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BASF

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December 22, 1993

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OFFICE OF POLLUTION  
PREVENTION AND TOXICS

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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



88940000093

Subject: Notice in Accordance with Section 8(e) - Preliminary Results  
of a Screening Program of the Prenatal Toxicity of Four Phthalates

Ladies and Gentlemen:

BASF Corporation is submitting preliminary results of a screening prenatal toxicity program for four commercially available phthalates conducted by BASF Aktiengesellschaft, Ludwigshafen, Germany. Although BASF Corporation does not feel that the information presents a substantial risk to health or environment, it is being submitted under Section 8(e) of TSCA.

The results for the following four phthalates are reported below:

- A. CAS No. 26761-40-0; Di(isodecyl)phthalate
- B. CAS No. 68515-48-0; Di(isononyl)phthalate 1
- C. CAS No. 28553-12-0; Di(isononyl)phthalate 2
- D. CAS No. 28553-12-0; Di(isononyl)phthalate 3

In this comparative screening program, the test substances were administered to pregnant Wistar rats (10/group) by gavage for 10 consecutive days (days 6 - 15 post coitum) in daily doses of 40, 200 and 1,000 mg/kg body weight. For comparison, a control group was dosed with olive oil.

Food consumption and body weights of the animals were recorded regularly throughout the study period. The state of health of the animals was checked daily.

On day 20 p.c., all surviving females were sacrificed and assessed by gross pathology (including weight determinations of liver, kidneys and the unopened uterus). The fetuses were dissected from the uterus, sexed, weighed and further investigated for any external, soft tissue and/or skeletal findings.

1-12-94

Following is a summary of the preliminary results:

#### Phthalate A

At the highest dose level (1,000 mg/kg body weight/day), mild signs of maternal toxicity were observed. Mean food consumption was statistically significantly lower than control values on days 8 - 10 p.c.; 3 dams showed vaginal hemorrhages and 2 dams showed urine-smear fur during the treatment period. Absolute and relative liver weights were statistically significantly increased.

The only sign of embryo-/fetotoxicity which was observed occurred at the highest dose level in the form of a markedly increased occurrence of skeletal variations (i.e. rudimentary cervical and/or accessory 14 ribs); no teratogenic effects, however, were recorded.

At the low dose (40 mg/kg body weight/day) and the intermediate dose (200 mg/kg body weight/day), no signs of maternal toxicity, no substance induced effects on gestational parameters, and no signs of embryo-/fetotoxicity (including teratogenicity) were recorded.

#### Phthalate B

At the highest dose level (1,000 mg/kg body weight/day), moderate signs of maternal toxicity were observed. Mean food consumption was statistically significantly lower than control values during most of the days of the treatment period. One dam showed vaginal hemorrhage between days 13 and 15 p.c. Relative kidney weights were statistically significantly increased.

The only sign of embryo-/fetotoxicity which was observed occurred at the highest dose level in the form of a markedly increased occurrence of skeletal variations (i.e. rudimentary cervical and/or accessory 14 ribs); no teratogenic effects, however, were recorded.

At the low (40 mg/kg body weight/day) dose and the intermediate dose (200 mg/kg body weight/day), no signs of maternal toxicity, no substance induced effects on gestational parameters, and no signs of embryo-/fetotoxicity (including teratogenicity) were recorded.

#### Phthalate C

At the highest dose level (1,000 mg/kg body weight/day), only very marginal - if any - signs of maternal toxicity were observed (one dam with vaginal hemorrhage on days 14 and 15 p.c.).

The only sign of embryo-/fetotoxicity which was observed occurred at 1,000 mg/kg in the form of a statistically significantly increased rate of one skeletal variation (accessory 14 rib(s)); no teratogenic effects, however, were seen.

At the low dose (40 mg/kg body weight/day) and the intermediate dose (200 mg/kg body weight/day) no signs of maternal toxicity, no substance induced effects on gestational parameters, and no signs of embryo-/fetotoxicity (including teratogenicity) were recorded.

## Phthalate D

At the highest dose level (1,000 mg/kg body weight/day), some overt signs of maternal toxicity were observed. Food consumption was statistically significantly reduced during several days of the treatment period, mean body weights were statistically significantly lower than the respective control values on days 13, 15 and 17 p.c. and body weight gains were clearly impaired (about 38% less than the corresponding control value). Relative liver weights were statistically significantly increased.

Clear signs of embryo-/fetotoxicity (including teratogenicity) occurred at the 1,000 mg/kg group. Some rare soft tissue and skeletal malformations (predominantly involving the urogenital tract and the long bones) were found. In addition, an increased occurrence of fetal soft tissue (hydro-urether) and skeletal variations (rudimentary cervical and/or accessory 14th ribs) and an increased rate of skeletal retardation (delays in the ossification of the sternbrae) were seen.

At the low (40 mg/kg body weight/day) dose and the intermediate dose (200 mg/kg body weight/day), no signs of maternal toxicity, no substance induced effects on gestational parameters, and no signs of embryo-/fetotoxicity (including teratogenicity) were recorded.

## Conclusion

In the present screening program involving four different phthalates, signs of developmental toxicity were only noted at 1,000 mg/kg body weight/day, a dose where at least some maternal toxicity was also evident. The most pronounced effects concerning developmental toxicity were recorded for Phthalate D. For Phthalate A, Phthalate B and Phthalate C, only increased rates of fetal skeletal variations (supernumerary ribs) were observed as the only sign of developmental toxicity. The effects from Phthalate C were less pronounced than were those of the other two.

BASF understands that this reporting of study results from the prenatal toxicity screening program with four phthalates under TSCA 8(e) is in accordance with EPA's policy. All persons handling these products will be informed of these results via updated Material Safety Data Sheets.

Please note that this letter does not contain any confidential business information.

Very truly yours,

BASF CORPORATION



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

/cs



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
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OFFICE OF  
PESTICIDES AND TOXIC  
SUBSTANCES

APR 12 1994

This letter formally acknowledges EPA's receipt of information submitted by your organization under Section 8(e), the "substantial risk" information reporting provision of the Toxic Substances Control Act (TSCA). For your reference, copies of the first page(s) of your submission(s) are enclosed and display the TSCA Section 8(e) Document Control Number (i.e., 8EHQ-0000-0000 Init.) assigned by EPA to your submission(s). Please refer to this cited number when submitting follow-up or supplemental information.

Please note that all submitted correspondence will be placed in the public files unless confidentiality is claimed according to the procedures outlined in Part X of EPA's TSCA Section 8(e) policy statement (43 FR 11110, March 16, 1978).

Confidential submissions submitted pursuant to the TSCA Section 8(e) Compliance Audit Program (CAP) should already contain information supporting confidentiality claims, because substantiation of CBI claims is required at the same time the 8(e) CAP is submitted to EPA. (If not done so already, please ensure that this information is provided to the Agency). When substantiating any/all claims, answer the questions detailed in the following attachment.

For NON-CAP submissions, any confidentiality claims should be supported by submission of information as described in the attachment(s).

12808 A

CECATS/IRIAGE TRACKING DBASE ENTRY FORM

CPCATS DATA:  
Submission # 8402-1293-12808 SEQ A

INFORMATION REQUESTED: FLWP DATE:  
0501 NO INFO REQUESTED  
0502 INFO REQUESTED (TECH)  
0503 INFO REQUESTED (VOL ACTIONS)  
0504 INFO REQUESTED (REPORTING RATIONALE)  
DISPOSITION:  
0679 REFER TO CHEMICAL SCREENING  
0678 CAP NOTICE

VOLUNTARY ACTIONS  
0401 NO ACTION REPORTED  
0402 STUDIES PLANNED/UNDERWAY  
0403 NOTIFICATION OF WORKER/OHHS RS  
0404 LABEL/MSDS CHANGES  
0405 PROCESS/HANDLING CHANGES  
0406 APP/USE DISCONTINUED  
0407 PRODUCTION DISCONTINUED  
0408 CONFIDENTIAL

TYPE: INT SUPP FLWP  
SUBMITTER NAME: BASF Corporation

SUB DATE: 12/22/93 OTS DATE: 12/29/93 CSB DATE: 01/12/94

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

CAS#  
26761-40-0  
68515-48-0  
28553-12-0

| INFORMATION TYPE:                 | P F C           | INFORMATION TYPE:              | P F C    | INFORMATION TYPE:      | P F C    |
|-----------------------------------|-----------------|--------------------------------|----------|------------------------|----------|
| 0201 ONCO (HUMAN)                 | 01 02 04        | 0216 EPI/CLIN                  | 01 02 04 | 0241 IMMUNO (ANIMAL)   | 01 02 04 |
| 0202 ONCO (ANIMAL)                | 01 02 04        | 0217 HUMAN EXPOS (PROD CONTAM) | 01 02 04 | 0242 IMMUNO (HUMAN)    | 01 02 04 |
| 0203 CELL TRANS (IN VITRO)        | 01 02 04        | 0218 HUMAN EXPOS (ACCIDENTAL)  | 01 02 04 | 0243 CHEM/PHYS PROP    | 01 02 04 |
| 0204 MUTA (IN VITRO)              | 01 02 04        | 0219 HUMAN EXPOS (MONITORING)  | 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. OCCC/REL/FATE        | 01 02 04 | 0246 CLASTO (HUMAN)    | 01 02 04 |
| <u>0207</u> REPRO/TERATO (ANIMAL) | <u>01</u> 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 REQEST DELAY     | 01 02 04 | 0248 PROD/USE/PROC     | 01 02 04 |
| 0209 NEURO (ANIMAL)               | 01 02 04        | 0224 PROD/COMP/CHEM ID         | 01 02 04 | 0251 MSDS              | 01 02 04 |
| 0210 ACUTE TOX. (HUMAN)           | 01 02 04        | 0225 REPORTING RATIONALE       | 01 02 04 | 0299 OTHER             | 01 02 04 |
| 0211 CHR. TOX. (HUMAN)            | 01 02 04        | 0226 CONFIDENTIAL              | 01 02 04 |                        |          |
| 0212 ACUTE TOX. (ANIMAL)          | 01 02 04        | 0227 ALLERG (HUMAN)            | 01 02 04 |                        |          |
| 0213 SUB ACUTE TOX (ANIMAL)       | 01 02 04        | 0228 ALLERG (ANIMAL)           | 01 02 04 |                        |          |
| 0214 SUB CHRONIC TOX (ANIMAL)     | 01 02 04        | 0239 METAB/PHARMACO (ANIMAL)   | 01 02 04 |                        |          |
| 0215 CHRONIC TOX (ANIMAL)         | 01 02 04        | 0240 METAB/PHARMACO (HUMAN)    | 01 02 04 |                        |          |

IRIAGE DATA: NON-CBI INVENTORY ONGOING REVIEW SPECIES TOXICOLOGICAL CONCERN: USE: PRODUCTION

YES (CONTINUE) YES (DROP/REFER) RAT LOW

NO (DROP) NO (CONTINUE) MED

IN TERMINI REFR HIGH

GAVAGE  
Maternal & embryo toxicity only at 1000 mg/kg  
1 hebelate D was most toxic.

COMMENTS: Y cap