UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE MAY 28 1981

SUBJECT PP#9E2145. Gibberellins A_3, A_4 and A_7 on all raw agricultural commodities. Request for an exemption. Amendment of 12/2/80.

FROM R.B. Perfetti, Ph.D., Chemist
Residue Chemistry Branch (TS-769)

TO Minor Crops Officer
Registration Division (TS-767)
and
Toxicology Branch
Hazard Evaluation Division (TS-769)

THRU: Charles L. Trichilo, Chief
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

This amendment is in response to our memo of 12/6/78 in which several deficiencies in the subject petition were outlined. These deficiencies and the petitioners responses to them will be discussed in the order in which they appeared in our memo cited above.

Deficiencies:

1a. When and if the deficiencies in this petition are resolved, we will need the inert ingredient statements for all of the formulations involved in order to determine whether inerts in the formulation are cleared under Section 180.1001 before a final favorable recommendation could be made by RCB.

1b. Specifics with respect to application rates, times of application PHI's etc. for each crop or crop grouping are needed and should be submitted in a revised Section B.

2. Tolerances for gibberellin A_3 or any other gibberellin, whether naturally occurring or artificial, on specific crops or crop grouping are needed. Tolerance regulation should be proposed in terms of gibberellin A_x for naturally occurring compounds. Artificial (synthetic) gibberellin tolerance regulations will be handled on a case by case basis. Determinations as to what metabolism data would be needed for each gibberellin on a specific crop or crop grouping will also be made on case by case basis depending on such considerations as the use proposed, the structure of the gibberellin to be used, the subject crop, etc.

3a. The PAM II method for gibberellin A_3 is acceptable for enforcement purposes only for thoses crops already having tolerances. In these crops one can obviously not distinguish between endogenous and added gibberellin A_3. The practical limit of detection in these crops is 0.1 ppm. This method cannot be extended to other crops unless information as to the level of naturally occuring gibberellin A_3 in the specific crop is submitted. Information regarding the level of gibberellin A_3 in specific crops or a representative number of crops in a crop grouping, as well as appropriate validation data on these r.a.c.'s is needed. A second method trial may also be needed. Therfore no adeuqate analytical method is presently available for enforcement of these tolerances.

3b. Tolerances requests for other gibberellins, whether naturally occurring or artifical will require adequate enforcement methodology including confirmatory procedures for these compounds (and possibly metabolites) which can distinguish between the different gibberellins involved. Appropriate control values and validation data will also be needed.

4a. Residue data submitted previously on several crops was quite limited and is not considered adequate to extend the present tolerances to all r.a.c.'s. Additional residue data on specific crops or a representative number of crops in a crop grouping is needed before tolerances for residues of gibberellin A_3 on all r.a.c.'s could be established. This data should reflect adequate geographical and varietal representation, maximum proposed uses, etc.

4b. Tolerance requests for uses of other gibberellins, whether naturally occurring or artificial, will activate the need for the same residue data requirements as any other new pesticide chemical.

5a. Tolerances for residues of gibberellin A_3 on all r.a.c.'s may place a significant additional burden of this compound on the diets of livestock depending on whether the levels of this compound in feed items are signficantly higher than endogenous levels. Therefore a final conclusion with respect to secondary residues in meat, milk, poultry and eggs will be made at such time as the deficiencies discussed above are resolved. Depending on the levels of gibberellin A_3 found in feed items, metabolism and feeding studies in ruminants and poultry along with appropriate methodology, validation data and a method trial may be needed.

5b. Tolerance requests for uses of other gibberellins, whether naturally occurring or artificial, could activate the need for the same metabolism and feeding studies and methodology (including a method trail) as would be required for a tolerance on a feed item for any new pesticide chemical.

Response to 1(a) and 1(b): The petitioner has submitted a revised Section B proposing specific uses for Gibberellin A_3 on grapefruit, limes and seckel pears. He has also submitted EPA registration numbers for seven formulations produced by Abbott Laboratories (3), Elanco Products Co. (2) and Merck & Co. (2). These formulations range from 2 to 29.6% of Gibberellin A_3. The use on grapefruit calls for a single application of 500 gallons of a 10 to 30 ppm spray/acre (19 to 57 gms of active ingredient/acre 3 to 4 months before harvest. The use on limes allows a single application of 47 gms active ingredient per acre 30 days or more before harvest. A 30 PHI is prescribed. The seckel pear use calls for application of 15 to 38 gms active ingredient/acre 30 days after bloom. A 30 day PHI is required. The petitioner has also submitted a list of amounts of Gibberellins applied to various crops. Application rates range from 0.03 gms per plant to 210 gms/acre.

We do not consider these deficiencies resolved.

Response to 4a and 4b: The petitioner in a paper entitled "Gibberellins - Are Residue Tolerances Necessary?" provided a table containing analyses for background levels for Gibberellin A_3 in artichokes (0.08 ppm), celery (0.07 ppm), cherries (0.01 ppm), seedless grapes (0.05 ppm), lime pulp (0.24 ppm), lime peel (0.23 ppm), prunes (0.05 ppm), tangelo pulp (0.04 ppm) and tangelo rind (0.07 ppm). We do not consider this limited information adequate to make a residue conclusion for all r.a.c.'s.

The petitioner has also submitted a revised Section F proposing an exemption for Gibberellins A_3, A_4 and A_7 on all r.a.c.'s when it is applied to growing crops only. The regulation also prescribes that for dosages exceeding 20 gms/acre a 14 day PHI should be observed.

We reaffirm our previous conclusion that tolerances are needed for specific Gibberellins on specific crops or crop groupings.

We do not consider these deficiencies resolved.

Response to remaining deficiencies 2, 3a, 3b, 5a, and 5b: The petitioner does not specifically address these deficiencies. He does however present an arugment based on the following:

1. He opines that gibberellins are not poisonous or deleterious substances but presents no scientific basis for this generalization. In fact, in the paper cited above the petitioner admits that the National Cancer Institute has selected gibberellin A_3 for further carcinogenic testing.

2. Gibberellins occur naturally and are not added substances. They are, however, added when growning crops are treated. In addition, there is no proof that Gibberellin A_3, Gibberelin A_4 and Gibberellin A_7 all occur in all r.a.c.'s.

3. Gibberellins are not likely to occur in treated r.a.c.'s at levels significantly higher than the background levels found in crops. There is no scientific basis for this opinion since there is not sufficient residue data available for Gibberellin A_3, Gibberellin A_4 or Gibberellin A_7 in a large number of different crops.

4. In every case where residue determinations have been made on crops treated with Gibberellin A_3, only negligible residues, if any, have been found on treated crops at harvest. As we have already pointed out there is not an overwhelming amount of residue data available for Gibberellin A_3, Gibberellin A_4 and Gibberellin A_7 with respect to either the number of crops treated on the number of studies performed.

5. The petitoner refers to the Agency's <u>proposed</u> policy, on biorational pesticides and states that in those cases when the application rate is less than 20 gms/acre an automatic exemption should be given for that crop. He further states that in these cases where the dosage rates exceed 20 gms/acre residue data may be needed to show that residues of applied gibberellins do not significantly exceed the background levels in the respective untreated crop.

We agree with the petitioner in that when and if the Agency's <u>proposed</u> policy is finalized and if the gibberellins fall under the definition of biorationals this could provide a mechanism by which the Gibberellins A_3, A_4 or A_7 could be exempted from the requirements of a tolerance on a <u>specific</u> crop provided the treatment rate for that crop does not exceed 20 gms/acre.

Since, however the petitioner concedes that, for those uses on crops which require application rates in excess of 20 gms/acre, additional residue data for that crop will be needed, we cannot understand his objection to obtaining this data which we have required as discussed in Conclusion 4a above. Once this residue data is provided, appropriate tolerance levels can be estimated. We would not consider imposition of an arbitrary 14 day PHI as being a viable alternative to the additional data required.

Based on our discussion of the five points raised by the petitionr above it is our judgment both that the outstanding deficiencies are not resolved and that tolerances for residues of Gibberellins on specific crops or crop groupings are appropriate. The International Tolerance Sheet is attached. We do not consider the present exemption proposal for all r.a.c.'s to be consistent with the established Canadian tolerances on specific commodities.

Conclusions:

1. None of the deficiencies listed above have been resolved by this amendment.

2. No clear proof that Gibberellins are not poisonous or deleterious substances has been presented.

3. There is no scientific basis for concluding that the subject Gibberellins are not likely to occur at levels significantly above background in all r.a.c.'s after treatment. Additional residue data is needed.

4a. When and if the Agency's proposed bio-rational pesticide policy is finalized this may provide a mechanism by which Gibberellins A_3, A_4 and A_7 could be exempted from the requirements of a tolerance on a specific crop provided the treatment rate does not exceed 20 gms/acre and if gibberellins are determined to fall under the biorational definitions.

4b. Tolerances for specific crops or crop groupings are appropriate for those uses of the subject Gibberellins where treatment rates are in excess of 20 gms/acre. This will require all of the data discussed in our original memo of 12/6/78. We do not consider the imposition of an arbitrary 14 day PHI a viable alternative to the additional data requirements in these cases.

5. The International Tolerance sheet is attached. We do not consider the present exemption proposal for all r.a.c.'s to be consistent with the established Canadian tolerances on specific commodities.

Recommendation

We recommend against the proposed exemption for the reasons given in conclusions 1-5 above. Also see our conclusons 1a-5b in our memo of 12/6/78.

The petitioner should be informed of the requirements for resolution of these deficiencies. These are also discussed in the appropriate conclusions.

TS-769:RCB:RBPerfetti:gs:X77484:CM#2:RM810: 5/18/81
cc: RF, Circ.(3), RBPerfetti, Watts, FDA, TOX, EEB, EFB, PP#9E2145
RDI: Quick, 4/15/81: Schmitt, 4/16/81

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL Gibberellins A_3, A_4 and A_7 PETITION NO. 9E2145

CCPR NO. ----

Codex Status

/ X / No Codex Proposal
Step 6 or above

Residue (if Step 9): NONE

Crop(s)	Limit (mg/kg)
NONE	

Proposed U.S. Tolerances

Exemption from the requirements of a tolerance for the three Gibberellins above on all raw agriculatural commodities.
Residue:

Crop(s)	Tol. (ppm)
SEE ABOVE	

CANADIAN LIMIT

Residue: Gibberellic acid

Crop	Limit (ppm)
Gibberellic acid	
rhubarb	0.015 ppm
barley malt	0.5 ppm
canning corn)	
citrus fruit)	0.1 ppm
seed potatoes)	
sour cherries)	

MEXICAN TOLERANCIA

Residue: NONE

Crop	Tolerancia (ppm)
NONE	

NOTES:

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