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8(e)

CAP

12330

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401 M Street., S.W.  
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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 process issues and clouds the appropriate reporting standard by which regulated persons can assure TSCA Section 8(e) compliance.

For Regulatee,

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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>;

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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<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 (Fm. 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

<b>NEUROTOXICITY</b>	<b>N</b>	<b>Y<sup>15</sup></b>
<b>CARCINOGENICITY</b>	<b>Y<sup>16</sup></b>	<b>Y<sup>17</sup></b>
<b>MUTAGENICITY</b>		
<i>In Vitro</i>	Y <sup>18</sup>	Y <sup>19</sup>
<i>In Vivo</i>	Y}	Y}
<b>ENVIRONMENTAL</b>		
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
<b>AVIAN</b>		
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# 10042-84-9; 868-18-8; 87-69-4; 77-85-0**

**CHEM: Sodium nitrilotriacetate; sodium tartrate; tartaric acid;  
methyltrimethylmethane; nitrogen triacetic acid; imino  
diacetic acid hydrochloride**

**TITLE: Preliminary Toxicity Tests**

**DATE: 12/18/47**

**SUMMARY OF EFFECTS: Some compounds relatively toxic**

## MEDICAL RESEARCH PROJECT MR-125

### Preliminary Toxicity Tests

Acute toxicity tests have been carried out on a group of compounds as per D. K. O'Leary's letter of July 30, 1947, to Dr. Foulger. The compounds and the details of the tests on each compound are as follows:

#### A-8122 Sodium Nitritotriacetate

The compound was given in a water solution containing 0.25 grams/ml. in one series of M L D Tests and 0.203 grams/ml. in a second series. All doses of sodium nitritotriacetate greater than 1500 mg/kg. killed the rats within 30 to 100 minutes. Prior to death the rats became weak, developed convulsions, and became cyanotic. At autopsy the lungs showed slight to severe congestion and edema. The mucosa of the stomach was slightly inflamed. One rat surviving 1500 mg/kg. was killed two days after treatment and did not show any gross or microscopic pathology.

#### A-8123 Sodium Tartrate

The Sodium Tartrate solution used contained an equivalent of 0.25 grams of tartaric acid per ml. The M F D for Sodium Tartrate is around 7500 mg/kg. The rats that survived this and lower doses did not show any gross or microscopic pathology when sacrificed forty-eight hours after treatment.

#### A-8041 Tartaric Acid

The M F D for Tartaric Acid is around 7500 mg/kg. Rats receiving doses of 5000 mg/kg. or less all survived and were killed 12 to 15 days after treatment. No gross or microscopic pathology was observed. One rat which died after a dose of 7590 mg/kg. showed edema and hemorrhages in the lung and acute inflammatory changes in

the stomach with superficial loss of tissue from the stomach mucosa.

A-2038 Methyltrimethylolmethane

The effect of this compound on the skin was tested on guinea pigs with the following results:

	<u>No. G.P.</u>	<u>Reactions</u>			
		<u>+</u>	<u>Sl+</u>	<u>VSl+</u>	<u>Neg.</u>
Initial Patch	10			1	9
Final Patch	10			1	9

These tests indicate that methyltrimethylolmethane is not particularly irritant to the skin and does not produce sensitization in guinea pigs.

Rats were fed doses as high as 7590 mg/kg. and aside from some discomfort immediately following treatment, they did not show any untoward effects. The rats were killed 8 to 15 days after treatment and did not show any gross or microscopic damage to the internal organs. The gain in weight of these rats between treatment and the time they were sacrificed was normal.

A-8039 Nitrogen Triacetic Acid

Rats survived single doses of this compound as high as 7590 mg/kg. Doses up to 2250 mg/kg. did not produce any apparent effect. Higher doses made the rats slightly uncomfortable following treatment, and doses of 7590 mg/kg produced considerable prostration and progressive loss in weight during the eight days following treatment. No gross or microscopic pathology was noted in the rats receiving 5000 mg/kg. or less nor in two rats receiving 7590 mg/kg. One rat receiving the latter dose showed minor changes in the liver at autopsy. The liver cells were slightly shrunken, and the nuclei were pyknotic.

A-8040 Imino Diacetic Acid Hydrochloride

Doses of this compound up to 2250 mg/kg. did not produce any apparent effect. Higher doses made the animals uncomfortable, and one rat fed a dose of 5060 mg/kg. died 18 hours after treatment. The stomach was badly burned, and there were extensive hemorrhages in the mucosa. This chemical necrosis extended to tissues adjacent to the stomach, such as the liver and abdominal wall. Microscopically the liver, stomach, and kidneys were superficially disintegrated where there had been contact with the chemical. The rats that survived doses ranging from 2250 to 1000 mg/kg. gained weight normally. Higher doses inhibited the normal increase in weight. Rats that survived doses up to 3375 mg/kg. did not show any gross or microscopic pathology when sacrificed 12 to 15 days after treatment.

Skin Tests

The remaining nine compounds were tested for skin irritation or sensitization, and the results of the tests are presented in tabular form. Ten guinea pigs were used in each test, and the standard technique was followed in making the tests.

Code	Compound	Reaction				Final Patch			
		+	SI+	VSI+	Neg.	+	SI+	VSI+	Neg.
A-8042	Bis(ethylene glycol) glutarate				10				10
A-8043	Bis(propylene glycol) glutarate				10				10
A-8044	Nonyl Alcohol	1	1		8	1			8*
A-8045	Dinonyl Phthalate	1	3	1	0	1			8*
A-8046	Trinonyl Phosphate	3	7	0	0	2	4	1	2*

\* 1 G. P. in group died during experiment.

Code	Compound	Reaction							
		Initial Patch			Final Patch				
		+	SI+	VSI+	Neg.	+	SI+	VSI+	Neg.
A-8047	Dicyanobutene				10				10
A-8048	Adiponitrile				10				10
A-8049	Tolualdehyde				10	1	4	2	3
A-8050	Benzaldehyde				10			1	9

Summary and Conclusion

None of the compounds tested orally are highly toxic and some of them are relatively non-toxic. The data on M F D are summarized as follows:

<u>Compound</u>	<u>Approx. MFD in mg/Kilo</u>
Sodium Nitrilotriacetate	2200
Sodium Tartrate	7500
Tartaric Acid	7500
Methyltrimethylolmethane	7500
Nitrogen Triacetic Acid	More than 7500
Imino Diacetic Acid Hydrochloride	More than 5000

With the exception of sodium nitrilotriacetate, death from these compounds resulted from an acute corrosive effect in the upper gastrointestinal tract. Sodium nitrilotriacetate produced marked prostration and convulsions in the rats before death. At autopsy pulmonary edema was present. It is possible this difference in toxicity between this compound and nitrogen triacetic acid may be due to an alkalosis produced by excess sodium ion.

Dinonyl phthalate and trinonyl phosphate appear to be irritant to guinea pig skin but do not sensitize. Tolualdehyde appears to produce sensitization in guinea pigs.

AJF:164

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