US EPA ARCHIVE DOCUMENT

4-25-84

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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Oryzalin, amendment to TOX Branch reviews of PP#3F2874, use in or on wheat and barley. CASWELL #623A.

TO: Robert Taylor, PM #25
Herbicides-Fungicides Branch
Registration Division (TS-767)

4-25-84

FROM: R. Bruce Jaeger, Section Head
Review Section #1
Toxicology Branch/HED (TS-769)

4/11/84

RE: Toxicology Branch memos, PP#2G2612 (3/24/82, Jaeger); TMRC Analysis (8/23/82, Jaeger); PP#3F2874 (7/13/83, Chen and 3/28/84, Ritter); and FR Notice, Vol. 48, No. 28, Feb. 9, 1983 pg. 5899.

Please note that TOX Branch considers oxyzalin to be a rat oncogen based upon our review of the rat onco. study, 3/24/82. Bert Litt concluded that "all statistical weight indicates that due to the increase in both sexes and earlier incidence of basal cell type tumors in males that this tumor be used as the basis for quantitative risk assessment." Mr. Litt examined the various mathematical models for goodness of fit and "concluded that the one-hit and multi-stage models were the most logical but that the multi-stage model provided a better fit to these data."

Practically all of the tolerance considerations to date have resulted in favorable recommendations because residue data demonstrate residues at or below the method sensitivity. We note that this was the determination by RCB with regards to spearmint and peppermint oils where both control and treatment samples were comparable (NDR to < 0.1 ppm), except for one sample at < 0.1 ppm from an exaggerated application rate. TB considers this result spurious and therefore, that residues of oxyzalin, per se, are at or below the limit of detection (0.01 ppm), if at all.

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The same considerations are equally valid for grains of barley and wheat, and their processed fractions (e.g. bran, shorts, flour, germ, etc.). The RCB determined there was no need for food/feed additive tolerances (RCB memo, M. Nelson, PP#3F2874, 11/18/83). They have further concluded that there is no reasonable expectation of residues occurring in meat, fat and meat by-products of cattle, horses, swine, sheep, goats, poultry, milk or eggs from these tolerances.

This evidences together with the available toxicity data support the proposed tolerances on wheat and barley grains.

The FR Notice for PP#2F2717, and 2F2718, Vol. 48 No. 28, 2/9/83 is inaccurate and should be corrected as noted on the attached Draft Notice for PP#3F2874. Also, delete the reference to the chronic feeding/oncogenicity study (rat) as it appeared in that 2/9/83 FR notice.

Toxicology Branch recommends that a long-term chronic feeding study in the dog (at least one year duration) be submitted to support permanent tolerances. At present, available toxicity data demonstrate the dog is the most sensitive species and therefore the PADI is based on a 90-day dog feeding study. Although, as previously indicated, food uses to date have been essentially "no detectable residue" situations (based on method of sensitivty, 0.01 ppm), the adverse findings in the 2-year rat feeding/oncogenicity study plus the determination that the dog is the most sensitive species (from short-term study) suggest the need for a more definitive long-term feeding study in the most sensitive species - the dog.

The corrected Draft FR notice is attached.

2F2717
2F2718

40 CFR Part 180

[PP 2F2717, 2F2718/R520; Ph-FRL 2304-6]

Oryzalin; Tolerance for Residue

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This rule establishes tolerances for residues of the herbicide oryzalin in or on the raw agricultural commodities potatoes, peppermint, and spearmint hay. This regulation to establish maximum permissible levels for residues of oryzalin was requested, pursuant to petitions, by the Elanco Product Company.

EFFECTIVE DATE: February 9, 1983.

ADDRESS: Written objections may be submitted to the: Hearing Clerk (A-110), Environmental Protection Agency, Rm. 3708, 401 M St., SW., Washington, D.C. 20460.

FOR FURTHER INFORMATION CONTACT: Robert Taylor, Product Manager (PM) 25, Registration Division (TS-767C), Office of Pesticide Programs, Environmental Protection Agency, Rm. 245, CM#2, 1921 Jefferson Davis Highway, Arlington, VA 22202, (703-557-1800).

SUPPLEMENTARY INFORMATION: EPA issued a notice, published in the Federal Register of August 18, 1982 (47 FR 36016), that announced that the Elanco Products Company, 740 South Alabama St., Indianapolis, IN 46285, had submitted pesticide petitions (PP) as follows proposing to amend 40 CFR 180.304 by establishing tolerances for residues of the herbicide oryzalin (3,5-dinitro-N^4, N^4-dipropylsulfanilamide:

1. *PP 2F2717.* Potatoes at 0.1 part per million (ppm). The petition was subsequently amended reducing the proposed tolerance to 0.05 ppm.

2. *PP 2F2718.* Peppermint and spearmint hay at 0.05 ppm.

There were no comments received in response to these notices of filing.

The data submitted in the petitions and relevant material have been evaluated. The pesticide is considered useful for the purpose for which the tolerances are sought. The toxicology data evaluated included a 90-day feeding study (rat) with a no-observed-effect level (NOEL) of 750 ppm (37.5 mg/kg/day); a 90-day feeding study (dog) with a NOEL of 750 ppm (18.75 mg/kg/day); a 3-generation reproduction study (rat) with a NOEL of 250 ppm (12.5 mg/kg/day), a teratology study (rat) with a NOEL of 2,250 ppm (112 mg/kg/day), the highest dose tested; a teratology study (rabbit) with a NOEL of 125 mg/kg/day, (highest dose tested); a chronic feeding/oncogenicity study (mouse) with a NOEL of 500 ppm (71.4 mg/kg/day) and no oncogenic effects observed up to 3,560 ppm (521 mg/kg/day), the highest dose tested; ~~and a chronic feeding/oncogenicity study (rat) with a NOEL of 300 ppm (15 mg/kg/day) and no oncogenic effects observed up to 2,700 ppm (135 mg/kg/day), the highest dose tested.~~ delete

Desirable data lacking are a dominant lethal study (rat). The company has been notified of the deficiency and has agreed to perform the study and to remove the use from the label should the results of the above study exceed the criteria for chronic toxicity as stated in 40 CFR 162.11. And A long-term feeding study in the dog

The acceptable daily intake (ADI) based on the 90-day dog feeding study (NOEL of 750 ppm (18.75 mg/kg/day)) and a 200-fold safety factor, is calculated to be 0.0094 mg/kg/day. The maximum permissible intake (MPI) for a 60-kg human is calculated to be 0.5625 mg/day. The theoretical maximum residue contribution (TMRC) from existing tolerances for a 1.5 kg diet is calculated to be 0.0091 mg/day. The current action will utilize 0.72 percent of the ADI. Published tolerances utilize 1.61 percent of the ADI. A related document (FAP 2H5360/R133), establishing tolerances for peppermint and spearmint oil at 0.1 ppm which appears in this issue of the Federal Register, will contribute 0.0001 mg/day (1.5 kg) to the TMRC and increase the ADI to 2.35 percent.

There are no regulatory actions pending against the continued registration of oryzalin. This product contains a nitrosoamine at levels less than 1 ppm. Based on an Agency policy published in the Federal Register of June 15, 1980 (45 FR 42854), this level of nitrosoamine falls below the currently acceptable risk criteria. The metabolism of oryzalin in plants and animals has been adequately delineated for the uses. An adequate analytical method, gas chromatography using an electron capture detector, is available for

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enforcement purposes. There is no reasonable expectation of residues occurring in meat, fat, and meat by-products of cattle, horses, swine, sheep, goats, poultry, milk or eggs from these tolerances.

The pesticide is considered useful for the purpose for which the tolerances are sought. It is concluded that the tolerances would protect the public health and are established as set forth below.

Any person adversely affected by this regulation may, within 30 days after publication of this notice in the Federal Register, file written objections with the Hearing Clerk, at the address given above. Such objections should specify the provisions of the regulation deemed objectionable and the grounds for the objections. If a hearing is requested, the objections must state the issues for the hearing and the grounds for the objections. A hearing will be granted if the objections are supported by grounds legally sufficient to justify the relief sought.

The Office of Management and Budget has exempted this rule from the requirements of section 3 of Executive Order 12291.

Pursuant to the requirements of the Regulatory Flexibility Act (Pub. L. 96-534, 94 Stat. 1164, 5 U.S.C. 601-612), the Administrator has determined that regulations establishing new tolerances or raising tolerance levels or establishing exemptions from tolerance requirements do not have a significant economic impact on a substantial number of small entities. A certification statement to this effect was published in the Federal Register of May 4, 1981 (46 FR 24950).

(Sec. 408(e), 68 Stat. 514 (21 U.S.C. 346(a)(e)))

List of Subjects in 40 CFR Part 180

Administrative practice and procedure, Agricultural commodities, Pesticides and pests.

Dated: February 1, 1983.

James M. Conlon,

Acting Director, Office of Pesticide Programs.

PART 180—[AMENDED]

Therefore, 40 CFR 180.304 is amended by adding and alphabetically inserting the commodities peppermint hay, potatoes, and spearmint hay to read as follows:

§ 180.304 Oryzalin; tolerances for residues.

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Commodities	Part per million
* * * * *	
Peppermint hay	0.05
* * * * *	
Potatoes	0.05
* * * * *	
Spearmint hay	0.05
* * * * *	

[FR Doc. 83-3643 Filed 2-8-83; 8:45 am]

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TITLE 40--PROTECTION OF ENVIRONMENT

CHAPTER I--ENVIRONMENTAL PROTECTION AGENCY

SUBCHAPTER E--PESTICIDE PROGRAMS

[3F2874]

PART 180--TOLERANCES AND EXEMPTIONS FROM TOLERANCES FOR PESTICIDE CHEMICALS IN OR ON RAW AGRICULTURAL COMMODITIES

ORYZALIN

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final Rule.

SUMMARY: This rule establishes tolerances for residues of the herbicide oryzalin in or on the raw agricultural commodities barley grain and wheat grain. This regulation to establish maximum permissible levels for residues of oryzalin was requested, pursuant to petitions, by the Elanco Product Company.

EFFECTIVE DATE: Effective on (insert date of publication in the FEDERAL REGISTER).

ADDRESS: Written objections may be submitted to the:

Hearing Clerk (A-110),

Environmental Protection Agency,

Rm. 3708,

401 M St., SW.,

Washington, DC 20460.

FOR FURTHER INFORMATION CONTACT:

Robert Taylor
Product Manager (PM) 25,
Registration Division (TS-767C),
Office of Pesticide Programs,
Environmental Protection Agency,
Rm. 245, CM#2,
1921 Jefferson Davis Highway,
Arlington, VA 22202
(703-557-1800).

SUPPLEMENTARY INFORMATION: EPA issued a notice, published in the FEDERAL REGISTER of June 8, 1983, (48 FR 26535) ~~that~~ which announced that Elanco Products Company, 740 South Alabama Street, Indianapolis, Indiana 46285, had submitted a pesticide petition (3F 2874) which proposed to amend 40 CFR 180.304 by establishing tolerances for residues of the herbicide oryzalin (3,5-dinitro-N^4, N^4-dipropylsulfanilamide) in or on the raw agricultural commodities barley grain at 0.05 part per million (ppm) and wheat grain at 0.05 part per million (ppm).

The data submitted in the petitions and relevant material have been evaluated. The pesticide is considered useful for the purpose for which the tolerances are sought. The toxicology data evaluated included a 90-day feeding study (rat) with a no-observed-effect level (NOEL) of 750 ppm (37.5 mg/kg/day); a 90-day feeding study (dog) with a NOEL of 750 ppm (18.75 mg/kg/day); a 3-generation reproduction study (rat) with a

NOEL of 250 ppm (12.5 mg/kg/day), a teratology study (rat) with a NOEL of 2,250 ppm (112 mg/kg/day), the highest dose tested; a teratology study (rabbit) with a NOEL of 125 mg/kg/day (highest level tested); a chronic feeding/oncogenicity study (mouse) with a NOEL of 500 ppm (71.4 mg/kg/day) and no observed oncogenic effects at any level tested (0, 500, 1350 and 3650 ppm; equivalent to 0, 71.4, 192.8 and 521.2 mg/kg/day); a chronic feeding/oncogenicity study (rat) demonstrated weak oncogenic effects in skin at all levels tested, including the control groups (0, 300, 900 and 2700 ppm; equivalent to 0, 15, 45 and 135 mg/kg/day); DNA repair synthesis in rat hepatocyte primary cultures (negative); and a Sister Chromatid Exchange assay in chinese hamster bone marrow (negative orally, positive intraperitoneally).

Statistical evaluation of the 2-year rat chronic feeding/oncogenicity study indicated that basal cell type tumors of the skin were significantly increased at 900 ppm (9 mg/kg/day human equivalent in the food of study rats). There were 11/120 basal cell tumors in control rats, 16/120 at 3 mg/kg/day and 32/120 at 9 mg/kg/day. Examination of the various models for goodness of fit demonstrated that the multi-stage model provided a better fit to these data. Both of the multi-stage models lead to approximately the same level of potency as estimated by the 95% upper confidence bound on the slope or dose response as indicated by $Q_1^* = 3.375 \times 10^{-2}$ for the male plus female data or $Q_1^* = 4.426 \times 10^{-2}$ for male data only. The $Q_1^* = 3.375 \times 10^{-2}$ has been used in lieu of the latter figure because it includes a larger sample size. Assuming that 100% of the crops are treated and residue levels are at tolerance levels, the upper bound estimate of dietary oncogenic risk is calculated to be 7.43×10^{-6}. However, dietary risk estimates are significantly lower when considering the percentage of the crop treated, together with the finding that actual residue data suggest NDR to < 0.04 ppm, in grains, and NDR in processed/milled fractions.

Desirable data lacking are a dominant lethal study (rat) and a long-term non-rodent (dog) feeding study (at least one-year duration).

The company has been notifed of the deficiency and has agreed to perform the study and to remove the use from the label should the results of the above study exceed the criteria for chronic toxicity as stated in 40 CFR 162.11.

The acceptable daily intake (ADI), based on the 90-day dog feeding study (NOEL of 750 ppm (18.75 mg/kg/day)) and a 2000-fold safety factor, is calculated to be 0.0094 mg/kg/day. The maximum permissible intake (MPI) for a 60-kg human is calculated to be 0.5625 mg/day. The theoretical maximum residue contribution (TMRC) from existing tolerances for a 1.5 kg diet is calculated to be 0.0132 mg/day. The current action will utilize an additional 1.39 percent of the ADI to the published tolerances which utilize 2.34 percent of the ADI.

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