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August 3, 1993



8EHQ-93-12009

.INIT 08/11/93

Document Processing Center (TS-790)  
Attention: 8(e) Coordinator  
Office of Pollution Prevention and Toxics  
U. S. Environmental Protection Agency  
401 M Street, SW  
Washington, DC 20460



88930000403

Ladies and Gentlemen:

Subject: Notice in Accordance with Section 8(e) - Two Week Rat Inhalation Study of a Poly(oxypropylene) poly(oxyethylene) poly(oxypropylene) polymer, having an average molecular weight of 2900 and a monomer ratio of 85 weight percent propylene oxide and a 15 weight percent ethylene oxide, described by CAS RN 106392-12-5.

BASF Corporation is submitting the report of a two week rat inhalation study of the subject polymer. This study was sponsored by AlliedSignal Inc., Morristown, N.J.

The referenced compound was found to produce target organ effects after repeated inhalation exposure of rats. Groups of rats were exposed to atmospheres containing liquid aerosols at target concentrations of 0, 5, 50, or 500 mg/m<sup>3</sup> for six hours per day, five days per week for two weeks (Groups I, II, III, IV respectively). Animals were sacrificed at the end of the tenth exposure. An additional group of animals was exposed to 500 mg/m<sup>3</sup> and was allowed to recover for two weeks prior to sacrifice.

All of the animals survived to the end of their scheduled test periods. Macroscopic findings were not related to compound administration. Microscopic findings of interstitial inflammation and alveolar/intraalveolar macrophages were seen in the lungs of all animals in a dose related manner. Effects were minimal to slight in Groups I, II and, in most cases in Group III. Moderate ratings were noted in Group IV. Slight to moderate hypertrophy/hyperplasia of the bronchiolar epithelium was seen at the high dose only. Partial recovery of these effects occurred. The NOEL for females was five mg/m<sup>3</sup>; there was no NOEL determined for males.

KS  
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6/27/96

Because of the marginal effects at the low dose levels, BASF Corporation does not feel that this information constitutes an adverse effect to health or the environment; however, we feel that the effects at the high dose are consistent with the reporting requirements defined under TSCA.

BASF Corporation will notify employees and customers of these new results via revised Material Safety Data Sheets and Hazard Communication training. Any additional reports that we receive will be forwarded to the Agency.

This submission does not contain confidential business information. If you have any questions, please feel free to contact me at 313-246-6207 or AlliedSignal Inc. of Morristown, N.J.

Very truly yours,

BASF CORPORATION

A handwritten signature in cursive script that reads "Edward Kerfoot".

Edward J. Kerfoot, Ph.D.  
Director, Toxicology and  
Product Regulations

/cs



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A Subchronic (2-Week) Inhalation Toxicity Study  
of Pluronic 31R1 (357-93A) in the Rat via Whole-Body Exposures  
Pathology Report

**SUMMARY:**

Sixty Sprague Dawley - derived (CD)<sup>1</sup> albino rats (30 males, 30 females) were randomly distributed into 4 groups (10/sex/Groups I and IV and 5/sex/Groups II and III). Groups II, III, and IV were exposed, whole-body, to atmospheres which contained liquid aerosols of Pluronic 31R1 (357-93A) at projected target concentrations of 5, 50, or 500 mg/m<sup>3</sup>, respectively, 6 hours/day, 5 days/week for 2 weeks. Group I, the control, was similarly exposed to clean air only. The animals were 6-8 weeks old at the start of the study.

All of the animals on test survived to the end of their respective exposure and post-exposure recovery periods. Macroscopic findings in the animals from both the exposure and the post-exposure periods were considered to be of sporadic occurrence and were not related to the whole body exposure to atmospheres which contained Pluronic 31R1 (357-93A).

Microscopically, subacute/chronic interstitial inflammation and alveolar/intraalveolar macrophages were seen in the lungs of all animals. At the end of the exposure period, the severities of both findings showed a dose-related increase in the males and were most severe for the females from Group IV (500 mg/m<sup>3</sup>) followed by Group III (50 mg/m<sup>3</sup>). Inflammatory cells/cell debris was seen in the bronchiolar lumens of 4 males; 3 from Group IV and 1 from Group II (5 mg/m<sup>3</sup>). Hypertrophy/hyperplasia of the bronchiolar epithelium was seen in the 5 males and in 2 females from Group IV only. At the end of the post-exposure recovery period, the severities and/or incidence of these findings in the animals of Group IV were less than those from the Group IV killed at the end of the exposure period. This indicated that recovery had occurred but was not yet complete.

At the end of the exposure period the NOEL (no observable effect level) for the females was 5 mg/m<sup>3</sup>; there was no NOEL for the males.

**INTRODUCTION:**

This study was designed to assess the potential inhalation toxicity of Pluronic 31R1 (357-93A). Sixty Sprague Dawley - derived (CD)<sup>1</sup> albino rats (30 males, 30 females) were randomly distributed into 4 groups (10/sex/Groups I and IV and 5/sex/Groups II and III). Groups II, III, and IV were exposed, whole-body, to atmospheres

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<sup>1</sup>Supplied by Charles River Breeding Laboratories, Kingston, N.Y.

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**INTRODUCTION (cont.):**

which contained liquid aerosols of Pluronic 31R1 (357-93A) at projected target concentrations of 5, 50, or 500 mg/m<sup>3</sup>, respectively, 6 hours/day, 5 days/week for 2 weeks. Group I, the control, was similarly exposed to clean air only. Group I of this study, was a common control for 2 other studies (92-6051 and 92-6052) conducted concurrently in this laboratory. The animals were 6-8 weeks old at the start of the study. The identification and disposition of the individual animals are presented in Table I.

**POSTMORTEM METHODS:**

At the end of 2 weeks of exposure, 5 animals/sex/group were killed by exsanguination under carbon dioxide anesthesia. Five animals/sex/Groups I and IV were maintained on test for a 2 week post-exposure recovery period, at the end of which they were similarly killed. Immediately after death, the external surfaces; all orifices; the external surfaces of the brain and spinal cord; the organs and tissues of the cranial, thoracic, abdominal, and pelvic cavities, and neck; and the remaining carcass were examined for the presence of macroscopic abnormalities. One animal was selected from each group (I, IV, III, II, in that order) until all were killed.

Organs listed below, from all of the animals on test, were dissected, trimmed to remove contiguous tissues in a uniform manner, and weighed as soon as possible after dissection to avoid drying. Paired organs were weighed together. The weights and the results of their analyses are presented with the antemortem findings.

adrenal glands	liver
brain	lungs
heart	spleen
kidneys	testes with epididymides

The following tissues and organs were sampled from all animals on test and preserved in 10% NBF (neutral buffered formalin). The lungs and the nasopharyngeal tissues were infused with 10% NBF prior to their immersion into a larger volume of the same fixative.

adrenal glands	lungs
brain	nasopharyngeal tissues
heart	spleen
kidneys	testes with epididymides
larynx	tissue lesions/masses
liver	

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**POSTMORTEM METHODS (cont.):**

After fixation the lungs from all of the animals on test were routinely processed, embedded in paraffin, cut at a microtome setting of 4-7 microns, mounted on glass slides, stained with hematoxylin and eosin and examined by light microscopy.

**RESULTS AND DISCUSSION:**

**Mortality:**

All of the animals on test survived to the end of their respective exposure and post-exposure recovery periods when they were killed and examined postmortem for the presence of morphologic abnormalities.

**Macroscopic Findings:**

All of the animals on test were examined postmortem for the presence of macroscopic abnormalities. Incidence summaries are presented in Tables II A and II B; findings in the individual animals are presented in Table III. Macroscopic findings in the animals from both the exposure and the post-exposure periods were considered to be of sporadic occurrence and not related to whole-body exposure to atmospheres which contained Pluronic 31R1 (357-93A).

**Microscopic Findings:**

Only the lungs from all of the animals on test were examined by light microscopy. Incidence summaries are presented in Tables IV A and IV B; findings in individual animals are presented in Table V.

**Exposure Period (2 Weeks):**

Subacute/chronic interstitial inflammation and alveolar/intraalveolar macrophages (both were minimal to moderate) were seen in the lungs of all animals which were killed at the end of the exposure period. In the males the severities of both findings showed a dose related increase. In the females, both findings were most severe in Group IV (500 mg/m<sup>3</sup>) followed by Group III (50 mg/m<sup>3</sup>); in Groups I and II (0 and 5 mg/m<sup>3</sup>, respectively) the severities were considered to be comparable. Inflammatory cells/cell debris (minimal to slight) was seen in the bronchiolar lumens of 4 males: 3 from Group IV and 1 from Group II. This was not seen in the females. Hypertrophy/hyperplasia (slight to moderate) of the epithelium lining the bronchioles was seen in the 5 males and in 2 females from Group IV only.

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A Subchronic (2-Week) Inhalation Toxicity Study  
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RESULTS AND DISCUSSION (cont.):

Microscopic Findings (cont.):

Exposure Period (2 Weeks) (cont.):

Table A  
Treatment Related Findings - Lungs - Exposure Period

SEX	MALE				FEMALE			
GROUP	I	II	III	IV	I	II	III	IV
EXPOSURE LEVEL (mg/m <sup>3</sup> )	0	5	50	500	0	5	50	500
NUMBER EXAMINED	5	5	5	5	5	5	5	5
subacute/chronic interstitial inflammation								
minimal	4	2	0	0	5	3	1	0
slight	1	3	4	0	0	2	4	1
moderate	0	0	1	5	0	0	0	4
alveolar/intraalveolar macrophages								
minimal	3	2	0	0	3	3	1	0
slight	2	3	5	0	2	2	4	1
moderate	0	0	0	5	0	0	0	4
bronchiolar lumen: inflammatory cells/cell debris								
minimal	0	1	0	2	0	0	0	0
slight	0	0	0	1	0	0	0	0
bronchiolar epithelium: hypertrophy/hyperplasia								
slight	0	0	0	3	0	0	0	2
moderate	0	0	0	2	0	0	0	0

Post Exposure Recovery Period (2 Weeks):

Subacute/chronic interstitial inflammation and alveolar/intraalveolar macrophages (both were minimal to moderate) were seen in all animals from Groups I and IV (0 and 500 mg/m<sup>3</sup> respectively). For both findings, the severities in males and females from Group IV were greater than those seen in the comparable controls. Hypertrophy/hyperplasia (minimal) of the epithelium lining the bronchioles was seen only in 2 males from Group IV. The severities and/or incidence of these findings in the animals of Group IV from the post-exposure recovery period were less than those in Group IV from the exposure period. This indicated that recovery had occurred but was not yet complete.

A Subchronic (2-Week) Inhalation Toxicity Study  
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RESULTS AND DISCUSSION (cont.):

Microscopic Findings (cont.):

Post Exposure Recovery Period (2 Weeks) (cont.):

Table B

Treatment Related Findings - Lungs - Post Exposure Recovery Period

SEX	MALE				FEMALE			
	I	II	III	IV	I	II	III	IV
GROUP								
EXPOSURE LEVEL (mg/m <sup>3</sup> )	0	5	50	500	0	5	50	500
NUMBER EXAMINED	5	0	0	5	5	0	0	5
subacute/chronic interstitial inflammation								
minimal	2	0	0	0	3	0	0	0
slight	3	0	0	3	2	0	0	5
moderate	0	0	0	2	0	0	0	0
alveolar/intraalveolar macrophages								
minimal	4	0	0	0	5	0	0	0
slight	1	0	0	4	0	0	0	5
moderate	0	0	0	1	0	0	0	0
bronchiolar lumens: inflammatory cells/cell debris	0	0	0	0	0	0	0	0
bronchiolar epithelium: hypertrophy/hyperplasia minimal	0	0	0	2	0	0	0	0

Other Morphologic Findings:

Foci/areas of hemorrhage were seen in the lungs of 1 or more animals from all groups. These appeared to be of recent origin and were considered to be agonal. Macroscopically, the lungs of a number of these animals had red foci. These focal hemorrhages were not considered to be related to the whole body exposure to atmospheres which contained Pluronic 31R1 (357-93A).

Other morphologic findings, macroscopic and microscopic, in animals from both the exposure and post-exposure recovery periods occurred with comparable incidence and severities in exposure and control groups or they occurred sporadically. These findings were also not considered to be related to the whole-body exposure to atmospheres which contained Pluronic 31R1 (357-93A).

A Subchronic (2-Week) Inhalation Toxicity Study  
of Pluronic 31R1 (357-93A) in the Rat via Whole-Body Exposures  
Pathology Report

**CONCLUSIONS:**

1. All of the animals on test survived to the end of their respective exposure and post-exposure recovery periods.
2. There were no treatment-related macroscopic findings.
3. There were treatment-related microscopic findings in the lungs of animals killed at the end of both the exposure period and the post-exposure recovery period
  - A. Exposure Period: subacute/chronic interstitial inflammation and alveolar/intraalveolar macrophages were seen in all animals; the severities of both findings showed a dose-related increase in the males and were most severe in the females from Group IV (500 mg/m<sup>3</sup>) followed by Group III (50 mg/m<sup>3</sup>). Inflammatory cells/cell debris was seen in the bronchiolar lumens of 4 males; 3 from Group IV and 1 from Group II (5 mg/m<sup>3</sup>). Hypertrophy/hyperplasia of the bronchiolar epithelium was seen in the 5 males and in 2 females from Group IV.
  - B. Post-Exposure Recovery Period: The severities and/or incidence of the aforementioned findings in the recovery animals from Group IV were less than those in the comparable animals in Group IV killed at the end of the exposure period. This indicated that recovery had occurred but was not yet complete.
4. At the end of the exposure period the NOEL (no observable effect level) for the females was 5 mg/m<sup>3</sup>; there was no NOEL for the males.

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Henry F. Bolte, D.V.M., Ph.D.                      Date  
Associate Director of Pathology

Reviewed by: 

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Ward R. Richter, D.V.M., M.S.                      Date  
Diplomate, A.C.V.P.  
Vice President and Director of  
Pathology

## Triage of 8(e) Submissions

Date sent to triage: 11-22-96

**NON-CAP**

**CAP**

Submission number: 12009 A

TSCA Inventory: Y N **D**

Study type (circle appropriate):

Group 1 - Gordon Cash (1 copy total)

ECO            AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX            **SBTOX**            SEN            w/NEUR

Group 3 -HERD (1 copy each)

STOX                            CTOX                            EPI                            RTOX                            GTOX

STOX/ONCO                    CTOX/ONCO                    IMMUNO                    CYTO                            NEUR

Other (FATE, EXPO, MET, etc.): \_\_\_\_\_

Notes:

- This is the **original** 8(e) submission; refile after triage evaluation.
- This **original** submission has been **split**; rejoin after triage evaluation.
- Other:

**Photocopies Needed for Triage Evaluation**

entire document:	0	1	2	3
front section and CECATS:	0	1	2	3
Initials: _____	Date: _____			

CECATS DATA:  
 Submission # BEHQ: 0893-12009 SEQ: A

TYPE: INT SUPP FLWP

SUBMITTER NAME: BASF Corporation

INFORMATION REQUESTED: FLWP DATE:

- 0501 NO INFO REQUESTED
  - 0502 INFO REQUESTED (TECH)
  - 0503 INFO REQUESTED (VOL ACTIONS)
  - 0504 INFO REQUESTED (REPORTING RATIONALE)
- DISPOSITION:  
 REFER TO CHEMICAL SCREENING  
 CAP NOTICE

VOLUNTARY ACTIONS:

- 0401 NO ACTION REPORTED
- 0402 STUDIES PLANNED/IN PROGRESS
- 0403 NOTIFICATION OF WORKER RIGHTS
- 0404 LABELING/MSDS CHANGES
- 0405 PROCESS/AND/OR INGREDIENTS
- 0406 APPL USE DISCONTINUED
- 0407 PRODUCTION DISCONTINUED
- 0408 CONFIDENTIAL

SUB DATE: 08/03/93 OTS DATE: 08/11/93 CSRAD DATE: 06/27/96

CHEMICAL NAME:

Poly(oxypropylene) poly(oxyethylene)  
poly(oxypropylene) polymer

CASE

106392-12-5

INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C
0201 ONCO (HUMAN)	01 02 04	0216 EPICLIN	01 02 04	0241 IMMUNO (ANIMAL)	01 02 04
0202 ONCO (ANIMAL)	01 02 04	0217 HUMAN EXPOS (PROD CONTAM)	01 02 04	0242 IMMUNO (HUMAN)	01 02 04
0203 CELL TRANS (IN VITRO)	01 02 04	0218 HUMAN EXPOS (ACCIDENTAL)	01 02 04	0243 CHEM/PHYS PROP	01 02 04
0204 MUTA (IN VITRO)	01 02 04	0219 HUMAN EXPOS (MONITORING)	01 02 04	0244 CLASTO (IN VITRO)	01 02 04
0205 MUTA (IN VIVO)	01 02 04	0220 ECO/AQUA TOX	01 02 04	0245 CLASTO (ANIMAL)	01 02 04
0206 REPRO/TERATO (HUMAN)	01 02 04	0221 ENV. OCCUR/REL/FATE	01 02 04	0246 CLASTO (HUMAN)	01 02 04
0207 REPRO/TERATO (ANIMAL)	01 02 04	0222 EMER INCI OF ENV CONTAM	01 02 04	0247 DNA DAM/REPAIR	01 02 04
0208 NEURO (HUMAN)	01 02 04	0223 RESPONSE REQUEST DELAY	01 02 04	0248 PROD/USE/PROC	01 02 04
0209 NEURO (ANIMAL)	01 02 04	0224 PROD/COM/CIHEM ID	01 02 04	0251 MSDS	01 02 04
0210 ACUTE TOX. (HUMAN)	01 02 04	0225 REPORTING RATIONALE	01 02 04	OTHER	01 02 04
0211 CHR. TOX. (HUMAN)	01 02 04	0226 CONFIDENTIAL	01 02 04		
0212 ACUTE TOX. (ANIMAL)	01 02 04	0227 ALLERG (HUMAN)	01 02 04		
<input checked="" type="checkbox"/> 0213 SUB ACUTE TOX (ANIMAL)	01 02 04	0228 ALLERG (ANIMAL)	01 02 04		
0214 SUB CHRONIC TOX (ANIMAL)	01 02 04	0229 METAB/PHARMACO (ANIMAL)	01 02 04		
0215 CHRONIC TOX (ANIMAL)	01 02 04	0240 METAB/PHARMACO (HUMAN)	01 02 04		

IMAGE DATA NON-CBI INVENTORY

YES YES (DROP/REFER)

CAS SR NO NO (CONTINUE)

SPECIES RAT

TOXICOLOGICAL CONCERN:

LOW  
 MED  
 HIGH

USE: PRODUCTION:

106392-12-5

IM N AMINI