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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

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MEMORANDUM

SUBJECT: Terbufos HED RED Chapter. Update to Incorporate FQPA Considerations.
P.C.Code 105001. Case No. 0109. DP Barcode D244918.

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This memorandum and attachments serve to update the HED RED Chapter for Terbufos (D. McCall, 10/17/95) by addressing considerations necessitated by the 1996 Food Quality Protection Act (FQPA). Attachments include the original HED RED Chapter by D. McCall date 10/17/95 (Attachment 1), the most recent HED Hazard Identification Review Committee (HAZID) report by J. Rowland dated 9/25/97 (Attachment 2), Current Occupational/Residential Status memorandum by J. Dawson dated 3/4/98 (Attachment 3), the most recent Terbufos usage information from BEAD (Attachment 4; E-Mail from A. Grube dated 2/26/98), 3/19/98 W. Hazel memorandum re. Terbufos anticipated residues for chronic dietary risk assessment (Attachment 5), the 4/3/98 Chronic Dietary Risk Assessment report by C. Swartz (Attachment 6), the 3/27/98 E. Doyle evaluation of the probabilistic acute dietary assessment submitted 10/21/97 by American Cyanamid (Attachment 7), and the 9/30/97 J. Breithaupt drinking water exposure assessment (Attachment 8).

Terbufos is an organophosphate insecticide. Cumulative risk assessment considering risks from other pesticides having a common mechanism of toxicity is not addressed in this document.

Terbufos is formulated as one of two granular formulations: a clay-based 15% G and an [REDACTED] polymeric 20% G (the 20 CR). Terbufos is registered for preplant, at-plant, or early postemergence, soil-incorporated use on bananas, corn (field, pop-, and sweet), sorghum, and sugar beets. Use is restricted to commercial applicators. There are no residential uses of terbufos.

Technical terbufos is classified as Toxicity Category I for oral and dermal toxicity. Death occurred to all test animals treated via the ocular route. An acute inhalation study is outstanding although one is planned for the 15%G. Cholinesterase inhibition and the attendant cholinergic signs were the principal toxic effects associated with all risk assessment endpoints. Neither developmental nor reproductive toxicity were associated with terbufos treatment. There was no evidence of carcinogenicity in any terbufos study.

Significant occupational exposure to terbufos is expected based on surrogate exposure estimates using the Pesticide Handler Exposure Database (PHED). Separate MOEs were estimated for the dermal and inhalation routes of exposure. For short and intermediate dermal risk assessment, the NOEL used was 0.005 mg/kg/day from a 28-day oral dog study in which plasma cholinesterase inhibition was observed at the LOEL of 0.015 mg/kg/day. Dermal absorption was assumed to be 100% in the absence of a dermal absorption study; the use of this conservative default assumption is supported by the available acute oral and dermal toxicity studies which, in fact, suggest that terbufos is highly toxic via the dermal route and/or is highly absorbed. The NOEL of 0.01 ug/L (0.0014 mg/kg/day) was used for inhalation risk assessment based on a 21-day rat study in which plasma, RBC, and brain cholinesterase inhibition was observed at the LOEL of 0.04 ug/L. Separate dermal and inhalation risk assessments resulted in MOEs of <6 for all exposure scenarios even utilizing PPE and engineering controls. A reevaluation of the use patterns and the available surrogate exposure data in PHED indicates that the risk estimates cannot be refined in any significant way. Although the corn use rate has been reduced by one-third since the 10/17/95 RED chapter, this is a relatively minor change considering that the MOEs associated with applications to corn were as low as 0.0042. We note that the relevant studies in the PHED data base are low quality data and that they cannot distinguish between conventional, clay-based granulars, such as the 15% G, and the low-dust, polymeric granulars such as the 20CR. We expect that the greatest impact on refinement of the occupational risk numbers would be achieved by the generation of chemical-specific worker exposure data and dermal toxicity studies on the 15% G and 20CR, all of which are planned or in progress.

Coffee? There is an acute dietary risk concern for terbufos. In the 1995 HED RED Chapter, acute oral MOEs were calculated to be 10-50. In support of the extension of the import tolerance for terbufos on bananas (PP#8E3574), American Cyanamid submitted an acute probabilistic dietary risk assessment. The toxicological endpoint used was plasma cholinesterase inhibition observed in the 28-day oral dog study having a NOEL of 0.005 mg/kg/day. An examination of this assessment has been performed but is considered tentative pending submission of additional information regarding data used in this assessment. MOEs at the 99.9th percentile of exposure (excluding water but including coffee) were reported as:

- 83 for total U.S. population,
- 43 for Children (1-6),
- 82 for Children (7-12),
- 53 for All infants, and
- 151 for Women (13 years and older).

Note that nursing and non-nursing infants are included in the category "All infants". We understand that a revised probabilistic assessment is being conducted in which terbufos metabolites in water are being included.

In anticipation of cumulative risk assessment of the organophosphates being conducted in the future, anticipated residues were calculated for terbufos to permit a refined chronic dietary risk assessment. Note that in the 1995 HED RED Chapter, anticipated residues contributed $\leq 81\%$ of the RfD to the various population subgroups; this assessment included percent-crop-treated data for all crops (except bananas) but did not refine the actual residue estimates, i.e., tolerance values were used. Both the 1995 and the 3/98 risk assessments used the same toxicological endpoint, i.e., plasma cholinesterase inhibition observed at the LOEL in 1-year and 28-day cocritical oral dog studies in which the NOEL was 0.005 mg/kg/day and the RfD was 0.00005 mg/kg/day. Attachments 4, 5, and 6 detail revised percent-crop-treated data, calculation of anticipated residues, and calculation of chronic dietary risk, respectively. Based on the new information and refined exposure estimates, chronic dietary risk is now estimated to be $\leq 16\%$ of the RfD for all population subgroups; note that non-nursing infants and children (1-6) had risks of 16 and 12% of the RfD, respectively. Bananas contributed the major portion of the risk; note, however, that HED has low confidence in the banana field trial data upon which the anticipated residue estimate was based. Coffee was included in the chronic dietary risk assessment: it comprised 42% of the risk to the General U.S. Population based on the assumption of residues at the expired import tolerance level and 100% crop treated.

The FQPA requirement to assess the potential for increased sensitivity of infants and children has been addressed by the HAZID (see Attachment 2). To assure that a consistent approach is used for all members of the organophosphates class of chemicals, HED's FQPA Safety Committee will revisit terbufos and all other members of this class later in the risk assessment/risk management process to determine the necessity and magnitude of any extra uncertainty factor to be applied to infants and children.

Aggregate exposure to terbufos will not be calculated at this time. There is no residential exposure expected. HED has been provided a terbufos drinking water assessment from EFED (see Attachment 8) which includes modeling as well as groundwater monitoring data. No attempt will be made to aggregate the food and water sources of exposure at this time. When SRRD is in need of aggregate risk calculations, we advise that HED, EFED, and SRRD reach agreement on the appropriateness of using the monitoring data for purposes of risk assessment.

Attachments: