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

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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#2F04154; Fenbuconazole, Indar® 2F Agricultural Fungicide, (EPA Reg. No. 707-EGR), in or on Bananas. Amendment of 3/31/94.
MRID No. 432051-01; CBTS No. 13647.
DP Barcode: D202611.

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William D. Wassell 8/1/94

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Summary / Background:

Rohm and Haas Company, Philadelphia, PA, requests the establishment of tolerances for residues resulting from the use of the fungicide fenbuconazole (ANSI/ISO) or RH-7592 [alpha-(2-(4-chlorophenyl)-ethyl)-alpha-phenyl-3-(1H-1,2,4-triazole)-1-propanenitrile] and its metabolites RH-9129 and RH-9130 and FIFRA Section 3 registration in or on the raw agricultural commodity bananas (whole fruit) at 0.3 ppm of which not more than 0.05 ppm is contained in the banana pulp.

The current submission is in response to our review of 10/06/93 (W.D. Wassell, PP#2F04154) and consists of revised Sections A, B and F and a response to the



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cited deficiencies in our original review of the subject petition. The previously cited deficiencies are restated below followed by the petitioner's response and finally our comments. In some cases, the petitioner's response to our conclusion has been paraphrased.

Detailed Considerations:

Conclusion 1a: Data gaps exist for Product Chemistry guideline reference numbers 61-1, 61-2, 61-3, 62-1, 62-3, 63-7, 63-8, 63-12 and 63-13 (see our review 2/25/93, N. Dodd, CBTS No. 8873). CBTS concludes the previously submitted product chemistry data are not adequate to support the proposed use of fenbuconazole on bananas.

Petitioner's Response: "Data gaps for Series 61, 62, and 63 from CBTS review dated 25FEB93 were discussed with N. Dodd 05APR93 and EPA concurred in writing with the summary of this phone conversation [letter dated 28JUL93]. A response addressing all data gaps was filed with EPA 15JUL93 [MRID's 428565-01, 428565-02, 428565-03]."

CBTS Response: The cited data was the subject of our review of 04/04/94 (N.Dodd, PP#1F3989 and PP#1F3995, CBTS Nos. 12265, 12266). In this review, we concluded data gaps under the Product Chemistry Guidelines §61-1, 61-2, 61-3, 62-1, 62-2, 62-3, 63-7, 63-8, 63-12, and 63-13 have been resolved by this submission. No additional product chemistry data are required for RH-7592 Technical Fungicide before permanent tolerances can be established. However, the PM should know that one component on the Confidential Statement of Formula for RH-7592 Technical Fungicide is misspelled (as discussed in 61-1 in the Confidential Appendix). Also, the Chemical Abstracts Service name for another component on the Confidential Statement of Formula should be added when available.

CBTS can now conclude the previously submitted product chemistry data are adequate to support the proposed use of fenbuconazole on bananas. This deficiency is resolved.

Conclusion 1b: The registrant has submitted CAS nomenclature for fenbuconazole and its metabolites RH-9129, RH-9130 and RH-6467 (see our memo of 9/29/93, N. Dodd). The Section B must be revised such that the CAS nomenclature for fenbuconazole is used on the proposed label.

Petitioner's Response: "The data gap for the nomenclature of fenbuconazole and its metabolites was filed with EPA 12AUG93 [no MRID Number was assigned to this document]. The label has been revised to reflect the appropriate nomenclature and is included with this submission."

CBTS Response: The registrant has revised the label as instructed. This deficiency is resolved.

Conclusion 1c: Fenbuconazole contains an asymmetrically substituted carbon atom. Therefore, the registrant must indicate which enantiomer of fenbuconazole is contained in the formulated product. If the product is a mixture of the two enantiomers, then the registrant must indicate which enantiomer is fungicidally active and the relative percentages of the two components.

Petitioner's Response: "See response to Item 1a. In addition the EPA was notified [RH Report 34-93-86; submitted 23SEP93; no MRID assigned] that the residue methods are not stereoisomer-specific. The methods were developed with the racemic mixture and detect the racemic mixture of the parent compound. There is no stereoisomer-specific fungicidal activity."

CBTS Response: As per a telephone conference between N. Dodd, CBTS and Dr. Richard Costlow, Dr. Deborah Graves and Dr. Ann Tillman of Rohm and Haas (see our memo of 3/29/93), the registrant indicated they expect the product to be a racemic mixture but had not conducted analyses to determine the relative percentages of the enantiomers. The registrant was instructed to indicate on the CSF that the technical is a racemic mixture or an approximately 50% mixture would be adequate if the petitioner indicates that no optically active reactants were used in the manufacturing process.

The petitioner has provided the requested discussion and it was the subject of a CBTS review (see our memo of 04/04/94, N.Dodd, PP#1F3989 and PP#1F3995, CBTS Nos. 12265, 12266). As all product chemistry deficiencies have been satisfied, this deficiency is resolved.

Conclusion 2: CBTS concludes the proposed directions for use of fenbuconazole on bananas are not adequate and the following deficiencies should be addressed: (i) the label should be revised to state that only EPA approved adjuvants should be added to the spray solution; and (ii) a restriction against the grazing of livestock in treated orchards/groves as well as a restriction against the cutting of cover crops for feeds must be included in the directions for use of the product on bananas.

Petitioner's Response: The petitioner has submitted a revised Section B. The registrant also requests that since livestock commodity tolerances are pending (see PP#2G4143 and 2F4127, fenbuconazole on wheat) that this review be written such that RD may approve the removal of the grazing/feeding restriction when the livestock commodity tolerances are established.

CBTS Response: The registrant has included the requested restrictions on the revised label. This deficiency is resolved.

In order to have the grazing/feeding restrictions removed from the label, the petitioner will need to submit additional residue data for all possible cover crops which may be used in banana groves reflecting a zero-day pregrazing interval and request the establishment of tolerances for fenbuconazole on these crops. Also the feeding studies would have to reflect the increased dietary burden due to the requested tolerances for the fungicide in/on cover crops. These restrictions should not be removed from the label without CBTS review of the applicable data.

Conclusion 3: For the purpose of this petition, we will consider the components included in the tolerance expression for stone fruit to constitute the residues of concern in bananas. The decision as to which metabolites should be included in the tolerance expression for stone fruit will be decided at a future date by the HED Metabolism Committee. If the Committee determines additional residues for which data are not submitted are of toxicological concern, then analytical methods, storage stability data and residue data will be needed for these residues.

The HED Metabolism Committee has determined that the tolerance expression for apples, bananas and wheat as a result of the proposed uses of fenbuconazole on these crops is to include, as a minimum, residues of the parent compound and its metabolites RH-9129 and RH-9130, provided the registrant provides data to show that the conjugated metabolite RH-4911 is a minor component of the residue in these crops. Since the lactone metabolites (RH-9129 and RH-9130) are to be included in the tolerance expression, then the iminolactone metabolite (RH-6468) is also included by virtue of the registrant's contention that this compound is converted to the lactones by the analytical methodology. Therefore, all data requirements from our initial reviews of these petitions concerning residues of fenbuconazole (RH-7592), RH-9129, RH-9130 and RH-6468 must be satisfied prior to a favorable recommendation from CBTS for the proposed uses of the fungicide on apples, bananas and wheat. Any data requirements for residues other than RH-7592, RH-9129, RH-9130 and RH-6468 need not be satisfied prior to a favorable recommendation from CBTS for the proposed use of the fungicide.

Petitioner's Response: "The HED Metabolism Committee (HEDMC) has concluded that residues of concern for all crops except peanuts are fenbuconazole (RH-7592), RH-6468, RH-9129, and RH-9130. The iminolactone metabolite, RH-6468, has never been observed in plants, it has only been detected in animals. This metabolite was only proposed as an intermediate in the metabolic pathway for plants and should not be part of the tolerance expression. Even if it occurred in

bananas, RH-6468 would be quantitated by the residue method used for bananas and would increase apparent residue."

"Since the existing residue data on bananas already reflects any possible contribution of RH-6468, and since RH-6468 has never been observed as a plant metabolite, the proposed tolerance for bananas was revised to be silent on RH-6468. This minor modification still faithfully reflects the decision of the HEDMC on fenbuconazole. The HEDMC concern for possible residues of RH-4911 will be addressed in the residue trials which will be done, as a condition of registration (*vide infra* Item 7a), on bagged and unbagged bananas."

CBTS Response: The registrant has not as yet submitted data to show that the metabolite RH-6468 is recovered by the analytical method described in Rohm and Haas Technical Report #34-90-47 (MRID No. 418750-38) or other similar analytical method (see the discussion of RH-6468 in our memo of 6/22/94, W.D. Wassell, DP Barcodes: D203274 through D203281), but this data is expected to be submitted in conjunction with other fenbuconazole petitions.

In conjunction with the petition requesting tolerances for fenbuconazole in or on peaches (PP#1F3989), the petitioner has submitted data that involved the reanalysis of peach samples from a metabolism study for residues of RH-4911 (see of review of 4/12/94, N. Dodd, DP Barcode: D197092 and D198819). The reanalysis of the samples indicated that RH-4911 was a minor component of the residue in peaches and we have concluded the residues of concern in stone fruit are parent (RH-7592) and its metabolites RH-9129 and RH-9130. Since, we have previously concluded that the components included in the tolerance expression for stone fruit are to constitute the residues of concern in bananas, this deficiency is resolved provided the data concerning RH-6468 is provided in conjunction with PP#2F4135 or PP#2F4127 and the samples from the additional field trials to be conducted to support this petition are analyzed for residues of RH-4911.

Conclusion 5a: Fenbuconazole and its metabolites, (RH-9129, RH-9130 and RH-6467) have been tested for recovery via FDA Multiresidue Protocols (PAM Vol. I). Pending the decisions of the HED Metabolism Committee, additional fenbuconazole metabolites may need to be tested for recovery by the FDA Multiresidue protocols.

Petitioner's Response: "The HEDMC has concluded that no residues other than fenbuconazole (RH-7592), RH-9129, and RH-9130 require validation, thus the residue methods for fenbuconazole use on bananas are adequate."

CBTS Response: No additional data are needed at this time, but if significant levels of RH-4911 are found in the additional field trials conducted to support the

proposed use on bananas, then additional data concerning recovery of this residue via the FDA Multiresidue Protocols may be needed.

Conclusion 5b: An analytical grade reference standard and a Material Safety Data Sheet (MSDS) for fenbuconazole are available from the Agency's Pesticide and Industrial Chemical Repository located in Research Triangle Park, NC. MSDS's and analytical grade reference standards are not available for the metabolites of fenbuconazole (RH-9129, RH-9130 and RH-6467). Pending the decisions of the HED Metabolism Committee, the petitioner must submit analytical grade reference standards and Material Safety Data Sheets for all compounds to be included in the tolerance expression for plant and animal commodities to the Agency's Pesticide and Industrial Chemical Repository.

Petitioner's Response: "Analytical standards for metabolites of concern [RH-7592, RH-9129, and RH-9130] have been sent to EPA at Research Triangle Park. A letter dated 12JAN94 was received from Mr. Seymour Gold at EPA/RTP and was sent via telefax to Ms. Dolphine Wilson on 30MAR94."

CBTS Response: This deficiency is resolved.

Conclusion 5c: The analytical method utilized for residue determinations in the submitted studies is described in Rohm and Haas Technical Report #34-90-47 (MRID No. 418750-38). CBTS concludes the analytical method TR #34-90-47 has been adequately validated for use as a data collection method for bananas. The petitioner should be aware that residue data should be reported as not corrected for procedural recoveries in future submissions to support this petition. Additionally, residue levels of the metabolites should be converted to fenbuconazole equivalents and reported as such.

Petitioner's Response: "The validation of the method was not included as a reason for recommending against the petition, but the issues of reporting uncorrected residue values and residues as parent compound equivalent are recent guidance from EPA and will be adhered to for the upcoming trials. The Rohm and Haas Company assumes that this is not an impediment to a registration for use of fenbuconazole on bananas. The banana residue data for fenbuconazole are reported in Table 1 as parent compound equivalents."

CBTS Response: Our comments were meant as guidance for the additional field trials to be conducted to support the proposed use of the fungicide on bananas and the petitioner is correct in assuming that this was not meant as an impediment to the registration. We are confused by the petitioner's statement that the reporting of residue values uncorrected for fortification recovery and as parent equivalent are

"recent guidance from EPA". Subdivision O, first published in October 1982, refers to reporting residues as uncorrected and as parent equivalents. No additional action concerning this item on the part of the petitioner are required.

Conclusion 5d: The method TR #34-90-47 was initially reviewed in conjunction with PP#1F3989 (fenbuconazole in/on stone fruit, see our memo of 3/10/93, N. Dodd). This method has undergone an Independent Laboratory Validation, as per PR Notice 88-5 and a validation study on peaches by the Agency's Analytical Chemistry Laboratory is pending for this method. CBTS concludes the method (TR No. 34-90-47) may be suitable for enforcement of the proposed tolerances provided the method is successfully validated by the Agency's Analytical Chemistry Laboratory.

Petitioner's Response: "It is our understanding from the Registration Division that this method has been validated at EPA for stone fruit and is, therefore, valid for bananas."

CBTS Response: The analytical method described in the Rohm and Haas Technical Report No. 34-90-47, "Residue Analytical Method for Parent RH-7592 and its Lactone Metabolites RH-9129 and RH-9130 in Stonefruit", has been successfully validated by the Agency's Analytical Chemistry Laboratory (ACL). ACL has concluded that the method with minor modifications is satisfactory as an enforcement method for the proposed tolerances for fenbuconazole on stone fruit (see our memo of 10/25/93, N. Dodd, DP Barcode: D195384). The petitioner has revised and submitted for review the method as instructed by CBTS and ACL (see our memo of 4/11/94, N. Dodd, DP Barcode: D197760). We have concluded that the method is acceptable and will be sent to FDA for publication in PAM Vol. II upon our recommendation for a permanent tolerance. CBTS has not yet favorably recommended for the tolerances for the active ingredient in/on stone fruit and the method has not yet been sent to the FDA for publication.

CBTS can now conclude that the method (TR No. 34-90-47) is adequate for enforcement of the proposed tolerances for fenbuconazole in/on bananas. The method will be forwarded to FDA for publication in the near future. This deficiency is resolved.

Conclusion 7a: Magnitude of residue data for fenbuconazole in/on bananas were submitted to support the requested tolerances. Tolerance levels for pesticides in/on bananas are based upon the highest residues resulting from applications to both bagged and unbagged bananas. The registrant has conducted only one study in which side-by-side trials were included with bagged and unbagged bananas. This trial showed higher residue levels in the unbagged

bananas (up to 0.24 ppm on peel versus <0.010 ppm for bagged bananas). Therefore, additional field trials reflecting applications to unbagged bananas are required to determine the appropriate tolerance level. Provided the other deficiencies (e.g. product chemistry, EPA method validations, revised Section B and F etc.) can be resolved, CBTS would have no objections to granting a tolerance with an expiration date while the additional field trials are being conducted. We suggest that a total of four additional trials be conducted (2 each in Hawaii and Puerto Rico) in which applications at the maximum proposed use rate are made to unbagged bananas. The residues should be reported on a whole fruit basis as well as for the banana pulp. In addition, our comment in Conclusion 7c should be noted with regard to conduct of the field trials.

Petitioner's Response: "Rohm and Haas Company plans to initiate 4 additional residue trials with fenbuconazole, as requested by EPA in this item. We understand that 'CBTS would have no objections to granting a tolerance with an expiration date while the additional field trials are being conducted' and these trials will be part of a conditional registration with a 'sunset' tolerance. Residues will be reported for whole fruit and pulp, and data uncorrected for recoveries will be included."

The petitioner also has expressed concern for the setting of the tolerance level based upon field trials in which the active ingredient is applied to unbagged bananas.

CBTS Response: The petitioner has not indicated where these four additional field trials will be conducted. Rohm and Haas should make note of our suggested locations for the additional field trials. CBTS policy concerning the setting of tolerances for pesticides on bananas has not changed; tolerances are based upon the residue levels on unbagged bananas. We reiterate our previous conclusion: CBTS would have no objections to granting a tolerance with an expiration date while the additional field trials are being conducted.

Conclusion 7b: The registrant has requested individual tolerances for banana pulp and peel. Tolerances are generally set on whole bananas or as X ppm in or on bananas (of which not more than Y ppm are in the pulp). CBTS requests a revised Section F in which tolerances are requested for fenbuconazole and its metabolites, expressed as the parent, in or on the raw agricultural commodity bananas as noted above.

Petitioner's Response: A revised Section F has been submitted in which tolerances for the combined residues of fenbuconazole and its metabolites RH-9129 and RH-9130 are requested on bananas (whole fruit) at 0.3 ppm of which not more than 0.05 ppm is contained in the banana pulp.

CBTS Response: The petitioner must submit a revised Section F in which the tolerances are requested for fenbuconazole and its metabolites, expressed as the parent compound. This deficiency is not resolved.

Conclusion 7c: The banana bunches were dipped in water and permitted to drip dry after harvest. The registrant indicates that this is a normal agricultural practice. We can find no documentation that indicates this dipping procedure is a normal agricultural practice. Therefore, CBTS would prefer residue data on bananas that are not dipped in water after harvest unless the registrant can provide published information indicating this a normal practice and all commercially produced bananas are handled in this manner.

Petitioner's Response: The petitioner has submitted copies of three references that indicate dipping of bananas is a standard agricultural practice.

CBTS Response: The petitioner's literature sources demonstrate that the dipping of bananas is most likely a common practice in Central and South America, but the requested tolerance is in relation to a domestic use of the fungicide. The submitted literature does not indicate if this is a common practice in the United States. No additional information concerning this practice is requested at this time, but the petitioner should submit additional information concerning this practice in conjunction with the requested additional residue data.

Recommendations:

Provided a revised Section F is submitted as instructed in Conclusion 7b, above, CBTS can recommend for a tolerance with an expiration date for the combined residues of fenbuconazole and its metabolites, RH-9129 and RH-9130, expressed as fenbuconazole, in or on bananas (whole fruit) at 0.3 ppm of which not more than 0.05 ppm is contained in the banana pulp while the additional field trials (see Conclusion 7a, above) are being conducted. A DRES run can be initiated using the 0.05 ppm residue value for banana pulp.

For a permanent tolerance, samples from the additional field trials should be analyzed for the fenbuconazole metabolite RH-4911 in addition to the compounds included in the tolerance expression (see Conclusion 3, above).

cc: WDWassell, RF, Circ., PP#2F04154

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