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

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Oxyfluorfen - Goal 1.6E - 89-OR-21 - Section 18 Request to Use Oxyfluorfen for Weed Control in Grasses Grown for Seed in Oregon

Caswell No.: 188AAA
Project No.: 9-1651A
Record No.: 296552

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Rdd 7/28/89

Requested Action

Review section 18 request from Oregon Department of Agriculture to use oxyfluorfen for weed control in grasses grown for seed.

Analysis of Request

The Oregon Department of Agriculture requests approval for a section 18 use of oxyfluorfen to control various weeds in grasses grown for seed. The formulation to be used is Goal 1.6E (EPA Registration No. 707-174). Inerts are cleared under 40 CFR 180.1001.

The time period for use of oxyfluorfen is September 1, 1989 to January 15, 1990.

The total amount of oxyfluorfen to be used for all crops is 51,400 lb ai.

The anticipated usage in the 1989 to 1990 growing season will be 165,800 acres of perennial grasses.

Background

On ~~June 25~~ May 24, 1989, the Agency Peer Review Committee met to evaluate the oncogenic potential of oxyfluorfen.

"The Committee considered the following facts regarding the toxicology data on oxyfluorfen to be of importance in a weight-of-the-evidence determination of oncogenic potential.

"1. Oxyfluorfen, when administered in the diet to male CD-1 strain mice at dietary doses of 0, 2, 20, and 200 ppm for 20 months, was associated with significant positive dose-related trends for liver adenoma, carcinoma, carcinoma and combined adenoma and/or carcinoma. There were no significant pairwise comparisons to untreated control.

"2. The increased incidence of the liver tumors was found to be above the laboratory's historical control incidences.

"3. There was no evidence for a reduction in the latency period for the time to liver tumor appearance in male mice.

"4. There was no compound-related increase in tumors observed in female mice or in male and female rats.

"5. Both the mouse and rat studies were not considered to have been tested adequately at high enough doses to fully assess the oncogenic potential of oxyfluorfen in either species.

"6. Technical grade oxyfluorfen was found positive for inducing gene mutations in the Salmonella and the mouse lymphoma assays suggesting it has mutagenic capability.

"7. Oxyfluorfen was associated with adverse developmental effects in rats and rabbits and adverse reproductive effects in rats.

"8. Oxyfluorfen is structurally related to four other diphenyl ether herbicides that have oncogenicity evidence associated with them. These chemicals include lactofen, acifluorfen (Blazer, Tackle), nitrofen, and fomesafen. The primary neoplastic lesions induced by these chemicals include hepatocellular carcinomas and adenomas in mice, similar to that seen in the oxyfluorfen study. These data provide strong support for the association of oncogenicity to this class of chemicals.

"The Peer Review Committee unanimously concluded that the data available for oxyfluorfen provided evidence to classify oxyfluorfen as a Category C oncogen ("Possible Human Carcinogen"). This was based on the significant positive dose-related trends in liver adenomas, carcinomas, and combined adenomas and/or carcinomas in male CD-1 mice. Supporting evidence included a strong association of oncogenicity with this class of chemical (diphenyl ether herbicides with nitro groups), some mutagenicity evidence and the appearance of increased carcinomas (although not significant by pairwise comparison).

"The Committee concluded that quantification of oncogenic risk by oxyfluorfen was not appropriate at this time. This was based on the data that included positive results in only one sex, one species, and no pairwise significant comparisons in tumor incidences. It was conjectured if higher doses in the mouse study had been used, more carcinomas may have appeared. However, additional studies may not be necessary at this time, but if they were needed, higher dosing would have to be used." [End of quotation].

Review

The toxicology data base for oxyfluorfen has been summarized in previous memoranda. There are no data gaps. Tolerances are established in 40 CFR 180.381 on a variety of raw agricultural commodities. There are no regulatory actions pending against the pesticide.

The acceptable daily intake (ADI) is based on the NOEL of 2.0 ppm in the chronic/oncogenic mouse feeding study.

A hundredfold safety factor was used to calculate the ADI.

$$ADI = \frac{NOEL}{100} = \frac{0.30 \text{ mg/kg/day}}{100}$$

$$ADI = 0.003 \text{ mg/kg/day}$$

The effect of the section 18 request on the TMRC and percent ADI utilized will be provided by a TAS analysis.

Conclusion and Recommendation

The requested section 18 can be toxicologically supported provided that Agency concerns regarding the potential oncogenic risks are resolved.