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

008422

JUN 24 1991

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: Hydrogen Cyanamide - Submission of a 2-Year Drinking Water Carcinogenicity Study in Mice

TOX Chem. No.: 485A
Project No.: 0-1901
Submission No.: S381969

FROM: William B. Greear, M.P.H. William B. Greear 4/23/91
Review Section II
Toxicology Branch I
Health Effects Division (H7509C)

TO: Robert Ikeda, PM Team 23
Fungicide-Herbicide Branch
Registration Division (H7505C)

THRU: Marion P. Copley, D.V.M., Section Head Marion Copley 6/15/91
Review Section II
Toxicology Branch I
Health Effects Division (H7509C)

I. CONCLUSIONS

The mouse oncogenicity drinking water study has been classified Core-Supplementary. The sponsor should provide the following data/information in order to upgrade the study:

- Analytical chemistry data to verify the stability of the dosing solutions;

- An explanation why a female in each of the 200 and 600 ppm groups that were "borderline with granulosa-theca tumors" were excluded from the tumor analysis and why a female in the control group showing necrosis with an equivocal diagnosis of granulosa-theca tumor should be included in the analysis; and

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- Detailed historical control data on the incidence of granulosa-theca tumors in this strain of mouse used at Hazleton, UK.

II. REQUESTED ACTION

The Registration Division has submitted a Data Package Record Bean Sheet dated September 14, 1990 to Toxicology Branch I requesting that a mouse carcinogenicity study on hydrogen cyanamide be reviewed.

III. PRODUCT INFORMATION

Hydrogen cyanamide is a plant growth regulator which has been approved for use on grapes under several Section 18 Emergency Exemptions. It has properties similar to disulfiram (Antabuse®) which is used to treat chronic alcoholism. Its chemical structure is presented below:

$$N = C\text{-}NH_2$$

IV. REQUIREMENTS FOR TERRESTRIAL FOOD-USE (40 CFR 158.340)

Hydrogen Cyanamide, #485A
Updated: April 1991

Technical	Required	Satisfied
81-1 Acute Oral Toxicity	Y[1]	Y
81-2 Acute Dermal Toxicity	Y[1]	Y
81-3 Acute Inhalation Toxicity	Y[1]	Y
81-4 Primary Eye Irritation	Y[1]	Y
81-5 Primary Dermal Irritation	Y[1]	Y
81-6 Dermal Sensitization	Y[1]	Y
81-7 Acute Delayed Neurotoxicity (Hen)	N	-
82-1 Subchronic Oral (Rodent)	Y	N
82-1 Subchronic Oral (Nonrodent)	Y	Y[2]
82-2 21-Day Dermal	N	-
82-3 90-Day Dermal	N	-
82-4 90-Day Inhalation	N	-
82-5 90-Day Neurotoxicity (Hen)	N	-
82-5 90-Day Neurotoxicity (Mammal)	N	-
83-1 Chronic Toxicity (Rodent)	Y	N
83-1 Chronic Toxicity (Nonrodent)	Y	Y
83-2 Carcinogenicity (Rat)	Y	N
83-2 Carcinogenicity (Mouse)	Y	N
83-3 Developmental Toxicity (Rat)	Y	Y
83-3 Developmental Toxicity (Rabbit)	Y	N
83-4 Two-Generation Reproduction	Y	N
83-5 Chronic/Carcinogenicity	-	-
84-2 Mutagenicity - Gene Mutation	Y	Y
84-2 Mutagenicity - Structural Chromosomal Aberration	Y	Y
84-2 Mutagenicity - Other Genotoxic Effects	Y	Y
85-1 General Metabolism	Y	N
85-2 Dermal Penetration	N	-
86-1 Domestic Animal Safety	N	-

Y = Yes; N = No.

[1]Also required for end-use product. (Note: the technical is also the end-use product).

[2]The chronic study in the dog (#2319-121, 5/10/89) may be used to satisfy the requirement for a subchronic dog study.

V. TOXICOLOGY PROFILE

GUIDE#	CITATIONS	RESULTS
81-1	Acute oral LD50 Species: rat CIVO-Cen. Inst Nutr & Food Res Study#: 2949 WN ACC#1: 073726 Tox Cat. II Date: 2/7/73 CORE - MINIMUM DOC#s: 005681	LD50 = 0.285 (0.250 - 0.325) ml/kg. or approx. 300 mg/kg (based on 100% Cyanamid L500). Levels tested: 0.20, 0.25, 0.30, and 0.35 ml/kg (gavage).
81-2	Acute Dermal LD50 Species: rabbit Hazleton Study#: 23129-122 MRID: 412888-01 Tox Cat. II Date: 2/9/88 CORE - ACCEPTABLE DOC#s: 008150	Doses: 1, 2.5 & 4 mg/kg. Route: dermal in str NZW. LD50 (M) = 850 mg/kg (1.7 ml/kg). 95% CL 1.1-2.7 ml/kg LD50 (F) = 1.4 ml/kg (700 mg/kg a.i.). 95% CL = 0.9-2.2 ml/kg.
81-3	Acute inhalation LC50 Species: rat CIVO-Cen. Inst Nutr & Food Res Study#: R 4083 ACC#1: 073726 Tox Cat. II Date: 5/73 CORE - MINIMUM DOC#s: 005681	LC50 > 2.0 mg/L/4 hrs. Level tested: 2.0 mg/L.
81-4	Primary eye irritation Species: rabbit CIVO-Cen. Inst Nutr & Food Res Study#: R 4398 ACC#1: 073726 Tox. Cat. II Date: 6/74 CORE - MINIMUM DOC#s: 005681	Slight corneal opacity. All displayed slight conjunctivitis on day 7.
81-5	Primary dermal irritation Species: rabbit Central Inst Voedingsonderzoek Study#: B82-006-4 ACC#1: Tox Cat. I Date: 1982 CORE - MINIMUM DOC#s: 005681	Corrosive at up to 7 days (end of test).
81-6	Dermal sensitization Species: guinea pig CIVO-Cen. Inst Nutr & Food Res Study#: V 82.096/220063 ACC#1: 073726 Date: 3/82 CORE - GUIDELINE DOC#s: 005681	The test material is a strong sensitizer.

GUIDE#	CITATIONS	RESULTS
82-1(a)	Feeding-3 month Species: rat CIVO-Cen. Inst Nutr & Food Res Study#: R 4595 ACC#1: 073727 Date: 1/75 CORE - SUPPLEMENTARY DOC#s: 005681	NOEL = 20 ppm. LEL = 60 ppm (histological changes in the thyroid). Levels tested: 20, 60, & 180 ppm in Wistar strain
82-1(b)	Feeding-3 month Species: dog TNO Study#: V82.084/210694 MRID: 413905-01 Date: 7/22/81 CORE - SUPPLEMENTARY DOC#s: 008150	Doses: 1.2, 4 & 12 mg/kg/day. Route: oral (by gavage) in beagle. NOEL < 1.2 mg/kg/d. LEL = 1.2 mg/kg/d. based on decr. HGB and HCT in males, decr. reticulocytes and thrombocytes, incr. monocytes in females, decr T3, decr T4 in males, slight incr. of mononuclear inflammatory cells in the parotid salivary gland, reduced spermatogenesis, atrophic seminiferous tubules, incr. cellular debris within the lumen of epididymal ducts and reduced spermatocytes. Most of these were magnified in animals at the higher dose levels. Additional signs observed were salivation prior to dosing, redness of the buccal mucosa, decr. body wt. decr. RBC, incr. cholesterol, decr. absolute and relative testes wt., testicular atrophy with giant cells, proliferation of testicular interstitial cells, and epididymitis.
83-1(a)	Feeding/oncogenic-2 year Species: rat National Cancer Inst. Study#: 79-1719 ACC#1: 073727 Date: 1979 CORE - MINIMUM DOC#s: 005681 008162	Levels tested at 100 & 200 ppm in F344 str. Onco NOEL > 200 ppm (HDT). Letter (May 4, 1987) in reference to conference April 4, 1987. The agreement reached in conference decided the NCI rat & mouse bioassays for calcium cyanamide were acceptable studies.
83-1(a)	Oncogenicity Species: mice National Cancer Inst. Study#: 79-1719 ACC#1: Date: 1979 CORE - SUPPLEMENTARY DOC#s: 005681 008150 008162	Levels tested at 500 & 2000 ppm in B6C3F1 str. Oncogenic NOEL > 2000 ppm. The conversion data, Calcium cyanamide ---> Hydrogen cyanamide, allows upgrading to minimum. - 11/9/90.
83-1(b)	Feeding-1 year Species: dog Hazleton Study#: 2319-121 ACC#1: Date: 5/10/89 CORE - GUIDELINE DOC#s: 008150	Doses: 0.4, 2.0 and 10 mg/kg/day (these dose were half as large during the 1st 2 weeks). Route: oral(by gavage) in strain beagle. NOEL = 0.4 mg/kg/day (0.2 mg/kg/day a.i.). LEL = 2.0 mg/kg/day based on decr. body wt. gains, decr. MCV and MCH, pale areas of the spleen. In addition, at 10.0 mg/kg/day there was a decrease in the relative weight of the thyroid-parathyroid in females, incr in brown pigment within Kupffer cells, small stones in the gall bladder, extramedullary hematopoiesis in the spleen, thymic atrophy, inflammation of the testes and decr. spermatogenic activity.
83-2	Oncogenicity - Species: mice Hazleton Study #: 6001-556/3 MRID: 415655-02 Doc#s:	Doses: 70, 200 and 700 ppm in water (M: 9.9, 27.1 and 73.6 mg/kg/day, F: 13.8, 33.8 and 98.0 mg/kg/day) NOEL = 70 ppm (M: 9.9 mg/kg/day; F: 13.8 mg/kg/day). LEL = 200 ppm (M: 27.1 mg/kg/day, F: 33.8 mg/kg/day) - increased mortality in females, increased urinary bladder and kidney lesions. In addition, at 200 ppm there were decreased in male body wt gain and increases in ovarian granulosa-theca tumors and ovarian adenoma/

GUIDE#	CITATIONS	RESULTS
83-3(a)	Developmental Toxicity Study Species: rat Hazleton Study#: 2339-124 MRID: 412888-06 Date: 5/2/89 CORE - Supplementary DOC#s: 008150	Doses: 10, 30 & 90 mg/kg/day; route oral (by gavage). Strain Crl:CDBR. Maternal NOEL < 10 mg/kg. Maternal LEL = 10 mg/kg (decr. body wt. gain). Developmental Tox NOEL = 30 mg/kg. Develop. Tox LEL = 90 mg/kg (based on increase in number of resorptions., decr. fetl body wt., incr in diaphramagtic hernia and wavy (bent) ribs>
83-3(b)	Developmental Toxicity Study Species: rabbit CIVO-Cen. Inst Nutr & Food Res Study#: V 84.4414/240171 ACC#1: 073727 Date: 11/84 CORE - GUIDELINE DOC#s: 005681	NOEL (developmental) = 12 mg/kg; LEL (developmental) = 36 mg/kg Maternal NOEL = 4 mg/kg; Maternal LEL = 12 mg/kg; A/D ratio = 0.33 Levels tested by gavage in N.Z. White: 4, 12 & 36 mg/kg
84-2(a)	Mutagenic-Ames Species: salmonella Hazleton Study#: 9583-0-401 MRID: 403896-08 Date: 10/21/87 CORE - ACCEPTABLE DOC#s: 006628	Doses: 0.10, 0.25, 0.5, 1, 5, 10 and 15 uL/plate in salmonella strains TA1535, TA1537, TA1538, TA98, and TA100. Results: negative.
84-2(b)	Mut- Chrom. aberr. in vitro Species: CHO cells Hazleton Study#: 9583-0-437 ACC#1: Date: 10/21/87 CORE - ACCEPTABLE DOC#s: 006628	Doses: 42.4, 56.5, 141 and 424 ug/ml (w/o activation); 32.1, 42.8, 438, 875, 1310 and 1750 ug/ml with activ. Results: Negative.
84-4	Mutagenic-unscheduled DNA synt Species: rat hepatocytes Hazleton Study#: 9583-447 MRID: 403896-07 Date: 10/21/87 CORE - ACCEPTABLE DOC#s: 006628	Doses: 5.95, 11.9, 23.8, 47.6, 71.4, 95.2, 143 & 190 ug/ml in F344 rat hepatocytes. Results: Negative.

VI. DATA GAPS FOR TERRESTRIAL FOOD-USE:

82-1 90-Day Subchronic Oral - Rodent
83-1 Chronic Toxicity - Rodent
83-2 Carcinogenicity - Rat
82-2 Carcinogenicity - Mouse
83-4 Two-Generation Reproduction
85-1 General Metabolism
83-3 Developmental Toxicity - Rabbit

VII. ACTION TAKEN TO REMOVE DATA GAPS AND OBTAIN ADDITIONAL INFORMATION

The sponsor is herein informed of the additional studies (data gaps) required for a terrestrial food-use.

VIII. REFERENCE DOSE (RfD)

A reference dose has not been established because of the absence of acceptable data.

IX. PENDING REGULATORY ACTIONS

None at present that TB-I is aware of.

X. TOXICOLOGIC ISSUES

A. The mouse drinking-water carcinogenicity study (#6001-556/3; May 3, 1990) is inadequate. The following data/information must be submitted in order to upgrade it to an acceptable study.

1. Analytical chemistry data to verify the stability of the dosing solutions should be submitted.

2. The sponsor should explain why one female in each of the 200 and 600 ppm groups that were diagnosed "borderline with granulosa-theca tumors" were excluded from the tumor analysis and why the female in the control group showing necrosis with an equivocal diagnosis of granulosa-theca tumor should be included in the analysis.

3. Historical control data on the incidence of granulosa-theca tumors in this strain of mouse used at Hazleton, UK, should be submitted. Each study should be separately reported with the duration of dosing, year of study, etc.

B. A two-generation reproduction study (#B84-1475; October 1986) was submitted in 1987. An evaluation of this study could not be completed because of several deficiencies (see memorandum of W. Greear dated November 30, 1987). The deficiencies are:

1. A missing page (#69).

2. Individual litter data were not submitted. Individual data on weight gain, etc., were not submitted.

3. The results of the gross necropsies of moribund pups and pups with physical behavioral abnormalities were not submitted.

4. It was unclear whether the test material was hydrogen cyanamide or calcium cyanamide.

5. The analytical concentration of the test material in the diet is questionable since the method of analysis ("spectrophotometric") was stated to be "not very specific." On analysis of the control diet, it was found that it contained 12 ppm of the test material. Obviously, there is the possibility of making large errors concerning dietary concentration of the test material. Concerning stability of the test material in the diet, it was stated ". . . that the concentrations both after a 7-day and a 17-day storage period at -20 °C were not altered in a way that could be measured with the method available." This requires an explanation if the study is to be used to support future actions.

NOTE: It is recommended that this memorandum be forwarded to the sponsor in its entirety.

cc: Kocialski (H7509C)
Chow (H7509C)

008422

EPA No.: 68D80056
DYNAMAC No.: 340-A
TASK No.: 3-40A
March 28, 1991

DATA EVALUATION RECORD

HYDROGEN CYANAMIDE

Oncogenicity Drinking Water Study in Mice

APPROVED BY:

Robert J. Weir, Ph.D.
Program Manager
Dynamac Corporation

Signature: William J. McClanahan for

Date: March 28, 1991

EPA No.: 68D80056
DYNAMAC No.: 340-A
TASK No.: 3-40A
March 28, 1991

DATA EVALUATION RECORD

HYDROGEN CYANAMIDE

Oncogenicity Drinking Water Study in Mice

REVIEWED BY:

Pia Lindström, DPH
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Signature: [signature]
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Signature: [signature]
Date: 4/16/91

DATA EVALUATION RECORD

GUIDELINE § 83-2

STUDY TYPE: Oncogenicity drinking water study in mice.

MRID NUMBER: 415665-02.

TEST MATERIAL: Hydrogen cyanamide.

SYNONYMS: Amidocyanogen, cyanamide, cyanogenamide, carbodiimide, carbamonitrile, carbimide, cyanogen nitride.

STUDY NUMBER: 6001-556/3.

SPONSOR: SKW Trostberg AG., Trostberg, Germany.

TESTING FACILITY: Hazleton UK, North Yorkshire, England.

TITLE OF REPORT: Hydrogen Cyanamide, up to 104 Week Oral (Drinking Water) Carcinogenicity Study in the Mouse.

AUTHOR: M.J. Goodyer.

REPORT ISSUED: May 3, 1990.

CONCLUSIONS: Hydrogen cyanamide was administered in the drinking water to groups of 60 CD-1 mice/sex for 100 weeks to males and for 104 weeks to females at levels of 0, 70, 200, or 600 ppm (for males: 0, 9.9, 27.1, and 73.6 mg/kg/day, respectively; for females: 0, 13.8, 33.8, and 98.0 mg/kg/day, respectively). Compound-induced oncogenicity was observed in females at 200 and 600 ppm as evidenced by increased incidences of ovarian granulosa-theca tumors (significant at 600 ppm). At 600 ppm, an MTD was achieved as evidenced by significantly decreased body weight gain in males and survival rate (Kaplan-Meier) in females. In addition, increased incidences of urinary bladder and kidney lesions in both sexes and ovarian stromal/luteal hyperplasia in females were observed at this dose level. At 200 ppm, only a nonsignificantly increased incidence of urinary bladder and kidney lesions and a nonsignificantly decreased survival rate (Kaplan-Meier) in females were observed. Based on these results, the NOEL and LOEL for systemic toxicity were 70 and 200 ppm, respectively.

Core Classification: This study is Supplementary. The study does not satisfy the requirement for a guideline series 83-1 Oncogenicity study in mice as specified in the discussion section. The study may be upgraded after submission of data on stability of dosing solutions, data for clinical signs and palpable masses for individual animals, and historical laboratory control data on ovarian granulosa-theca tumors.

A. MATERIALS:

1. Test Compound: Hydrogen cyanamide; description: colorless 50% aqueous solution; batch numbers 150586, 031286, 062987, and 200188; purity: approximately 50%.

2. Test Animals: Species: mouse; strain: Crl:CD-1(ICR)BR; age: approximately 6 weeks at start of study; weight: males--range 18.5-35.7 g, females--range 17.8-30.7 g at start of study; source: Charles River (UK) Ltd., Margate, England.

B. STUDY DESIGN:

1. Animal Assignment: Animals were acclimated to laboratory conditions for 18 days and were randomly assigned by sex (based on body weight) to the following test groups:

Test group	Dose in water (ppm)	Main study (up to 24 months) Males	Females
1 Control	0	60	60
2 Low	70	60	60
3 Mid	200	60	60
4 High	600	60	60

Mice were housed three/cage in a temperature-controlled room (19-25°C) with a minimum of 15 air changes/hour. A 12-hour dark/light cycle was maintained (light from 6 a.m. to 6 p.m.). Humidity ranged from 40 to 70%.

Dose levels were selected based on the results of a pilot study. However, no results were reported from that pilot study.

2. Preparation of Dosing Solutions: The sponsor supplied five batches of the test article in 50% aqueous solution. Fresh solutions of the test article for each dose group were prepared weekly in filtered tapwater and stored at room temperature. Each day, a fresh solution was given to the mice. Samples to determine the concentration of the test material in water were collected from all dose groups and kept frozen until time of analysis. Samples were taken during weeks 1, 13, 26, 39, 52, 65, 78, 91, and 104. Stability was determined in the dose range-finding study (HUK Proj. No. 556/2).

   Results: Analyses of the sponsor-supplied solutions indicated a mean value of 49.9% (range 49.0-50.3) of the active ingredient (w/w). Concentrations of the dosing solutions ranged from 93 to 117% of nominal concentrations. The author stated that stability at room temperature for at least 7 days was confirmed on samples from the dose range-finding study. However, no data were submitted to enable the reviewers to verify this statement.

3. Food and Water Consumption: Animals received food (SQC Rat and Mouse Maintenance Diet No. 1, Expanded Ground Fine) and water ad libitum.

4. Statistics: The following procedures were utilized in analyzing the numerical data: ANOVA followed by a t-test--body weight gain, food and water consumption, and organ weights; Kaplan-Meier technique--survival

probability; and Log-rank method (Peto et al., 1980)--ovarian granulosa-theca tumors.

5. Quality Assurance: A quality assurance statement was signed and dated May 2, 1990.

C. METHODS AND RESULTS:

1. Observations: Animals were observed twice daily for moribundity and mortality and once daily for clinical signs of toxicity. Once a week the animals were given a thorough clinical examination.

Results: Table 1 presents selected data on mortality and percent survival. During week 52, accidental death occurred in one high-dose male, one low-dose female, and two mid-dose females; during week 100, accidental death occurred in one control and one low-dose male (no details were reported). In males, no treatment-related effects were observed in mortality/morbidity; at termination, the percent survival was 37, 38, 43, and 37% in the control, 70-, 200-, and 600-ppm dose groups, respectively. About two-thirds of the males died from nonneoplastic conditions such as amyloidosis and urogenital tract lesions. In females, mortality/morbidity increased during the second year at 200 and 600 ppm (significantly different from controls at 600 ppm). About half of the females died from various types of neoplasia, but no particular neoplasia was more common than others. At termination, the percent survival for females was 40, 33, 23, and 23% in the control, 70-, 200-, and 600-ppm dose groups, respectively.

No treatment-related clinical signs of toxicity or palpable masses were observed. Summary and/or individual animal data (to verify these statements) were not submitted.

2. Body Weight: Body weight was recorded weekly for the first 16 weeks. Thereafter, it was recorded once every 4 weeks throughout the study and at termination.

Results: Table 2 summarizes selected data on mean body weight gain. Among males during the first study week, 2 control and 16 high-dose animals lost weight (data not shown); of these, 1 control and 3 high-dose animals continued to lose weight during the second week. Among females during the first study week, 7 control and 12 high-dose animals lost weight (data not shown); of these, one control and 1 high-dose animal continued to lose weight during the second week. Body weight gain for males was significantly below controls during weeks 0-6 at 70 ppm ($p < 0.01$), at 200 ppm ($p < 0.01$), and at 600 ppm ($p < 0.001$);

TABLE 1. Cumulative Mortality and Percent Survival in Mice Administered Hydrogen Cyanamide in the Drinking Water for up to 2 Years[a,b]

Level in Drinking Water (ppm)	Cumulative Mortality and (Percent Survival) at Week: 52	76	100/104[c]
	Males		
0	5 (92)	14 (77)	38 (37)
70	2 (97)	12 (80)	37 (38)
200	3 (95)	12 (80)	34 (43)
600	7 (88)	18 (70)	38 (37)
	Females		
0	3 (95)	7 (88)	36 (40)
70	5 (92)	13 (78)	40 (33)
200	6 (90)	14 (77)	46 (23)
600	7 (88)	18 (70)	46* (23)

[a]Data were extracted from Study No. 6001-556/3, Table 1.

[b]Percent survival was based on 60 mice/sex/dose.

[c]Males and females were sacrificed at weeks 100 and 104, respectively.

*Significantly different from control ($p < 0.05$) using a pairwise test when data on mortality were analyzed by the Kaplan-Meir method.

TABLE 2. Mean Body Weight Gain at Representative Intervals in Mice Administered Hydrogen Cyanamide in the Drinking Water for up to 2 Years[a]

Level in Drinking Water (ppm)	Body Weight Gain (g ± S.D.) for Weeks:				
	0 - 6	6 - 16	16 - 28	28 - 52	52 - 100[b]
			Males		
0	6.6 ± 2.4	3.0 ± 1.9	2.1 ± 1.4	2.8 ± 2.1	-1.8 ± 3.7
70	5.5 ± 1.4** (83)[c]	2.4 ± 1.9 (80)	2.5 ± 1.6 (119)	1.7 ± 4.2 (61)	-1.3 ± 4.0
200	5.4 ± 2.1** (82)	3.1 ± 1.4 (103)	2.0 ± 2.0 (95)	2.4 ± 2.4 (86)	-0.8 ± 3.1
600	4.8 ± 2.1*** (73)	2.8 ± 1.9 (93)	1.6 ± 1.0* (76)	0.8 ± 3.2** (29)	-2.4 ± 4.2
			Females		
0	5.1 ± 1.4	3.0 ± 2.2	2.2 ± 2.3	3.0 ± 2.6	1.9 ± 2.8
70	4.7 ± 1.8 (92)	2.8 ± 1.4 (93)	1.9 ± 1.9 (86)	3.0 ± 2.7 (100)	2.0 ± 4.9 (105)
200	4.4 ± 1.5* (86)	2.8 ± 1.8 (93)	1.8 ± 2.1 (82)	2.7 ± 2.4 (90)	1.9 ± 6.3 (100)
600	3.8 ± 2.3*** (75)	3.0 ± 2.2 (100)	1.2 ± 2.0 (55)	2.7 ± 2.2 (90)	2.3 ± 3.1 (121)

[a]Data were extracted from study No. 6001-556/3, Table 2.2.

[b]For males, weeks 52-100; for females, weeks 52-104.

[c]Weight gain as percent of control.

*Significantly different from control ($p < 0.05$).

**Significantly different from control ($p < 0.01$).

***Significantly different from control ($p < 0.001$).

during weeks 16-28 at 600 ppm ($p < 0.05$); and during weeks 28-52 at 600 ppm ($p < 0.01$). At termination, surviving high-dose males had gained 62% of the weight gain observed in control males. Body weight gain for females was significantly below controls during weeks 0-6 at 200 ppm ($p < 0.05$) and 600 ppm ($p < 0.001$). At termination, surviving high-dose females had gained 90% of the weight gain observed in control females. No differences were observed in body weight gain between control and treated males and females during the second year.

3. Food Consumption: Food consumption was recorded weekly for the first 16 weeks. Thereafter, it was recorded once every 4 weeks throughout the study.

   Results: Table 3 summarizes selected data on mean cage food consumption. During weeks 1-72, food consumption for treated males was slightly less than controls; however, the decrease never exceeded 6%, but was statistically significant ($p < 0.05$) at 200 and 600 ppm during weeks 1-6 (data not shown). No differences were observed between treated and control males after week 72. During weeks 1-60, food consumption for mid- and high-dose females was slightly less than controls; however, the decrease never exceeded 7%, but was statistically significant ($p < 0.05$) at 200 and 600 ppm during weeks 24-28. No differences were observed between treated and control females after week 60. Food consumption for low-dose females was comparable to or higher than controls throughout the study. These reductions were considered to be slight; overall, the food intake was satisfactory in all groups. With the exception of high-dose males during week one, no differences among groups were noted in food efficiency. The decreased food efficiency in high-dose males during week one (control 5.8% versus high-dose group 1.9%) was considered to be a result of the decreased body weight in this group.

4. Water and Test Compound Intake: Water consumption was recorded weekly for the first 16 weeks. Thereafter, it was recorded once every 4 weeks throughout the study.

   Results: Table 4 summarizes selected data on mean cage water consumption. In males, significant ($p < 0.01$ or 0.001) reductions were observed at 200 ppm during weeks 1-6 (14%) and at 600 ppm during weeks 1-6 (20%) and 13-16 (22%). In females, significant ($p < 0.01$ or 0.001) reductions were observed at 200 ppm (10, 14, and 17% for weeks 1-6, 13-16, and 24-28, respectively) and at 600 ppm (22, 23, and 20% for weeks 1-6, 13-16, and 24-28, respectively). Water consumption for low-dose animals was comparable to or higher than controls throughout the study. Although water consumption was reduced in a dose-related

TABLE 3. Mean Cage Food Consumption in Mice Administered Hydrogen Cyanamide in the Drinking Water for up to 2 Years[a]

Level in Drinking Water (ppm)	Food Consumption (g/animal/week ± S.D.) for Weeks:				
	1 - 6	13 - 16	24 - 28	48 - 52	96 - 100[b]
			Males		
0	39.8 ± 2.6	39.7 ± 2.2	39.4 ± 2.8	36.5 ± 4.3	37.5 ± 4.6
70	38.7 ± 2.6	38.2 ± 3.0	37.1 ± 3.3	35.0 ± 3.6	37.5 ± 4.3
200	37.8 ± 2.5*	38.5 ± 3.3	38.5 ± 5.2	36.4 ± 3.2	35.4 ± 3.9
600	38.1 ± 1.5*	38.7 ± 2.8	37.6 ± 2.2	35.9 ± 4.5	35.6 ± 5.7
			Females		
0	41.5 ± 3.1	43.8 ± 3.5	43.1 ± 3.5	37.9 ± 3.5	37.7 ± 7.5
70	41.1 ± 3.0	44.9 ± 4.1	42.7 ± 3.1	38.1 ± 3.7	42.1 ± 10.1
200	40.3 ± 2.6	42.3 ± 4.3	40.7 ± 3.4*	35.8 ± 2.9	42.0 ± 7.6
600	39.7 ± 3.9	42.0 ± 5.1	40.3 ± 3.9*	35.8 ± 4.1	36.2 ± 5.6

[a]Data were extracted from study No. 6001-556/3, Table 3.2.

[b]Last period measured for females was weeks 100-104.

*Significantly different from control ($p < 0.05$).

TABLE 4. Mean Cage Water Consumption in Mice Administered Hydrogen Cyanamide in the Drinking Water for up to 2 Years[a]

Level in Drinking Water (ppm)	Water Consumption (g/animal/week ± S.D.) for Weeks: 1 - 6	13 - 16	24 - 28	48 - 52	96 - 100[b]
			Males		
0	39.6 ± 7.5	38.1 ± 9.3	39.6 ± 11.0	38.0 ± 9.5	43.2 ± 17.4
70	38.7 ± 6.5	37.3 ± 8.4	38.5 ± 7.4	43.2 ± 12.8	41.9 ± 11.3
200	34.1 ± 4.8**	33.5 ± 9.9	38.6 ± 14.2	39.5 ± 11.1	37.5 ± 10.1
600	31.5 ± 4.4***	29.6 ± 12.3**	32.0 ± 10.7	37.9 ± 14.6	33.5 ± 19.5
			Females		
0	37.9 ± 3.5	39.2 ± 5.6	47.3 ± 7.9	47.7 ± 10.3	44.7 ± 14.9
70	37.7 ± 2.5	38.5 ± 5.2	45.6 ± 9.0	44.8 ± 7.4	58.7 ± 33.7
200	34.0 ± 3.2***	33.8 ± 6.2**	39.1 ± 6.8***	42.9 ± 7.6	41.9 ± 17.2
600	29.7 ± 3.9***	30.2 ± 4.7***	37.7 ± 6.0***	40.2 ± 10.3	39.8 ± 10.7

[a]Data were extracted from study No. 6001-556/3, Table 4.2.

[b]Last period measured for females was weeks 100-104.

**Significantly different from control ($p < 0.01$).

***Significantly different from control ($p < 0.001$).

manner in both sexes (which sometimes reached statistical significance in the mid- and high-dose groups) and may have been due to a palatability problem, overall it was considered to be satisfactory.

Table 5 summarizes test compound intake for selected weeks. Mean test compound intake was 9.9 (8.4-12.9), 27.1 (24.3-34.7), and 73.6 (59.1-92.2) mg/kg/day for males and 13.8 (11.0-16.4), 33.8 (26.8-43.5), and 98.0 (77.9-124.2) for females in the 70-, 200-, and 600-ppm dose groups, respectively.

5. Ophthalmological Examinations: No ophthalmologic examinations were reported.

6. Hematology and Clinical Chemistry: Total white cell counts were performed on blood samples from all surviving animals in week 52, from all surviving males in week 100, and from all surviving females in week 104. Blood smears were also prepared to determine the differential white blood cell count for control and high-dose animals in weeks 52, 100, and 104, and whenever possible, for moribund animals. No clinical chemistry was performed.

   Results: No differences were observed in total and differential white blood cell counts between control and high-dose animals. Therefore, the counts for the low- and mid-dose groups were not determined.

7. Urinalysis: No urinalysis results were reported.

8. Sacrifice and Pathology: All animals that died, were sacrificed *in extremis* during the study, and were sacrificed at termination were necropsied. CHECKED (X) tissues were collected for histological examination. In addition, from 10 animals per sex per group the (XX) organs were weighed:

TABLE 5. Mean Cage Compound Consumption for Selected Weeks in Mice Administered Hydrogen Cyanide in the Drinking Water for up to 2 Years[a]

Level in Drinking Water (ppm)	Compound Consumption (mg/kg/day) for Week: 1	20	40	60	80
			Males		
0	0	0	0	0	0
70	12.9	9.4	9.4	9.2	9.1
200	34.7	24.3	27.3	24.7	27.3
600	92.2	60.6	75.3	72.9	67.9
			Females		
0	0	0	0	0	0
70	16.4	13.7	12.6	11.5	11.4
200	43.5	33.1	34.8	32.4	30.0
600	112.9	98.1	107.3	113.8	77.9

[a]Data were extracted from study No. 6001-556/3, Table 5.

Digestive System	Cardiovasc./Hemat.	Neurologic
Tongue	X Aorta, dorsal	XX Brain
X Salivary glands†	X Heart†	X Peripheral nerve (sciatic nerve)†
X Esophagus†	X Bone marrow†	X Spinal cord (3 levels)
X Stomach†	X Lymph nodes†	X Pituitary†
X Duodenum†	X Spleen	X Eyes, optic nerve
X Jejunum†	X Thymus	X Sciatic nerve
X Ileum†		
X Cecum†		
X Colon†		
X Rectum	Urogenital	Glandular
XX Liver†	XX Kidneys†	X Adrenals†
X Gallbladder†	X Urinary bladder†	Lacrimal gland
X Pancreas†	XX Testes†	X Mammary glands†
	X Epididymides	X Thyroids (with parathyroids)†
	X Prostate gland	Harderian glands
	X Seminal vesicles	
Respiratory	X Ovaries	
X Trachea†	X Uterus	
X Lungs†	Cervix	Other
		X Femur with articular surface†
		X Skeletal muscle†
		X Skin
		X All gross lesions
		Larynx
		Ribs/costochondral junction
		Skull
		X Sternum

Samples of all available tissues for all animals in the control and high-dose groups and for decedent animals in the low- and mid-dose groups were examined histologically. For other animals, gross lesions and masses, lungs, liver, kidneys, thyroids, and urinary bladder were examined histologically.

Results:

a. Organ weights: Slight increases were observed in high-dose males in relative (to body weight) testes (10%) and brain (13%) weight. The increase was significant ($p < 0.05$) for brain weight but not for testes weight. No changes on the mean absolute weight of these organs was observed, however.

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†Recommended by Subdivision F (October 1982) Guidelines.

b. Gross pathology: No remarkable findings were observed. Findings were either single events or occurred in all dose groups, and therefore, were not considered to be treatment-related.

c. Microscopic pathology: Table 6 summarizes the most frequently observed nonneoplastic lesions, Table 7 summarizes incidence and severity of kidney and urinary bladder changes, and Table 8 summarizes malignant and benign neoplastic lesions. All tables include animals sacrificed at termination, as well as those that died or were sacrificed moribund during the study.

1) Nonneoplastic: Incidences of chronic cystitis in the urinary bladder were increased in a dose-related manner in both males and females at 200 and 600 ppm (for males 9, 13, 30, and 68% and for females 10, 15, 42, and 64% in the 0, 70-, 200-, and 600-ppm dose groups, respectively). The severity of the finding also increased, predominantly in the high-dose groups (Table 7). The incidences of atrophic/basophilic tubules in the kidneys were marginally increased in males (62 versus 47% in controls) and females (43 versus 33% in controls) at 600 ppm, and the severity of the finding was somewhat greater in the high-dose groups than in other groups. Vacuolar degeneration in the kidney was also increased at 200 ppm (0 and 5% in controls versus 20.6 and 15.5% in exposed males and females, respectively) (Table 7). All other microscopic nonneoplastic findings were reported to be within the normal range of background pathology in mice of this strain and age and occurred with similar frequencies in all dose groups.

Amyloidosis occurred with similar frequency in control and treated animals as evidenced by the summary of 'organ by organ' data. No dose-or sex-related patterns were observed and incidences were not unusually high for this strain of mice.

2) Neoplastic: Neoplasms in the lung and hemolymphoreticular system in both sexes, in the liver in males, and in the reproductive system in females were the most frequently observed tumors (Table 8). However, no dose relationships were noted. Neoplasms in the lung occurred with similar frequencies in both sexes in all dose groups, while neoplasms in the liver in the males decreased with increasing dose (which was attributed to the

TABLE 6. Selected Nonneoplastic Lesions in Mice Administered Hydrogen Cyanamide in the Drinking Water for up to 2 Years[a]

Organ/Finding	Level in Drinking Water (ppm)							
	Males				Females			
	0	70	200	600	0	70	200	600
Kidney	(59)[b]	(59)	(59)	(58)	(60)	(60)	(59)	(58)
Cyst(s)	13	15	9	7	12	5	4	5
Pigment	1	2	3	1	6	4	3	1
Leukocyte foci	24	30	29	19	30	32	22	24
Fibrosis/scarring	1	1	1	7	0	1	1	6
Atrophic/basophilic tubules	28	28	29	36	20	19	15	25
Tubular dilation	8	11	12	8	8	6	9	15
Granular cast	1	0	2	6	1	0	2	5
Vacuolar degeneration/necrosis	0	1	5	12	3	1	5	9
Glomerulonephritis/nephropathy	6	5	4	2	12	16	18	9
Hyaline droplets	1	0	1	1	4	2	7	6
Hydronephrosis	10	13	5	6	1	5	3	4
Pyelitis	1	4	3	0	4	3	1	6
Mineralization	2	1	2	2	0	0	3	0
Ovary	(0)	(0)	(0)	(0)	(60)	(59)	(60)	(58)
Stromal/luteal hyperplasia	0	0	0	0	16	13	13	22
Cysts	0	0	0	0	49	49	46	43
Urinary Bladder	(56)	(56)	(57)	(57)	(59)	(54)	(55)	(56)
Chronic cystitis	5	7	17	39	6	8	23	36
Leucocyte foci	9	10	8	4	20	20	7	5
Congestion/hemorrhage	6	7	2	2	0	0	0	0
Colloid plug	1	2	1	5	1	0	0	0
Urothelial hyperplasia	6	0	0	0	0	0	1	0

[a]Data were extracted from study No. 6001-556/3, Table 8.7.

[b]Indicates the number of tissues examined.

TABLE 7. Incidence and Severity of Selected Kidney and Urinary Bladder Changes in Mice Administered Hydrogen Cyanamide in the Drinking Water for up to Two Years[a]

Organ/Finding	Dietary Level (ppm)							
	Males				Females			
	0	70	200	600	0	70	200	600
Kidney	(59)[b]	(59)	(59)	(58)	(60)	(60)	(59)	(58)
Atrophic/basophilic tubules								
Minimal	22	19	25	16	16	14	12	15
Slight	4	9	4	12	4	5	3	6
Moderate	2	0	0	5	0	0	0	3
Moderate to Severe	0	0	0	3	0	0	0	1
Total	28	28	29	36	20	19	15	25
Urinary Bladder	(56)	(56)	(57)	(57)	(59)	(54)	(55)	(56)
Chronic cystitis								
Minimal	3	4	11	18	6	8	18	16
Slight	0	2	6	10	0	0	5	16
Moderate	2	1	0	11	0	0	0	4
Total	5	7	17	39	6	8	23	36

[a]Data were extracted from study No. 6001-556/3, page 27.

[b]Indicates the number of tissues examined.

TABLE 8. Selected Neoplastic Lesions in Mice Administered Hydrogen Cyanamide in the Drinking Water for up to 2 Years[a,b]

Organ/Finding	Dietary Level (ppm)							
	Males				Females			
	0	70	200	600	0	70	200	600
Hemolymphoreticular	(9)[c]	(4)	(6)	(10)	(13)	(15)	(19)	(16)
Lymphoma mixed	2	1	0	2	2	4	6	3
Lymphoma lymphocytic	4	2	3	4	7	6	12	11
Leukemia	1	0	0	1	3	0	0	0
Liver	(59)	(57)	(57)	(58)	(60)	(59)	(55)	(57)
Adenoma	10	1	4	2	0	0	0	0
Carcinoma	6	10	3	6	0	0	1	1
Carcinoma/adenoma	2	0	0	0	0	0	0	0
Lung	(58)	(60)	(58)	(60)	(60)	(60)	(60)	(59)
Adenoma	19	18	14	19	13	9	16	10
Carcinoma	3	3	3	7	2	2	2	2
Ovary	(0)	(0)	(0)	(0)	(60)	(60)	(60)	(58)
Granulosa-theca tumor	0	0	0	0	3[d]	1	6[e]	8[e]
Papillary adenoma	0	0	0	0	6	0	4	2

[a]Data were extracted from study No. 6001-556/3, Table 8.10.

[b]Metastatic tumours are not tabulated.

[c]Indicates the number of tissues examined.

[d]One lesion was necrotic and the diagnosis was equivocal.

[e]Excludes one animal diagnosed as "borderline with granulosa-theca tumor".

significant reduction in body weight gain (see Reviewers' Conclusions for further discussion). The incidences of ovarian granulosa-theca tumors were increased above controls at 200 and 600 ppm. The ovary in one control animal was necrotic and the diagnosis was, therefore, equivocal. If this animal was excluded, the increased frequency at 600 ppm was statistically significant ($p < 0.05$). The study author excluded two females (one at 200 and one at 600 ppm) diagnosed "borderline with granulosa-theca tumors" (see Reviewers' Conclusions for further discussion).

D. STUDY AUTHOR'S CONCLUSIONS:

Treatment with hydrogen cyanamide (administered in the drinking water to groups of 60 CD-1 mice at nominal concentrations of 0, 70, 200, and 600 ppm for 100 weeks to males and for 104 weeks to females) decreased the female survival rate at 200 and 600 ppm, decreased the male body weight gain at 600 ppm, and increased the incidence of urinary bladder and kidney lesions in both sexes at 200 and/or 600 ppm. No treatment-related effects were observed at 70 ppm; this, therefore, was considered a NOEL. At 200 ppm, no changes were observed in the tumor profile, although systemic toxicity was sometimes evident.

A maximum tolerated dose (MTD) was exceeded at the high-dose level as evidenced by the magnitude of the reduced body weight gain in males and survival rates in females as well as the histopathologic findings in the urinary bladder and kidney in both sexes. Treatment-related changes in the tumor profile at this dose level included a decreased number of males with liver tumors and an increased number of females with ovarian granulosa-theca tumors. The decreased number of liver tumors was considered to be a secondary effect of reduced body weight gain. Because the MTD was exceeded, the significance of the granulosa-theca tumors is complicated to assess; "it is unreasonable to include the changes in tumor profile in the evaluation of the test article." Consequently, the incidence and morphology of tumors in this test system were considered unaffected by hydrogen cyanamide treatment.

E. REVIEWERS' DISCUSSION AND INTERPRETATION OF RESULTS:

In general, the data reporting was acceptable and the summary means that were validated were supported by the individual animal data. However, a Tissue Inventory Tabulation would have been useful. This would have facilitated the evaluation of autolyzed tissues and possible effects of the severity of autolysis on the histopathologic evaluation.

The following study deficiencies were noted: Concentrations of the dosing solutions varied from 93 to 117% of nominal; this is outside the commonly accepted range of ±10%. Analytical chemistry data to verify stability of the dosing solutions were not reported. No individual animal data were submitted for clinical signs of toxicity and palpable masses. No historical control data from U.K. were submitted. This above missing information should be submitted.

The reviewers agree with the study author's conclusions with the following exceptions: First, an MTD was achieved at 600 ppm as evidenced by decreased body weight gain in males, increased mortality in females, and increased incidences of urinary bladder and kidney lesions in both sexes. The MTD was, however, not exceeded. Second, the reviewers consider the increased incidences of ovarian granulosa-theca tumors to be a compound-related effect. No trend for decreased latency of the tumors was observed; 19/20 animals with granulosa-theca tumors died during week 78 or later, and the tumor was considered to be the cause of demise in only one animal. However, two females (one mid-dose and one high-dose animal) were excluded without an explanation from the study author's calculations. These animals were diagnosed "borderline with granulosa-theca tumors," and when included along with the necrotic control animal, they further strengthen the significance of these tumors (3/60, 1/59, 7/60, and 9/58 tumors diagnosed in the control, 70-, 200-, and 600-ppm dose groups, respectively). An explanation is needed for this discrepancy in diagnosing ovarian granulosa-theca tumors. In addition, a comparison of these tumor incidences with historical control data from Hazleton, US (overall total 6/293), revealed that they indeed were elevated and should be compared with historical control data from Hazleton, UK.

Third, the reviewers noted increased incidences in both sexes of kidney fibrosis/scarring and granular casts at 600 ppm and kidney vacuolar degeneration/necrosis at 200 and 600 ppm and in females of ovarian stromal/luteal hyperplasia at 600 ppm. The reviewers support the study author's conclusion that the decreased incidence of liver neoplasms with increased dose of hydrogen cyanamide in high-dose males, is due to decreased body weight gain. It is a common observation that mice age faster (i.e., neoplasms increase faster) with increasing body weight.

Thus, the reviewers concluded that an MTD was achieved at 600 ppm and that at 200 and 600 ppm, compound-related increases in ovarian granulosa-theca tumors were observed. Based on increased incidences of urinary bladder and kidney lesions in both sexes at 200 and 600 ppm and ovarian stromal/luteal hyperplasia in females at 600 ppm, decreased body weight gain in males at 600 ppm, the NOEL and LOEL for systemic toxicity were 70 and 200 ppm, respectively.

APPENDIX A

Written or oral warning must be given to workers who are expected to be in treated area or in an area about to be treated with this product. Specific oral warning will inform workers of areas or fields that may not be entered without specific protective clothing, period of time before entering field must be calculated and appropriate action to take in case of accidental exposure. When oral warnings are given, warnings shall be given in a language customarily understood by workers. Oral warning must be given of there is reason to believe that written warnings cannot be understood by workers. Written warnings must include the following information: **DANGER** - Area treated with Dormex (hydrogen cyanimide) on (date of application).

Preharvest Interval: 110 days

Effective Date: December 1, 1992

Expiration Date: February 15, 1992

Other Requirements:

1. All mixing and loading will be carried out in a closed system. Mixers and loaders will wear long-sleeved shirt, long-legged pants or coveralls, chemically-resistant boots and gloves, chemically resistant apron, NIOSH/MSHA approved organic vapor/dust-fume-mist respirator, goggles. A full face respirator may be substituted for goggles.

2. Applicants will be made with ground spray rig with closed cab and low pressure nozzle. Applicators will wear long-sleeved shirt, long-legged pants or coveralls, chemically-resistant boots and gloves, NIOSH/MSHA approved organic vapor/dust-fume-mist respirator, goggles. A full face respirator may substitute for goggles. A respirator and goggles will not be required if the closed cab is equipped with activated charcoal air-intake filters. If the applicator leaves cab to perform repairs or adjustments, the person must wear the above cited respirator and eye protection.

3. No person shall be within 100 yards of the application vehicle or mixing/loading site unless wearing a long-sleeved shirt, long-legged pants or coveralls, chemically-resistant boots and gloves. NIOSH/MSHA approved organic vapor/dust-fume-mist respirator, goggles, A full face respirator may substitute for goggles.

4. Any person who will be working or entering within 100 yards of the application vehicle and/or the mixing/loading site must be given verbal notification that alcoholic beverages may not be consumed immediately before, during or 24 hours after exposure.

5. To avoid possible exposure to the endangered Coachella Valley fringe-toed lizard in the vineyards located within boundaries of the Coachella Valley Preserve, applications may not be made within 50 feet of the boundary of the Coachella Valley Preserve along the southern boundary of the vineyard; no applications will be made when wind velocity exceeds 5 miles per hour; and the manager of the Coachella Valley Preserve will be notified a minimum of 24 hours prior to application.

6. Do not apply this product in such a manner as to directly or through drift expose workers or other persons. The area being treated must be vacated by unprotected persons.

7. A maximum of 18,800 acres of table grapes in the Coachella Valley of Riverside County, a maximum of 800 acres of table grapes in the Cadiz Valley of San Bernardino County and a maximum of 270 acres of table grapes in the Coachella Valley of Imperial Valley may be treated.

8. Applications made in accordance with the above provisions are not expected to result in residues of hydrogen cyanamide in or on grapes in excess of 0.1 ppm. The USEPA has determined that this level is adequate to protect the public health.

Analytical methodology is available from Dietary Exposure Branch, HED (H7509C), EPA, 401 M. Street, S.W., Washington, D.C. 20460. The Food and Drug Administration, DHHS, has been advised of this action.

9. Only nonionic surfactants cleared for use on growing crops under 40 CFR 180.1001 may be used as a spray additive as described under "Frequency/Timing of Application".

All applicable directions, restrictions, and precautions on the USEPA registered label and this label must be followed.

This labeling must be in the possession of the user at the time of pesticide application.

The Department shall be immediately informed of any adverse effects resulting from the use of this exemption.

Please note: The USEPA expects concerned growers or grower groups to work toward the registration of use patterns that may be needed on a continuing basis. It will, therefore, be necessary to require applicants wishing to renew emergency exemptions to provide a progress report on residue tolerance and registration along with requests for reissuance of an emergency exemption renewals. Without substantial progress in pursuing a tolerance and registration for the use in question, it will be difficult to obtain an emergency exemption for a another season. The pesticide manufacturer or Western Region IR-4 may be contacted regarding the initiation of a pesticide petition for residue tolerance.

A final report must be submitted by the county agricultural commissioner to Pesticide Registration, Department of Pesticide Regulation, within 45 days of the expiration date of this exemption. This report must include the following information:

a. Amount of product used.
b. Units (i.e., acres, trees, cattle) treated.
c. Number of applications.
d. Estimate of effectiveness.
e. Any adverse effects noted.

Prior to use under this exemption, a permit must be obtained from the county agricultural commissioner. The permit shall state the maximum amount of

13544

009508

Chemical:	**Cyanamide**
PC Code:	**014002**
HED File Code	**16000 Water Assessment Reviews**
Memo Date:	**06/24/91**
File ID:	**TX008422**
Accession Number:	**412-02-0004**

HED Records Reference Center
10/01/2001