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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Date: April 28, 2005

**MEMORANDUM**

SUBJECT: Topramezone (BAS670H). Report of the Risk Assessment Review Committee (RARC1)

FROM: Sarah Winfield, Recorder
Risk Assessment Review Committee
Health Effects Division (7509C)

TO: Mary Clock-Rust, Biologist, Risk Assessor
Registration Branch 1
Health Effects Division (7509C)

THROUGH: Ray Kent, Co-Chair
Risk Assessment Review Committee
Health Effects Division (7509C)

*PC Code*: 123009

*Team Members*: Mark I. Dow, Ph.D., Biologist
George F. Kramer, Ph.D., Chemist
Sarah J. Levy, M.S., Chemist
Yung Yang, Ph.D., Toxicologist
Silvia Termes, EFED
James Wolf, EFED

*Assessment Type*: Section 3 Registration, New Active Ingredient, Single Chemical

*RARC Members*: Norman Birchfield, Rebecca Daiss, Danette Drew, Jeff Evans, Diana Locke, Michael Metzger, PV Shah, Christina Swartz, Dana Vogel, Karen Whitby

*Other attendees:* Jim Stone, Joanne Miller, and PMRA (via telephone): Michael Honeyman, Zahra Galehdar, Andrea Katynski, Ron Bell, Suzan Mathew

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**MAJOR POINTS OF DISCUSSION:**

The RARC noted that the document was well-written.

***1.0 Executive Summary***

1. The RARC recommends the Team characterize the elevated serum tyrosine levels in the hazard characterization section of the executive summary (p. 6).

***3.0 Metabolism Assessment***

1. The RARC recommends the Team include information regarding the toxicological nature/hazard of the degradates in their justification for including/excluding degradates in the risk assessment (p. 17).

2. The RARC recommends the Team check to make sure the text describing the metabolites (p. 12 and 13) jibes with what is outlined in Table 3.4 (p. 15 and 16).

3. The RARC recommends removing M670H05 from the rotational crop tolerance expression (label restrictions [plant-back intervals] prevent exposure, nor is it considered toxic) and the drinking water tolerance expression (it is not considered toxic) in Table 3.6.1 (p. 17).

***4.0 Hazard Characterization/Assessment***

1. The RARC recommends clarifying what is meant by "there are no data of critical threshold for tyrosine-related toxic effects" under Section 4.1.1.2 (p. 18).

2. The RARC recommends clarifying in Section 4.1.4 FQPA, that the adverse effects observed in the toxicological studies relevant to FQPA are of concern, but that the endpoints utilized in the risk assessment are protective of these adverse effects (p. 20).

3. The RARC recommends including a paragraph summarizing the 8 developmental toxicity studies at the start of Section 4.2.3, followed by each study's DER executive summary (p. 30).

4. The RARC recommends the Team adjust the dermal absorption factor (*i.e.*, multiply by 5X), to account for the 20% oral absorption factor (p. 45).

5. The RARC recommends expanding on the rationale for the short-term incidental oral, dermal and inhalation exposure scenarios, by including the information that at day 41 in the carcinogenicity study in the rat (on which the endpoint is based) relevant adverse effects were observed (p. 51).

6. The RARC recommends altering the language re: the cancer classification, to read "not likely to be carcinogenic to humans at doses that do not alter thyroid hormone homeostasis" (p. 52).

7. The RARC recommends the Team describe the dietary drinking water assessment as Tier 2, in Section 4.5 Special FQPA Safety Factor (p. 53).

8. The RARC recommends the Team mention the adverse effect increased time to preputial separation observed in the reproduction and fertility effects study in the rat under Section 4.6 Endocrine Disruption (p. 53).

***6.0 Exposure Characterization/Assessment***

1. The RARC recommends the Team explain what compounds (parent, metabolites, degradates) were employed in the drinking water assessment, and then explain why the assessment is appropriate and protective. The RARC further recommends characterizing the drinking water assessment as "high-end," rather than "worst case" (p. 8, 55, 56, 58, 59).

2. The RARC recommends the Team clarify why rotational crops RACs are not included in the dietary assessment, *i.e.*, that the plant-back interval label requirement allows dissipation of the residues to non-detectable levels (p. 55).

3. The RARC recommends the Team replace the terms "acute" and "chronic" with "peak" and average," respectively, when describing the EDWCs (p. 57).

cc: Karen Whitby, Branch Chief
PV Shah, Senior Scientist
RARC Members