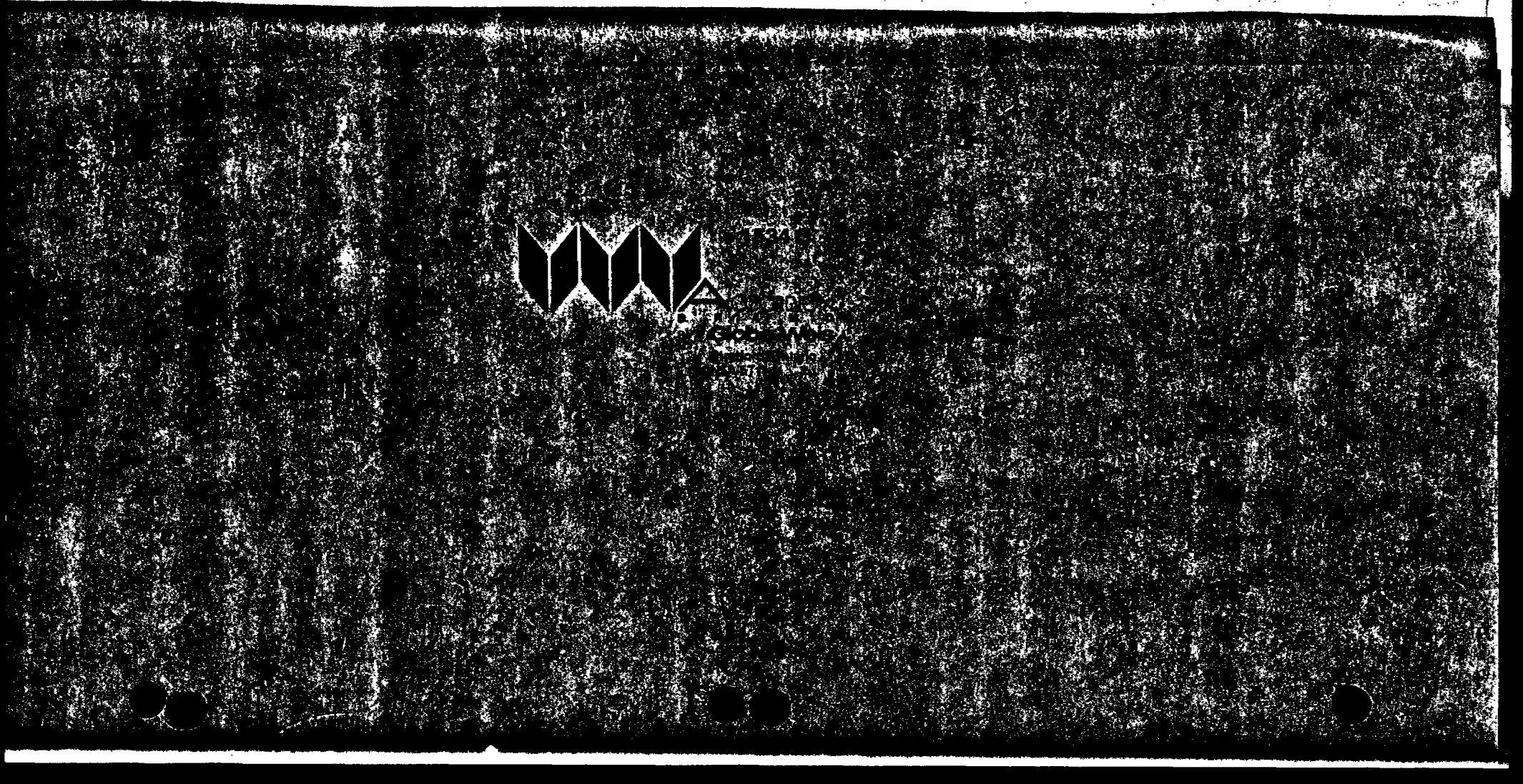

Toxicology
Files

Vinyl Resin VYEE

4

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UNION CARBIDE **INTERNAL CORRESPONDENCE**

UNION CARBIDE CORPORATION 39 OLD RIDGEBURY ROAD, DANBURY, CT 06817-0001

RECEIVED

JUL 16 1985

M. R. HUFFMAN

To (Name) Dr. J. E. McKeon
Division
Location
Area

Date July 9, 1985
Originating Dept HS&EA
Area P-2

Copy to Dr. W. F. Gorham
Dr. D. L. Heywood
Mr. M. R. Huffman

Subject UCAR(Tm) Resin VYEE

Dear Dr. McKeon:

I have reviewed the physical and chemical properties of UCAR(Tm) Resin VYEE, a vinyl chloride-vinyl acetate hydroxyl modified copolymer, with the bjective of preparing a Health Effects Statement by analogy to similar materials. In this case I cannot trace a material having a sufficiently close structure, and of known toxicity, to allow a credible comparison and extrapolation of health hazard data.

I recommend that UCAR(Tm) Resin VYEE be subjected to the following toxicity tests:

Acute peroral, percutaneous and saturated vapor studies
Primary skin and eye irritancy
Ames bacterial mutagenicity assay

Sincerely yours,

Bryan Ballantyne, M.D., D.Sc., Ph.D.
Director of Applied Toxicology

BB/rjk

UCC
049556

UNION CARBIDE

INTERNAL CORRESPONDENCE

HEALTH, SAFETY & ENVIRONMENTAL AFFAIRS

P-2
39 Old Ridgebury Road
Danbury, CT 06817-0001

TO: R. C. Wise

DATE: July 23, 1986

COPY: Dr. B. Ballantyne
Mr. M. R. Huffman
Dr. R. W. Tyl

SUBJECT: UCAR VINYL RESIN VYEE

Dick:

Enclosed is a preamble to the protocol:

> Reproductive Toxicity Evaluation of Generic UCAR Vinyl Resin VYEE Administered in the Feed to the CD Sprague-Dawley) Rat

this, upon your approval, will be given to Alison Kerester in Mr. Conner's office for submission to the EPA. Please let me know if you have any questions or comments.

Sincerely,

Tipton R. Tyler, Ph.D., D.A.B.T.
Assistant Director Applied Toxicology

RECEIVED
JUL 23 1986
M. R. HUFFMAN

TRT:jmc
Enclosure

UCC
049557

PROPOSAL FOR INVESTIGATING THE POTENTIAL FOR VYEE
TO CAUSE ADVERSE POSTNATAL EFFECTS IN ANIMALS

In order to alleviate the Agency's concern over the possible postnatal toxic effects of UCAR Vinyl Resin, VYEE, Union Carbide is proposing to conduct a reproductive toxicity evaluation. The Agency's concern is based upon the results of a reproduction range-finding study in rats on a chlorinated paraffin of intermediate chain length and containing 52% by weight chlorine. In that study there was no evidence of treatment related toxicity to the parental animals, nor was there any evidence of adverse effects on the measured reproductive indicies in the treated animals. There was, however, a profound effect, at the highest dosage level employed (6250 ppm in feed), on pup survival from lactation day 10 and onward. In fact, there was complete mortality of all pups in this dosage level group. The results of that study clearly demonstrate that the intermediate chain length, 52% chlorinated paraffin does not express reproductive toxicity, but does exhibit potential for postnatal toxicity. Based upon what the Agency believes to be a chemical structural analogy, therefore, a suspicion exists that UCAR Vinyl Resin VYEE, may exhibit some similar toxicological activity.

Union Carbide is proposing to conduct a study of similar design to that conducted at the International Research and Development Corporation (IRDC) under sponsorship of the Chlorinated Paraffins Industry Association (CPIA). Since that study was sufficient to identify the postnatal toxic potential of the chlorinated paraffin, it seems reasonable to assume that a study of similar design would be sufficient to define the postnatal toxic potential of the VYEE resin. In addition, certain modifications have been made in the companies proposal based upon experience and information gained from the CPIA study. Thus, the number of animals per group has been increased to improve the sensitivity of the assay, and the postpartum time decreased, since the toxic effect is manifest well within the 21-day lactation period. These modifications both improve the design of the study within the scope of the defined toxic effect, and increase the cost effectiveness of the hazard assessment program. The salient features of Union Carbide's proposal, along with the side-by-side comparison with the CPIA study design are shown in Table 1.

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The study proposed by Union Carbide offers the following advantages over that of conducting a traditional 2-generation reproductive study as pointed below.

1. The postnatal toxicity evaluation is more cost effective than conducting a 2-generation reproductive study. Since the specific toxic concern has been identified a priori, it seems justified to design the study in the most cost effective manner to address the specific concern. The proposed study will answer the question of whether or not UCAR Vinyl Resin expresses potential postnatal toxicity and can be conducted for about one-half the cost of a 2-generation oral reproductive study.

2. Decreasing the cost of testing will result in the ability for the product to support the testing program within a shorter time interval. Therefore, the testing would be initiated at an earlier stage in the products life and this would allow for more rapid data collection and hazard evaluation.

In summary, Union Carbide is proposing to conduct a reproductive toxicity evaluation in rats in order to alleviate the Agency's concerns on possible toxic effects of UCAR Vinyl Resin VYEE. This study will address and r solve the issue of postnatal toxicity which has arisen from the Agency's belief that there is a chemical structural analogy between the PMN material and chlorinated paraffins. The study is cost effective and, therefore, the product will support the testing in a shorter time period then if a full 2-generation reproductive toxicity test were required. Pending the possibility that additional data become available on the chlorinated paraffins which might clarify the postnatal toxic response and could be used to modify the protocol for the testing, Union Carbide's proposal would appear to address and answer the Agency's concerns on UCAR Vinyl Resin VYEE.

Tipton R. Tyler, Ph.D., D.A.B.T.
Assistant Director Applied Toxicology

TRT:jmc
0695E

TABLE 1: COMPARISON OF UNION CARBIDE PROPOSED STUDY AND CPIA REPRODUCTION RANGE FINDING STUDY

UNION CARBIDE PROPOSED STUDY ON VYEE	CHLORINATED PARAFFIN (52% CHLORINE, INTERMEDIATE CHAIN LENGTH)
Sprague Dawley rats [Crl:CD^{R}(SD)BR].	COBs CD rats.
25 females/dosage group. 1 male mated with 1 female.	10 females/dosage group. 1 male mated with 2 females.
6-weeks of age at start of dosing.	12-weeks at start of dosing.
Test material to be administered orally in diet.	Test material administered orally in diet.
Dosing to commence 6-weeks prior to mating.	Dosing commenced 14-days prior to mating.
Parental observations will include: clinical condition, weekly body weight (including gestation and postpartum period for females), food consumption, complete gross necropsey on sacrifice (both males and females). Selected tissues fixed for possible histological examination.	Parental observations included: clinical condition, weekly body weight (including gestation and postpartum period for females), food consumption, estrous cycle determination.
Progency observations will include: clinical condition, mortality (litter size), external examination, necropsy on abnormal or dead pups.	Progency observations included: clinical condition, litter size, external examination, necropsy on abnormal or dead pups.
Study terminated at day-21-postpartum. Full gross necropsy on 10 pups/sex per dosage level.	Study terminated 10-weeks postpartum. At day-21 postpartum, 10 pups/sex per dosage level subjected to full necropsy. At 10-weeks postpartum, 10 female and 5 male rats subjected to full necropsy. Hematology conducted. Selected tissues fixed for possible histological examination.

UNION CARBIDE CORPORATION 39 OLD RIDGEBURY ROAD, DANBURY, CT 06817-0001
LAW DEPARTMENT

September 8, 1987

Ms. Jeralene Green (A-101)
Freedom of Information
U.S. Environmental Protection Agency
401 M Street, S. W.
Washington, D.C. 20460

Re: Freedom of Information Act Request

Dear Ms. Green:

Pursuant to the Freedom of Information Act, 5 U.S.C. § 522, and EPA's implementing regulations, 40 C.F.R. Part 2, I hereby request a copy of the following document:

> A study submitted by Imperial Chemical Industries PLC to EPA about October 1986 entitled "Chlorinated Paraffin (52% Chlorination of Intermediate Chain Length N-Paraffins): Reproductive Study of the Haemorrhagic Effects in Offspring Rats".

I understand that this study was submitted to EPA in connection with (but possibly not as a formal part of) a negotiated testing agreement under Section 4 of the Toxic Substances Control Act ("TSCA") with the Consortium of Chlorinated Paraffins Manufacturers, described at 47 Fed. Reg. 1017 (Jan. 8, 1982). This study is not referenced in the index to the docket for that testing agreement.

I further understand that the submitter may have asked EPA to keep the study confidential. Section 14(b) of TSCA provides that the statute's provision on protection from disclosure of data, Section 14(a),

> does not prohibit the disclosure of - (A) any health and safety study which is submitted under this Act with respect to - (i) any chemical substance or mixture which, on the date on which such study is to be disclosed has been offered for commercial distribution. . . .

This study is a "health and safety study" on a chemical which "has been offered for commercial distribution", and hence is not subject to TSCA's protections from disclosure.

Moreover, under 40 C.F.R. § 2.306, a health and safety study such as this is subject to mandatory disclosure notwithstanding claims of confidentiality, because "health and safety data are not eligible for confidential treatment". 40 C.F.R § 2.306(g). That section applies because (i) the study was submitted in connection with a testing agreement under Section 4 of TSCA, and (ii) the study was subject to mandatory submission under Section 8(d) of TSCA (chlorinated paraffins were included in the first 8(d) list; see 40 C.F.R. § 716.120(c)). 40 C.F.R. § 2.306(b). Thus, the study was not "voluntarily submitted". 40 C.F.R. § 2.306(g).

You make take this letter as assurance that I will pay whatever fee is assessed for complying with this request, up to $50.00.

I look forward to receiving a response within 10 days of your receipt of this letter.

Thank you for your assistance.

Sincerely,

Mark N. Duvall

Mark N. Duvall

MND:mm

bcc: T. R. Tyler
R. C. Wise

PRIVELEGED

DOCUMENT

Bates number UCC049563–04 96 08 has been skipped

CAT/SOT 1985 - 108

DATE: December 18, 1985

SUBJECT: UCAR SOLUTION VINYL VYEE: Significance of Acute Toxicity and Primary Irritancy Studies. BRRC Project Report 48-169: Draft dated December 4, 1985.

INTERPRETATION

Acute Peroral Toxicity

Due to its high viscosity, UCAR Solution Vinyl VYEE had t be diluted with dimethyl sulfoxide (DMSO) to make a solution (50% w/v) suitable for dosing perorally. Aqueous vehicles and vegetable oil were found to be unsuitable as diluents. The solution in DMSO was administered by gavage to groups of 5 male and 5 female rats at a dose of 8.0 g VYEE/kg, which was the maximum achievable dose. There were neither deaths nor signs of toxicity during a 14 day postdosing observation period. Also, during this time there was a normal gain in weight.

Animals were sacrificed at the end of the observation period and subjected to necropsy. No gross pathological features were seen which could be related to dosing.

The above findings indicate that UCAR Solution Vinyl VYEE is of a low order of acute peroral toxicity.

Acute Percutaneous Toxicity

In order to determine the potential for systemic toxicity by absorption across the skin, UCAR Solution Vinyl VYEE was applied to the shaven trunk skin of groups containing 5 male and 5 female rabbits. The applied dose was 16.0 ml/kg, and the material was maintained in contact with the skin for 24 hours by means of an occlusive dressing. No animals died, and there were no signs of systemic toxicity during the contact peri d, or in a subsequent 2 week observation period. At necropsy, carried out immediately following sacrifice at the end of the observation period, there were no gross pathological features.

On removal of the occlusive dressing, erythema and edema were seen. In general, the erythema persisted for 7 to 14 days, and edema for one to 7 days. Desquamation was seen from the seventh to fourteenth day.

These findings indicate that UCAR Solution Vinyl VYEE is of a low order of acute percutaneous toxicity, but that sustained occlusive contact may result in the appearance of local signs of inflammation.

Acute Inhalation Toxicity

In order to determine the potential for adverse health effects by exposure to the vapor generated from UCAR Solution Vinyl VYEE at ambient temperature, groups of 5 male and 5 female rats were exposed for 6 hours to an atmosphere substantially saturated with vapor from the material. To achieve this atmosphere, samples of the material were introduced into the inhalation exposure chambers, and the vapor allowed to equilibrate overnight (c. 18 hours) at 24°C. The animals were then introduced into this test atmosphere.

Within 1.5 hours from the start of the exposure, the animals became ataxic, and, by 2.5 hours, became prostrated. Labored breathing was seen by 3.5 hours of exposure. On removal of the animals from the exposure chamber, they wer seen to have periocular wetness, slow breathing, and some loss of co-ordination of movement. No animals died, and there was recovery from these effects by one day. Animals gained weight during the 14 day postexposure period, and no further signs of irritation or toxicity were seen.

At necropsy, carried out immediately following sacrifice at the end of the observation period, no gross pathology was seen.

The above findings indicate that exposure to high vap r concentrations from UCAR Solution Vinyl VYEE at ambient temperature, may cause irritant effects in the eye and respiratory tract, from which recovery will occur.

Primary Skin Irritation

To determine the skin irritating effects of UCAR Solution Vinyl VYEE under standardized conditions, 0.5 ml of the material was applied to the shaven dorsal skin of each of 6 rabbits. The material was held in contact with the skin for 4 hours by means of an occlusive dressing. On removal of this dressing, there were no signs of local inflammation. At 24 hours, one animal showed a just detectable local redness, but no other signs of inflammation developed.

With the more demanding conditions of the acute percutaneous toxicity test, involving a more prolonged occluded contact (24 hours) with a substantially large amount of material (16 ml/kg), there developed erythema and edema.

The above findings indicate that UCAR Solution Vinyl VYEE is not irritant to the skin by close contact for a few hours, but very prolonged singled occluded contact may produce mild t moderate local inflammation.

Primary Eye Irritation

The eye irritating potential of UCAR Solution Vinyl VYEE was investigated by placing 0.1 ml of the material into the inferior conjunctival sac of one eye of each of 6 rabbits. This resulted in the development of a just detectable to mild conjunctivitis, as evidenced by excess redness and swelling of the conjunctiva. The effect was apparent by one hour, and healed by 2 days. There was no accompanying iritis or corneal injury.

The above results indicate that UCAR Solution Vinyl VYEE is a mild eye irritant.

In Summary: UCAR Solution Vinyl VYEE is of a low order of acute toxicity perorally and percutaneously, may be irritant and slightly toxic by exposure to high vapor concentrations generated at ambient temperature, marginally irritant to the skin, and mildly irritant to the eye.

IMPLICATIONS

1. Handling Hazards

Due to the physical properties of the material, it is extremely unlikely that UCAR Solution Vinyl VYEE could be swallowed. However, in the remote likelihood of this occurring, it is not expected that short-term adverse health effects will develop.

Contact with the skin for a few hours will not result in the development of any local signs of inflammation, but very prolonged single occluded contact may result in the development of mild local redness and swelling, but it is not anticipated that harmful amounts will be absorbed.

Exposure to moderately high vapor concentrations generated at ambient temperature may result in the development of signs and symptoms of irritation of the eye and respiratory tract.

Contamination of the eye will cause a mild conjunctivitis of a few days duration, but injury to the cornea is not expected.

2. Protective and Precautionary Measures

When UCAR Solution Vinyl VYEE is likely to be handled for prolonged periods, protective clothing should be worn.

Due to the irritant and possible toxic effects of vapor from UCAR Solution Vinyl VYEE at ambient temperature, places

where the material is handled should be well ventilated. If it is anticipated that high vapor concentrations will be encountered, then appropriate respiratory protective equipment should be worn.

When used in conditions where it is possible that the eyes could become contaminated, then eye protection should be worn.

3. First-Aid and Medical Considerations

In the unlikely event that UCAR Solution Vinyl VYEE has been swallowed, water should be given to drink and the advice of a physician sought.

Contaminated eyes should be flushed with water, and the washing continued for about 15 minutes. The advice of a physician should be sought.

If overexposure to the vapor occurs, remove to fresh air. If breathing is difficult, administer oxygen. Seek medical advice.

4. Product Safety Information

(A) Label: The acute toxicity and primary irritancy studies indicate a need for the following label statement for UCAR Solution Vinyl VYEE:

"Causes Eye Irritation
Harmful by Inhalation"

[NA. The extreme conditions needed to produce any skin irritation suggest that this does n t require precautionary label warning.]

(B) MSDS's and other forms of Product Safety Literature should draw attention to the following for UCAR Solution Vinyl VYEE:

(a) Acute Swallowing: Low toxicity. May cause mild nausea.

(b) Acute Skin Absorption: Toxicology studies indicate the absence of any significant short-term adverse health effects.

(c) Acute Inhalation: Exposure to high concentrations of vapor generated at ambient temperature may result in chest discomfort, cough, difficulty

		with breathing, and nasal discomfort and discharge.
(d)	Skin Contact:	Contact for a few hours may not result in the development of any local signs of inflammation. Sustained single contact of many hours may result in th development of local mild to moderate redness and swelling.
(e)	Eye Contact:	There may be mild discomf rt with the development of a slight conjunctivitis, seen as excess redness and swelling. Injury to the cornea is not expected. Vapor will cause discomfort, excess tear production and blinking.
(f)	Effects of Repeated Overexposure:	None known.
(g)	Emergency and First-Aid Procedure:	The considerations presented in item (3) should be mentioned.
(h)	Medical Conditions Aggravated:	None known.
(i)	Notes to Physician:	(i) Low acute toxicity. (ii) Mild irritant. (iii) No known antidote.

5. Health Hazards Manual Ratings

The following Health Hazards Manual Ratings are appropriate for UCAR Solution Vinyl VYEE:

Swallowing	= 1
Skin Penetration	= 1
Breathing	= 2
Irritation (Skin)	= 2
Irritation (Eye)	= 2

6. D.O.T. Considerations

(A) Skin: A 4 hour occluded contact with 0.5 ml of UCAR Solution Vinyl VYEE did not produce any inflammatory effects (erythema and edema) or necrosis in each of 6 rabbits. Therefore, the material is not a D.O.T. Corrosive material.

(B) Poison: The acute peroral LD_{50} (>8 g/kg) in rats, and acute percutaneous LD_{50} (>16.0 ml/kg) in rabbits are clearly in excess of those defining a D.O.T. Class B Poison. Also, a 6 hour exposure of rats to a substantially saturated vapor atmosphere from UCAR Solution Vinyl VYEE at ambient temperature produced irritant effects, but no mortalities. Therefore, UCAR Solution Vinyl VYEE is not a Class B Poison by breathing, swallowing or skin contact.

7. Health Effects Statement

[NB. The following brief nontechnical summary of the acute toxicology of UCAR Solution Vinyl VYEE, and its implications, may be of use for certain Product Literature purposes.]

UCAR Solution Vinyl VYEE is of a low order of acute toxicity by swallowing, and short-term adverse health effects are not expected from swallowing of the material on a single occasion.

Contact with skin for a few hours will not produce any local inflammatory effects. Sustained single contact of many hours may produce a local slight to moderate redness and swelling. It is not expected that such contact will result in the absorption of potentially harmful amounts of material.

Exposure to moderately high concentrations of the vapor generated at ambient temperature may result in mild irritant effects on the eye and respiratory tract. These will includ discomfort in the eye, with excess tear production and blinking, nasal discomfort and discharge, discomfort in the chest with cough, and possibly difficulty with breathing. For this reason, workplaces where UCAR Solution Vinyl VYEE is handled should be well ventilated.

Contamination of the eye will result in mild conjunctivitis, seen as excess redness and swelling of th conjunctiva. Injury to the cornea is not expected to occur.

Bryan Ballantyne, M.D., D.Sc., Ph.D.
Director of Applied Toxicology

BB/rr
0108s

Daniel Baugh Institute of Anatomy
Department of Anatomy
Office of the
Director and Chairman

Philadelphia, 19107
(215) 928-7820

May 21, 1986

Dr. Tipton R. Tyler
Union Carbide Corporation
Applied Toxicology
39 Old Ridgebury Rd.
P-2592
Danbury, CT 06817

Dear Tip:

Fascinating situation. Thank you for the opportunity to review it. I tried to be as brief and to the point as possible in my review without being telegraphic.

In my opinion, the CP group was very poorly served in its studies. Some of the problems I noticed were:

1) Animals aged while the laboratory cleaned up coccidiosis.
2) Infection breaks down the rabbits later on when they are pregnant.
3) Use of tap water instead of reverse osmosis or similar.
4) Pilots made with too few animals (coccidiosis status = ?, age = ?).
5) Credibility probably lost at Agency by obfuscation regarding animal status.
6) Dose level for entire study based on day 6 weight and thereby excess variability generated.
7) Loose use of terms "variations" and "genetic" effects with little if any relationship to developmental biology.

Enclosed is a copy of my brief review. Please call me if I have done violence to any point etc. Also, if I slighted a needed topic it can be revised upward.

Sincerely,

E. Marshall Johnson, Ph.D.
Professor and Chairman
Director, Daniel Baugh Institute

EMJ/rd

UNION CARBIDE CORPORATION OLD RIDGEBURY ROAD, DANBURY, CT 06817
Corporate Health, Safety and Environmental Affairs Department

CONTAINS CONFIDENTIAL BUSINESS INFORMATION

Via Federal Express

January 31, 1986

Document Control Officer
Office of Toxic Substances, TS-793
U.S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

Dear Sir:

With regard to:

Premanufacture Notification PMN P-85-1388;
Submitted by Union Carbide Corporation;
Currently under suspension of review period;

Enclosed is the report of the short term toxicology study on the PMN substance, identified as follows:

UCAR Solution Vinyl VYEE, Acute Toxicity and Primary Irritancy Studies; R. C. Myers, Bushy Run Research Center, Project Report 48-169.

It should be apparent from the test of the report that the toxicity studies were on a ketone solvent solution of the PMN substance, and that the toxicological results found may be largely attributable to the solvent. A sanitized copy will be forwarded for the public file as soon as possible.

Very truly yours,

D. L. Heywood

D. L. Heywood
Principal Technical Contact

DLH/cr
Enclosure

0788J

UCC
049615

UNION CARBIDE

BUSHY RUN RESEARCH CENTER

R. D. 4, Mellon Road, Export, Pennsylvania 15632 Telephone (412) 733-5200

PROJECT REPORT 48-169

TITLE: UCAR® Solution Vinyl VYEE
Acute Toxicity and Primary Irritancy Studies

AUTHOR: R. C. Myers

SPONSOR: W. F. Gorham
Specialty Chemicals Division
Union Carbide Corporation

DATE: December 27, 1985

BUSHY RUN RESEARCH CENTER
R. D. 4, Mellon Road, Export, Pennsylvania 15632 Telephone (412) 733-5200

UCC BUSINESS CONFIDENTIAL: Not to be released outside UCC without the written consent of the UCC-sponsoring Division HS&EA Manager.

Project Report 48-169
10 Pages
December 27, 1985

UCAR® Solution Vinyl VYEE

Acute Toxicity and Primary Irritancy Studies

Sponsor: Specialty Chemicals Division
Union Carbide Corporation

* * * * *

SUMMARY

Peroral, Rat (Fasted)
Males: 8.0 g/kg (of contained VYEE) killed 0 of 5; sample dosed as a 50% (w/v) dilution in DMSO.
Females: 8.0 g/kg (of contained VYEE) killed 0 of 5; sample dosed as a 50% (w/v) dilution in DMSO.

Percutaneous, Rabbit
Males: 16.0 ml/kg, killed 0 of 5; sample dosed as received.
Females: 16.0 ml/kg, killed 0 of 5; sample dosed as received.

Inhalation, Rat; Substantially Saturated Vapor (Static)
Males: 6.0 hours killed 0 of 5 (signs noted).
Females: 6.0 hours killed 0 of 5 (signs noted).

Skin Irritation, Rabbit (4-hr occluded)
Minor, transient erythema on 3 of 6 rabbits from 0.5 ml (reaction delayed on 2).

Eye Irritation, Rabbit
No corneal injury or iritis in any of 6 eyes, minor to moderate transient conjunctival irritation in 6 from 0.1 ml (all healed at 48 hours).

INTERPRETATION

UCAR® Solution Vinyl VYEE was no more than slightly toxic following its administration by single peroral intubation. It had an extremely low order of toxicity following single dermal application. A single static inhalation exposure to substantially saturated vapor produced no deaths, but signs of inhalation toxicity included respiratory distress, coordination loss and

Exposure to a statically-generated, substantially-saturated vapor produced no deaths after 6.0 hours of exposure. During the exposure, hypoactivity, ataxia, labored breathing and prostration were evident. Immediately after exposure, signs included periocular wetness, slow breathing (bradypnea), coordination loss and slow righting reflex. These signs possibly resulted from the ketone component of the solution. All animals recovered after one day. At necropsy, there were no remarkable gross lesions in any animal.

A 4-hour application of 0.5 ml of UCAR® VYEE to covered skin resulted in minor erythema on 3 of 6 rabbits. This reaction appeared on one animal at ne day, but was not evident on 2 others until 7 days. In each instance the irritation subsided by the subsequent examination. No edema was observed during the 10 days of observation.

In 6 of 6 rabbit eyes, 0.1 ml of UCAR® VYEE produced minor to moderate conjunctival irritation. After 24 hours, there was slight conjunctival redness in each eye. No irritation persisted in any of 6 eyes at 48 hours. No corneal injury or iritis developed in any eye from the 0.1 ml dose.

Reviewed and Approved by:

Roy C. Myers, B.S.
Study Director

Ronald S. Slesinski, Ph.D.
Assistant Director

Fred R. Frank, Ph.D.
Director

Acknowledgements:

Single Peroral Tests	Susan M. Christopher, B.S. Research Technologist
Percutaneous, Skin and Eye Irritation tests	Kathleen R. Hufford, AALAS Cert. II Technologist
	Nick S. Bellich, AALAS Cert. II Master Technologist
Inhalation Studies	David W. Fait, B.S., AALAS Cert II Master Technologist

WPC/fcw/0433Z-2; 12-04-85

Table 2

Dermal Application, Single Dose to Rabbits

Material: UCAR® Solution Vinyl VYEE — Sample No.: 48-257

Dosage, ml/kg	Dead/ Dosed	Days to Death	Weight, g ± S.D. 0 Day	7 Day	14 Day	Skin Irritation	Signs of Toxicity	Gross Path logy
Male Rabbits								
16.0	0/5	-	2806 ± 209	2800 ± 257	2917 ± 259	Sample residue at 1 through 14 days; edema at 1 through 7 days; erythema at 1 day persisting on 2 through 14 days; desquamation at 7 through 14 days.	None noted.	Nothing remarkable.
Female Rabbits								
16.0	0/5	-	2738 ± 159	2633 ± 246	2773 ± 181	Sample residue at 1 through 14 days; edema at 1 day; erythema at 1 day persisting on 2 at 7 days; desquamation at 7 through 14 days.	None noted.	Intestines f 1 filled with soft fecal material.

LD50s:

Males: 16.0 ml/kg killed 0 of 5; sample dosed as received.
Females: 16.0 ml/kg killed 0 of 5; sample dosed as received.

Table 4

Primary Skin Irritation - Rabbit

Material: UCAR® Solution Vinyl VYEF Sample No.: 48-257 Conditions: 0.5 ml dosed

	Date: 09-23-85	Date: 09-23-85	Date: 09-23-85	Date: 09-23-85	Date: 09-23-85	Date: 09-23-85
	Rabbit No.: 85-3275	Rabbit No.: 85-3276	Rabbit No.: 85-3277	Rabbit No.: 85-18806	Rabbit No.: 85-18810	Rabbit No.: 85-18815
	Sex: Male	Sex: Male	Sex: Male	Sex: Female	Sex: Female	Sex: Female

Erythema & Eschar Formation

Time (After Initiation f Contact):	Score	Score	Score	Score	Score	Score	Ave. Score
5 hours	0	0	0	0	0	0	0.0
1 day	0	0	0	0	1	0	0.2
2 days	0	0	0	0	0	0	0.0
3 days	0	0	0	0	0	0	0.0
7 days	0	0	1	0	0	1	0.3
10 days	0	0	0	0	0	0	0.0

Edema Formation

Time:	Score	Score	Score	Score	Score	Score	Ave. Score
5 hours	0	0	0	0	0	0	0.0
1 day	0	0	0	0	0	0	0.0
2 days	0	0	0	0	0	0	0.0
3 days	0	0	0	0	0	0	0.0
7days	0	0	0	0	0	0	0.0
10 days	0	0	0	0	0	0	0.0

Other Irritation or Effects

Time:	Effect	Effect	Effect	Effect	Effect	Effect	
5 hours	None	None	None	None	None	None	
1 day	None	None	None	None	None	None	
2 days	None	None	None	None	None	None	
3 days	None	None	None	None	None	None	
7 days	None	None	None	None	None	None	
10 days	None	None	None	None	None	None	

Remarks: Sample residue present on the dose site of each rabbit at 5 hr through 3 days, persisting on 1 through 10 days.

WPC/fcw/0433Z-2; 12-04-85

Table 5 (Continued)

Primary Eye Irritation-Rabbit

Material: UCAR® Solution Vinyl VYEE Sample No.: 48-257 Amount: 0.1 ml

Rabbit No:		85-18921	85-18925	85-18977	85-18953	85-18967	85-19025	
Sex/Eye Dosed		Male/R	Male/L	Male/R	Female/L	Female/R	Female/L	
Date Dosed		10-22-85	10-22-85	10-22-85	10-22-85	10-22-85	10-22-85	
		Scores/Effects at 72 hr						Mean
Cornea:	Opacity	0	0	0	0	0	0	0.0
	Area	0	0	0	0	0	0	0.0
Iris:	Inflam.	0	0	0	0	0	0	0.0
Conjunct:	Redness	0	0	0	0	0	0	0.0
	Chemosis	0	0	0	0	0	0	0.0
	Discharge	0	0	0	0	0	0	0.0
Fluorescein Exam.		0%	0%	0%	0%	0%	0%	0%
Other Effects/Remarks:								
		Scores/Effects at 7 days						Mean
Cornea:	Opacity	0	0	0	0	0	0	0.0
	Area	0	0	0	0	0	0	0.0
Iris:	Inflam.	0	0	0	0	0	0	0.0
Conjunct:	Redness	0	0	0	0	0	0	0.0
	Chemosis	0	0	0	0	0	0	0.0
	Discharge	0	0	0	0	0	0	0.0
Fluorescein Exam.		0%	0%	0%	0%	0%	0%	0%
Other Effects/Remarks:								

WPC/fcw/0433Z-2;
12-04-85

APPENDIX 1

STANDARD TEST PROCEDURES

For all tests, the animals are maintained on appropriate commercial diet and municipal water. Both are available ad libitum except during periods of fasting (rat peroral test) or manipulation. Dosage levels for the toxicity tests normally differ by a factor of 2 in a geometric series, but may differ by other constant factors if required. The maximum dosage for the peroral and percutaneous tests is 16 ml/kg. Dosages are reduced until significant signs of toxicity are not observed. LD50's and the estimated LD50 slopes are calculated by the moving average method (Thompson, 1947; Weil, 1983) and are based on a 14-day observation period. Animal weights are recorded at 0 days (before dose), 7 days and 14 days (just prior to sacrifice). At death or sacrifice, each animal is subjected to gross pathologic evaluation.

Toxicity terminology used for peroral and percutaneous LD50's includes:

Term	LD50	Term	LD50
Extremely low order	>15 ml(or g)/kg	Highly	0.05-0.5 ml(or g)/kg
Slightly	5-15 ml(or g)/kg	Seriously	0.001-0.05 ml(or g)/kg
Moderately	0.5-5 ml(or g)/kg	Dangerously	<0.001 ml (or g)/kg

Peroral Intubation

Sprague-Dawley albino rats, weighing between 200 and 300 g, receive the test material by stomach intubation with a ball-end stainless steel needle. The sample is injected through the needle by means of a syringe and doses are varied by adjusting the volume of the test material or its dilution. The rats are fasted overnight before dosing. Five males and 5 females are included on each level used for the LD50 calculations.

Application

New Zealand White rabbits, weighing between 2.0 and 3.0 kg, are subjected to 24 hours of contact with the test material which is retained under impervious sheeting on the clipped, intact skin of the trunk. As necessary for larger doses, gauze is wrapped around the trunk over the sample to prevent leakage. Vetrap® Bandaging Tape is wrapped over the impervious sheeting and the animal is returned to its cage for the contact period. Doses are varied by adjusting the volume or weight of the test material. Solids are dosed as powders and are moistened with a sufficient amount of water or other suitable vehicle to form a paste. After the contact period, excess fluid is removed to diminish ingestion. Observations for skin reaction are made at one hour, 7 days and 14 days after the contact period. Five male and 5 females are included on each level used for the LD50 calculation.

Inhalation Exposure

Sprague-Dawley albino rats, weighing between 200 and 300 g, are exposed to substantially saturated vapor for 6 hours. The vapor is produced by enclosing the test material in a sealed 120-liter animal chamber for approximately 18 hours (static conditions) or by passing air (at 2.5 liters/min) through the sample and then through a 9-liter animal chamber (dynamic conditions). Oxygen is added, as needed, for static exposures to maintain a chamber oxygen content of approximately 20%. If deaths occur, exposure times are varied to determine an LT50. Five males and 5 females are included for each exposure period.

SCALE FOR SCORING OCULAR LESIONS

Cornea:

A. Opacity--degree of density (most dense area taken for reading)

No opacity	0
Scattered or diffuse area, iris details clearly visible	1
Easily discernible translucent areas, iris details slightly obscured	2
Opalescent areas, iris details not visible, pupil size barely discernible	3
Opaque, iris invisible	4

B. Area of cornea involved

One-quarter or less, but not zero	1
Greater than one-quarter, but less than half	2
Greater than half, but less than three-quarter	3
Greater than three-quarter, up to whole area	4

Iris:

A. Normal	0
Folds above normal, congestion, swelling, circumcorneal injection (any or all), iris still reacting to light	1
No reaction to light, hemorrhage, gross destruction	2

Conjunctivae:

A. Vessels normal	0
Vessels definitely injected above normal	1
Diffuse, deep crimson red, individual vessels not readily discernible	2
Diffuse beefy red	3
B. No chemosis	0
Any swelling above normal (includes nictitating membrane)	1
Obvious swelling with partial eversion of lids	2
Swelling with lids about half closed	3
Swelling with lids about half closed to completely closed	4
C. No discharge	0
Any amount of discharge different from normal	1
Discharge with moistening of the lids and hairs adjacent to lids	2
Discharge with considerable moistening around the eyes	3

WPC/fcw/0433Z-1
11-25-85

D & H

UNION CARBIDE CORPORATION OLD RIDGEBURY ROAD, DANBURY, CT 06817
Corporate Health, Safety and Environmental Affairs Department

CONTAINS CONFIDENTIAL BUSINESS INFORMATION

Certified Mail
Return Receipt Requested

January 31, 1986

Document Control Officer
Office of Toxic Substances (TS-793)
Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

Attention: J. Alwood, Program Manager

Dear Jim:

With regard to PMN 85-1388, submitted by the Union Carbide Corporation, Union Carbide hereiwth requests an additional suspension of the review period for PMN 85-1388 from the date of receipt of this letter until March 15, 1986. Please continue to communicate with my office with questions relating to this PMN.

Very truly yours,

D. L. Heywood
Principal Technical Contact
(203) 794-5224

DLH/cr

bcc: R. E. Bollinger
M. N. Duvall
D. R. Rink
D. F. Smith
R. C. Wise

0785J

UCC
049625

=> s l2 and (carcinogen? or cancer)
        20306 CARCINOGEN?
        17612 CANCER
L4   1 L2 AND (CARCINOGEN? OR CANCER)

CAS - CHEM ABS

=> display l4 bib abs
ENTER ANSWER NUMBER OR RANGE (1):1

Poly Vinyl Acetate & cancer

L4 ANSWER 1 OF 1

AN CA93(4):31731p
TI Controlled slow release of chemotherapeutic drugs for cancer from matrixes prepared by radiation polymerization at low temperatures
AU Kaetsu, Isao; Yoshida, Masaru; Yamada, Akio
CS Takasaki Radiat. Chem. Res. Establ., JAERI
LO Takasaki, Japan
SO J. Biomed. Mater. Res., 14(3), 185-97
SC 63-6 (Pharmaceuticals)
DT J
CO JBMRBG
IS 0021-9304
PY 1980
LA Eng
AB Vinyl polymer-chemotherapeutic agent composites of various shapes (rod, tablet, membrane, microsphere, and powder) were prepd. by radiation polymn. at low temps. for the purpose of durable controlled slow release of drugs from implanted matrixes. Bleomycin-HCl [66703-07-5], mitomycin C [50-07-7], and 5-fluorouracil [51-21-8] were tested as chemotherapeutic drugs entrapped in poly(diethylene glycol dimethacrylate) [25101-18-2] including a small quantity of a polymer such as polystyrene [9003-53-6], poly(vinyl formal), poly(vinyl acetate) [9003-20-7], poly(me methacrylate) [9011-14-7] or polyethylene glycol 600 [25322-68-3]. The release rates from the matrixes depended much on the kind of polymer, drug, and monomer concn. in polymn. and also on the shape of the composite. The release of these drugs from polymer matrixes obeyed the diffusion-controlled release mechanism based on Higuchi's equation and was durable for more than 30 days. The release rate can be controlled easily by design of the shapes and structures of the polymer matrixes.

CAS — CHEMICAL ABSTRACT

```
=> s 9003-20-7
L2          7346 9003-20-7

=> s l2 and metabolism?
         250061 METABOLISM?
L3            2 L2 AND METABOLISM?

=> display l3 1-2 bib abs
```

POLY VINYL ACETATE & METABOLISM

L3 ANSWER 1 OF 2

AN CA102(3):19031g
TI Cutaneous absorption of corrosion inhibitors of metals
AU Paustovskaya, V. V.
LO USSR
SO Gigiena Truda, Kiev, (20), 74-8
From: Ref. Zh., Khim. 1984, Abstr. No. 14I455
SC 4-3 (Toxicology)
DT J
PY 1984
LA Russ
AB Title only translated.

L3 ANSWER 2 OF 2

AN CA87(4):28211q
TI Metabolism of the most important electrolytes in workers of a poly(vinyl acetate) plant
AU Melik-Israelyan, S. S.; Avakyan, M. A.
LO USSR
SO Biol. Zh. Arm., 29(10), 99-102
SC 59-3 (Air Pollution and Industrial Hygiene)
SX 36
DT J
CO BZARAZ
PY 1976
LA Russ
AB The workers of poly(vinyl acetate) [9003-20-7] plant revealed disordered electrolytic metab. The changes in K, Na, and Cl ions caused by impaired acid-base-equil. have compensatory significance. The escape of Na and K ions into erythrocytes lead to the inhibition of alk. properties of HCO3-, rendering, therefore blood plasma active reaction less alk. and increasing the concn. of Cl-.

obtain copy of 1

2 and teratology (sn) or 2 and cancer (sn)

PROG:
TIME OVELW: CONT? (Y/N)

USER:
Y
prt ss 5 compr

Poly Vinyl Acetate and (Teratology and cancer)

TOXLINE 76-80

PROG:

1
AU - Kaetsu I : Yoshida M : Yamada A
TI - Controlled slow release of chemotherapeutic drugs for cancer from matrixes prepared by radiation polymerization at low temperatures
SI - CA/093/031731P
SO - J. Biomed. Mater. Res.: VOL 14. ISS 3, 1980.185-97

2
AU - SHCHERBAK BI
TI - Long-term effects of chronic poisoning of animals with polyvinyl acetate extracts.
SI - HERP/78/08382
SO - GIG SANIT; (4). 1977 99-100

SS 7 /C?
USER:

#2 admin copy

UCC
049828

... needs the standard reagents on Friday morning. (5-16-86)

Literature Search

Chemical/Subject Polyvinyl Acetate

Requested by DR T R Taylor CAS # 9003-20-7

Division _____ Searched by JN

Date Submitted 5-13-86 Date of Search 05/15/86

Sources Searched:

1. BIOASSAY FOR POSSIBLE CARCINOGENICITY, NCI _____
2. BUSHY RUN RESEARCH CENTER DATA CARDS _____
3. CATALOG OF TERATOGENIC AGENTS (1980), Shepard, T. H. _____
4. CHEMICAL HAZARDS OF THE WORKPLACE (1978), Proctor, N. _____
5. CLINICAL TOXICOLOGY OF COMMERCIAL PRODUCTS 5th Ed. (1984), Gosselin, R. E. _____
6. CURRENT INTELLIGENCE BULLETIN, NIOSH _____
7. DANGEROUS PROPERTIES OF INDUSTRIAL CHEMICALS 6th Ed. (1984), Sax. N. I. _____
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11. GOODMAN & GILMAN'S - THE PHARMACOL. BASIS OF THERAP. 6th ED. (1980) _____
12. HANDBOOK OF INDUSTRIAL TOXICOLOGY (1976), Plunkett, E. R. _____
13. HANDBOOK OF POISONING, DREISBACH, R.H. _____
14. HANDBOOK OF TOXIC AND HAZARDOUS CHEMICALS (1985), 2nd Ed., Sittig, M. _____
15. HAZARDOUS CHEMICALS DATA BOOK (1980), Weiss, G _____
16. HAZARDOUS & TOXIC EFFECTS OF INDUSTRIAL CHEMICALS (1979), Sittig, M. _____
17. IARC MONOGRAPHS: EVALUATION OF CARCINOGENIC RISK _____
18. INDUSTRIAL TOXICOLOGY, Hamilton & Hardy, 3rd Ed., 1974 _____
19. MERCK INDEX 10th Ed. (1983) _____
20. OCCUPATIONAL EXPOSURE TO: _____, NIOSH _____
21. OCCUPATIONAL HEALTH GUIDELINES FOR CHEMICAL HAZARDS (1981), NIOSH/OSHA _____
22. OHS MSDS _____
23. OSHA HAZARDOUS CHEMICALS LIST - ATTACHMENT 1 _____
24. PATTY'S INDUSTRIAL HYGIENE AND TOXICOLOGY - Vol. _____ _____
25. POISONING 4th Ed. (1979), Arena, J. M. _____
26. POTENTIAL INDUSTRIAL CARCINOGENS AND MUTAGENS (1979), Fishbein, L. _____
27. TIS PRODUCT FILES _____
28. TOXIC & HAZARDOUS INDUSTRIAL CHEMICALS SAFETY MANUAL (1977) _____
29. TOXICOLOGY OF THE EYE, W. Morton Grant, (1974) _____
30. UCC MSDS _____
31. Other (Specify): _____

_____ _____

0030V

UCC
049629

BUSHY RUN RESEARCH CENTER
R. D. 4, Mellon Road, Export, Pennsylvania 15632 Telephone (412) 733-5200

October 9, 1986

Dr. T. R. Tyler
Assistant Corporated Toxicologist
Union Carbide Corporation
39 Old Ridgebury Road - P2592
Danbury, CT 06817-0001

Dear Dr. Tyler:

Enclosed are two (2) originals of the protocol entitled "Reproductive Toxicity Evaluation of Generic UCAR® Vinyl Resin VYEE Administered in the Feed to the CD® (Sprague-Dawley) Rat". This final version incorporates all of the EPA's requested changes. Mr. Wise has received the estimated costs for this study from Dr. Frank.

If the protocol meets with your approval, please sign both originals, forward them to Mr. Wise for his signature as soon as possible, and return one original fully signed protocol to me for distribution to involved BRRC personnel. Please also request that Mr. Wise send a copy of the fully signed protocol to Attorney A. A. Kerester for inclusion in the VYEE Consent Order.

Thank you for your cooperation.

Sincerely,

R. W. Tyl, Ph.D., DABT
Study Director

PATH/esk/0779P-1

Enclosures

cc: Dr. F. R. Frank, Director BRRC
Mr. R. C. Wise, UCC
Ms. A. A. Kerester, Esq., McKenna, Conner and Cuneo
Dr. J. P. Van Miller
Ms. L. J. Calisti, QA
Ms. T. A. Savine

BUSHY RUN RESEARCH CENTER
R. D. 4, Mellon Road, Export, Pennsylvania 15632 Telephone (412) 733-5200

PROTOCOL

TITLE: Reproductive Toxicity Evaluation of Generic UCAR® Vinyl Resin VYEE Administered in the Feed to the CD® (Sprague-Dawley) Rat

BRRC PROJECT NUMBER: 86-13-18830

SPONSOR: Solvents and Coatings Materials Division
Union Carbide Corporation
39 Old Ridgebury Road - K4440
Danbury, CT 06817-0001

TESTING FACILITY: Bushy Run Research Center (BRRC)
Union Carbide Corporation
R. D. #4, Mellon Road
Export, PA 15632
Attention: R. W. Tyl
(412) 733-5277

Reviewed and Approved by:

Bushy Run Research Center:

Rochelle W. Tyl, Ph.D., DABT Date
Study Director/Manager, Reproductive and Developmental Toxicology Section

Linda J. Calisti, B.S. Date
Group Leader, Good Laboratory Practices/Quality Assurance

Fred R. Frank, Ph.D. Date
Director

Union Carbide Corporation:

Tipton R. Tyler, Ph.D., DABT Date
Assistant Director of Applied Toxicology

Division:

Richard C. Wise Date

0694P-3

I. PURPOSE

This study is intended to evaluate the potential of UCAR® vinyl resin VYEE administered in the diet to CD® rats to produce alterations in parental fertility, maternal pregnancy and lactation, and growth and development of the F1 offspring until weaning.

II. GENERAL

A. Sponsor

Union Carbide Corporation
Solvents and Coatings Materials Division
39 Old Ridgebury Road - K4440
Danbury, CT 06817-0001

B. Government Representative: Chief Premanufacture Notice Management Branch, Chemical Control Division, Office of Toxic Substances

C. Project Monitor: Tipton R. Tyler, Ph.D., DABT

D. Testing Facility: Bushy Run Research Center, Export, PA 15632

E. BRRC Project No.: 86-13-18830

F. Personnel

Study Director:	R. W. Tyl, Ph.D., DABT Manager, Reproductive and Developmental Toxicology
Teratology Personnel:	D. L. Fait, AALAS Cert. II L. C. Fisher, B.S. M. F. Kubena, B.S. D. J. McNeil, AHT, A.S., AALAS Cert. I T. A. Rebick, AHT, A.S., AALAS Cert. I T. A. Savine, HT(ASCP)
Chronic Oral Personnel:	J. P. Van Miller, Ph.D., DABT, Manager N. S. Bellich, AALAS Cert. II J. A. DeNinno, AALAS Cert. II E. J. Mika J. E. Negley, B.S. A. G. Chiarmonte, AALAS Cert. I. G. W. Klingensmith, AALAS Cert. I E. V. Weaver, B.A.
Analytical Support:	J. P. Van Miller, Ph.D., DABT, Manager M. A. Vrbanic, B.A.
Attending Veterinarian:	P.E. Losco, VMD, Diplomate ACVP
Necropsy:	M. A. McGee, HT(ASCP), Supervisor
Histology:	M. A. McGee, HT(ASCP), Supervisor
Pathologist:	E. H. Fowler, DVM, Ph.D., Diplomate ACVP
Animal Care:	To be assigned

Other study team members to be determined.

G. Starting Date of Acclimation To be added to the protocol by amendment

H. Starting Date of Administration To be added to the protocol by amendment

I. Proposed Date for Completion of In-Life Phase To be added to the protocol by amendment

J. Proposed Date for Submission of the Draft Final Report To be added to the protocol by amendment

K. Basis for the Study

This study will be performed in compliance with the following guidelines and regulations, to the extent possible given the study design.

EPA (1983). Part III EPA Toxic Substances Control, Good Laboratory Practice Standards; Final Rule. Fed. Reg. 48(230), 53922-53944.

OECD Guideline for Testing of Chemicals, No. 416, May 26, 1983.

L. Alteration of Design

Alterations of this protocol by the Study Director may be made with agreement of the Sponsor as the study progresses. Examples of such alterations are additional histopathology or laboratory studies.

Any alterations will be described in detail in amendment form, signed by the Study Director and the Project Monitor and added to this protocol.

III. METHODS

A. Test Animals

Species:	Sprague Dawley Derived Outbred Albino Rat [Crl:CD®(SD)BR], known as the Charles River CD® Rat
Supplier:	Charles River Breeding Laboratories, Kingston, NY
Rationale:	The albino rat is the species of choice for multi-generation reproduction studies (according to guidelines).
Number and sex:	One hundred thirty (130) virgin female and the same number of virgin male rats will be ordered for the study. Females will be nulliparous and nonpregnant. There will be 200 animals (100 males and 100 females) assigned to the study at the initiation of the treatment period (See Section III.E).

Age and Weight: The animals will be twenty-eight days of age on the scheduled animal receipt date (approximate weights upon arrival: 75 grams for males and 65 grams for females). Dosing will begin when the animals are approximately six weeks old (males approximately 150 grams, females approximately 125 grams).

Quality Control: Quality control will be performed within one day after the receipt of the animals. Three animals per sex will be subjected to histopathologic examination of salivary glands, trachea, lungs, liver, kidneys, cervical lymph nodes and nasal cavities. Five animals per sex will be given fecal examinations (for possible intestinal parasites) by zinc sulfate floatation of the feces, and five animals per sex will be subjected to serum analyses for possible viral antibody titers.

Acclimation: Animals will be acclimated for at least two weeks under test conditions. They will be observed daily for general health status and ability to adapt to the automatic watering system.

Body Weight: All animals will be weighed at least once during acclimation. The weight variation of the study animals at initiation will not exceed ± 20% of the mean weight for each sex.

Identification: Animals shall be uniquely identified prior to initiation of the study by both toe clip and ear tag (Monel, Gey Band and Tag Co., Morristown, PA) and the method and numbers documented in the study records.

Culled Animals: Animals received with the initial shipment but not used in the study will be euthanized or removed from the study room prior to the start of the treatment period, and used for methods development and training of the BRRC staff. Records will be kept documenting the fate of all animals received for the study.

B. Husbandry

Conditions: The experiment will be carried out under standard laboratory conditions. The animals will be housed two-three per cage separated by sex during the acclimation period and they will be individually housed upon the initiation of the treatment period in stainless steel cages with wire mesh floors. Study animals will be housed two per cage (one male: one female from the same dose level) during

the mating period (see section III.F). Females will be caged separately and individually nce they have been successfully mated (or at the end of the mating period). Successfully mated females will be transferred to shoe-box cages and furnished with appropriate nesting materials and water bottles with stainless steel sipper tubes on day 20 of gestation. Specific information on the cages (dimensions, etc.) will be included in the study data.

All animals will be housed in BRRC animal room (number to be added to the protocol by amendment) for the duration of the study. Temperature and humidity will be recorded continuously using an automatic recorder and checked regularly. The animal room will be maintained at a temperature of 22 ± 3°C and a relative humidity of 30-70% with a 12-hour light cycle per day. The BRRC animal ro m is air-conditioned and is equipped with laminar air flow (approximately 150 air changes/hour).

Diet: Ground Purina Certified Rodent Chow® #5002 (Ralston Purina Co., Richmond, IN) will be available ad libitum.

Water: Tap water (Municipal Authority of Westmoreland County, Greensburg, PA) will be available ad libitum by automatic watering system with demand control valves mounted on each rack during the pre-breed, mating, and gestation period until gd 20 when females will be provided with water bottles and stainless steel sipper tubes (for use in the shoe-box cages). Contaminant levels will be measured at regular intervals per EPA specifications, to include the 129 "priority" pollutants, identified in the Federal Register 45(98), Appendix D, Part 122, and shall comply with human requirements.

C. Test Substance

Name: Generic UCAR® Vinyl Resin VYEE (hereafter designated as VYEE)

CAS No.: To be added to the protocol by amendment.

Reference Number: To be added to the protocol by amendment.

BRRC Number: To be added to the protocol by amendment.

Purity: To be added to the protocol by amendment.

Description: To be added to the protocol by amendment.

Stability of Test Substance: To be added to the protocol by amendment.

Storage Conditions: Test substance will be stored in a refrigerator.

Estimated Quantity Needed: To be added to the protocol by amendment.

Safety Precautions: Exposure will be restricted by the use of latex rubber gloves and suitable disposable clothing (lab coats or jumpsuits, booties, and hair covers).

D. Administration of Test Substance

Route: Oral; mixed in the diet. This is the route agreed to by the Sponsor and the EPA.

Diet Preparation and Storage: The basic diet will be ground Purina Certified Rodent Chow® #5002 (Ralston Purina Co., St. Louis, MO). The analyses of chemical composition and possible contaminants (including nitrosamine) of each batch of diet will be performed by Raltech Scientific Services, St. Louis MO and Hazleton Laboratories, Inc., Madison, WI. The results of such analyses will be incorporated into the final report.

Test diets will be prepared as follows: All measurements of the test material will be made by weight and corrected for purity of the active ingredient, VYEE. VYEE will be mixed with the feed to generate a concentrated premix. Diets will be prepared from the premix in a manner to ensure homogeneous distribution of the test material. Control diets will be mixed as long as the test diets. Details of the procedures, including mixing times, will be documented in the raw data. All premixes and diets will be prepared weekly and stored frozen.

Analysis of Diet: Details of the analysis of VYEE in the animal diets will be added to the pr tocol by amendment. Homogeneity and stability of the test material in the animal diets at the concentrations to be used in this study will be determined. Analysis of diet concentrations f VYEE will be performed on all doses and control for the first four weeks of the study. These analyses will be completed prior to administration of the test diets to the animals. Thereafter, one randomly selected sample from a dosed diet will be retained frozen from each week's preparation and analyzed every four weeks with one control sample.

Feeding Levels:

Group No.	Level (to be added to the protocol by amendment)
1 control	0 ppm
2 low	ppm
3 middle	ppm
4 high	ppm

Duration of Treatment: The test diet for all animals assigned to each dosage level will be administered throughout the study beginning when the parental animals are approximately 6 weeks old and ending at study termination when the F1 animals are weaned (postnatal day 21).

E. Study Design

Number of Animals per Group: The study will begin with 25 males/group and 25 females/group to yield at least 20 pregnant females/group at or near term.

Animals will be assigned to the different groups by means of computer-generated randomization such that the body weights of all groups are homogeneous by statistical analysis at study initiation.

Organization:

Group	Number of Animals Male	Number of Animals Female	Dietary Level of Test Material (ppm)
Control	25	25	0
Low	25	25	(To be added to
Middle	25	25	the protocol by
High	25	25	amendment)

F. Experimental Evaluations

PARENTAL ANIMALS

Mortality: Observations for mortality will be made twice daily (a.m. and p.m.)

General Conditions: The general condition of all animals will be checked daily.

Symptoms: Clinical examinations will be conducted and recorded daily throughout the course of the study. This record will include the time of onset, degree and duration of symptoms.

These cage-side observations will include, but not be limited to, changes in: skin and fur, eyes, and mucous membranes, respiratory system, circulatory system, autonomic and central nervous system, somatomotor activity, and behavior pattern.

Body Weight: The body weights of the male rats will be determined and recorded initially and weekly through the mating period when the males will be sacrificed. The body weights of female rats will be recorded in the same manner until confirmation of mating. During gestation, females will be weighed on gestational days 0, 7, 14 and 20. Dams producing litters will be weighed on days 0, 4, 7, 14 and 21 postpartum. Body weight gains will be computed.

Food Consumption: Food consumption determinations will be conducted weekly for each parental animal during the pre-mating period of this study. During gestation and lactation food consumption determination will be made for the parental females for gestational days 0-7, 7-14, and 14-20 and for lactational days 0-4, 4-7, 7-14 and 14-21. These measurements will correspond with the collection of the animals' body weight data and will be employed to calculate their actual exposure to the test article on a mg of test article/kg of body weight ratio.

During the three-week mating phase of this study, food consumpti n will be monitored visually but feed intake measurements will not be conducted (since animals will be housed two, one male:one female, per cage).

Mating Procedures: Animals of the F0 generation will be approximately 6 weeks of age at the commencement of treatment. They will be maintained on their respective diets for at least six (6) weeks prior to mating, i.e. until they are approximately 12 weeks of age. The animals will then be mated on the basis of one male to one female selected randomly within each dose group for a period of 20 days. The observation of dropped copulation plugs will be considered evidence of successful mating. The day a copulation plug is observed will be designated gestational day (gd) 0 [Hafez, E. W. E. (ed) (1970) Reproduction and Breeding Techniques for Laboratory Animals Lea and Febiger, Philadelphia, PA]. Once a plug has been observed, the male and female from that mating pair will be individually housed (See Section III.B). For any mating pairs which do not show evidence of successful mating (i.e., no copulation plug is observed) the last scheduled mating day will be considered gd 0 for that female and the animals will be treated accordingly for subsequent events. On gd 20, each female will be transferred to a shoe-box cage with appropriate bedding (see Section III.B). Females will be observed twice daily beginning on gd 20 for evidence of littering. The dams will be allowed to rear their young to Day 21 postpartum. When the last litter has reached Day 21 postpartum, one F1 pup/sex/litter will be randomly selected for necropsy. Additionally, one pup/sex/litter will be selected as possible parents of the F2 generation. Following the necropsy of the selected F1 pups, a decision will be made by the Chief, Premanufacture Notice Management Branch of EPA with the concurrence of the Study Director and Project Monitor as to whether the remaining F1 pups will be necropsied or euthanized and discarded, based on the results of the necropsy of the selected animals.

PROGENY

Mortality: All pups will be sexed and examined as soon as possible after birth to determine the number of viable and stillborn members of each litter. Litters will be evaluated twice daily for survival.

Standardization of Litter Sizes:	On day 4 after birth, the size of each litter will be adjusted by eliminating extra pups by random selection to yield, as nearly as possible, four males and four females per litter. Culled pups will be sacrificed by decapitation and discarded.
Survival Data:	Survival indices will be calculated at 0, 4, 7 and 14 days after birth and at weaning (postnatal day 21).
Body Weight and Sex Determination:	All live pups will be sexed and weighed individually at day 0; and 4, 7 and 14 days after birth and at weaning. The body weights and sexes will be recorded on an individual basis but the pups will not be uniquely identified at this stage.
Symptoms:	All pups will be examined for physical abnormalities at birth and throughout the lactation period. All pups dying during lactation will be necropsied when possible to investigate the cause of death.
Selection:	After the weaning of the last litter, one pup/sex/litter from all dose groups will be selected for necropsy with tissues saved (see below), and one pup/sex/litter from all dose groups will be selected as possible parents of the F2 generation. All pups will be available for selection. The results from the necropsy of selected F1 weanlings shall be provided t the Chief, Premanufacture Notice Management Branch of EPA (and the Project Monitor) within 48 hours of the completion of necropsy. He (or she) shall then have 72 hours from receipt of the data to decide whether the remaining F1 weanlings will be necropsied with tissues saved (see below) or euthanized and discarded. If the Branch Chief determines that it is necessary (with the concurrence of the Study Director and Project Monitor) that the remaining weanlings be necropsied, they will be processed as soon as possible. If the Branch Chief decides that this procedure is unnecessary, the remaining weanlings will be euthanized and discarded. The F1 pups, selected as possible parents for the F2 generation, will remain on the same dietary concentration of VYEE as their parents for a maximum of three (3) weeks. On or before that time the EPA Branch Chief with the concurrence of the Study Director and Project Monitor will determine, based on draft data from the F1 breed, whether the selected F1 animals will

continue on the test diets and be bred (as described above for the F0 animals) or euthanized and discarded. During their exposures these F1 animals will be weighed weekly and examined daily for clinical signs. Feed consumption will also be measured weekly.

Gross Pathology: A gross internal examination will be made on any pup appearing abnormal or dying on test, and on one pup/sex/litter randomly selected from each test group of the F1 generation (see below).

Pathology

Parental and Weanling Animals: All adult F0 (parental) animals in all groups shall be subjected to a complete gross necropsy. Parental males will be sacrificed after the mating period is completed; parental females will be sacrificed after their litters are weaned. The tissues specified below from all F0 adults and necropsied F1 weanlings will be retained in fixative. The tissues listed below from the 25 male and 25 female F0 adults from the control and high dose groups shall be subjected to histopathologic examination:

pituitary
vagina
uterus
ovaries

testes
epididymides
seminal vesicles
prostate
target organ(s) if any

Any of the above organs or tissues exhibiting gross changes will be evaluated microscopically in F0 animals from the other dose groups.

Animals Dying on Test: A complete gross necropsy will be conducted for any parental animals dying on test and tissues listed above will be retained for possible subsequent histopathology.

Nonpregnant Females: The fixed (buffered neutral 10% formalin) uteri from any females of the F0 generation failing to produce a litter will be stained with potassium ferricyanide for confirmation of pregnancy status. This staining procedure will not affect any subsequent histopathologic examination.

Gross Necropsy

The gross necropsy will include: examination of the external surfaces; all orifices; cranial cavity; carcass; external and cut surfaces of the brain and spinal cord; the thoracic, abdominal, and pelvic cavities and their viscera; and cervical tissues and organs.

Statistical Analyses

The unit of comparison will be the male or the pregnant female (or the litter). Results of the quantitative continuous variables (e.g. body weights, food consumption, etc.) will be intercompared for the three treatment groups and one control group by use of Levene's test for equal variances, analysis of variance (ANOVA), and t-tests with Bonferroni probabilities. The t-tests will be used when the F value from the ANOVA is significant. When Levene's test indicates homogeneous variances and the ANOVA is significant, the pooled t-test will be used for pairwise comparisons. When Levene's test indicates heterogeneous variances, all groups will be compared by an ANOVA for unequal variances followed, when necessary, by the separate variance t-test.

Nonparametric data will be statistically evaluated using the Kruskal-Wallis test followed by the Mann-Whitney U test for pairwise comparisons when appropriate. Frequency data (such as the various indices) will be compared using the Fisher's Exact Test. For all statistical tests, the fiducial limit of 0.05 (two-tailed) will be used as the criterion f r significance.

Retention of Specimens and Records

All specimens and records which remain the responsibility of Bushy Run Research Center (BRRC) will be retained in the BRRC archives for the length of time specified in the appropriate guidelines and regulations (see Section II K).

Good Laboratory Practices

The Bushy Run Research Center, through administration of a quality assurance program by the Good Laboratory Practices Committee and Quality Assurance Unit, assures compliance of all phases of toxicological studies with existing regulations and generally accepted good laboratory practices.

IV. REPORTING

Status Reports: Status reports will be provided to the Sponsor indicating the number of survivors in each group, mean body weights with statistical significance, and any compound-related effects. The frequency and format of the reports are flexible.

Final Report: A draft report will be issued prior to the issuance of the final report. Complete signed copies (number to be specified) of the final report will be submitted following termination of the study. The final report will include:

Abstract
Introduction
Experimental Design
Materials and Methods
Narrative discussion of parameters evaluated
Individual Maternal Data for F0 Generation:

a. Identification number
b. Age at beginning of study
c. Age at death and manner of death.
d. Weekly body weights prior to mating and gestational and lactational body weights taken thereafter
e. Weekly food consumption prior to mating and food consumption during gestation and lactation
f. Male rat (by identification number) used for mating.
g. Date of delivery and gestation length in days.
h. Total number of offspring per litter.
i. Number and percent of live and dead offspring.
j. General condition of offspring and mother through weaning.

Summary of Maternal Data for F0 Generation:

a. Mean maternal body weights and survival indices.
b. Mean food and compound consumption (expressed as mg/kg/day).
c. Mean litter size.
d. Mean number of live and dead offspring.
e. Number and percent of mothers showing behavioral abnormalities in nesting and nursing.
f. Mating index =

$$\frac{\text{Number of plugged females}}{\text{Number of paired females}} \times 100$$

g. Fecundity index =

$$\frac{\text{Number of pregnancies}}{\text{Number of plugged females}} \times 100$$

h. Fertility indices (also expressed as percentages) =

$$\frac{\text{Number of females pregnant}}{\text{Total number of females paired}} \times 100$$

Individual Paternal Data for F0 Generation:

a. Identification number.
b. Age at beginning of study.
c. Age at death and manner of death.
d. Weekly body weights prior to mating.
e. Weekly food consumption.

Summary of Paternal Data for F0 Generation:

a. Mean male body weights (weekly prior to mating) and survival indices
b. Mean food and compound consumption (expressed as mg/kg/day)
c. Fertility indices (also expressed as percentages):

$$\frac{\text{Number of males shown to be fertile}}{\text{Total number of males paired}} \times 100$$

Data From Each F1 Litter Arranged by Dose Level:

a. Total litter size.
b. Number and percent of stillborn.
c. Number and percent of live births.
d. Periodic viability counts.
e. Periodic body weights by sex per litter from day 0 of life to weaning (taken on days 0, 4, 7, 14, and 21 of lactation).
f. Number and nature of physical abnormalities observed.
g. Pup survival indices (also expressed as percentages).
h. Sex ratio

Gestational index =

$$\frac{\text{Number of females with live litters}}{\text{Number of females pregnant}}$$

Live birth index =

$$\frac{\text{Number of live pups at birth}}{\text{Total number of pups born}}$$

4-Day survival index =

$$\frac{\text{Number of pups surviving 4 days}}{\text{Total number of live pups at birth}}$$

7-Day survival index =

$$\frac{\text{Number of pups surviving 7 days}}{\text{Total number of live pups at 4 days}}$$

14-Day survival index =

$$\frac{\text{Number of pups surviving 14 days}}{\text{Total number of live pups at 7 days}}$$

21-Day survival index =

$$\frac{\text{Number of pups surviving 21 days}}{\text{Total number of live pups at 14 days}}$$

Lactation Index =

$$\frac{\text{Number of pups surviving 21 days}}{\text{Total number of live pups at 4 days}}$$

Summary of F1 Litter Data:

a. Mean body weights of all pups through weaning (taken on day 0, 4, 7, 14 and 21).
b. Number and percent of pups with physical or behavioral abnormalities.
c. Mean pup survival indices through lactation day 21.

Protocol and any amendments

Summary and details of dietary analyses

Summary and individual data on gross F0 parental necropsy

Summary and individual data on gross necropsy of selected F1 weanlings

Summary and individual data on the F0 histopathologic evaluations

Resumes of the professional personnel associated with the study

WPC/esk/0694P-4
09-18-86

UNION CARBIDE

BUSHY RUN RESEARCH CENTER

R. D. 4, Mellon Road, Export, Pennsylvania 15632 Telephone (412) 733-5200

September 18, 1986

Mr. R. C. Wise
Solvents and Coatings Materials Division
Union Carbide Corporation
39 Old Ridgebury Road - K440
Danbury, CT 06817-0001

Dear Mr. Wise:

Enclosed is the revised draft protocol for the VYEE Reproductive Toxicity Evaluation. I have addressed all of the changes requested by EPA and specifically identified an EPA officer (title supplied by Alison Kerester) to whom the necropsy data from selected F1 weanlings and the F1 breed data will be sent, and the time frame in which he/she must respond (section entitled Selection, Pages 10-11 in the protocol). At Alison's suggestion, I'm also sending draft copies of this protocol to Dr. T. R. Tyler, Mr. M. Duvall and Ms. A. Kerester. If everyone is satisfied with the protocol (please let me know at your earliest convenience - no later than Wednesday, September 24, 1986), I'll finalize the protocol and send it to Tip and you for signatures. At that point, one of us should send a fully signed copy to Alison for inclusion in the Consent Order.

Dr. Frank will provide you with the revised costs of this protocol. Dr. John Van Miller is working with the Carbide chemists (thank you for setting this up); we do not yet know what the analytical costs will be. As soon as Dr. Van Miller knows, Dr. Frank will give you those costs.

Thank you for your continued cooperation.

R. W. Tyl

R. W. Tyl, Ph.D., DABT
Study Director

WPC/esk/0765P-1

Enclosure

RECEIVED
SEP 2 2 1986
T. R. TYLER, Ph. D.

cc: Dr. F. R. Frank, Director
Dr. J. P. Van Miller
Dr. T. R. Tyler, UCC
Dr. M. N. Duvall, UCC
Ms. A. A. Kerester, McKenna, Conner and Cuneo

DRAFT

BUSHY RUN RESEARCH CENTER

R. D. 4, Mellon Road, Export, Pennsylvania 15632 Telephone (412) 733-5200

PROTOCOL

TITLE: Reproductive Toxicity Evaluation of Generic UCAR® Vinyl Resin VYEE Administered in the Feed to the CD® (Sprague-Dawley) Rat

BRRC PROJECT NUMBER: 86-13-18830

SPONSOR: Solvents and Coatings Materials Division
Union Carbide Corporation
39 Old Ridgebury Road - K4440
Danbury, CT 06817-0001

TESTING FACILITY: Bushy Run Research Center (BRRC)
Union Carbide Corporation
R. D. #4, Mellon Road
Export, PA 15632
Attention: R. W. Tyl
(412) 733-5277

Reviewed and Approved by:

Bushy Run Research Center:

Rochelle W. Tyl, Ph.D., DABT Date
Study Director/Manager, Reproductive and Developmental Toxicology Section

Linda J. Calisti, B.S. Date
Group Leader, Good Laboratory Practices/Quality Assurance

Fred R. Frank, Ph.D. Date
Director

Union Carbide Corporation:

Tipton R. Tyler, Ph.D., DABT Date
Assistant Director of Applied Toxicology

Division:

Richard C. Wise Date

0694P-3

I. PURPOSE

This study is intended to evaluate the potential of UCAR® vinyl resin VYEE administered in the diet to CD® rats to produce alterations in parental fertility, maternal pregnancy and lactation, and growth and development f the F1 offspring until weaning.

II. GENERAL

A. Sponsor

Union Carbide Corporation
Solvents and Coatings Materials Division
39 Old Ridgebury Road - K4440
Danbury, CT 06817-0001

B. Government Representative: Chief Premanufacture Notice Management Branch, Chemical Control Division, Office of Toxic Substances

C. Project Monitor: Tipton R. Tyler, Ph.D., DABT

D. Testing Facility: Bushy Run Research Center, Export, PA 15632

E. BRRC Project No.: 86-13-18830

F. Personnel

Study Director:	R. W. Tyl, Ph.D., DABT Manager, Reproductive and Developmental Toxicology
Teratology Personnel:	D. L. Fait, AALAS Cert. II L. C. Fisher, B.S. M. F. Kubena, B.S. D. J. McNeil, AHT, A.S., AALAS Cert. I T. A. Rebick, AHT, A.S., AALAS Cert. I T. A. Savine, HT(ASCP)
Chronic Oral Personnel:	J. P. Van Miller, Ph.D., DABT, Manager N. S. Bellich, AALAS Cert. II J. A. DeNinno, AALAS Cert. II E. J. Mika J. E. Negley, B.S. A. G. Chiarmonte, AALAS Cert. I. G. W. Klingensmith, AALAS Cert. I E. V. Weaver, B.A.
Analytical Support:	J. P. Van Miller, Ph.D., DABT, Manager M. A. Vrbanic, B.A.
Attending Veterinarian:	P.E. Losco, VMD, Diplomate ACVP
Necropsy:	M. A. McGee, HT(ASCP), Supervisor
Histology:	M. A. McGee, HT(ASCP), Supervisor
Pathologist:	E. H. Fowler, DVM, Ph.D., Diplomate ACVP
Animal Care:	To be assigned

Other study team members to be determined.

G. Starting Date of Acclimation To be added to the protocol by amendment

H. Starting Date of Administration To be added to the protocol by amendment

I. Proposed Date for Completion of In-Life Phase To be added to the protocol by amendment

J. Proposed Date for Submission of the Draft Final Report To be added to the protocol by amendment

K. Basis for the Study

This study will be performed in compliance with the following guidelines and regulations, to the extent possible given the study design.

EPA (1983). Part III EPA Toxic Substances Control, Good Laboratory Practice Standards; Final Rule. Fed. Reg. 48(230), 53922-53944.

OECD Guideline for Testing of Chemicals, No. 416, May 26, 1983.

L. Alteration of Design

Alterations of this protocol by the Study Director may be made with agreement of the Sponsor as the study progresses. Examples of such alterations are additional histopathology or laboratory studies.

Any alterations will be described in detail in amendment form, signed by the Study Director and the Project Monitor and added to this protocol.

III. METHODS

A. Test Animals

Species:	Sprague Dawley Derived Outbred Albino Rat [Crl:CD®(SD)BR], known as the Charles River CD® Rat
Supplier:	Charles River Breeding Laboratories, Kingston, NY
Rationale:	The albino rat is the species of choice for multi-generation reproduction studies (according to guidelines).
Number and sex:	One hundred thirty (130) virgin female and the same number of virgin male rats will be ordered f r the study. Females will be nulliparous and nonpregnant. There will be 200 animals (100 males and 100 females) assigned to the study at the initiation of the treatment period (See Section III.E).

Age and Weight: The animals will be twenty-eight days of age on the scheduled animal receipt date (approximate weights upon arrival: 75 grams for males and 65 grams for females). Dosing will begin when the animals are approximately six weeks old (males approximately 150 grams, females approximately 125 grams).

Quality Control: Quality control will be performed within one day after the receipt of the animals. Three animals per sex will be subjected to histopathologic examination of salivary glands, trachea, lungs, liver, kidneys, cervical lymph nodes and nasal cavities. Five animals per sex will be given fecal examinations (for possible intestinal parasites) by zinc sulfate floatation of the feces, and five animals per sex will be subjected to serum analyses for possible viral antibody titers.

Acclimation: Animals will be acclimated for at least two weeks under test conditions. They will be observed daily for general health status and ability to adapt to the automatic watering system.

Body Weight: All animals will be weighed at least once during acclimation. The weight variation of the study animals at initiation will not exceed ± 20% of the mean weight for each sex.

Identification: Animals shall be uniquely identified prior to initiation of the study by both toe clip and ear tag (Monel, Gey Band and Tag Co., Morristown, PA) and the method and numbers documented in the study records.

Culled Animals: Animals received with the initial shipment but not used in the study will be euthanized or removed from the study room prior to the start of the treatment period, and used for methods development and training of the BRRC staff. Records will be kept documenting the fate of all animals received for the study.

B. Husbandry

Conditions: The experiment will be carried out under standard laboratory conditions. The animals will be housed two-three per cage separated by sex during the acclimation period and they will be individually housed upon the initiation of the treatment period in stainless steel cages with wire mesh floors. Study animals will be housed two per cage (one male: one female from the same dose level) during

the mating period (see section III.F). Females will be caged separately and individually once they have been successfully mated (or at the end of the mating period). Successfully mated females will be transferred to shoe-box cages and furnished with appropriate nesting materials and water bottles with stainless steel sipper tubes on day 20 of gestation. Specific information on the cages (dimensions, etc.) will be included in the study data.

All animals will be housed in BRRC animal room (number to be added to the protocol by amendment) for the duration of the study. Temperature and humidity will be recorded continuously using an automatic recorder and checked regularly. The animal room will be maintained at a temperature of 22 ± 3°C and a relative humidity of 30-70% with a 12-hour light cycle per day. The BRRC animal r om is air-conditioned and is equipped with laminar air flow (approximately 150 air changes/hour).

Diet: Ground Purina Certified Rodent Chow® #5002 (Ralston Purina Co., Richmond, IN) will be available ad libitum.

Water: Tap water (Municipal Authority of Westmoreland County, Greensburg, PA) will be available ad libitum by automatic watering system with demand control valves mounted on each rack during the pre-breed, mating, and gestation period until gd 20 when females will be provided with water bottles and stainless steel sipper tubes (for use in the shoe-box cages). Contaminant levels will be measured at regular intervals per EPA specifications, to include the 129 "priority" pollutants, identified in the Federal Register 45(98), Appendix D, Part 122, and shall comply with human requirements.

C. Test Substance

Name: Generic UCAR® Vinyl Resin VYEE (hereafter designated as VYEE)

CAS No.: To be added to the protocol by amendment.

Reference Number: To be added to the protocol by amendment.

BRRC Number: To be added to the protocol by amendment.

Purity: To be added to the protocol by amendment.

Description: To be added to the protocol by amendment.

Stability of Test Substance: To be added to the protocol by amendment.

Storage Conditions: Test substance will be stored in a refrigerator.

Estimated Quantity Needed: To be added to the protocol by amendment.

Safety Precautions: Exposure will be restricted by the use of latex rubber gloves and suitable disposable clothing (lab coats or jumpsuits, booties, and hair covers).

D. Administration of Test Substance

Route: Oral; mixed in the diet. This is a possible route of human exposure and the route requested by the Sponsor.

Diet Preparation and Storage: The basic diet will be ground Purina Certified Rodent Chow® #5002 (Ralston Purina Co., St. Louis, MO). The analyses of chemical composition and possible contaminants (including nitrosamine) of each batch of diet will be performed by Raltech Scientific Services, St. Louis MO and Hazleton Laboratories, Inc., Madison, WI. The results of such analyses will be incorporated into the final report.

Test diets will be prepared as follows: All measurements of the test material will be made by weight and corrected for purity of the active ingredient, VYEE. VYEE will be mixed with the feed to generate a concentrated premix. Diets will be prepared from the premix in a manner to ensure homogeneous distribution of the test material. Control diets will be mixed as long as the test diets. Details of the procedures, including mixing times, will be documented in the raw data. All premixes and diets will be prepared weekly and stored frozen.

Analysis of Diet: Details of the analysis of VYEE in the animal diets will be added to the protocol by amendment. Homogeneity and stability f the test material in the animal diets at the concentrations to be used in this study will be determined. Analysis of diet concentrations of VYEE will be performed on all doses and control for the first four weeks of the study. These analyses will be completed prior to administration of the test diets to the animals. Thereafter, one randomly selected sample from a dosed diet will be retained frozen from each week's preparation and analyzed every four weeks with one control sample.

Feeding Levels:

Group No.	Level (to be added to the protocol by amendment)
1 control	0 ppm
2 low	ppm
3 middle	ppm
4 high	ppm

Duration of Treatment: The test diet for all animals assigned t each dosage level will be administered throughout the study beginning when the parental animals are approximately 6 weeks old and ending at study termination when the F1 animals are weaned (postnatal day 21).

E. Study Design

Number of Animals per Group: The study will begin with 25 males/group and 25 females/group to yield at least 20 pregnant females/group at or near term.

Animals will be assigned to the different groups by means of computer-generated randomization such that the body weights of all groups are homogeneous by statistical analysis at study initiation.

Organization:

Group	Number of Animals Male	Number of Animals Female	Dietary Level of Test Material (ppm)
Control	25	25	0
Low	25	25	(To be added to
Middle	25	25	the protocol by
High	25	25	amendment)

F. Experimental Evaluations

PARENTAL ANIMALS

Mortality: Observations for mortality will be made twice daily (a.m. and p.m.)

General Conditions: The general condition of all animals will be checked daily.

Symptoms: Clinical examinations will be conducted and recorded daily throughout the course of the study. This record will include the time of onset, degree and duration of symptoms.

These cage-side observations will include, but not be limited to, changes in: skin and fur, eyes, and mucous membranes, respiratory system, circulatory system, autonomic and central nervous system, somatomotor activity, and behavior pattern.

Body Weight: The body weights of the male rats will be determined and recorded initially and weekly through the mating period when the males will be sacrificed. The body weights of female rats will be recorded in the same manner until confirmation of mating. During gestation, females will be weighed on gestational days 0, 7, 14 and 20. Dams producing litters will be weighed on days 0, 4, 7, 14 and 21 postpartum. Body weight gains will be computed.

Food Consumption: Food consumption determinations will be conducted weekly for each parental animal during the pre-mating period of this study. During gestation and lactation food consumption determination will be made for the parental females for gestational days 0-7, 7-14, and 14-20 and for lactational days 0-4, 4-7, 7-14 and 14-21. These measurements will correspond with the collection of the animals' body weight data and will be employed to calculate their actual exposure to the test article on a mg of test article/kg of body weight ratio.

During the three-week mating phase of this study, food consumption will be monitored visually but feed intake measurements will not be conducted (since animals will be housed two, one male:one female, per cage).

Mating Procedures: Animals of the F0 generation will be approximately 6 weeks of age at the commencement of treatment. They will be maintained on their respective diets for at least six (6) weeks prior to mating, i.e. until they are approximately 12 weeks of age. The animals will then be mated on the basis of one male to one female selected randomly within each dose group for a period of 20 days. The observation of dropped copulation plugs will be considered evidence of successful mating. The day a copulation plug is observed will be designated gestational day (gd) 0 [Hafez, E. W. E. (ed) (1970) Reproduction and Breeding Techniques for Laboratory Animals Lea and Febiger, Philadelphia, PA]. Once a plug has been observed, the male and female from that mating pair will be individually housed (See Section III.B). For any mating pairs which do not show evidence of successful mating (i.e., no copulation plug is observed) the last scheduled mating day will be considered gd 0 for that female and the animals will be treated accordingly for subsequent events. On gd 20, each female will be transferred to a shoe-box cage with appropriate bedding (see Section III.B). Females will be observed twice daily beginning on gd 20 for evidence of littering. The dams will be allowed to rear their young to Day 21 postpartum. When the last litter has reached Day 21 postpartum, one F1 pup/sex/litter will be randomly selected for necropsy. Additionally, one pup/sex/litter will be selected as possible parents of the F2 generation. Following the necropsy of the selected F1 pups, a decision will be made by the Chief, Premanufacture Notice Management Branch of EPA with the concurrence of the Study Director and Project Monitor as to whether the remaining F1 pups will be necropsied or euthanized and discarded, based on the results of the necropsy of the selected animals.

PROGENY

Mortality: All pups will be sexed and examined as soon as possible after birth to determine the number of viable and stillborn members of each litter. Litters will be evaluated twice daily for survival.

Standardization of Litter Sizes: On day 4 after birth, the size of each litter will be adjusted by eliminating extra pups by random selection to yield, as nearly as possible, four males and four females per litter. Culled pups will be sacrificed by decapitation and discarded.

Survival Data: Survival indices will be calculated at 0, 4, 7 and 14 days after birth and at weaning (postnatal day 21).

Body Weight and Sex Determination: All live pups will be sexed and weighed individually at day 0; and 4, 7 and 14 days after birth and at weaning. The body weights and sexes will be recorded on an individual basis but the pups will not be uniquely identified at this stage.

Symptoms: All pups will be examined for physical abnormalities at birth and throughout the lactation period. All pups dying during lactation will be necropsied when possible to investigate the cause of death.

Selection: After the weaning of the last litter, one pup/sex/litter from all dose groups will be selected for necropsy with tissues saved (see below), and one pup/sex/litter from all dose groups will be selected as possible parents of the F2 generation. All pups will be available for selection. The results from the necropsy of selected F1 weanlings shall be provided t the Chief, Premanufacture Notice Management Branch f EPA (and the Project Monitor) within 48 hours of the completion of necropsy. He (or she) shall then have 72 hours from receipt of the data to decide whether the remaining F1 weanlings will be necropsied with tissues saved (see below) or euthanized and discarded. If the Branch Chief determines that it is necessary (with the concurrence of the Study Director and Project Monitor) that the remaining weanlings be necropsied, they will be processed as soon as possible. If the Branch Chief decides that this procedure is unnecessary, the remaining weanlings will be euthanized and discarded. The F1 pups, selected as possible parents for the F2 generation, will remain on the same dietary concentration of VYEE as their parents for a maximum of three (3) weeks. On or before that time the EPA Branch Chief with the concurrence of the Study Director and Project Monitor will determine, based on draft data from the F1 breed, whether the selected F1 animals will

continue on the test diets and be bred (as described above for the F0 animals) or euthanized and discarded. During their exposures these F1 animals will be weighed weekly and examined daily for clinical signs. Feed consumption will also be measured weekly.

Gross Pathology: A gross internal examination will be made on any pup appearing abnormal or dying on test, and on one pup/sex/litter randomly selected from each test group of the F1 generation (see below).

Pathology

Parental and Weanling Animals: All adult F0 (parental) animals in all groups shall be subjected to a complete gross necropsy. Parental males will be sacrificed after the mating period is completed; parental females will be sacrificed after their litters are weaned. The tissues specified below from all F0 adults and necropsied F1 weanlings will be retained in fixative. The tissues listed below fr m the 25 male and 25 female F0 adults from the control and high dose groups shall be subjected to histopathologic examination:

pituitary
vagina
uterus
ovaries

testes
epididymides
seminal vesicles
prostate
target organ(s) if any

Any of the above organs or tissues exhibiting gross changes will be evaluated microscopically in F0 animals from the other dose groups.

Animals Dying on Test: A complete gross necropsy will be conducted for any parental animals dying on test and tissues listed above will be retained for possible subsequent histopathology.

Nonpregnant Females: The fixed (buffered neutral 10% formalin) uteri from any females of the F0 generation failing to produce a litter will be stained with potassium ferricyanide f r confirmation of pregnancy status. This staining procedure will not affect any subsequent histopathologic examination.

Gross Necropsy

The gross necropsy will include: examination of the external surfaces; all orifices; cranial cavity; carcass; external and cut surfaces of the brain and spinal cord; the thoracic, abdominal, and pelvic cavities and their viscera; and cervical tissues and organs.

Statistical Analyses

The unit of comparison will be the male or the pregnant female (or the litter). Results of the quantitative continuous variables (e.g. body weights, food consumption, etc.) will be intercompared for the three treatment groups and one control group by use of Levene's test for equal variances, analysis of variance (ANOVA), and t-tests with Bonferroni probabilities. The t-tests will be used when the F value from the ANOVA is significant. When Levene's test indicates homogeneous variances and the ANOVA is significant, the pooled t-test will be used for pairwise comparisons. When Levene's test indicates heterogeneous variances, all groups will be compared by an ANOVA for unequal variances followed, when necessary, by the separate variance t-test.

Nonparametric data will be statistically evaluated using the Kruskal-Wallis test followed by the Mann-Whitney U test for pairwise comparisons when appropriate. Frequency data (such as the various indices) will be compared using the Fisher's Exact Test. For all statistical tests, the fiducial limit of 0.05 (two-tailed) will be used as the criterion for significance.

Retention of Specimens and Records

All specimens and records which remain the responsibility of Bushy Run Research Center (BRRC) will be retained in the BRRC archives for the length of time specified in the appropriate guidelines and regulati ns (see Section II K).

Good Laboratory Practices

The Bushy Run Research Center, through administration of a quality assurance program by the Good Laboratory Practices Committee and Quality Assurance Unit, assures compliance of all phases of toxicological studies with existing regulations and generally accepted good laboratory practices.

IV. REPORTING

Status Reports: Status reports will be provided to the Sponsor indicating the number of survivors in each group, mean body weights with statistical significance, and any compound-related effects. The frequency and format of the reports are flexible.

Final Report: A draft report will be issued prior to the issuance of the final report. Complete signed copies (number to be specified) of the final report will be submitted following termination of the study. The final report will include:

Abstract
Introduction
Experimental Design
Materials and Methods
Narrative discussion of parameters evaluated
Individual Maternal Data for F0 Generation:

a. Identification number
b. Age at beginning of study
c. Age at death and manner of death.
d. Weekly body weights prior to mating and gestational and lactational body weights taken thereafter
e. Weekly food consumption prior to mating and food consumption during gestation and lactation
f. Male rat (by identification number) used for mating.
g. Date of delivery and gestation length in days.
h. Total number of offspring per litter.
i. Number and percent of live and dead offspring.
j. General condition of offspring and mother through weaning.

Summary of Maternal Data for F0 Generation:

a. Mean maternal body weights and survival indices.
b. Mean food and compound consumption (expressed as mg/kg/day).
c. Mean litter size.
d. Mean number of live and dead offspring.
e. Number and percent of mothers showing behavioral abnormalities in nesting and nursing.
f. Mating index =

$$\frac{\text{Number of plugged females}}{\text{Number of paired females}} \times 100$$

g. Fecundity index =

$$\frac{\text{Number of pregnancies}}{\text{Number of plugged females}} \times 100$$

h. Fertility indices (also expressed as percentages) =

$$\frac{\text{Number of females pregnant}}{\text{Total number of females paired}} \times 100$$

Individual Paternal Data for F0 Generation:

a. Identification number.
b. Age at beginning of study.
c. Age at death and manner of death.
d. Weekly body weights prior to mating.
e. Weekly food consumption.

Summary of Paternal Data for F0 Generation:

a. Mean male body weights (weekly prior to mating) and survival indices
b. Mean food and compound consumption (expressed as mg/kg/day)
c. Fertility indices (also expressed as percentages):

$$\frac{\text{Number of males shown to be fertile}}{\text{Total number of males paired}} \times 100$$

Data From Each F1 Litter Arranged by Dose Level:

a. Total litter size.
b. Number and percent of stillborn.
c. Number and percent of live births.
d. Periodic viability counts.
e. Periodic body weights by sex per litter from day 0 of life to weaning (taken on days 0, 4, 7, 14, and 21 of lactation).
f. Number and nature of physical abnormalities observed.
g. Pup survival indices (also expressed as percentages).
h. Sex ratio

Gestational index =

$$\frac{\text{Number of females with live litters}}{\text{Number of females pregnant}}$$

Live birth index =

$$\frac{\text{Number of live pups at birth}}{\text{Total number of pups born}}$$

4-Day survival index =

$$\frac{\text{Number of pups surviving 4 days}}{\text{Total number of live pups at birth}}$$

7-Day survival index =

$$\frac{\text{Number of pups surviving 7 days}}{\text{Total number of live pups at 4 days}}$$

14-Day survival index =

$$\frac{\text{Number of pups surviving 14 days}}{\text{Total number of live pups at 7 days}}$$

21-Day survival index =

$$\frac{\text{Number of pups surviving 21 days}}{\text{Total number of live pups at 14 days}}$$

Lactation Index =

$$\frac{\text{Number of pups surviving 21 days}}{\text{Total number of live pups at 4 days}}$$

Summary of F1 Litter Data:

a. Mean body weights of all pups through weaning (taken on day 0, 4, 7, 14 and 21).
b. Number and percent of pups with physical or behavioral abnormalities.
c. Mean pup survival indices through lactation day 21.

Protocol and any amendments

Summary and details of dietary analyses

Summary and individual data on gross F0 parental necropsy

Summary and individual data on gross necropsy of selected F1 weanlings

Summary and individual data on the F0 histopathologic evaluations

Resumes of the professional personnel associated with the study

WPC/esk/0694P-4
09-18-86

PRIVELEGED

DOCUMENT

Bates number UCC049662 - 049689 has been skipped

UNION CARBIDE

INTERNAL CORRESPONDENCE

HEALTH, SAFETY & ENVIRONMENTAL AFFAIRS

P-2
39 Old Ridgebury Road
Danbury, CT 06817-0001

TO: R. C. Wise

DATE: July 23, 1986

COPY: Dr. B. Ballantyne
Mr. M. R. Buffman
Dr. R. W. Tyl

SUBJECT: UCAR VINYL RESIN VYEE

Dick:

Enclosed is a preamble to the protocol:

> Reproductive Toxicity Evaluation of Generic UCAR Vinyl Resin VYEE Administered in the Feed to the CD Sprague-Dawley) Rat

this, upon your approval, will be given to Alison Kerester in Mr. Conner's office for submission to the EPA. Please let me know if you have any questions or comments.

Sincerely,

Tipton R. Tyler, Ph.D., D.A.B.T.
Assistant Director Applied Toxicology

TRT:jmc
Enclosure

PROPOSAL FOR INVESTIGATING THE POTENTIAL FOR VYEE
TO CAUSE ADVERSE POSTNATAL EFFECTS IN ANIMALS

In order to alleviate the Agency's concern over the possible postnatal toxic effects of UCAR Vinyl Resin, VYEE, Union Carbide is proposing to conduct a reproductive toxicity evaluation. The Agency's concern is based upon the results of a reproduction range-finding study in rats on a chlorinated paraffin of intermediate chain length and containing 52% by weight chlorine. In that study there was no evidence of treatment related toxicity to the parental animals, nor was there any evidence of adverse effects on the measured reproductive indicies in the treated animals. There was, however, a profound effect, at the highest dosage level employed (6250 ppm in feed), on pup survival from lactation day 10 and onward. In fact, there was complete mortality of all pups in this dosage level group. The results of that study clearly demonstrate that the intermediate chain length, 52% chlorinated paraffin does not express reproductive toxicity, but does exhibit potential for postnatal toxicity. Based upon what the Agency believes to be a chemical structural analogy, therefore, a suspicion exists that UCAR Vinyl Resin VYEE, may exhibit some similar toxicological activity.

Union Carbide is proposing to conduct a study of similar design to that conducted at the International Research and Development Corporation (IRDC) under sponsorship of the Chlorinated Paraffins Industry Association (CPIA). Since that study was sufficient to identify the postnatal toxic potential of the chlorinated paraffin, it seems reasonable to assume that a study of similar design would be sufficient to define the postnatal toxic potential of the VYEE resin. In addition, certain modifications have been made in the companies proposal based upon experience and information gained from the CPIA study. Thus, the number of animals per group has been increased to improve the sensitivity of the assay, and the postpartum time decreased, since the toxic effect is manifest well within the 21-day lactation period. These modifications both improve the design of the study within the scope of the defined toxic effect, and increase the cost effectiveness of the hazard assessment program. The salient features of Union Carbide's proposal, along with the side-by-side comparison with the CPIA study design are shown in Table 1.

The study proposed by Union Carbide offers the following advantages over that of conducting a traditional 2-generation reproductive study as pointed below.

1. The postnatal toxicity evaluation is more cost effective than conducting a 2-generation reproductive study. Since the specific toxic concern has been identified a priori, it seems justified to design the study in the most cost effective manner to address the specific concern. The proposed study will answer the question of whether or not UCAR Vinyl Resin expresses potential postnatal toxicity and can be conducted for about one-half the cost of a 2-generation oral reproductive study.

2. Decreasing the cost of testing will result in the ability for the product to support the testing program within a shorter time interval. Therefore, the testing would be initiated at an earlier stage in the products life and this would allow for more rapid data collection and hazard evaluation.

In summary, Union Carbide is proposing to conduct a reproductive toxicity evaluation in rats in order to alleviate the Agency's concerns on possible toxic effects of UCAR Vinyl Resin VYEE. This study will address and resolve the issue of postnatal toxicity which has arisen from the Agency's belief that there is a chemical structural analogy between the PMN material and chlorinated paraffins. The study is cost effective and, therefore, the product will support the testing in a shorter time period then if a full 2-generation reproductive toxicity test were required. Pending the possibility that additional data become available on the chlorinated paraffins which might clarify the postnatal toxic response and could be used to modify the protocol for the testing, Union Carbide's proposal would appear to address and answer the Agency's concerns on UCAR Vinyl Resin VYEE.

Tipton R. Tyler, Ph.D., D.A.B.T.
Assistant Director Applied Toxicology

TRT:jmc
0695E

TABLE 1: COMPARISON OF UNION CARBIDE PROPOSED STUDY AND CPIA REPRODUCTION RANGE FINDING STUDY

UNION CARBIDE PROPOSED STUDY ON VYEE	CHLORINATED PARAFFIN (52% CHLORINE, INTERMEDIATE CHAIN LENGTH)
Sprague Dawley rats [Crl:CD^{R}(SD)BR].	COBs CD rats.
25 females/dosage group. 1 male mated with 1 female.	10 females/dosage group. 1 male mated with 2 females.
6-weeks of age at start of dosing.	12-weeks at start of dosing.
Test material to be administered orally in diet.	Test material administered orally in diet.
Dosing to commence 6-weeks prior to mating.	Dosing commenced 14-days prior to mating.
Parental observations will include: clinical condition, weekly body weight (including gestation and postpartum period for females), food consumption, complete gross necropsey on sacrifice (both males and females). Selected tissues fixed for possible histological examination.	Parental observations included: clinical condition, weekly body weight (including gestation and postpartum period for females), food consumption, estrous cycle determination.
Progency observations will include: clinical condition, mortality (litter size), external examination, necropsy on abnormal or dead pups.	Progency observations included: clinical condition, litter size, external examination, necropsy on abnormal or dead pups.
Study terminated at day-21-postpartum. Full gross necropsy on 10 pups/sex per dosage level.	Study terminated 10-weeks postpartum. At day-21 postpartum, 10 pups/sex per dosage level subjected to full necropsy. At 10-weeks postpartum, 10 female and 5 male rats subjected to full necropsy. Hematology conducted. Selected tissues fixed for possible histological examination.

UNION CARBIDE

BUSHY RUN RESEARCH CENTER

R. D. 4, Mellon Road, Export, Pennsylvania 15632 Telephone (412) 733-5200

July 3, 1986

Dr. T. R. Tyler
Assistant Corporate Director of Applied Toxicology
UNION CARBIDE CORPORATION
39 Old Ridgebury Road - P2
Danbury, CT 06817-0001

Dear Dr. Tyler:

Enclosed please find the draft protocols you requested from Dr. Tyl for the evaluation of VYEE for reproductive toxicity and postnatal toxicity in CD® rats.

The cost for the reproductive toxicity evaluation is $72,000.00. The cost for the postnatal toxicity evaluation is $33,000.00. Please note that as you requested, the following aspects of the studies are not included: analyses of the dosed feed in both studies for homogeneity, stability and dosage level, histopathology of parental and weanling tissues in the reproduction study, and any clinical chemistry on the offspring in both studies. Please note also that, for both studies, it is assumed that the dosed feed will be stable for one week. If this is not the case, more frequent formulations and feeding (at extra cost) will be necessary.

If you have any questions or if you need additional information please call Dr. Tyl who will be Study Director for both of the studies.

Sincerely,

F. R. Frank

F. R. Frank, Ph.D.
Director

FRF/md
Enclosure
CC: Dr. R. W. Tyl
Ms. T. A. Savine
Ms. L. C. Fisher
Mr. K. J. Castora
Dr. W. M. Snellings

McKENNA, CONNER & CUNEO

WASHINGTON, D. C.

OFFICE MEMORANDUM

MEMORANDUM

TO: Union Carbide Corporation
Witnesses

FROM: C. A. O'Connor, III, Alison A. Kerester,
William A. McCue WAM

DATE: June 27, 1986

RE: VYEE

The following is a list of action items which have been identified as a result of the meeting held with EPA personnel on June 24 and the conference call with EPA on June 27, 1986.

1. Explain the reason that the ratio of oxygenated monomers to vinyl chlorides in low MW VYEE as stated in the PMN differs from that resulting from subsequent measurements performed on low MW VYEE and described in the June 24th meeting. Explain the analytical techniques used to derive these measurements. (Dr. Smith)

2. Supply the NMR spectrum and assignments and supply additional GPC information. Supply original NMR data. Supply copy, if possible, of the GPC chromatogram. Describe the detailed GPC procedure: from raw data to weight percentages. (Dr. Smith)

3. Assess the usefulness of supplying a carbonyl detector response in addition to the refractive index response for the GPC curve; determine if any useful mass spectroscopy data can be obtained. (Dr. Smith)

4. Provide the most current information concerning the actual percentage of the low MW species in VYEE. (Dr. Smith)

5. Provide a reasoned estimate of the maximum percentage of the low MW species which could theoretically consist of polyvinyl chloride oligomers and which could conceivably be analogized to chlorinated paraffins. (Dr. Smith)

6. Determine the amount of free formaldehyde present in the melamine formaldehyde cross-linkers. (Dr. Smith)

7. Describe the typical composition of the isocyanate formulations and identify the isocyanates used. (Dr. Smith)

8. Provide the log P calculation for the low molecular weight species. (Dr. Smith)

9. Ascertain from Myron Ottley (EPA-Reproductive Toxicologist) whether EPA possesses the purported ICI study of chlorinated paraffins and, if so, whether the Study concluded that post-natal exposures were essential to producing post-natal effects. (Dr. Tyl)

10. Modify the protocols for the Chernoff study to extend the dosing period in order to compare the post-natal effects of low MW VYEE with chlorinated paraffins. (Dr. Tyl)

11. Recalculate, and provide to EPA, the percentage of VYEE which will be present in the coatings formulations. (Dr. Smith)

12. Obtain an expert statement from the National Paint and Coatings Association's industrial hygienist, Steven Sider, concerning the standard workplace practices and precautions of Original Equipment Manufacturers ("OEM's") who apply high solids coatings. The expert's statement should indicate the following:

a. Whether applications are entirely by airless or electrostatic applications;

b. Whether respirators are worn routinely, even where applications take place in a spray booth;

c. Whether the masks worn for vapor protection will protect against mist as well. (Mr. Keough/MC&C)

13. Estimate the cancer risk of VYEE based upon the analogy to C-12 (58% chlorine). (Dr. Turnbull)

14. Ascertain from EPA attorney Jim Nelson the following:

a. Whether the Agency's concern over low molecular weight VYEE disappears if it is less than 2% of the PMN substance;

b. Ascertain whether by answering satisfactorily all of Mr. Israel's questions on VYEE chemistry, Union Carbide will have succeeded in destroying the analogy.

c. Whether EPA understands that respirators must be worn in the OEM workplace and, therefore, should be assumed for purposes of risk assessment.

15. Ascertain whether EPA accepts that in the OEM workplace there will be no air spray of VYEE formulations. (MC&C).

16. Make sure that EPA understands that UCC's difficulty with putting a carcinogen warning on the label for VYEE is that UCC strongly believes that such a warning will kill the product.

cc: Mark N. Duvall, Esq.

UNION CARBIDE CORPORATION
OLD RIDGEBURY ROAD DANBURY CONN 06817
LAW DEPARTMENT

May 1, 1986

D. L. Heywood
P. F. Smith
T. R. Tyler
R. C. Wise

Re: VYEE Stategy Meeting

On April 30, 1986 a meeting was held at the Boundbrook plant to discuss preparation of objections to EPA's proposed order concerning PMN85-1388, VYEE. Attending were M. N. Duvall, D. F. Smith, T. R. Tyler, R. C. Wise, and outside consultant, D. J. Jollow. Because of concerns for potential carcinogenicity, developmental toxicity, reproductive effects, and substantial exposure, the proposed order would prohibit the manufacture or importation of VYEE pending the development of information judged necessary by EPA for a reasoned evaluation of the health effects of VYEE, and the completion of EPA's review of that information. The preamble discusses 3 tests needed to provide the necessary information: a 2-year bioassay (estimated cost of $850,000), a 2-generation reproductive study (estimated cost of $109,400), and a developmental toxicity (teratology) test (estimated cost of $53,492), with a total estimated cost of $1,012,892.

The group discussed the proposed order and concluded that: (1) the proposed order is generally well written; (2) it clarified the basis for EPA's objections (essentially, it discusses virtually every objection raised by EPA during the negotiations and adopts none of UCC's arguments); and (3) UCC should prepare written objections to the proposed order. Objections are due by Saturday, May 24.

The group agreed to retain Dr. Jollow as a consultant in this matter, both for preparation of objections to the proposed order and for defense of a subsequent injunction action expected to be brought by EPA. Dr. Jollow is in the Department of Pharmacology at the Medical University of South Carolina in Charleston; is Chairman of the Safe Drinking Water Committee of the National Academy of Sciences; has held

NTP estimates 1.1 million for 2 species feeding studies
(NTP spokesman via SOCMA Alan Bailo

several positions at the National Institutes of Health; and has published approximately 70 articles, primarily in the field of pharmocokinetics. R. C. Wise agreed to send him a letter formally retaining him and specifying the financial arrangements. Wise also agreed to arrange with R. L. Crawford to provide Dr. Jollow with a copy of the standard UCC confidentiality agreement for his signature.

After further discussion, the group agreed that the objections to the proposed order:

(1) should discuss why EPA's asserted analogy of VYEE to chlorinated paraffins is inapposite (this would include (a) a primary argument that VYEE is structurally different from chlorinated paraffins and would be expected to have different pharmocokinetic properties - Dr. Jollow will focus on this argument; and (b) a secondary argument that within the family of chlorinated paraffins, some structurally quite similar members do not appear to exhibit the hazards of concern to EPA, further suggesting that the structural analogy to VYEE is weak);

(2) should discuss how a different chemical or family of chemicals which do not appear to exhibit the effects of concern to EPA are more structurally analogous to VYEE than are chlorinated paraffins (Dr. Jollow will assist T. R. Tyler in identifying such a closer structural analogue; Jollow will question his professional colleagues and Tyler will consult with other corporations);

(3) should discuss briefly the evidence cited by the proposed order for the carcinogenicity of chlorinated paraffins (it should note that (a) the NTP studies have not been peer reviewed and have not yet been issued in final; (b) the NTP studies obtained positive or equivocal results only at extremely high doses; and (c) the proposed order did not express a no observable effect level ("NOEL") for carcinogenicity, although one could be calculated from the NTP studies);

(4) perhaps should discuss the evidence cited by the proposed order for developmental toxicity and reproductive effects of chlorinated paraffins, depending upon the results of a critical review of the studies cited by the proposed order (T. R. Tyler will discuss the studies with S. Tyl of Bushy Run Research Center and with an outside expert, possibly H. Marshall Johnson, of the Jefferson Medical College, Philadelphia);

(5) should discuss the proposed order's suggestions of substantial exposure potential for VYEE (D. F. Smith will be the expert for this issue);

(6) should discuss the proposed order's estimates of VYEE's margins of safety ("MOSs") for the effects of concern to EPA (this will include (a) discussion of the proposed order's estimate of a 10% degree of absorption through skin contact rather than the usual estimate of a 1% degree; and (b) any helpful statements in EPA's published risk assessment guidelines for carcinogenicity and developmental toxicity);

(7) should discuss the public interest in use of VYEE as a component in low VOC coatings, which are substitutes for coatings requiring the use of high VOC solvents; and

(8) should discuss how the proposed order fails to meet the legal standards under Section 5(e) of TSCA for an order prohibiting manufacture pending receipt of additional information.

In light of the May 24 deadline for the filing of objections, the group agreed on the following schedule:

(1) on Thursday, May 1, M. N. Duvall and T. R. Tyler will discuss strategy with outside counsel, Chuck O'Connor and Alison Kerester, at a meeting in Washington, D. C.;

(2) by Friday, May 9, Dr. Jollow will send out a first draft of his paper discussing (a) the inappropriateness of chlorinated paraffins as a structural analogue for VYEE; (b) (possibly) a closer structural analogue which does not appear to exhibit the effects of concern to EPA; and (c) considerations relating to skin absorption of chemicals such as VYEE);

(3) by the same date, a first draft of the objections will have been prepared by outside counsel and other members of the group and will be distributed for review;

(4) on Tuesday, afternoon, May 13, and most of Wednesday, May 14, Dr. Jollow will meet with outside counsel and any necessary members of the group in Washington, D. C. to discuss the first draft of the objections and his paper; and

(5) on Friday, May 23, outside counsel will serve the final draft of the objections and Dr. Jollow's paper on EPA; if necessary, outside counsel will arrange on May 23 for filing with EPA on Saturday, May 24.

Given the deadline for filing comments, the group concluded that it is impractical to initiate any additional short-term testing of VYEE.

M. N. Duvall

cc: A. Kerester
C. A. O'Conner
B. L. White

PRIVELEGED

DOCUMENT

Bates number UCC49702-49705 has been skipped

D. L Heywood RECEIVED

DEC 18 198

D. L. HEYWOOD

INTERNAL CORRESPONDENCE

UNION CARBIDE CORPORATION P.O. BOX 670 BOUND BROOK, NEW JERSEY 08805

SPECIALTY CHEMICALS DIVISION

To (Name): D. L. Heywood
Dept: R. C. Wise
Location: UCC - Danbury
Area:

Copy to:

Date: December 12, 1985

Originating Dept:

Area:

Subject: December 5 Meeting with EPA on the VYEE PMN

The following is a summary of our December 5 meeting with EPA on the VYEE PMN. The purpose of this meeting was for EPA to relay the basis f their concerns and regulatory recommendation.

Jim Alwood led off with the following assessment:

1. The substance is recognized as a polymer.

2. EPA has a major concern about the fraction with MW less than 500. They decided that this material is polyvinyl chloride oligomers and contained no HPA, HEA or EA. Their analysis leads them to the conclusion that this low MW material is very similar to a chlorinated parafin.

3. There have been 2 NTP bioassay studies on chlorinated parafins which show toxicity problems. These are NTP-TR 305 on $C_{23}Cl_7H_{19}$ (40% chlorine) which showed problems at 3750 mg/Kg dose (gavage) and NTP-TR 308 on $C_{12}Cl_7H_{19}$ (58% chlorine) which showed problems at 625 mg/Kg. The 40% chlorine material showed considerably less toxic effects in these studies.

4. Also, the Chlorinated Parafin Institute has a study showing reproductive effects at high dose for a C_{15} material with 52% chlorine.

5. EPA is also concerned about the exposure scenario: manufacturer, coatings formulator, end user; and potential dermal as well as inhilation exposure during spray operations.

6. The CTA is not an issue at all. Alternate CTA would not change their assessment.

We presented our analytical characterization of the low MW fraction of VYEE, which is shown on the attached sheet. Bob Israel and Peter Tong were very interested in these results and the details of the Analytical methods. We agreed to provide this information through Don Heywood.

UCC
049706

Our assessment is that EPA may modify their position due to this chemical composition information but that they will still see a correlation with the chlorinated Parafins.

Our immediate courses of action are to obtain copies of the three toxicity studies mentioned above for internal review and to forward the Analytical information.

D. F. Smith

DFS:lms

Meeting Agenda
P85-1388

TSCA CONFIDENTIAL
BUSINESS INFORMATION

Date: December 5, 1985
Time: 2:00 P.M.
Place: Environmental Protection Agency
401 M Street, S.W., East Tower Room 542
Washington, D.C. 20460

Submitter: [Union Carbide Corp.]

Premanufacture Notice: 85-1388

EPA Representatives:

Stephanie Roan, Section Chief
James Alwood, Program Manager
Jon Silberman, Attorney-Advisor
Peter Tong, Technical Integrator
Bob Israel, Chemist
Jim Long, Economist

[Union Carbide Corp.] Representatives:

[D. L. Heywood, Assistant Corporate Director, Product Safety
R. C. Wise, Director of Health, Safety, and Environmental Affairs, SCME
D. F. Smith, Technology Director, SCME]

Purpose of Meeting

- Discuss Chemistry of Low Molecular Weight Species
- Discuss Basis of Health Concerns
- Discuss Exposure Scenario

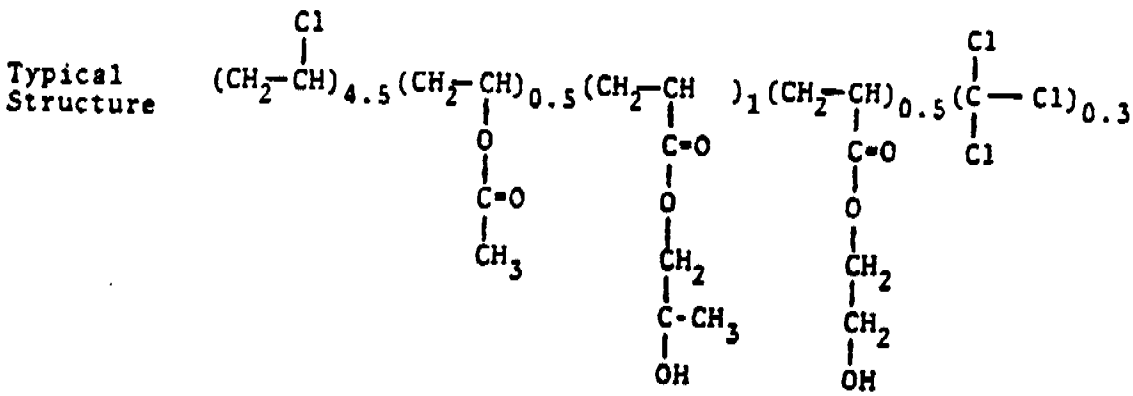
Summary

The meeting should relay to Union Carbide the basis of EPA's concerns and regulatory recommendation. It should also identify specific actions Union Carbide might take to facilitate a regulatory recommendation that will allow the PMN substance to be marketed.

UCC
049708

VYEE (500 molecular weight species)

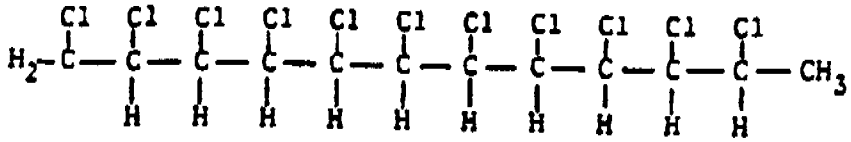
Typical Structure



Diamond Shamrock Co.	Average Molecular Formula	Average Molecular Weight	Chlorine Content, %
Chlorowax 40	$C_{24}H_{44}Cl_6$	545	40-42
Chlorowax 50	$C_{24}H_{42}Cl_8$	614	48-54
Chlorowax 70	$C_{24}H_{29}Cl_{21}$	1062	70
Chlorowax 500C	$C_{12}H_{19}Cl_7$	170	60-65
Chlorowax 70L	$C_{12}H_{15}Cl_{11}$	549	70

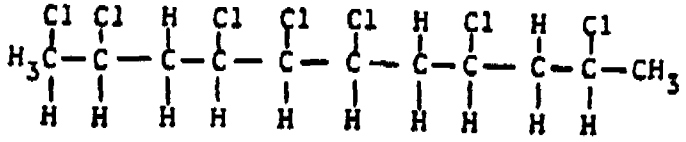
Chlorowax 70L (average formula $C_{12}H_{15}Cl_4$)

Typical Structure



Chlorowax 500C (average formula $C_{12}H_{19}Cl_7$)

Typical Structure



60-65 wt. percent chlorine

UNION CARBIDE INTERNAL CORRESPONDENCE

To: D. L. Heywood - DB P2 1-3

From: L. Brydia - BB/200

UNION CARBIDE CORPORATION

D. F. Smith
Solvents & Coatings Materials
Bound Brook, NJ

Date: December 10, 1985

Organization: R&D - Analytical

Area:

Subject: Characterization of VYEE

Copies to:
R. A. Gregory - BB
D. L. Heywood - DB P2
I. E. Treble - BB
R. C. Wise - DB K4

As you requested, we have characterized VYEE and the portion of this vinyl resin that is below a molecular weight of 500 to determine whether the composition of the low molecular weight species is appreciably different than the complete resin. Comparison of the chlorine concentrations of VYEE and the low molecular weight fraction of the resin is of particular interest. The analytical techniques employed in this investigation were carbon-13 nuclear magnetic resonance spectroscopy (NMR), gel permeation chromatography (GPC), Dohrmann microcoulometry (MCTS), liquid chromatography/size exclusion chromatography (LC/SEC), and fourier transform-infrared spectroscopy (FT-IR).

The sample of VYEE used for all of the analyses was labelled "VYEE Texas City #1." The sample as received was reported to be 67.3% solids in methylethylketone. The initial analyses consisted of determining the composition of VYEE and the isopropanol soluble (10.8%) and insoluble portions (89.2%) of VYEE. The isopropanol soluble fraction was obtained by diluting the VYEE with 10 parts isopropanol/pentane (50/50) to 1 part of VYEE followed by coagulation in dry ice acetone, filtering the residue, and evaporating the solvent with a vacuum pump for 1 hour. The purpose of the isopropanol extraction was to isolate sufficient low molecular weight material for NMR analysis. GPC (using μ-Styragel columns) of each fraction confirmed that the concentration of low molecular weight material was enhanced in the alcohol soluble fraction.

	Wt. % of Material with MW < 500	Mn
VYEE	12.0	~2100
Isopropanol Solubles	49.5	~500
Isopropanol Insolubles	5.6	~2900

4.5 - 1. Stab [illegible]

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049713

2-3

Analysis of the three samples by C-13 NMR gave the following results:

	Weight Percent			
	VCl	VAc	HPA	HEA
VYEE	60	4	26	11
Isopropanol Solubles	56	8	24	12
Isopropanol Insolubles	63	4	21	12

These data show that the composition of VYEE does not change appreciably with molecular weight.

The chlorine content of the material between molecular weights 500 and 100 was determined by microcoulometric analysis of a fraction collected from the gel permeation chromatograph. The chlorine concentration in the fraction below 500 molecular weight was 33.0 compared to ~~34~~.0 in VYEE. Therefore, the chlorine content of VYEE between 500 ~~and 100~~ molecular weight is the same as that of the resin itself.

Further comparison of the compositions of different molecular weight fractions of VYEE was obtained from infrared analysis of fractions of the polymer which were isolated by size exclusion chromatography (Ultra-Styragel columns). Three fractions were collected and analyzed which represent; (a) the average molecular weight of VYEE; (b) an average molecular weight of about 500; and (c) a fraction of molecular weight less than 500. The infrared spectra of these three fractions were qualitatively very similar and representative of a vinyl resin such as VYEE. Through band ratioing it was shown that the concentration of the chlorinated species does not change with molecular weight.

In summary, our analyses show that there is no significant compositional difference between VYEE of different molecular weights. No data were obtained during this investigation to indicate that the chlorine concentration of VYEE increases with decreasing molecular weight.

L. E. Brydia

LEB:jja
Att.

INSTRUMENTS USED IN CHARACTERIZATION OF VYEE

- IBM Model WP-270/SY Nuclear Magnetic Resonance Spectrometer
- Digilab Model FTS-15 Fourier Transform Infrared Spectrometer
- Dohrmann Microcoulometric Titration System
- Waters Associates Model 244 Liquid Chromatograph with 10^5, 10^4, 10^3, and 500Å μ-Styragel Columns
- Waters Associates Liquid Chromatograph with 100 and 500Å Ultra-Styragel Columns

UNION CARBIDE CORPORATION P.O. BOX 670, BOUND BROOK, NJ 08805
SOLVENTS AND COATINGS MATERIALS DIVISION PHONE: (201) 563-5000

May 23, 1986

Dr. D. J. Jallow
Department of Pharmacology
Medical University of South Charleston
171 Ashley Ave.
Charlotte, South Carolina 29425

Dr. J. V. Rodricks
Environ Corporation
1000 Patomac St., N.W.
Washington, D.C. 20007

Dear Drs. Jallow and Rodricks:

Attached are the calculated Octanol/Water Partition Coefficients which we had calculated as part of our work on VYEE.

Sincerely,

D. F. Smith

DFS:lms
Attachment

cc: Dr. T. Tyler
Union Carbide Corp.
Danbury, CT

OCTANOL/WATER PARTITION COEFFICIENTS

These partition coefficients were calculated for a number of species potentially present in the low molecular weight fraction of VYEE. These calculations were performed by Mr. T. Engle of Union Carbide Corporation, Research Triangle Park, N.C. using a C Log P Computer Program which has been developed by Dr. Leo of Pamona College in California.

		Log P
Reference:	$(VCl)_6$	5.32
	$(VCl)_5$	4.55
	$(VCl)_4$	3.75
Species:	$(VCl)_3(HEA)$	2.05
	$(VCl)_3(HPA)$	2.65
	$(VCl)_3(VAc)$	2.98
	$(VCl)_2(HEA)$	1.28
	$(VCl)_2(HEA)(VCl)_3(VAc)$	3.64
	$(VCl)_2(HEA)(VCl)_3(HEA)$	3.0

Conclusions

- Log P increases as the oligomer size increases.
- Insertion of an hydroxy alkyl acrylate group into the chain lowers log P by 1 to 1.5 units; this says that the distribution in the water phase is increased by a factor of 10 to 30.

PRIVELEGED

DOCUMENT

Bates number UCC49718-49720 has been skipped

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ALISON A. KERESTER
DIRECT DIAL (202) 789- 7644

May 6, 1986

BY HAND

Dr. Joseph V. Rodericks
Environs, Inc.
1000 Potomac Street, N.W.
Washington, D.C. 20007

Re: NTP Bioassays on Chlorinated Paraffins

Dear Dr. Rodericks:

We are very pleased that you are able to assist us in the preparation of formal objections to EPA's proposed TSCA § 5(e) order on Union Carbide Corporation's ("UCC") compound, VYEE.

EPA has determined that VYEE is structurally analogous to chlorinated paraffins. EPA has further determined that because the two NTP bioassays appear to indicate that chlorinated paraffins are carcinogenic, that by analogy VYEE is also expected to be a potential carcinogen.

We ask that you review and critique the two NTP bioassays and determine what these studies demonstrate with respect to the potential carcinogenicity of chlorinated paraffins, and what the implication of these studies is for VYEE. In addition, we ask that you perform a qualitative risk assessment on the carcinogenic potential. We would welcome any thoughts you may have with respect to other areas addressed in the proposed order, e.g., structure activity relationship, developmental and reproductive health effects.

With respect to the general format of your report, we suggest the following:

Identification of Author -- A brief introductory statement should identify your qualifications and describe your familiarity with the facts.

Issues Examined -- The report should describe the issue(s) examined including the bases for the Agency concern.

Summary of Conclusions -- The report should state your overall conclusions with respect to the issue(s) investigated.

Issue-By-Issue Discussion -- The report should provide a separate discussion of each issue examined by you. The discussion should address the particular test performed or study reviewed, the results of the study or review, your analysis of, and observations about the results, and your conclusions.

Overall Conclusions -- This section should summariz the conclusions with respect to each issue and then provide an overall conclusion or opinion.

References/Data Tables -- Provide a list of references relied upon and data tables, if appropriate, should be attached.

Curriculum Vitae -- Attach your CV including any publications.

The idea is to make your report a self-contained document and thus any relevant materials relied upon by you should either be incorporated into the text or attached as an appendix.

Please note that the information contained in the proposed TSCA § 5(e) order is regarded by UCC as highly confidential (including the fact that EPA has issued the proposed order) and therefore should be treated by you as such.

If you have any questions, please feel free to contact me at 789-7644.

Sincerely,

Alison Kerester

Alison A. Kerester

cc: Mark Duvall, Esquire
Encl.
AAK:py

Xerox TR Tyler

UNION CARBIDE CORPORATION 39 OLD RIDGEBURY ROAD, DANBURY, CT 06817-0001
Corporate Health, Safety and Environmental Affairs Department

CONTAINS CONFIDENTIAL BUSINESS INFORMATION

Certified Mail
Return Receipt Requested

December 26, 1985

Document Control Officer
Office of Toxic Substances, TS-793
U.S. Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460

Attention: Jim Alwood, TS-794

Dear Mr. Alwood:

On behalf of the Union Carbide representatives, I extend our appreciation for the discussions with you and members of the EPA staff on December 5 regarding PMN 85-1388, which is for the substance described generically as "vinyl chloride-vinyl acetate hydroxyl modified copolymer". You have by now received and filed Union Carbide's written agreement to further suspension of the review period.

During the meeting, the question of analytical characterization of the lower molecular weight fraction of the subject resin arose, and we agreed to provide the Agency with further data that were being developed at the time of and subsequent to the meeting. Following is a summary report of additional information.

> The analytical techniques employed in this investigation were carbon-13 nuclear magnetic resonance spectroscopy (NMR), gel permeation chromatography (GPC), Dohrmann microcoulometry (MCTS), liquid chromatography/size exclusion chromatography (LC/SEC), and fourier transform-infrared spectroscopy (FT-IR).
>
> The sample of VYEE used for all of the analyses was labelled "VYEE Texas City #1." The sample as received was reported to be 67.3% solids in methyl ethyl ketone. The initial analyses consisted of determining the composition of VYEE and the isopropanol soluble (10.8%) and insoluble

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portions (89.2%) of VYEE. The isopropanol soluble fraction was obtained by diluting the VYEE with 10 parts isopropanol/pentane (50/50) to 1 part of VYEE followed by coagulation in dry ice/acetone, filtering the residue, and evaporating the solvent with a vacuum pump for 1 hour. The purpose of the isopropanol extraction was to isolate sufficient low molecular weight material for NMR analysis. GPC (using - Styragel columns) of each fraction confirmed that the concentration of low molecular weight material was enhanced in the alcohol soluble fraction.

	Wt. % of Material with MW 500	Mn
VYEE	12.0 (a)	2100
Isopropanol Solubles	49.5 (a)	500
Isopropanol Insolubles	5.6	2900

Note (a): These values should be corrected downward to read "7.0-8.0" and "44.5-45.5", respectively, since they include 4-5% of a soluble, non-polymeric, resin stabilizer.

Analysis of the three samples by C-13 NMR gave the following results:

	Weight Percent				
	VCl	VAc	HPA	HEA	Mn
VYEE	60	4	26	11	2100
Isopropanol Solubles	56	8	24	12	500
Isopropanol Insolubles	63	4	21	12	2900

These data show that the composition of VYEE does not change appreciably with molecular weight.

The chlorine content of the material between molecular weights 500 and 100 was determined by microcoulometric analysis of a fraction collected from the gel permeation chromatograph. The chlorine concentration in the fraction below 500 molecular weight was 33.0 compared to 34.0 in VYEE. Therefore, the chlorine content of VYEE below 500 molecular weight is essentially the same as that of the resin itself.

Further comparison of the compositions of different molecular weight fractions of VYEE was obtained from infrared analysis of fractions of the polymer which were isolated by size exclusion chromatography (Ultra-Styragel columns). Three fractions were collected and analyzed which represent; (a) the average molecular weight of VYEE; (b) an average molecular weight of about 500; and (c) a fraction of molecular weight

less than 500. The infrared spectra of these three fractions were qualitatively very similar and representative of a vinyl resin such as VYEE. Through band ratioing it was shown that the concentration of the chlorinated species does not change with molecular weight.

In summary, these analyses show that there is no significant compositional difference between VYEE of different molecular weights. No data were obtained during this investigation to indicate that the chlorine concentration of VYEE increases with decreasing molecular weight.

We are obtaining copies of and reviewing the three reports of the toxicological properties of the chlorinated paraffins that were discussed during the meeting, and will contact you in early January when we have comments or questions based on our review of those documents. Please continue to communicate through my office regarding PMN 85-1388.

Very truly yours,

D. L. Heywood
Principal Technical Contact
(203) 794-5224

DLH/cr

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UNION CARBIDE

D. L. HEYWOOD
Corporate Product Safety
P2599, Danbury, CT
(203) 794-5224

12/27/85

To: R. E. Bollinger
D. F. Smith
B-L. White
R. C. Wise