Bill Dykstra (46)

Glyphosate/Tox

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

Releasable

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Transmittal of the Final FIFRA Scientific Advisory Panel Reports on the February 11-12, 1986 Meeting

TO: Steven Schatzow, Director
Office of Pesticide Programs (TS-766)

The above mentioned meeting of the FIFRA Scientific Advisory Panel (SAP) was an open meeting held in Arlington, Virginia to review the following topics:

(1) A set of scientific issues being considered by the Agency in connection with the Registration Standard for Glyphosate;

(2) A set of scientific issues in connection with the Agency's proposed action on the non-wood uses of Pentachlorophenol as set forth in the Position Document 4;

(3) A set of scientific issues being considered by the Agency in connection with the Registration Standard for Oryzalin;

(4) A set of scientific issues being considered by the Agency in connection with the Registration Standard for Amitraz;

(5) A set of scientific issues being considered by the Agency in connection with the Registration Standard for Acephate;

(6) A set of scientific issues being considered by the Agency in connection with Subdivision U of the Pesticide Assessment Guidelines.

Please find attached the SAP's final reports on the six issues discussed at the meeting.

Stephen L. Johnson, Executive Secretary
FIFRA Scientific Advisory Panel (TS-769)

Attachments

cc: Panel Members
John A. Moore
James Lamb
Al Heier
Susan Sherman
John Melone
Douglas Campt
EPA Participants

FEDERAL INSECTICIDE, FUNGICIDE, AND RODENTICIDE ACT

SCIENTIFIC ADVISORY PANEL

A Set of Scientific Issues Being Considered by the Agency in Connection with the Registration Standard for Glyphosate

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The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Scientific Advisory Panel (SAP) has completed review of the data base supporting the Environmental Protection Agency's (EPA) decision to reclassify Glyphosate as a class C (possible human) carcinogen. The review was conducted in an open meeting held in Arlington, Virginia, on February 11, 1986. All Panel members, except Dr. Thomas W. Clarkson, were present for the review. In addition, Dr. David Gaylor, Director of the Biometry Staff at the National Center for Toxicological Research, served as an ad hoc member of the Panel.

Public notice of the meeting was published in the Federal Register on Friday, January 17, 1986 (Citation 51-FR2568).

Oral statements were received from staff of the Environmental Protection Agency and from Mr. Robert Harness and Dr. Timothy Long of Monsanto Company.

In consideration of all matters brought out during the meeting and careful review of all documents presented by the Agency, the Panel unanimously submits the following report.

REPORT OF SAP RECOMMENDATIONS

General Comments on Carcinogen Classification

The Panel concurs that it is necessary to categorize chemicals as to their apparent carcinogenic risk to man. The Panel is concerned that the categories outlined in the Agency's Cancer Guidelines are somewhat limited in scope. For only a small number of specific chemicals is there epidemiologic evidence of their carcinogenicity in man, either sufficient evidence (Group A) or limited evidence (Group B-1). Thus, most chemicals that are carcinogenic for animals have been placed in Groups B-2 and C. Category D has apparently not been used. The Panel urges the Agency to attempt to develop a more discriminatory classification scheme.

Glyphosate

The Agency requested the Panel to focus its attention upon a set of issues relating to the pesticide Glyphosate. There follows a list of the issues and the SAP's response to each question.

1. Based on the Agency's weight of the evidence assessment with emphasis on the mouse kidney tumors, the Agency has classified Glyphosate as a class C (possible human) carcinogen. The Agency specifically requests any comment that the Panel may wish to present with regard to its assessment of the weight of evidence and subsequent determination of carcinogenicity according to the Agency's Cancer Guidelines.

2. The Agency requests also that the Panel consider what weight should be given to this marginal increase in kidney tumors, the importance of this type of tumor in the assessment of the carcinogenicity of Glyphosate, and the weight placed on historical and concurrent controls for this type of evaluation.

Panel Response:

In the instance of Glyphosate, the Panel concurs that the data on renal tumors in male mice are equivocal. Only small numbers of tumors were found in any group, including those at the highest dose which appear to have exceeded the maximal tolerated dose. The vast majority of the pathologists, who examined the proliferative lesion in the male control animal, agreed that the lesion represented a renal adenoma. Therefore, statistical analysis of the data should utilize this datum. In addition, the statistical analysis shall be age-adjusted; when this is done, no oncogenic effect of Glyphosate is demonstrated using concurrent controls. Nevertheless, the occurrence of three neoplasms in high dose male mice is unusual and using historical controls is statistically highly significant. Furthermore, categorization of the oncogenic risk of Glyphosate is complicated by the fact that doses used in the rat study do not appear to have reached the maximal tolerated dose. Under these circumstances, the Panel does not believe that it is possible to categorize Glyphosate clearly into Group C (possible human carcinogen) or Group E (no evidence of carcinogenicity for humans). The Panel proposes that Glyphosate be categorized as Group D (not classified) and that there be a data call-in for further studies in rats and/or mice to clarify unresolved questions.

Regarding the issue of using historical or concurrent controls, the Panel believes that this has to be decided on a case-by-case basis. For Glyphosate, the historical control data support that there may be reason for concern. However, the level of concern raised by historical control data was not great enough to displace putting primary emphasis on the concurrent controls.

FOR THE CHAIRMAN

Certified as an accurate report of Findings:

Stephen L. Johnson
Executive Secretary
FIFRA Scientific Advisory Panel

Date: 2/24/86