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

AUG 27 1991

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM:

SUBJECT: 91-IA-0003. Section 18 Specific Exemption.
Chlorothalonil (Bravo 720, EPA Reg. No. 50534-188) on
corn grown for seed and fed to livestock.
No. MRID No. DEB No. 8333. DP Barcode No. D167032.

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TO: Susan Stanton, PM-41 Team
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and

Toxicology Branch
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The Iowa Department of Agriculture and Land Stewardship has requested a Section 18 specific exemption for the use as livestock feed of corn seed screenings treated with the fungicide Bravo® 720 to control foliar diseases on corn grown for seed. The active ingredient is chlorothalonil (2,4,5,6-tetrachloroisophthalonitrile). The request is to use ISK Biotech Corporation product Bravo 720 (EPA Reg. No. 50534-188). Up to 330,000 acres of seed corn may be treated. If 10 percent of grain produced in seed corn fields could not be processed into seed and were fed to livestock, 1.58 million bushels of corn grain would be fed, which would represent 0.27 percent of the Iowa corn grain feed supply. At the maximum application rate if the entire corn acreage were treated, up to 495,000 lb ai would be used for each application; petitioner assumes only one application should be necessary in most cases. The assignment instructions are to examine whether residue data support the removal of the feeding restriction on the present label.

Tolerances for chlorothalonil and its metabolite 4-hydroxy-2,5,6-trichloroisophthalonitrile (common name SDS-3701) have been established on a variety of commodities at levels ranging from 0.05 ppm to 15 ppm (40 CFR 180.275). Tolerances are established at 1 ppm in or on sweet corn only. No tolerances are established on any animal commodity. A Registration Standard (Guidance Document) was issued in September 1984; a Final Registration Standard and Tolerance Reassessment (FRSTR), Residue Chemistry Chapter, was issued in February 1988.

Proposed use would allow an initial application of 0.75 to 2 pints (0.56 to 1.5 lb ai) of Bravo 720 per acre. Begin applications when conditions favor disease development and repeat at 4 to 7 day intervals or as required to maintain control. Under severe disease conditions, use 1.5 to 2 pt per acre. Do not apply within 14 days of harvest. Do not allow livestock to graze in treated fields. Do not ensile treated corn or use as livestock forage. Corn grain screenings, not acceptable for seeds, may be fed to livestock.

The federally registered label allows treatment of sweet corn and corn grown for seed, but prohibits use on sweet corn to be processed and contains the restrictions indicated above on animal feeding. Consistent with the intent of the label to prevent animal feeding, petitioner has interpreted the label as prohibiting use of treated seed as animal feed. The proposed use is consistent with the label except that this Section 18 exemption would remove the restriction on feeding corn seed screenings; the exemption would expire 10/31/91.

Residues of concern under 40 CFR 180.275 consist of chlorothalonil and its metabolite 4-hydroxy-2,5,6-trichloroisophthalonitrile (SDS-3701). In addition, the FRSTR Residue Chemistry Chapter notes that hexachlorobenzene (HCB) and pentachlorobenzonitrile (PCBN), impurities in technical chlorothalonil, have been detected in many plant commodities. The Chapter concludes that for the purposes of reregistration, the metabolism of chlorothalonil in plants is not adequately understood. Toxicology Branch subsequently concluded that "the toxicological profile of the [chlorothalonil] technical product reflects the toxicity of PCBN as an impurity.... Further, the toxicity of CTN, per se, as well as the toxicity of hexachlorobenzene (HCB), as an oncogenic contaminant of potential concern in racs, are the controlling factors governing the use(s) of CTN products. Thus, the magnitude of the residues of PCBN in comparison are not of toxicological concern." (Chlorothalonil Reg. Standard File, R.B. Jaeger, 7/27/88) For the purposes of this Section 18 request only, residues of concern in plants consist of the parent chlorothalonil, the metabolite SDS-3701, and the impurity in technical chlorothalonil HCB.

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Analytical method. A method using gas chromatography and electron capture detection is available for enforcement of tolerances for the combined residues of chlorothalonil and SDS-3701, and is published as method I in PAM Vol. II. Residue data were submitted with this Section 18 request, including a modification to this method which permits detection of the impurities HCB and PCBN.

The modified analytical method is described in the following report, a copy of which was submitted with this Section 18 request:

Residues of Tetrachloroisophthalonitrile (Chlorothalonil), SDS-2787), 4-Hydroxy-trichloroisophthalonitrile (SDS-3701), HCB and PCBN on Corn Seed and Corn Stover, Document 638-3CR-83-0054-001, SDS Biotech Corporation.

Under this method, plant material is extracted in acidified acetone. The homogenate is filtered and acetone evaporated. The residue is dissolved in acidified aqueous solution and partitioned with petroleum ether, which separates SDS-3701 from the other compounds. SDS-3701 is converted to its methyl ester derivative by the methylating agent 3-methyl-1-p-tolyltriazine. The SDS-3701 derivative is cleaned up on an alumina column. The sample containing the other compounds is divided and cleaned up on a Florisil column; this produces separate fractions of chlorothalonil, HCB, and PCBN. Each compound is quantitated separately by gas chromatography with detection by electron capture.

The analytical method was validated with corn seed samples fortified at concentrations from 0.05 to 1 ppm chlorothalonil; 0.03 to 0.5 ppm SDS-3701; and 0.01 to 0.05 ppm for HCB. Recoveries ranged from 70-80% for chlorothalonil, 67-80% for SDS-3701, and 98-110% for HCB. Stated limits of detection were 0.01 ppm for chlorothalonil and SDS-3701 and 0.003 ppm for HCB.

According to the FRSTR Residue Chemistry Chapter, the adequacy of available analytical methods cannot be determined because the nature of the residue in plants is not adequately understood. For the purposes of this Section 18 request only, the method described in Document 638-3CR-83-0054-001 is adequate for enforcement purposes.

Residue data were submitted with this Section 18 request. In addition to the SDS Biotech Corporation document cited above, the request also included:

Summary of Study: Residues of Tetrachloroisophthalonitrile (Chlorothalonil, SDS-2787), SDS-3701, SDS-46581, HCB and PCBN on Sweet Corn Seed-1985, Document 1166-86-0047-CR-001, Ricerca, Inc.

This document was previously submitted as MRID 40000113 and has been reviewed in the Chlorothalonil FRSTR Residue Chemistry Chapter. Field trials were conducted in IL on sweet corn using 8 foliar applications of Bravo at a rate of 1.4 lb ai per acre, applied with ground equipment, at intervals of 3-4 days or 7 days, with a PHI of 14 days. Residues on corn seed were all nondetectable for chlorothalonil (<0.01 ppm), SDS-3701 (<0.01 ppm), HCB (<0.003 ppm). Residues were also undetectable for SDS-46851 (<0.03 ppm). According to the FRSTR Residue Chemistry Chapter, metabolite SDS-46851 has been sought and detected in plants treated in crop field trials, but has not been identified as a ¹⁴C-residue in studies of plant metabolism.

The SDS Biotech document cited above, which described the analytical method, also included data from field trials conducted in IL and IN, using 3 applications of Bravo at 1-2 lb ai per acre, with PHIs at 35 or 61 days. In one composite sample of corn seed, chlorothalonil residues were 0.02 ppm. Residues of chlorothalonil on all other samples, and all other compounds on all samples, were nondetectable.

Present policy is to assume that residues of HCB will be 0.5% the residues of chlorothalonil on all crops (Chlorothalonil Subject File, D.F. Edwards, 8/23/88). If residues of chlorothalonil are no more than 0.02 ppm, the residues of HCB would not be expected to exceed 0.0001 ppm (0.1 ppb) HCB.

For the purposes of this Section 18 request only, residues on corn seed resulting from the proposed use are expected to be no more than 0.02 ppm chlorothalonil, 0.01 ppm SDS-3701, and 0.1 ppb HCB.

The FRSTR Residue Chemistry Chapter notes that no tolerance presently exists for chlorothalonil and metabolites in or on sweet corn forage. The Chapter concludes that the label restriction on treatment of sweet corn grown for processing is not enforceable, and the restriction on grazing or feeding corn forage is not practical since utilization of sweet corn forage is under grower control only in FL. For reregistration, the registrant must remove the unenforceable restriction on sweet corn grown for processing and must propose tolerances, supported by residue data, for sweet corn forage. These requirements for reregistration are provided for information purposes only, and are not meant to be resolved as part of this Section 18 request.

Meat, milk, poultry, and eggs. At present, no tolerances exist for chlorothalonil in meat, milk, poultry, or eggs. Tolerances will be established through the reregistration process after all required livestock metabolism and feeding studies and feed commodity residue studies have been received and evaluated,

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No animal feeding studies were submitted with this Section 18 request. Chlorothalonil animal feeding studies were described in the Registration Standard Residue Chemistry Chapter (September 1983) and were summarized in the FRSTR Residue Chemistry Standard. In one study, residues of chlorothalonil were 0.02-0.04 ppm in milk from cows fed chlorothalonil at 25-250 ppm in the diet for 30 days. In a second study, residues of SDS-3701 were up to 0.3, 0.7, and 1.34 ppm in milk samples after 18-30 days of feeding chlorothalonil plus SDS-3701 at 25 ppm + 0.2 ppm, 75 ppm + 0.6 ppm, and 250 ppm + 2 ppm, respectively.

In a third study, cows fed 250 ppm chlorothalonil plus 2 ppm of SDS-3701 produced milk containing up to 1.3 ppm chlorothalonil on the 8th day of treatment, and up to 1.54 ppm of SDS-3701 on the 20th day. Residues of SDS-3701 were up to 0.12 ppm in muscle, 0.34 ppm in fat, 0.76 ppm in kidney, and 0.15 ppm in liver from cattle fed chlorothalonil at 25 ppm plus SDS-3701 at 0.2 ppm for 30 days. Residues of parent chlorothalonil were not detected in tissues from the same feeding group.

Combined residues, parent plus SDS-3701, on corn seed treated under this proposed Section 18 use would be expected to be no more than 0.03 ppm. This is at least three orders of magnitude smaller than the combined dietary burdens (25-250 ppm) used in the cattle feeding studies. Levels of chlorothalonil and SDS-3701 are therefore not expected to be detectable on cattle meat or milk as a result of this proposed Section 18 use.

Chlorothalonil poultry feeding studies were submitted with a previous petition and have been reviewed (PP 3F2875, M.F. Kovacs, 11/7/83). In the first study, laying hens were fed daily for 21 days with ¹⁴C-labeled chlorothalonil and SDS-3701 (8:1 ratio) at doses of 2, 6, and 20 ppm. No detectable (≤ 0.03 ppm) ¹⁴C residues were detected in egg white at any dose level, nor in egg yolk at the 2 and 6 ppm feeding levels. At a dose of 20 ppm, yolks contained up to 0.047 ppm ¹⁴C. The only detectable tissue residues were found in liver; residues were 0.098 ppm ¹⁴C in liver at the 6 ppm feeding level.

In the second poultry study, laying hens were dosed daily for 21 days with 0.1, 0.3, and 1.0 ppm [¹⁴C]SDS-3701. No detectable residues were found in egg whites at any dose level. Maximum ¹⁴C levels in egg yolk were 0.12 ppm at the 0.3 ppm feeding level, and 0.42 ppm at the 1.0 ppm feeding level. The highest concentrations of ¹⁴C residues in tissue were 0.056 ppm, 0.27 ppm, and 0.78 ppm in liver at feeding levels of 0.1, 0.3, and 1.0 ppm labeled SDS-3701, respectively. The reviewer remarked that as with the cattle feeding studies, SDS-3701 rather than the parent chlorothalonil is the primary secondary residue transferred from animal feed to meat, milk, and tissue. (PP 3F2875, M.F. Kovacs, 11/7/83) Nonetheless, there was no concentration of parent or

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SDS-3701 in meat or eggs in either of the poultry feeding studies. Considering the low level of residues expected on corn seed from this Section 18 requested use, detectable residues are not expected on eggs or poultry.

Animal feeding studies have not been performed with HCB. The Chlorothalonil Registration Standard noted that according to data in the published literature, HCB can bioaccumulate in fat tissues and eggs. HCB can concentrate up to 9X its level in the diet in sheep fat, up to 31X the level in the diet in poultry fat and up to 8X the level in the diet in eggs. Even accounting for such concentration factors, considering the expected low levels of residues of HCB on seed corn, and the low usage involved (0.27% of IA corn grain feed supply), residues of HCB in meat, milk, poultry, and eggs resulting from this use are unlikely to exceed detectable levels, and are unlikely to be higher than levels resulting from uses on feed items having established tolerances.

Conclusions

1. For the purposes of this Section 18 request only, the residues of concern are chlorothalonil, its metabolite SDS-3701, and the impurity in technical chlorothalonil HCB.
2. For the purposes of this Section 18 request only, residues on corn seed resulting from the proposed use are expected to be no more than 0.02 ppm chlorothalonil, 0.01 ppm SDS-3701, and 0.1 ppb HCB.
3. For the purposes of this Section 18 request only, secondary residues on meat, milk, poultry, and eggs of chlorothalonil, SDS-3701, and HCB are expected to be below detectable levels as a result of the proposed use. Furthermore, due to the low usage involved, residues of chlorothalonil, SDS-3701, and HCB in meat, milk, poultry, and eggs resulting from this use are unlikely to be higher than those resulting from use on other feed commodities having established tolerances (beans, peanuts, tomatoes, etc.)
4. For the purposes of this Section 18 request only, the method described by SDS Biotech Corporation Document 638-3CR-83-0054-001 is considered adequate for enforcement purposes.
5. Analytical reference standards are available from the Pesticides and Industrial Chemicals Repository at Research Triangle Park, NC
6. Residue data evaluated in this review were generated by SDS Biotech Corporation and Ricerca, Inc. No data from Craven Laboratories were used in reviewing this Section 18 request.

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Recommendation

Toxicological considerations permitting, CBRS has no objections to the issuance of this Section 18 exemption. An agreement should be made with FDA regarding the legal status in commerce of the meat, milk, poultry, and egg commodities from animals fed treated corn seed.

cc:Circ, Abbotts, SACB (E.Saito), Section 18, Chlorothalonil SF,
RF, PIB/FOD (C.Furlow)

RDI:FBSuhre:8/23/91:EZager:8/26/91

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