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

OFFICE OF PREVENTION, PESTICIDES AND TOXIC SUBSTANCES

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

MEMORANDUM

Date: April 22, 2008

SUBJECT: **Triadimefon; Chemical Screen of Newly Submitted Toxicology Studies.**

PC Code: 109901
Decision No.: 391164
Petition No.: NA
Risk Assessment Type: NA
TXR No.: NA
MRID No.: 47377101

DP Barcode: D351351
Registration No.: NA
Regulatory Action: New Chemicals Screen
Case No.: NA
CAS No.: 43121-43-3
40 CFR: NA

Ver.Apr.08

FROM: Kelly M. Schumacher, Biologist 4/22/2008
Registration Action Branch 2
Health Effects Division (7509P)

THROUGH: Richard Loranger, Ph.D., Branch Senior Scientist
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TO: Tony Kish, RM 22
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I. CONCLUSIONS

The newly submitted developmental neurotoxicity (DNT) study on triadimefon has been screened for completeness and general acceptability. This study has passed the screen and is eligible for complete review; however, the registrants should first submit historical control data for rearing by offspring in the FOB, particularly for PND 60 males and females, as there was a statistically significant decrease in both the mid- and high-dose groups. During review, the Health Effects Division (HED) may wish to consult with experts in brain morphometry at the Office of Research and Development (ORD), regarding changes seen in the PND 75 female cerebellum and the accompanying assessment provided by an independent pathologist.

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II. ACTION REQUESTED

The Registration Division (RD) of the Office of Pesticide Programs (OPP) has requested that HED screen the DNT study on triadimefon, in accordance with screening criteria based on the 870 series guidelines for toxicology studies.

III. RESULTS/DISCUSSION

The newly submitted developmental neurotoxicity (DNT) study on triadimefon has passed the screen for completeness and general acceptability and is eligible for complete review. Please refer to the attached summary tables and screening criteria appendixes for specific details. Note that the registrants should first submit historical control data for rearing by offspring in the FOB, particularly for PND 60 males and females, as there was a statistically significant decrease in both the mid- and high-dose groups

In general, it does not appear that HED will request any further data or conduct further statistical analyses, pending full review of the study. Preliminary review suggests that, in contrast to the study authors, the EPA may conclude no maternal LOAEL was observed because the magnitude of the maternal body weight changes was not great enough to be considered adverse. Auditory startle and passive avoidance effects appear to be limited to the highest dose tested, so more thorough statistical analyses by HED are not warranted at this time. Where statistically significant morphometric changes were seen at the high dose, analogous measurements were provided at the mid and low doses, so there does not appear to be any missing morphometric data.

During review, the Health Effects Division (HED) may wish to consult with Karl Jensen of the Office of Research and Development (ORD), or another expert in brain morphometry. A statistically significant decrease in the PND 75 female cerebellum was seen at all doses. The study authors explain that this finding was due to the non-homology of lobule 1 and provide an assessment by an independent pathologist. EPA reviewers should carefully consider this issue.

Table 1. Toxicology Data Requirements Screening Results

Chemical: Triadimefon
PC Code(s): 109901 Food Use: _____ Non-Food Use: ____X_____

Guideline	Study Title	MRID	GLP[a]	Test Article[b]	Dosing[c]	Animal Observations[d]	Control Data[e]
870.6300	Developmental Neurotoxicity Study in Rats	47377101	-	-	-	-	-

Comments:

- The overall data submission is of high quality and acceptable for placement into full review.

_ Indicates study passed the screen for the parameter specified

a GLP/Compliance statement present

b Test article, including stability, homogeneity, concentration, purity

c Dosing adequacy (including appropriate levels and numbers of animals) and route of administration

d Animal parameters observed, including (as applicable) body weight, food consumption, survival, hematology, clinical chemistry, urinalysis, histopathology, necropsy findings, study-specific parameters such as tumors, developmental toxicity, etc.

e Control data including (as applicable) historical controls and positive controls

Table 2. Preliminary Hazard for New Triadimefon Study.

PC Code: 109901		Based on Study Report		
Toxicity Study	Target Organ(s)/Effects	NOAEL (mg/kg/day)	LOAEL (mg/kg/day)	MRID
Developmental neurotoxicity (rat)	**Maternal:** Decreased body weight and body weight gain. **Offspring:** Decreased body weight and body weight gain, deviated snout, auditory startle effects (PND 60), and passive avoidance effects (F only).	**Maternal:** 23.9 mg/kg/day **Offspring:** 23.9 mg/kg/day	**Maternal:** 71.3 mg/kg/day **Offspring:** 71.3 mg/kg/day	47377101

Table 3. Bibliography of Newly Submitted Toxicology Studies for Triadimefon.

47377101	Sheets, L., Gilmore, R., Hoss, H. (2008) A Developmental Neurotoxicity Study with Technical Grade Triadimefon in Wistar Rats. Project Number: 07/D72/IL, 201766. Unpublished study prepared by Bayer CropScience. 1179 p.