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October 15, 1992

Document Processing Center (TS-790)
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 6/28/91 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,

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

we
1/26/93

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 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 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)	} 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

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
Reprodutive	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 # 302-01-2

Chem: Hydrazine; hydrazine hydrate

**Title: Preliminary data on the acute toxicity of hydrazine
and hydrazine hydrate**

Date: 12/10/49

**Summary of Effects: convulsions; salivation; highly
toxic; skin and eye damage**

1798

MEDICAL DIVISION
ARMY CHEMICAL CENTER
MARYLAND

10 December 1949

PRELIMINARY DATA ON THE ACUTE TOXICITY OF
HYDRAZINE AND HYDRAZINE HYDRATE

This work was performed under Chemical Corps Project No. 4-61-14-02, "Health Hazards of Military Chemicals". The data reported herein are preliminary and subject to revision on the basis of experimental work in progress.

ACUTE INHALATION TOXICITY OF HYDRAZINE AND HYDRAZINE HYDRATE

Exposure of rats to saturated hydrazine vapors for a half hour resulted in fatalities in about 17% of the animals exposed. Behavior and symptoms were observed during the exposure. Restlessness was evident during the first half of the exposure. In the second half of the exposure, nasal bleeding appeared. There was pronounced salivation. Neurological disturbances manifested themselves, terminating with convulsions. Death in most cases was delayed, occurring approximately two days after exposure. Nasal bleeding was the only symptom observed in some cases.

Hydrazine hydrate offers less hazard by inhalation, as indicated by saturated vapor exposures. 4-hour exposure of rats to saturated hydrazine hydrate vapors resulted in no fatalities during a 14-day observation period. It appears that the toxicity of hydrazine hydrate is due to its hydrazine content. Symptoms for this compound are essentially the same as those for hydrazine, except that in the case of the hydrate there was no pronounced salivation. The animals exhibited more violent neurological disturbances and survival time was longer.

Rats killed as a result of exposure or sacrificed after exposure showed comparable pathological changes. The constant lesion present was erosion of the bronchiolar mucosa. Apparently this effect was a predisposing factor in the subsequent development of pneumonia.

HYDRAZINE AND HYDRAZINE HYDRATE INJECTION TOXICITY

The LD₅₀ value for hydrazine on rapid intravenous injection into

rabbits was found to be approximately 26 mg./kg. By this route, results indicated that the toxicity of the hydrate is due to the hydrazine it contains.

HYDRAZINE AND HYDRAZINE HYDRATE PERCUTANEOUS TOXICITY

Hydrazine and hydrazine hydrate were applied to the clipped skin of rabbits. The LD₅₀ for hydrazine by this route was found to be approximately 91 mg./kg., and for the hydrate, 283 mg./kg. This difference, contrary to that found by the intravenous route, is considerably greater than can be accounted for on the basis of the water of hydration.

Application of undiluted hydrazine to the clipped skin of rabbits produced a fairly prompt local effect and a delayed systemic effect. The local effect consisted of development of a purplish discoloration which appeared in 2 to 5 minutes, reached maximum in 10 minutes, and gradually disappeared over the next 48 hours. Both forms of the material seemed to produce permanent injury to the skin in some cases. The discoloration was apparently subcutaneous hemorrhage which sometimes resulted in sloughing of the overlying skin and subsequent scar formation. The systemic effect was the development of extensor rigidity of the forelegs and occasionally of the hind legs. Shortly thereafter the animals developed clonic convulsions which in some instances were very severe. The convulsions were intermittent and death seemed to occur more often between convulsions than during.

HYDRAZINE AND HYDRAZINE HYDRATE INTRAOCULAR TOXICITY

Application of amounts of undiluted hydrazine as low as 0.3 mm³ produced moderately severe irritation when applied to the corneas of rabbits. When 5 mm³ was applied to the cornea, an area of hemorrhage appeared in the nictitating membrane. This developed within 5 minutes after application and persisted for 24 to 48 hours. Hydrazine hydrate produced comparable irritating effects in 3 or 5 mm³ amounts. However, 1 mm³ of the hydrate was less irritating than 0.3 mm³ of the anhydrous form. This indicates a significant difference in the threshold amounts.

SUMMARY, CONCLUSIONS, AND RECOMMENDATIONS

1. The inhalation hazard offered by hydrazine is moderately severe, so that respiratory protection is indicated where possibilities of gross spillage exist. Hydrazine hydrate is less toxic by this route so that precautions used for hydrazine would be adequate for the hydrate.

2. Hydrazine skin toxicity is of a high order of magnitude. Splashes on the skin should be removed as soon as possible by washing freely with water. Threshold values have not been defined to date. On the basis of rabbit results reported herein, personnel receiving hydrazine in amounts in excess of 1-2 mls., which have not been washed off immediately, should be referred to a physician for observation. Hydrazine hydrate is about one-third as toxic by this route, and should be handled accordingly.

3. Eye protection is indicated for both compounds.

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

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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

12333A



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Triage of 8(e) Submissions

AUG 24 1985

Date sent to triage: _____

NON-CAP

CAP

Submission number: 12333A

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:

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entire document: 10 1 2 pages 1st TAB pages 17 TABS

Notes:

Contractor reviewer: POK Date: 3/21/95

CECATS DATA: Submission # BEHQ-1092-12333 SEQ. A

TYPE: SUPP FLWP

SUBMITTER NAME: E. I. Dupont de Nemours and Company

INFORMATION REQUESTED: FLWP DATE: _____
 0501 NO INFO REQUESTED
 0502 INFO REQUESTED (TECH)
 0503 INFO REQUESTED (VOL ACTIONS)
 0504 INFO REQUESTED (REPORTING RATIONALE)
 DISPOSITION:
 REFER TO CHEMICAL SCREENING
 CAP NOTICE

VOLUNTARY ACTIONS:
 0401 NO ACTION REPORTED
 0402 STUDIES PLANNED/IN PROGRESS
 0403 MODIFICATION OF WORK PRACTICES
 0404 LABELING/MSDS CHANGES
 0405 PROCESS/ANALYSIS CHANGES
 0406 APPAUSE DISCONTINUED
 0407 PRODUCTION DISCONTINUED
 0408 CONFIDENTIAL

SUB. DATE: 10/15/92 OTR DATE: 10/27/92 CSRAD DATE: 01/25/95

CHEMICAL NAME:
Hydrazine
Hydrazine hydrate

CASE
302-01-2
302-01-2 UNKNOWN

INFORMATION TYPE:	P.F.C.	INFORMATION TYPE:	P.F.C.	INFORMATION TYPE:	P.F.C.
0201 ONCO (HUMAN)	01 02 04	0216 EPICLIN	01 02 04	0241 IMMUNO (ANIMAL)	01 02 04
0202 ONCO (ANIMAL)	01 02 04	0217 HUMAN EXPOS (PROD CONTAM)	01 02 04	0242 IMMUNO (HUMAN)	01 02 04
0203 CELL TRANS (IN VITRO)	01 02 04	0218 HUMAN EXPOS (ACCIDENTAL)	01 02 04	0243 CHEMPHYS PROP	01 02 04
0204 MUTA (IN VITRO)	01 02 04	0219 HUMAN EXPOS (MONITORING)	01 02 04	0244 CLASTO (IN VITRO)	01 02 04
0205 MUTA (IN VIVO)	01 02 04	0220 ECO/AQUA TOX	01 02 04	0245 CLASTO (ANIMAL)	01 02 04
0206 REPRO/ITERATO (HUMAN)	01 02 04	0221 ENV. OCCURENCE/FATE	01 02 04	0246 CLASTO (HUMAN)	01 02 04
0207 REPRO/ITERATO (ANIMAL)	01 02 04	0222 EMER INCI OF ENV CONTAM	01 02 04	0247 DNA DAM/REPAIR	01 02 04
0208 NEURO (HUMAN)	01 02 04	0223 RESPONSE REQEST DELAY	01 02 04	0248 PRODUSE/PROC	01 02 04
<input checked="" type="checkbox"/> 0209 NEURO (ANIMAL)	01 02 04	0224 PROD/COMP/CHEM ID	01 02 04	0251 MSDS	01 02 04
0210 ACUTE TOX. (HUMAN)	01 02 04	0225 REPORTING RATIONALE	01 02 04	0299 OTHER	01 02 04
0211 CHR. TOX. (HUMAN)	01 02 04	0226 CONFIDENTIAL	01 02 04		
<input checked="" type="checkbox"/> 0212 ACUTE TOX. (ANIMAL)	01 02 04	0227 ALLERG (HUMAN)	01 02 04		
0213 SUB ACUTE TOX (ANIMAL)	01 02 04	0228 ALLERG (ANIMAL)	01 02 04		
0214 SUB CHRONIC TOX (ANIMAL)	01 02 04	0239 METAB/PHARMACO (ANIMAL)	01 02 04		
0215 CHRONIC TOX (ANIMAL)	01 02 04	0240 METAB/PHARMACO (HUMAN)	01 02 04		

<u>TRACE DATE:</u>	<u>NON-CBI INVENTORY</u>	<u>ONGOING REVIEW</u>	<u>SPECIES</u>	<u>TOXICOLOGICAL CONCERN:</u>	<u>USE:</u>	<u>PRODUCTION:</u>
	<input checked="" type="checkbox"/> YES	YES (DROP/REFER)	Rbt	LOW		
CAS SR	NO	NO (CONTINUE)	RAT	<input checked="" type="checkbox"/> MED		
	IN PROGRESS	REFER		<input checked="" type="checkbox"/> HIGH		

-CPSS-

> <ID NUMBER>

8(E)-12333A

> <TOX CONCERN>

H/M/H/H

> <COMMENT>

HYDRAZINE: ACUTE INHALATION TOXICITY IN RATS IS ASSIGNED NO LEVEL OF BECAUSE AN EXPOSURE LEVEL WAS NOT REPORTED. A SINGLE ONE-HALF HOUR EXPOSURE TO SATURATED VAPORS IN RATS (NUMBERS UNSPECIFIED) WAS ASSOCIATED WITH 17% FATALITY AND SIGNS OF NEUROTOXICITY INCLUDING CONVULSIONS. OTHER CLINICAL SIGNS OF TOXICITY INCLUDED NASAL BLEEDING AND PRONOUNCED SALIVATION. NECROPSY OF BOTH SURVIVING AND DECEDENT ANIMALS REVEALED EROSION OF THE BRONCHIOLAR MUCOSA CORRELATING TO INCIDENCE OF PNEUMONIA.

HYDRAZINE HYDRATE: ACUTE INHALATION TOXICITY IN RATS IS ASSIGNED NO LEVEL OF CONCERN BECAUSE AN EXPOSURE LEVEL WAS NOT REPORTED. A SINGLE FOUR-HOUR EXPOSURE TO SATURATED VAPORS IN RATS (NUMBERS UNSPECIFIED) WAS ASSOCIATED WITH SOME VIOLENT SIGNS OF NEUROTOXICITY AND NO MORTALITY THROUGHOUT 14-DAY POST-EXPOSURE OBSERVATION. NECROPSY REVEALED EROSION OF THE BRONCHIOLAR MUCOSA CORRELATING TO INCIDENCE OF PNEUMONIA.

HYDRAZINE: ACUTE INTRAVENOUS (RAPID INJECTION) TOXICITY IN RABBITS IS ASSIGNED NO LEVEL OF CONCERN. AN LD50 WAS 26 MG/KG.

HYDRAZINE: ACUTE DERMAL TOXICITY IN RABBITS IS OF HIGH CONCERN. A SINGLE APPLICATION TO THE CLIPPED SKIN OF RABBITS WAS ASSOCIATED WITH SIGNS OF NEUROTOXICITY AND MORTALITY SUCH THAT AN LD50 WAS 91 MG/KG. DERMAL IRRITATION MANIFESTED AS EARLY TRANSIENT PURPLISH DISCOLORATION OR OCCASIONAL PERMANENT INJURY. SIGNS OF SYSTEMIC TOXICITY WERE APPARENT LATER AND INCLUDED RIGIDITY OF THE FORELEGS AND, OCCASIONALLY, THE HINDLEGS FOLLOWED BY INTERMITTENT CLONIC CONVULSIONS AND DEATH.

HYDRAZINE HYDRATE: ACUTE DERMAL TOXICITY IN RABBITS IS OF MEDIUM CONCERN. A SINGLE APPLICATION TO THE CLIPPED SKIN OF RABBITS WAS ASSOCIATED WITH SIGNS OF NEUROTOXICITY MORTALITY SUCH THAT AN LD50 WAS 283 MG/KG. DERMAL IRRITATION MANIFESTED AS EARLY TRANSIENT PURPLISH DISCOLORATION OR OCCASIONAL PERMANENT INJURY. SIGNS OF SYSTEMIC TOXICITY WERE APPARENT LATER AND INCLUDED RIGIDITY OF THE FORELEGS AND, OCCASIONALLY, THE HINDLEGS FOLLOWED BY INTERMITTENT CLONIC CONVULSIONS AND DEATH.

HYDRAZINE: EYE IRRITATION IN RABBITS IS OF HIGH CONCERN. A SINGLE INTRAOCULAR APPLICATION OF 0.33 - 5.00 MM3 IN RABBITS WAS ASSOCIATED WITH SEVERE CORNEAL IRRITATION. 5 MM3 PRODUCED EARLY HEMORRHAGE OF THE NICTITATING MEMBRANE PERSISTING FOR 24 TO 48 HOURS.

HYDRAZINE HYDRATE: EYE IRRITATION IN RABBITS IS OF HIGH CONCERN. A

SINGLE INTRAOCULAR APPLICATION OF 3 TO 5 MM3 IN RABBITS WAS ASSOCIATED WITH SEVERE CORNEAL IRRITATION. 5 MM3 PRODUCED EARLY HEMORRHAGE OF THE NICTITATING MEMBRANE PERSISTING FOR 24 TO 48 HOURS. AN APPLICATION OF 1 MM3 PRODUCED LESS CORNEAL IRRITATION THAN DID 0.33 MM3 OF HYDRAZINE.

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