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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:

SECAP-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  
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mm  
2/16/95

**ATTACHMENT 1**

Submission of information is made under the 6/28/91 CAP Agreement, Unit II. This submission is made voluntarily and is occasioned by recent changes in EPA's TSCA §8(e) reporting standard; such changes made, for the first time in 1991 and 1992 without prior notice and in violation of Regulatee's constitutional due process rights. Regulatee's submission of information under this changed standard is not a waiver of its due process rights; an admission of TSCA violation or liability, or an admission that Regulatee's activities with the study compounds reasonably support a conclusion of substantial risk to health or to the environment. Regulatee has historically relied in good faith upon the 1978 Statement of Interpretation and Enforcement Policy criteria for determining whether study information is reportable under TSCA §8(e), 43 Fed Reg 11110 (March 16, 1978). EPA has not, to date, amended this Statement of Interpretation.

After CAP registration, EPA provided the Regulatee the June 1, 1991 "TSCA Section 8(e) Reporting Guide". This "Guide" has been further amended by EPA, EPA letter, April 10, 1992. EPA has not indicated that the "Reporting Guide" or the April 1992 amendment supersedes the 1978 Statement of Interpretation. The "Reporting Guide" and April 1992 amendment substantively lowers the Statement of Interpretation's TSCA §8(e) reporting standard<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 criteri. Regulatee supports and has no objection to the Agency's amending reporting criteria *provided that* such amendment is not applied to the regulated community in an unfair way. However, with the unilateral announcement of the CAP under the auspices of an OCM enforcement proceeding, EPA has wrought a terrific unfairness since much of the criteria EPA has espoused in the June 1991 Reporting Guide and in the Agency's April 2, 1992 amendment is new criteria which does not exist in the 1978 Statement of Interpretation and Enforcement Policy.

The following examples of new criteria contained in the "Reporting Guide" that is not contained in the Statement of Interpretation follow:

- o even though EPA expressly disclaims each "status report" as being preliminary evaluations that should not be regarded as final EPA policy or intent<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

<b>NEUROTOXICITY</b>	N	Y <sup>15</sup>
<b>CARCINOGENICITY</b>	Y <sup>16</sup>	Y <sup>17</sup>
<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
Reprodcutive	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 *invitro* 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 # 75-87-6**

**Chem: Chloral**

**Title: The possible toxicity of chloral**

**Date: 9/5/45**

**Summary of Effects: At 12 ppm 2-hour inhalation exposures, mortality in rats. At 31 ppm 2-hour inhalation exposure, mortality in one dog.**

Medical Research Project No. MR-136The Possible Toxicity of ChloralSummary and Conclusions

Chloral is used in the manufacture of DDT. The hazards incident to inhalation of this compound were not known and this project was undertaken to determine the effect of chloral on the lungs when inhaled and its general physiological action if absorbed into the body.

Our experiments show that chloral is highly toxic when inhaled and exposure to concentrations as low as 12 p.p.m. in the atmosphere for two hours gives rise to fatal pulmonary edema in rats.

Exposures to concentrations ranging from 15 to 31 p.p.m. for two hours produced fatal pulmonary edema in one dog, and severe pulmonary edema in another. A third dog developed severe respiratory symptoms from exposures to concentrations ranging from 3.7 to 7.2 p.p.m.

Chloral in concentrations around 5 p.p.m. may cause depression of the circulation with a fall in systolic and diastolic pressure.

If the pulmonary edema produced from inhaling chloral was not fatal, the recovery of the experimental animals was good and no residual damage to the lungs was noted at autopsy one week after the last exposure.

The degree of exposure to chloral in our experiments did not produce demonstrable damage to organs in the body other than the lungs.

Since chloral is a potent pulmonary irritant, every precaution should be taken to avoid inhalation of its vapor. Individuals accidentally gassed with chloral vapors should be carried to the plant hospital in a stretcher at once and given inhalations of oxygen under 6 cm. of water pressure. With the possible omission of platelet counts, the procedure already recommended to our plant physicians for the treatment of pulmonary edema from nitrous fumes should be followed in cases accidentally gassed with chloral vapor.

HASKELL LABORATORY OF  
INDUSTRIAL TOXICOLOGY

John H. Foulger, M. D.  
Director

By: *Allan J. Fleming* M.D.  
Allan J. Fleming, M.D.  
Assistant Director

Medical Research Project No. MR-136

The Possible Toxicity of Chloral

Although there is considerable information in the medical literature on chloral hydrate, there is no information about chloral ( $\text{CCl}_3\text{CHO}$ ) with reference to the possible hazards from inhalation of chloral as a vapor or a mist. This project was undertaken to determine what effect chloral has on the lungs and upper respiratory passages when inhaled, as well as its physiological effect when absorbed into the body. The method of determining chloral in the atmosphere is given in Appendix I.

I. Acute Exposures

Preliminary tests on rats were carried out to determine the acute effects of chloral vapors when inhaled. The results of these tests are summarized below:

<u>Date</u>	<u>No. Rats</u>	<u>Period of Exposure</u>	<u>Concentration</u>	<u>No. of Exposures</u>	<u>Results</u>
10-4-44	10	2 hours	406 p.p.m.	1	All rats died overnight of acute pulmonary edema.
10-6-44	2	2 hours	44 p.p.m.	1	1 rat died, 1 very ill of acute pulmonary edema.
10-9-44	2	2 hours	10 p.p.m.	5	Both rats survived but showed a great loss in weight. They were killed 4 days after the last treatment. There was no gross pathology at autopsy but one rat showed a trace of pulmonary edema on microscopic examination.
to 10-14-44					

II. Subacute Exposures

Ten rats were exposed to chloral vapors in concentrations around 10 p.p.m. for 2 hours daily\*. Seven out of the 10 died in from 2 to 12 treatments of acute pulmonary edema. The remaining 3 rats were killed 5 days after the 13th exposure and did not show any gross or microscopic pathology other than deposits of hemosiderin in the spleen of one rat, congestion in the liver of one rat and in the

\*A 2 hour exposure period was chosen in place of the usual 6 hour period due to the drastic effect of chloral.

kidneys of two other rats. During the experiment the rats showed a 10 to 14 per cent loss in weight during each 5 day (Monday through Friday) treatment period with a 5 to 6 per cent gain in weight over the week-end (rest period). Control rats kept under identical conditions gained weight steadily during both periods. The degree of exposure and the times at which death occurred are summarized below.

<u>Date</u>	<u>No. Rats</u>	<u>Exposure</u>	<u>Average Concentration in P.P.M.</u>	<u>Deaths</u>
10-16-44	10	1	11.2	
10-17-44	9	2	11.3	1
10-18-44	9	3	10.4	
10-19-44	9	4	10.6	
10-20-44	7	5	13.6	2
10-23-44	7	6	14.5	
10-24-44	7	7	11.8	
10-25-44	7	8	12.1	
10-26-44	6	9	14.2	1
10-27-44	6	10	13.4	
10-30-44	5	11	13.2	1
10-31-44	3	12	12.5	2
11-1 -44	3	13	14.3	
		<u>Average</u>	12.5	7

Experiments on Dogs

Dog 136A was exposed for 2-1/3 hours to an average concentration of chloral of 24 p.p.m. The maximum concentration attained was 45 p.p.m. This concentration produced an abnormal blood pressure (low systolic and diastolic pressure) which persisted for 24 hours. The second exposure of this dog occurred six days later when it inhaled an average concentration of 15 p.p.m. (maximum 31 p.p.m.) for one and three-quarters hours. The dog vomited after being in the chamber for an hour and continued to vomit after removal from the chamber. The pulse and respirations were slow, the respirations were labored, and the breath sounds noisy. The lower half of the abdomen was very full as if the muscle tonus of the abdominal wall was diminished. Again, the systolic and diastolic blood pressure dropped and remained low during the day of exposure and the day following exposure. By the second day the dog had developed severe pulmonary edema. It was placed in an oxygen-CO<sub>2</sub> mixture at 9:45 a.m. and in pure oxygen from 11:00 a.m. until 3:30 p.m. at which time oxygen therapy was discontinued. The respiratory rate was 80 per minute when the dog

was breathing oxygen and 180 per minute when breathing air. It died during the night, some 30 to 40 hours after the second exposure.

At autopsy the heart was dilated. The lungs were voluminous and mottled throughout. The darker portions resembled areas of congestion rather than hemorrhage. The bronchial mucosa was normal. Marked pulmonary edema was present. Microscopically the lungs showed edema and focal congestion. There was moderate emphysema, but no evidence of bronchitis. The heart, spleen, adrenals and pancreas were normal. The liver, kidney and brain were congested, but otherwise normal.

#### Dog 136B

This dog received its first exposure on 11-21-44 (first week of exposure, Table I) to an average concentration of 24 p.p.m. chloral (maximum 45 p.p.m.) for 2 hours and 20 minutes. The blood pressure readings taken immediately after the dog was removed from the chamber were not abnormal but both morning and afternoon readings the day following exposure were abnormal. There were no clinical signs of pulmonary edema, although the respiratory rate was 36 per minute (control 16), suggesting possible involvement of the lung.

The second exposure was on 11-27-44 (second week of exposure, Table I) when the dog inhaled an average concentration of 15 p.p.m. chloral (maximum 31 p.p.m.) for an hour and three-quarters. The dog had clinical signs of pulmonary edema on removal from the chamber. A watery discharge came from the nose (not edema fluid) and lacrimation was excessive. The respiratory rate was 48 (control 16). The following day, 11-28-44, the respiratory rate was still high (40 to 44) and the respirations were labored and noisy.

The third exposure to 3.7 to 7.2 p.p.m. (third week of exposure, Table I) for 2 hours was given on 12-4-44. The dog tolerated this concentration well and there was no respiratory disturbance or increase in respiratory rate.

Beginning 12-11-44 the dog was exposed two hours daily 5 days a week for two weeks (fourth and fifth weeks of exposure, Table I) to concentrations ranging between 2.6 and 7 p.p.m. These concentrations did not have any drastic effect on the circulation, but did produce irritation of the nose and upper respiratory passages. The blood pressure scores of this dog for the various exposure periods are given in Table I. The dog was autopsied on 12-28-44, six days after the last exposure. There was no gross or microscopic pathology noted.

Dog 136C

Dog 136C was never exposed to concentrations above 7.2 p.p.m. Its first exposure was on 12-4-44 (first week of exposure, Table I) for 2 hours to concentrations ranging between 3.7 to 7.2 p.p.m. The dog vomited just before removal from the chamber. The respirations were deep with expirations greatly prolonged, giving rise to typical asthmatic type of breathing. The eyes were irritated. The following day and for the remainder of the week the breath sounds remained noisy and bronchial in character and the dog coughed considerably. The respiratory rate was high. The circulation was abnormal during the week.

Its second exposure was on 12-11-44 (second week of exposure, Table I) when it inhaled for 2 hours concentrations ranging from 2.6 to 5.1 p.p.m. Asthmatic breathing was again noted when the dog was removed from the chamber and it is possible some edema was present in the lungs. The dog was exposed again on 12-13-44 and 12-14-44. The respiratory difficulty persisted.

The blood pressure scores were several times in the doubtful zone during the week in which these three exposures were given, but did not fall into the abnormal range (See Table I, second week's exposure). During the week of 12-18-44, the dog was exposed 2 hours daily for 5 days to concentrations ranging between 2.8 and 6.8 p.p.m. The respiratory rate was high after each exposure and the breath sounds were bronchial in character and excessively noisy. The dog's cough persisted during the week, and the blood pressure scores became definitely abnormal.

See Table I for the abnormal pulse pressure - diastolic pressure scores during the control and exposure periods. This dog was autopsied six days after the last exposure and did not show any gross or microscopic pathology.

The Effect of Chloral Inhalations on the Blood and Urine

No significant change was noted in the blood or urine of the three rats that survived thirteen 2 hour exposures to an average concentration of 12.5 p.p.m. chloral in the atmosphere.

Dogs 136B and C showed an appreciable rise in the red blood cells over the control values without a corresponding rise in hemoglobin. There was little change in the white blood cell count or differential.

Pulmonary edema produced by the administration of chloral does not produce a rise in blood platelets as has been found in pulmonary edema resulting from exposure to nitrous fumes.

TABLE I

Dog 136A

Period	No. Exams		No. Abn.	No. Expected Abnormal		*Ratio	No. Exposures During Week	Concentrations in P.P.M.	
	63	5		8	1			Average	Maximum
Control	63	5	2	8	1	0.25	1 (Tues.)	24	45
1st wks. exposure	4	4	3	1	1	2.00	1 (Mon.)	15	31
2nd "						3.00			

This dog died of acute pulmonary edema following the second exposure.

Dog 136B

Control	59	5	5	7	0.71	1 (Tues.)	24	45
1st wks. exposure	5	3	3	1	3.00	1 (Mon.)	15	31
2nd "	8	1	1	2	0.50	1 (Mon.)	3.7	7.2
3rd "	8	1	1	2	0.50	1 (Mon. - Fri.)	3.3	5.7
4th "	11	2	2	2	1.00	"	3.1	5.4
5th "	9	1	1	2	0.50	"		

Dog 136C

Control	77	7	7	9	0.77	1 (Mon.)	3.7	7.2
1st wks. exposure	8	4	4	2	2.00	3 (Mon., Wed. & Thurs.)	3.3	5.7
2nd "	9	0	0	2	0.00	5 (Mon. - Fri.)	3.1	5.4
3rd "	9	5	5	2	2.50			

\* The observed abnormal scores divided by the expected number of abnormal scores by chance alone in the given group gives a ratio which is abnormal if its value exceeds one.

- 5 -

Examination of the urine of dogs 136B and C did not reveal any abnormality of the excretory function of the kidney or gross damage to the urinary tract as a result of inhalation of chloral.

AJF:vem  
9-5-45

## APPENDIX I

### The Determination of Chloral in Air

Marjorie H. Morrison

For the quantitative estimation of chloral (trichloroacetaldehyde  $\text{CCl}_3\text{CHO}$ ) vapors in air, the colorimetric method of Fujiwara frequently used for compounds having three halogens was found satisfactory with slight modifications.

#### Collection of Sample

A measured volume of air containing chloral is passed slowly through two bubble tubes each containing 20 ml. of distilled water. The volume of sample taken depends upon the concentration. For a concentration of 5 p.p.m., a sample not less than 11 liters should be taken if the contents of the two collecting tubes are mixed and tested. However, as the amount of chloral in the second tube is negligible at this concentration, a 6 liter sample and testing of the first tube only is satisfactory. For a concentration of 100 p.p.m., a 5 liter sample may be taken and 20 ml. of the mixture of the two tubes diluted to 100 ml. and tested.

#### Testing of Sample

Of the aqueous solution to be tested (the sample from one tube, or a 1-1 mixture of the samples from the two tubes, or the diluted mixture) 5 ml. are added to a test tube containing 5 ml. of 35% NaOH in  $\text{H}_2\text{O}$  and 2 ml. of pyridine. A control tube is prepared containing 5 ml.  $\text{H}_2\text{O}$  instead of the test solution. The two tubes are placed in a water bath at  $85^\circ \text{C}$ . and shaken constantly and vigorously for 5 minutes, then cooled in running water for 3 minutes. To each tube, 10 ml. of 95% ethyl alcohol are added and mixed by shaking. When two layers have formed, not less than 10 cc. of the top layer is transferred by pipette to a colorimeter tube. With the 490 filter and the 10 cc. slit, the galvanometer of the Evelyn Photoelectric Colorimeter is set at 100 for the control tube. Replacing the control tube by the sample tube, the galvanometer reading is obtained.

A mechanical shaker was used consisting of a wire basket suspended from a cam on the shaft of a motor. It is important that the motor be run rapidly enough to produce thorough shaking as otherwise the color is not fully developed. It is also important that the level of the water and the temperature be constant. As the color is not stable but fades fairly rapidly, it is desirable that the time required for each manipulation be always the same. The following schedule was used:

- 0 - Time taken from completed preparation of control and sample tubes.
- 2 min. - Put in bath (2 min. are allowed for adjustment of temperature of bath)
- 7 min. - Remove from bath to running water, turn on colorimeter lamp.
- 10 min. - Remove from water.
- 15 min. - Read galvanometer (5 min. are allowed for adding alcohol, shaking, separating, transferring top layer, bubbles rising, setting galvanometer for control)

Several known solutions of chloral in water were prepared from the sample of chloral submitted by Grasselli Chemicals. Each was tested in duplicate by the above procedure and the galvanometer readings plotted against mg./ml. on the attached graph. From this curve, the mg./ml. corresponding to the galvanometer reading for an unknown sample may be obtained. From mg./ml., p.p.m. are calculated by multiplying by the dilution ratio if sample was diluted and by the number of ml. through which air was passed, dividing by the number of liters of air taken, and multiplying by 165.9 (conversion factor for mg./L to p.p.m. for compounds of mol. wt. 147.37).

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JHF

cc: H. M. Rosencrans - 5028 D  
J. C. Woodhouse - 4040 D

October 24, 1944

MR-136

Mr. A. H. Miller  
5044 Du Pont Building

Re: Chloral Toxicity

Mr. Rudolph Seiden of the Haver-Glover Laboratories, Kansas City, Missouri, has given us a literature reference dealing with the toxicity of chloral hydrate which, we believe, may be of interest to you in connection with our DDT operations. The reference is to an article by Prof. O. Gustav Nebele in his book entitled, "Handlet: Kon Der Tieraztlichen Praxis" (1938, Vol. 1, pg. 239). A free translation of this reference reads as follows: Chloral hydrate causes excitement, then collapse due to paralysis of heart and respiratory failure. . . . . Secondly, if in the blood, it contributes to its coagulation and, thus, to thrombosis . . . . .

S/ W. E. Gordon

W. E. GORDON

FILE

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

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

OFFICE OF  
PREVENTION, PESTICIDES AND  
TOXIC SUBSTANCES

APR 18 1995

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

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

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

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

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

Sincerely,

*Terry R. O'Bryan*

Terry R. O'Bryan  
Risk Analysis Branch

Enclosure

12016A



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**Triage of 8(e) Submissions**

Date sent to triage: APR 20 1995

NON-CAP

CAP

Submission number: 12016A

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**

<b>For Contractor Use Only</b>	
entire document: <u>0</u> 1 2 pages <u>1, 1st TAB</u>	pages <u>1, TABS</u>
Notes:	
Contractor reviewer: <u>POK</u>	Date: <u>3/29/95</u>

CECATS DATA: 10/2 - 12016 SEQ: A  
 Submission # BEHO: 10/2 - 12016

TYPE: INT 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 RATIONAL/F)  
 DISPOSITION:  
 (0639) REFER TO CHEMICAL SCREENING  
 (0678) CAP NOTICE

SUB DATE: 10/15/92 OTS DATE: 10/27/92 CSRAD DATE: 02/16/95

CHEMICAL NAME: \_\_\_\_\_

CAS# 75-87-6

VOLUNTARY ACTIONS:  
 (040) NO ACTION REPORTED  
 0402 STUDIES PLANNED/IN PROGRESS  
 0403 NOTIFICATION OF WORK REQUIRED  
 0404 LABEL/MSDS CHANGES  
 0405 PROCESS/HANDLING CHANGES  
 0406 APPAUSE DISCONTINUED  
 0407 PRODUCTION DISCONTINUED  
 0408 CONFIDENTIAL

INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C
0201 ONCO (HUMAN)	01 02 04	0216 EPI/CLIN	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 CHEM/PHYS PROP	01 02 04
0204 MUTA (IN VITRO)	01 02 04	0219 HUMAN EXPOS (MONITORING, ECO/AQUA TOX)	01 02 04	0244 CLASTO (IN VITRO)	01 02 04
0205 MUTA (IN VIVO)	01 02 04	0220 ECV/AQUA TOX	01 02 04	0245 CLASTO (ANIMAL)	01 02 04
0206 REPRO/ITERATO (HUMAN)	01 02 04	0221 ENV. OCCUR/EL/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 REQUEST DELAY	01 02 04	0248 PROD/USE/PROC	01 02 04
0209 NEURO (ANIMAL)	01 02 04	0224 PROD/COMP/CHEM ID	01 02 04	MSDS	01 02 04
0210 ACUTE TOX. (HUMAN)	01 02 04	0225 REPORTING RATIONALE	01 02 04	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 METAB/PHARMACO (ANIMAL)	01 02 04		
0215 CHRONIC TOX (ANIMAL)	01 02 04	0240 METAB/PHARMACO (HUMAN)	01 02 04		

TRIAZE DATA: NON-CBI INVENTORY ONGOING REVIEW: YES (DROP/REFER) SPECIES: RAT TOXICOLOGICAL CONCERN: LOW USE: \_\_\_\_\_ PRODUCTION: \_\_\_\_\_

CAS SR NO YES NO (CONTINUE)

TM TMMINI

MED HIGH

UNRECD

8(E) -12016A

H/H/H

ACUTE INHALATION TOXICITY IN RATS IS OF HIGH CONCERN BASED ON MORTALITY. DOSAGES (2-HOURS) AND MORTALITY DATA ARE AS FOLLOWS: 10 PPM (0/2); 44 PPM (1/2); AND 406 PPM (10/10). SIGNS OF TOXICITY INCLUDED SIGNIFICANT WEIGHT LOSS AND PULMONARY EDEMA.

SUBACUTE INHALATION TOXICITY IN RATS IS OF HIGH CONCERN DUE TO LETHALITY. 10 RATS WERE EXPOSED TO CHLORAL VAPORS IN CONCENTRATIONS AROUND 12.5 PPM FOR 2 HOURS DAILY FOR 13 DAYS. 7/10 RATS DIED FROM 2 TO 12 TREATMENTS OF PULMONARY EDEMA. THE REMAINING THREE RATS WERE SACRIFICED 5 DAYS AFTER THE LAST EXPOSURE AND DID NOT EXHIBIT ANY GROSS OR MICROSCOPIC PATHOLOGY OTHER THAN DEPOSITS OF HEMOSIDERIN IN THE SPLEEN OF ONE RAT, CONGESTION IN THE LIVER OF ONE RAT AND IN THE KIDNEYS OF TWO OTHER RATS. DURING THE EXPERIMENT THE RATS SHOWED A 10 TO 14% WEIGHT LOSS ON TREATMENT DAYS AND A 5 TO 6% WEIGHT GAIN ON THE WEEKEND REST DAYS.

SUBACUTE INHALATION TOXICITY IN DOGS IS OF HIGH CONCERN BASED ON MORTALITY. TWO DOGS (SEX AND BREED NOT INDICATED) WERE EXPOSED TO VARYING CONCENTRATIONS OF THE TEST SUBSTANCE, APPROXIMATELY 2 HOURS/WEEK FOR TWO OR MORE WEEKS. SIGNS OF TOXICITY FROM THE WEEK 1 EXPOSURE (24 PPM AVERAGE CONCENTRATION, MAXIMUM 45 PPM) WERE LOW OR ABNORMAL BLOOD PRESSURE AND A HIGH RESPIRATORY RATE. ONE DOG DIED APPROXIMATELY 30-40 HOURS AFTER THE WEEK 2 EXPOSURE (15 PPM AVERAGE CONCENTRATION, MAXIMUM 31 PPM); TOXIC SIGN DURING AND IMMEDIATELY AFTER LETHAL EXPOSURE WERE REPEATED VOMITING, SLOW PULSE, SLOW AND LABORED RESPIRATION, LOW BLOOD PRESSURE, NOISY BREATHING, DISTENDED ABDOMEN, AND PULMONARY EDEMA. SIGNS IN THE SURVIVOR WERE WATERY DISCHARGE FROM THE NOSE, PULMONARY EDEMA, LACRIMATION, AND ELEVATED RESPIRATORY RATE. THE SURVIVOR WAS EXPOSED ON WEEK 3 FOR 2 HOURS TO 3.7-7.2 PPM, WITH NO NOTED EFFECTS, FOLLOWED BY EXPOSURE FOR 2 HOURS/DAY, 5 DAYS/WEEK FOR 2 WEEKS TO 2.6 TO 6 PPM, WITH FINDINGS OF NOSE AND UPPER RESPIRATORY TRACT IRRITATION BUT NO GROSS OR MICROSCOPIC FINDINGS AT NECROPSY. A THIRD DOG WAS REPEATEDLY EXPOSED FOR 2-HOUR PERIODS TO CONCENTRATIONS RANGING FORM 2.6 TO 7.2 PPM. SIGNS OF TOXICITY INCLUDED VOMITING IN THE EXPOSURE CHAMBER, ASTHMATIC BREATHING, EYE IRRITATION, PERSISTENT COUGH, ASTHMATIC BREATHING, HIGH RESPIRATORY RATE, AND ABNORMAL BLOOD PRESSURE, WITH NO GROSS OR MICROSCOPIC FINDINGS AT NECROPSY.