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

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANC

MEMORANDUM

SUBJECT: Cover Memo for Azinphos-methyl (Guthion)

TO: Larry Schnaubelt, Acting PM 12
Insecticide-Rodenticide Branch
Registration Division (TS-767C)

THRU: Amy S. Rispin, Director
Science Integration Staff
Hazard Evaluation Division (TS-769C)

INTRODUCTION

Azinphos-methyl is an organophosphate insecticide registured for use on a variety of tree fruit and nut, field and vegetable crops. It is formulated as a dust, flowable concentrate, emulsifiable concentrate, granular, wettable powder and soluble concentrate/liquid. The primary effect of guthion is acute toxicity to humans and wildlife.

TOXICOLOGY

Carcinogenicity - Weight-of-the-Evidence

In an oncogenicity bioassay performed by NCI, Azinphos-methyl was administered in the diet of Osborne-Mendal rats and B6C3F1 mice. Neoplasms of the thyroid and pancreatic islets suggest, but did not provide sufficient evidence for the carcinogenicity of azinphos-methyl in male Osborne-Mendel rats. Because there were too few matched control animals (only 10 per sex), this study does not meet guideline requirements and there is a data gap for rat oncogenicity study. The concurrent NCI mouse feeding study was negative for oncogenic effects.

Azinphos-methyl failed to induce unscheduled DNA synthesis in primary rat hepatocytes. Gene mutation and chromosomal aberration studies must be submitted.

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The Toxicology Branch Peer Review Committee held an abbreviated peer review on May 27, 1986 and concluded that there was inadequate human and animal evidence of carcenogenicity of azinphos-methyl. Pending receipt of another rat oncogenicity-chronic feeding study and of the mutagenicity assays, azinphos-methyl has been tentatively classified as a Group D oncogenic (inadequate data).

Acute Toxicity

Azinphos-methyl is a Category I toxicant by the oral and dermal routes of exposure. Azinphos-methyl is currently classified, based on inhalation hazard to humans, as a restricted use pesticide for all liquids with a concentration greater than 13.5 percent for all uses. Although, the inhalation study on which restricted use classification was based is no longer available, we recommend that no change be made in this classification. Data on both the inhalation and dermal toxicity of wettable powder formulation are needed to determine if these formulations should also be restricted.

ECOLOGICAL EFFECTS

Azinphos-methyl is very highly toxic to mammals and aquatic organisms, and slightly to highly toxic for avian species. While theoretical calculations indicate that azinphos-methyl is likely to cause adverse effects to fish and wildlife, there is only limited evidence from the field to support the predictions. Pesticide Incident Monitoring System (PIMS) reports only one bird kill where azinphos-methyl alone was involved. In addition, 14 fish kills were reported to PIMS from 1966 to 1981 involving azinphos-methyl alone. Fish kill information available from US EPA Office of Water for the years 1978-1982 cited 6 kills involving azinphos-methyl alone. EEB has been checking with the States and Regions and have confirmed only one fish kill since 1982.

We recommend a full scale terrestrial field study for the apple site for both avian and mammals. For cherry and walnut orchards, a field study to include dietary exposure and thorough carcass search is recommended. A field study with carcass searching, is recommended for 10% ai granular formulations in sugarcane. The walnut and sugarcane sites should also be monitored for aquatic residues (i.e., water column and sediments). The following sites should also be monitored for aquatic residues: potatoes, blueberries, cotton, soybeans and pine forest. In addition, a simulated field study (mesocosm) should be applicable to use patterns covered in the RS, if conducted at appropriate loading rates.

If a full-scale aquatic field study is performed as an alternative to the mesocosm study, it must be conducted on the cotton site. However, a mesocosm study is likely to be more applicable to other registered sites than the full-scale aquatic field study.

Endangered Species

The EEB chapter indentifies use patterns and endangered species for which precautionary labeling is required. This labeling is required for cropland, forest, range and pastureland uses of azinphos-methyl. The cropland label includes aquatic organisms, avain species, insects and reptiles and includes 20 states. The forest use also includes 20 states and covers aquatic organisms and avian species. The range and pastureland includes 11 states east of the Mississippi and covers aquatic organisms, reptiles and avian species. If the forest use areas are defined more clearly, the endangered species labeling can be refined. A consultations with OES will be initiated to cover all current use patterns and all taxonomic catagories.

ENVIRONMENTAL FATE

Ground Water

Azinphos-methyl was one of the chemicals for which a ground water DCI was issued. Field dissipation studies demonstrate that azinphos-methyl is not persistent (greater than 90 percent degraded within 30 days). The leaching studies showed that azinphos-methyl has low mobility and precludes a potential for leaching of azinphos-methyl to ground water.

Reentry

A 24-hour reentry interval has been established under 40 CFR 170.3 (b) (2). A DCI for reentry was issued in February 1985 requesting soil and foliar dissipation studies Until these studies have been submitted and reviewed, the 24 hour reentry interval will remain in effect.

Rotational Crops

Rotational crop field studies demonstrate that an interim rotational crop restriction of 6 months for root crops and 30 days for all other crops be included on the label. (See attached memo from Creeger 6/23/86).

TOLERANCE REASSESSMENT

It should be noted that data gaps exist for plant and animal metabolism. Because the requested residue data and perhaps the continued adequacy of all established tolerances are dependent upon the results of the above studies, we recommend that metabolism data be obtained and submitted prior to any required residue data. Tolerances for residues in or on animal commodities will not be assessed until the animal metabolism studies are completed and reviewed.

Additional data are required to ascertain the adequacy of the established tolerances for residues in or on all crops with the exception of potatoes, parsley, pistachios, sugarcane and sugarcane bocgasse. Data may be translated for certain crops, however, translated data may not be used to support a crop group tolerance.

The toxicology base is inadequate to support establishment of an ADI for azinaphos-methyl. A Provisional Limiting Dose (PLD) based on a two year dog study with an uncertainity factor of 100 has been established. The Maximum Permissible Intake (MPI) is 0.075 mg/kg for 60 kg person.

The Theoretical Maximum Residue Contribution (TMRC) to the human diet from the existing tolerances is 0.6678 mg for a 1.5 kg diet which is 900 percent of the PLD. (This percentage is very high. The PLD was based on a NOEL for cholinesterase inhibition from a two year dog study. The dog appears to be more sensitive than the rat for which a cholinesterase-inhibition NOEL has been reported in a chronic feeding study. This study is at present unavailable for review. In addition. because the existing data base was insufficient, a 100-fold uncertainty factor was used instead of the customary 10 fold safety factor for this effect. When the additional studies necessary to establish an ADI i.e., a rodent chronic feeding, a two generation reproductive and two teratogenicity studies are submitted, a safety factor of 10, can be used.

Tolerances are established to prevent crops in interstate commerce, treated at maximum label rates and applications with the shortest Preharvest Interval (PHI), from being seized. Thus, the TMRC, calculated from these tolerances, is an upper bound of possible dietary levels and will probably not be attained in actuality. The FDA monitoring data from FY 1978 to 1985 of approximately 50000 samples showed residues of azinphos-methyl on 431 samples (less than 1%). Only 14 positive residue findings were made in the FDA's revised Total Diet Study from April 1982 to April 1985. The residues ranged from 0.001 ppm to 0.082 ppm which is well below the

established 2.0 ppm tolerance level for these commodities. Therefore, we may conclude that the TMRC is far greater than dietary residues of azinphos-methyl which may be reasonably expected in practice.

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Attachment

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