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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:

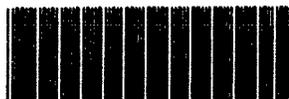
8ECAP-0025

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

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Better Things for Better Living

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.

Comparison:

Reporting triggers found in the Policy, 43 Fed Reg 11110 (3/16)

TEST TYPE 197
CR

ACUTE LETHALITY

- Oral
- Dermal
- Inhalation (Vapors)
- aerosol
- dusts/ particles

SKIN IRRITATION

SKIN SENSITIZATION (ANIMALS)

EYE IRRITATION

**SUBCHRONIC
(ORAL/DERMAL/INHALATION)**

REPRODUCTION STUDY

DEVELOPMENTAL TOX

⁶43 Fed Reg at 11114, comment 14:
"This policy statement directs Administrator. Many routine chemical, unknown effects or they are those of concern to h 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



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
Reprodcutive	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 # 75-87-6

Chem: Chloral

**Title: Acute Inhalation Toxicity Study with Chloral
In Albino Rats**

Date: 12/6/72

Summary of Effects: LC50 0.44 mg/L

Industrial BIO-TEST Laboratories, Inc.

1810 FRONTAGE ROAD
NORTHBROOK, ILLINOIS 60062
December 6, 1972

Dr. Henry Sherman
Haskell Laboratory for Toxicology
and Industrial Medicine
E. I. DuPont De Nemours & Co.
Elkton Road
Newark, Delaware 19711

Dear Dr. Sherman:

Re: IBT No. T2458 - Acute Vapor Inhalation Toxicity Study
with Chloral in Albino Rats

We are submitting herewith our laboratory report dated
December 6, 1972 prepared in connection with the above study.

Very truly yours,



J. C. Calandra
President

JCC/mp

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REPORT TO

E. I. du PONT de NEMOURS & COMPANY

ACUTE VAPOR INHALATION TOXICITY STUDY WITH
CHLORAL
IN ALBINO RATS

DECEMBER 6, 1972

IBT NO. T2458

I. Introduction

A sample identified as Chloral was received October 16, 1972, from E. I. du Pont de Nemours & Company for the purpose of conducting an acute vapor inhalation toxicity study using albino rats as experimental animals.

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Inhalation of the test material vapor caused moderate to severe diffuse discoloration of the lungs in animals which died during the observation period. Surviving rats revealed slight to minimal focal lung discoloration.

Respectfully submitted,

INDUSTRIAL BIO-TEST LABORATORIES, INC.

Report prepared by:

Victor M. Bowers
Victor M. Bowers, B.A.
Assistant Toxicologist
Inhalation Toxicity

Report approved by:

Kenneth J. Schadeberg
Kenneth J. Schadeberg, B.S.
Group Leader
Inhalation Toxicity

John W. Goode
John W. Goode, Ph. D.
Manager
Decatur Research Laboratories

M. L. Keplinger
M. L. Keplinger, Ph. D.
Manager, Toxicology

dm:psh

0 0 1 4

II. Summary

Five groups of ten rats each were used to determine the inhalation median lethal vapor concentration (LC50) of Chloral. Each group of animals was exposed to the vapor in a plexiglas chamber. After exposure, all surviving rats were observed for 14 days.

The acute vapor inhalation median lethal concentration was found to be 0.44 mg/L air (nominal concentration) based on a four-hour period of exposure. Untoward behavioral reactions exhibited by the animals included sneezing, hypoactivity, ptosis, dyspnea, prostration, and gasping. Body weight gains of most survivors at the end of the 14-day observation period were within normal limits.

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III. Procedure

Young, adult, male albino rats (Sprague-Dawley strain*) having an average body weight of 144 grams were employed as test animals. Five groups of ten rats each were selected after having been under observation for at least five days to insure their general health and suitability for testing. The animals were housed individually in stock cages and permitted a standard laboratory diet** plus water ad libitum, except during inhalation exposure.

Each exposure was designed to run for a four-hour period, during which time observations were made with respect to incidence of mortality and reactions displayed. At the end of the exposure period, the rats were returned to their stock cages and observed for the following 14 days.

A body weight was determined for each animal prior to inhalation exposure and for each surviving animal at the end of the 14-day observation period. The data were recorded as an index to body weight effects.

Gross pathologic examinations were scheduled to be conducted upon all animals which might succumb during the test period and upon those sacrificed at the end of the 14-day observation period.

*ARS/Sprague-Dawley, Madison, Wis.

**Purina Rat Chow, Ralston Purina Company, St. Louis, Mo.

Test animals were exposed in a specially constructed Plexi-las inhalation chamber having a capacity of 700 liters. The chamber was designed so that the animals could be introduced to the test atmosphere after 99 percent of the desired vapor concentration was established. Each animal was caged separately during exposure to minimize filtration of inspired air by animal fur.

Vapor was generated by bubbling a stream of clean dry air (-40°C dewpoint) through the undiluted test material. The resulting air-vapor stream was mixed with additional clean dry air, when necessary, to achieve the desired final vapor concentration. The test atmosphere was then introduced into the exposure chamber at the top center, dispersed by a baffle plate and exhausted at the bottom of the chamber. Air flow rates through the system were measured with rotameters connected in the air supply lines upstream of vapor contamination. The rotameters were calibrated with a wet-test meter after each exposure was completed. Average nominal vapor concentrations were calculated by dividing the total weight of test material vaporized by the total volume of air used during each inhalation exposure. Temperature and pressure of the test atmosphere were also measured.

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At the conclusion of the 14-day investigational period, all data were collected and the acute vapor inhalation median lethal concentration (LC₅₀) of the test material was calculated employing the method of Litchfield and Wilcoxon*.

An outline of the test conditions is presented in Table I.

* Litchfield, J. T., Jr. and Wilcoxon, F., "A Simplified Method of Evaluating Dose-Effect Experiments," J. Pharm. & Exp. Ther. 96, 99 (1949).

TABLE I
 TEST MATERIAL: Chloral
 Acute Vapor Inhalation Toxicity Study - Albino Rats
 Outline of Test Conditions

Group	Number of Animals Tested	Duration of Exposure (minutes)	Air Delivery Rates			Test Atmosphere Temperature (°C)	Test Atmosphere Pressure (inches Hg)	Average Nominal Vapor Concentration (mg/L air at 29.92 inches Hg and 25°C)
			Vapor Generator	Additional	Total			
I	10	240	0.08	88.0	88.1	25	30.08	0.24
II	10	240	0.07	47.4	47.5	25	29.94	0.36
V	10	240	0.08	54.0	54.1	24	30.01	0.38
	10	240	0.16	50.4	50.6	24	30.08	0.71
	10	240	0.60	30.1	30.7	24	30.02	6.32

IV. Results

A. Mortality

Mortality data and the LC₅₀ are presented in Table II.

B. Body Weight Effects

The average two-week body weight gains of surviving animals in Groups I, II, and III were 70, 39, and 58 grams respectively. All of these average weight gains are within the normal limits.

C. Behavioral Reactions

Untoward behavioral reactions exhibited by the animals, in order of their appearance, included sneezing, hypoactivity, ptosis, dyspnea, gasping, and prostration. In Groups I through IV, the onset and duration of these reactions were essentially the same. Sneezing was noted approximately one-half hour after the start of the inhalation period. Hypoactivity, ptosis, and dyspnea occurred at about one hour, with gasping and prostration at two to three hours. Rats in Group V exhibited these same reactions; however, all occurred within one hour into the exposure.

Normal behavior, if the animals survived, resumed within two to ten days. Death of rats in Groups II and III was observed at four to five days after the inhalation exposure. In Groups IV and V, death was noted at one to three days.

TABLE II
 TEST MATERIAL: Chloral
 Acute Vapor Inhalation Toxicity Study - Albino Rats

Mortality Data

Group	Average Nominal Vapor Concentration (mg/L air)	Number of Animals Tested	Observed Percent Dead	Expected Percent Dead
I	0.24	10	0	0.01
II	0.36	10	10	12.10
III	0.38	10	20	20.00
IV	0.71	10	100	99.86
V	6.32	10	100	100

Acute Vapor Inhalation $LC_{50} = 0.44$ mg/L air (four-hour exposure)
 Limits of LC_{50} at the 95% Level of Confidence = 0.38 - 0.50 mg/L air

D. Gross Pathologic Findings

Necropsy of rats which died during the 14-day observation period revealed moderate to severe diffuse red discoloration of the lungs. Most animals surviving the observation period revealed minimal to slight focal red discoloration of the lungs. Three rats from Group II did not reveal any gross pathologic alterations. There were no findings in any of the other tissues and organs examined.