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

OFFICE OF PREVENTION,
PESTICIDES AND
TOXIC SUBSTANCES

June 21, 2000

MEMORANDUM

SUBJECT: Thiamethoxam -- Report of the Risk Assessment Review Committee

FROM: Kathleen Martin, Recorder
Risk Assessment Review Committee
Health Effects Division (7509C)

THROUGH: Paula Deschamp, Chair
Risk Assessment Review Committee
Health Effects Division (7509C)

TO: Pamela Hurley, Risk Assessor and Toxicologist
G. Jeff Herdon, Chemist
Steven Weiss, Industrial Hygienist
Registration Branch 2
Health Effects Division (7509C)

PC Code:	060109
Presenters:	P. Hurley, J. Herdon, and S. Weiss (EPA); G. Cockell; C. Norman, and H. Bietlot (Health Canada)
Assessment Type:	New Pesticide

"☼" Refers to Items that will be added to the RARC Guidance on Lotus Notes.
"☞" Refers to an item that requires RARC follow-up (i.e., a RARC action item).

BRIEF PROFILE:

Thiamethoxam is a new broad spectrum pesticide in the new class of compounds, the neonicotinoids. The review and risk assessment was conducted jointly with Health Canada: Gordon Cockell is their toxicologist; Christine Norman the occupational and residential exposure assessor, and Henri Bietlot the chemist. There is only one other pesticide in this new class that has undergone review thus far: imidacloprid.

The registrant is requesting several crop uses, tobacco, seed-treatment, and turf. This risk assessment does not include the seed-treatment and turf uses; this will be assessed later, when the corresponding exposure data arrive and are reviewed. Also, canola was not included in the occupational risk assessment as seed-treatment data for this crop are expected.

The toxicological effects of thiamethoxam are minimal. All the acute studies are in categories 3 and 4. Thiamethoxam does not inhibit cholinesterase. Subchronic and chronic studies indicate four primary targets for this chemical: the liver, kidney, hematopoietic system, and testes, with the testicular effects driving the toxicological endpoint selection for risk assessment because they are observed at very low dose levels and they may potentially be induced after short- up to long-term exposure, particularly when exposure occurs *in utero*. Thiamethoxam has been classified as a likely carcinogen for humans. The FQPA Safety Factor was retained because of the need for a developmental neurotox study. A dermal absorption estimate of 27% was used in the risk assessment. This is thought to be conservative.

Risk assessments were conducted for the following exposure scenarios: acute dietary exposure (food only) and aggregate acute exposure (food + water); chronic/cancer dietary exposure (food only) and aggregate chronic exposure (food + water); short-term, intermediate-term, and cancer occupational exposure. Risk estimates for short- and intermediate-term aggregate exposures were not conducted because the proposed non-occupational uses for thiamethoxam are not being considered at this time.

On the dietary side, there are no risks of concern. On the occupational front, there are no handler risks of concern; there is some concern regarding aerial application. Postapplication risks were estimated to meet the target MOE of 100 at postapplication intervals ranging from 0 to 35 days.

MAJOR TOPICS OF DISCUSSION:♦

- Kudos!!!!!!! This is a beautifully-prepared risk assessment. The hazard characterization was particularly good. The length and level of detail in the Executive Summary was just about perfect; it was very concise.

  - Toxicological Significance of Effects. How wonderful to have this sort of information in a risk assessment.

  - Dermal Absorption. Conservative but very well characterized.

  - ORE. Nice to have all the assumptions listed out.

  - ORE, page 36. Very nice–MOE's at harvest. Great table–should be used across the board.

- Question on Uses Included in Risk Assessment. The proposed labels include lawn and pet uses, however these were not included in the risk assessment. RARC asked for clarification. The Team responded that pet uses are not included because this is not a common US/Canada use. Regarding turf, the Team is awaiting studies that are now being conducted.

  - *RARC Recommends* that on page 21 the Team clarify which uses are being considered in this risk assessment.

Toxicity

- Conservatism of Reproductive Toxicity Assessment. RARC pointed out that the Team's reproductive toxicity assessment is a bit conservative. The Team explained its rationale for taking the approach it did, saying that some toxicologists in the field who are familiar with this pesticide believe the results of the study are equivocal. The Team and RARC discussed the possibility of having the registrant re-do the study or perhaps just part of the study. The Team pointed out that re-running just part of the study is not really feasible. The bottom line is that the study is expensive to conduct, the Team has data (albeit conservative) to conduct the risk assessment, and the risks are not of concern. RARC had no recommendations.

- ❖ NOAEL Selection in Rabbit Developmental Study, page 19, 20. The RARC asked why a NOAEL of 100 was selected instead of 50 and why an acute endpoint for females 13-50 was not established. The Team did not have the reasoning available; however, they did remember discussing the hazard assessment approach. They will follow-up on this and include more rationale in the document regarding their approach.

- ❖ Toxicity Endpoint for Chronic. The RARC asked if this applied to the general population as it's from a reproductive study and it's not clear whether the effect is specific to males or females. Could it be passed from either gender? RARC Recommends moving this discussion before the dietary section.

Dietary

- ❖ Cancer Risk Estimate: Is there a risk concern? The cancer risk for food is in the $3x10^{-6}$ range. And the Team asked for guidance on what should be considered as a level of concern. There have been some pesticides (EBDC Special Review; bromoxynil) where the risk cutoff was $3x10^{-6}$. *RARC Recommended* that the Team talk to OGC.

  - ♦ Quantifying Drinking Water Risk. A related question–is it appropriate to do the back calculation using $3x10^{-6}$? The RARC recommends that to remain consistent with other assessments drinking water for cancer not be quantified.

☼ - ❖ Tobacco Use. The Team quantified the risk resulting from exposure to thiamethoxam from tobacco use. Only an acute assessment was done as OPP believes that with regard to chronic toxicity, the adverse health effects resulting from tobacco use would affect an individual before chronic thiamethoxam exposure resulting from tobacco use.

  - ♦ RARC will post this in the RARC library.

- ❖ Estimating Residues in Liver from a Goat Study by Adding a 10x Factor. Because reliable liver data were unavailable, the Team applied a 10x factor to the metabolism data to estimate liver residues. While this approach has merit, it has not been validated as a standard policy. The RARC recommended that the Team characterize the rationale for developing their estimated value in qualitative terms to the effect "even if the liver residue were 10x greater than the goat residue, the risk would be....."

Drinking Water

- DWLOC. RARC noted that information regarding fate characteristics or assumptions and inputs used to calculate surface water EECs were omitted from the document. *RARC Recommends* reporting in the risk assessment at least the EFED input parameters. More information and documentation is needed on groundwater.

Occupational

- Page 3. Foliar based on screens. Discuss the potential impact of the DFR and/or ARETF data that are coming in.

- Page 30. Provide a little more explanation for the selection of the time intervals. Also, why is 30 a high-end value?

- Page 29. Include a use summary. How frequently, how applied, etc.

- Page 35. Include aerial application assumptions.

- Page 36. Remove scouting at harvest as it does not make sense: at this point they would be out picking; just use NA. Why are you concerned about foliar – clarify.

- Page 34, paragraph 2. There were no estimates for postapplication cancer risk. RARC recommended that the Team validate that postapplication cancer risks are of less concern than postapplication non-cancer risks which drive the REIs and provide a full explanation in the document.

OTHER ITEMS

- Changes to the Proposed Label. RARC asked for clarification regarding the proposed label changes–are they specific to residue chemistry? The Team responded yes.

- Dermal Absorption Study in Progress. The Team and RARC discussed the fact that the registrant is conducting a dermal absorption study which is expected to significantly lower the occupational risk estimates.

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pc: Richard Loranger, BSS
Donna Davis, BC