8EHQ-0497-12956

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April 9, 1997

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Document Processing Center (7407)
Attention: 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
401 M Street SW
Washington, D.C. 20460-0001

Dear 8(e) Coordinator:

Contains No CBI

8EHQ-0494-12956
Dimethylacetamide (DMAC)
C.A.S Registry No. 127-19-5

This letter is to inform you of the preliminary results of a recently completed rat developmental toxicity study with the test material.

This study was sponsored by BASF AG (Ludwigshafen, Germany), DuPont Deutschland (Bad Homburg, Germany), Ertisa S.A. (Madrid, Spain), and Montefibre S.P.A. (Milano, Italy).

Dimethylacetamide (DMAC) in water was administered to groups of 25 mated rats over days 7-21 of gestation (days 7-21G) at daily dose levels of either 0, 20, 65, 150, or 400 mg/kg. On day 22G, all rats were euthanized and necropsied. The fetuses were removed from the uterus and were weighed, sexed, and examined for external, visceral, head, and skeletal alterations. Significant, adverse maternal and developmental toxicity were produced at 400 mg/kg. There were significant dose-related reductions in mean maternal body weight, weight gain, and food consumption. Developmental toxicity was evident as increased embryolethality (increased resorptions per litter), significantly decreased mean fetal weight, increased fetal malformations (including anasarca, distended brain ventricles, malformations of the heart and greater vessels, naris atresia, synotia), and slightly increased fetal variations (including delayed ossification of the skull bones and sternebrae). Minimal developmental toxicity was seen at 150 mg/kg. At 150 mg/kg, mean maternal weight gain was reduced over the first four days of the dosing period indicative of maternal toxicity. Developmental toxicity was evident as significantly decreased mean fetal weight. In addition, there were some malformations (consistent with those seen at 400 mg/kg) seen occurring in single fetuses (including synotia, naris atresia, malformation of the heart and greater vessels). No evidence of maternal or developmental toxicity was seen at either 65 or 20 mg/kg.

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Prior to the conduct of the current study, a pilot developmental toxicity study was conducted at dose levels of 0, 62.5, 125, 250, and 500 mg/kg. The results of the pilot study and the results of a previously conducted study (Johannsen et al., 1987[1]) were both considered to determine the dose levels of the current study. The dose levels evaluated in the Johannsen study were 0, 65, 160, and 400 mg/kg. The results reported for the Johannsen study were largely consistent with what was seen in the current study in that clear evidence of maternal and developmental toxicity was seen at 400 mg/kg. However, some of the fetal malformations seen in the current study at 400 mg/kg were not reported in the Johannsen study (synotia, naris atresia, distended brain ventricles). At 160 mg/kg, Johannsen et al. reported a reduction in mean fetal weight and the data included in the paper indicate that a slight reduction in maternal weight gain was evident at this level as well. These findings are consistent with what was seen in the current study at 150 mg/kg. No effects were seen at 65 mg/kg; this result is consistent with the current study as well.

Thus, the overall conclusions drawn from the current study data are consistent with those drawn from the previously reported Johannsen study. Despite this similarity, we are reporting the current study to EPA as meeting the requirements for reporting studies under TSCA 8(e) because of the slight differences in some of the specific findings observed at the two higher dose levels.

These results do not warrant a change in the existing safe exposure limit of the chemical (10 ppm, 8- and 12-hr TWA) nor a change in current handling practices; with both providing adequate protection to workers having exposure potential to the compound.

Sincerely,

A. Michael Kaplan

A. Michael Kaplan, Ph.D.
Manager, Regulatory Affairs

AMK/SMM:jat
(302) 366-5260

[1] Johannsen, F.R., G.J. Levinskas, and J.L. Schardein, "Teratogenic Response of Dimethylacetamide in Rats", Fundamental and Applied Toxicology, 9: 550-556 (1987)