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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 6/28/91CAP 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

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**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<sup>2</sup>. This is particularly troublesome as the "Reporting Guide" states criteria, applied retroactively, which expands upon and conflicts with the Statement of Interpretation.<sup>3</sup> 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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<sup>2</sup>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".

<sup>3</sup>A 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 intent<sup>4</sup>, 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.<sup>5</sup>
- 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.

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<sup>4</sup>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.

<sup>5</sup> 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>
<b>ACUTE LETHALITY</b>		
Oral	N}	Y}
Dermal	N}	Y}
Inhalation (Vapors)	} <sup>6</sup>	} <sup>7</sup>
aerosol	N}	Y}
dusts/ particles	N}	Y}
<b>SKIN IRRITATION</b>	N	Y <sup>8</sup>
<b>SKIN SENSITIZATION (ANIMALS)</b>	N	Y <sup>9</sup>
<b>EYE IRRITATION</b>	N	Y <sup>10</sup>
<b>SUBCHRONIC (ORAL/DERMAL/INHALATION)</b>	N	Y <sup>11</sup>
<b>REPRODUCTION STUDY</b>	N	Y <sup>12</sup>
<b>DEVELOPMENTAL TOX</b>	Y <sup>13</sup>	Y <sup>14</sup>

<sup>6</sup>43 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."

<sup>7</sup>Guide at pp.22, 29-31.

<sup>8</sup>Guide at pp-34-36.

<sup>9</sup>Guide at pp-34-36.

<sup>10</sup>Guide at pp-34-36.

<sup>11</sup>Guide at pp-22; 36-37.

<sup>12</sup>Guide at pp-22

<sup>13</sup>43 Fed Reg at 11112

"Birth Defects" listed.

<sup>14</sup>Guide at pp-22

NEUROTOXICITY	N	Y <sup>15</sup>
CARCINOGENICITY	Y <sup>16</sup>	Y <sup>17</sup>
MUTAGENICITY		
<i>In Vitro</i>	Y <sup>18</sup>	Y <sup>19</sup>
<i>In Vivo</i>	Y}	Y}
ENVIRONMENTAL		
Bioaccumulation	Y}	N
Bioconcentration	Y <sup>20</sup>	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

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<sup>15</sup>Guide at pp-23; 33-34.

<sup>16</sup>43 Fed Reg at 11112  
"Cancer" listed

<sup>17</sup>Guide at pp-21.

<sup>18</sup>43 Fed Reg at 11112; 11115 at Comment 15

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

<sup>19</sup>Guide at pp-23.

<sup>20</sup>43 Fed Reg at 11112; 11115 at Comment 16.

**CAS # 137-26-8; 97-94-5**

**Chem: Thiuram M, Thiuram E; Thionex; Penzone E; Permalux  
Retarder W; carbamic acid, N,N'-(4-methyl-metaphenylene)-  
di-, difurfuryl ester**

**Title: Maternal toxicity, embryotoxicity and teratogenic  
potential of neoprene accelerators applied to skin of  
rats during organogenesis**

**Date: 7/12/73**

**Summary of Effects: Thiorex was teratogenic at lethal doses**

# BEST COPY AVAILABLE

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

Haskell Laboratory Report No. 344-73

MR No. 1658-011

<u>Materials Submitted</u>	<u>Haskell Nos.</u>	<u>Other Codes</u>
1) Thiuram M (tetramethylthiuram disulfide) <u>187-26-8</u>	1 7788	1) LRT-179
2) Thiuram E (tetraethylthiuram disulfide) <u>97-77-8</u>	2 7789	2) LRT-179
3 Thionex® (tetramethylthiuram monosulfide) <u>97-74-5</u>	3 7790	LRT-180
4 Penzone E (N,N'-diethyl thiourea) <u>105-55-5</u>	4 7791	4) LRT-181
5 Permalux® (di-o-tolylguanidine salt of dicatechol borate)	5 7792	5) LRT-182
6 Retarder W (salicylic acid) <u>69-72-7</u>	6 7793	6) LRT-183
7 Carbamic acid, N,N'-(4-methyl-meta- phenylene)di-, difurfuryl ester	7 7794	7) LRT-184

Submitted by: P. R. Johnson, Elastomer Chemicals Department.

MATERNAL TOXICITY, EMBRYOTOXICITY AND  
TERATOGENIC POTENTIAL OF NEOPRENE  
ACCELERATORS APPLIED TO SKIN OF RATS  
DURING ORGANOGENESIS

Introduction: These materials used as accelerators for neoprene were tested on pregnant rats in a preliminary procedure to estimate relative toxicity to female and embryos.

The results and method are described in the attached Pathology Report No. 64-73.

Report by:

O. Louis Dashiell  
O. Louis Dashiell

Approved by:

Charles F. Reinhardt  
Charles F. Reinhardt  
Assistant Director

PATHOLOGY REPORT NO. 64-73

Maternal Toxicity, Embryotoxicity and Teratogenic Potential of  
Neoprene Accelerators Applied to Skin of Rats During Organogenesis

H-7788-7794 - MR-1660-001 - Elastomers Dept.

Screening Tests

June 29, 1973

The purpose of this study was to determine the Approximate Lethal Dose (ALD) of seven neoprene accelerators for pregnant rats and to compare their embryotoxic and teratogenic potential. The materials were dissolved or suspended in dimethylsulfoxide (DMSO) and a single dose was applied on the clipped back skin of primigravida Charles River-CD rats on day 12 of gestation at dose levels of 450, 670, 1000, 1500, and 2250 mg/kg of body weight. Five pregnant females were treated with DMSO and served as controls. The animals were sacrificed on the twentieth day of gestation and the following observations and determinations were made: (1) gross examinations of uterus and fetuses; (2) number of implantation sites; (3) number of live fetuses; (4) number of early resorptions; (5) number of late resorptions; (6) fetal weight and (7) fetal crown-rump length. All fetuses were saved in appropriate fixatives for possible future determination of skeletal and visceral anomalies.

Summary of the Results:

The effects of a single skin application of DMSO and the seven neoprene accelerators on the survival of pregnant rats, outcome of pregnancy and fetal development are summarized in the attached table.

Thiuram M

Moderately toxic to mothers and lethal to embryos. All but one implanted conceptuses were resorbed after the treatment (late resorptions) at all levels while only the highest dose (2250 mg/kg) caused death of the mother.

Thionex®

Lethal to pregnant rats at 1500 mg/kg, was teratogenic but, was not embryo-lethal. Five and three fetuses with exencephaly were found in litters from mothers treated with 670 and 1000 mg/kg, respectively. A slightly higher number of early resorptions, compared with that of the control animals, was found in this and other groups. These early resorptions were not treatment-related. At the time of treatment, the process of resorption was already in progress.

Summary of the Results (Continued):

Retarder W

Very similar to Thionex®. A dose level of 1500 mg/kg was lethal to pregnant rats. One fetus with exencephaly was detected in a litter at 450 mg/kg. The material was not embryo-lethal.

Permalux®

Slightly toxic and possibly teratogenic. At the highest dose level of 2250 mg/kg the gain in body weight of the female and the weights of the fetuses were significantly lower than those of females treated with Permalux® at lower levels or of control females treated with DMSO. One fetus, from a litter of eight, exposed to 450 mg/kg, was thought to have mild exencephaly. The fetus was stunted and extremely small. Ossification of all bones, including those of the skull were retarded. This, and the fact that no other fetuses from dams exposed to higher concentrations of Permalux® showed similar changes, suggests that this may not be compound-related.

Thiuram E, Penzone E and Difurfuryl-2,4-tolylene diurethane

Not toxic to pregnant rats, not embryo-lethal and not teratogenic under the conditions of this test at levels ranging from 450 to 2250 mg/kg. All animals (at all levels) delivered normal litters. All parameters used to measure the outcome of pregnancy and fetal development were similar to those of the control DMSO-treated females.

Note: Due to incorrect information given to us by the supplier of the pregnant rats, (Charles River Breeding Laboratories, Wilmington, Mass.) regarding the exact day of breeding, most of the animals were treated on day 12 and a few on day 11 of gestation rather than on day 13. Variations in the size of the fetuses (weight and length) and the extent of the ossification of the bones occurred in all treatment groups. However, this discrepancy in the breeding dates did not significantly alter the primary purpose of this study which was to screen the teratogenic potential of these candidates.

Report by: \_\_\_\_\_

*R. Culik*  
R. Culik  
Research Pathologist

RC:ljm

Effects of a Single Topical Application of Various Neoprene Accelerators on the Outcome of Pregnancy and Fetal Development

Haskell Number	Compound	Number of Females		Number per Pregnant Female			Live Fetuses	No. Fetuses With Major Gross Anomalies at Treatment Level <sup>1</sup>	
		Preg.	Not Preg.	Implant-ation Sites	Early Re-sorptions	Late Re-sorptions			
7788	DMSO (Control)	4	1	0	10.8	0.3	0	10.5	None
7788	Thiuram M	3	1	1*	8.7	0.4	8.3	0	All fetuses resorbed at all treatment levels
7789	Thiuram E	5	0	0	9.6	0.6	0	9.0	None
7790	Thionex®	3	0	2**	9.7	1.7	0	8.0	5 Exencephaly at 670 mg/kg 3 Exencephaly at 1000 mg/kg
7791	Penzone E	4	1	0	10.0	1.5	0	8.5	None
7792	Permalux®	5	0	0	10.0	0.6	0	9.4	1 Questionable exencephaly at 450 mg/kg
7793	Retarder W	3	0	2***	8.0	1.0	0	7.0	1 Exencephaly at 450 mg/kg
7794	Difurfuryl-2,4-tolyene diurethane	4	1	0	9.0	0.8	0	9.8	None

Died at dose levels:

- \* 2250 mg/kg
- \*\* 1500 and 2250 mg/kg
- \*\*\* 1500 and 2250 mg/kg

<sup>1</sup> Petechial hemorrhages and small hematomas were found in several fetuses in all groups. They were not treatment-related.

**Triage of 8(e) Submissions**

Date sent to triage: 2/5/96

NON-CAP

CAP

Submission number: 12209A

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**

*Only permalux and difuryl ester were assessed.  
Please complete the other 5 chemicals.*

*Thanks*

		<b>For Contractor Use Only</b>	
entire document:	<u>0</u> 1 2	pages <u>1, 1<sup>st</sup> tab</u>	pages <u>1, all tabs</u>
Notes:			
Contractor reviewer:	<u>LPS</u>	Date:	<u>5/17/95</u>

CECATS/TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA  
Submission # SEHQ-1092-12209 SEQ. A

TYPE: (NT) 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:  
0505 REFER TO CHEMICAL SCREENING  
0506 CAP NOTICE

VOLUNTARY ACTIONS:  
0401 NO ACTION REPORTED  
0402 STUDIES PLANNED/IN PROGRESS  
0403 NOTIFICATION IN WORK PROGRESS  
0404 LABELS/MSDS (CHANGE)  
0405 PROCESS/ASIAN/ING (CHANGE)  
0406 APPAUSE DISCONTINUED  
0407 PRODUCTION DISCONTINUED  
0408 CONFIDENTIAL

SUB. DATE: 10/15/92 OTS DATE: 10/27/92 CSRAD DATE: 03/30/95

CHEMICAL NAME: Dicatenol borate, di-o-tolyl guanidine salt of Permalux  
Permalux  
Carbamic acid, N,N'-(4-methyl-metaphenylene) di-  
diFurfuryl ester

137-26-8 Thiuran M  
97-77-8 Thiuran E  
97-74-5 Thionex  
105-55-5 Penzone E  
69-72-7 Retarder W

INFORMATION TYPE:	P.F.C.	INFORMATION TYPE:	P.F.C.	INFORMATION TYPE:	P.F.C.
0201 ONCO (HUMAN)	01 02 04	0216 EPICLEN	01 02 04	0201 IMMUNO (ANIMAL)	01 02 04
0202 ONCO (ANIMAL)	01 02 04	0217 HUMAN EXPOS (PROD CONTAM)	01 02 04	0202 IMMUNO (HUMAN)	01 02 04
0203 CELL TRANS (IN VITRO)	01 02 04	0218 HUMAN EXPOS (ACCIDENTAL)	01 02 04	0203 CHEMPHYS PROP	01 02 04
0204 MUTA (IN VITRO)	01 02 04	0219 HUMAN EXPOS (MONITORING)	01 02 04	0204 CLASTO (IN VITRO)	01 02 04
0205 MUTA (IN VIVO)	01 02 04	0220 BODWQUA TOX	01 02 04	0205 CLASTO (ANIMAL)	01 02 04
0206 REPRO/TERATO (HUMAN)	01 02 04	0221 ENV. OCCUREL/PATE	01 02 04	0206 CLASTO (HUMAN)	01 02 04
<u>0207</u> REPRO/TERATO (ANIMAL)	01 02 04	0222 EMER INCI OF ENV CONTAM	01 02 04	0207 DNA DAM/REPAIR	01 02 04
0208 NEURO (HUMAN)	01 02 04	0223 RESPONSE REQEST DELAY	01 02 04	<u>0208</u> PRODUCE/PROC	01 02 04
0209 NEURO (ANIMAL)	01 02 04	0224 PROD/COMP/CHM ID	01 02 04	0209 MSYS	01 02 04
0210 ACUTE TOX. (HUMAN)	01 02 04	0225 REPORTING RATIONALE	01 02 04	0209 OTHER	01 02 04
0211 CHR. TOX. (HUMAN)	01 02 04	0226 CONFIDENTIAL	01 02 04		
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	0229 METABPHARMACO (ANIMAL)	01 02 04		
0215 CHRONIC TOX (ANIMAL)	01 02 04	0230 METABPHARMACO (HUMAN)	01 02 04		

IRADIATION: NON-CELL INVENTORY  
CAS SR: YES  
ONGOING REVIEW: YES (DROP/REFER)  
SPECIES: RAT  
TOXICOLOGICAL CONCERN: LOW

USE: accelerators for neoprene  
PRODUCTION:

Short-term Developmental, dermal

~~Acute~~ dose: 450, 670, 1000, 1500, and 2250 mg/kg/gestation day 12

Permalux  
At 2250mg/kg: ↓ maternal and fetal body wt gain  
... diFurfuryl ester  
no treatment-related effects in either dams or fetuses.

THIURAM M

137-26-8

“12209A-01”=H”=“ABSTRACT BASED ON SUMMARIZED RESULTS SUBMITTED WITHOUT A REPORT. THIURAM M (CAS# 137-26-8) WAS DISSOLVED IN DMSO AND A SINGLE DOSE OF EITHER 0, 450, 670, 1000, 1500, OR 2250 MG/KG WAS APPLIED TO THE CLIPPED BACK SKIN OF PRIMIGRAVIDA CHARLES RIVER-CD RATS ON DAY 12 OF GESTATION. THE NUMBER OF RATS PER GROUP WAS NOT GIVEN. ANIMALS WERE SACRIFICED ON DAY 20 OF GESTATION AND EXAMINED FOR FETAL AND MATERNAL TOXICITY. ALL BUT ONE IMPLANTED FETUS WERE RESORBED AFTER THE TREATMENT AT ALL LEVELS. MATERNAL MORTALITY WAS ONLY SEEN AT 2250 MG/KG.”

THIONEX

97-74-5

“12209A-03”= M ”=“ABSTRACT BASED ON SUMMARIZED RESULTS SUBMITTED WITHOUT A REPORT. THIONEX (CAS# 97-74-5) WAS DISSOLVED IN DMSO AND A SINGLE DOSE OF EITHER 0, 450, 670, 1000, 1500, OR 2250 MG/KG WAS APPLIED TO THE CLIPPED BACK SKIN OF PRIMIGRAVIDA CHARLES RIVER-CD RATS ON DAY 12 OF GESTATION. THE NUMBER OF RATS PER GROUP WAS NOT GIVEN. ANIMALS WERE SACRIFICED ON DAY 20 OF GESTATION AND EXAMINED FOR FETAL AND MATERNAL TOXICITY. MATERNAL MORTALITIES OCCURRED AT 1500 AND 2200 MG/KG. FETUSES WITH EXENCEPHALY WERE FOUND IN LITTERS AT 670 AND 1000 MG/KG.”

RETARDER W

69-72-7

"12209A-06"=M"=" ABSTRACT BASED ON SUMMARIZED RESULTS SUBMITTED WITHOUT A REPORT. RETARDER W (CAS# 69-72-7) WAS DISSOLVED IN DMSO AND A SINGLE DOSE OF EITHER 0, 450, 670, 1000, 1500, OR 2250 MG/KG WAS APPLIED TO THE CLIPPED BACK SKIN OF PRIMIGRAVIDA CHARLES RIVER-CD RATS ON DAY 12 OF GESTATION. THE NUMBER OF RATS PER GROUP WAS NOT GIVEN. ANIMALS WERE SACRIFICED ON DAY 20 OF GESTATION AND EXAMINED FOR FETAL AND MATERNAL TOXICITY. MATERNAL MORTALITIES OCCURRED AT 1500 AND 2200 MG/KG. ONE FETUS WITH EXENCEPHALY WAS FOUND AT 450 MG/KG."

THIURAM E

97-77-8

“12209A-04j”= L ”=“ABSTRACT BASED ON SUMMARIZED RESULTS SUBMITTED WITHOUT A REPORT. THIURAM E (CAS# 97-77-8) WAS DISSOLVED IN DMSO AND A SINGLE DOSE OF EITHER 0, 450, 670, 1000, 1500, OR 2250 MG/KG WAS APPLIED TO THE CLIPPED BACK SKIN OF PRIMIGRAVIDA CHARLES RIVER-CD RATS ON DAY 12 OF GESTATION. THE NUMBER OF RATS PER GROUP WAS NOT GIVEN. ANIMALS WERE SACRIFICED ON DAY 20 OF GESTATION AND EXAMINED FOR FETAL AND MATERNAL TOXICITY. NO MORTALITIES OR CLINICAL SIGNS OF TOXICITY WERE OBSERVED IN EITHER MOTHERS OR FETUSES.”

PENZONE E

105-55-5

“12209A-~~08~~<sup>H</sup>”=L”=“ABSTRACT BASED ON SUMMARIZED RESULTS SUBMITTED WITHOUT A REPORT. PENZONE E (CAS# 105-55-5) WAS DISSOLVED IN DMSO AND A SINGLE DOSE OF EITHER 0, 450, 670, 1000, 1500, OR 2250 MG/KG WAS APPLIED TO THE CLIPPED BACK SKIN OF PRIMIGRAVIDA CHARLES RIVER-CD RATS ON DAY 12 OF GESTATION. THE NUMBER OF RATS PER GROUP WAS NOT GIVEN. ANIMALS WERE SACRIFICED ON DAY 20 OF GESTATION AND EXAMINED FOR FETAL AND MATERNAL TOXICITY. NO MORTALITIES OF SIGNS OF CLINICAL TOXICITY WERE OBSERVED IN MOTHERS OR FETUSES.”