQUESTED
 0102 INFO REQUESTED (TOXIC)
 0103 INFO REQUESTED (VOL. ACTIONS)
 0104 INFO REQUESTED (REPORTING RATIONALE)
 0105 INFO
 0106 REFER TO CHEMICAL SCREENING
 0107 CAP NOTICE

EXEMPTION ACTIONS
 0401 NO ACTION REPORTED
 0402 STUDIES PLANNED/IN PROGRESS
 0403 NOTIFICATION OF WORKER RIGHTS
 0404 LABELING/STORAGE CHANGES
 0405 PROCESS/PLANTING CHANGES
 0406 APPRAISE DISCONTINUED
 0407 PRODUCTION DISCONTINUED
 0408 CONFIDENTIAL

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CASE
91-15-6

INFORMATION TYPE	P.F.C.	INFORMATION TYPE	P.F.C.	INFORMATION TYPE	P.F.C.
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0102	01 02 04	0217	01 02 04	0242	01 02 04
0103	01 02 04	0218	01 02 04	0243	01 02 04
0104	01 02 04	0219	01 02 04	0244	01 02 04
0105	01 02 04	0220	01 02 04	0245	01 02 04
0106	01 02 04	0221	01 02 04	0246	01 02 04
0107	01 02 04	0222	01 02 04	0247	01 02 04
0108	01 02 04	0223	01 02 04	0248	01 02 04
0109	01 02 04	0224	01 02 04	0249	01 02 04
0110	01 02 04	0225	01 02 04	0250	01 02 04
0111	01 02 04	0226	01 02 04	0251	01 02 04
0112	01 02 04	0227	01 02 04	0252	01 02 04
0113	01 02 04	0228	01 02 04	0253	01 02 04
0114	01 02 04	0229	01 02 04	0254	01 02 04
0115	01 02 04	0230	01 02 04	0255	01 02 04
		0231	01 02 04	0256	01 02 04
		0232	01 02 04	0257	01 02 04
		0233	01 02 04	0258	01 02 04
		0234	01 02 04	0259	01 02 04
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		0236	01 02 04		
		0237	01 02 04		
		0238	01 02 04		
		0239	01 02 04		
		0240	01 02 04		

YES CAS SR NO
 YES (DROU/REFER) NO (CONTINUE)
 REF-R

SPECIES: RAT

TOXICOLOGICAL CONCERN:
 (LOW) Subacute Dermal Toxicity, Subacute Inhalation Toxicity
 (MED) Acute Oral Toxicity
 (HIGH) Subacute Oral Toxicity

USE: ... PRODUCTION: ...

#12329A

H

Subacute oral toxicity is of high concern based on 2/4 deaths in rats repeatedly exposed to doses ranging from 40-59 mg/kg for 6 or 13 treatments. Convulsions were observed in 2/4. Mortality (5/5) and convulsions (2/5) were observed in rats repeatedly exposed to doses ranging from 110-119 mg/kg for 4, 6 or 7 treatments. Autopsy revealed hemorrhagic lungs and gastric abnormalities for both dose ranges.

M

Acute oral toxicity is of medium concern based on the following mortality data in rats exposed to dose ranges in mg/kg: 0/4 (40-59), 0/5 (110-119), 2/5 (120-139 and 200-219), 1/5 (140-159), 0/3 (160-179), 4/8 (180-199), 4/5 (220-239), 6/6 (240-259) and 3/3 (260-309). Clinical signs included irritation, discomfort, weak and unable to stand, tremors, cyanosis and convulsions. Hemorrhagic lungs and gastric abnormalities were noted at autopsy.

L

Subacute dermal toxicity is of low concern based on no signs of toxicity or gross pathology in 5 rats exposed to a 5% suspension in agar for 9 treatments. Daily exposure to the same suspension for 13 treatments resulted in hemorrhagic lungs in 2/5 rats, liver pitting in 3/5, and liver mottling in 1/5. Daily exposure to a 5% suspension in olive oil in rats for 10 treatments resulted in weight loss, and slight pitting (2/6) and mottling (1/6) in the liver.

L

Subacute inhalation toxicity is of low concern based on no mortality in 2 rats exposed for 1 hour on 2 successive days (exposure concentration not reported). Clinical signs included irritation, sleepiness and slight cyanosis. Small hemorrhages in the lungs were noted at sacrifice.