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PP#DF2373. Pendimethalin (Prowl®) in or on sunflower seeds.
Evaluation of analytical methodology and residue data.

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The American Cyanamid Company proposes the establishment of a tolerance for combined residues of the herbicide pendimethalin [N-[(1-ethylpropyl)-3,4-dimethyl-2,6-dinitrobenzenamine] [Trade name: Prowl®] and its metabolite, 4-[(1-ethylpropyl)amino]-2-methyl-3-,5-dinitrobenzyl alcohol, in or on sunflower seeds at 0.1 ppm.

Tolerances on several crops (soybeans, corn, cottonseed) are presently established (40 CFR 180.361) for aforesaid combined residues; tolerances on several other crops (e.g., wheat, peanuts, sorghum) are currently co-pending. Both the proposed and established tolerances are all at 0.1 ppm.

A temporary tolerance for the aforesaid combined residues in or on sunflower seeds at 0.1 ppm was established in October, 1977 in re PP#761896.

In the developmental stage, pendimethalin was also known as CL 92,553.

Conclusions

1. A nitrosamine, [redacted] has been identified as an impurity in technical pendimethalin [redacted] and Prowl® [redacted]. The residue level of this impurity to be expected in sunflower seeds (or by-products) has been calculated to be <0.1 ppb. We defer to TOX whether they require actual residue analyses for the presence of this impurity in sunflowers.
2. The nature of the residue in plants and animals is sufficiently understood. Pendimethalin plus its benzyl alcohol metabolite are the residues of concern.
3. Adequate analytical methodology (EC-SLC) is available to enforce the proposed tolerance.

- 4a. Residues, if any, in sunflower seeds and by-products (meal, oil, hulls, soapstock) are not expected to exceed the proposed tolerance level of 0.1 ppm (which represents the combined method sensitivities of pendimethalin plus the benzyl alcohol metabolite). Detectable residues were not encountered, even under exaggerated rate conditions.
- 4b. No residue data were submitted for sunflower forage. Its feed use is restricted by labeling, as is grazing in treated fields.
5. Based on the information cited in Conclusions 4a and 4b, there is no reasonable expectation of residues occurring in meat, milk, poultry, or eggs as a result of the proposed use.
6. There is no conflict between the proposed tolerance level and any international residue limit(s) for pendimethalin/sunflower seeds, since there are none (see attached sheet).

Recommendations

Contingent upon a favorable response from TOX re our deferral (see Conclusion #1) and if other toxicological and EFB (crop rotation) considerations permit, we could recommend in favor of the proposed tolerance.

DETAILED CONSIDERATIONS

Manufacture and Formulation

The manufacturing process for pendimethalin technical was detailed in our review (A. Smith, 5/8/75) of PP#5F1556, which see.

The technical product is 91-94% pure. One impurity is noteworthy: technical pendimethalin

The formulated product to be used is Prowl® herbicide (EPA Reg. No. 241-243-AA), an emulsifiable concentrate containing 42.3% ai and 57.7% inert ingredients (cleared under §180.1001). One gallon of formulated product contains 4 lbs. ai.

The Prowl formulation also contains

MANUFACTURING PROCESS INFORMATION IS NOT INCLUDED

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Assuming the residue behavior patterns of Prowl and its nitrosamine component are similar, we would then expect nitrosamine residues in sunflower seed of <0.1 ppb (i.e., <1/1000th of the proposed tolerance level for pendimethalin). If TOX considers this level toxicologically significant, then actual residue analyses by validated analytical methodology will need to be submitted for the nitrosamine component. We defer to TOX on this.

Proposed Use

For the control of various specified annual grasses and broadleaf weed species in the cultivation of sunflowers, Prowl is to be applied to soil via broadcast spray or band treatment either immediately before planting to sunflowers or up to 60 days prior to planting, and preplant incorporated.

Recommended application rates (broadcast basis; use proportionately less for band treatment) vary between 1.0 to 3.0 pts of formulation (i.e., 0.5-1.5 lbs ai) per acre, depending on the degree of infestation, soil texture and type, and geographic location.

The recommended Prowl treatment is to be applied either in 10 or more gallons of water or in 20 or more gallons of liquid fertilizer per acre by ground equipment or in 5 or more gallons of water per acre by aircraft.

Do not feed forage or graze livestock in treated sunflower fields. If sunflower crop loss occurs due to weather conditions, sunflowers, soybeans, or cotton can be replanted. Prowl-treated land can be planted to other crops the following year.

Nature of the Residue

Metabolism studies of pendimethalin in various r.a.c.'s (corn, cottonseed, soybeans, potatoes, peanuts, et al.) and animals (rats, goats, cows) have previously been submitted and reviewed (e.g., ref. PP's 5F1556, 6G1739-40).

In brief, pendimethalin is absorbed from soils, translocated in plants, and metabolized/degraded via oxidative pathways. Plant residues consist primarily of the parent compound and its benzyl alcohol metabolite, and these are considered the residues of concern. Other components present in low concentration are believed to be various carboxylic acid derivatives. No binding or conjugation of residues has been noted.

while no data has been submitted to specifically show the metabolism of pendimethalin in sunflower plants, we believe the behavior therein would be similar to that in the other plant species studied. Accordingly, we consider the nature of the residue in sunflowers to be sufficiently understood.

In animals, extensive and rapid metabolism/degradation and excretion of pendimethalin residues has been shown to occur via oxidative pathways. Some deposition of residues occurs in tissues, but no tendency towards storage or concentration has been noted. The main sites for oxidation are the 4-methyl group on the benzene ring and the N-alkyl side chain. In addition to the parent compound and the benzyl alcohol metabolite, a variety of metabolites--most of which appear to contain one or more carboxylic acid groups--have been reported as minor components of the residue. We consider the nature of the residue in animals to be adequately defined; the parent and benzyl alcohol metabolite are the residues of concern.

Analytical Methodology

Residues of pendimethalin (aka CL 92,453) were determined as such in samples of sunflower seed, straw, meal, oil, hulls, and soapstock by analytical methodology entailing solvent extraction, one or more clean-up steps (liquid-liquid partitioning and/or adsorption chromatography on Florisil), and quantitation by electron-capture GLC, with procedural specifics dependent on the particular substrate involved. The validated sensitivity of the methodology for determination of pendimethalin residues in each substrate was reported as 0.05 ppm. (Actual limit of detection is less than 0.01 ppm.)

Residues of the benzyl alcohol metabolite (aka CL 202,347) in these substrates were extracted and cleaned-up by procedures similar to those for pendimethalin per se, with the addition of a derivatization step so that the benzyl alcohol metabolite was determined by EC-GLC as its acetylated derivative. The validated sensitivity of the methodology for such determination in each substrate was also reported as 0.05 ppm. (Actual limit of detection is less than 0.01 ppm.)

Validation data were submitted for the recovery of pendimethalin and its benzyl alcohol metabolite from fortified samples of sunflower seed, straw, meal, oil, hulls, and soapstock. Substrates were fortified over the range of 0.05-5.0 ppm; recoveries ranged 79-121% for pendimethalin and 64-120% for the benzyl alcohol metabolite. Control values were less than or equal to 0.00% ppm for both pendimethalin and its benzyl alcohol metabolite.

A trial of similar methods for determining residues of pendimethalin and its benzyl alcohol metabolite in cottonseed has previously been run by Agency chemists (in re PP#5F1556). Adequate recoveries (more than or equal to 76%) were obtained from fortification at levels of 0.05 and 0.1 ppm; blanks were less than 0.01 ppm.

A confirmatory method for pendimethalin was discussed in our (A. Smith, 5/8/75) review of PP#5F1556. It is based on a chromophoric reaction; other nitroanilide compounds reportedly do not interfere.

We conclude that adequate analytical methodology is available for the determination of pendimethalin and its benzyl alcohol metabolite in sunflower seeds and related by-products and for enforcement of the proposed tolerance.


Residue Data

Data for pendimethalin and benzyl alcohol metabolite residues in sunflower seeds are submitted from the states of MN, ND, SD, TX, and CA for the crop years 1975 and 1977-79. These data were from 12 field studies involving different soil textures (5), percent organic matter, sunflower varieties (11), preplant incorporated treatment rates (0.5-4.0 lbs. ai/A; maximum proposed rate, 1.5 lb ai/A), and PHI's (125-160 days). Two of the field studies (1975) were submitted previously with PP#7G1896, and constituted the residue base for the establishment of the 0.1 ppm temporary tolerance on sunflower seeds.

In none of these 12 field studies was a detectable residue of either pendimethalin or its benzyl alcohol metabolite (validated method sensitivity level for each component, 0.05 ppm) reported. All values are indicated to be ≤ 0.05 ppm, each component. The proposed tolerance level, 0.1 ppm, reflects the combined method sensitivities of the two components (pendimethalin plus its benzyl alcohol metabolite) to be regulated.

Samples of sunflower seeds from 3 of the above field studies (SD and MN, 1979; 1.25-1.5 lb ai/A treatment rate) were processed into refined oil, meal, hulls, and soapstock. MDR were observed in any of these by-products based on the validated sensitivities of the methodology (0.05 ppm for each compound in all commodities).

Based on the available data, we conclude that residues, if any, of pendimethalin and its benzyl alcohol metabolite in or on sunflower seeds and sunflower by-products (except forage, for which no residue data were submitted and no conclusion can be drawn; feed use of the forage is label restricted) will not exceed the proposed tolerance level of 0.1 ppm for sunflower seeds.



Residues in Meat, Milk, Poultry, or Eggs

Sunflower forage is a livestock feed item, but its feed use in the instant case is prohibited by label restriction. There is also a label restriction against grazing in treated fields.

Sunflower by-products (meal, etc.) are also items of livestock feed, and poultry feed as well. However, since no detectable residues (validated method sensitivity, 0.05 ppm, for parent; also, for benzyl alcohol metabolite; proposed tolerance reflects these combined sensitivities) have been reported in sunflower seeds or any by-products under proposed (or exaggerated) conditions of use, no transfer of residues to meat, milk, poultry, or eggs is anticipated.

Other Considerations

There is no conflict between the proposed tolerance and international residue limit(s) for such a use (there are none; see attached sheet).

Attachment

TS-769:RCB:M. Nelson:gs:X77324:HC#2:R1010:8/6/80
cc: RF, Circ., M. Nelson, Watts, FDA, TOX, EEB, EFB, PP#0F2373
RDI:R.S. Quick:7/31/80:R.D. Schmitt:7/31/80



INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL Pendimethalin

OF2373

PETITION NO.
Reviewer: M. Nelson

CCPR NO. None

Codex Status

/ X - / No Codex Proposal
Step 6 or above

Proposed U. S. Tolerances

40 CFR 180.361

Residue (if Step 9): _____

None

Residue: pendimethalin and its
metabolite [4-(1-ethylpropyl)amino]-2-
methyl-3,5-dinitrobenzyl alcohol]

Crop(s) Limit (mg/kg)

None

Crop(s) Tol. (ppm)

Sunflower seeds 0.1

CANADIAN LIMIT

Residue: _____

None

Crop Limit (ppm)

None

MEXICAN TOLERANCIA

Residue: _____
None

Crop Tolerancia (ppm)

None

Notes: