

FAP # 2H5640



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

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HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

OCT 18 1995

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Memorandum

Subject: PP#6F3333/FAP#2H5640. Cyromazine on Tomatoes. Response to RD Request Dated 07/25/95 to Reevaluate the Need for 409 Tolerances. Reevaluation of Need for Additional Tolerances for Animal Commodities. CBTS# 15912. No MRID#'s. DP Barcode# D217689.

From: Jerry B. Stokes, Chemist
Chemistry Branch I/Tolerance Support
Health Effects Division (7509C)

Thru: Michael Metzger, Chief
Chemistry Branch I/Tolerance Support
Health Effects Division (7509C)

To: George LaRocca/Linda Deluise, PM-13
Insecticide/Rodenticide Branch
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and

Karen Whitby, Acting Section Head
Risk Characterization and Analysis Branch
Health Effects Division (7509C)

RD has now requested CBTS to determine if cyromazine residues (parent and metabolite melamine) concentrate in tomato processed commodities based on the new analytical methodology for cyromazine residues, and to determine if 409 tolerances are still required for cyromazine residues in these commodities based upon recent changes in residue chemistry review procedures.

Background:

Since all residue data deficiencies cited for PP#6F3333 had been satisfied, CBTS recommended for the proposed tolerances for the combined residues of cyromazine (N-cyclopropyl-1,3,5-triazine-2,4,6-triamine), its metabolite, melamine (1,3,5-triazine-2,4,6-triamine), all expressed as cyromazine: tomatoes, 1.0 ppm;



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processed tomato products (except juice), 2.5 ppm; tomato pomace (wet and dried), 2.5 ppm; milk, 0.02 ppm; meat, fat, and meat by-products of cattle, goats, hogs, horses, and sheep, 0.05 ppm. CBTS also recommended tolerances for the combined residues of cyromazine (N-cyclopropyl-1,3,5-triazine-2,4,6-triamine), its metabolites, melamine (1,3,5-triazine-2,4,6-triamine), and 1-methylcyromazine, all expressed as cyromazine: liver and kidney of cattle, goats, hogs, horses, and sheep, 0.05 ppm. (See memo of 05/26/95, J. Stokes).

Need for 409 Tolerances:

CBTS has now reevaluated the processing study based on new CBTS/CBRS policy (See memo of 07/17/95, M. Metzger and E. Zager). CBTS has determined that the highest average field trial residue (HAFT) in/on harvested tomatoes for the proposed label at a maximum of 6 applications and 0-day PHI is 0.59 ppm (combined residues for cyromazine and metabolite melamine) [Note: CBTS previously concluded that since the field trial residue data suggested that 7- and 14-day PHIs have little effect on overall residue levels, the tolerance would be based on 0-day PHI data (See memo of 04/02/93, R. Lascola). Therefore, CBTS recommended a 1.0 ppm tolerance in/on tomato.]. In the petitioner's tomato processing data (See MRID# 422551-01), fruit were harvested from a field trial that was conducted at a 1X rate with 7-day PHI. Although the petitioner reported combined residues of 0.15 ppm, 4 additional rac samples analyzed from the same field trial averaged 0.30 ppm. The average residue for the five rac samples is 0.27 ppm. Therefore, since the average rac residues better reflect the residues that might be on the rac before processing, CBTS has now determined that the average combined residues on the unwashed tomato was of 0.27 ppm. The processing study using the rac harvested from the 1X trial showed combined residues of cyromazine and metabolite melamine in tomato puree at 0.23 ppm and in tomato paste at 0.34 ppm. Therefore, the concentration factors for puree and paste are 0.8x and 1.2x, respectively, based on only the processing study using 1X treated tomatoes.

Likewise, the petitioner reported combined residues on the rac unwashed tomato from a field trial conducted at a 2X rate with a 7-day PHI at 0.35 ppm. However, three additional rac samples analyzed from the same field trial averaged 1.3 ppm. Based on the above comments for the 1X trial, CBTS has now determined the average combined residues of the rac before processing at 1.1 ppm. Fruit harvested from a field trial that was conducted at a 2X rate yielded 0.33 ppm for puree and 0.72 ppm for paste. Therefore, the concentration factors for puree and paste are 0.3x and 0.7x, respectively, based on only the second processing study.

Therefore, the average concentration factors for the two processing studies are 0.6x for puree and 1x for paste. Since the residues in puree and paste are below or equal to the proposed rac (raw

agricultural commodity) tolerance of 1.0 ppm in/on tomato, a 409 tolerance is not needed for tomato processed products. The recommended 1.0 ppm rac tolerance will cover any residues in processed tomato products from the proposed use of cyromazine on tomato. The analytical data also show that combined cyromazine residues are reduced by as much as 50% following the normal washing procedure included in the commercial process for tomato.

A revised Section F must be submitted with the previous request for the 2.5 ppm tolerance in/on tomato processed products removed.

Other Considerations:

Feed Additive Tolerances:

Based upon recent changes of residue data requirements as a result of Table II (September 1995), tolerances are no longer needed for tomato pomace, wet, or tomato pomace, dried. A revised Section F must be submitted with the request for tolerances in/on the tomato pomaces removed.

Tolerances for Animal Commodities (excluding poultry):

Based on the petitioner's metabolic and feeding studies for ruminant animals, CBTS determined that cyromazine and its metabolite melamine should be regulated in milk, and meat, fat, and meat byproducts of cattle, goats, hogs, horses, and sheep. CBTS also determined that the animal metabolite 1-methylcyromazine should be regulated in the liver and kidney of cattle, goats, hogs, horses, and sheep. These recommendations were based on 1) the proposed use on tomato and the resulting livestock feedstuffs, wet tomato pomace and dried tomato pomace, and 2) the proposed use of cyromazine on carrots (See PP#6F3332) and the resulting feedstuff, carrot culls. The petitioner requested the withdrawal of proposed use in/on carrots, PP#6F3329 (See letter dated 06/10/95, N. Beth Carroll, Regulatory Manager, Ciba-Geigy Corporation, PP#6F3329).

Therefore, neither tomato pomace, wet or dried, nor cull carrots are considered in the dietary burden. These feedstuffs were controlling the need for rac tolerances for cyromazine and its metabolite melamine in the milk, meat, fat, and meat byproducts of cattle, goats, hogs, horses, and sheep. These feedstuffs were also controlling the need for tolerances for the animal metabolite 1-methylcyromazine in the liver and kidney of cattle, goats, hogs, horses, and sheep. Thus, based on the above discussion, cyromazine residues will not be observed in animal commodities for the proposed cyromazine use in/on tomato.

In addition, the petitioner has submitted a request for rac tolerances in/on sweet corn forage and cannery waste for the proposed inadvertent use on sweet corn in crop rotation (See PP#6F3332). Based on the 5.0 ppm ruminant feeding study, and an

estimated dietary burden of sweet corn forage and cannery waste in livestock (estimated at 0.25 ppm), expected levels of the combined residues of cyromazine, its metabolites melamine and 1-methylcyromazine, will be <0.005 ppm in milk and \leq 0.01 ppm in meat, fat, meat byproducts of cattle, goats, hogs, horses, and sheep. These estimated combined residues are below the levels of detection (cyromazine, 0.3 ppm; melamine, 0.1 ppm; 1-methylcyromazine, 0.01 ppm) in animal commodities of milk, meat, fat, or meat byproducts of cattle, goats, hogs, horses, and sheep. CBTS does not consider these potential residues resulting from crop rotation to be significant, and does not recommend that tolerances be established for meat, fat, and meat byproducts of cattle, goats, hogs, horses, and sheep. The existing 0.25 ppm tolerance for milk will be adequate to cover any inadvertent cyromazine residues. The sweet corn inadvertent use will not affect poultry commodities.

Thus a revised Section F must be submitted with the removal of the previously requested tolerances for cyromazine and its metabolite melamine in meat, fat, and meat byproducts of cattle, goats, hogs, horses, and sheep, including the requested tolerance for the metabolite 1-methyl-cyromazine in the liver and kidney of cattle, goats, hogs, horses, and sheep.

Revision of Poultry Tolerances:

Based upon CBTS's request the petitioner proposed revision of tolerances for poultry commodities for the proposed use on tomato, and resulting residues on the poultry feedstuff, dried tomato pomace.

"(6a). Combined residues of cyromazine and its metabolite melamine could occur in eggs and meat of poultry, hogs, and horses. However, residues in eggs and poultry would be adequately covered by the level of the existing tolerances for layer hens (0.05 ppm). The established tolerance should be revised to reflect poultry, in general. As a result, revised tolerance proposals are needed and should be submitted." (See memo of 02/12/87, A. Smith, PP#6F3333).

However, since dried tomato pomace is no longer considered significant feedstuff, this revision is not necessary. Thus, a revised Section F must be submitted with the removal of the requested tolerances for cyromazine and its metabolite melamine in "other poultry". The established tolerances for layer and breeder hens is adequate to cover the existing cyromazine use as a feed additive in the feed for layer and breeder hen only [See 40 CFR §186.1400 (a)]. The "other poultry" would have included chicken broilers and turkeys plus other minor poultry stock. The proposed inadvertent use on sweet corn in crop rotation (See PP#6F3332) will not affect poultry commodities of eggs or layer and breeder hen meat, fat, and meat byproducts.

Summary of Tolerances Needs:

- 1) A food additive tolerance is not needed for cyromazine residues, including metabolite melamine, in tomato processed products.
- 2) Feed additive tolerances are not needed for tomato pomace, wet, or tomato pomace, dried.
- 3) Rac tolerances for cyromazine and its metabolite melamine in meat, fat, and meat byproducts of cattle, goats, hogs, horses, and sheep are not needed.
- 4) A tolerance for the metabolite 1-methylcyromazine in the liver and kidney of cattle, goats, hogs, horses, and sheep is not needed.
- 5) Expansion of the established rac tolerances from "layer and breeder hens" to "poultry" is not necessary.

Recommendations:

TOX considerations permitting, CBTS can recommend for the proposed tolerances for the combined residues of cyromazine (N-cyclopropyl-1,3,5-triazine-2,4,6-triamine), its metabolite, melamine (1,3,5-triazine-2,4,6-triamine), all expressed as cyromazine in/on tomatoes at 1.0 ppm. However, the petitioner must submit a revised Section F to reflect all of the above changes. A DRES run can be initiated at this time using 1 ppm for raw tomatoes, puree, and paste.

cc: J. Stokes, RF, Circu, PP#6F3329, PP#6F3332, PP#6F3333/
FAP#2H5640
RDI: Perrico:10/12/95:RLoranger:10/17/95:MMetzger:10/18/95
7509C:CBTS:JStokes/js:CM#2:Rm803:305-7561:10/18/95

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FAP # 5640



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MAY 26 1995

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TOXIC SUBSTANCES

Memorandum

Subject: PP#6F3333/FAP#2H5640: Cyromazine on Tomato. Amendment of 05/04/95. CBTS#15420. MRID#'s 436077-00 and 436077-01. DP Barcode#D214217.

From: Jerry B. Stokes, Chemist
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Health Effects Division (7509C)

Through: Ed Zager, Acting Chief
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Health Effects Division (7509C)

To: George LaRocca, PM 13
Insecticide/Rodenticide Branch
Registration Division (7505C)

and

Jane Smith, Acting Section Head
Risk Characterization and Analysis Branch
Health Effects Division (7509C)

The petitioner, CIBA-GEIGY, has submitted an amendment dated 05/04/95 in response to CBTS comments (See memo 02/13/95, J. Stokes). The petitioner has proposed tolerances for the combined residues of cyromazine (N-cyclopropyl-1,3,5-triazine-2,4,6-triamine), its metabolite, melamine (1,3,5-triazine-2,4,6-triamine), all expressed as cyromazine: tomatoes, 1.0 ppm; processed tomato products (except juice), 2.5 ppm; tomato pomace (wet and dried), 2.5 ppm; milk, 0.02 ppm; meat, fat, and meat by-products of cattle, goats, hogs, horses, and sheep, 0.05 ppm. The petitioner has also proposed tolerances for the combined residues of cyromazine (N-cyclopropyl-1,3,5-triazine-2,4,6-triamine), its metabolites, melamine (1,3,5-triazine-2,4,6-triamine), and 1-methylcyromazine, all expressed as cyromazine: liver and kidney of cattle, goats, hogs, horses, and sheep, 0.05 ppm. Tolerances are established for eggs (0.25 ppm) and poultry meat, fat, and meat byproducts (0.05 ppm) under 40 CFR §180.414 (a), (b), and (c).

(See Revised Section F dated June 10, 1994, PP#3F3333)



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Detailed Considerations:

Deficiency 3a, memo of 04/02/93, R. Lascola:

Analytical Methods. The recovery data, chromatograms, and other data submitted in this report indicate that the proposed method, AG-584A, may be adequate for the determination of 1-methylcyromazine in liver and kidney. However, the petitioner has not submitted an independent laboratory validation, as required under PR 88-5. This must be submitted before this method can be sent to EPA's Beltsville laboratories for a petition method validation. CBTS cannot accept this method at this time.

Petitioner Response, 06/10/94:

The petitioner has submitted an "independent" validation of the proposed enforcement analytical methodology AG-584A. (MRID#432742-02). According to the petitioner this method validation was performed in-house by the company using an analyst with no prior experience with the method.

CBTS Comments/Conclusions, memo of 02/13/95, J. Stokes:

The petitioner must verify that not only the analyst had no prior experience, but also that the analytical equipment and columns, standards, reagents, and any other materials needed to run the method, are different from those used to develop the method, and that there was no contact with persons responsible for the development of the method, other than that allowed by USEPA PR Notice 88-5.

Deficiency 3a is still outstanding. This data requested above must be submitted before this method can be sent to EPA's Beltsville laboratories for a petition method validation. CBTS cannot accept this method at this time. The petitioner's response to this deficiency should be submitted under PP#6F3329.

Petitioner Response, 05/04/95:

The petitioner has submitted additional comments as requested by CBTS.

CBTS Comments/Conclusions:

Deficiency 3a cited in PP#6F3333 (See memo of 04/02/93, R Lascola) has been satisfied in regards to verification of the "independent" lab validation as requested by CBTS (See memo 02/13/95, J. Stokes).

The analytical methodology for the detection of 1-methylcyromazine, method AG-584A (MRID# 422243-04), is nearly identical to method AG-398, which has been previously determined to be adequate for the determination of 1-methylcyromazine in milk and tissues and was

recommended to be incorporated into PAM II as a letter method. (See memo of 01/28/87, A. Smith). In addition, residues of cyromazine and its metabolites may be analyzed by the several FDA multiresidue protocols (II and III, with marginal detectability).

The petitioner previously has submitted a feeding study (MRID# 422243-03) of lactating dairy cattle fed cyromazine for 28 days at either rates of 10, 50, or 100 ppm. Maximum combined residues observed in milk (cyromazine plus melamine plus 1-methylcyromazine, all expressed as cyromazine) were as follows: 10 ppm feeding level, 0.09 ppm; 50 ppm feeding level, 0.38 ppm; 100 ppm feeding level, 0.69 ppm. No residues of 1-methylcyromazine were found in milk. Residues of 1-methylcyromazine were found only in liver and kidney, and only at the higher feeding levels. (See memo of 04/03/93, R. Lascola). Since the petitioner's request to withdraw the proposed use on carrots, the previous 8.0 ppm dietary burden estimated by CBTS will now be less than 3.0 ppm if a proposed diet includes sweet corn forage [0.5 ppm proposed tolerance (PP#6F3332), 50% intake] and wet tomato pomace [2.5 ppm proposed tolerance (PP#6F3333), 10% intake]. Based on this diet, the maximum expected residues of 1-methylcyromazine would be <0.1 ppm in liver and <0.2 ppm in kidney. Residues would not be expected in muscle tissue or milk.

Therefore CBTS has now determined that a PMV for the proposed methodology for the animal metabolite 1-methylcyromazine will no longer be required to recommend the establishment of tolerances in/on raw tomato and tomato processed products. CBTS will submit the proposed analytical methodology to FDA for inclusion in PAM II as a letter method. Deficiency 3a is now resolved.

Recommendations:

TOX considerations permitting, CBTS can now recommend for the proposed tolerances for the combined residues of cyromazine (N-cyclopropyl-1,3,5-triazine-2,4,6-triamine), its metabolite, melamine (1,3,5-triazine-2,4,6-triamine), all expressed as cyromazine: tomatoes, 1.0 ppm; processed tomato products (except juice), 2.5 ppm; tomato pomace (wet and dried), 2.5 ppm; milk, 0.02 ppm; meat, fat, and meat by-products of cattle, goats, hogs, horses, and sheep, 0.05 ppm. CBTS can also recommend tolerances for the combined residues of cyromazine (N-cyclopropyl-1,3,5-triazine-2,4,6-triamine), its metabolites, melamine (1,3,5-triazine-2,4,6-triamine), and 1-methylcyromazine, all expressed as cyromazine: liver and kidney of cattle, goats, hogs, horses, and sheep, 0.05 ppm. All outstanding deficiencies with PP#6F3333 has been resolved.

Note to PM: In previous CBTS memo (02/13/95, J. Stokes) stated that the livestock tolerances must be established under PP#3F3329. However, after reevaluation, CBTS has determined that the petitioner had previously submitted a revised Section

F dated June 10, 1994, requesting the livestock tolerances under PP#3F3333/FAP#2H5640 in addition to a similar request under PP#F3329. Therefore, the livestock tolerances can be established under PP#3F3333 when appropriate.

cc: J. Stokes, RF, Circu, PP#6F3329, PP#6F3332, PP#6F3333/
FAP#2H5640
RDI: RPerfetti:05/25/95:RLoranger:05/25/95:E Zager:05/25/95
7509C:CBTS:JStokes/js:CM#2:Rm803:305-7561:05/26/95

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PP# 5640



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EPA SERIES 361

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OFFICE OF
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TOXIC SUBSTANCES

Memorandum

Subject: PP#6F3333/FAP#2H5640. Cyromazine on Tomato. Response to FR Notice, Revised Section F, and Correction to Previous Comment in CBTS (J. Stokes) Memorandum dated 10/18/95. No MRID#'s. CBTS#17083. DP Barcode #D224826.

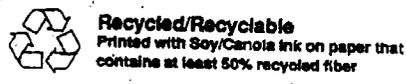
From: Jerry B. Stokes, Chemist
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Health Effects Division (7509C)

Thru: Ed Zager, Acting Chief
Chemistry Branch I/Tolerance Support
Health Effects Division (7509C)

To: George LaRocca/Linda Deluise, PM-13
Insecticide/Rodenticide Branch
Registration Division (7505C)

CBTS has reviewed the proposed FR notice and changes/corrections have been made on the attached draft copy. A Section F (dated 11/21/95) with corrected tolerance requests has been submitted. The previous cyromazine (and its metabolites melamine) tolerance requests for tomato processed products, tomato pomace, and livestock commodities (i.e., meat, fat, meat byproducts), expansion of established tolerances for "layer and breeder hens" to "poultry", and the requested establishment of a 1-methylcyromazine tolerance in livestock liver and kidney, have been removed per the recommendation of CBTS. However, the petitioner still requests a 0.02 ppm milk tolerance. The inclusion of this milk tolerance request is probably a result of a comment in the CBTS memorandum dated 10/18/95 [J. Stokes, comment (p.4)] in regards to an existing 0.25 ppm milk tolerance. This is incorrect. There is not an existing milk tolerance for cyromazine. Furthermore, a milk tolerance is not needed for the proposed use on tomato. CBTS recommends that RD request the petitioner to submit a corrected Section F to reflect the proposed establishment of a 1.0 ppm cyromazine tolerance in/on tomato only. CBTS does not need to review this revised Section F, but a copy should be sent to CBTS for their petition files.

cc: J. Stokes, RF, Circu, PP#6F3333/FAP#2H5640
RDI: EHaerberer:04/03/96:EZager:04/03/96
7509C:CBTS:JStokes/js:CM#2:Rm803:305-7561:04/03/96



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