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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

RECEIVED
2/17/95

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]

---

[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 #115-25-3; 75-68-3; 75-71-8; 76-14-2; 75-69-4
Chem: Octafluorocyclobutane (Freon C-318); 1-chloro-1,1-difluoroethane (fluorocarbon 142b); dichlorodifluoromethane (Freon 12); 1,2-dichlorotetrafluoroethane (Freon 114); trichlorofluoromethane (Freon 11)
Title: Cardiac sensitization - Fright Exposures
Date: 2/20/70
Summary of Effects: Severe convulsions; generalized clonic, tonic seizures

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Copies to: T. D. Johnson, Jr.
R. M. Glover
C. L. Gray, Jr.
C. W. Maynard
D. E. Kvalnes
R. C. Downing
T. D. Armstrong, Jr.
J. H. James

E. I. du Pont de Nemours and Company
Haskell Laboratory for Toxicology and Industrial Medicine

HASKELL LABORATORY REPORT NO. 81-70 MR NO. 1262-CC1

Materials Tested:	Haskell Nos.:
Octafluorocyclobutane (Freon® C-318)	5501
1-chloro-1,1-difluoroethane (fluorocarbon 142b)	6163
Dichlorodifluoromethane (Freon® 12)	5450-4
1,2-dichlorotetrafluoroethane (Freon® 114)	5798-2
Trichlorofluoromethane (Freon® 11)	6404-2

Materials Submitted by: T. D. Armstrong, Jr., Freon® Products Laboratory, Organic Chemicals Department, Chestnut Run

CARDIAC SENSITIZATION - FRIGHT EXPOSURES

Purpose:

This experiment was performed to determine whether some of the fluorocarbon compounds previously tested and found to sensitize the beagle dog heart to the effect of intravenously injected adrenalin chloride (see Haskell Lab. Report Nos. 14-69, 52-69, 354-69) would produce a similar effect on the heart if a dog's own circulating level of epinephrine were raised sufficiently. The compounds tested were some of those which have been involved in aerosol sniffing deaths. The conditions of the experiment (simultaneous fright and inhalation of a high level of compound for a short period of time) simulate what actually happens in aerosol sniffing.

Procedure:

The equipment used to expose the dogs has been previously described in Haskell Laboratory Report No. 14-69. The experimental procedure was the one described in that report modified as outlined here. No epinephrine was administered exogenously. After a one-and-a-half minute control electrocardiogram was taken, an amplified sound effect tape recording (sirens, gongs, animal roars, etc.) was played in order to frighten the dogs and stimulate the release of endogenous epinephrine while they were simultaneously inhaling an 80 per cent compound/20 per cent oxygen mixture. This exposure period lasted 30 seconds and was followed by a 2 minute recovery period. Continuous electrocardiograms were taken throughout the experiment. The number of abnormal beats before, during and after exposure were recorded.

This procedure was decided upon because after preliminary testing it was found that the sound effect tape recording produced more fright than did other trial methods of frightening the dogs; an exposure time of 30 seconds was decided upon

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because in those compounds which affected the central nervous system (i.e., fluorocarbon 142b) a longer exposure was not tolerated.

With the exception of Freon® 11, all of the compounds studied were in the vapor or gaseous phase at normal ambient temperature and pressure and therefore, were stored in pressure cylinders. The desired concentrations (calculated) were achieved by delivering a metered volume of gas from the cylinder into a metered volume of pure oxygen vapor in an 80 to 20 per cent by volume ratio. Freon® 11, a liquid at temperatures below 75°F, was vaporized from a heated one liter cylinder and delivered to the flow meter. Oxygen was then added as above. During the Freon® 11 experiments the room temperature was maintained at 85° F to guard against condensation of the Freon® in the generation system tubing. All metal tubing was wrapped with heating tape for the same reason. The flow meters used for delivering the flow of the test compounds and the oxygen had been calibrated using a dry gas test meter. The concentration of oxygen was monitored throughout the experiment using a Beckman oxygen analyzer. It was found that the fluorocarbons exerted a slightly negative effect (<2%) on the oxygen reading. Thus, a reading of 18 or 19 per cent oxygen on the Beckman analyzer during the exposure period corresponded to an actual oxygen concentration of 20 per cent and a fluorocarbon concentration of 80 per cent.

Results and Conclusions:

Preliminary testing was done on Freon® C-318 to develop a test procedure. The results of these tests are given in Table I. All other compounds were administered as described above and the results of these exposures are given in Table II. The number of animals that had "marked" cardiac responses (cardiac arrythmias which are considered to pose a serious threat to life) and the number that had convulsions are reported. Fluorocarbon 142b was the most potent compound tested, resulting in 41.7 per cent marked responses; Freon® 12 resulted in none. With Freon® 11 there were two cases of questionable marked responses and one with Freon® 114. These questionable marked responses were not the classical multiple consecutive ventricular beats usually seen, but consisted mainly of a bigeminal rhythm with some areas highly suggestive of multiple ventricular beats. A marked tachycardia (300-350 beats per minute) was frequently observed with exposure to Freon® 12 and Freon® 114.

Because there was a high percentage of marked responses with fluorocarbon 142b, the effect of the compound without noise was tested. Without the noise, fewer marked responses were found and the convulsions were not as severe as those seen with the compound and noise together.

The convulsions observed with fluorocarbon 142b and Freon® 12 were severe, generalized clonic, tonic seizures, occasionally associated with fecal and urinary incontinence. Those seen with Freon® 114 were mild and characterized by spasticity of the extremities. Although Freon® 11 did not result in convulsions, the dogs did not tolerate the compound and struggled violently.

Whether the loud noise by itself resulted in sufficient endogenous epinephrine to produce cardiac sensitization is questionable. It is probable that the convulsions and struggling which occurred at these high concentrations also resulted in an

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Results and Conclusions: (Cont'd.)

increase in the level of endogenous epinephrine. Thus, it is felt that most likely a combination of these factors was involved and that the noise increased the severity of the struggling and convulsions. This reasoning is supported by the finding that the number and severity of the convulsions seen with fluorocarbon 142b and noise together were greater than those with either noise or compound alone.

Report by: Linda S. Mullin
Linda S. Mullin

Approved by: John W. Zapp, Jr.
John W. Zapp, Jr.
Director

LSM/jtd

Date: February 20, 1970

Report No. 21-70

N.B.: 4-67:52, 42, 96, 118-119, 114-116, 106-107, 5-69:76-94

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TABLE II

RESULTS OF FRIGHT EXPOSURES

80% Compound/20% Oxygen For 30 Seconds With Noise

Compound	Number of Dog Exposures	Number of Marked Responses	Per Cent Marked Responses	Number of Convulsions	Per Cent Convulsions	Comments
None - Noise Control	6	0	0	0	0	
Fluorocarbon 142b	12	5	41.7	9	75.0	
Fluorocarbon 142b without noise	12	1	8.3	5	41.7	
Freon® 12	12	0	0	9	75.0	
Freon® 114	12	1[a]	8.3	5	41.7	
Freon® 11	12	2[a]	16.7	0	0	Compound not well tolerated

a - Bigeminal rhythm with some areas suggestive of multiple ventricular beats.

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TABLE I

RESULTS OF PRELIMINARY FRIGHT EXPOSURES

Fluorocarbon C-318 - 80% Compound/20% oxygen Mixture

Duration of Exposure (min.)	Duration of Fright[a] (min.)	Type of Fright	Number of Dog Exposures	Number of Marked Responses	Per Cent Marked Responses	Comments
1	Approx. 0.1	Cymbals	2	0	0	
3	Approx. 0.1	Cymbals	1	0	0	
5	Approx. 0.1	Cymbals	1	0	0	
3	1.0	Noise Tape	3	0	0	
3	0.5	Gun Shots	3	0	0	
3.5	1.5	Noise Tape	6	1	16.7	
3.5	None	None	6	1	16.7	Dog that showed marked responses also had convulsion.
2.5	0.5	Electric Shock	4	0	0	

[a]Duration of fright was calculated to end at same time the exposure ended.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

Mark H. Christman
Counsel
E. I. Du Pont De Nemours and Company
Legal D-7010-1
1007 Market Street
Wilmington, Delaware 19898

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

APR 18 1995

EPA acknowledges the receipt of information submitted by your organization under Section 8(e) of the Toxic Substances Control Act (TSCA). For your reference, copies of the first page(s) of your submission(s) are enclosed and display the TSCA §8(e) Document Control Number (e.g., 8EHQ-00-0000) assigned by EPA to your submission(s). Please cite the assigned 8(e) number when submitting follow-up or supplemental information and refer to the reverse side of this page for "EPA Information Requests".

All TSCA 8(e) submissions are placed in the public files unless confidentiality is claimed according to the procedures outlined in Part X of EPA's TSCA §8(e) policy statement (43 FR 11110, March 16, 1978). Confidential submissions received pursuant to the TSCA §8(e) Compliance Audit Program (CAP) should already contain information supporting confidentiality claims. This information is required and should be submitted if not done so previously. To substantiate claims, submit responses to the questions in the enclosure "Support Information for Confidentiality Claims". This same enclosure is used to support confidentiality claims for non-CAP submissions.

Please address any further correspondence with the Agency related to this TSCA 8(e) submission to:

Document Processing Center (7407)
Attn: TSCA Section 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
Washington, D.C. 20460-0001

EPA looks forward to continued cooperation with your organization in its ongoing efforts to evaluate and manage potential risks posed by chemicals to health and the environment.

Sincerely,

Terry R. O'Bryan

Terry R. O'Bryan
Risk Analysis Branch

Enclosure 12405A

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Triage of 8(e) Submissions

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NON-CAP (CAP)

Submission number: 12405A

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

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STOX CTOX EPI RTOX GTOX

STOX/ONCO CTOX/ONCO IMMUNO CYTO NEUR

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

Notes:

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CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:
Submission # 8EHQ- 1092 -12405 SEQ. A

TYPE: (INT) SUPP FLWP

SUBMITTER NAME: E. I. Du ont de Nemours and Company

SUB. DATE: 10/15/92 OTS DATE: 10/27/92 CSRAD DATE: 02/17/95

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
(0639) REFER TO CHEMICAL SCREENING
(0678) CAP NOTICE

VOLUNTARY ACTIONS:
(0401) NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKERS/USERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP/USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

CHEMICAL NAME:	CAS#
Freon C-318	115-25-3
Fluorocarbon 1426	75-68-3
Freon 12	75-71-8
Freon 114	76-14-2
Freon 11	75-69-4

INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04
0202	ONCO (ANIMAL)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04
0204	MUTA (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04
0208	NEURO (HUMAN)	01 02 04
(0209)	NEURO (ANIMAL)	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04
0212	ACUTE TOX. (ANIMAL)	01 02 04
0213	SUB ACUTE TOX (ANIMAL)	01 02 04
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04
0215	CHRONIC TOX (ANIMAL)	01 02 04

INFORMATION TYPE:		P F C
0216	EPI/CLIN	01 02 04
0217	HUMAN EXPOS (PROD CONTAM)	01 02 04
0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04
0219	HUMAN EXPOS (MONITORING)	01 02 04
0220	ECO/AQUA TOX	01 02 04
0221	ENV. OCCC/REL/FATE	01 02 04
0222	EMER INCI OF ENV CONTAM	01 02 04
0223	RESPONSE REQEST DELAY	01 02 04
(0224)	PROD/COMP/CHEM ID	01 02 04
0225	REPORTING RATIONALE	01 02 04
0226	CONFIDENTIAL	01 02 04
0227	ALLERG (HUMAN)	01 02 04
(0228)	ALLERG (ANIMAL)	01 02 04
0239	METAB/PHARMACO (ANIMAL)	01 02 04
0240	METAB/PHARMACO (HUMAN)	01 02 04

INFORMATION TYPE:		P F C
0241	IMMUNO (ANIMAL)	01 02 04
0242	IMMUNO (HUMAN)	01 02 04
(0243)	CHEM/PHYS PROP	01 02 04
0244	CLASTO (IN VITRO)	01 02 04
0245	CLASTO (ANIMAL)	01 02 04
0246	CLASTO (HUMAN)	01 02 04
0247	DNA DAM/REPAIR	01 02 04
0248	PROD/USE/PROC	01 02 04
0251	MSDS	01 02 04
0299	OTHER	01 02 04

TRIAGE DATA:

NON-CBI INVENTORY	ONGOING REVIEW	SPECIES	TOXICOLOGICAL CONCERN:	USE:	PRODUCTION:
(YES)	YES (DROP/REFER)	DOG	(LOW)		
CAS SR NO	NO (CONTINUE)		MED		
IN TERMINI	REFER		HIGH		

COMMENTS

8(E)-12405A

L/L/L/L/L

FREON C-318: INHALATION CARDIAC SENSITIZATION IN BEAGLE DOGS IS OF LOW CONCERN. DOGS WERE EXPOSED TO A FRIGHT STIMULUS (AN AMPLIFIED SOUND EFFECT OR AN ELECTRIC SHOCK) TO STIMULATE THE RELEASE OF ENDOGENOUS EPINEPHRINE WHILE THEY WERE SIMULTANEOUSLY INHALING AN 80% TEST SUBSTANCE/20% OXYGEN ATMOSPHERE. A 1-MINUTE EXPOSURE AND 0.1 MINUTE OF FRIGHT STIMULUS (CYMBALS) RESULTED IN 0/2 MARKED CARDIAC ARRHYTHMIAS; A 3-MINUTE EXPOSURE WITH 0.1 MINUTE OF FRIGHT STIMULUS (CYMBALS) RESULTED IN 0/1 RESPONSES; A 5-MINUTE EXPOSURE AND 0.1 MINUTE OF FRIGHT STIMULUS (CYMBALS) RESULTED IN 0/1 RESPONSES; A 3-MINUTE EXPOSURE AND 1 MINUTE OF FRIGHT STIMULUS (NOISE TAPE) RESULTED IN 0/3 RESPONSES; A 3-MINUTE EXPOSURE AND 0.5 MINUTE OF FRIGHT STIMULUS (GUN SHOTS) RESULTED IN 0/3 RESPONSES; A 3.5-MINUTE EXPOSURE WITH NO FRIGHT STIMULUS RESULTED IN 1/6 RESPONSES WITH CONVULSIONS IN THE RESPONDING ANIMAL; AND A 2.5-MINUTE EXPOSURE WITH 0.5 MINUTE OF FRIGHT STIMULUS (ELECTRIC SHOCK) RESULTED IN 0/4 RESPONSES.

FLUOROCARBON 142B: INHALATION CARDIAC SENSITIZATION IN BEAGLE DOGS IS OF LOW CONCERN. DOGS WERE EXPOSED TO A FRIGHT STIMULUS (AN AMPLIFIED SOUND EFFECT TAPE RECORDING) TO STIMULATE THE RELEASE OF ENDOGENOUS EPINEPHRINE WHILE THEY WERE SIMULTANEOUSLY INHALING AN 80% TEST SUBSTANCE/20%OXYGEN ATMOSPHERE. EXPOSURE FOR 30 SECONDS RESULTED IN 5/12 CARDIAC RESPONSES (ARRHYTHMIAS) AND SEVERE CONVULSIONS WITH FECAL AND URINARY INCONTINENCE IN 9/12. IN ANOTHER EXPERIMENT WITH NO FRIGHT STIMULUS, 1/12 HAD CARDIAC RESPONSES AND 5/12 HAD CONVULSIONS.

FREON 12: INHALATION CARDIAC SENSITIZATION IN BEAGLE DOGS IS OF LOW CONCERN. DOGS WERE EXPOSED TO A FRIGHT STIMULUS (AN AMPLIFIED SOUND EFFECT TAPE RECORDING) TO STIMULATE THE RELEASE OF ENDOGENOUS EPINEPHRINE WHILE THEY WERE SIMULTANEOUSLY INHALING AN 80% TEST COMPOUND/20% OXYGEN ATMOSPHERE. EXPOSURE FOR 30 SECONDS RESULTED IN 0/12 CARDIAC RESPONSES (ARRHYTHMIAS) BUT SEVERE CONVULSIONS WITH FECAL AND URINARY INCONTINENCE IN 9/12.

FREON 114: INHALATION CARDIAC SENSITIZATION IN BEAGLE DOGS IS OF LOW CONCERN. DOGS WERE EXPOSED TO A FRIGHT STIMULUS (AN AMPLIFIED SOUND EFFECT TAPE) TO STIMULATE THE RELEASE OF ENDOGENOUS EPINEPHRINE WHILE THEY WERE SIMULTANEOUSLY INHALING AN 80% TEST COMPOUND/20% OXYGEN ATMOSPHERE. EXPOSURE FOR 30 SECONDS RESULTED IN 1/12 CARDIAC RESPONSES (ARRHYTHMIAS) WITH BIGEMINAL RHYTHM WITH SOME AREAS SUGGESTIVE OF MULTIPLE VENTRICULAR BEATS, AND MILD CONVULSIONS WITH SPASTICITY OF EXTREMITIES IN 5/12.

FREON 11: INHALATION CARDIAC SENSITIZATION IN BEAGLE DOGS IS OF LOW CONCERN. DOGS WERE EXPOSED TO A FRIGHT STIMULUS (AN AMPLIFIED SOUND EFFECT TAPE) TO STIMULATE THE RELEASE OF ENDOGENOUS EPINEPHRINE WHILE THEY WERE SIMULTANEOUSLY INHALING AN 80% TEST COMPOUND/20% OXYGEN ATMOSPHERE. EXPOSURE FOR 30 SECONDS RESULTED IN 2/12 CARDIAC RESPONSES (ARRHYTHMIAS) WITH BIGEMINAL RHYTHM WITH SOME

AREAS SUGGESTIVE OF MULTIPLE VENTRICULAR BEATS, AND VIOLENT STRUGGLING BUT NO CONVULSIONS.