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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP# 3F2874. Oryzalin in or on wheat and barley.
Evaluation of analytical methodology and residue
data.

FROM: M. Nelson, Chemist *mjn*
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

THRU: C. Trichilo, Chief
Residue Chemistry Branch
Hazard Evaluation Division (TS-769) *CT*

TO: R. Taylor, PM 25
Registration Division (TS-767)
and
Toxicology Branch
Hazard Evaluation Division (TS-769)

The petitioner, Elanco Products Company, proposes the establishment of permanent tolerances for residues of the herbicide oryzalin in or on wheat grain and barley grain at 0.05 ppm.

A temporary tolerance of 0.1 ppm for oryzalin residues in or on "wheat" is presently in effect (exp. 2/3/84) as a result of PP# 6G1802.

Permanent tolerances are established (40 CFR 180.304 and 21 CFR 193.462) on a variety of commodities at levels ranging from 0.05 to 0.1 ppm.

Conclusions

1. Low levels [redacted] occur in technical oryzalin and its formulations. However, detectable residues (> 0.2 ppb) [redacted] have not been found in analyses of wheat grain or soybeans.

2a. The label prohibition against the grazing or feeding of treated forage and straw needs to be revised to apply to forage and hay. An amended Section B is needed.

INFORMATION WHICH MAY REVEAL THE IDENTITY OF A PRODUCT IMPURITY IS NOT INCLUDED

2b. A restriction against grazing/feeding of the straw is not considered practical due to economic considerations. A tolerance proposal (revised Section F) will therefore be needed for wheat and barley straws.

2c. A single application to the crops is implied, but not specified. Since the field study data reflect only a single application, we request that it be clarified on the label that the intended use is for but a single application per crop.

3a. We request a further examination of the water-extractable (aka neutral aqueous) fraction of wheat and barley straws for the presence/identification of conjugates, and of the methanol extract of barley straw for characterization of residues. (Ref.: "Radiochemical Studies with ^{14}C Oryzalin on Wheat, Barley, and Alfalfa" by T. Golab and H. Wooten, 10/80.)

Pending receipt/review of this additional information, we defer judgment as to whether the residue of concern in plants consists of more than just the parent compound. [In that eventuality, suitable enforcement methodology and supporting field trial data, as well as tolerance levels based upon the total residue of concern, will be needed.]

3b. The existing low-level "metabolism"/feeding studies with cattle, swine, and hens which demonstrated only minute amounts of total ^{14}C activity in animal tissues and in which no characterization of residues was therefore attempted, will be adequate for purposes of this petition, provided the estimated daily ingestion exposure to animals (including poultry) from proposed tolerances to be associated with this petition do not exceed the feeding levels reflected by these feeding studies. Oryzalin per se is considered the residue of concern in the absence of characterized residues.

However, in the eventuality that the estimated daily ingestion exposure to animals should exceed the feeding levels reflected by these available studies, then higher level animal "metabolism"/feeding studies will probably be required to support this petition.

In such an eventuality, characterization of the residues in animals (tissues, milk, eggs) would be required if sufficient radioactivity permitted it. [Demonstration of any metabolite(s) of concern in animals would warrant inclusion in the regulations, suitable enforcement methodology, and tolerance levels taking the total residue of concern into account.]

4a. We conclude that adequate enforcement methodology (EC-GLC) exists for regulating residues of oryzalin per se in or on wheat and barley grains and straws. Should plant metabolite(s) of concern be demonstrated (see Conclusion 3a), appropriate enforcement methodology will be required for it/them also.

4b. Proposed enforcement methodologies (GLC and HPLC) are submitted for regulating residues of oryzalin per se in animal substrates (tissues, eggs, milk). A MTO will be needed prior to the establishment of meat/milk tolerances. Pending resolution of other related deficiencies (see discussion under Analytical Methodology, Animals), however, we defer recommending for such a trial at this time.

Provided oryzalin per se remains the sole residue of concern in animals (see Conclusion 3b), we propose to eventually subject the GLC procedure (AM-AA-CA-RO77-AA-755) to test.

If metabolite(s) of concern should be demonstrated in animals, however (cf Conclusion 3b), then enforcement methodology suitable for regulating the total residue of concern in animal substrates would be needed, and it would be that methodology which would be MTO'd.

5a. Frozen storage stability data is lacking for oryzalin. As best we can deduce (comparing sampling dates with G-L chromatogram dates) from the partial data available, some of the treated field samples may have been stored in excess of two years prior to analysis (e.g., DAA 5-7 trial). This raises the question as to the validity (integrity) of the field samples at the time of analysis. To clarify this issue we require: (a) information as to the length and manner of storage of all the submitted wheat and barley field trial and processing samples prior to analysis; (b) frozen storage stability data for oryzalin residues in crops that encompasses a time frame similar to (a) above; and, (c) if other than parent is to be regulated, frozen stability data in crops for the metabolite(s) of concern.

5b. The nature of the residue is still not sufficiently delineated for a determination at this time as to whether there are plant metabolite(s) of regulatory concern (see Conclusion 3a). For this reason, and because of the storage stability question raised in Conclusion 5a above, we defer any conclusion re the adequacy of the proposed tolerance level on wheat and barley grains until those issues are resolved. If metabolite(s) of concern are identified in the elucidation of the nature of the residue, then residue data reflecting the total residue of concern will be needed from field trial studies.

5c. Tolerance proposals for the straws of wheat and barley will also be needed (revised section F). For the above-stated reasons (see Conclusions 3a and 5a), we defer judgment at this time as to what an appropriate level would be. If metabolite(s) of concern are identified in the elucidation of the nature of the residue, then residue data reflecting the total residue of concern will be needed from field trial studies.

5d. Based on the processing study data available, there does not appear to be a need for food/feed additive tolerances. We will reconsider this conclusion once information on storage stability (see Conclusion 5a) and elucidation of the nature of the residue in plants (see Conclusion 3a) become available.

6. Based upon the feeding study data presently available, we would have to classify the likelihood for secondary residues in meat/milk/poultry/eggs from the proposed use as a Sec. 180.6(a)(2) situation. Therefore, at a minimum, method sensitivity level tolerances will be needed (revised section F).

Method sensitivity in animal substrates is reportedly 0.05 ppm. A MTO (to be conducted once uncertainties over the residue of concern are resolved; see Conclusion 4b) will confirm/refute this contention and ascertain the availability of a suitable enforcement method for meat/milk/poultry/eggs.

We defer judgment at this time as to what tolerance level(s) should be proposed for meat/milk/poultry/eggs. We also note that at this time (see Conclusion 3b) we can not entirely preclude the need for higher level feeding studies to support this petition.

7. There are no international tolerances noted on the Codex sheet associated with the proposed use. Thus, this is not presently an area of conflict.

Recommendations

We recommend against the establishment of the proposed tolerances at this time. For further consideration the petitioner should address the deficiencies raised in Conclusions 2a, 2b, 2c, 3a, 5a, 5c, and 6.

Our comments in Conclusions 3b, 4a, 4b, 5b, and 5d should also be transmitted to the petitioner.

The Codex Sheet is attached to this review.

Detailed Considerations

Manufacture and Formulation

The manufacturing process, a listing of impurities, and nitrosamine information are all contained in the correspondence file to PP# 9E2219, and were most recently discussed in our (R. Loranger) review of 6/18/82, PP# 2G2612.

To summarize, the technical product is typically 96.9-98.8% pure. Impurities are not expected to present a residue problem. Low

However, detectable residues have been found in analyses of wheat grain or soybeans.

Two formulations are involved in the proposed use: Surflan® 75W (EPA Reg. No. 1471-96), a wettable powder containing 75% ai, and Surflan® A.S. (EPA Reg. No. 1471-112), an aqueous suspension containing 4 lbs ai/gallon (41.3% ai). The inerts in both formulations are cleared for use under 40 CFR 180.1001 (Confidential Statements of Formula are contained within Section A of this petition).

Proposed Use

For weed control in wheat or barley: Apply Surflan® at 1.0-1.5 lbs ai (1-1/3 to 2 lbs 75W or 1 to 2-1/2 qts A.S.), depending on soil texture, per broadcast acre as an OTS (over-the-top) spray anytime after the small grain is fully tillered and jointing has been initiated, but prior to heading.

Do not apply to soils containing more than 5% organic matter. Do not apply to winter wheat or barley prior to the fully tillered stage as crop injury may result. Do not graze or feed treated forage and straw.

Tank mix: Surflan may be tank-mixed with 2,4-D. Follow 2,4-D application recommendations, precautions, and limitations. [Note: there are 2,4-D/wheat and barley tolerances; see 40 CFR 180.142.]

Comments. The label prohibition against the grazing or feeding of treated forage (presumably both immature and mature) and straw needs to be revised to apply to forage and hay. A restriction against grazing/feeding of the straw is not considered practical due to economic considerations. A tolerance proposal will therefore be needed for wheat and barley straws.

INFORMATION WHICH MAY REVEAL THE IDENTITY OF A PRODUCT IMPURITY IS NOT INCLUDED

A single application to the crops is implied, but not specified. The field study data reflect only a single application. We request it be clarified on the label that the intended use is for but a single application per crop.

Nature of the Residue

Plants. A report entitled "Radiochemical Studies with ^{14}C Oryzalin on Wheat, Barley, and Alfalfa" by T. Golab and H. Wooten (10/80) was submitted in re PP# 2G2612 (oryzalin/alfalfa), and was extensively discussed in our (R. Loranger) 6/18/82 review thereof, which discussion is herein incorporated by reference. No additional metabolism information is provided in this current petition.

Comments. For consistency with our requirements for a permanent tolerance on alfalfa (see R. Loranger reviews of 10/19/82 and 5/17/83, PP# 2G2612), and since the same shortcomings also apply to our tolerance considerations on barley and wheat, we request a further examination of the water-extractable (aka neutral aqueous) fraction of wheat and barley straws for the presence/identification of conjugates (we forego data in the grains because of the low levels of total radioactivity therein), and of the methanol extract of barley straw for characterization of residues.

Pending receipt/review of this additional information, we defer judgment as to whether the residue of concern in plants consists of more than just the parent compound. In that eventuality, suitable enforcement methodology and supporting field trial data, as well as tolerance levels based upon the total residue of concern will be needed.

Animals. A new cattle balance-excretion study and radiolabeled (^{14}C) "metabolism"/ feeding studies for cattle (0.4 ppm feeding level), swine (0.2 ppm feeding level), and hens (0.2 ppm feeding level) were also submitted in re PP# 2G2612 (oryzalin/alfalfa) and were discussed in our (R. Loranger) 6/18/82 review thereof, which discussion is also incorporated herein by reference.

Comments. Only minute amounts of total ^{14}C activity were reported in animal tissues as a result of those feeding studies and, consequently, no attempt was made to characterize the residue. Oryzalin per se was considered to be the residue of concern in the absence of characterization of the residue.

Provided the estimated daily ingestion exposure to animals (including poultry) from the appropriate tolerance levels to be associated with this petition do not exceed the feeding levels reflected by these available data, we can conclude these studies are adequate for purposes of this petition. The petitioner reportedly has higher level feeding studies underway (and, if residues of significance result, characterization of the residues will be attempted) to support future petitions with feed items involved.

However, in the eventuality that the estimated daily ingestion exposure to animals should exceed the feeding levels reflected by these available studies, then higher level animal "metabolism"/feeding studies will probably be required to support this petition.

In that event, characterization of the residues in animals (tissues, milk, eggs) would be required if sufficient radioactivity permitted it. Demonstration of any metabolite(s) of concern in animals would warrant inclusion in the regulations, suitable enforcement methodology, and tolerance levels taking the total residue of concern into account.

Analytical Methodology

Plants. Samples were analyzed for oryzalin residues via EC-GLC following organic extraction, clean-up (liquid-liquid partitioning; column), and derivatization steps. Either procedure 5801615 or AM-AA-CA-RO29-AA-755 (which supersedes procedure 5801615) was utilized. These are both similar in principle -- measuring the residue as the dimethyl derivative of oryzalin via EC-GLC -- but differ in minor aspects in the clean-up steps. The limit of detection of both procedures is claimed to be 0.01 ppm.

Recovery data are available for samples of wheat grain (0.01, 0.04, 0.2 ppm spikes), milled by-products (0.04 ppm spike), and straw (0.04 and 0.05 ppm spikes). Recoveries from grain ranged 46-50%, 60-136%, and 84-94% at the respective spike levels. Recoveries from the milled by-products were: flour, 50%; germ, 70%; bran, 93%; shorts, 80%; and red dog, 48%. Recoveries from straw were 40-87%. Control values in grain were NDR (<0.01 ppm) to trace (>0.01 - <0.04 ppm), and in straw were NDR (<0.01 ppm) to 0.076 ppm. Similar recoveries would be expected from barley substrates.

We conclude that adequate enforcement methodology exists for regulating residues of oryzalin per se in or on wheat and barley grains and straws. (No by-products tolerances appear necessary in this instance.) Should plant metabolites(s) of concern be demonstrated (see Nature of the Residue, Plants), appropriate enforcement methodology (and supporting field trial data) will be required for it/them also.

Animals. Two methods (GLC, HPLC) were submitted in re PP#2G2612 (Amendment of 3/10/83) to quantitate oryzalin residues in meat/milk/poultry/eggs. These procedures are discussed in our (R. Loranger) review of 5/17/83, which discussion is incorporated herein by reference.

In both procedures the claimed limit of detection is 0.05 ppm. Neither method has as yet undergone a method trial, and such a trial will be needed prior to the establishment of any meat/milk/poultry/egg tolerances (such as will be needed in re this petition).

We tentatively propose to subject the GLC procedure (AM-AA-CA-R077-AA-755) to method trial. (This is an arbitrary choice based mainly on its similarity to the plant substrates procedure and the wider availability of GLC vs HPLC equipment for enforcement purposes.) The petitioner should be alerted to this and advised to inform us if there are any overriding considerations that, in their opinion, would make the HPLC procedure (AM-AA-CA-R078-AA-755) a better choice for enforcement purposes.

However, because of the present uncertainties as to whether the residue of concern in plants is parent only (see Nature of the Residue, Plants), and because this determination will affect what component(s) is/are to be regulated, what tolerance levels are needed, and thereby exposure levels to animals (which directly impacts on the adequacy of the existing animal "metabolism"/feeding studies), we defer initiation of the method trial until such time as the issue of the nature of the residue in plants is resolved.

As stated under Nature of the Residue, Animals, in the eventuality that the estimated daily ingestion exposure to animals should exceed the feeding levels reflected by the available studies, then higher level animal "metabolism"/feeding studies will probably be required to support this petition.

If higher level animal "metabolism"/feeding studies are run, it is possible that sufficient radioactivity would then accrue in animal tissues (including poultry), milk and eggs to necessitate characterization of residues therein and, possibly as a result, metabolite(s) of concern in animals might be identified which would necessitate regulation and suitable enforcement methodology. So, for this reason and the others stated above, we defer a MTO of meat/milk/poultry/egg methodology at this time.

Residue Data

Data on oryzalin residue levels are available from 14 field experiments conducted in 1975, 1976, and 1979 using Surflan 75W (FL, GA, IL, IN, KY, MS, OK, VA, MD, NC) and 6 field experiments conducted in 1981 and 1982 using Surflan 4 AS (DE, IL, IN, OR, WA).

In each experiment, the herbicide was applied once in the spring as an over-the-top spray for weed control in fall-planted wheat or barley. The treatment rate ranged from 0.75-1.5 lbs ai/A and included use on fine, medium, and coarse soil types and various varieties of wheat and barley.

In all trials, mature grain was harvested and submitted for the determination of oryzalin residues. Straw samples were also collected from ca half of the wheat studies for analysis of oryzalin residues; no barley straw samples were collected. Additionally, some of the collected wheat grain (but not barley) from three of the field trials was processed into milled by-products and subsequently analyzed for residues of oryzalin. All residue results reported have been corrected for recoveries.

Analyses of the wheat and barley grain samples indicated an oryzalin residue range of NDR (<0.01 ppm) to <0.04 ppm (which the petitioner claims reflects contamination) at the proposed use rate. Residues in wheat straw (1X rate) ranged from NDR (<0.01 ppm) to 0.17 ppm; although no barley straw data is available, we would expect residue of the same magnitude as in wheat straw.

Of the three processing studies conducted (with wheat grain), two utilized grain containing detectable levels of oryzalin (0.011 and 0.014 ppm). In the resultant flour, germ, and red dog fractions, NDR (<0.01 ppm) were reported. In the bran and shorts fractions, a low level residue was often reported at, or slightly above, method sensitivity (0.01 ppm) but, with one exception, still lower than in the grain from which it was processed; in the one exception, 0.01 ppm (the limit of detection) was reported in the bran from grain reportedly containing NDR (<0.01 ppm).

Comments. (1) Frozen storage stability data is lacking for oryzalin. As best we can deduce (comparing sampling dates with G-L chromatogram dates) from the partial data available, some of the treated field samples may have been stored in excess of two years prior to analysis (e.g., DAA 5-7 trial). This raises the question as to the validity (integrity) of the field samples at the time of analysis. To clarify this issue we require: (a) information as to the length and manner of storage of all the submitted wheat and barley field trial and processing samples prior to analysis; (b) frozen storage stability data for oryzalin residues in crops that encompasses a time frame similar to (a) above; and, (c) if other than parent is to be regulated, frozen stability data in crops for the metabolite(s) of concern.

(2) The nature of the residue is still not sufficiently delineated for a determination at this time as to whether there are plant metabolite(s) of regulatory concern. For this reason, and because of the storage stability question raised in (1) above, we defer any conclusion re the adequacy of the proposed tolerance level on wheat and barley grains until those issues are resolved. If metabolite(s) of concern are identified in the elucidation of the nature of the residue, then residue data reflecting the total residue of concern will be needed from field trial studies.

(3) Tolerance proposals for the straws of wheat and barley will also be needed (revised Section F). For the above-stated reasons, we defer judgment at this time as to what an appropriate level would be. If metabolite(s) of concern are identified in the elucidation of the nature of the residue, then residue data reflecting the total residue of concern will be needed from field trial studies.

(4) Based on the processing study data available, there does not appear to be a need for food/feed additive tolerances. We will reconsider this conclusion once information on storage stability and elucidation of the nature of the residue in plants becomes available.

Residues in Meat, Milk, Poultry, and Eggs

Based upon the feeding study data presently available (ref. R. Loranger review of 6/18/82, PP# 2G2612, for discussion), we would have to classify the likelihood for secondary residues in meat/milk/poultry/eggs from the proposed use as a Sec. 180.6(a)(2) situation. Therefore, at a minimum, method sensitivity level tolerances will be needed (revised Section F). Method sensitivity in animal substrates is reportedly 0.05 ppm (GLC or HPLC; ref. R. Loranger review of 5/17/83, PP# 2G2612). A MTO (to be conducted once uncertainties over the residue of concern are resolved) will confirm/refute this contention and ascertain the availability of a suitable enforcement method for meat/milk/poultry/eggs.

We defer judgment at this time as to what tolerance level(s) should be proposed for meat/milk/poultry/eggs. We also note that at this time (see Nature of the Residue, Animals) we can not entirely preclude the need for higher level feeding studies to support this petition.

Other Considerations

Codex. There are no international tolerances noted on the Codex sheet. Thus, this is not presently an area of potential conflicts.

Attachment

cc: R.F., Circu, Reviewer, TOX. EEB, EAB, Petition No 3F2874
FDA, Robert Thompson
RDI:Section Head:MJN>Date:11/4/83:RDS>Date:11/4/83
TS-769:RCB:Reviewer(mjn):Typist (LM)RM:810:CM#2>Date:11/10/83
DCR-44809

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL oryzalin

PETITION No. 3F2874

CCPR NO. none

Codex Status

Proposed U. S. Tolerances

No Codex Proposal
 Step 6 or above

for 180.304

Residue (if Step 9): _____

Residue: oryzalin

Crop(s) Limit (mg/kg)

Crop(s) Tol. (ppm)

barley, grain 0.05
wheat, grain 0.05

CANADIAN LIMIT

MEXICAN TOLERANCIA

Residue: _____

Residue: _____

Crop Limit (ppm)

Crop Tolerancia (ppm)

none

none

Notes: