



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

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File

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

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MEMORANDUM

SUBJECT: Arsenal® (Imazypyr) - PP#8H5547 and PP#8H5548 -
Response to Deferral from DEB Regarding Exemption
from Tolerance for Arsenal

Caswell No.: 221G
No Project Number

FROM: William Dykstra, Reviewer *William Dykstra 11/26/90*
Review Section I
Toxicology Branch I - Insecticide, Rodenticide Support
Health Effects Division (H7509C)

TO: R.D. Schmitt, Ph.D., Chief
Dietary Exposure Branch
Health Effects Division (H7509C)

THRU: Roger Gardner, Acting Section Head *Roger Gardner for 6/14/91*
Review Section I
Toxicology Branch I - Insecticide, Rodenticide Support
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Requested Action

DEB requests input from TB-I on the toxicological
significance of imazypyr to assess if exemptions are appropriate
as requested by the petitioner.

Conclusion and Recommendation

In response to the DEB request, TB-I is currently assessing the toxic potential of imazypyr. Most of the animal toxicity data have been reviewed.

Based on secondary reviewed data, the oncogenic potential in mice is negative, but historical control data are needed to determine the NOEL, if any, for pulmonary edema (a non-neoplastic lesion) in female mice.

The NOEL for toxicity in a 1-year dog study was 10,000 ppm (HDT).

The NOEL for toxicity in a 2-generation rat reproduction study was 10,000 ppm (HDT).

In the 2-year rat study, recently reviewed, the NOEL for non-neoplastic lesions appears to be 5000 ppm (mid-dose). The lesions at the high dose (10,000 ppm) were increased incidence and grade of severity of extramedullary hematopoiesis of the spleen and thyroid cysts.

The oncogenic potential of imazypyr may be positive.

Both brain tumors in male rats and pheochromocytoma in female rats are of current serious concern. The chemical is likely to go to the Peer Review Committee.

Additionally, in the 2-year rat study, an MTD may not have been used.

The 2-year rat study is undergoing secondary review.

The mutagenicity studies have been reviewed by Dr. Irving Mauer and additional data are needed.

Although imazypyr is certainly less toxic than other pesticides by some criteria, this thinking is immature.

TB-I cannot envision a total absence of toxicity by all present and future criteria and cannot predict the possibility of future concerns, e.g., immunotoxicity or the possibility of toxic plant and/or ruminant metabolites, which are currently not disclosed.

Exemption from tolerance would allow legally, at least, (this may be checked with OGC), the unrestricted use of imazypyr and the possibility of additional exposure which could result in toxic levels. This would be of special concern if there were, for example, mutagenic plant and ruminant metabolites to which rats and mice have not been exposed.

Based on current knowledge, TB-I cannot predict the toxicological consequences to humans and domestic animals of this regulatory request and, therefore, recommends against the exemption.