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CODEX COMMITTEE ON PESTICIDE RESIDUES

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PROPOSED MAXIMUM RESIDUE LIMITS FOR PESTICIDES IN FOOD AND FEED

*Comments at Step 3 in reply to CL 2020/6-PR submitted by
Australia, Brazil, Canada, Chile, Egypt, European Union
and the United States of America*

Steps in the CCPR-Codex procedure

- Step 1 Recommendation of priority compounds by CCPR, involving the *Ad Hoc* Working group on Priorities
- Step 2 First evaluation of the compound by the Joint FAO/WHO Meeting on Pesticide Residues; estimation of an ADI and of MRLs (draft MRLs or proposed Codex MRLs)
- Step 3 Submission of the proposed Codex MRLs to governments for a first round of comments
- Step 4 First discussion of the proposed MRLs by the CCPR in the light of the comments received
- Step 5 Submission of the proposed Codex MRLs to the Codex Alimentarius Commission in the light of the CCPR-discussion, for consideration
- Step 6 Submission of the proposed Codex MRLs to governments for a second round of comments
- Step 7 Final discussion of the proposed Codex MRLs by the CCPR in the light of comments received
- Step 8 Consideration by the CAC in view of adoption of the proposal as Codex MRL (CXL)
- Step 5/8 The proposed codex MRL is submitted to the Commission at Step 5; as there seems to be no controversy and no need for further discussion at Steps 6 and 7, omission of these Steps is recommended to the Commission

Part I of the document contains comments on MRLs for consideration by CCPR52.

Part II of this document contains concern forms for consideration by CCPR52.

PART I: COMMENTS ON MRLs**GENERAL COMMENTS****Chile**

Chile supports all the recommendations made by the JMPR, as scientific advisory body to this Codex Committee, and therefore the advancement in the corresponding step for their early adoption.

Rationale: It is important for the Codex to advance in the study and determination of MRLs of those active substances which are extensively used.

Egypt

Egypt agrees on the proposed draft MRLs that correspond to Step 3 of the Codex Procedure as proposed by the 2019 JMPR Extraordinary and Regular Meetings.

European Union

The EU would like to **comment** that the MRLs and also the currently taken positions for thiabendazole, tebuconazole and metconazole might be revised in future, pending an evaluation of triazole derivative metabolites in the EU.

An assessment strategy for triazole derivative metabolites has recently been adopted in the EU and is applicable since September 2019. Toxicological reference values have been endorsed for these metabolites.

SPECIFIC COMMENTS**Dimethoate (027)****Australia**

Australia notes the data did not allow a residue definition to be established for dietary risk assessment. Australia suggests that CCPR should seek advice from the manufacturer to determine whether new data will be submitted to resolve the toxicological issues.

Canada

Canada acknowledges JMPR's recommendation to withdraw all MRLs in the absence of data for omethoate, the major metabolite. Dimethoate was recently re-evaluated by Canada. See [PRVD2011-12](#) and [RVD2015-04](#) for details.

Egypt

Egypt disagrees to withdraw the previously established maximum residue limit of "Dimethoate (027)" in (Wheat) and proposing to keep the limit set (0.05 mg/kg).

Omethoate (055)**Australia**

Australia notes that the current CXLs for omethoate on spices are based on residues from use of dimethoate. If the manufacturer does not commit to providing new data to resolve toxicological issues for dimethoate, Australia supports the withdrawal of MRLs for omethoate on spices.

Thiabendazole (065)**Australia**

Australia supports advancement of the MRLs to Step 5/8.

Canada

Canada supports the JMPR recommended MRLs for the new uses on pulses and legume vegetables.

European Union

The EU introduces a **reservation to the advancement** of the proposed draft MRLs for the following commodities, pending the outcome of ongoing import tolerance requests in the EU:

- **Mango**
- **Sweet potato**

The EU **notes** that for beans with pods, the description of the commodity related to the code VP 2060 should be corrected (to include the suffix '(includes all commodities in this subgroup)').

Carbendazim (072)

Australia

Australia supports advancement to step 5/8 for MRLs for carbendazim on spices (seeds).

European Union

The EU introduces a **reservation to the advancement** of the proposed draft MRLs for the following commodities, pending the outcome of an ongoing evaluation of benomyl, carbendazim and thiophanate-methyl in the EU:

- **Spices, seeds, Subgroup of**

Moreover, the EU invites clarification of the status of benomyl, carbendazim and thiophanate-methyl, as outlined in the concern form submitted by the EU.

Chlorothalonil (081)

Australia

Australia supports advancement of the MRL to Step 5/8.

Canada

Canada has no objection to the JMPR recommended MRL for the cranberry new use. Chlorothalonil was recently re-evaluated in Canada. See [PRVD2011-14](#) and [RVD2018-11](#) for details.

European Union

The EU introduces a **reservation to the advancement** of the proposed draft MRLs for the following commodities:

- **Cranberry**

In a recent EU assessment, a genotoxicity concern could not be excluded for residues to which consumers will be exposed. In the absence of EU toxicological reference values for metabolite SDS-3701 (R182281), even an indicative consumer risk assessment using preliminary residue definitions could not be conducted.

Iprodione (111)

European Union

The EU identified a concern about the safety of iprodione residues. The EU thanks JMPR for their review of the EU's concern and supports JMPR's strong recommendation that iprodione be prioritized for periodic re-evaluation.

Cypermethrin (118)

Australia

Australia supports advancement of the MRL to Step 5/8.

Canada

Canada has no objection to the JMPR recommended MRLs. Cypermethrin was recently re-evaluated by Canada. See [PRVD2016-18](#) and [RVD2018-22](#) for details.

European Union

The EU introduces a **reservation to the advancement** of the proposed draft MRLs for the following commodities, pending the outcome of the ongoing periodic re-evaluation in the EU:

- **Ginseng, dried including red ginseng**

Diflubenzuron (130)

European Union

The EU identified a concern about a plant metabolite of diflubenzuron, 4-chloroaniline. The EU takes note of the assessment recently conducted by JECFA.

Methoprene (147)

Australia

Australia supports advancement of the MRLs to Step 5/8.

Canada

Canada has no objection to the JMPR recommended MRL for the new use on peanut.

European Union

The EU introduces a **reservation to the advancement** of the proposed draft MRLs for the following commodities:

- **Peanut, whole**

A chronic risk for European consumers could not be excluded. Considering the significant background exposure from the existing EU MRLs, there is no scope to raise the MRLs. Further refinements of the chronic exposure calculation are possible; however the relevant data have not yet been assessed in the EU.

Studies investigating the metabolic behaviour after post-harvest treatment and on the nature and magnitude of residues in processed products are lacking.

Glyphosate (158)

Australia

Australia supports advancement of the MRLs to Step 5/8.

Canada

Canada has no objection to the JMPR recommended MRLs for the new uses. Glyphosate was recently e-evaluated in Canada. See [PRVD2015-01](#) and [RVD2017-01](#) for details.

European Union

The EU introduces a **reservation to the advancement** of the proposed draft MRLs for the following commodities, pending the outcome of the ongoing periodic re-evaluation in the EU:

- **Dry beans, Subgroup of (except soya beans)**
- **Dry peas, Subgroup of**

Propiconazole (160)

Australia

Australia supports advancement of the MRLs to Step 5/8.

Canada

Canada has no objection to the JMPR recommended MRL on the peaches subgroup.

European Union

The EU introduces a **reservation to the advancement** of the proposed draft MRLs for the following commodities:

- **Peach**

Following a recent EU evaluation, the active substance was not approved in the EU. In that framework, the consumer risk assessment could not be finalised due to data gaps, and no conclusion could be drawn on the genotoxicity and the general toxicity of several metabolites.

Specifically on peaches, an acute consumer risk has been identified for European consumers. Moreover, the proposed Codex MRL is not acceptable because the number of residue trials is insufficient according to the Information Document on the Application of the Guidance to Facilitate the Establishment of MRLs for Pesticides for Minor Crops (referred to in Annex D to the Risk Analysis Principles applied by the Codex Committee on Pesticide Residues, Codex Procedural Manual).

Buprofezin (173)

Australia

Australia supports advancement of the MRLs to Step 5/8.

Canada

Canada has no objection to the JMPR recommended ADI and ARfD for the aniline metabolite and the recommended JMPR MRLs for buprofezin in the various new uses.

European Union

The EU introduces a **reservation to the advancement** of the proposed draft MRLs for the following commodities:

- **Group of tree nuts**
- **Eggs**
- **Mammalian fats except milk fats**
- **Poultry, edible offal of**
- **Poultry fats**
- **Poultry meat**

The EU identified a concern about the potential for the formation of aniline from residues of buprofezin in commodities which are subject to processing. The EU thanks JMPR for their review of the EU's concern and notes that JMPR took into consideration new data including a new in vivo genotoxicity study on aniline not yet assessed in the EU.

The EU notes that JMPR derived a Codex MRL proposal for crude olive oil, although no MRL proposal is made for unprocessed olives for oil production (SO 0305). It is the EU's understanding that a Codex MRL for the corresponding raw agricultural commodity needs to be established before a Codex MRL for a processed product can be set. However, the concern about the potential for the formation of aniline from residues of buprofezin would still apply. ~~for the raw agricultural commodity olives for oil production.~~

Bifenthrin (178)

Australia

Australia notes the JMPR identified an acute exposure risk associated with strawberry and does not support advancement of this MRL. Australia supports advancement of the MRL for straw and fodder dry of cereal grains to Step 5/8.

Brazil

Brazil would like to inform that the Brazilian Health Regulatory Agency (ANVISA) has conducted short-term dietary risk assessment for compounds and commodities reported on CL 2020/06-PR.

The risk assessment methodology was based on WHO/FAO guidelines. The individual food consumption and body weight of people older than 10 years was based on the Brazilian household budget survey report released in 2009.

Based on the results of the short-term dietary risk assessment, Brazil has a concern regarding the MRL proposed for strawberry on compound Bifenthrin (178). In this case, the acute dietary exposure to residues for the consumption of strawberries present a public health concern for Brazilian consumers. It is worth mentioning that ANVISA considered 0.01 mg/kg bw as ARfD.

Canada

Canada acknowledges the acute dietary risk of concern identified by JMPR from exposure to bifenthrin residues in strawberries.

European Union

The EU **opposes to the advancement** of the proposed draft MRLs for the following commodities:

- **Strawberry**

JMPR concluded that the estimated acute dietary exposure to residues of bifenthrin for the consumption of strawberries may present a public health concern.

The EU notes that:

For strawberries, also the CXL of 1 mg/kg, adopted in 1995, may pose a public health concern. Therefore, the EU considers that the existing CXL for strawberries should be revoked.

For celery and lettuce the proposed MRLs were retained at step 4 by 2016 CCPR under the four-year rule. As no additional data has been submitted, the EU considers that the proposed draft MRLs for celery and lettuce should be withdrawn.

Clethodim (187)

Australia

Australia notes the data did not allow a residue definition to be established for dietary risk assessment. Australia suggests that CCPR should seek advice from the manufacturer to determine whether new data will be submitted to resolve the toxicological issues.

Canada

Clethodim was recently re-evaluated by Canada. See [PRVD2016-11](#) and [RVD2017-10](#) for details.

While Canada has no objection to the JMPR recommended ADI, Canada is concerned with the withdrawal of the maximum residue level for rapeseed/canola based on the insufficient number of crop field trials conducted in accordance to the cGAP.

Canada respectfully requests that the existing CXL be maintained for a period of no more than four years pending the commitment from a registrant to conduct additional crop field trials on rapeseed/canola. Should this commitment not be fulfilled prior to CCPR52, Canada will withdraw its request.

Tebuconazole (189)

Australia

Australia supports advancement of the MRLs to Step 5/8.

Canada

Canada has no objection to the JMPR recommended MRLs for the various citrus crops.

European Union

The EU introduces a **reservation to the advancement** of the proposed draft MRLs for the following commodities, pending the outcome of the ongoing periodic re-evaluation in the EU:

- **Mandarins (including Mandarin-like hybrids) Subgroup of**
- **Oranges, Sweet, Sour, subgroup of**

Tolclofos-methyl (191)

Australia

Australia supports advancement of the MRL to Step 5/8.

Canada

Canada has no objection to the JMPR recommended ADI and MRLs. Tolclofos-methyl is not registered for use in Canada, nor have any import MRLs been established.

European Union

The EU introduces a **reservation to the advancement** of the proposed draft MRLs for the following commodities:

- **Potatoes**

An acute consumer risk has been identified for European consumers. The EU has set an acute reference dose, based on a 9-month mouse study and an uncertainty factor of 100.

Kresoxim-methyl (199)

Australia

Australia supports advancement of the MRLs to Step 5/8.

Canada

Canada has no objection to the JMPR recommended MRLs.

Pyriproxyfen (200)

Australia

Australia supports advancement of the MRLs to Step 5/8.

Cyprodinil (207)

Australia

Australia supports advancement of the MRL to Step 5/8.

Canada

Canada has no objection to the JMPR recommended MRL for the soya bean (dry) new use.

European Union

- **Soya bean (dry)**

The EU **notes** that the approach taken by JMPR is not in line with point 4 of Annex C to the Risk Analysis Principles Applied by the Codex Committee on Pesticide Residues (Codex Alimentarius Commission, Procedural Manual). The proportionality approach was applied despite deviation from the cGAP by more than one parameter.

Pyraclostrobin (210)

Australia

Australia supports advancement of the MRL to Step 5/8

Boscalid (221)

Australia

Australia supports advancement of the MRLs to Step 5/8.

Canada

Canada has no objection to the JMPR recommended MRLs for the new uses.

European Union

The EU introduces a **reservation to the advancement** of the proposed draft MRLs for the following commodities:

- **Pome fruits (subgroup)**

The OECD MRL calculator derives a lower MRL of 1.5 mg/kg.

Azoxystrobin (229)

Australia

Australia supports advancement of the MRLs to Step 5/8.

Canada

Canada has no objection to the JMPR recommended MRL for the new use on guava.

Chlorantraniliprole (230)

Australia

Australia supports advancement of the MRLs to Step 5/8.

Canada

Canada acknowledges that the recommended MRLs for the new subgroups of dry peas and beans are lower than the Canadian MRL for legume vegetables based on different crop field trial data.

European Union

- **Palm fruit (African oil palm)**

The **EU notes** that in accordance with the Information Document on the Application of the Guidance to Facilitate the Establishment of MRLs for Pesticides for Minor Crops (referred to in Annex D to the Risk Analysis Principles applied by the Codex Committee on Pesticide Residues, Codex Procedural Manual) palm fruit (oil) is a major crop. The EU considers that the setting of Codex MRLs in palm kernels and palm fruit should be further discussed.

Spirotetramat (234)

Australia

Australia supports advancement of the MRLs to Step 5/8.

Canada

Canada acknowledges that the JMPR recommended MRLs are lower than the Canadian MRLs for the same crops based on different residue definitions for enforcement.

Metaflumizone (236)

Australia

Australia supports advancement of the MRLs to Step 5/8.

Canada

Canada has no objection to the JMPR recommended MRLs for the new uses. Metaflumizone is not registered for use in Canada, nor have any import MRLs been established.

European Union

The EU introduces a **reservation to the advancement** of the proposed draft MRLs for the following commodities:

- **Grape**

For grape an acute consumer risk has been identified for European consumers. The EU has set an ARfD based on reduced body weight gain observed in a rat developmental study.

Dicamba (240)

Australia

Australia supports advancement of the MRLs to Step 5/8.

Canada

Canada has no objection to the JMPR recommended MRLs for the new uses.

European Union

The EU introduces a **reservation to the advancement** of the proposed draft MRLs for the following commodities pending the outcome of the ongoing periodic re-evaluation in the EU:

- **Cotton seed**
- **Maize**
- **Soya beans**

The EU notes that for **soya bean hulls** and **soya bean meal** the processing factor derived from the GAP in dicamba-tolerant soybeans was used to propose draft MRLs, which reflect different uses in conventional crops.

Acetamiprid (246)

Australia

Australia supports advancement to step 5/8 for MRLs for acetamiprid on spices (seeds).

Penthiopyrad (253)

Australia

Australia supports advancement of the MRLs to Step 5/8.

Canada

Canada has no objection to the JMPR recommended MRLs on the various berry crops/crop groups.

European Union

The EU introduces a **reservation to the advancement** of the proposed draft MRLs for the following commodities:

- **Bush berries, Subgroup of**
- **Cane berries, Subgroup of**

In the EU, a separate residue definition for risk assessment for the metabolite 1-methyl-3-trifluoromethyl-1H-pyrazole-4-carboxamide (PAM) applies. Individual levels of penthiopyrad and PAM were not reported separately in the JMPR Report.

- **Elderberries**

An extrapolation from blueberries to elderberries is not foreseen in the Codex extrapolation rules. The EU understands that JMPR derived the proposed draft CXL for elderberries based on the scope of the underlying authorisation. However, the EU considers that the extrapolation from blueberries to elderberries and guelder rose should be discussed by the eWG on Classification to determine whether such extrapolation is appropriate.

Fluxapyroxad (256)

Australia

Australia supports advancement of the MRLs to Step 5/8.

Canada

Canada has no objection to the JMPR recommended MRLs for the citrus crop subgroups.

European Union

The EU **notes** that the proposed extrapolation from lemons to mandarins is not in accordance with the agreed Codex extrapolations rules.

Picoxystrobin (258)

Australia

Australia supports advancement of the MRLs to Step 5/8.

Canada

Canada has no objection to the JMPR recommended MRLs on the various crops.

European Union

The EU **introduces a reservation** to the advancement of the proposed draft MRLs the following commodities due to several health concerns identified in the EFSA peer review, including possible genotoxicity of picoxystrobin and its main plant metabolites:

- **Coffee bean**
- **Cottonseed**
- **Edible offal (Mammalian)**
- **Mammalian fats (except milk fats)**
- **Meat (from mammals other than marine mammals)**
- **Milks**
- **Sorghum grain**
- **Tea, green, black (black, fermented and dried)**

Benzovindiflupyr (261)

Australia

Australia supports advancement of the MRL to Step 5/8.

Canada

Canada has no objection to the JMPR recommended MRLs for the bulb onion and sugar cane new uses.

Fluensulfone (265)

Australia

Australia supports advancement of the MRLs to Step 5/8.

Canada

Canada has no objection to the JMPR recommended MRLs for the various crops/crop groups.

European Union

The EU introduces a **reservation to the advancement** of proposed draft MRLs for the following commodities:

- Barley, similar grains, and pseudo cereals with husks, Subgroup of
- Citrus fruit, Group of
- Coffee bean
- Maize cereals, Subgroup of
- Pome fruit, Group of (except Persimmon, Japanese)
- Rice cereals, Subgroup of
- Small fruit vine climbing, Subgroup of
- Sorghum grain and millet, Subgroup of
- Stone fruit, Group of
- Sugar cane
- Sweet corns, Subgroup of
- Tree nuts, Group of
- Wheat, similar grains, and pseudo cereals without husks, Subgroup of

The metabolism studies are not representative for the residue behaviour observed in the residue trials. In addition the EU is of the opinion that the genotoxic potential of MeS cannot be excluded and that further genotoxicity tests would be needed to follow up on the positive results in vitro.

Tolfenpyrad (269)

Australia

With the exception of tomatoes and eggplants for which an acute exposure concern was identified by the JMPR, Australia supports advancement of the MRL to Step 5/8.

Canada

Canada has no objection to the JMPR recommended MRLs for the citrus and fruiting vegetable crop subgroups and animal commodities.

European Union

The EU introduces a **reservation to the advancement** of the proposed draft MRLs for the following commodities, pending the outcome of ongoing import tolerance requests in the EU:

- Edible offal (mammalian)
- Eggs
- Lemons and limes, Subgroup of
- Mammalian fats except milk fats
- Mandarins, Subgroup of
- Meat (from mammals other than marine mammals)
- Milks
- Oranges, sweet, sour, Subgroup of
- Peppers, Subgroup of (except okra, martynia, and roselle)
- Pummelo and grapefruits, Subgroup of
- Poultry, edible offal of
- Poultry fats
- Poultry meat

For mandarins, oranges and peppers, based on the toxicological reference values derived by JMPR, an acute consumer risk has been identified for European consumers.

The EU **opposes to the advancement** of the proposed draft MRLs for the following commodities:

- Eggplants, Subgroup of
- Tomatoes, Subgroup of

JMPR concluded that the estimated acute dietary exposure to residues of tolfenpyrad for the consumption of tomatoes and eggplants may present a public health concern.

Mesotrione (277)

Australia

Australia supports advancement of the MRLs to Step 5/8.

Canada

Canada has no objection to the JMPR recommended MRLs for the new uses on orchard crops.

Acetochlor (280)

Australia

Australia supports advancement of the MRLs to Step 5/8.

Canada

Canada has no objection to the JMPR recommended MRLs for the new uses. Acetochlor is not registered for use in Canada, nor have any import MRLs been established.

European Union

The EU introduces a **reservation to the advancement** of the proposed draft MRLs for the following commodities:

- **Edible offal (mammalian)**
- **Soya bean (dry)**

The enforcement residue definitions for plant and animal commodities in the EU differ from the definitions applied by JMPR.

Flonicamid (282)

Australia

Australia supports advancement of the MRLs to Step 5/8.

Canada

Canada has no objection to the JMPR recommended MRLs for the new uses.

European Union

The EU introduces a **reservation to the advancement** of the proposed draft MRLs for the following commodities:

- **Lemons and Limes (subgroup)**
- **Oranges, Sweet, Sour (subgroup)**
- **Pumelo and grapefruit (including Shaddock-like hybrids) (subgroup)**

The enforcement residue definition for plant commodities in the EU differs from the definition applied by JMPR.

For oranges an acute consumer risk has been identified for European consumers. The EU has set an ARfD based on rabbit developmental study.

Fluazifop-p-butyl (283)

Australia

Australia notes the decision of CCPR 2017 to withdraw the draft MRLs for sweet potato and yam has resolved the long-term dietary exposure concern.

Australia supports advancement of the MRL to Step 5/8.

Canada

Canada has no objection to the JMPR recommended MRLs for the various berry crops/crop groups.

European Union

The EU introduces a **reservation to the advancement** of the proposed draft MRLs for the following commodities:

- **Elderberries**

An extrapolation from blueberries to elderberries is not foreseen in the Codex extrapolation rules. The EU understands that JMPR derived the proposed draft CXL for elderberries based on the scope of the underlying authorisation. However, the EU considers that the extrapolation from blueberries to elderberries and guelder rose should be discussed by the eWG on Classification to determine whether such extrapolation is appropriate.

- **Strawberry**

An acute consumer risk has been identified for European consumers.

Moreover, a chronic consumer risk has been identified for European consumers, with strawberries as the main contributor among the crops under consideration.

Flupyradifurone (285)

Australia

Australia supports advancement of the MRLs to Step 5/8.

Canada

Canada has no objection to the JMPR recommended MRLs for the new uses.

Isofetamid (290)

Australia

Australia supports advancement of the MRLs to Step 5/8.

Canada

Canada acknowledges that the JMPR recommended MRLs are lower than the Canadian MRLs for the same crops based on different residue definitions for enforcement and scaling of residues conducted by JMPR.

Pendimethalin (292)

Australia

Australia supports advancement of the MRLs to Step 5/8.

Canada

Canada has no objection to the JMPR recommended MRLs for the new uses on the various cane and bush berry subgroups including strawberries.

Cyclaniliprole (296)

Canada

Canada supports the JMPR recommended MRLs.

European Union

The EU introduces a reservation to the advancement of the proposed draft MRLs for the following commodities:

- **Almonds**
- **Bush berries, Subgroup of**
- **Cabbages, head**
- **Cane berries, Subgroup of**
- **Cherries, Subgroup of**
- **Citrus fruit, Group of**
- **Cucumbers and summer squashes, Subgroup of**
- **Eggs**
- **Eggplants, Subgroup of**
- **Flowerhead Brassicas, Subgroup of**
- **Grapes**
- **Leaves of Brassicaceae, Subgroup of,**
- **Low growing berries, Subgroup of (except cranberries)**
- **Melons, pumpkins and winter squashes, Subgroup of**
- **Peaches (including Apricots and Nectarines), Subgroup of**
- **Peppers, Subgroup of (except Martynia, Okra and Roselle)**
- **Plums, Subgroup of**
- **Pome fruits, Group of (excluding Japanese persimmons)**
- **Tea, green, black (black, fermented and dried)**
- **Tomatoes, Subgroup of**
- **Tuberous and corn vegetables, Subgroup of**

In a recent EU evaluation, the consumer risk assessment could not be finalised due to data gaps, and no conclusion could be drawn on the genotoxicity and the general toxicity of several metabolites.

The EU notes that for the subgroup of leaves of Brassicaceae ~~and tea~~, the proposed Codex MRLs are not acceptable because the number of residue trials is insufficient.

Fenazaquin (297)

Australia

Australia supports advancement of the MRLs to Step 5/8.

Canada

Canada has no objection to the JMPR recommended MRLs for the new uses. Fenazaquin is in the process of being reviewed in Canada to support a domestic registration.

Fosetyl-Al (302)

Australia

Australia supports advancement of the MRLs to Step 5/8.

Canada

Canada has no objection to the JMPR recommended MRLs for the new uses. Fosetyl-aluminum was recently re-evaluated in Canada. See [PRVD2017-19](#) and [RVD2019-08](#) for details.

European Union

The EU introduces a **reservation to the advancement** of the proposed draft MRLs for the following commodities:

- **Coffee beans**

In accordance with the Information Document on the Application of the Guidance to Facilitate the Establishment of MRLs for Pesticides for Minor Crops (referred to in Annex D to the Risk Analysis Principles applied by the Codex Committee on Pesticide Residues, Codex Procedural Manual), coffee beans are a major crop. Therefore, the number of residue trials submitted is insufficient.

Mandestrobin (307)

Australia

Australia supports advancement of the MRLs to Step 5/8.

Canada

Canada has no objection to the JMPR recommended ADI and ARfD but acknowledges that the JMPR recommended MRL for rapeseed is lower than the Canadian MRL based on a different interpretation of the residue data. Canada has received an application from the sponsor to reassess its MRL to align with that recommended by JMPR.

European Union

The EU introduces a **reservation to the advancement** of the proposed draft MRLs for the following commodities:

- **Rape seed**

In the EU, a different residue definition for risk assessment applies, which includes also the metabolites De-Xy-S-2200, 4-OH-S-2200 conjugate, and 2-CH₂OH-S-2200 conjugate. A conversion factor to recalculate residues according to the residue definition for monitoring to the EU residue definition for risk assessment is not available for rape seed.

Pydiflumetofen (309)

Australia

With the exception of leafy greens for which an acute exposure concern was identified by the JMPR, Australia supports advancement of the MRL to Step 5/8.

Canada

Canada acknowledges that several of the JMPR recommended MRLs are lower than the Canadian MRLs based on the different interpretation and application of residue uptake from soil as evidenced in the field accumulation studies.

European Union

The EU introduces a **reservation to the advancement** of the proposed draft MRLs for the following commodities, pending the outcome of the ongoing approval procedure in the EU:

- Barley, similar grains, and pseudocereals with husks, Subgroup of
- Brassica vegetables (except Brassica leafy vegetables), Group of
- Cotton seed
- Dry beans, Subgroup of
- Dry peas, Subgroup of
- Edible offal (Mammalian)
- Eggs
- Fruiting vegetables, cucurbits, Group of
- Fruiting vegetables, other than cucurbits, Group of (except Martynia, Okra and Roselle)
- Leaves of Brassicaceae, Subgroup of
- Leaves of root and tuber vegetables, Subgroup of (except leaves of tuber vegetables)
- Legume vegetables, Group of
- Maize cereals, Subgroup of
- Mammalian fats (except milk fats)
- Meat (from mammals other than marine mammals)
- Milks
- Okra
- Peanut
- Poultry, edible offal of
- Poultry fats
- Poultry meat
- Rice cereals, Subgroup of
- Root vegetables, Subgroup of
- Small seed oilseeds, Subgroup of
- Sorghum grain and Millet, Subgroup of
- Stems and petioles, Subgroup of
- Sunflower seeds, Subgroup of
- Sweet corns, Subgroup of
- Tuberous and corm vegetables, Subgroup of
- Wheat, similar grains, and pseudocereals without husks, Subgroup of

The EU notes that for the subgroup of stems and petioles an acute consumer risk has been identified for European consumers.

The EU **opposes to the advancement** of the proposed draft MRLs for the following commodities:

- Leafy greens, Subgroup of

JMPR concluded that the estimated acute dietary exposure to residues of pydiflumetofen for the consumption of leafy greens may present a public health concern. An acute consumer risk has been identified for European consumers.

Pyriofenone (310)

Australia

Australia supports advancement of the MRL to Step 5/8.

Canada

Canada has no objection to the JMPR recommended MRLs for animal commodities.

Afidopyropen (312)

Australia

Australia supports advancement of the MRL to Step 5/8.

Canada

Canada has no objection to the JMPR recommended ADI, ARfDs and MRLs. Afidopyropen was recently registered in Canada. See [PRD2018-15](#) and [RVD2018-18](#) for details.

European Union

The EU introduces a **reservation to the advancement** of the proposed draft MRLs for the following commodities, pending the outcome of ongoing import tolerance requests in the EU:

- Cabbages, Head
- Cherries, Subgroup of
- Citrus Fruit, Group of
- Coriander, leaves
- Cotton seed
- Cucumber
- Dill, leaves
- Edible offal (mammalian)
- Eggs
- Eggplants, Subgroup of
- Flowerhead Brassicas, Subgroup of
- Fruiting vegetables, cucurbits – melon, pumpkins and winter squashes, Subgroup of
- Ginger, rhizome (fresh)
- Leafy greens, Subgroup of
- Leaves of Brassicaceae, Subgroup of
- Mammalian fats (except milk fats)
- Meat (from mammals other than marine mammals)
- Milks
- Parsley, leaves
- Peaches, Subgroup of
- Peppers, Subgroup of, excluding okra, martynia and roselle
- Pome fruit, Group of, excluding persimmon
- Plums, Subgroup of
- Poultry, edible offal of
- Poultry, fats
- Poultry, meat
- Soya bean (dry)
- Stem and petioles, Subgroup of
- Summer squash
- Tomatoes, Subgroup of
- Tree nuts, Group of
- Tuberous and corm vegetables, Subgroup of
- Turmeric, root (fresh)

The EU notes that:

For leaves of Brassicaceae, based on the toxicological reference values derived by JMPR, an acute consumer risk has been identified for European consumers.

For coriander, dill and parsley leaves, JMPR considered mustard greens to be more representative for herbs than leaf lettuce or spinach. However, the agreed extrapolations rules (Appendix VIII of REP18/PR) specify that trials on basil, mint, leaf lettuce or spinach should be used to derive an MRL for herbs. By considering the residue trials in leaf lettuce and spinach, a lower MRL proposal of 2 mg/kg is derived.

Metconazole (313)

Australia

Australia supports advancement of the MRLs to Step 5/8.

Canada

Canada has no objection to the JMPR recommended ADI and ARfD but acknowledges that the JMPR recommended MRLs for the subgroup of dry peas and dry soya bean are lower than the Canadian MRL based on a different crop grouping approach and interpretation of the residue data.

European Union

The EU introduces a **reservation to the advancement** of the proposed draft MRLs for the following commodities, pending the outcome of the ongoing periodic re-evaluation in the EU:

- Banana
- Beans with pods (*Phaseolus spp.*) immature pods and succulent seeds)
- Blueberries
- Cherries, Subgroup of
- Cotton seed
- Dry beans, Subgroup of (except soya beans)
- Dry peas, Subgroup of
- Edible offal (mammalian)
- Eggs
- Garlic
- Maize
- Mammalian fats (except milk fats)
- Meat (from mammals other than marine mammals)
- Milks
- Onion, bulb
- Peaches, Subgroup of
- Peanut
- Plums, Subgroup of
- Poultry, edible offal of
- Poultry fats
- Poultry meat
- Rape seed
- Soya bean (dry)
- Sugar beet
- Sugar cane
- Sunflower seeds, Subgroup of
- Sweet corn (Corn-on-the-cob)
- Tree nuts, Group of
- Tuberous and corm vegetables, Subgroup of

The EU notes that:

For peaches, an MRL of 0.15 mg/kg is sufficient according to the OECD calculator.

For sweet corn (corn-on-the-cob), the asterisk should be deleted, as an MRL of 0.015 mg/kg is derived with the OECD calculator.

For plums, subgroup of, the number of residue trials submitted is insufficient. In accordance with the Information Document on the Application of the Guidance to Facilitate the Establishment of MRLs for Pesticides for Minor Crops (referred to in Annex D to the Risk Analysis Principles applied by the Codex Committee on Pesticide Residues, Codex Procedural Manual), plums are a major crop.

For cherries, sunflower and sugar beet, fewer residue trials have been submitted to JMPR than to the EU for import tolerance requests for the same commodities. The EU considers that JMPR should base its recommendations on the most comprehensive dataset possible, and that submission of a reduced dataset, intentionally or unintentionally, is not acceptable. The EU calls on all sponsors to ensure that all available studies are submitted to JMPR.

Pyflubumide (314)

Australia

Australia notes the JMPR identified an acute exposure concern for apple and tea consumption. Australia does not support advancement of the MRLs.

Canada

Canada acknowledges the acute dietary risk of concern from exposure to pyflubumide residues in apples and tea. Pyflubumide is not registered for use in Canada, nor have any import MRLs been established.

European Union

The EU **opposes to the advancement** of the proposed draft MRLs for the following commodities:

- **Apple**
- **Tea, Green, Black (black, fermented and dried)**

JMPR concluded that the estimated acute dietary exposure to residues of pyflubumide for the consumption of apple and tea may present a public health concern.

The EU **notes** that the use in apples would trigger a dietary burden calculation for livestock and an assessment of residues in animal products, which were not reported in the JMPR report.

Pyridate (315)

Canada

Canada has no objection to the JMPR recommended MRLs for the new uses. Pyridate is in the process of being reviewed in Canada to support a domestic registration.

European Union

The EU notes differences in the toxicological reference values derived from JMPR. Studies selected as point of departure (multi-generation study and developmental rat toxicity study) and application of UF (applied because of the severity of effect) would lead to lower TRV.

The EU agrees with the information provided by JMPR considering that toxicity of the metabolites pyridafol CL 9673-N-glucoside (pyridafol-N-glucoside) and pyridafol-O-methyl (CL 9869) could be covered by parent compound.

Pyrifluquinazon (316)

Canada

Canada has no objection to the JMPR recommended ADI, ARfDs and acknowledges that JMPR could not recommend MRLs as the Meeting was unable to reach a conclusion on the residue definition for risk assessment for animal commodities. Pyrifluquinazon is not registered for use in Canada, nor have any import MRLs been established.

Triflumuron (317)

Canada

Canada acknowledges that JMPR could not recommend MRLs as the Meeting was unable to reach a conclusion on the residue definition for risk assessment. Triflumuron is not registered for use in Canada, nor have any import MRLs been established.

Valifenalate (318)

Australia

Australia supports advancement of the MRL to Step 5/8.

Canada

Canada has no objection to the JMPR recommended ADI and MRLs. Valifenalate is not registered for use in Canada, nor have any import MRLs been established.

PART II: CLARIFICATION / CONCERN FORMS ON MRLs**European Union**

**FORM FOR EXPRESSING CONCERNS WITH ADVANCEMENT OF AN MRL
OR REQUEST FOR CLARIFICATION OF CONCERNS
Benomyl (69), Carbendazim (72) and Thiophanate-methyl (77)**

Submitted by: <i>The European Union</i>			
Date: <i>March 2021</i>			
Pesticide / Pesticide Code Number:	Food(s) / Food Code Number(s)	MRL (mg/kg)	Present Step
<i>Benomyl (69) Carbendazim (72) Thiophanate-methyl (77)</i>	<i>All commodities</i>	<i>All MRLs</i>	<i>CXL</i>
Is this a request for clarification?			
<i>Yes</i>			
Request for clarification (Specific statement of clarification requested)			
<p>Benomyl was initially evaluated by JMPR before 1995 and reviewed a few times for toxicology and residues (last review in 1998 for residues; in 1995 for toxicology).</p> <p>Carbendazim was initially evaluated by JMPR before 1973 and reviewed several times for toxicology and residues (last review in 2005). A toxicological periodic review took place in 1995; in 2005 only an Assessment concerning an ARfD was done.</p> <p>Thiophanate-methyl was initially evaluated by JMPR in 1973 and reviewed several times for toxicology and residues (last periodic review in 1998 for residues; in 2017 for toxicology). The JMPR in 2017 noted that it did not receive any information on the toxicology of carbendazim. The meeting was unable to complete its evaluation for residues.</p> <p>In 2003 it was decided to combine the residue definitions for benomyl, carbendazim and thiophanate-methyl to "Sum of benomyl, carbendazim and thiophanate-methyl, expressed as carbendazim". At that time, Germany noted "that benomyl is no longer supported in the EU and the USA, but was also advised that benomyl still had uses in Australia. The delegation of Germany also pointed out that the majority of MRLs came from the use of benomyl and that in its opinion all the MRLs should be reconsidered." (ALINORM 03/24A).</p> <p>At the same time benomyl and thiophanate-methyl were transferred to table 1 "LIST OF PESTICIDES WHOSE MRLS(CXLS) OR GLS HAVE BEEN DELETED BY THE CODEX ALIMENTARIUS COMMISSION AND FOR WHICH NO MRLS HAVE BEEN PROPOSED" with the note "see Carbendazim" within the document on DRAFT AND PROPOSED DRAFT MAXIMUM RESIDUE LIMITS IN FOODS AND FEEDS AT STEPS 7 AND 4. This is misleading due to the heading of the table but correct since CXLS were not deleted yet. As a result, both substances are no longer part of table 3 in the priority lists!</p> <p>The EU is seeking advice on the following questions:</p> <ul style="list-style-type: none"> • In case the entries in Table 1 of DRAFT AND PROPOSED DRAFT MAXIMUM RESIDUE LIMITS IN FOODS AND FEEDS AT STEPS 7 AND 4 are correct why do we have qualifiers for benomyl and thiophanate-methyl in the list of CXLS for Carbendazim? • In case the entries in Table 1 of DRAFT AND PROPOSED DRAFT MAXIMUM RESIDUE LIMITS IN FOODS AND FEEDS AT STEPS 7 AND 4 are not correct how is it possible to perform a periodic re-evaluation for toxicology and residues for benomyl as the substance is no longer part in the priority lists? How was it possible to perform a periodic re-evaluation for toxicology for thiophanate-methyl in 2017 as the substance is no longer part in the priority lists? 			
Is this a concern?			
<i>Yes</i>			
Is this a continuing concern?			
<i>No</i>			

Concern (Specific statement of reason for concern to the advancement of the proposed MRL)

As stated above in 2003 it was mentioned that benomyl is no longer approved in the EU and USA. EU takes note on the fact that the toxicological evaluation for thiophanate-methyl could not be finalized due to a missing actual evaluation of the toxicology of carbendazim.

EU acknowledges that carbendazim is scheduled for periodic review in 2022. This substance is no longer approved in the EU since 2014. It is also noted that up to now no information was made available how the results of the toxicological re-evaluation of carbendazim will fit into the toxicological review of thiophanate-methyl and benomyl.

The re-evaluation process for thiophanate-methyl in the EU was terminated in 2020, following the withdrawal of the application for renewal of approval by the applicant. The substance is thus no longer approved in the EU.

A re-evaluation of the toxicological properties and MRLs for carbendazim and thiophanate-methyl in the EU is ongoing, taking into account information available under different legal frameworks and for both substances. The opinion of the European Food Safety Authority is expected to be published in the third quarter of 2021.

Do you wish this concern to be noted in the CCPR Report?

Yes

Data/Information (Description of each separate piece of data/information which will be provided to the appropriate JMPR secretary within one month of the CCPR meeting)

United States of America

Dear CCPR Secretariat:

The United States appreciates the opportunity and would like to provide the following comments in response to Circular Letter CL 2020/6(REV2)-PR --Request for comments on the recommendations of the 2019 Joint FAO/WHO Meetings on Pesticide Residues (JMPR).

Specific Comments

The United States received a total of four Concern Forms from pesticide registrants/sponsors. After careful review, we believe that three of these had merit and should be considered further by JMPR. As per practice, we have limited the submitted Concern Forms to those that deal with specific technical issues and corrections that were raised to the U.S. Delegation by the sponsors; simply disagreeing with a JMPR decision or JMPR judgement is not a valid reason for submitting a Concern Form.

Given that and in response to CL 2020/6(REV2)-PR, the United States submits Concern Forms on the following for consideration by the JMPR Secretariat:

1. Flensulfone-Pome and Citrus Juice (265)
2. Metaconazole-Wheat (313)
3. Afidopyropen (312)

We hope the Concern Forms provide sufficient information to be fully considered by the JMPR Secretariat and welcome any clarifying questions in advance of CCPR52. If you have any questions or issues, please feel free to contact U.S. Delegate David Miller (miller.davidj@epa.gov) and Aaron Niman (niman.aaron@epa.gov) directly.

**FORM FOR EXPRESSING CONCERNS WITH ADVANCEMENT OF AN MRL
OR REQUEST FOR CLARIFICATION OF CONCERNS
FLUENSULFONE (265)**

Submitted by: U.S. Delegation			
Date: February 28, 2021			
Pesticide/ Pesticide Code Number	Commodity/ Commodity Code Number	MRL (mg/kg)	Present Step
Fluensulfone (265)	Pome fruit (FB 0272)	N/A	New uses
Is this a Request for Clarification? No			
Is this a Concern? Yes			
Is this a Continuing Concern? No			
Concern (<i>Specific statement of reason for concern to the advancement of the proposed MRL.</i>) This concern is regarding the MRL value of 0.2 ppm proposed for pome fruit and also proposals for calculation of MRLs/processing factors for orange/citrus juice.			
Request for Clarification (<i>Specific statement of clarification requested.</i>)			
Do you wish this Concern to be Noted in the CCPR Report? Yes			
Data/Information (Description of each separate piece of data/information which is attached or will be provided to the appropriate JMPR secretary within one month of the CCPR meeting.) Pome fruit In the evaluation, the residue values for pear in the decline study were incorrect (Hoi and Jones, 2016, R-35572, trial PR-WA). At the 128 day PHI, residues of BSA were 0.138 and 0.140 mg/kg giving a giving sum of fluensulfone + BSA expressed as fluensulfone of 0.22 mg/kg instead of the value reported in the JMPR evaluation of <0.025 mg/kg. Using the above-corrected values, both the apple and pear data would still be shown to be from the same population and could be combined into a single joint dataset and used to calculate the MRL. Apples: < 0.025 (10), 0.028 (3), 0.031, 0.037 and 0.16 mg/kg (n = 16); Pears: < 0.025 (4), 0.026, 0.11 0.17 and 0.22 mg/kg (n = 8). Using the above corrected values, the OECD calculator predicts an MRL of 0.3 mg/kg fluensulfone (total residues). The HR and the STMR remain unchanged at 0 mg/kg fluensulfone. Citrus juice MRLs for citrus juice were not calculated for orange juice as there were no detectable levels in the citrus RAC. This is true for fluensulfone parent but detectable residues of BSA metabolite were present. Therefore, a processing factor based on total residues in citrus could be calculated, but JMPR did not do so. With a comparable data set, the approach of using a processing factor based on total residues was taken by the JMPR when calculating processing factors for pome fruit/apple juice. There were two processing factors calculated in the two processing studies done for citrus juice: 0.44 and 1.8; however, the higher value is very similar to that for apple juice (1.7) and should be considered the appropriate processing factor for calculating the MRL for citrus/orange juice.			

**FORM FOR EXPRESSING CONCERNS WITH ADVANCEMENT OF AN MRL
OR REQUEST FOR CLARIFICATION OF CONCERNS
METCONAZOLE (313)**

Submitted by: U.S. Delegation to CCPR			
Date: February 28, 2021			
Pesticide/ Pesticide Code Number	Commodity/ Commodity Code Number	MRL (mg/kg)	Present Step
Metconazole / 313	Wheat / GC 0654	-	-
Is this a Request for Clarification?			
Is this a Concern? Yes			
Is this a Continuing Concern? No			
<p>Concern (<i>Specific statement of reason for concern to the advancement of the proposed MRL.</i>)</p> <p>JMPR 2019 concluded that no MRL could be proposed for metconazole on wheat grain based on insufficient number of trials matching the US label application parameters (within 25%).</p> <p>More specifically: JMPR considered only the 4 residue trials with pre-harvest intervals (PHIs) longer than 21 days since these were the only ones considered to fall within 25% of the label 30-day PHI, despite that most of the trials had PHIs of 20-22 days. However, according to the current FAO Manual, tolerances on the application parameters should be those that would result in a 25% change in the <u>residue concentration</u>, not 25% changes in the <u>parameters themselves</u>.</p> <p>It is requested that JMPR re-assess its determination that a MRL could not be established and consider the other eleven US wheat trials with PHI 20-22 days. These trials should be considered because residue decline behavior for wheat grain between PHI 14 and 35/36 days measured in the two decline trials clearly demonstrate that the residue trials with PHI 20-22 days will result in a residue deviation of less than 25% from the expected residue level at a PHI 30 days.</p>			
Request for Clarification (<i>Specific statement of clarification requested.</i>)			
Do you wish this Concern to be Noted in the CCPR Report? Yes			
<p>Data/Information (<i>Description of each separate piece of data/information which is attached or will be provided to the appropriate JMPR secretary within one month of the CCPR meeting.</i>)</p> <p>BASF submitted residue data and labels from US metconazole residue trials on several cereals (wheat, rye, oat, barley and maize) to the 2019 JMPR. The request for Codex MRLs in these cereals was primarily to support US growers. The critical GAP for wheat, barley, oat, rye and triticale in the USA allows two outdoor foliar applications of metconazole at 112 g ai/ha each with a retreatment interval of 6 days and a PHI of 30 days. The current US tolerance for metconazole on wheat grain is 0.15 ppm (<i>sum of cis and trans isomers</i>) and is based on the wheat residue data included in the JMPR dossier.</p> <p>JMPR 2019 concluded that no maximum residue levels could be proposed for metconazole on wheat grain based on an insufficient number of trials matching the US label application parameters (within 25%). Only residue trials with pre-harvest intervals (PHIs) longer than 21 days (4 trials) were considered to fall within 25% of the label 30-day PHI, despite that most of the trials had PHIs of 20-22 days. However, according to the current FAO Manual, tolerances on the application parameters should be those that would result in a 25% change in the residue concentration, not 25% changes in the parameters themselves. Application of the "25% rule" to pre-harvest interval is explained in detail in the 2016 FAO Manual. In chapter 5.2.3 of the manual it is stated, "<i>The latitude of acceptable intervals around the PHI depends on the rate of decline of residues of the compound under evaluation. The allowable latitude should relate to a ±25% change in residue level and may be estimated from residue decline studies.</i>"</p>			

What follows in the 2016 FAO Manual chapter is a mathematical approach to calculating the acceptable intervals for pre-harvest interval that will lead to a maximum deviation of 25% in the final residue values in the harvested commodity.

BASF kindly asks JMPR to consider also the eleven other US/Canada wheat trials with PHI 20-22 days, as the residue decline behavior for wheat grain between PHI 14 and 35/36 days measured in the two decline trials clearly demonstrate that the residue trials with PHI 20-22 days will result in a residue deviation of less than 25% from the expected residue level at the label PHI of 30 days.

Crop / commodity	Decline Trial	Residue values mg/kg (total <i>cis+trans</i> metconazole)		Calculated half-life (days)
		PHI	Residue	
Winter wheat grain	R05047 (IL)	14	0.034, 0.045	387 (R ² = 0.0041)
		21	0.077, 0.062	
		28	0.051, 0.051	
		35	0.036, 0.048	
Spring wheat grain	R05050 (ND)	14	0.018, 0.022	32 (R ² = 0.886)
		22	0.014, 0.016	
		28	0.013, 0.013	
		36	0.012, 0.013	

The winter wheat trial from the state of Illinois (IL) did not show typical residue decline behavior. Residues actually increased between the first and second sampling dates resulting in a very long half-life and poor fit to the expected first-order decay. However, the decline trial conducted in spring wheat in the state of North Dakota (ND) had acceptable fit to first-order decay and resulted in a calculated half-life of 32 days. Based on an estimated 32-day half-life for metconazole in wheat grain, the acceptable variance around a label PHI of 30 days is 20 to 43 days (see calculations below). Assuming that the other application parameters match the registered label, the residue values from samples collected within this PHI range of 20 to 43 days will fall within 25% of the residue values expected from the label PHI of 30 days.

From the FAO Manual (2016), page 86:

$$t_1 - t_2 = \ln\left(\frac{C_1}{C_2}\right) \times \frac{t_{1/2}}{\ln(0.5)}$$

Where $t_1 - t_2$ is the time (days) between the registered PHI (t_1) and the residue trial PHI (t_2)

C_1 is the residue level expected from the registered PHI

C_2 is the residue level measured in the field trials

$t_{1/2}$ is the half-life (days)

When C_2 is 25% greater than C_1 then $C_2 = 1.25 \times C_1$

And when C_2 is 25% less than C_1 then $C_2 = 0.75 \times C_1$

With these constraints, the equation results in the following intervals for the time between the registered PHI and the trial PHI:

$t_1 - t_2 = 0.32 \times t_{1/2}$ (when the trial PHI is shorter than the registered PHI)

$t_2 - t_1 = 0.42 \times t_{1/2}$ (when the trial PHI is longer than the registered PHI)

So, for metconazole on wheat grain where the observed half-life was at least 32 days, the acceptable PHI range that will lead to residues that are within 25% of the expected residue at the label PHI is 20-43 days.

In summary, BASF kindly requests that JMPR consider the full set of 15 submitted US/Canada residue trials to support the Caramba® label as they *do* fall within the FAO interpretation of the "25% rule" with regard to expected residue levels in wheat grain when calculated as per FAO Manual-directed practice.

**FORM FOR EXPRESSING CONCERNS WITH ADVANCEMENT OF AN MRL
OR REQUEST FOR CLARIFICATION OF CONCERNS
AFIDOPYROPEN (312)**

Submitted by: U.S. Delegation to CCPR			
Date: February 28, 2021			
Pesticide/ Pesticide Code Number	Commodity/ Commodity Code Number	MRL (mg/kg)	Present Step
Afidopyropen/ 312	All commodities	All MRLs	First Request
Is this a Request for Clarification? Yes			
Is this a Concern? Yes, it is mostly a concern			
Is this a Continuing Concern? No, but it impacts previously reviewed CXLs and a new submission made in 2020.			
Concern (<i>Specific statement of reason for concern to the advancement of the proposed MRL</i>).			
Concern # 1: BASF has concern with the numeric calculations used to implement the JMPR proposed risk assessment residue definition for plants for Afidopyropen. <ul style="list-style-type: none"> • JMPR established definition of the residue for dietary risk assessment for plant commodities: sum of afidopyropen + M440I007, <i>expressed as afidopyropen</i> • To express M440I007 as parent the ratio of Molecular Weights should be employed as an adjustment factor; the expression of M440I007 as parent requires a scaling of 0.5 X based on scaled molecular weights = MW where afidopyropen / M440I007 = (593.7/1187.3) • However, the final JMPR report clearly shows that the residues of parent and M440I007 were just summed; summation implies that they are applying a special dimer rule to count M440I007 = 2 molecules of parent. • BASF provided JMPR 3 different lines of evidence (a rat ADME study with ¹⁴C M440I007, a comparative tox ratio argument, and a quantum chemical calculation on the strength of the dimer bridge) for why the M440I007 will not reform 2 molecules of parent as a residue. • Finally, we believe that without the MW adjustment, the HR and STMR values in the draft document are currently incorrectly too high for all plant commodities. As an example, please refer to the attached US EPA HED document. An excerpt of Table 5.3.1 from the US EPA Analytical Summary (correctly) depicts calculations using the MW conversion factor already summarized for M440I007. (And while the document also has a “combined” set with M440I007; we note the final US decision <u>did not</u> include M440I007.) The full US EPA residue chemistry document is provided as a further convenient reference which is attached to this concern form. • We ask that the HR and STMR values in the draft JMPR document be recalculated using the appropriate scaling factor based on MWs rather than the incorrect simple summing of parent Afidopyropen and metabolite M440I007. 			
Concern # 2 The Meeting is also asked to reconsider the very low MRL drafted for milk at 0.001 ppm. While this is supported by the current methods, the value is very low for practical monitoring in trade. A typical default of 0.01* ppm would be better harmonized with enforcement practices and more useful to the international trading community and we recommend that this 0.01 ppm* CXL value be used instead.			
Request for Clarification (<i>Specific statement of clarification requested</i>).			
BASF welcome any further clarifications from JMPR in any Fall, 2021 review that were not included in the final report related to the inclusion on M440I007 in the risk assessment definition. Further information from BASF is provided below on the request for clarification.			

- In our dossier and further correspondence, we noted that addition of the M440I007 in the risk assessment definition does not reflect the known significantly lower toxicity of the M440I007 metabolite; it is very conservative to add the parent and M440I007 metabolite and then assess against the parent reference doses (especially for the ARfD, where there is no evidence of acute toxicity). A clearer explanation addressing this point should be provided by JMPR.

Do you wish this Concern to be Noted in the CCPR Report?

Data/Information (Description of each separate piece of data/information which is attached or will be provided to the appropriate JMPR secretary within one month of the CCPR meeting.)

Attachments:

- Appendix 1. BASF Sept 23, 2019 Response for Afidopyropen JMPR Residue Appraisal Draft
Please refer to pgs. 3-4 of Appendix 1 for a detailed example of calculations using the correct MW conversion factor for M440I007.



Attachment
1_Appendix BASF Re

- Appendix 2. U.S. EPA (D439679). Afidopyropen. Summary of Analytical Chemistry and Residue Data. April 3, 2018.



Attachment 2_U.S.
EPA_Afidopyropen_5

Attachments 1 and 2 as follows.

BASF appreciates the opportunity to provide feedback on the 2019 JMPR Draft Residue Appraisal for afidopyropen. We recognize this was a large submission and it took significant time and dedication to assess and consolidate the information for The Meeting. Please consider our comments in order to further improve the evaluation for the final report.

- 1) We are pleased that JMPR proposed MRLs for our uses based on submitted trials and label GAPs. We especially appreciate the inclusion of the reviewer's written rationale for distinctions made between proposing an MRL for a crop group, a subgroup or a single commodity. We would appreciate an inclusion of rationale when submitted residue trials were not used in the distribution (e.g. R140682 was not included in the residue distribution, but no explanation was given). We also agree the *parent-only* residue definition is appropriate for enforcement and note this definition is harmonized with countries of current registrations.
- 2) However, we have **concern with the numeric calculations used to implement the JMPR proposed risk assessment residue definition for plants**. The residue definition for plant is drafted as parent plus M440I007, *expressed as parent*.
 - But the calculation to add the metabolite **has not included a molecular weight correction for parent equivalence**. We note our original dossier submission did not provide a summation or correction to parent equiv. because we proposed that parent only was appropriate. Alternatively, the raw M440I007 values could also be used if a separate reference dose was set for M440I007 based lower and non-comparable toxicity to the parent. Our dossier did clearly state methodology for the calculation of parent equivalence for M440I007 if needed. No explanation has been given as to why our information and conversion was not used for the proposed definition.
 - Moreover, in late August, BASF responded to initial questions regarding M440I007 and BASF gave JMPR three separate points of evidence for why M440I007 (a *photolytic* dimer) does not metabolize back to the parent and thus the expression of M440I007 as parent **requires a scaling of 0.5 X based on scaled molecular weights = MW where afidopyropen / M440I007 = (593.7/1187.3)**.
 - Our August response included two key pieces of information which support this important interpretation. First is the metabolism study 2013/8001821; the study is fit for purpose to determine that parent (or closely related metabolites) is not reformed via metabolism in the rat. The second is the lower toxicity observed with the M440I007 metabolite (comprised of 2 parent halves) compared to the higher observed toxicity of the parent afidopyropen. In addition, quantum chemical calculations also further support our position; additional information on the relative stability of the dimer bridge (which is formed photolytically) is discussed.
 - We also request that each place in the JMPR writeup where the document says "dimer" the term "photolytic dimer" or M440I007 be used, because this is a better reflection of the afidopyropen situation.
 - Without a MW adjustment, we believe **the HR and STMR values in the draft document are currently incorrectly too high** for all plant commodities. As an example, we include an excerpt of Table 5.3.1 from the US EPA Analytical Summary with calculations using the MW conversion factor already summarized for M440I007. (And while the document also has a "combined" set with M440I007; we note the final US decision did not include M440I007.) The full US EPA document is provided a further convenient reference in the email as part of our response.
 - As noted in the following table, when the M440I007 calculations are completed with the MW scaling, **the resulting exposure to a parent equivalent of M440I007 is lower by a factor of 2X relative to JMPR draft**. We suggest a further discussion of our August comments (reattached) and the parent equivalence methodology for M440I007 within the appraisal is appropriate.

Table 5.3.1 from US EPA Analytical Summary¹

Table 5.3.1. Summary of Residues from Crop Field Trials Conducted with Afidopyropen.											
Crop Matrix	Analyte	Total Application Rate (lb ai/A) [g ai/ha]	PHI (days)	n ¹	Residues (ppm parent equivalents)						
					Min. ²	Max. ²	LAFT ³	HAFT ³	Median ³	Mean ³	SD ³
Leafy Vegetables (U.S. Field Trials)											
[Proposed Use Pattern – 0.11 lb ai/A total application rate @ 0-day PHI]											
Celery	Afidopyropen	0.105-0.110 (117-123)	0	7	0.024	1.894	0.027	1.275	0.283	0.434	0.446
Head lettuce, w/wrapper		0.106-0.112 (119-125)	0	8	0.011	0.287	0.014	0.278	0.164	0.149	0.079
Head lettuce, wo/wrapper		0.106-0.112 (119-125)	0	8	<0.01	0.275	<0.01	0.272	0.020	0.051	0.090
Leaf lettuce		0.106-0.111 (119-124)	0	8	0.030	0.969	0.042	0.944	0.496	0.482	0.312
Spinach		0.107-0.111 (119-124)	0	8	0.041	1.168	0.042	1.074	0.629	0.651	0.337
Celery	M440I007	0.105-0.110 (117-123)	0	7	0.007	0.131	0.013	0.076	0.043	0.042	0.024
Head lettuce, w/wrapper		0.106-0.112 (119-125)	0	8	0.009	0.254	0.012	0.240	0.097	0.115	0.086
Head lettuce, wo/wrapper		0.106-0.112 (119-125)	0	8	<0.005	0.216	<0.005	0.209	0.011	0.040	0.070
Leaf lettuce		0.106-0.111 (119-124)	0	8	0.022	0.654	0.033	0.644	0.201	0.284	0.204
Spinach		0.107-0.111 (119-124)	0	8	0.005	0.787	0.006	0.787	0.403	0.391	0.246
Celery	Combined	0.105-0.110 (117-123)	0	7	0.042	2.025	0.046	1.350	0.295	0.476	0.459

- 3) Equally important, we are concerned that the current addition of the M440I007 in the risk assessment definition **does not account for the known significantly lower toxicity of the M440I007** metabolite; it is very conservative to add the parent and M440I007 metabolite and then assess against the parent reference doses (especially for the ARfD, where there is no evidence of acute toxicity). Addition of the M440I007 metabolite to the risk assessment is currently not decided for EU, but it was discussed with authorities in early 2019. The April 2019 EU dossier includes a derivation of references doses for M440I007 which is reproduced here:

¹ P. Savoia, **D439679**, D443666, and D444876, 04/03/2018, Afidopyropen. Section 3 Registration of the New Insecticide Active Ingredient Afidopyropen for Use on Brassica Head and Stem Vegetable Crop Group 5-16, Citrus Fruit Crop Group 10-10, Cotton, Cucurbit Vegetable Crop Group 9, Fruiting Vegetable Crop Group 8-10, Leaf Petioles Vegetable Subgroup 22B, Leafy Greens Subgroup 4-16A, Brassica Leafy Greens Subgroup 4-16B, Pome Fruit Crop Group 11-10, Soybean, Stone Fruit Crop Group 12-12, Tree Nut Crop Group 14-12, and Tuberous and Corm Vegetable Subgroup 1C. **Summary of Analytical Chemistry and Residue Data**

Table of Reference Doses for Afidopyropen and M440I007

	Source	Value	Study relied upon	Safety factor
Afidopyropen				
ADI		0.08 mg/kg bw/day	Dog, 1 year oral	100
ARfD		0.32 mg/kg bw	Rabbit, developmental toxicity	100
Metabolite M440I007				
ADI		3.58 mg/kg bw/day	Rat, 90 day oral	200
ARfD		None proposed		

Therefore, given the JMPR residue definition for risk assessment for plants includes M440I007, then we respectfully ask the JMPR to consider improved **operational methodology for the implementation of the risk assessment definition for plants such that:**

- The acute risk assessment definition = afidopyropen only (because no ARfD for 440I007 is warranted)
- The chronic risk assessment definition uses **a toxicology scaling factor for the metabolite** such that:

$$\text{Total afidopyropen} = \text{afidopyropen} + 0.1 \times \text{M440I007 (expressed as parent eq.)}$$

To support our comments, a table is provided below demonstrating the important impact on examples for Mustard Greens and Cabbage with leaves. These crops were chosen as an example for the revision, because they have a high residues and/or impact on the animal feed burden.

Residue Distribution Calculations Related to Afidopyropen (ppm)

Matrix	Trial	440I	M007	M007 as parent eq.	BASF Total 440I+ 0.1*M007	JMPR Draft Total	Ratio of Overexposure
Mustard Leaves							
	R140676	2.7	1.5	0.73	2.8	4.2	1.5
	R140675	1.3	1.5	0.77	1.4	2.8	2.0
	R140677	1.8	1.5	0.77	1.9	3.3	1.8
	R140678	1.8	0.6	0.30	1.9	2.4	1.3
	R140679	0.7	1.3	0.65	0.7	2.0	2.7
	R140680	1.1	1.4	0.7	1.1	2.5	2.2
	R140681	1.1	0.19	0.1	1.1	1.3	1.2
	R140682	Not used?					
Cabbage with leaves							
	R140665	0.049	0.047	0.023	0.05	0.096	1.9
	R140666	0.034	0.026	0.013	0.04	0.06	1.7
	R140667	0.28	0.027	0.013	0.28	0.30	1.1
	R140668	0.038	0.047	0.023	0.04	0.085	2.1
	R140669	0.14	0.024	0.012	0.14	0.16	1.2
	R140670	0.01	0.01	0.001	0.01	<0.02	1.2
	R140671	0.043	0.046	0.023	0.04	0.088	2.0
	R140672	0.012	0.014	0.01	0.01	0.026	2.1
	R140673	0.041	0.011	0.005	0.042	0.052	1.2
	R140674	0.27	0.12	0.06	0.27	0.39	1.4

The proposed revision requires recalculation of several numbers but using the highest residues, the revision concept is demonstrated, to be refined in the final report writeup. The high-end “overexposure” in the current JMPR draft is 2X. The revised section on mustard greens is as follows:

Residue trials, performed in the USA and Australia, approximating the critical GAP were submitted on mustard greens. Residues levels (parent only) in ranked order were (n=7): 0.67, 1.1, 1.1, 1.3, 1.8, 1.8, and 2.7 mg/kg. **The HR for acute risk assessment is 2.7.**

For estimating STMRs ~~and HRs~~-total residues (parent + 0.1 * M440I007 as parent eq.) in ranked order were (n=7): **0.7, 1.1, 1.1, 1.4, 1.9, 1.9 and 2.8** mg/kg (highest individual value: 4.8 mg/kg)

Noting that mustard greens is a representative crop for the Subgroup of Brassica Leafy vegetables, the Meeting estimated an MRL for the Subgroup of Brassica Leafy vegetables (VL 2054) of 5 mg/kg and an STMR and HR of **1.4** and **2.7** mg/kg.

The revised text for cabbage for the portion regarding with leaves is:

Head cabbage (with wrapper leaves=WWL) (n=10): 0.010, 0.012, 0.034, 0.038, 0.041, **0.043**, 0.049, 0.14, 0.27, and 0.28 mg/kg. **The HR for maximum animal burden assessment is 0.28.**

For estimating STMRs ~~and HRs~~-total residues (parent + 0.1 * M440I007 as parent eq.) in ranked order were:

Cabbage (WWLs) (n=10) for animal dietary burden calculation: **0.01 (2x), 0.04 (3X), 0.042, 0.05, 0.14, 0.27, 0.28** mg/kg.

- 4) In addition, finalizing a more realistic addition of the M440I007 metabolite into the animal feeds for risk assessment would also result in a lower animal burdens by ~2X and hence lower animal commodity exposures in the human diet as well.
- 5) The Meeting is also asked to **reconsider** very low MRL drafted for milk at 0.001 ppm. While this is supported by the current methods, the value is very low for practical monitoring in trade. A **typical default of 0.01* ppm** would be better harmonized with enforcement practices and more useful to the international trading community.
- 6) Finally, we are also providing in a separate email to follow, the **appraisal report back** with a number of edits, small corrections and comments for reviewer consideration in a **tracked changes file**. We hope this tracked changes file will be considered helpful for improving the final document.

In summary, we are grateful to be able to provide meaningful input and insight for afidopyropen into the Meeting, this fall. We thank you for careful consideration of this set of comments.



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

OFFICE OF CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM

Date: 03-Apr-2018

Subject: **Afidopyropen.** Section 3 Registration of the New Insecticide Active Ingredient Afidopyropen for Use on Brassica Head and Stem Vegetable Crop Group 5-16, Citrus Fruit Crop Group 10-10, Cotton, Cucurbit Vegetable Crop Group 9, Fruiting Vegetable Crop Group 8-10, Leaf Petioles Vegetable Subgroup 22B, Leafy Greens Subgroup 4-16A, Brassica Leafy Greens Subgroup 4-16B, Pome Fruit Crop Group 11-10, Soybean, Stone Fruit Crop Group 12-12, Tree Nut Crop Group 14-12, and Tuberous and Corm Vegetable Subgroup 1C. **Summary of Analytical Chemistry and Residue Data.**

PC Code: 026200	DP Barcode: D439679, D443666, and D444876
Decision No.: 516381 and 516391	Registration No.: 7969-XXX
Petition No.: 6F8468	Regulatory Action: Section 3
Risk Assessment Type: NA	Case No.: NA
TXR No.: NA	CAS No.: 915972-17-7
MRID Nos.: See Appendix F	40 CFR: §180.XXX

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1.0 Executive Summary

Afidopyropen, [(3S,4R,4aR,6S,6aS,12R,12aS,12bS)-3-[(cyclopropylcarbonyl)oxy]-1,3,4,4a,5,6a,12,12a,12b-decahydro-6,12-dihydroxy-4,6a,12b-trimethyl-11-oxo-9-(3-pyridinyl)2H,11H-naphtho[2,1-b]pyrano[3,4-e]pyran-4-yl)methyl cyclopropanecarboxylate, is a new insecticide active ingredient developed by the BASF Corporation. It provides effective residual control of piercing-sucking pests such as aphids and whiteflies. In developing afidopyropen, BASF has submitted petition PP#6F8468 requesting to establish its use on a number of food commodities and ornamentals. For this petition, tolerances are requested for *Brassica* head and stem vegetable crop group 5-16, citrus fruit crop group 10-10, cotton, cucurbit vegetable crop group 9, fruiting vegetable crop group 8-10, leaf petioles vegetable subgroup 22B, leafy greens subgroup 4-16A, *Brassica* leafy greens subgroup 4-16B, pome fruit crop group 11-10, soybean, stone fruit crop group 12-12, tree nut crop group 14-12, and tuberous and corm vegetable subgroup 1C. Afidopyropen is a North American Free Trade Agreement (NAFTA) joint submission for review by the United States (U.S.) Environmental Protection Agency (EPA) and Canada's Pest Management Regulatory Agency (PMRA) with Australia as an observer. The proposed uses of afidopyropen span both the U.S., and Canada.

Two dispersible concentrate formulations of afidopyropen are proposed for registration. These end-use products are the Versys™ 100 g ai/L and Sefina™ 50 g ai/L formulations. Copies of the proposed labels were provided by the petitioner. The proposed single application rate ranges from 0.009 lbs ai/A (10 g ai/ha) to 0.045 lbs ai/A (50 g ai/ha), and the seasonal application rate ranges from 0.018 lbs ai/A (20 g ai/ha) to 0.11 lbs ai/A (125 g ai/ha). Pre-harvest intervals (PHI) range from 0 day to 7 days. The minimum retreatment interval (RTI) is 7 days.

Acceptable data were submitted depicting metabolism in crops and livestock; analytical methods; storage stability; and residues in target crops, rotational crops, processed foods/feeds, and livestock commodities. These data are presented as Tier 2 summaries prepared by the USEPA and PMRA and referenced throughout this document. These data are adequate to support the establishment of the recommended tolerances and human health risk assessment. The Residues of Concern Knowledgebase Subcommittee (ROCKS) has determined the residue definition for tolerance enforcement to be parent afidopyropen for both plant and livestock commodities (ROCKS Decision Memo D441491, I. Negron-Encarnacion, 01/30/2018). For risk assessment, the residue definition was also determined to be parent afidopyropen for both plant and livestock commodities. Adequate analytical methods, utilizing solvent extraction and liquid chromatography with tandem mass spectrometry (LC-MS/MS) analyses are available to enforce tolerances in crops and livestock.

Field trials and feeding studies with afidopyropen indicate that tolerances are needed for crops but not for livestock. Low livestock dietary burdens paired with low residue transfer rates into livestock commodities indicate there is no reasonable expectation of finite residues in livestock commodities [40 CFR §180.6(a)(3)]. The submitted limited rotational crop data indicate that no residues of concern are expected to be present in rotational crops following a 30-day plant-back interval (PBI). In the processing studies, residues were found to concentrate in apple wet pomace, citrus oil, and dried tomatoes. The tolerance levels recommended by HED are summarized in Table 2.2.2. These tolerances have been harmonized with those recommended by PMRA.

2.0 Regulatory Recommendations

Pending submission of revised Sections B (see Label Recommendations) and F (see requirements under Revisions to Petitioned-For Tolerances), there are no residue chemistry considerations that preclude granting the requested Section 3 registration of afidopyropen for the recommended tolerances on the commodities as listed in Table 2.2.2.

A human health risk assessment is forthcoming.

2.1 Data Deficiencies/Data Needs

The registrant should submit a revised Section F to specify the recommended tolerances and correct commodity definitions listed in Table 2.2.2. No residue chemistry conditional registration data needs are associated with this tolerance petition.

2.2 Tolerance Considerations

2.2.1 Enforcement Analytical Method

B.5.2 Residue Analytical Methods

Plant and Livestock Methods – tolerance enforcement methods for plants and livestock using LC-MS/MS analyses were submitted for the analysis of afidopyropen. Independent laboratory validations were provided for each tolerance enforcement method put forward in this petition. The tolerance enforcement method for plants performs sample extraction through shaking with acetonitrile, or acetonitrile and water for dry matrices. The sample extracts are then centrifuged followed by liquid/liquid partitioning with shaking using a mixture of several salts (sodium chloride, magnesium sulfate, and citrate buffering agents). The residues in the acetonitrile layer are further purified with the addition of a second magnesium sulfate salt mixture to remove residual water. An amine and sorbent are then added to remove sugars and fatty acids, and the sample extract is then centrifuged. Following this sequence, the resulting sample extracts are then analyzed by LC-MS/MS. The tolerance enforcement method for livestock performs sample extraction using methanol except for fat. In fat, dichloromethane is used for the extraction of parent afidopyropen and the metabolite M440I003 and water is used for the metabolites M440I001 and cyclopropanecarboxylic acid carnitine (CPCA-carnitine). Following extraction, solid phase extraction is used for purification and the sample extracts are then analyzed by LC-MS/MS analysis. Radiovalidation was not needed since the solvent systems used in the proposed enforcement methods were also used in the metabolism studies to adequately demonstrate extraction efficiency.

Studies to evaluate FDA multi-residue method testing for determining the residues of afidopyropen were not performed in support of this petition. However, a QuEChERS multi-residue method based on AOAC method 2007.01 using LC-MS/MS analysis was developed by the registrant for plants and included in this submission to satisfy this data requirement.

2.2.2 Recommended Tolerances

HED has reviewed the available residue data and has determined the appropriate tolerance levels for residues of afidopyropen which are presented below in Table 2.2.2. The recommended tolerance expression is as follows:

(a) General. (1) Tolerances are established for residues of afidopyropen, including its metabolites and degradates, in or on the commodities in the table below. Compliance with the tolerance levels specified below is to be determined by measuring only afidopyropen, [(3*S*,4*R*,4*aR*,6*S*,6*aS*,12*R*,12*aS*,12*bS*)-3-[(cyclopropylcarbonyl)oxy]-1,3,4,4*a*,5,6*a*,12,12*a*,12*b*-decahydro-6,12-dihydroxy-4,6*a*,12*b*-trimethyl-11-oxo-9-(3-pyridinyl)2*H*,11*H*-naphtho[2,1-*b*]pyrano[3,4-*e*]pyran-4-yl]methyl cyclopropanecarboxylate, in or on the commodity.

Table 2.2.2. Tolerance Summary for Afidopyropen.			
Commodity	Proposed Tolerance (ppm)	HED-Recommended Tolerance (ppm)	Comments (correct commodity definition)
Almond, hulls	0.15	0.15	
Apple, wet pomace	0.05	0.05	
Vegetable, brassica, head and stem, group 5-13	0.5	0.50	<i>Brassica, head and stem, group 5-16</i>
Vegetable, leafy, subgroup 4-13B	5	5.0	<i>Brassica, leafy greens, subgroup 4-16B</i>
Citrus, oil	0.3	0.40	<i>Tolerance is harmonized to the Canadian MRL</i>
Cotton, gin byproducts	2	2.0	
Cotton, undelinted seed	0.1	0.08	
Fruit, citrus, group 10-10	0.15	0.15	
Fruit, pome, group 11-10	0.03	0.02	
Fruit, stone, group 12-12	0.03	0.03	
Vegetable, leafy, subgroup 4-13A	2	2.0	<i>Leafy Greens, subgroup 4-16A</i>
Vegetable, leaf petioles, subgroup 22B	3	3.0	<i>Leaf petiole vegetable subgroup 22B</i>
Nut, tree, group 14-12	0.01	0.01	
Plum, prune	0.06	Not Recommended	
Soybean, aspirated grain fractions	0.4	0.15	<i>Grain, aspirated fractions</i>
Soybean, seed	0.01	0.01	
Tomato, dried	None Requested	0.50	<i>Tolerance is harmonized to the Canadian MRL</i>
Vegetable, cucurbit, group 9	0.7	0.70	
Vegetable, fruiting, group 8-10	0.15	0.20	
Vegetable, tuberous and corm, subgroup 1C	0.01	0.01	

2.2.3 Revisions to Petitioned-For Tolerances

Several proposed tolerances requested by the registrant are different from those recommended by HED. For citrus oil, and cotton undelinted seed, these differences are attributable to the rounding of the maximum residue limits (MRLs) followed for setting these recommended tolerances. The recommended pome fruit tolerance is different because of differences in the MRL calculation for pear. Two pear field trials were concluded to be replicates for calculation and the registrant also used an additional residue value which is believed to be a transcription error. In regard to prunes and aspirated grain fractions (AGF), it is unclear how the registrant calculated the tolerance levels that were proposed, but these limits were not comparable to the Agency's determination. As a result, the proposed tolerance for prunes is not needed because the crop tolerance is protective of this processed commodity. For fruiting vegetables, these differences are attributable to the registrant having combined both the bell and non-bell pepper

data together for calculation. In addition, the petitioner did not propose a tolerance for residues in/on the dried tomato processed commodity but a limit is being recommended for harmonization with Canada. Therefore, the petitioner should submit a revised Section F in which the proposed tolerances and commodity definitions are the same as those recommended by HED.

2.2.4 International Harmonization

Afidopyropen is a new active ingredient and no MRLs have yet been established by Codex, Canada, or Mexico. For this joint review, the participating countries all agreed to use the Organization for Economic Co-operation and Development (OECD) calculation procedures to determine the recommended MRLs. In doing so, the highest average field trial (HAFT) data from each field trial site were entered into the calculator for all commodities. For crop groupings, the field trial data for the representative commodities were entered into the calculator and the highest recommended tolerance was selected for the entire crop group. In all, the residue definition and recommended MRLs are harmonized between Canada and the U.S.

2.3 Label Recommendations

All afidopyropen labels should be revised to specify that a 30-day PBI is required for rotation to non-labeled crops.

3.0 Introduction

Afidopyropen, company experimental name BAS 440 I, is a new insecticide active ingredient developed by the BASF corporation. It is undergoing NAFTA joint review with Canada for registration on a number of food uses and ornamentals. Afidopyropen is a non-systemic insecticide with contact activity that provides effective residual control of piercing-sucking pests such as aphids and whiteflies. Its mode of insecticidal action is as an insect behavior modifier that reduces feeding behavior. Afidopyropen is being proposed for foliar use on *Brassica* head and stem vegetable crop group 5-16, citrus fruit crop group 10-10, cotton, cucurbit vegetable crop group 9, fruiting vegetable crop group 8-10, leaf petioles vegetable subgroup 22B, leafy greens subgroup 4-16A, *Brassica* leafy greens subgroup 4-16B, pome fruit crop group 11-10, soybean, stone fruit crop group 12-12, tree nut crop group 14-12, tuberous and corm vegetable subgroup 1C and ornamentals.

3.1 Chemical Identity

The chemical structure and nomenclature of afidopyropen is presented below in Table 3.1.

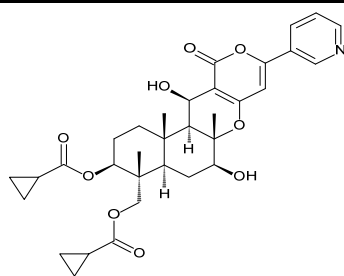
Table 3.1. Afidopyropen Nomenclature.	
Compound	
Afidopyropen	
Common name	Afidopyropen

Table 3.1. Afidopyropen Nomenclature.	
Company experimental name	BAS 440 I
IUPAC name	[(3 <i>S</i> ,4 <i>R</i> ,4 <i>aR</i> ,6 <i>S</i> ,6 <i>aS</i> ,12 <i>R</i> ,12 <i>aS</i> ,12 <i>bS</i>)-3-(cyclopropylcarbonyloxy)-1,2,3,4,4 <i>a</i> ,5,6,6 <i>a</i> ,12,12 <i>a</i> ,12 <i>b</i> -decahydro-6,12-dihydroxy-4,6 <i>a</i> ,12 <i>b</i> -trimethyl-11-oxo-9-(3-pyridyl)-11 <i>H</i> ,12 <i>H</i> -benzo[<i>f</i>]pyrano[4,3- <i>b</i>]chromen-4-yl]methyl cyclopropanecarboxylate
CAS name	[(3 <i>S</i> ,4 <i>R</i> ,4 <i>aR</i> ,6 <i>S</i> ,6 <i>aS</i> ,12 <i>R</i> ,12 <i>aS</i> ,12 <i>bS</i>)-3-[(cyclopropylcarbonyl)oxy]-1,3,4,4 <i>a</i> ,5,6 <i>a</i> ,12,12 <i>a</i> ,12 <i>b</i> -decahydro-6,12-dihydroxy-4,6 <i>a</i> ,12 <i>b</i> -trimethyl-11-oxo-9-(3-pyridinyl)2 <i>H</i> ,11 <i>H</i> -naphtho[2,1- <i>b</i>]pyrano[3,4- <i>e</i>]pyran-4-yl]methyl cyclopropanecarboxylate
CAS #	915972-17-7
End-use product/EP	EPA Reg. No. 7969-GIO(389) Versys™ Insecticide EPA Reg. No. 7969-GOG(393) Ventigra™ Insecticide EPA Reg. No. 7969-GOR(391) Sefina™ Insecticide

3.2 Physical/Chemical Characteristics

The physical/chemical characteristics of afidopyropen are presented below in Table 3.2.

Table 3.2. Physicochemical Properties of the Technical Grade Test Compound: Afidopyropen.		
Parameter	Value	Reference
Melting point/range	150 °C	MRID No. 49688912
Molecular mass (molecular formula)	C ₃₃ H ₃₉ NO ₉ MW: 593.7	MRID No. 49688922
pH	5.3 – 5.8	MRID No. 49688912
Density	1.300 g/cm ³	MRID No. 49688907
Aqueous solubility (20°C)	25.1 mg/L	MRID No. 49688920
Solvent solubility (mg/L at 25°C)	n-Hexane: 7.66 mg/L Toluene: 5.54 g/L Dichloromethane: > 500 g/L Acetone: > 500 g/L Methanol: > 500 g/L Ethyl Acetate: > 500 g/L	MRID No. 49688921
Vapor pressure (Torr)	<7.49x10 ⁻⁸ at 25 °C <1.13x10 ⁻⁷ at 50 °C	MRID No. 49688908
Henry's Law Constant (20°C, pH 7)	2.34x10 ⁻⁷ kPa·m ³ /mol 1.76x10 ⁻⁶ torr·m ³ /mol	MRID No. 49688909
Dissociation constant (pKa)	not determined	MRID No. 49688927
Log octanol-to-water partition coefficient (log K _{ow}) (20°C)	3.45	MRID No. 49688922
UV/visible absorption spectrum	In Methanol: 231 nm: ε = 20900 L mol ⁻¹ cm ⁻¹ 321 nm: ε = 13200 L mol ⁻¹ cm ⁻¹ In Aqueous Solution (pH 7.44): 231 nm: ε = 20900 L mol ⁻¹ cm ⁻¹ 317 nm: ε = 14100 L mol ⁻¹ cm ⁻¹ In Acidic Solution (pH 1.03): 231 nm: ε = 19100 L mol ⁻¹ cm ⁻¹ 330 nm: ε = 10700 L mol ⁻¹ cm ⁻¹ In Basic Solution (pH 13.36): 231 nm: ε = 21400 L mol ⁻¹ cm ⁻¹ 320 nm: ε = 13500 L mol ⁻¹ cm ⁻¹	MRID No. 49688914

Technical grade afidopyropen is an odorless solid (yellow powder) at room temperature and at all environmentally relevant temperatures. The compound is not volatile, so there is no likelihood for exposure to afidopyropen in the vapor phase. Afidopyropen is moderately soluble having an aqueous solubility value of 25.1 mg/L in pure water at 20°C. It also exhibits an octanol/water partition coefficient with a log K_{ow} value of 3.45 at 20°C which indicates it is lipophilic with an affinity to dissolve more readily in fats, oils, lipids, and non-polar solvents. This is exhibited in the supporting livestock metabolism and feeding study data which do show afidopyropen concentrations are highest in fat.

3.3 Pesticide Use Pattern/Directions for Use (860.1200)

B.7.6.1 Residues in Target Crops

The petitioner provided labels for the two end-use products of afidopyropen which are being proposed for registration. The petitioner used both the 100 g ai/L and 50 g ai/L dispersible concentrate formulations of afidopyropen for study in the field trials. No greenhouse uses were requested with this submission. If greenhouse uses are requested in the future, then additional data would be required. The proposed critical good agricultural practice (cGAP) use directions are detailed below in Table 3.3.

Table 3.3. Summary of Directions for Use of Afidopyropen.						
Applic. Timing, Type, and Equip.	EPA File Symbol Formulation	Max. Applic. Rate g ai/ha (lb ai/A)	Max. No. Applic. per Season	Max. Seasonal Applic. Rate g ai/ha (lb ai/A)	PHI (days)	Use Directions and Limitations
Cotton						
Ground, Aerial, and Chemigation	Sefina™ 50 g ai/L Dispersible Concentrate	10-50 (0.009-0.045)	NS	125 (0.11)	7	Apply in sufficient volume to coverage Begin applications at first sign of pest presence 7 day RTI
Fruits, Citrus, Group 10-10						
Ground, and Aerial	Sefina™ 50 g ai/L Dispersible Concentrate Versys™ 100 g ai/L Dispersible Concentrate	10-50 (0.009-0.045)	NS	125 (0.11)	0	Apply in sufficient volume to coverage Begin applications prior to first sign of infestation Do not use sprinkler irrigation 7 day RTI
Fruits, Pome, Group 11-10						
Ground, and Aerial	Versys™ 100 g ai/L Dispersible Concentrate	10-25 (0.009-0.022)	NS	50 (0.044)	7	Apply in sufficient volume to coverage Begin applications prior to first sign of infestation Do not use sprinkler irrigation 7 day RTI

Table 3.3. Summary of Directions for Use of Afidopyropen.						
Applic. Timing, Type, and Equip.	EPA File Symbol Formulation	Max. Applic. Rate g ai/ha (lb ai/A)	Max. No. Applic. per Season	Max. Seasonal Applic. Rate g ai/ha (lb ai/A)	PHI (days)	Use Directions and Limitations
Fruits, Stone, Group 12-12						
Ground, and Aerial	Versys™ 100 g ai/L Dispersible Concentrate	10 (0.009)	NS	20 (0.018)	7	Apply in sufficient volume to coverage Begin applications prior to first sign of infestation Do not use sprinkler irrigation 7-day RTI
Nuts, Tree, Group 14-12						
Ground, and Aerial	Versys™ 100 g ai/L Dispersible Concentrate Sefina™ 50 g ai/L Dispersible Concentrate	10 (0.009)	NS	20 (0.018)	7	Apply in sufficient volume to coverage Begin applications prior to first sign of infestation Do not use sprinkler irrigation 7-day RTI
Soybeans						
Ground, Aerial, and Chemigation	Sefina™ 50 g ai/L Dispersible Concentrate	10 (0.009)	NS	20 (0.018)	7	Begin applications at first sign of pest presence 7-day RTI Do not feed or graze soybean hay or forage
Vegetables, Brassica, head and Stem Group 5-16						
Ground, Aerial, and Chemigation	Versys™ 100 g ai/L Dispersible Concentrate	10-50 (0.009-0.045)	NS	125 (0.11)	0	Apply in sufficient volume to coverage Begin applications prior to first sign of pest presence 7-day RTI
Vegetables, Cucurbit, Group 9						
Ground, Aerial, and Chemigation	Versys™ 100 g ai/L Dispersible Concentrate Sefina™ 50 g ai/L Dispersible Concentrate	10-50 (0.009-0.045)	NS	125 (0.11)	0	Apply in sufficient volume to coverage Begin applications prior to first sign of pest presence 7-day RTI

Table 3.3. Summary of Directions for Use of Afidopyropen.						
Applic. Timing, Type, and Equip.	EPA File Symbol Formulation	Max. Applic. Rate g ai/ha (lb ai/A)	Max. No. Applic. per Season	Max. Seasonal Applic. Rate g ai/ha (lb ai/A)	PHI (days)	Use Directions and Limitations
Vegetables, Fruiting, Group 8-10						
Ground, Aerial, and Chemigation	Versys™ 100 g ai/L Dispersible Concentrate	10-50 (0.009-0.045)	NS	125 (0.11)	0	Apply in sufficient volume to coverage Begin applications prior to first sign of pest presence 7-day RTI
	Sefina™ 50 g ai/L Dispersible Concentrate					
Vegetables, Leaf Petioles, Subgroup 22B						
Ground, Aerial, and Chemigation	Versys™ 100 g ai/L Dispersible Concentrate	10-50 (0.009-0.045)	NS	125 (0.11)	0	Apply in sufficient volume to coverage Begin applications prior to first sign of pest presence 7-day RTI
Vegetables, Leafy Greens, Subgroup 4-16A						
Ground, Aerial, and Chemigation	Versys™ 100 g ai/L Dispersible Concentrate	10-50 (0.009-0.045)	NS	125 (0.11)	0	Apply in sufficient volume to coverage Begin applications prior to first sign of pest presence 7-day RTI
Vegetables, Brassica Leafy Greens, Subgroup 4-16B						
Ground, Aerial, and Chemigation	Versys™ 100 g ai/L Dispersible Concentrate	10-50 (0.009-0.045)	NS	125 (0.11)	0	Apply in sufficient volume to coverage Begin applications prior to first sign of pest presence 7-day RTI
Vegetables, Tuberous and Corm, Subgroup 1C						
Ground, Aerial, and Chemigation	Sefina™ 50 g ai/L Dispersible Concentrate	10-50 (0.009-0.045)	NS	125 (0.11)	7	Apply in sufficient volume to coverage Begin applications prior to first sign of infestation 7-day RTI
	Versys™ 100 g ai/L Dispersible Concentrate					

Conclusions: The submitted use directions are adequate to allow evaluation of the residue data relative to the proposed uses. Refer to section 2.3 for recommended modifications to the proposed labels.

4.0 Metabolite/Degradate Residue Profile

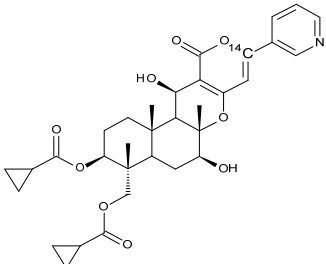
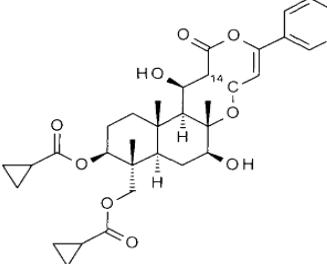
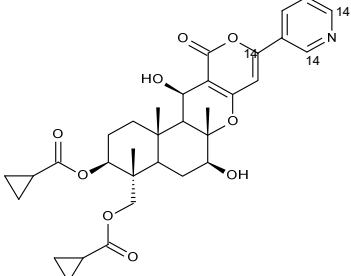
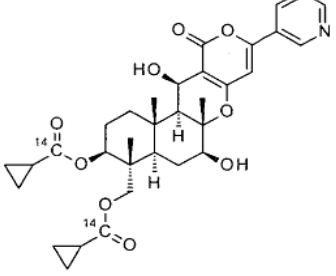
4.1 Nature of the Residue

4.1.1 Summary of Plant Metabolism (860.1300)

B.7.1 Metabolism, Distribution and Expression of Residues in Plants

The metabolism of afidopyropen (BAS 440 I) was investigated in commodities from three different crop categories, tomato (fruits), cabbage (leafy crops), and soybean (pulses and oilseeds). These studies were performed with radiolabeled ^{14}C -afidopyropen. Four different radiolabels were used in the studies. Each commodity was investigated with at least two different radiolabeled afidopyropen test substances. Tomato and cabbage studies were done with the radiolabel on the nicotinic acid position (^{14}C -NCA label). Tomato and cabbage studies were also done with the label on the pyranone-4- ^{14}C position (pyranone-4- ^{14}C label). Soybean metabolism was investigated with test substances using three different radiolabels. These studies were conducted with the pyranone label and ^{14}C -NCA label (multiply labeled on pyranone-6- ^{14}C , pyridine-2,6- ^{14}C) along with the carbonyl labeled on both cyclopropane carboxylic acid groups (CPCA- ^{14}C label). The locations of the radiolabel in the test substances used in the metabolism studies are shown below in Table 4.1.1.

Table 4.1.1. Radiolabeled Test Substances Used in Plant Metabolism Studies.

	
<p>Short name: Nicotinic Acid label Label position: nicotinic acid 9-^{14}C- Also described as pyranone -6-^{14}C Tomato, cabbage</p>	<p>Short name: Pyranone label Label position: pyranone-4-^{14}C Tomato, cabbage, soybean</p>
	
<p>Short name: Nicotinic acid label Label position pyranone-6-^{14}C, pyridine-2,6-^{14}C Soybean</p>	<p>Short name: cyclopropane carboxylic acid label or CPCA-^{14}C label Label position: carbonyl of both cyclopropane carboxylic acid groups Soybean</p>

4.1.1.1 Tomato [Nicotinic Acid Position (^{14}C -NCA Label)]

The metabolism of afidopyropen was investigated in tomato using radiolabeled nicotinic acid-9- ^{14}C -afidopyropen (^{14}C -NCA label). During the experimental period, the plants were located

indoors in a glasshouse. For testing, one at-planting soil application was done at 406 g ai/ha (0.362 lbs ai/A). This was followed by two sequential, late-season broadcast foliar sprays of 144 g ai/ha/application (0.129 lbs ai/A/application) and 157 g ai/ha/application (0.134 lbs ai/A/application), with 55- and 14-day retreatment intervals, for a total of 0.707 kg ai/ha (0.631 lbs ai/A). The two foliar applications were made at fruiting, 21 and 7 days before the first harvest (7-day PHI) and 28 and 14 days before the second “mature” harvest (14-day PHI). Samples of tomato fruit were harvested 7 and 14 days after the last application (DALA) and leaves were harvested at 14 DALA. Table 4.1.1.1 summarizes the reported results for foliar applications to tomatoes.

The overall total radioactive residues (TRRs) were 0.336 and 0.300 ppm in fruit harvested at 7 and 14 DALA, respectively, and 4.296 ppm in leaves at 14 DALA. Collectively, a substantial amount of the radioactivity was removed from both the fruit and leaves by the surface rinse with acetonitrile (fruit 27.9% and 12.1% of the TRRs and leaf 22.0% of the TRRs) and by solvent extraction with acetone:water (fruit 53.6% and 65.2% of the TRRs and leaf 54.7% of the TRRs). The radioactivity in the post-extraction solids was 18.5% and 22.7% of the TRRs in tomato fruit and 23.3% of the TRRs in tomato leaf and were not analyzed further (≤ 0.06 ppm).

[^{14}C]-Afidopyropen decreased in/on fruit from 32.1% of the TRRs at 7 DALA to 16.1% of the TRRs at 14 DALA. M440I007, a dimer of afidopyropen likely formed by photo-transformation on the plant surface, accounted for 10.2% of the TRRs in fruit at 7 DALA and 6.7% of the TRRs at 14 DALA. Except for afidopyropen and M440I007, the level of radioactive components in the surface rinses and the organosoluble fraction, as characterized by solid-phase extraction (SPE) followed by high-performance liquid chromatography (HPLC) fractionation analysis, was $\leq 2.9\%$ of the TRRs (0.009 ppm), for each fraction. The aqueous-soluble ^{14}C -residues, characterized by ion exchange columns, contained trace amounts of nicotinic acid, detected in the acidic fraction. Overall accountabilities ranged from 96% to 98%.

The metabolism of afidopyropen included dimerization to form M440I007. Cleavage of the ring system also occurred to form nicotinic acid and numerous unidentified minor components, including metabolites with a range of polarities and others which were incorporated into natural products.

Compound	Fruit, 7 DALA (TRR=0.3363 ppm)		Fruit, 14 DALA (TRR=0.3004 ppm)		Leaves, 14 DALA (TRR=4.2961 ppm)	
	%TRR	ppm	%TRR	ppm	%TRR	ppm
Afidopyropen	32.09	0.1079	16.12	0.0484	24.76	1.0443
M440I007	10.22	0.0344	6.70	0.0201	15.20	0.6277
Nicotinic acid	Trace	--	Trace	--	--	--
Total identified	42.31	0.1423	22.82	0.0685	39.96	1.672
Total characterized	37.31	0.1255	69.74	0.2096	55.69	2.438
Total extractable	79.62	0.2678	92.56	0.2781	95.65	4.110
Unextractable (PES)	18.54 ¹	0.0623	3.30	0.0099	0.07	0.0032
Accountability (calculated TRR)²	98%		96%		96%	

1. Not further fractionated / analyzed.

2. Accountability = (Total extractable, ppm + Total unextractable, ppm)/(calculated TRR, ppm) * 100.

4.1.1.2 Tomato (Pyranone-4-¹⁴C Label)

The metabolism of afidopyropen was investigated in tomato using radiolabeled afidopyropen at position 4 of the pyranone ring (pyranone-4-¹⁴C label). Tomato plants were treated twice using an automatic spray track system at 62.5 g ai/ha (0.056 lbs ai/A) for a total rate of 125.0 g ai/ha (0.112 lbs ai/A), at 8 days and 1-day PHI, respectively. The tomato plants were harvested 1 day after the last treatment and were separated into tomato fruits, tomato fruits (unripe) and tomato leaves. Leaves and stems were minced with scissors. The matrix tomato fruits (unripe) were not extracted. All samples were stored in a freezer at $\leq -18^{\circ}\text{C}$, and were extracted 83 days after sampling and the extracts were analyzed 16 days after extraction. Table 4.1.1.2 summarizes the reported results for foliar applications to tomatoes.

In tomato fruits and tomato leaves, parent afidopyropen was the most abundant component (0.033 ppm or 61.3 % of the TRRs and 0.63 ppm or 27.2 % of the TRRs, respectively). In tomato fruits, metabolites M440I007 and M440I020 were identified, but were significantly less abundant than the parent compound (≤ 0.008 ppm or ≤ 14.2 % of the TRRs). In tomato leaves, metabolites M440I001, M440I019, M440I002, M440I017, M440I007, and M440I020 were identified, which were also significantly less abundant than the parent compound, each component ≤ 8.4 % of the TRRs (0.193 ppm). In tomato fruits, 80.8 % of the TRRs were identified and additional 8.7 % of the TRRs were characterized. In tomato leaves, 49.7 % of the TRRs were identified and additional 41.0 % of the TRRs were characterized.

This study showed afidopyropen is converted to some extent into the dimer M440I007 in tomato fruits and leaves and to very low levels of metabolites M440I001, M440I002, M440I017, M440I019, and M440I020 in tomato leaves. It also showed that in tomato leaves, very small amounts of afidopyropen are incorporated into carbohydrates and proteins.

Designation	Tomato fruits		Tomato leaves	
	[ppm]	[% of the TRRs]	[ppm]	[% of the TRRs]
Overall TRRs	0.054	100	2.307	100
Afidopyropen	0.033	61.3	0.627	27.2
M440I001	n.d.	n.d.	0.053	2.3
M440I019	n.d.	n.d.	0.071	3.1
M440I002	n.d.	n.d.	0.082	3.6
M440I017	n.d.	n.d.	0.193	8.4
M440I007	0.008	14.2	0.048	2.1
M440I020	0.003	5.3	0.070	3.0
Total identified	0.044	80.8	1.144	49.7
Total characterized	0.005	8.7	0.945	41.0
Total extractables	0.049	89.5	2.089	90.7
PES	0.007	13.2	0.219	9.5
Accountability	103.7		100	

n.d. not detected

4.1.1.3 Cabbage [Nicotinic Acid Position (¹⁴C-NCA Label)]

The metabolism of afidopyropen was investigated in cabbage after one at-planting soil application followed by two sequential, late-season broadcast foliar sprays using ¹⁴C-NCA radiolabeled afidopyropen. Cabbage seedlings at the 4-5 leaf stage (BBCH growth stage 14-15) were transplanted into four plastic containers filled with sandy loam soil located outdoors in a netted tunnel. Application rates were 844 g ai/ha (0.753 lbs ai/A) for the soil application and 144 g ai/ha (0.128 lbs ai/A) and 151 g ai/ha (0.135 lbs ai/A) for the foliar applications. These applications were made at 163- and 14-day retreatment intervals, for a total rate of 1.14 kg ai/ha (1.02 lbs ai/A). The foliar applications were made during the development of harvestable vegetative plant parts (BBCH growth stage not reported), 21 and 7 days before the first harvest, and 28 and 14 days before the second “mature” harvest. Samples of whole cabbage plants were harvested 7 and 14 days after the last application (DALA) and separated into outer leaves and head portions. Table 4.1.1.3 summarizes the reported results for foliar applications to tomatoes.

At 7 DALA, overall TRRs were 1.47 ppm in cabbage (0.685 ppm in surface washes; 0.644 ppm in washed outer leaves; and 0.141 ppm in heads). At 14 DALA, TRRs declined to 1.06 ppm in cabbage (0.462 ppm in surface washes; 0.516 ppm in washed outer leaves; and 0.083 ppm in heads). The TRRs characterized as natural products accounted for 10.7% (0.158 ppm) and 13.9% (0.147 ppm) of the TRRs in cabbage harvested at 7-DALA and 14-DALA, respectively. The total identified radioactivity accounted for 44.0% (0.642 ppm) and 27.4% (0.292 ppm) of the TRRs in cabbage harvested at 7-DALA and 14-DALA, respectively.

At intermediate harvest, unchanged parent afidopyropen accounted for a total of 13.8% of the TRRs (0.202 ppm) in cabbage heads, and 2.8% of the TRRs (0.041 ppm) in washed outer leaves. M440I007 was a major component, accounting for a total of 16.7% of the TRRs (0.244 ppm) in cabbage heads, and 2.2% of the TRRs (0.032 ppm) in washed outer leaves. In the polar fraction, nicotinamide accounted for 2.8% of the TRRs (0.041 ppm) in heads and 7.0% of the TRRs (0.102 ppm) in washed outer leaves. Nicotinic acid represented 0.7% of the TRRs (0.010 ppm) and 3.0% of the TRRs (0.043 ppm) in heads and washed outer leaves, respectively. Unidentified polar components individually accounted for a total of ≤2.0% of the TRRs (≤0.029 ppm). A total of 15 other minor components were observed, each accounting for a total of ≤3.4% of the TRRs (≤0.050 ppm).

At final harvest, afidopyropen accounted for a total of 6.9% of the TRRs (0.073 ppm) in cabbage heads, and 1.6% of the TRRs (0.017 ppm) in washed outer leaves. M440I007 accounted for a total of 9.9% of the TRRs (0.105 ppm) in cabbage heads, and 1.6% of the TRRs (0.017 ppm) in washed outer leaves. In the polar fraction, nicotinamide and nicotinic acid respectively represented 2.7% of the TRRs (0.029 ppm) and 0.3% of the TRRs (0.004 ppm) in heads, and 5.4% of the TRRs (0.058 ppm) and 2.2% of the TRRs (0.023 ppm) in washed outer leaves. Unidentified polar components individually accounted for a total of 13.5% of the TRRs (0.143 ppm). All other components (15 in total) each accounted for a total of ≤3.7% of the TRRs (≤0.039 ppm).

The ¹⁴C-residues in post-extraction solids (after solvent extraction and/or exhaustive extraction of bound residues) were insignificant, accounting for 1% of the TRRs (0.011-0.015 ppm). The metabolism of afidopyropen included dimerization to form M440I007. Cleavage of the ring system also occurred to form nicotinamide, nicotinic acid and numerous unidentified minor components, including polar metabolites and incorporation into natural products.

Table 4.1.1.3. Summary of characterization and identification of radioactive residues in cabbage harvested 7 or 14 days after the last application of NCA-¹⁴C-Afidopyropen.				
Compound	Cabbage, 7 DALA		Cabbage, 14 DALA	
	TRR=1.47 ppm		TRR=1.06 ppm	
	%TRR	ppm	%TRR	ppm
Afidopyropen	13.8	0.202	6.9	0.073
M440I007	16.7	0.244	9.9	0.105
1. M440I044 (Nicotinamide)	9.8	0.143	8.1	0.087
M440I045 (Nicotinic acid)	3.7	0.053	2.5	0.027
Total identified	44.0	0.642	27.4	0.292
Total characterized	52.2	0.767	72.3	0.766
By HPLC / TLC	41.4	0.610	58.4	0.619
Exhaustive Extraction of Bound Residues (pectin, lignin, hemicellulose, cellulose)	10.7	0.158	13.9	0.147
Total extractable	96.2	1.41	99.7	1.06
Final Unextractable (PES)	1.0	0.015	1.0	0.011
%Accountability (calculated TRR)	97		101	

Accountability = (Total extractable + Total unextractable)/(calculated TRR) * 100.

4.1.1.4 Cabbage (Pyranone-4-¹⁴C Label)

The metabolism of afidopyropen was investigated in greenhouse cabbage using radiolabeled afidopyropen at position 4 of the pyranone ring (pyranone-4-¹⁴C label). The cabbage plants were treated with two 62.5 g ai/ha (0.056 lbs ai/A) spray applications for a total rate of 125.0 g ai/ha (0.112 lbs ai/A). The cabbage heads were harvested 1 day after the last treatment and separated into outer and inner leaves. The TRRs were 1.751 ppm for cabbage outer leaves and 0.436 ppm for cabbage head leaves. The extractability with methanol and water accounted for 83.2 % of the TRRs for cabbage outer leaves and 86.4 % of the TRRs for cabbage inner leaves. Table 4.1.1.4 summarizes the reported results for foliar applications to tomatoes.

In cabbage outer leaves and cabbage inner leaves, parent afidopyropen was the most abundant component (0.398 ppm or 22.7 % of the TRRs and 0.094 ppm or 21.6 % of the TRRs, respectively). Metabolite M440I007, the predominant metabolite, was identified in cabbage outer leaves and cabbage inner leaves; in cabbage inner leaves it was less abundant than in cabbage outer leaves (0.060 ppm or 13.8 % of the TRRs vs 0.302 ppm or 17.3 % of the TRRs). In cabbage outer leaves, metabolite M440I017 was identified (0.037 ppm or 2.1 % of the TRRs), which was significantly less abundant than the parent compound and M440I007; it was also detected in cabbage inner leaves (0.012 ppm or 2.8 % of the TRRs). Carbohydrates, as sugars, were identified in cabbage outer leaves (0.167 ppm or 9.5 % of the TRRs) and cabbage inner leaves (0.062 ppm or 14.2 % of the TRRs).

In cabbage outer leaves, 0.933 ppm or 53.3 % of the TRRs were identified and additional 0.713 ppm or 40.7 % of the TRRs were characterized. In cabbage inner leaves, 0.240 ppm or 55.0 % of the TRRs were identified and additional 0.170 ppm or 38.9 % of the TRRs were characterized.

Afidopyropen was metabolized to an extent in cabbage but was still the predominant residue. The M440I007 dimer was the main metabolite in both the outer and inner leaves; low levels of the N-oxide metabolite M440I017 were also seen in cabbage outer and inner leaves. The study also found low amounts of ¹⁴C- residues were incorporated into carbohydrates, indicating some degradation of the parent afidopyropen molecule with incorporation of small fragments into natural products.

Table 4.1.1.4. Summary of characterization and identification of radioactive residues in cabbage harvested 1 day after the last application of Pyranone-4-¹⁴C-Afidopyropen.				
Designation	Cabbage outer leaves [TRR = 1.751 ppm]		Cabbage inner leaves [TRR = 0.436 ppm]	
	[ppm]	[% of the TRRs]	[ppm]	[% of the TRRs]
Carbohydrates	0.167	9.5	0.062	14.2
M440I017	0.037	2.1	0.012	2.8
BAS 440 I	0.398	22.7	0.094	21.6
M440I020	0.029	1.6	0.011	2.6
M440I007	0.302	17.3	0.060	13.8
Total identified	0.933	53.3	0.240	55.0
Total characterized	0.713	40.6	0.169	38.9
Final PES	0.100	5.7	0.026	6.0
%Accountability	1.746	99.7	0.435	99.8

Accountability = (Total extractable + Total unextractable)/(calculated TRR) * 100.

4.1.1.5 Cabbage (Pyranone-6-¹⁴C Label)

The metabolism of afidopyropen was previously investigated in cabbage with the ¹⁴C-NCA radiolabel (also described as pyranone-6-¹⁴C) characterized the trigonelline metabolite in cabbage leaves which was also identified in the soybean metabolism study. To investigate the possible presence of trigonelline in cabbage matrices, a study was initiated to further analyze homogenized cabbage leaf samples and surface washes. For this study, cabbage plants were treated with ¹⁴C-afidopyropen labeled at position 6 of the pyranone ring (pyranone-6-¹⁴C label). Treatments were made as a 0.844 kg ai/ha (0.753 lbs ai/A) soil application at planting followed by two foliar applications of 0.150 kg ai/ha (0.134 lbs ai/A) at 7 and 14 days before harvest of the mature cabbage.

The extractability of washed cabbage outer leaves was 82.3 % of the TRRs (0.892 ppm) when extracted with methanol and water from the washed outer leaves. The major part of radioactivity was extracted with methanol (69.6 % of the TRRs), with smaller amounts extracted with water (12.7 % of the TRRs). Analysis of the polar fraction of the methanol extract of the cabbage outer leaves using HPLC method LC01 resulted in a pattern of 17 peaks. M440I031 was identified as trigonelline by co-chromatography using a reference item, and comprised 7% of the TRRs.

4.1.1.6 Soybean [Nicotinic Acid Position (¹⁴C-NCA) & Pyranone-4-¹⁴C Labels]

The metabolism of afidopyropen was investigated in soybean after post-emergence spray application of a radiolabeled test product made as two 62.5 g ai/ha (0.056 lb ai/A) treatments. For this metabolism study, afidopyropen was either ¹⁴C-labeled in the pyranone and pyridine ring (pyranone-6-¹⁴C, pyridine-2,6-¹⁴C, Nicotinic Acid label) or only in the pyranone ring (pyranone-4-¹⁴C, Pyranone Label). The soybean plants were harvested 14 days after the last treatment and were separated into leaf, seed, pod and rest of plant. Table 4.1.1.6 summarizes the reported results for foliar applications to tomatoes.

Fractionation and isolation from a soybean leaf methanol extract (Pyranone Label) followed by HPLC-MS analysis led to the identification of an isomer of afidopyropen and metabolites

M440I033, M440I014, M440I022 (label-specific) and M440I007. In soybean seed (Nicotinic Acid Label), the label-specific metabolite M440I031 (trigonelline), was identified as the predominant residue. In the soybean leaf and pod, trigonelline (M440I031) / Polar Components and parent afidopyropen, M440I007 were the predominant residues for the Nicotinic Acid Label, and afidopyropen and M440I007 were the predominant residues for the Pyranone Label. The level of the afidopyropen isomer and metabolites M440I033, M440I014 and M440I022 did not exceed 4.0 % of the TRRs in either label.

The metabolism in soybean showed afidopyropen is converted to the dimer M440I007, trigonelline / carbohydrates and low levels of an isomer of afidopyropen and metabolites M440I033, M440I014 and M440I022 in soybean plant leaves and to trigonelline and carbohydrates in the soybean seed. Trigonelline, a product of niacin metabolism, occurs naturally in a wide range of plants, particularly in legumes.

Table 4.1.1.6. Summary of identified/characterized components in soybean matrices from the NCA-¹⁴C and Pyranone-4-¹⁴C-Afidopyropen labels.								
Component	Leaves		Seeds		Hulls		Rest of Plants	
	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR
	TRR=16.859 ppm		TRR=0.378 ppm		TRR=1.507 ppm		TRR=0.401 ppm	
Nicotinic Acid Label								
Afidopyropen	2.944	17.5	n.d.	n.d.	0.189	12.6	0.033	8.2
M440I031	0.432	2.6	0.179	47.3	n.a.	n.a.	n.a.	n.a.
M440I033	0.216	1.3	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
M440I014	0.421	2.5	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
M440I007	2.566	15.2	n.d.	n.d.	0.397	26.3	0.055	13.7
Total extractables	13.850	82.2	0.361	95.1	1.330	88.1	0.367	91.5
Total identified	5.940	35.2	0.179	47.3	0.587	38.9	0.330	69.5
Total characterized	7.910	47.0	0.182	47.8	0.743	49.2	0.037	22.0
Remaining bound (PES)	2.861	17.0	0.014	3.7	0.262	17.4	0.032	8.0
Accountability %*	99		99		106		100	
Pyranone-4-¹⁴C Label								
	TRR=20.076 ppm		TRR=0.166 ppm		TRR=1.567 ppm		TRR=0.356 ppm	
Afidopyropen	3.800	18.9	0.001	0.4	0.278	17.8	0.063	17.7
Carbohydrates	0.892	4.4	0.069	41.6	0.120	7.7	0.050	13.9
M440I033	0.148	0.7	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
M440I007	3.532	17.6	0.002	1.0	0.782	49.9	0.136	38.1
Total extractables	16.761	83.5	0.132	79.4	1.316	84.0	0.323	91.0
Total identified	8.3724	41.6	0.071	42.9	1.181	75.4	0.248	69.7
Total characterized	8.389	41.9	0.061	36.5	0.135	8.6	0.075	21.3
Remaining bound (PES)	3.073	15.3	0.028	16.7	0.292	18.6	0.026	7.2
Accountability %*	99		96		103		98	
<i>n.d. = not detected; n.a. = not applicable</i>								
<i>*Accountability = Sum of identified + characterized + PES (all in ppm)/overall TRR (ppm) x 100</i>								

4.1.1.7 Soybean (CPCA-¹⁴C Label)

The metabolism of afidopyropen was investigated in soybean using a radiolabeled CPCA-¹⁴C-afidopyropen following two spray applications of 62.5 g ai/ha (0.056 lb ai/A). The soybeans were grown in climatic chambers and harvested 14 days after the last treatment. The TRRs observed in the study were 4.965 ppm for soybean leaves, 2.603 ppm for soybean hulls (pods)

and 0.172 ppm for green pods. The TRRs in soybean seeds were significantly lower at 0.015 ppm. Extractability with methanol followed by water ranged from 57% of the TRRs for seed to 75% of the TRRs for leaves. Table 4.1.1.7 summarizes the reported results for foliar applications to tomatoes.

The study found afidopyropen was metabolized to only trace amounts of parent in the soybean seeds. In the methanol extract of soybean seeds, metabolite M440I007 was the only component identified using two HPLC systems (12.1 % of the TRRs; 0.002 ppm), while two other components were characterized as polar, each present at 0.002 ppm. In soybean leaves, hulls (pods) and green pods, parent afidopyropen and metabolite M440I007 were the predominant residues. In soybean leaves, metabolite M440I033, a glucoside of parent (1.5% of the TRRs), and M440I014, formed by dehydration of parent (3.9% of the TRRs), were also present as was a low level component identified as a sugar (1.6% of the TRRs). An isomer of afidopyropen, present in the application solution, was seen in leaves and hulls (≤ 4.1 % of the TRRs), and considered a contaminant.

The metabolism observed in soybeans found total residues in the seeds to be very low. It demonstrated afidopyropen is converted into the dimer M440I007, the only metabolite exceeding 10% of the TRRs, and into low levels of a glucoside of parent (M440I033), a dehydration product (M440I014) and very low levels of sugars.

Table 4.1.1.7. Summary of characterized and identified metabolites in soybean matrices treated with CPCA-¹⁴C.

Designation	Soybean seeds		Soybean leaves		Soybean hulls (pods)		Soybean green pods	
	[ppm]	[% of the TRRs]	[ppm]	[% of the TRRs]	[ppm]	[% of the TRRs]	[ppm]	[% of the TRRs]
	TRR= 0.015 ppm		TRR= 4.965 ppm		TRR= 2.603 ppm		TRR= 0.173 ppm	
M440I033	n.d.	n.d.	0.074	1.5	n.d.	n.d.	n.d.	n.d.
Afidopyropen	n.d.	n.d.	1.572	31.7	0.441	17.0	0.031	17.8
M440I014	n.d.	n.d.	0.193	3.9	0.029	1.1	n.d.	n.d.
M440I007	0.002	12.1	0.457	9.2	0.614	23.6	0.056	32.2
Total identified	0.002	12.1	2.375	47.9	1.084	41.7	0.087	50.0
Total characterized	0.011	75.0	1.634	32.9	0.904	34.7	0.052	29.8
Final PES	0.001	5.9	0.636	12.8	0.423	16.3	0.029	16.7
Accountability (%)*	93		94		93		97	

n.d. not detected

*Accountability = Identified (ppm) + Characterized (ppm) + PES (ppm)/Overall TRR (ppm) * 100

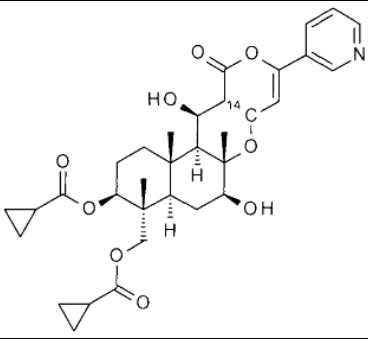
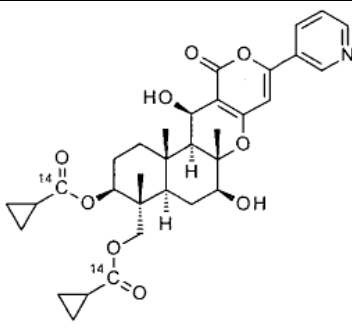
Conclusions: The submitted plant metabolism studies for afidopyropen are adequate to satisfy data requirements. The petitioner has provided plant metabolism studies in three diverse crops (tomato, cabbage, and soybean). In addition, a confined rotational crop study is also available for depicting the nature of the residue in root vegetables as well. Based upon these studies, the nature of the residue of afidopyropen is concluded to be adequately understood in plants.

4.1.2 Summary of Livestock Metabolism (860.1300)

B.7.2 Metabolism, Distribution and Expressions of Residues in Livestock (Annex IIA 6.2)

The metabolism of afidopyropen was investigated in the laying hen and lactating goat. One goat

study was performed with ^{14}C -afidopyropen with the label on the pyranone-4- ^{14}C position (pyranone label). The hen study and a second goat study were done with the label on the carbonyl of both cyclopropane carboxylic acid groups (CPCA- ^{14}C label). The locations of the radiolabel in the test substances used in the metabolism studies are shown below in Table 4.1.2.

Table 4.1.2. Radiolabeled Test Substances Used in Livestock Metabolism Studies.

Short name: Pyranone label Label position: Pyranone-4- ^{14}C goat
Table 4.1.2. Radiolabeled Test Substances Used in Livestock Metabolism Studies.

Short name: Cyclopropane carboxylic acid label or CPCA label Label position: Carbonyl of both cyclopropane carboxylic acid groups goat, hen

4.1.2.1 Poultry Metabolism (Laying Hen CPCA- ^{14}C Label)

The metabolism of afidopyropen was investigated in poultry by dosing ten laying hens with radiolabeled CPCA- ^{14}C -afidopyropen for 14 consecutive days at a level of 12 ppm dry feed (12000x). The radiolabel was in both carbonyl carbons of the cyclopropylcarbonyl esters. The carbon-14 labeled form of afidopyropen was radiodiluted with ^{14}C -afidopyropen and non-radiolabeled afidopyropen at a ratio of 4:3:3. The final specific activity of the radiolabeled afidopyropen was 2.99 MBq/mg. Dose capsules were prepared daily for each hen based on the previous day's food consumption. Hens were offered commercially available concentrate ad libitum throughout the acclimatization and dosing period. Tables 4.1.2.1.1-4.1.2.1.3 summarize the reported results of the residues found in the hen matrices.

Eggs were collected during the dosing period at least twice daily (am and pm) until sacrifice. Excreta were collected from the metabolism cages, along with cage washes for total radioactivity analysis. Approximately 10 hours after administration of the final dose, the hens were sacrificed for analysis. Edible tissues (liver, kidney, peritoneal fat, skin with fat, combined leg and thigh muscle, breast muscle, GI tract and contents, bile, blood and carcass) were collected post mortem. Composite egg white, egg yolk and excreta samples were prepared by pooling samples

from Day 10-13. Liver, muscle, egg white and excreta were extracted with methanol and water, and fat and egg yolk were extracted with dichloromethane, methanol and water.

The overall TRRs were 0.409 ppm in liver, 0.046 ppm in muscle, and 0.101 ppm in fat. Radioactive residues in egg white and egg yolk were 0.138 ppm and 0.368 ppm; respectively, from Day 10-13. TRRs reached a maximum of 0.275 ppm in whole eggs on day 7 of dosing.

The extractability of tissues ranged from 85.4% of the TRRs for liver to 99.3% of the TRRs for fat. Extractability was also high in eggs, ranging from 98.8% (egg white) to 99.4% (egg yolk) of the TRRs. The predominant residues identified in liver extract were afidopyropen (0.241 ppm; 59.1% of the TRRs) and the metabolite M440I017 (0.085 ppm; 20.9% of the TRRs), with the cyclopropane carboxylic acid metabolite M440I061 as a minor component (CPCA, 0.017 ppm; 4.1% of the TRRs). The major metabolites identified in muscle extract were afidopyropen (0.021 ppm; 46.5% of the TRRs), CPCA-carnitine metabolite M440I060 (0.017 ppm; 37.7% of the TRRs) and a minor metabolite (0.004 ppm; 9.0% of the TRRs), which was only characterized. The predominant residue identified in fat was afidopyropen (0.097 ppm; 96.1% of the TRRs) and a minor metabolite (0.002 ppm; 1.9% of the TRRs), which was only characterized. The predominant residue identified in egg white extract was afidopyropen (0.125 ppm; 90.5% of the TRRs) and a minor metabolite identified as M440I017 (0.007 ppm; 5.4% of the TRRs). Analysis of the egg yolk extract identified the major residue as BAS 440 I (0.355 ppm; 96.6% of the TRRs).

The metabolic pathway of afidopyropen in poultry included oxidation of the pyridine ring of afidopyropen to form the N-oxide, M40I017 as well as cleavage to form cyclopropane carboxylic acid (CPCA, M440I061), which further interacts with carnitine to form O-(cyclopropylcarbonyl)-carnitine (CPCA-carnitine, M440I060).

Designation	Liver		Muscle		Fat	
	ppm	%TRR	ppm	%TRR	ppm	%TRR
	TRR = 0.409 ppm		TRR = 0.046 ppm		TRR = 0.101 ppm	
Identified						
*MeOH:H ₂ O Extracts (liver, muscle) *DCM:MeOH, MeOH:H ₂ O Extracts (fat)	0.341	83.7	0.043	93.2	0.099	98.0
BAS 440 I (including protease/acid hydrolysis in liver)	0.241	59.1	0.021	46.5	0.097	96.1
(CPCA-carnitine) M440I060	--	--	0.017	37.7	--	--
(CPCA) M440I061	0.017	4.1	--	--	--	--
M440I017	0.085	20.9	--	--	--	--
Total Identified in Extractable Radioactivity	0.343	84.1	0.038	84.2	0.097	96.1
Other Radioactivity not Further Processed	0.011	2.6	0.002	5.4	0.001	1.3
Total Characterized	0.030	7.4	0.006	13.2	0.004	3.9
Post-Extraction Solid (PES)	0.060	14.6	0.001	1.4	0.001	0.7
Final Post-Extraction Solid (PES) After Protease Extraction	0.031	7.5	--	--	--	--
% Accountability**	101		102		102	

*The TRR values (% and mg equiv./kg) reported are slightly different from Table B.7.2.1-7 as they are based on the TRRs measured after workup of the extracts analyzed by HPLC.

**%Accountability = Total ppm (identified + characterized + PES)/Overall TRR ppm * 100

Table 4.1.2.1.2. Summary of identified and characterized ¹⁴C-residues extracted from egg yolk and egg white after 14 daily doses of [¹⁴C-CPCA]-Afidopyropen at 12 ppm feed (12000x).				
Designation	Egg Yolk		Egg White	
	ppm	%TRR	ppm	%TRR
	TRR = 0.368 ppm		TRR = 0.138 ppm	
Identified				
Methanol: Water Extract	0.365	99.4	1.36	98.8
BAS 440 I	0.355	96.6	0.125	90.5
M440I017			0.007	5.4
Total Identified in Extractable Radioactivity	0.355	96.6	0.132	95.9
Other Radioactivity not Further Processed	0.010	2.8	0.004	2.9
Total Characterized	0.007	1.8	--	--
Post-Extraction Solid (PES)	0.003	0.7	0.002	1.3
% Accountability (total ppm/TRR ppm * 100)	102		100	

Table 4.1.2.1.3. Summary of Identified and Characterized ¹⁴C-Residues Extracted from Excreta after 14 Daily Doses of [¹⁴C-CPCA]-Afidopyropen at 12 ppm (12000x).		
Designation	Excreta	
	% of Administered Dose	% of the TRR
Identified		
Methanol:Water Extract	25.3	93.5
BAS 440 I	13.3	49.2
M440I017	12.0	44.3
Total Identified in Extractable Radioactivity	25.3	93.5
Other Radioactivity not Further Processed	0.7	2.4
Total Characterized	<0.1	0.1
Post-Extraction Solid (PES)	1.1	4.1
Grand Total	27.1	100.1

4.1.2.2 Ruminant Metabolism (Lactating Goat Pyranone-4-¹⁴C Label)

The metabolism of afidopyropen was investigated in ruminants by dosing a single lactating goat using radiolabeled afidopyropen at position 4 of the pyranone ring (pyranone-4-¹⁴C label). The lactating goat was dosed for seven consecutive days at an average of 17.3 mg [¹⁴C]-afidopyropen per kg food consumed (dry weight equivalent; 1790x), with a specific activity of 1.79 MBq/mg. Urine and feces samples were collected for the 24-hour period prior to first dose and for each 24-hour period until sacrifice. The goat was milked twice daily and immediately prior to sacrifice. At approximately 8 hours after the final dose the goat was sacrificed and edible tissues (liver, kidney, muscle and fat), bile, blood and the GI tract were collected for analysis. Tables 4.1.2.2.1-4.1.2.2.2 summarize the reported results of the residues found in the goat matrices.

Approximately 91% of the total dose was recovered, the majority of which was present in the feces (66.5%) and GI tract contents (20.7%). Relatively low amounts were recovered in urine (2.5%) and cage wash (1.4%). Radioactivity associated with edible portions (milk and tissues) accounted in total for ≤0.1% of the administered dose.

The extractability of residues was acceptable in milk and tissues ranging from 94.1% of the TRRs to 97.6% of the TRRs. The remaining post-extraction solids (PES) in milk and tissues ranged from 2.4% to 10.8% of the TRRs. The overall radioactive residues (TRR calculated) were highest in liver (0.193 ppm), with lower residues in kidney (0.037 ppm), composite muscle (0.008 ppm), composite fat (0.005 ppm), and milk (0.006 ppm). The overall residues were also higher in the pooled feces samples (5.012 ppm), with lower residues in bile (3.223 ppm), and urine (0.292 ppm).

[Pyranone-4-¹⁴C]-afidopyropen was extensively metabolized in the lactating goat. The unchanged parent was not detected in samples of urine and bile and was found in portions below 35% of the TRRs in matrices, except in composite fat where parent comprised 49% of the TRRs. The main component in extracts of milk, liver, and kidney and a significant component in muscle was M440I001, formed by hydrolytic cleavage of ester bonds of both cyclopropyl carboxylic acid moieties. The metabolite M440I003, formed by ester cleavage of one cyclopropyl carboxylic acid moiety, was present in significant levels in muscle and kidney. In milk, in addition to the de-esterification to form the predominant metabolite M440I001, the metabolic transformation involved oxidation of an alcohol group of the metabolite M440I002 or M440I003 to give rise to the ketone metabolite M440I005 or M440I006, respectively. Transformations involving oxidation of the same alcohol group to the ketone metabolite M440I004 occurred at low levels in liver and to the ketone metabolite M440I006 at low levels in muscle and fat.

Component	Composite Whole Milk		Liver		Kidney		Composite Muscle		Composite Fat	
	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR
	TRR = 0.005		TRR = 0.193		TRR = 0.037		TRR = 0.008		TRR = 0.005	
Total Extractables ¹	0.006	77.9	0.176	90.7	0.036	99.1	0.007	87.5	0.003	67.2
Afidopyropen	<0.001	6.8	0.068	35.0	0.006	16.6	0.002	26.3	0.002	49.3
M440I001	0.002	45.0	0.089	46.3	0.025	65.8	0.002	23.5	<0.001	4.6
M440I002	--	--	0.004	2.1	--	--	--	--	--	--
M440I003	<0.001	3.6	0.009	4.4	0.005	12.1	0.002	22.4	<0.001	8.1
M440I004	--	--	0.006	2.9	--	--	--	--	--	--
M440I005	0.001	17.1	--	--	--	--	--	--	--	--
M440I006	<0.001	5.4	--	--	--	--	<0.001	5.3	<0.001	5.2
Total Identified	0.006	77.9	0.176	90.7	0.036	94.5	0.007	77.5	0.005	67.2
Unknowns	--	--	--	--	0.002	4.5	0.001	10.0	--	--
Post-Extraction Solid (PES)	<0.001	4.5	0.005	2.7	0.001	2.4	0.002	22.3	0.001	10.8
Protease hydrolysate	--	--	--	--	--	--	0.001	16.4	--	--
Remaining PES	--	--	--	--	--	--	0.001	9.9	--	--
% Accountability**	140		94		105		113		120	

¹The TRR values (% and mg equiv./kg) reported are different from Table B.7.2.2-7 as they are based on the TRRs measured after workup of the extracts analyzed by HPLC.

**The values less than LOQ were taken into account as absolute values only once. **%Accountability = Total ppm (identified + characterized + PES)/Overall TRR ppm * 100

Table 4.1.2.2.2. Pyranone-4-¹⁴C Labeled Afidopyropen Residues Identified and Characterized in Goat Urine, Feces, and Bile.

Component	Pooled Urine		Pooled Feces		Bile	
	ppm	%TRR	ppm	%TRR	ppm	%TRR
Afidopyropen	--	--	1.419	28.9	--	--
M440I001	0.110	57.1	0.847	17.3	1.099	34.1
M440I002	--	--	0.098	2.0	--	--
M440I003	--	--	0.357	7.3	--	--
M440I004	--	--	--	--	--	--
M440I005	--	--	--	--	--	--
M440I006	0.027	13.9	--	--	0.935	29.0
Total Identified	0.137	71.0	2.721	55.5	2.034	63.1
Total Characterized	0.057	29.0	--	--	1.19	36.9
Total Identified/Characterized	0.194	100	2.721	55.5	3.224	100

4.1.2.3 Ruminant Metabolism (Lactating Goat CPCA-¹⁴C Label)

The metabolism of afidopyropen was investigated in ruminants by dosing a single lactating goat with radiolabeled CPCA-¹⁴C-afidopyropen (CPCA-¹⁴C label). The lactating goat was dosed by capsule for 9 consecutive days at a nominal level of 12 ppm of test item per kg of feed (dry weight equivalent; 1200x). The carbon-14 labeled form of afidopyropen was radiodiluted with [¹⁴C]-afidopyropen and non-radiolabeled afidopyropen in a ratio of 2:4:3. Approximately 10 hours after administration of the final dose the goat was sacrificed for analysis. Edible tissues (liver, kidney, subcutaneous fat, omental fat, perirenal fat loin muscle, flank muscle, GI tract and contents, bile, blood and carcass) were collected post mortem. Tables 4.1.2.3.1-4.1.2.3.2 summarize the reported results of the residues found in the goat matrices.

Approximately 78.3% of the total dose was recovered with 49.9% in the feces, 13.2% in the urine and 0.1% in bile. A proportion remained in the GI tract (2.8%) and GI tract contents (7.3%). Radioactivity in the cage wash accounted for 2.3% of the administered dose. Radioactivity associated with edible portions (milk and tissues) accounted for 2.7% of the total dose.

Radioactivity in plasma rose steadily to a maximum of 0.011 ppm at 10 hours post first dose. Residues in the milk did not reach a plateau after 9 days of dosing. The ratio of residues associated with the skimmed milk and cream was determined in a representative 24-hour composite sample as 1:14 (0.185 ppm to 2.57 ppm).

Overall TRRs were determined by the sum of the extractable and non-extracted residues as 0.237 ppm (composite milk), 2.007 ppm (cream), 0.207 ppm (liver) and 0.479 ppm (kidney). Soluble radioactive residues extracted with methanol and methanol/water mixtures in milk and tissues ranged from 76.9% of the TRRs (0.182 ppm) in composite whole milk to 98.3% of the TRRs (0.306 ppm) in composite muscle.

Only 7.3% of the TRRs were identified in urine, with 79.9% of the TRRs characterized as polar components. Only minor metabolites were identified (<10% of the TRRs) as afidopyropen,

M440I002, M440I005, M440I017, M440I060, and M440I061. In feces, 45.3% of the TRRs were identified, whereas 8.6% of the TRRs were characterized. Afidopyropen was the predominant residue (33.5%) along with minor metabolites M440I002, M440I003, and M440I005.

A total of 70.8% of the TRRs were identified in liver, of which afidopyropen, M440I003, and M440I061 were predominant residues. Minor components were identified as M440I002, M440I017 (tentative), and M440I060. Only 9.0% of the TRRs (0.019 ppm) were characterized, leaving 9.5% of the TRRs (0.020 ppm) as post-extraction solids following protease treatment.

Of the 71.3% of the TRRs identified in kidney, M440I061 was the only predominant residue. Minor metabolites identified were M440I003, and M440I060. A total of 19.3% of the TRRs (0.092 ppm) were characterized, with 3.7% of the TRRs (0.020 ppm) remaining as post-extraction solids following protease treatment.

In muscle, of the 93.5% of the TRRs identified, M440I060 was the only predominant residue (91.0% of the TRRs; 0.283 ppm). The only minor components identified were M440I003, and M440I061. The total characterized residues were 4.7% of the TRRs (0.014 ppm), with remaining post-extraction solids of 1.7% of the TRRs (0.005 ppm).

In whole milk, no metabolites were identified. A total of 76.9% of the TRRs (0.182 ppm) was characterized as very polar in nature, with 23.2% of the TRRs (0.055 ppm) remaining as post-extraction solids. Despite lipase treatment, different HPLC systems, and normal phase TLC, the characterized residues were shown to be multiple co-eluting components with various polarities. Cream was partitioned into a hexane fraction (75.9% of the TRRs; 1.523 ppm) and an aqueous fraction (1.3% of the TRRs; 0.026 ppm). Further analysis of the hexane fraction was not successful due to the fatty nature of the sample. The aqueous fraction analyzed by TLC showed the presence of 4 components, of which one was polar in nature. Following lipase treatment, the aqueous fraction was also analyzed by HPLC resulting in many components with a range of polarities. M440I061 was tentatively identified (2.6% of the TRRs; 0.052 ppm) based on co-chromatography with the reference standard.

For this study, the following metabolic transformations was observed:

- Oxidation of the pyridine ring of parent to form the N-oxide, M440I017
- Cleavage of the cyclopropane carboxylic ester at hydroxymethyl group of afidopyropen to form M440I003 and release cyclopropane carboxylic acid (CPCA) (M440I061)
- Cleavage of alternate cyclopropanecarboxylic ester group of afidopyropen to form M440I002 and release cyclopropane carboxylic acid (CPCA) (M440I061)
- CPCA (M440I061) interacts with carnitine to form O-(cyclopropylcarbonyl)carnitine (CPCA-carnitine, M440I060)

Table 4.1.2.3.1. Summary of characterized and identified residues in goat tissues following administration of [¹⁴C-CPCA]-Afidopyropen.

Matrix ¹	Liver		Kidney		Composite Muscle		Whole Milk	
	mg equiv/kg	%TRR	mg equiv/kg	%TRR	mg equiv/kg	%TRR	mg equiv/kg	%TRR
	TRR = 0.207 ppm		TRR = 0.480 ppm		TRR = 0.311 ppm		TRR = 0.237 ppm	
Solvent Extractable Residues ²	0.165	79.8	0.434	90.6	0.306	98.3	0.182	76.9
Afidopyropen	0.038	18.5	ND	ND	ND	ND	ND	ND
M440I002	0.003	1.5	ND	ND	ND	ND	ND	ND
M440I003	0.026	12.4	0.007	1.4	0.001	0.2	ND	ND
M440I005	ND	ND	ND	ND	ND	ND	ND	ND
M440I017 (tentative id)	0.008	3.7	ND	ND	ND	ND	ND	ND
M440I060 (CPCA-carnitine)	0.014	6.9	0.028	5.8	0.283	91.0	ND	ND
M440I061 (CPCA)	0.057	27.8	0.307	64.1	0.007	2.3	ND	ND
Total identified	0.146	71.0	0.342	71.3	0.291	93.5	--	--
Total characterized	0.019	9.3	0.092	19.3	0.014	4.7	0.182	76.9
Post extraction solid	0.032	15.5	0.042	8.7	0.005	1.7	0.055	23.2
Protease treatment	0.012	6.0	0.024	5.0	--	--	--	--
Remaining PES	0.020	9.5	0.020	3.7	--	--	--	--
Accountability* (%)	100		100		100		100	

ND= Not Detected

¹ The presence of the metabolite M440I001, produced by the loss of both ester groups, could not be detected with radiometric detection due to the location of the label in the CPCA moiety.

² The TRR values (% and mg equiv./kg) reported are different from Table B.7.2.3-8 as they are based on the TRRs measured after workup of the extracts analyzed by HPLC.

*%Accountability = Total ppm (identified + characterized + PES)/Overall TRR ppm * 100

Table 4.1.2.3.2. Summary of characterized and identified residues in goat urine and feces following administration of [¹⁴C-CPCA]-Afidopyropen.

Matrix	Urine	Feces
	% of the TRRs	% of the TRRs
Metabolite ¹		
Afidopyropen	0.1	33.5
M440I002	0.1	2.6
M440I003	ND	8.7
M440I005	0.1	0.5
M440I017	1.5	ND
M440I060	4.1	ND
M440I061	1.4	ND
Total identified	7.3	45.3
No. of peaks characterized but not identified	19	7
Total characterized	79.9	8.6

ND= Not Detected- This equates to an LOQ of ≤0.002 ppm;

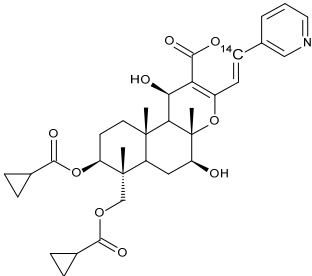
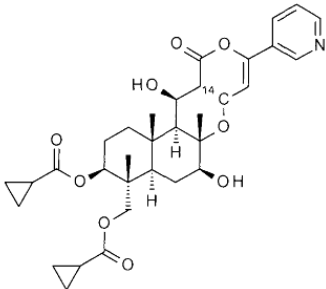
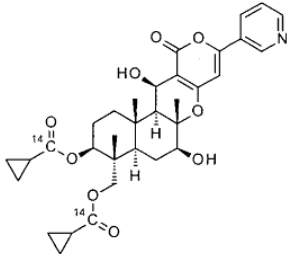
¹ The presence of the metabolite M440I001, produced by the loss of both ester groups, could not be detected with radiometric detection due to the location of the label in the CPCA moiety.

Conclusions: The submitted livestock metabolism studies for afidopyropen are adequate to satisfy data requirements. The metabolic pathways in livestock are found to be similar to the profile observed in the rat. This includes hydrolytic loss of one or both CPCA ester moieties, N-oxidation at the pyridine ring, hydroxylation of one of the methyl groups, and conjugation of hydroxyl groups of the metabolites. Based upon these studies, the nature of the residue of afidopyropen is concluded to be adequately understood in livestock.

4.1.3 Summary of Confined Rotational Crops (860.1850)

B.7.9. Residues in Succeeding Crops or Rotational Crops

The metabolism of ^{14}C -Afidopyropen in confined rotational crops was investigated in three separate studies following spray application of a radiolabeled test item to bare sandy loam soil (USDA scheme). Three differently radiolabeled test products were used for these studies which included radiolabels at the ^{14}C -NCA and Pyranone-4- ^{14}C positions along with the carbonyl labeled on both cyclopropane carboxylic acid groups (CPCA- ^{14}C label). The locations of the radiolabel in the test substances used in these metabolism studies are shown in Table 4.1.3.

Table 4.1.3. Radiolabeled Test Substances Used in Confined Rotational Crop Studies	
	
Short name: Nicotinic acid label Label position: 9- ^{14}C - Also described as pyranone-6- ^{14}C -	Short name: Pyranone label Label position: pyranone-4- ^{14}C
Table 4.1.3. Radiolabeled Test Substances Used in Confined Rotational Crop Studies	
	
Short name: Cyclopropane carboxylic acid (CPCA) label Label position: carbonyl of both cyclopropane carboxylic acid groups	

For the three confined rotational crop studies that were performed, the first study was conducted at a nominal rate of 125 g ai/ha (approximately 0.11 lbs ai/A; 1x) which is the maximum total rate proposed for treating fruits and vegetables. For this study, the ^{14}C -NCA and Pyranone-4- ^{14}C radiolabeled test substances were applied to bare soil and then planted with spinach, radish, and wheat at PBIs of 30-, 120-, and 365-days. For the PBIs characterized 30 days was used to simulate an emergency plantback, 120 days to simulate a fall plantback, and 365 days to correspond to a one year after treatment.

The second study was performed using a ^{14}C -NCA radiolabeled test substance applied to bare soil at the rate of 20 g ai/ha (0.02 lbs ai/A; 0.2x) which is the maximum rate for treating soybeans. For this study only winter wheat was sown at PBIs of 30-, 60-, and 90-days for characterization. In the third study, a CPCA radiolabeled test substance was used for treating bare soil at the rate of 20 g ai/ha (0.02 lb ai/A; 0.2x) with spinach, radish, and wheat being planted afterwards at PBIs of 30-, 120-, and 365-days for characterization.

4.1.3.1 Spinach, Radish, and Wheat (^{14}C -NCA and Pyranone-4- ^{14}C Labels)

A comparison of the two labels showed slightly higher total radioactive residue (TRR) values for the ^{14}C -NCA label over all PBIs and rotational crops. For all crops, the level of total radioactive residues was low and decreased with time in the different PBIs. Table 4.1.3.1 summarizes the reported results of the residues found in the rotated crop matrices.

The overall calculated TRRs were 0.004-0.009 ppm (immature spinach), 0.003-0.012 ppm (mature spinach), 0.003-0.012 ppm (mature spinach), 0.003-0.014 ppm (radish top), 0.004-0.008 ppm (radish root), and 0.009-0.024 ppm (wheat forage) at a PBI of 29-31 days for both radiolabels. In wheat hay, overall calculated TRRs were 0.044-0.064 ppm (29-31 d PBI), 0.019-0.039 ppm (119-122 d PBI), and 0.018 ppm (364 d PBI) for both radiolabels. In wheat straw, overall calculated TRRs were 0.037-0.097 ppm (29-31 d PBI), 0.025-0.050 ppm (119-122 d PBI), and 0.022 ppm (364 d PBI) for both radiolabels. In wheat grain, overall calculated TRRs were 0.044-0.061 ppm (29-31 d PBI), 0.014-0.050 ppm (119-122 d PBI), and 0.018 ppm (364 d PBI) for both radiolabels.

Afidopyropen was not identified in any of the samples from both radiolabels. The only metabolite identified was M440I003 in wheat straw at trace amounts (0.001 ppm, 0.9 % of the TRRs) at a plant-back interval of 31 days for the ^{14}C -NCA label. Overall accountabilities ranged from 83% to 106% for the nicotinic acid label and 75% to 133% for the pyranone label.

Afidopyropen is extensively metabolized into multiple components. Cleavage of afidopyropen occurred to form trace amounts of M440I003 and multiple unidentified minor metabolites with a range of polarities, including incorporation of afidopyropen into biomolecules. Figure 4.1.3.1 presents the proposed metabolic pathway in rotated crops.

Compound	31 days		122 days		364 days	
	ppm	%TRR	ppm	%TRR	ppm	%TRR
Immature Spinach	TRR= 0.009 ppm		TRR= 0.004 ppm ²		TRR= 0.003 ppm ²	
Total Identified	-	-	-	-	-	-
Total Characterized	0.005	62.0	-	-	-	-
Final PES	0.003	38.0	-	-	-	-
Accountability ¹	88.9%		-	-	-	-
Mature Spinach	TRR= 0.012 ppm		TRR= 0.004 ppm ²		TRR= 0.003 ppm ²	
Total Identified	-	-	-	-	-	-
Total Characterized	0.007	61.9	-	-	-	-
Final PES	0.004	38.1	-	-	-	-
Accountability ¹	91.7%		-	-	-	-
Radish Tops	TRR= 0.014 ppm		TRR= 0.005 ppm ²		TRR= 0.002 ppm ²	
Total Identified	-	-	-	-	-	-
Total Characterized	0.008	59.9	-	-	-	-
Final PES	0.006	40.1	-	-	-	-
Accountability ¹	100%		-	-	-	-

Table 4.1.3.1. Summary of characterization and identification of radioactive residues in rotational crop matrices following an application of NCA-¹⁴C Radiolabeled Afidopyropen at 125 g ai/ha.						
Compound	31 days		122 days		364 days	
	ppm	%TRR	ppm	%TRR	ppm	%TRR
Radish roots	TRR= 0.008 ppm		TRR= 0.003 ppm²		TRR= 0.001 ppm²	
Total Identified	-	-	-	-	-	-
Total Characterized	0.005	63.8	-	-	-	-
Final PES	0.003	36.2	-	-	-	-
Accountability ¹	100%		-	-	-	-
Wheat Forage	TRR= 0.024 ppm		TRR= 0.009 ppm²		TRR= 0.003 ppm²	
Total Identified	-	-	-	-	-	-
Total Characterized	0.015	64.7	-	-	-	-
Final PES	0.006	25.4	-	-	-	-
Accountability ¹	88%		-	-	-	-
Wheat Hay	TRR= 0.064 ppm		TRR=0.039 ppm		TRR=0.018 ppm	
Total Identified	-	-	-	-	-	-
Total Characterized	0.038	59.6	0.026	66.7	0.010	59.7
Final PES	0.016	24.3	0.009	22.4	0.008	45.5
Accountability ¹	83%		87%		100%	
Wheat Straw	TRR=0.097 ppm		TRR=0.050 ppm		TRR=0.022 ppm	
<i>M440I003</i>	0.001	0.9	-	-	-	-
Total Identified	0.001	0.9				
Total Characterized	0.042	42.7	0.029	59.4	0.010	46.8
Final PES	0.046	45.3	0.015	30.6	0.010	47.4
Accountability ¹	92%		90%		91%	
Wheat Grain	TRR= 0.061 ppm		TRR=0.050 ppm		TRR=0.018 ppm	
Total Identified						
Total Characterized	0.048	79.5	0.038	76.9	0.014	73.0
Final PES	0.007	10.9	0.009	17.2	0.005	26.5
Accountability ¹	90%		94%		106%	

¹ Accountability = (Total extractable, ppm + Total unextractable, ppm)/(overall calculated TRR, ppm)

² Combustion value. TRR was not calculated due to low radioactivity.

- Not analyzed/identified

4.1.3.2 Wheat (¹⁴C-NCA Label)

The metabolism of afidopyropen was investigated in wheat after one spray application of 19.9 g ai/ha (0.02 lbs ai/A) of an ¹⁴C-NCA-afidopyropen radiolabeled test product to soil. This application rate was made to reflect the highest total application rate of 2 x 10 g ai/ha requested for soybean. Samples of wheat were harvested at 30, 61 and 90 days.

The overall TRRs were ≤0.004 ppm for wheat forage (combustion), 0.021-0.024 ppm for wheat hay, 0.027-0.066 ppm for wheat straw and 0.011-0.021 ppm for wheat grain (calculated). In wheat forage, none of the TRRs were characterized due to low levels of radioactivity.

At PBIs of 30 days and 61 days, 34.8-51.5% of the TRRs (0.008-0.011 ppm) were characterized, with 48.5-65.2% of the TRRs (0.010-0.016 ppm) remaining as unextractable in wheat hay. In wheat straw, 62.8-70.2% of the TRRs (0.017-0.046 ppm) were characterized, with 29.8-37.2% of the TRRs (0.010-0.020 ppm) remaining as unextractable. In wheat grain, 23.2-41.5% of the TRRs (0.005 ppm) were characterized, with 58.5-76.8% of the TRRs (0.007-0.016 ppm) remaining as unextractables. Parent afidopyropen was not identified in any sample.

4.1.3.3 Spinach, Radish, and Wheat (CPCA-¹⁴C Label)

The metabolism of afidopyropen was investigated in wheat after one spray application to soil at 125 g ai/ha (0.11 lbs ai/A; 1x) and in spinach and radish after one spray application to soil at 20 g ai/ha (0.02 lbs ai/A; 0.2x) made with a CPCA-¹⁴C-afidopyropen radiolabeled test product. Samples of spinach and radish were harvested at 31 and 90 days while wheat samples were harvested at 30 and 61 days. Table 4.1.3.3 summarizes the reported results of the residues found in the rotated crop matrices.

The overall TRRs were 0.004-0.012 ppm for immature spinach, ≤0.009 ppm for mature spinach, ≤0.008 ppm for radish tops, and ≤0.006 ppm for radish roots at PBI of 31 days and 90 days. At PBIs of 30 days and 61 days, overall TRRs were 0.009-0.015 ppm for wheat forage, 0.043-0.103 ppm for wheat hay, 0.066-0.083 ppm for wheat straw and 0.019-0.041 ppm for wheat grain.

At a PBI of 31 days, overall TRRs extracted were 54-55% (0.005-0.006 ppm), with 45-46% of the TRRs (0.004-0.005 ppm) remaining as PES in immature and mature spinach. Overall TRRs extracted in wheat matrices (forage, hay, straw, and grain) at a PBI of 30 days were 22-61% of the TRRs (0.004-0.051 ppm), with 39-78% of the TRRs (0.010-0.064 ppm) remaining as PES. Overall TRRs extracted in wheat matrices (forage, hay, straw, and grain) at a PBI of 61 days were 15-39% of the TRRs (0.003-0.026 ppm), with 61-85% of the TRRs (0.006-0.040 ppm) remaining as PES. Afidopyropen and its metabolites were not identified in any of the samples from the CPCA-¹⁴C radiolabel.

Table 4.1.3.3. Summary of characterization and identification of radioactive residues in rotational crop matrices following an application of Pyranone-4-¹⁴C Radiolabeled Afidopyropen at 125 g ai/ha.						
Compound	31 days		122 days		364 days	
	ppm	%TRR	ppm	%TRR	ppm	%TRR
Immature Spinach	TRR= 0.004 ppm		TRR= 0.003 ppm³		TRR= 0.001 ppm³	
Total Identified	-	-	-	-	-	-
Total Characterized	0.002	48.1	-	-	-	-
Final PES	0.002	51.9	-	-	-	-
Accountability ²	100%		-	-	-	-
Mature Spinach	TRR= 0.003 ppm		TRR= 0.002 ppm³		TRR= 0.001 ppm³	
Total Identified	-	-	-	-	-	-
Total Characterized	0.002	46.6	-	-	-	-
Final PES	0.002	53.4	-	-	-	-
Accountability ²	133%		-	-	-	-

Table 4.1.3.3. Summary of characterization and identification of radioactive residues in rotational crop matrices following an application of Pyranone-4-¹⁴C Radiolabeled Afidopyropen at 125 g ai/ha.						
Compound	31 days		122 days		364 days	
	ppm	%TRR	ppm	%TRR	ppm	%TRR
Radish Tops	TRR= 0.003 ppm		TRR= 0.003 ppm ³		TRR= <0.001 ppm ³	
Total Identified	-	-	-	-	-	-
Total Extractable	0.001	31.6	-	-	-	-
Final PES	0.002	68.4	-	-	-	-
Accountability ²	100%		-	-	-	-
Radish roots	TRR= 0.004 ppm		TRR= 0.001 ppm ³		TRR= <0.001 ppm ³	
Total Identified	-	-	-	-	-	-
Total Characterized	0.002	61.6	-	-	-	-
Final PES	0.001	38.4	-	-	-	-
Accountability ²	75%		-	-	-	-
Wheat Forage	TRR= 0.009 ppm		TRR= 0.003 ppm ³		TRR= 0.001 ppm ³	
Total Identified	-	-	-	-	-	-
Total Characterized	0.005	58.6	-	-	-	-
Final PES	0.003	33.0	-	-	-	-
Accountability ²	89%		-	-	-	-
Wheat Hay	TRR= 0.044 ppm		TRR= 0.019 ppm		TRR= 0.001 ppm ³	
Total Identified	-	-	-	-	-	-
Total Characterized	0.026	58.7	0.014	72.8	-	-
Final PES	0.014	32.0	0.005	24.1	-	-
Accountability ²	91%		100%		-	-
Wheat Straw	TRR= 0.037 ppm		TRR= 0.025 ppm		TRR= 0.001 ppm ³	
Total Identified	-	-	-	-	-	-
Total Characterized	0.019	51.9	0.014	55.8	-	-
Final PES	0.015	39.6	0.009	36.8	-	-
Accountability ²	92%		92%		-	-
Wheat Grain	TRR= 0.044 ppm		TRR= 0.014 ppm		TRR= 0.001 ppm ³	
Total Identified	-	-	-	-	-	-
Total Characterized	0.034	78.9	0.011	81.9	-	-
Final PES	0.008	19.1	0.002	15.8	-	-
Accountability ²	95%		93%		-	-

¹ Unidentified metabolite

² Accountability = (Total extractable, ppm + Total unextractable, ppm)/(overall calculated TRR, ppm)

³ Combustion value. TRR not calculated due to low radioactivity.

- Not analyzed/identified

Conclusions: The submitted confined rotational crop studies for afidopyropen are adequate to satisfy data requirements. Sufficient studies at the maximum 1x rate were appropriately conducted in the three different crop categories. Because nicotinic acid can potentially be metabolized into trigonelline in legumes, additional studies were also conducted at the 0.2x labeled rate for soybeans. These studies all indicate that no residues of concern are expected to be present in rotational crops following a 30-day PBI. Given these results, field rotational crop studies are not needed to set plantback restrictions for the various uses proposed for registration (see Section 5.3.2).

4.1.4 Summary of Metabolites and Degradates

A summary of the metabolites of afidopyropen in plants, livestock, and rats is included in Appendix A, with proposed metabolic pathways in Appendix B.

4.2 Comparison of Metabolic Pathways

Studies depicting the nature of the residue in target crops (tomato, cabbage, and soybean), rotational crops (spinach, radish, and wheat) and livestock (laying hens and lactating goat) were provided to support registration. These metabolism studies are all recently conducted and are sufficient for supporting the petition. For the determination of plant metabolism, three diverse crop categories were appropriately used for study. The metabolic profile in plants was observed to be similar with some variation on the nature and extent of conjugations between crops. Metabolism proceeded by dimerization to form the metabolite M440I007. It also involved to some extent, cleavage of the ring system to form several minor metabolites as well as numerous unidentified minor components, including polar metabolites and incorporation into natural products. For livestock, the studies conducted with the laying hen and lactating goat showed metabolism to be similar in these species. The metabolic pathway in livestock included the hydrolytic loss of one or both CPCA ester moieties, N-oxidation at the pyridine ring, hydroxylation of one of the methyl groups, and conjugation of hydroxyl groups of the metabolites. Generally, these metabolic processes are found to be similar to the profile which has been observed in the rat.

4.3 Residues of Concern Summary and Rationale

ROCKS Decision Memo D441491, I. Negron-Encarnacion, January 30, 2018

The Residues of Concern Knowledgebase Subcommittee (ROCKS) met on August 17, 2017 to discuss the residue definitions for afidopyropen. Their recommendations are listed below in Table 4.3 and summarized as follows:

Water: The ROCKS recommends including parent afidopyropen and all structurally similar monomeric degradates (18 in total) as the residues of concern for risk assessment in drinking water. Considering the limited available data, most degradates are known or expected to be comparably mobile to the parent compound and the sum of minor metabolites observed in the aerobic soil metabolism study (study termination) is at levels comparable to the sum of major metabolites. In addition, the ROCKS recommends inclusion of CPCA as a residue of concern for risk assessment in drinking water. Given its anionic character at ambient pH, CPCA is expected to be highly mobile, and given its hydrolytic stability is likely to leach to groundwater.

Plants (Primary Crops): Parent afidopyropen was identified as major residue in most primary crop metabolism studies and/or crop field trials. It is considered an appropriate marker of misuse; therefore, is recommended as the residue of concern (ROC) for tolerance enforcement. Parent afidopyropen is also recommended as the residue of concern for risk assessment. Although, the metabolite M440I007 (afidopyropen dimer) was observed at levels >10% TRR in primary crop metabolism studies and at levels lower than half of those for parent in crop field trials, it is not recommended as a residue of concern. This is concluded based on its lower toxicity and exposure in comparison to parent afidopyropen.

Rotational Crops: As with primary crops, parent afidopyropen is recommended as the ROC for both tolerance enforcement and risk assessment. Parent afidopyropen accounted for a significant

proportion of the residue in all three primary crop metabolism studies. Moreover, no residues were identified in any of the matrices analyzed in the confined rotational study.

Livestock: The ROCKS recommends parent afidopyropen as the residue of concern for both tolerance enforcement and risk assessment in ruminant commodities. Based on the metabolism study conducted on the lactating goat, parent afidopyropen and the metabolites M440I001, M440I003, M440I005, CPCA-carnitine, and CPCA were the major components found in most ruminant commodities. However, given a low estimated dietary burden, there is little potential for exposure from these other analytes in the human diet. For poultry, the residues of concern in these matrices were not established since there is no expectation of finite residues for poultry matrices at this time and feeding studies have not been conducted.

Matrix		Residues Included In Risk Assessment	Residues Included In Tolerance Expression
Plants	Primary Crop	Afidopyropen	Afidopyropen
	Rotational Crop	Afidopyropen	Afidopyropen
Livestock	Ruminant ²	Afidopyropen	Afidopyropen
	Poultry	Not Determined	Not Determined
Drinking Water ³		Afidopyropen, the 18 identified structurally similar degradates and CPCA (M440I061)	Not Applicable

¹ Afidopyropen is [(3S,4R,4aR,6S,6aS,12R,12aS,12bS)-3-(cyclopropanecarbonyloxy-6,12-dihydroxy-4,6a,12b-trimethyl-11-oxo-9-(pyridin-3-yl)-1,2,3,4,4a,5,6,6a,12a,12b-decahydro-11H,12H-benzo[f]pyrano[4,3-b]chromen-4-yl)methyl cyclopropanecarboxylate.

² ROCKS recommends to include parent only based on the low exposure concern at this time.

³ The 18 transformation products include M440I001, M440I002, M440I003, M440I005, M440I006, M440I014, M440I015, M440I016, M440I021, M440I024, M440I046, M440I047, M440I048, M440I049, M440I050, M440I052, M440I053, and M440I057 (refer to Appendix A for metabolite structures). If refinement of the DWA is needed in the future, the exposure to these transformation products may be evaluated in more detail. CPCA may be included in a separate risk assessment to parent afidopyropen.

5.0 Residue Profile

5.1 Residue Analytical Methods (860.1340)

5.1.1 Data Collection Methods

B.5.2. Residue Analytical Methods

For this petition, the registrant used the proposed plant and livestock tolerance enforcement methods for data collection. Refer to section 5.1.3 for a detailed summary of the proposed tolerance enforcement methods.

5.1.2 Multi-Residue Methods (860.1360)

DER Reference: 49083746.der.docx

Afidopyropen was not evaluated for FDA multi-residue method determination. To satisfy this data requirement, the registrant has developed a QuEChERS multi-residue method (D1514/01) based on AOAC method 2007.01 using LC-MS/MS analysis for the determination of afidopyropen and its metabolites in plants. For this method, residues are extracted using acetonitrile, or acetonitrile and water for dry matrices. Sample purification is performed using a salt mixture (sodium chloride, magnesium sulphate, and citrate buffering agents), followed by a

second salt mixture (containing MgSO₄ to remove residual water and primary secondary amine, PSA sorbent, to remove sugars and fatty acids) and centrifuged. Sample analysis is performed by LC-MS/MS analysis for the determination of afidopyropen. Two ion transitions characteristic of the analyte are monitored for analysis (Table 5.1.2).

Table 5.1.2. Summary of Ion Transitions Monitored for Plant Analyses.		
Analyte	Ion Transitions Monitored	
	Quantitation	Confirmation
Afidopyropen	<i>m/z</i> 594→148	<i>m/z</i> 594→202

The reported limit of quantitation (LOQ) for the method is 0.01 ppm for the afidopyropen analyte. Validation of the QuEChERS multi-residue method D1514/01 was performed using a wide range of crop commodities which included orange, apple, potato, kidney bean and canola. It was conducted over the concentration range of 0.01-1.0 ppm. The individual recoveries were within the range of 66-115% for afidopyropen. Repeatability data were generated from at least 5 samples fortified at the LOQ and at least 5 samples fortified at 100-fold LOQ for each matrix and analyte. The relative standard deviations (RSDs) obtained for each fortification level were less than 20%.

For the determination of afidopyropen in livestock commodities, the registrant did not propose a QuEChERS multi-residue method for these analyses at this time.

Conclusions. The QuEChERS multi-residue method D1514/01 is considered suitable for the analysis of afidopyropen in plants. Low livestock dietary burdens paired with low residue transfer rates into livestock commodities indicate there is no reasonable expectation of finite residues in livestock commodities [40 CFR §180.6(a)(3)]. Should additional feed commodities be requested for registration requiring establishment of livestock tolerances, a QuEChERS multi-residue method for livestock matrices should be proposed to support registration.

5.1.3 Tolerance Enforcement Methods

Plants

Samples of crop commodities from the storage stability, crop field trial, and processing studies submitted with this petition were analyzed for afidopyropen using the proposed LC-MS/MS plant enforcement method, D1103/01. A complete method description with method validation (MRID No. 49688943) and independent laboratory validation (MRID No. 49688938) were submitted to demonstrate the adequacy of this proposed enforcement method.

For this method, samples are extracted with acetonitrile and water. The samples are then placed in a mechanical shaker, followed by centrifugation. Residues in the extracts are cleaned-up in the presence of a mixture of salts (MgSO₄, NaCl, citric acid disodium salt sesquihydrate, and citric acid trisodium salt dihydrate), and centrifuged. An aliquot of the upper phase (ACN) is further purified by shaking with a second salt mixture (MgSO₄, PSA) followed by centrifugation. An aliquot of the extract was diluted with water and formic acid, then determined by LC-MS/MS analysis. For this method, two ion transitions characteristic of each analyte are monitored for analysis (Table 5.1.3.1).

Table 5.1.3.1. Summary of Ion Transitions Monitored for Plant Analyses.		
Analyte	Ion Transitions Monitored	
	Quantitation	Confirmation
Afidopyropen	<i>m/z</i> 594→202	<i>m/z</i> 594→148

The reported LOQ of the method is 0.01 ppm for afidopyropen.

A successful independent laboratory validation (ILV) was conducted using samples of lettuce (high water content), oranges (high acid content), dry beans (difficult commodity), soybean seeds (high oil content) and potatoes (high starch content). For these analyses, each sample was fortified with afidopyropen at levels ranging from 0.01 to 1.0 ppm. The ILV followed method procedures as currently written. Recovery from fortified samples ranged from 80-94% for afidopyropen, with maximum relative standard deviations of 6%. Based upon these analyses, the validating laboratory recommended including instructions for sample dilution when matrix-matched standards are used, and the LOD and LOQ values should be noted as 0.002 and 0.01 µg/g (ppm), not µg/kg.

No radiovalidation data were submitted. Because the extraction solvents used in the metabolism studies are identical to those used in the proposed plant enforcement method, no radiovalidation data are required for crop commodities.

Livestock

Samples of livestock commodities from the submitted cattle feeding study were analyzed for residues of afidopyropen using the proposed LC-MS/MS livestock enforcement method, D15074/01. A complete method description with method validation (MRID No. 49688944) and independent laboratory validation (MRID No. 49688939) were submitted to demonstrate the adequacy of this proposed enforcement method.

For this method, samples of muscle, liver, and egg are diluted with water, purified on a solid phase extraction (SPE) column, eluted with acetonitrile:water (80:20, v/v), and diluted with acidified water for extraction of afidopyropen. For fat samples, residues of afidopyropen in an aliquot of the DCM extract are concentrated, diluted with cyclohexane, acetonitrile, and water, cleaned up on an SPE column, eluted with acetonitrile:water (80:20, v/v), and then diluted with acidified water. For milk, residues of afidopyropen are purified, as described above, on an SPE column eluted with acetonitrile:water (80:20, v/v), and then are diluted with acidified water. Following extraction, the resulting sample extracts are analyzed by LC-MS/MS analysis. For this method, two ion transitions characteristic of the afidopyropen analyte are monitored for analysis (Table 5.1.3.2).

Table 5.1.3.2. Summary of Ion Transitions Monitored for Livestock Analyses.		
Analyte	Ion Transitions Monitored	
	Quantitation	Confirmation
Afidopyropen	<i>m/z</i> 594→148	<i>m/z</i> 594→202

The reported LOQ is 0.01 ppm for afidopyropen in muscle, liver, fat and egg, and 0.0001 ppm in milk.

A successful ILV was conducted using samples of livestock tissues (bovine muscle, fat and liver) and poultry eggs fortified with afidopyropen at levels ranging from 0.01 to 1.0 ppm. Samples of bovine milk were fortified with afidopyropen at levels ranging from 0.001 to 0.1 ppm. The ILV

followed method procedures as currently written. Recovery of analytes from fortified samples ranged from 72.1 to 118% for afidopyropen with maximum relative standard deviations of 15%. Based upon these analyses, the validating laboratory recommended the solution prior to injection be diluted 1:1 with water to decrease the organic percentage for better peak resolution.

No radiovalidation data were submitted. Because the extraction solvents used in the metabolism studies are identical to those used in the proposed livestock enforcement method, no radiovalidation data are required for crop commodities.

Conclusions. BASF has submitted LC-MS/MS methods D1103/01 for plants and D15074/01 for livestock to determine the residues of afidopyropen for the purposes of tolerance enforcement. The reported LOQ of each method is 0.01 ppm for afidopyropen. These methods have been adequately validated by the registrant as well as by an independent laboratory. Identical extraction solvents were used in conducting the metabolism study analyses which serves to demonstrate the completeness of the extraction procedures developed in these methods. Following the criteria specified in the Tolerance Method Validation checklist (SOP No. ACB 019, Revision 1.0), these methods meet the conditions for depicting the suitability of an enforcement methodology. There are adequate recovery data and chromatograms provided at the method LOQ of 0.01 ppm for the afidopyropen analyte in each matrix. Concurrent fortification recoveries were acceptable in all matrices over the range of expected residues. The methods use standard analytical techniques and commercially available instrumentation. The methods displayed good linearity, specificity, and repeatability, and include the use of two ion transitions (primary quantitation and confirmatory) monitored by MS/MS. Therefore, method D1103/01 for plants and method D15074/01 for livestock are acceptable for determining the residues of afidopyropen for tolerance enforcement pending that the revisions recommended by the validating laboratory are addressed.

5.1.4 Submittal of Analytical Reference Standards (860.1650)

Analytical standards for afidopyropen are currently available in the EPA National Pesticide Standards Repository (personal communication with Gregory Verdin, BEAD, 10/19/2017). These standards are set to expire on 06/01/2018. As a reminder to the petitioner, supplies of analytical standards must be replenished as requested by the repository as long as the tolerance is published in 40 CFR. Please follow the process for submitting these materials as recommended in the guidance letter from Theresa Cole attached as Appendix C.

5.2 Storage Stability (860.1380)

B.7.6.2 Stability of Residues Prior to Analysis

Plants

Samples collected from the field trial studies conducted for the proposed new crop uses of afidopyropen were stored frozen for durations ranging from 297 days (9.8 months) for cabbage up to 555 days (18.2 months) for grapefruit (Table 5.2.1). Data depicting the stability of afidopyropen and its metabolite M440I007 at a level of 0.1 ppm stored frozen at $\leq -20^{\circ}\text{C}$ were acquired to support this petition. The commodities tested for determining storage stability were barley grain, lettuce, navy bean, soybean oil, orange, soybean hay, and soybean seed for durations of approximately 0, 1, 3, 4 (lettuce and orange only), 6, 9, 12, 15, 18, and 24 months. An additional 28-month time point was performed to monitor the stability of M440I007 in soybean hay. These commodities are representative of the high water, high oil, high protein and

high starch commodity groups specified in EU Guidance (SANCO 7032/VI/95 rev. 5), and the high water, high oil, high protein, high starch, and high acid commodity groups specified in OECD Guidelines (OECD Guideline 506). These commodities also are representative of an oilseed, non-oily grain, leafy vegetable, root crop and acidic fruit specified in EPA Guidelines (OCSPP 860.1380).

Crop Commodity	Crop Category	Days	Months
Potatoes	High Starch	361	11.9
Head lettuce	High Water	348	11.4
Leaf lettuce	High Water	375	12.3
Spinach	High Water	343	11.3
Celery	High Water	346	11.4
Broccoli	High Water	407	13.4
Cabbage	High Water	297	9.8
Mustard greens	High Water	468	15.4
Soybean forage	Other	341	11.2
Soybean hay	Other	320	10.5
Soybean seed	High Oil	369	12.1
Tomatoes	High Water	376	12.4
Peppers	High Water	337	11.1
Cucumber	High Water	302	9.9
Squash	High Water	324	10.7
Cantaloupe	High Water	325	10.7
Apples	High Water	336	11
Pears	High Water	326	10.7
Peaches	High Water	377	12.4
Plums	High Water	367	12.1
Cherries	High Water	483	15.9
Pecan	High Oil	240	7.9
Pistachio	High Oil	286	9.4
Almond	High Oil	370	12.2
Almond hulls	Other	355	11.7
Lemon	High Acid	479	15.7
Grapefruit	High Acid	555	18.2
Orange	High Acid	488	16
Cottonseed	High Oil	244	8.0
Cotton gin byproduct	Other	253	8.3

Tables 5.2.2 and 5.2.3 summarize the reported results for the stability of afidopyropen and the metabolite M440I007 in crop commodities. Concurrent recoveries were used to correct the residues in the stored samples.

Table 5.2.2. Storage Stability of Afidopyropen in Plant Matrices.														
Mean Recovery of Afidopyropen (%)														
A: Corrected in stored samples, % of nominal B: procedural, in freshly fortified sample														
Day	A	B	A	B	A	B	A	B	A	B	A	B	A	B
Method No. D1103														
Matrices	Barley grain		Lettuce		Navy bean		Soybean oil		Orange		Soybean Hay		Soybean Seed	
	High Starch	High Water	High Protein	High Oil	High Acid	Other	High Oil							
0	97	101	97	105	97	106	94	93	96	104	95	107	96	98
32	96	109	95	108	92	111	66	112	92	112	90	107	96	106
98	84	119	--	--	86	103	83	109	--	--	80	89	87	119
124	--	--	86	97	--	--	--	--	81	97	--	--	--	--
196-197	105	101	75	94	81	108	90	94	99	87	103	85	73	126
278-280	102	110	90	112	88	109	83	97	92	118	88	114	95	118
369-372	96	110	90	102	96	104	88	93	98	106	92	102	96	105
488	95	99	89	98	94	98	80	91	96	100	89	101	95	101
550	89	98	86	102	86	102	77	93	91	101	85	96	89	98
742	88	105	94	109	91	115	93	98	95	106	89	105	93	111

Note: Bolded values indicate the corrected values.

Mean recoveries of afidopyropen from stored-fortified samples (corrected for the mean of duplicate concurrent recoveries) were 88% (barley grain), 94% (lettuce), 91% (navy bean), 93% (soybean oil), 95% (orange), 89% (soybean hay) and 93% (soybean seed) at the latest sampling interval.

The overall mean concurrent recoveries of afidopyropen in freshly-fortified samples (0.1 ppm) were 106±7% (barley grain), 103±6% (lettuce), 106±6% (navy bean), 98±8% (soybean oil), 103±9% (orange), 101±9% (soybean hay), and 109±10% (soybean seed).

Table 5.2.3. Storage Stability of Metabolite M440I007 in Plant Matrices.														
Mean Recovery of M440I007 (%)														
A: Corrected mean in stored samples, % of nominal B: mean procedural, in freshly spiked sample														
Day	A	B	A	B	A	B	A	B	A	B	A	B	A	B
Matrices	Barley Grain		Lettuce		Navy Bean		Soybean Oil		Orange		Soybean Hay		Soybean Seed	
	High Starch	High Water	High Protein	High Oil	High Acid	Other	High Oil							
0	96	73	97	83	87	91	98	67	109	76	86	100	105	70
32	86	90	89	89	99	83	82	85	87	93	89	95	83	89
98	83	101	--	--	92	83	85	81	--	--	85	74	92	96
124	--	--	82	100	--	--	--	--	87	97	--	--	--	--
196-197	88	103	91	87	105	87	93	81	80	76	73	102	83	93
278-280	92	95	71	115	97	97	88	81	91	94	76	110	97	94
369-372	116	86	67	116	88	101	104	68	110	76	77	96	76	94
488	94	88	85	88	108	88	101	75	105	85	76	90	97	91
550	79	83	85	85	89	88	72	75	85	85	69	86	88	83
742	79	87	81	94	90	99	89	76	91	91	63	95	83	89
841	--	--	--	--	--	--	--	--	--	--	67	95	--	--

Mean recoveries of M440I007 from stored-fortified samples (corrected for the mean of duplicate concurrent recoveries) were 79% (barley grain), 81% (lettuce), 90% (navy bean), 89% (soybean oil), 91% (orange), 67% (soybean hay) and 83% (soybean seed), after the latest sampling interval.

Although M440I007 in soybean hay had a corrected stored recovery of 67% at the 28-month sampling interval, the 0-day recovery for M440I007 in soybean hay was 86%. This is an observed decline of approximately 19%, therefore M440I007 is considered stable for at least 28 months of frozen storage in soybean hay. Although there is evidence of degradation of M440I007 in soybean hay during the 24-month frozen storage interval, recoveries were still within the acceptable range after 28 months.

The overall mean concurrent recoveries of M440I007 in freshly-fortified samples (0.1 ppm), were 90±12% (barley grain), 95±15% (lettuce), 91±9% (navy bean), 76±8% (soybean oil), 86±9% (orange), 95±10% (soybean hay), and 89±9% (soybean seed). These data indicate that the LC-MS/MS method is adequate for the determination of M440I007 residues in/on plant commodity storage stability samples.

Processed Commodities

To support this petition, processing studies were conducted for potato, tomato, soybean, orange, apple, plums, and cotton. These samples were stored frozen at $\leq -20^{\circ}\text{C}$ for durations of 87 days (2.9 months) for potato up to 504 days (16.6 months) for oranges. No supporting storage stability data for the processed commodities acquired in these studies were submitted. Because the residues of afidopyropen were examined in five crop commodity categories and are shown to be stable, storage stability can be assumed for all crops including processed commodities.

Livestock

In support of this petition, a ruminant livestock feeding study was conducted on lactating cattle. The cattle matrices were analyzed for afidopyropen, and the metabolites M440I001, and CPCA-carnitine in milk, cream, skim milk, meat, fat, liver, and kidney. In addition, metabolite M440I003 was also analyzed in meat, liver and kidney, as well as metabolite M440I005 in milk matrices. Tissue samples for this study were stored frozen for a maximum of 113-121 days in liver, kidney, muscle, and 134 days in fat, except for CPCA-carnitine in liver and fat which was stored frozen for a maximum of 161 days. Samples of whole milk were stored frozen for a maximum of 71 days from collection to extraction for analysis.

A storage stability study was performed in conjunction with the livestock feeding study. Table 5.2.4 summarizes the reported results for the stability of afidopyropen residues in livestock commodities. For this study, homogenized milk, liver, muscle, and fat samples were fortified separately with each analyte (in acetonitrile or in water for CPCA-carnitine) at 10-fold the respective LOQ. The fortified and unfortified samples were placed in plastic containers and stored frozen until analysis. Each sample set consisted of one control, two samples to serve as freshly fortified at the time of analysis and two stored fortified samples. A set of samples was analyzed when the samples were fortified as the time-zero analysis. The freezer stored samples were analyzed after approximately 0, 1, and 3 months of frozen storage.

Table 5.2.4. Stability of Residues of Afidopyropen in Livestock Commodities.						
Analyte	Fortification Level (ppm)	Storage Interval (days)	Recovered Residues (ppm)	% Recovery (mean)	% Procedural Recovery (mean)	% Corrected Recovery
Milk						
Afidopyropen	0.01	0	0.0081, 0.0072	81, 72 (76)	83, 84 (84)	91
	0.01	43	0.0089, 0.0089	89, 89 (89)	83, 84 (84)	107
	0.01	99	0.0091, 0.0081	91, 81 (86)	90, 89 (89)	97
M440I001	0.01	0	0.0096, 0.0097	96, 97 (96)	92, 100 (96)	100
	0.01	43	0.0105, 0.0095	105, 95 (100)	92, 100 (96)	104
	0.01	99	0.0127, 0.0129	127, 129 (128)	99, 117 (108)	118
M440I005	0.01	0	0.0090, 0.0079	90, 79 (85)	100, 82 (91)	93
	0.01	43	0.0081, 0.0102	81, 102 (92)	100, 82 (91)	101
	0.01	99	0.0112, 0.0113	112, 113 (113)	99, 101 (100)	113
CPCA-carnitine	0.05	0	0.0365, 0.0389	73, 78 (75)	90, 64 (77)	98
	0.05	43	0.0367, 0.0461	73, 92 (83)	90, 64 (77)	108
	0.05	99	0.0384, 0.0366	77, 73 (75)	78, 78 (78)	96
Liver						
Afidopyropen	0.1	0	0.0788, 0.0879	79, 88 (83)	91, 97 (94)	89
		41	0.0864, 0.1017	86, 102 (94)	91, 97 (94)	100
		96	0.0750, 0.0816	75, 82 (78)	88, 89 (89)	88
M440I001	0.1	0	0.0896, 0.0877	90, 88 (89)	85, 96 (91)	98
		41	0.0908, 0.0830	91, 83 (87)	85, 96 (91)	96
		96	0.1082, 0.1121	108, 112 (110)	110, 114 (112)	98
M440I003	0.1	0	0.0872, 0.0904	87, 90 (89)	88, 93 (90)	98
		41	0.0845, 0.0857	84, 86 (85)	88, 93 (90)	94
		96	0.0970, 0.0918	97, 92 (94)	82, 89 (85)	111
CPCA-carnitine	0.5	0	0.3847, 0.3681	77, 74 (75)	93, 71 (82)	92
		41	0.3886, 0.3523	78, 70 (74)	93, 71 (82)	90
		96	0.3189, 0.3447	64, 69 (66)	69, 63 (66)	100
Muscle						
Afidopyropen	0.1	0	0.1029, 0.1098	103, 110 (106)	124, 85 (105)	102
		42	0.0874, 0.0949	87, 95 (91)	124, 85 (105)	87
		90	0.0918, 0.0801	92, 80 (86)	95, 88 (91)	94
M440I001	0.1	0	0.0988, 0.1020	99, 102 (100)	96, 94 (95)	106
		42	0.0888, 0.0970	89, 97 (93)	96, 94 (95)	98
		90	0.1080, 0.1305	108, 131 (119)	103, 93 (98)	122
M440I003	0.1	0	0.0958, 0.0955	96, 96 (96)	102, 101 (101)	94
		42	0.0931, 0.0966	93, 97 (95)	102, 101 (101)	94
		90	0.0995, 0.0997	99, 100 (100)	86, 95 (90)	110
CPCA-carnitine	0.5	0	0.4075, 0.3859	81, 77 (79)	82, 76 (79)	100
		42	0.3369, 0.4956	67, 99 (83)	82, 76 (79)	105
		90	0.4167, 0.4341	83, 87 (85)	81, 76 (79)	108
Fat						
Afidopyropen	0.1	0	0.0777, 0.0940	78, 94 (86)	82, 79 (80)	107
		42	0.0885, 0.0829	89, 83 (86)	82, 79 (80)	107
		86	0.0682, 0.0795	68, 80 (74)	90, 85 (88)	84
M440I001	0.1	0	0.0965, 0.0815	97, 82 (89)	76, 89 (82)	108
		42	0.0792, 0.0850	79, 85 (82)	76, 89 (82)	100
		86	0.1132, 0.1029	113, 103 (108)	96, 98 (97)	111
M440I003	0.1	0	0.0797, 0.0958	80, 96 (88)	93, 78 (86)	102
		42	0.0742, 0.0906	74, 91 (82)	93, 78 (86)	96
		86	0.0981, 0.0959	98, 96 (97)	91, 93 (92)	106
CPCA-carnitine	0.5	0	0.4907, 0.4113	98, 82 (90)	78, 88 (83)	109
		42	0.4344, 0.3846	87, 77 (82)	78, 88 (83)	99
		86	0.3637, 0.3878	73, 78 (75)	68, 73 (70)	107

The storage stability data acquired for livestock commodities showed no analyte degradation in any sample matrix for durations of frozen storage up to approximately 3 months. A request to waive the need for additional data was submitted by the registrant since the interval of sample storage incurred for the cattle feeding study did exceed that of the storage stability study (MRID No. 49688951). The waiver explains that further freezer storage stability data in livestock matrices are not required because the submitted data adequately establishes stability. In consideration of these data, the storage stability study shows no apparent loss of residues greater than 30% of the initial test value. These losses are not considered to be significant by EU and OECD guidelines (SANCO 7032/VI/95rev.5 and OECD Guideline 506). Even assuming some degradation during the extended intervals of storage incurred for the cattle feeding study, analyte degradation in any additional freezer storage stability data would be marginal. Further, the waiver also notes that analyses conducted in the accompanying lactating goat metabolism study are available which show residues of afidopyropen are stable in liver at an interval of 224 days (7.3 months).

Conclusions: The submitted storage stability data are adequate to support the field trials and processing studies. These data demonstrate that afidopyropen and the metabolite M440I007 are stable in crop commodities when stored at or below -20°C for at least 24 months. For livestock commodities, storage stability was demonstrated at 10 times the LOQ in samples of whole milk, liver, muscle, and fat frozen at or below -20°C for up to ~3 months. These data are sufficient to support the holding times and conditions incurred for all of the samples comprising the crop field trial, processing, and livestock feeding studies submitted in support of this action. It should be noted that in the event of a use expansion, which could increase the poultry dietary burden, matrix-specific storage stability data on relevant analytes in poultry matrices would be required. The predominant residues in the hen metabolism study were afidopyropen in all poultry matrices, M440I017 (liver), and M440I060 (muscle).

5.3 Residue Data

5.3.1 Crop Field Trials (860.1500)

B.7.6.1 Residues in Target Crops

For this action, BASF has submitted petition PP#6F8468 which requests to establish tolerances for its new insecticide active ingredient afidopyropen on *Brassica* head and stem vegetable crop group 5-16, citrus fruit crop group 10-10, cotton, cucurbit vegetable crop group 9, fruiting vegetable crop group 8-10, leaf petioles vegetable subgroup 22B, leafy greens subgroup 4-16A, *Brassica* leafy greens subgroup 4-16B, pome fruit crop group 11-10, soybean, stone fruit crop group 12-12, tree nut crop group 14-12, and tuberous and corm vegetable subgroup 1C. For these uses, supervised crop field trials with afidopyropen were conducted in the U.S. and Canada employing the maximum labelled use patterns to yield the highest possible residue levels for assessment (MRID Nos. 49689030-49689040 and 49689121-49689124). It should be noted that field trials conducted in Australia on potatoes, leafy and *Brassica* leafy vegetables, fruiting vegetables, and cotton were included in this submission for review. All matrices were analyzed for residues of afidopyropen and the metabolite M440I007 according to the data-collection methods described in Section 5.1.1. The geographic distribution of the North American field trials is summarized in Appendix D. Sufficient numbers of trials were conducted in geographically appropriate regions to support the establishment of tolerances. Table 5.3.1 below provides a summary of the field trial results for determining the magnitude of the residue in crops.

Table 5.3.1. Summary of Residues from Crop Field Trials Conducted with Afidopyropen.											
Crop Matrix	Analyte	Total Application Rate (lb ai/A) [g ai/ha]	PHI (days)	n ¹	Residues (ppm parent equivalents)						
					Min. ²	Max. ²	LAFT ³	HAFT ³	Median ³	Mean ³	SD ³
Potato (U.S. and Canadian Field trials) [Proposed Use Pattern – 0.11 lb ai/A total application rate @ a 7-day PHI]											
Potato, tuber	Afidopyropen	0.1061-0.1124 [118.9-126.0]	6-7	19	<0.01	<0.01	<0.01	<0.01	0.01	0.01	N/A
Potato, tuber	M440I007	0.1061-0.1124 [118.9-126.0]	6-7	19	<0.005	<0.005	<0.005	<0.005	0.005	0.005	N/A
	Combined		6-7	19	<0.015	<0.015	<0.015	<0.015	0.015	0.015	N/A
Potato (Australian Field trials) [Proposed Use Pattern – Not Specified]											
Potato, tuber	Afidopyropen	0.1079-0.1086 [121.0-121.7]	7	2	<0.01	<0.01	N/A	N/A	0.01	0.01	N/A
	M440I007		7	2	<0.005	<0.005	N/A	N/A	0.005	0.005	N/A
	Combined		7	2	<0.015	<0.015	N/A	N/A	0.015	0.015	N/A
Leafy Vegetables (U.S. Field Trials) [Proposed Use Pattern – 0.11 lb ai/A total application rate @ 0-day PHI]											
Celery	Afidopyropen	0.105-0.110 (117-123)	0	7	0.024	1.894	0.027	1.275	0.283	0.434	0.446
Head lettuce, w/wrapper		0.106-0.112 (119-125)	0	8	0.011	0.287	0.014	0.278	0.164	0.149	0.079
Head lettuce, wo/wrapper		0.106-0.112 (119-125)	0	8	<0.01	0.275	<0.01	0.272	0.020	0.051	0.090
Leaf lettuce		0.106-0.111 (119-124)	0	8	0.030	0.969	0.042	0.944	0.496	0.482	0.312
Spinach		0.107-0.111 (119-124)	0	8	0.041	1.168	0.042	1.074	0.629	0.651	0.337
Celery	M440I007	0.105-0.110 (117-123)	0	7	0.007	0.131	0.013	0.076	0.043	0.042	0.024
Head lettuce, w/wrapper		0.106-0.112 (119-125)	0	8	0.009	0.254	0.012	0.240	0.097	0.115	0.086
Head lettuce, wo/wrapper		0.106-0.112 (119-125)	0	8	<0.005	0.216	<0.005	0.209	0.011	0.040	0.070
Leaf lettuce		0.106-0.111 (119-124)	0	8	0.022	0.654	0.033	0.644	0.201	0.284	0.204
Spinach		0.107-0.111 (119-124)	0	8	0.005	0.787	0.006	0.787	0.403	0.391	0.246
Celery	Combined	0.105-0.110 (117-123)	0	7	0.042	2.025	0.046	1.350	0.295	0.476	0.459
Head lettuce, w/wrapper		0.106-0.112 (119-125)	0	8	0.020	0.523	0.025	0.518	0.264	0.264	0.160
Head lettuce, wo/wrapper		0.106-0.112 (119-125)	0	8	<0.015	0.491	<0.015	0.481	0.032	0.091	0.160
Leaf lettuce		0.106-0.111 (119-124)	0	8	0.052	1.267	0.075	1.225	0.880	0.766	0.418
Spinach		0.107-0.111 (119-124)	0	8	0.047	1.843	0.048	1.829	1.088	1.042	0.553

Table 5.3.1. Summary of Residues from Crop Field Trials Conducted with Afidopyropen.											
Crop Matrix	Analyte	Total Application Rate (lb ai/A) [g ai/ha]	PHI (days)	n ¹	Residues (ppm parent equivalents)						
					Min. ²	Max. ²	LAFT ³	HAFT ³	Median ³	Mean ³	SD ³
Brassica Leafy Vegetables (U.S. Field Trials)											
[Proposed Use Pattern – 0.11 lb ai/A total application rate @ 0-day PHI]											
Broccoli	Afidopyropen	0.106-0.108 (119-121)	0	10	0.036	0.235	0.043	0.205	0.104	0.112	0.054
Cabbage, w/wrapper		0.104-0.110 (117-124)	0	10	<0.01	0.294	<0.01	0.276	0.042	0.091	0.101
Cabbage, wo/wrapper		0.104-0.110 (117-124)	0	10	<0.01	0.028	<0.01	0.024	0.010	0.013	0.006
Mustard greens		0.107-0.109 (118-122)	0	8	<0.01	3.137	<0.01	2.733	1.196	1.315	0.825
Broccoli	M440I007	0.106-0.108 (119-121)	0	10	<0.005	0.071	<0.005	0.064	0.016	0.022	0.019
Cabbage, w/wrapper		0.104-0.110 (117-124)	0	10	<0.005	0.067	<0.005	0.060	0.013	0.018	0.016
Cabbage, wo/wrapper		0.104-0.110 (117-124)	0	10	<0.005	0.008	<0.005	0.008	0.005	0.005	0.001
Mustard greens		0.107-0.109 (118-122)	0	8	<0.005	0.849	<0.005	0.771	0.670	0.501	0.316
Broccoli	Combined	0.106-0.108 (119-121)	0	10	<0.041	0.273	<0.048	0.234	0.122	0.134	0.068
Cabbage, w/wrapper		0.104-0.110 (117-124)	0	10	<0.015	0.361	<0.015	0.326	0.064	0.109	0.111
Cabbage, wo/wrapper		0.104-0.110 (117-124)	0	10	<0.015	<0.033	<0.015	0.030	0.015	0.018	0.006
Mustard greens		0.107-0.109 (118-122)	0	8	<0.015	3.986	<0.015	3.460	1.917	1.816	1.025
Leafy and Brassica Leafy Vegetables (Australian Field Trials)											
[Proposed Use Pattern- Not Specified]											
Chinese cabbage; Baby Wombok (Head)	Afidopyropen	0.1068 [119.70]	0	1	0.086	0.086	N/A	N/A	N/A	N/A	N/A
	M440I007		0	1	0.007	0.007	N/A	N/A	N/A	N/A	N/A
	Combined		0	1	0.093	0.093	N/A	N/A	N/A	N/A	N/A
Leaf lettuce; Vicinity (Leaves)	Afidopyropen	0.1059 [118.70]	0	1	1.12	1.12	N/A	N/A	N/A	N/A	N/A
	M440I007		0	1	0.006	0.111	N/A	N/A	N/A	N/A	N/A
	Combined		0	1	1.45	1.45	N/A	N/A	N/A	N/A	N/A
Broccoli; Iron Man (Head & Stem)	Afidopyropen	0.1081 [121.20]	0	1	0.064	0.064	N/A	N/A	N/A	N/A	N/A
	M440I007		0	1	0.008	0.008	N/A	N/A	N/A	N/A	N/A
	Combined		0	1	0.072	0.072	N/A	N/A	N/A	N/A	N/A

Table 5.3.1. Summary of Residues from Crop Field Trials Conducted with Afidopyropen.											
Crop Matrix	Analyte	Total Application Rate (lb ai/A) [g ai/ha]	PHI (days)	n ¹	Residues (ppm parent equivalents)						
					Min. ²	Max. ²	LAFT ³	HAFT ³	Median ³	Mean ³	SD ³
Brussels sprouts; Speedia F1 (Buttons)	Afidopyropen	0.1083 [121.40]	0	1	0.012	<0.005	N/A	N/A	N/A	N/A	N/A
	M440I007		0	1	<0.005	<0.005	N/A	N/A	N/A	N/A	N/A
	Combined		0	1	<0.017	<0.017	N/A	N/A	N/A	N/A	N/A
Cabbage; Endeavor (Head)	Afidopyropen	0.1105 [123.90]	0	1	0.029	0.029	N/A	N/A	N/A	N/A	N/A
	M44040I007		0	1	<0.005	<0.005	N/A	N/A	N/A	N/A	N/A
	Combined		0	1	<0.034	<0.034	N/A	N/A	N/A	N/A	N/A
Soybean (U.S. and Canadian Field Trials) [Proposed Use Pattern – 0.018 lb ai/A total application rate @ 7-day PHI]											
Soybean, forage	Afidopyropen	0.0171-0.0186 [19.2-20.9]	6-8	20	0.014	0.075	0.017	0.070	0.034	0.039	0.018
Soybean, hay			6-8 (0-13)	20	0.044	0.229	0.045	0.206	0.117	0.121	0.053
Soybean, seed			6-8	20	<0.01	<0.01	<0.01	<0.01	0.01	0.01	N/A
Soybean, forage	M440I007	0.0171-0.0186 [19.2-20.9]	6-8	20	<0.005	0.015	<0.005	0.015	0.005	0.006	0.002
Soybean, hay			6-8 (0-13)	20	<0.005	0.053	<0.005	0.052	0.009	0.012	0.010
Soybean, seed			6-8	20	<0.005	<0.005	<0.005	<0.005	0.005	0.005	N/A
Soybean, forage	Combined	0.0171-0.0186 [19.2-20.9]	6-8	20	<0.019	<0.080	<0.022	<0.075	0.039	0.044	0.018
Soybean, hay			6-8 (0-13)	20	<0.049	0.252	<0.050	0.219	0.123	0.133	0.057
Soybean, seed			6-8	20	<0.015	<0.015	<0.015	<0.015	0.015	0.015	N/A
Fruiting Vegetables (U.S. Field Trials) [Proposed Use Pattern – 0.11 lb ai/A total application rate @ 0-day PHI]											
Bell pepper	Afidopyropen	0.107-0.116 (120-130)	0	7	<0.01	0.057	<0.01	0.046	0.022	0.023	0.012
Non-bell pepper			0	3	0.040	0.061	0.046	0.059	0.055	0.053	0.007
Tomato			0	19	<0.01	0.103	<0.01	0.097	0.019	0.029	0.025
Bell pepper	M440I007	0.107-0.116 (120-130)	0	7	<0.005	0.008	<0.005	0.007	0.005	0.005	0.001
Non-bell pepper			0	3	<0.005	0.026	<0.005	0.024	0.007	0.012	0.010
Tomato			0	19	<0.005	0.011	<0.005	0.010	0.005	0.005	0.001
Bell pepper	Combined	0.107-0.116 (120-130)	0	7	<0.015	0.065	<0.015	0.053	0.027	0.028	0.013
Non-bell pepper			0	3	<0.045	0.087	<0.051	0.079	0.066	0.065	0.014
Tomato			0	19	<0.015	0.109	<0.015	0.102	0.024	0.034	0.025

Table 5.3.1. Summary of Residues from Crop Field Trials Conducted with Afidopyropen.											
Crop Matrix	Analyte	Total Application Rate lb ai/A (g ai/ha)	PHI (days)	n ¹	Residues (ppm parent equivalents)						
					Min. ²	Max. ²	LAFT ³	HAFT ³	Median ³	Mean ³	SD ³
Fruiting Vegetables (Australian Field Trials) [Proposed Use Pattern – Not Specified]											
Pepper; Hugo (Fruit minus Stems)	Afidopyropen	0.1072 [120.10]	0	1	<0.01	<0.01	N/A	N/A	N/A	N/A	N/A
	M440I007		0	1	<0.005	<0.005	N/A	N/A	N/A	N/A	N/A
	Combined		0	1	<0.015	<0.015	N/A	N/A	N/A	N/A	N/A
Tomato; Nija (Fruit minus Stems)	Afidopyropen	0.1080 [121.10]	0	1	0.013	0.013	N/A	N/A	N/A	N/A	N/A
	M440I007		0	1	<0.005	<0.005	N/A	N/A	N/A	N/A	N/A
	Combined		0	1	<0.018	<0.018	N/A	N/A	N/A	N/A	N/A
Cucurbit Vegetables (U.S. Field Trials) [Proposed Use Pattern – 0.11 lb ai/A total application rate @ 0-day PHI]											
Cucumber	Afidopyropen	0.106-0.109 (118-122)	0	9	0.0455	0.443	0.0530	0.406	0.112	0.162	0.120
Cantaloupe		0.106-0.110 (117-123)	0	8	<0.01	0.0255	<0.01	0.0231	0.018	0.017	0.005
Squash, summer		0.106-0.110 (119-123)	0	5	<0.01	0.0383	<0.01	0.0334	0.018	0.020	0.010
Squash, winter		0.106-0.113 (119-127)	0	5	<0.01	0.0375	<0.01	0.0367	0.011	0.018	0.012
Cucumber	M440I007	0.106-0.109 (118-122)	0	9	<0.005	0.0875	<0.005	0.0838	0.015	0.026	0.026
Cantaloupe		0.106-0.110 (117-123)	0	8	<0.005	<0.005	<0.005	<0.005	0.005	0.005	N/A
Squash, summer		0.106-0.110 (119-123)	0	5	<0.005	0.0058	<0.005	<0.0054	0.005	0.005	<0.001
Squash, winter		0.106-0.113 (119-127)	0	5	<0.005	0.0057	<0.005	<0.0053	0.005	0.005	<0.001
Cucumber	Combined	0.106-0.109 (118-122)	0	9	<0.0505	0.523	<0.0580	0.489	0.143	0.188	0.145
Cantaloupe		0.106-0.110 (117-123)	0	8	<0.015	<0.0305	<0.015	<0.0281	0.023	0.022	0.005
Squash, summer		0.106-0.110 (119-123)	0	5	<0.015	0.0441	<0.015	0.0388	0.023	0.025	0.011
Squash, winter		0.106-0.113 (119-127)	0	5	<0.015	<0.0425	<0.015	<0.0417	0.017	0.023	0.012

Table 5.3.1. Summary of Residues from Crop Field Trials Conducted with Afidopyropen.											
Crop Matrix	Analyte	Total Application Rate lb ai/A (g ai/ha)	PHI (days)	n ¹	Residues (ppm parent equivalents)						
					Min. ²	Max. ²	LAFT ³	HAFT ³	Median ³	Mean ³	SD ³
Citrus Fruit (U.S. Field Trials)											
[Proposed Use Pattern – 0.11 lb ai/A total application rate @ 0-day PHI]											
Grapefruit	Afidopyropen	0.109-0.114 (122-128) Conc.	0	6	<0.01	0.062	<0.01	0.062	0.025	0.031	0.022
		0.109-0.114 (122-128) Dilute	0	6	<0.01	0.041	<0.01	0.041	0.026	0.025	0.012
Lemon		0.109-0.114 (123-128) Conc.	0	8	<0.01	0.070	<0.01	0.070	0.025	0.033	0.025
		0.109-0.114 (123-128) Dilute	0	8	<0.01	0.055	<0.01	0.055	0.038	0.032	0.016
Orange		0.109-0.114 (122-128) Conc.	0	12	<0.01	0.069	<0.01	0.069	0.049	0.045	0.021
		0.109-0.114 (122-128) Dilute	0	12	<0.01	0.072	<0.01	0.072	0.043	0.044	0.020
Grapefruit	M440I007	0.109-0.114 (122-128) Conc.	0	6	<0.005	<0.005	<0.005	<0.005	0.005	0.005	N/A
		0.109-0.114 (122-128) Dilute	0	6	<0.005	<0.005	<0.005	<0.005	0.005	0.005	N/A
Lemon		0.109-0.114 (123-128) Conc.	0	8	<0.005	<0.005	<0.005	<0.005	0.005	0.005	N/A
		0.109-0.114 (123-128) Dilute	0	8	<0.005	<0.005	<0.005	<0.005	0.005	0.005	N/A
Orange		0.109-0.114 (122-128) Conc.	0	12	<0.005	0.006	<0.005	0.006	0.005	0.005	<0.001
		0.109-0.114 (122-128) Dilute	0	12	<0.005	0.007	<0.005	0.007	0.005	0.005	0.001
Grapefruit	Combined	0.109-0.114 (122-128) Conc.	0	6	<0.015	<0.067	<0.015	<0.067	0.030	0.036	0.022
		0.109-0.114 (122-128) Dilute	0	6	<0.015	<0.046	<0.015	<0.046	0.031	0.030	0.012
Lemon		0.109-0.114 (123-128) Conc.	0	8	<0.015	<0.075	<0.015	<0.075	0.030	0.035	0.022
		0.109-0.114 (123-128) Dilute	0	8	<0.015	<0.060	<0.015	<0.060	0.043	0.037	0.016

Table 5.3.1. Summary of Residues from Crop Field Trials Conducted with Afidopyropen.											
Crop Matrix	Analyte	Total Application Rate lb ai/A (g ai/ha)	PHI (days)	n ¹	Residues (ppm parent equivalents)						
					Min. ²	Max. ²	LAFT ³	HAFT ³	Median ³	Mean ³	SD ³
Orange		0.109-0.114 (122-128) Conc.	0	12	<0.015	0.075	<0.015	0.075	0.054	0.050	0.021
		0.109-0.114 (122-128) Dilute	0	12	<0.015	0.079	<0.015	0.079	0.048	0.049	0.020
Pome Fruit (U.S. and Canadian Field Trials) [Proposed Use Pattern – 0.044 lb ai/A total application rate @ 7-day PHI]											
Apple	Afidopyropen	0.043-0.046 [49-51] Conc.	6-7	14	<0.01	0.011	<0.01	<0.011	0.01	0.010	<0.001
		0.043-0.046 [49-51] Dilute	6-7	14	<0.01	<0.01	<0.01	<0.01	0.01	0.01	N/A
Pear		0.043-0.046 [48-51] Conc.	7	8	<0.01	0.015	<0.01	0.014	0.01	0.011	0.001
		0.043-0.046 [48-51] Dilute	7	8	<0.01	0.013	<0.01	0.012	0.01	0.010	0.001
Apple	M440I007	0.043-0.046 [49-51] Conc.	6-7	14	<0.005	<0.005	<0.005	<0.005	0.005	0.005	N/A
		0.043-0.046 [49-51] Dilute	6-7	14	<0.005	<0.005	<0.005	<0.005	0.005	0.005	N/A
Pear		0.043-0.046 [48-51] Conc.	7	8	<0.005	<0.005	<0.005	<0.005	0.005	0.005	N/A
		0.043-0.046 [48-51] Dilute	7	8	<0.005	<0.005	<0.005	<0.005	0.005	0.005	N/A
Apple	Combined	0.043-0.046 [49-51] Conc.	6-7	14	<0.015	<0.016	<0.015	<0.016	0.015	0.015	<0.001
		0.043-0.046 [49-51] Dilute	6-7	14	<0.015	<0.015	<0.015	<0.015	0.015	0.015	N/A
Pear		0.043-0.046 [48-51] Conc.	7	8	<0.015	<0.020	<0.015	0.019	0.015	0.016	0.001
		0.043-0.046 [48-51] Dilute	7	8	<0.015	<0.018	<0.015	<0.017	0.015	0.015	0.001

Table 5.3.1. Summary of Residues from Crop Field Trials Conducted with Afidopyropen.											
Crop Matrix	Analyte	Total Application Rate lb ai/A (g ai/ha)	PHI (days)	n ¹	Residues (ppm parent equivalents)						
					Min. ²	Max. ²	LAFT ³	HAFT ³	Median ³	Mean ³	SD ³
Stone Fruit (U.S. and Canadian Field Trials) [Proposed Use Pattern – 0.018 lb ai/A total application rate @ 7-day PHI]											
Cherry	Afidopyropen	0.017-0.019 [19-21] Conc.	7	8	<0.01	0.017	<0.01	0.014	0.01	0.011	0.001
		0.017-0.019 [19-21] Dilute	7	8	<0.01	0.021	<0.01	0.021	0.01	0.012	0.004
Peach		0.017-0.019 [20-21] Conc.	7	13	<0.01	<0.01	<0.01	<0.01	0.01	0.01	N/A
		0.017-0.019 [20-21] Dilute	7	13	<0.01	0.012	<0.01	<0.011	0.01	0.010	<0.001
Plum		0.017-0.019 [20-21] Conc.	7	10	<0.01	<0.01	<0.01	<0.01	0.01	0.01	N/A
		0.017-0.019 [20-21] Dilute	7	10	<0.01	<0.01	<0.01	<0.01	0.01	0.01	N/A
Cherry	M440I007	0.017-0.019 [19-21] Conc.	7	8	<0.005	<0.005	<0.005	<0.005	0.005	0.005	N/A
		0.017-0.019 [19-21] Dilute	7	8	<0.005	<0.005	<0.005	<0.005	0.005	0.005	N/A
Peach		0.017-0.019 [20-21] Conc.	7	13	<0.005	<0.005	<0.005	<0.005	0.005	0.005	N/A
		0.017-0.019 [20-21] Dilute	7	13	<0.005	<0.005	<0.005	<0.005	0.005	0.005	N/A
Plum		0.017-0.019 [20-21] Conc.	7	10	<0.005	<0.005	<0.005	<0.005	0.005	0.005	N/A
		0.017-0.019 [20-21] Dilute	7	10	<0.005	<0.005	<0.005	<0.005	0.005	0.005	N/A
Cherry	Combined	0.017-0.019 [19-21] Conc.	7	8	<0.015	<0.022	<0.015	<0.019	0.015	0.016	0.001
		0.017-0.019 [19-21] Dilute	7	8	<0.015	<0.026	<0.015	<0.026	0.015	0.017	0.004
Peach		0.017-0.019 [20-21] Conc.	7	13	<0.015	<0.015	<0.015	<0.015	0.015	0.015	N/A
		0.017-0.019 [20-21] Dilute	7	13	<0.015	<0.017	<0.015	<0.016	0.015	0.015	<0.001

Table 5.3.1. Summary of Residues from Crop Field Trials Conducted with Afidopyropen.											
Crop Matrix	Analyte	Total Application Rate lb ai/A (g ai/ha)	PHI (days)	n ¹	Residues (ppm parent equivalents)						
					Min. ²	Max. ²	LAFT ³	HAFT ³	Median ³	Mean ³	SD ³
Plum		0.017-0.019 [20-21] Conc.	7	10	<0.015	<0.015	<0.015	<0.015	0.015	0.015	N/A
		0.017-0.019 [20-21] Dilute	7	10	<0.015	<0.015	<0.015	<0.015	0.015	0.015	N/A
Tree Nuts (U.S. Field Trials)											
[Proposed Use Pattern – 0.018 lb ai/A total application rate @ 7-day PHI]											
Almond, nutmeat	Afidopyropen	0.018 [20.2] Conc.	7	5	<0.01	<0.01	<0.01	<0.01	0.01	0.01	N/A
		0.018 [20.2] Dilute	7	5	<0.01	<0.01	<0.01	<0.01	0.01	0.01	N/A
Almond, hulls		0.018 [20.2] Conc.	7	5	0.018	0.060	0.019	0.058	0.025	0.030	0.016
		0.018 [20.2] Dilute	7	5	0.015	0.057	0.016	0.056	0.039	0.036	0.015
Pecan, nutmeat		0.018 [20.2] Conc.	6-8	5	<0.01	<0.01	<0.01	<0.01	0.01	0.01	N/A
		0.018 [20.2] Dilute	6-8	5	<0.01	<0.01	<0.01	<0.01	0.01	0.01	N/A
Pistachio, nutmeat		0.018 [20.2] Conc.	7	3	<0.01	<0.01	<0.01	<0.01	0.01	0.01	N/A
		0.018 [20.2] Dilute	7	3	<0.01	<0.01	<0.01	<0.01	0.01	0.01	N/A
Almond, nutmeat	M440I007	0.018 [20.2] Conc.	7	5	<0.005	<0.005	<0.005	<0.005	0.005	0.005	N/A
		0.018 [20.2] Dilute	7	5	<0.005	<0.005	<0.005	<0.005	0.005	0.005	N/A
Almond, hulls		0.018 [20.2] Conc.	7	5	<0.005	<0.005	<0.005	<0.005	0.005	0.005	N/A
		0.018 [20.2] Dilute	7	5	<0.005	<0.005	<0.005	<0.005	0.005	0.005	N/A
Pecan, nutmeat		0.018 [20.2] Conc.	6-8	5	<0.005	<0.005	<0.005	<0.005	0.005	0.005	N/A
		0.018 [20.2] Dilute	6-8	5	<0.005	<0.005	<0.005	<0.005	0.005	0.005	N/A
Pistachio, nutmeat		0.018 [20.2] Conc.	7	3	<0.005	<0.005	<0.005	<0.005	0.005	0.005	N/A
		0.018 [20.2] Dilute	7	3	<0.005	<0.005	<0.005	<0.005	0.005	0.005	N/A
Almond, nutmeat	Combined	0.018 [20.2] Conc.	7	5	<0.015	<0.015	<0.015	<0.015	0.015	0.015	N/A
		0.018 [20.2] Dilute	7	5	<0.015	<0.015	<0.015	<0.015	0.015	0.015	N/A
Almond, hulls		0.018 [20.2] Conc.	7	5	<0.023	<0.065	<0.024	<0.063	0.030	0.035	0.016
		0.018 [20.2] Dilute	7	5	<0.020	<0.062	<0.021	<0.061	0.044	0.041	0.015
Pecan, nutmeat		0.018 [20.2] Conc.	6-8	5	<0.015	<0.015	<0.015	<0.015	0.015	0.015	N/A
		0.018 [20.2] Dilute	6-8	5	<0.015	<0.015	<0.015	<0.015	0.015	0.015	N/A

Table 5.3.1. Summary of Residues from Crop Field Trials Conducted with Afidopyropen.											
Crop Matrix	Analyte	Total Application Rate lb ai/A (g ai/ha)	PHI (days)	n ¹	Residues (ppm parent equivalents)						
					Min. ²	Max. ²	LAFT ³	HAFT ₃	Median ³	Mean ³	SD ³
Pistachio, nutmeat		0.018 [20.2] Conc.	7	3	<0.015	<0.015	<0.015	<0.015	0.015	0.015	N/A
		0.018 [20.2] Dilute	7	3	<0.015	<0.015	<0.015	<0.015	0.015	0.015	N/A
Cotton (U.S. Field Trials)											
[Proposed Use Pattern – 0.11 lb ai/A total application rate@ 7-day PHI]											
Cotton, undelinted seed	Afidopyropen	0.106-0.110 [119-124]	6-8	12	<0.01	0.061	<0.01	0.059	0.010	0.018	0.015
Cotton, gin byproducts		0.107-0.108 [120-121]	6-7	3	0.42	0.65	0.46	0.60	0.54	0.53	0.073
Cotton, undelinted seed	M440I007	0.106-0.110 [119-124]	6-8	12	<0.005	0.025	<0.005	0.023	0.005	0.007	0.005
Cotton, gin byproducts		0.107-0.108 [120-121]	6-7	3	0.048	0.21	0.059	0.20	0.085	0.11	0.075
Cotton, undelinted seed	Combined	0.106-0.110 [119-124]	6-8	12	<0.015	0.083	<0.015	0.082	0.015	0.025	0.020
Cotton, gin byproducts		0.107-0.108 [120-121]	6-7	3	0.47	0.84	0.54	0.80	0.60	0.65	0.14
Cotton (Australian Field Trials)											
[Proposed Use Rate – Not Specified]											
Cotton, undelinted seed	Afidopyropen	0.109-0.112 [122-125]	7	3	<0.01	<0.01	N/A	N/A	0.01	0.01	N/A
Cotton, simulated gin trash			7	3	0.15	0.69	N/A	N/A	0.31	0.38	0.28
Cotton, undelinted seed	M440I007	0.109-0.112 [122-125]	7	3	<0.005	<0.005	N/A	N/A	0.005	0.005	N/A
Cotton, simulated gin trash			7	3	0.013	0.108	N/A	N/A	0.031	0.050	0.051
Cotton, undelinted seed	Combined	0.109-0.112 [122-125]	7	3	<0.015	<0.015	N/A	N/A	0.015	0.015	N/A
Cotton, simulated gin trash			7	3	0.18	0.80	N/A	N/A	0.32	0.43	0.32

¹ n = number of field trials.

² Values based on total number of samples.

³ Values based on total number of samples because single samples were analyzed. LAFT = lowest average field trial, HAFT = highest average field trial, SD = standard deviation. For computation of the LAFT, HAFT, median, mean, and standard deviation, values <LOQ are assumed to be at the LOQ (0.01 ppm for afidopyropen and 0.005 ppm for M440I007). N/A = Not Applicable.

Conclusions. The submitted residue data are adequate to satisfy all data requirements for determining the magnitude of the residue for the crops listed in Table 5.3.1. An adequate number of trials were performed for each subject crop in the countries where the use of afidopyropen is proposed and did represent the critical good agricultural practices (cGAP) of that

region. There were no distinct differences with residue levels between concentrated and dilute spray applications. Residue decline studies generally showed a decrease in residue levels with increasing PHIs. No labels were provided to assess the field trials that were conducted in Australia. A review of this data finds that the Australian field trials were conducted following the same pattern of use and generally resulted in lower mean residue levels in the crops that were studied.

5.3.2 Field Rotational Crops (860.1900)

B.7.9. Residues in Succeeding Crops or Rotational Crops

For this action, BASF has requested to waive the requirement for field rotational crop studies since no residues of afidopyropen were identified in the confined rotational crop studies in any of the matrices at any PBI (MRID No. 49689133).

Conclusions: The submitted confined rotational crop studies for afidopyropen indicate that no residues of concern are expected to be present in rotational crops. Given these results, field rotational crop studies are not needed to set plant-back restrictions. Because no residues are evident in the confined study at the 30-day PBI (i.e.; shortest PBI studied), these data demonstrate that a 30-day plant-back interval is appropriate for non-labeled crops.

5.3.3 Processed Food and Feed (860.1520)

B.7.7. Effects of Industrial Processing and/or Household Preparation (Annex IIA 6.5)

For this action, BASF is requesting to establish tolerances for the residues of afidopyropen on a number of crops and corresponding processed commodities. To satisfy data requirements, BASF has submitted processing studies made for this new insecticide active ingredient on potatoes, tomatoes, soybeans, oranges, apples, plums, and cotton. A summary of the data acquired from these processing studies is presented below in Table 5.3.3.

Table 5.3.3. Mean Processing Factors Determined for Residues of Afidopyropen.		
Processed Commodity	Median Pf- Afidopyropen	Median Pf - M4401007
	Expressed as parent equivalents	
Potato Processing Studys		
Baked Potatoes	NR ¹	NR
Boiled Potatoes	NR	NR
Potato Chips	NR	NR
Potato Pulp	NR	NR
Ensiled Potatoes	NR	NR
Potato Granules/Flakes	NR	NR
Potato Wet Peel	NR	NR
Peeled Potato	NR	NR
Potato Proteins	NR	NR
Potato Processed Waste	NR	NR
Potato Starch	NR	NR
Potato Crisps	NR	NR

Table 5.3.3. Mean Processing Factors Determined for Residues of Afidopyropen.		
Processed Commodity	Median Pf- Afidopyropen	Median Pf - M440I007
	Expressed as parent equivalents	
Tomato Processing Study		
Washed Tomatoes	0.5	0.4
Canned Tomatoes	0.1	0.3
Peeled Tomatoes	0.2	0.3
Tomato Peel	2.4	1.5
Sundried Tomato	4.4	1.9
Wash Water	0.2	0.4
Tomato Paste	0.6	0.3
Tomato Purée	0.2	0.3
Raw Tomato Juice	0.1	0.3
Wet Pomace	1.8	1.2
Dry Pomace	13.5	10.2
Ketchup after Pasteurization	0.6	0.4
Dry Tomato Peels	20.7	8.2
Soybean Processing Study		
Soybean Aspirated Grain Fractions	>12.5	>1.3
Soybean Crude Oil	NR	NR
Soybean Flour	NR	NR
Soybean Hulls	NR	NR
Soybean Meal	NR	NR
Soybean Miso	NR	NR
Soybean Refined Oil	NR	NR
Soybean Pollards	NR	NR
Soy Milk	NR	NR
Soy Sauce	NR	NR
Soybean Toasted Meal	NR	NR
Soy Tofu	NR	NR
Orange Processing Study		
Juice	0.1	1.0
Wet pomace	0.5	1.0
Dry pomace	2.5	1.0
Pulp	0.1	1.0
Dried pulp	0.4	1.0
Peel	1.9	1.0
Peel after oil extraction	0.5	1.0
Oil	4.6	1.1
Marmalade	0.1	1.0
Apple Processing Study		
Apple Sauce	1.0	1.0
Dried Apples	0.5	1.0
Canned Apples	1.0	1.0
Wet Pomace	3.9	2.0
Washed Whole Apples	1.0	1.0
Apple Juice	1.0	1.0
Dried Pomace	6.4	1.0
Wash Water	1.0	1.0
Fruit Syrup	1.0	1.0

Table 5.3.3. Mean Processing Factors Determined for Residues of Afidopyropen.		
Processed Commodity	Median Pf- Afidopyropen	Median Pf - M440I007
	Expressed as parent equivalents	
Plum Processing Study		
Washed Whole Plums	1.0	1.0
Purée	1.0	1.0
Dried Prunes	1.0	1.0
Wash Water	1.0	1.0
Depitted Plums	1.0	1.0
Juice	1.0	1.0
Cotton Processing Study		
Cotton seed hulls	0.77	1.0
Cotton seed meal	0.23	0.26
Refined oil	0.14	0.26

¹ NR = Not Reported; NA = Not Applicable

Conclusions. The processing studies that were submitted are acceptable. The samples in these studies were analyzed for parent afidopyropen and its metabolite M440I007 using the proposed tolerance enforcement method described in Section 5.1.3 and are supported by adequate storage stability data. The data indicate that residues of afidopyropen may concentrate in dried tomatoes, soybean aspirated grain fractions (AGF), apple wet pomace and dried pomace, and citrus peel and oil.

In summarizing these findings, the tomato processing study data demonstrated parent residues concentrate in dried tomatoes at 4.4x. This is a processed commodity the Agency normally does not set tolerances on and the registrant did not include it in their petition. However, Canada (PMRA) is proposing to set an MRL at 0.50 ppm for this processed commodity. Using the HAFT of 0.097 ppm equates to a calculated value of 0.43 ppm which is rounded to 0.50 ppm following the OECD rounding classes. Following the HED *Processing Factor Focus Group (PFFG) Guidance Document* (2014, in draft), this tolerance is recommended for harmonization. For AGF, the soybean processing study demonstrated that residues concentrate at 12.5x in this commodity. Using the HAFT of 0.01 ppm equates to a calculated value of 0.125 ppm which is rounded to 0.15 ppm following the OECD rounding classes. The apple processing study conducted for afidopyropen demonstrated that parent residues concentrate in wet pomace at 3.9x and dried pomace at 6.4x. The Agency does not set tolerances on apple dried pomace and none were proposed by the registrant. In regard to apple wet pomace, using the HAFT of 0.011 ppm equates to a calculated tolerance value of 0.0429 ppm which is rounded to 0.05 ppm. In regard to citrus commodities, the processing study demonstrated that parent residues concentrate in peel at 1.9x and in oil at 4.6x. Using the HAFT of 0.07 ppm for orange equates to a calculated tolerance value of 0.133 ppm for peel which is rounded to 0.15 ppm. The recommended tolerance for citrus fruit is 0.15 ppm which covers the calculated limit for peel; therefore, a separate tolerance is not needed. For oil, using the HAFT of 0.07 ppm for lemon equates to a tolerance value of 0.331 which is rounded to 0.40 ppm following the OECD rounding classes.

5.3.4 Meat, Milk, Poultry, and Eggs (860.1480)

B.7.2 Metabolism, Distribution and Expressions of Residues in Livestock and B.7.8 Livestock Feeding Studies

Afidopyropen is being proposed for use on several commodities that are fed to livestock which include: almond hulls, apple wet pomace, citrus dried pulp, cotton gin byproducts, cotton hulls, cotton meal, cotton undelinted seed, AGF, potato culls, potato processed waste, soybean hulls, soybean meal, and soybean seed. Soybean forage and hay are not a consideration because the

proposed afidopyropen labels restrict the feeding of these commodities to livestock. As such, there is the potential for transfer of residues to livestock commodities, and the registrant conducted a dairy cattle feeding study.

Cattle

A feeding study was conducted with lactating Holstein dairy cows by dosing the animals with encapsulated afidopyropen via a balling gun at levels equivalent to 1.54 ppm, 4.61 ppm, and 15.34 ppm in feed (dry weight basis).

At the 1.54 ppm feeding level, the only quantifiable residue was afidopyropen (AFIDOPYROPEN) in liver (0.017 ppm). All other analytes in tissues (M440I001, M440I003, and CPCA-carnitine) were less than LOQ. Whole milk samples were not analyzed at this feeding level.

At the 4.61 ppm feeding level, CPCA-carnitine, expressed as parent equivalents, was <0.005–0.021 ppm in whole milk, and 0.05-0.149 ppm in muscle. The only other quantifiable analyte was afidopyropen (BAS 440 I) in liver (0.040-0.056 ppm).

At the 15.34 ppm feeding level, afidopyropen (BAS 440 I) was <0.001-0.0029 ppm (whole milk), <0.001-0.0014 ppm (skim milk), <0.001-0.0018 ppm (cream), and 0.17-0.20 ppm (liver). Metabolite M440I001 (expressed as parent equivalents) was only quantified in liver (0.021-0.033 ppm). CPCA-carnitine (expressed as parent equivalents) was quantifiable in whole milk (<0.005-0.065 ppm), skim milk (0.029-0.058 ppm), cream (0.015-0.048 ppm), and muscle (0.268 ppm). All other analytes were less than LOQ in all milk (1 to 28 days) and tissue samples (day 29).

The summary of the residues obtained in the ruminant matrices examined following dosing with afidopyropen are presented below in Table 5.3.4.1.

Matrix / analyte	Study day	Dose Level (ppm)	n	Minimum	Maximum	Median	Mean	Std. Dev.
Afidopyropen								
Whole Milk	1 to 28	1.54	30	NA ²	NA	NA	NA	NA
		4.61	30	<0.001	<0.001	<0.001	<0.001	0.00
		15.34	60	<0.001	0.0029	<0.001	<0.001	0.00
Skim Milk	22	15.34	6	<0.001	0.0014	<0.001	<0.001	0.00
Cream	22	15.34	6	<0.001	0.0018	0.0011	0.0010	0.00
Liver	29	1.54	3	0.015	0.019	0.017	0.017	0.002
		4.61	3	0.040	0.056	0.041	0.046	0.009
		15.34	3	0.17	0.20	0.19	0.187	0.015
Kidney	29	1.54	3	<0.01	<0.01	<0.01	<0.01	0.00
		4.61	3	<0.01	<0.01	<0.01	<0.01	0.00
		15.34	3	<0.01	0.010	<0.01	<0.01	0.00
Muscle	29	1.54-15.34	9	<0.01	<0.01	<0.01	<0.01	0.00
Fat	29	1.54-15.34	27	<0.01	<0.01	<0.01	<0.01	0.00

Matrix / analyte	Study day	Dose Level (ppm)	n	Minimum	Maximum	Median	Mean	St Dev.
CPCA-Carnitine (M440I060) expressed as parent equivalents								
Whole Milk	1 to 28	1.54	30	<0.005	<0.005	<0.005	<0.005	0.000
		4.61	30	<0.005	0.021	0.013	0.013	0.004
		15.34	60	<0.005	0.065	0.029	0.028	0.013
Skim Milk	22	15.34	6	0.029	0.058	0.044	0.044	0.011
Cream	22	15.34	6	0.015	0.048	0.036	0.035	0.013
Liver	29	1.54-15.34	9	<0.05	<0.05	<0.05	<0.05	0.00
Kidney	29	1.54-15.34	9	<0.05	<0.05	<0.05	<0.05	0.00
Muscle	29	1.54	3	<0.05	<0.05	<0.05	<0.05	0.00
		4.61	3	<0.05	0.149	<0.05	<0.05	0.054
		15.34	3	0.268	0.268	0.268	0.268	0
Fat	29	1.54-15.34	27	<0.05	<0.05	<0.05	<0.05	0.00
M440I001³ expressed as parent equivalents								
Liver	29	1.54, 4.61	6	<0.01	<0.01	<0.01	<0.01	0.00
		15.34	3	0.021	0.033	0.021	0.026	0.007
M440I003 expressed as parent equivalents								
All tissues	29	1.54-15.34	54	<0.01	<0.01	<0.01	<0.01	0.00
M440I005 expressed as parent equivalents								
Whole Milk	1 to 28	4.61, 15.34	90	<0.001	<0.001	<0.001	<0.001	0.00
Skim Milk	22	15.34	6	<0.001	<0.001	<0.001	<0.001	0.00
Cream	22	15.34	6	<0.001	<0.001	<0.001	<0.001	0.00

¹ The LOQ for residues in milk is 0.001 ppm each for Afidopyropen, M440I001, and M440I005, and 0.005 ppm for M440I060 (CPCA-carnitine). The LOQ for residues in tissues is 0.01 ppm each for Afidopyropen, M440I001, and M440I003, and 0.05 ppm for M440I060 (CPCA-carnitine).

² NA = Not applicable (the low dose milk samples were not analyzed for parent, M440I001 or M440I005 based on the results for the mid- and high-dose analyses).

³ M440I001 was found only in liver (shown here) and then only at the high-dose level; therefore, for brevity, the other milk and tissue matrices are not shown.

Following withdrawal of the dose, residues of afidopyropen were non-quantifiable in samples of whole milk throughout depuration (study days 31, 35, 38, and 42), except for CPCA-carnitine (as parent equivalents), which was observed initially (Day 31) at <0.005-0.017 ppm (Table 5.3.4.2). Residues of afidopyropen in tissues at study day 32 were non-detectable, except for afidopyropen at 0.01 ppm in liver and CPCA-carnitine (expressed as parent equivalents) at 0.29 ppm in muscle, and were <LOQ in all tissue samples from the animals sacrificed on study days 36 and 43 (Table 5.3.4.3).

Animal Id #	Matrix/ Collection Time	Feeding Level (ppm)	Residues (ppm) ^a			
			BAS 440 I	M440I001	M440I005	CPCA-carnitine
13	Whole Milk / Day 31	15.34	<0.001	<0.001	<0.001	0.017
14			<0.001	<0.001	<0.001	0.012
15			<0.001	<0.001	<0.001	< 0.005
14	Whole Milk / Day 35		<0.001	<0.001	<0.001	< 0.005
15			<0.001	<0.001	<0.001	< 0.005
15			Whole Milk / Day 38	<0.001	<0.001	<0.001
	Whole Milk / Day 42		<0.001	<0.001	<0.001	< 0.005

Table 5.3.4.3. Summary of Residues of Afidopyropen in Tissues From the Depuration Study. ¹						
Animal Id #	Matrix/ Collection Time	Feeding Level (ppm)	Residues (ppm) ²			
			BAS 440 I	M440I001	M440I003	CPCA-carnitine
13	Liver / Day 32	15.34	0.011	<0.002	<0.002	<0.01
	Kidney		<0.002	<0.002	<0.002	<0.01
	Muscle		<0.002	<0.002	<0.002	0.290
	Fat (mesenterial)		<0.002	<0.002	<0.002	<0.01
	Fat (perirenal)		<0.002	<0.002	<0.002	<0.01
	Fat (subcutaneous)		<0.002	<0.002	<0.002	<0.01
14	Liver / Day 36		<0.002	<0.002	<0.002	<0.01
	Kidney		<0.002	<0.002	<0.002	<0.01
	Muscle		<0.002	<0.002	<0.002	<0.05
	Fat (mesenterial)		<0.002	<0.002	<0.002	<0.01
	Fat (perirenal)		<0.002	<0.002	<0.002	<0.01
	Fat (subcutaneous)		<0.002	<0.002	<0.002	<0.01
15	Liver / Day 43		<0.002	<0.002	<0.002	<0.01
	Kidney		<0.002	<0.002	<0.002	<0.01
	Muscle		<0.002	<0.002	<0.002	<0.05
	Fat (mesenterial)		<0.002	<0.002	<0.002	<0.01
	Fat (perirenal)		<0.002	<0.002	<0.002	<0.01
	Fat (subcutaneous)		<0.002	<0.002	<0.002	<0.01

¹. The LOQ for residues in milk is 0.001 ppm each for afidopyropen, M440I001, and M440I005, and 0.005 ppm for CPCA-carnitine.

². The LOQ and LOD for residues in tissues are 0.01 and 0.002 ppm each for afidopyropen, M440I001, and M440I003, and 0.05 and 0.01 ppm for CPCA-carnitine.

Swine

Based on the results of the goat and hen metabolism studies, HED determined that there is no reasonable expectation of finite residues of afidopyropen in swine matrices resulting from the uses which are being requested. If additional uses are proposed in the future that result in a significant increase in dietary burden for swine, then this conclusion will be reconsidered.

Poultry

The petitioner requested a waiver for a poultry feeding study (MRID No. 49689041), based on the results of the hen metabolism study. HED determined that there is no reasonable expectation of finite residues of afidopyropen in poultry matrices resulting from the uses which are being requested. If additional uses are proposed in the future that result in a significant increase in dietary burden for poultry, then this conclusion will be reconsidered and a poultry feeding study may be required.

Conclusions. The submitted cattle feeding study for depicting the magnitude of the residue in ruminants is adequate to support the proposed use of afidopyropen. The analyses conducted in this study were generated using the proposed tolerance enforcement method described in Section 5.1.3 and are supported by adequate storage stability data. HED notes that if additional uses are proposed which will increase dietary burden for poultry, then a poultry feeding study may be required.

5.3.4.1 Dietary Burden

The more balanced diet (MBD) calculations of livestock for afidopyropen are summarized below in Table 5.3.4.4. These calculations were determined using the Dietary Burden Calculator PMRA v.2.8, which is based on the Guidance Document on Residues in Livestock, 04-SEP-2013 (OECD ENV/JM/MONO(2013)8).

Table 5.3.4.4. Maximum Reasonably Balanced Dietary Burden (MRDB) of Livestock for Afidopyropen. ¹							
More Balanced Diet (MBD)							
Crop	Commodity	Type	Residue		%DM	%Diet	Dietary Contribution ppm
			ppm	input			
Beef Cattle							
Cotton	Gin byproducts	R	0.54	Median	90	5	0.03
Cotton	Hulls	R	0.0077	Median	90	10	0.0009
Soybean	Seed	PC	0.005	Median	89	5	0.0003
Untreated feed	NA	NA	NA	NA	NA	80	0
Total	NA	NA	NA	NA	NA	100	0.03
Dairy Cattle							
Soybean	Hulls	R	0.005	Median	90	20	0.001
Apples	Pomace, wet	CC	0.039	Median	40	10	0.010
Cotton	Undelinted seed	PC	0.01	Median	88	10	0.001
Untreated feed	NA	NA	NA	NA	NA	60	0
Total	NA	NA	NA	NA	NA	100	0.01
Poultry							
Soybean	Meal	PC	0.005	Median	92	25	0.001
Untreated feed	NA	NA	NA	NA	NA	75	0
Total	NA	NA	NA	NA	NA	100	0.001
Swine							
Soybean	Meal	PC	0.005	Median	92	15	0.0008
Untreated feed	NA	NA	NA	NA	NA	85	0
Total	NA	NA	NA	NA	NA	100	0.0008

¹ ½ LOQ (0.005 ppm) is used for non-detected residue values.

5.3.4.2 Estimated Secondary Residues in Livestock

The results of the cattle feeding study and the MBDs calculated above in Section 5.3.4.1 were used to determine the anticipated residue levels expected in ruminant commodities. The registrant performed the dairy cattle feeding study at the dosing levels of 1.54 ppm, 4.61 ppm, and 15.34 ppm. The feeding levels turned out to be approximately 154X, 461X, and 1534X the MBD level that HED calculated for dairy cattle. A poultry feeding study was not provided but the metabolism study for the laying hen reflects a 12000x rate.

Comparison of these dietary burden estimates to residue levels observed in the lactating cattle feeding study and laying hen metabolism study result in the projected secondary residues shown in Tables 5.3.4.5 and 5.3.4.6. Based on conservative assumptions, which are appropriate for deriving tolerance levels in livestock commodities, quantifiable residues are not expected in commodities from cattle, horses, goats, and sheep may occur. For poultry, residues are expected to also be substantially less than the LOQ.

Table 5.3.4.5. Summary of Anticipated Residues of Afidopyropen in Tissues and Milk of Cattle.							
Commodity	Feeding Level (ppm)	Highest Residues (ppm)	TF ¹	MBD ² (ppm)		Anticipated Residues at MBD (ppm) ³	
Afidopyropen							
				Beef	Dairy	Beef	Dairy
Whole milk	1.54	<0.001	6.5×10^{-4}	0.03	0.01	2.0×10^{-5}	6.5×10^{-6}
Fat		<0.01	6.5×10^{-3}			2.0×10^{-4}	6.5×10^{-5}
Liver		0.017	1.1×10^{-2}			3.3×10^{-4}	1.0×10^{-4}
Kidney		<0.01	6.5×10^{-3}			2.0×10^{-4}	6.5×10^{-5}
Muscle		<0.01	6.5×10^{-3}			2.0×10^{-4}	6.5×10^{-5}

¹ Transfer Factor (TF) = commodity highest residue result/feeding level.

² MBD – More Balanced Diet

³ Anticipated Residue = TF x MBD

Table 5.3.4.6. Summary of Anticipated Residues of Afidopyropen in Tissues and Eggs of Poultry.						
Commodity	Feeding Level (ppm) – Hen Metabolism	Highest Residues (ppm)	TF ¹	MBD ² (ppm)		Anticipated Residues ³ at MBD (ppm)
Afidopyropen						
				Poultry		Poultry
Egg white	12	0.125	1.0×10^{-2}	0.001		1.0×10^{-5}
Egg yolk		0.355	3.0×10^{-2}			3.0×10^{-5}
Fat		0.097	8.1×10^{-3}			8.1×10^{-6}
Muscle		0.021	1.8×10^{-3}			1.8×10^{-6}
Liver		0.241	2.0×10^{-2}			2.0×10^{-5}

¹ Transfer Factor (TF) = commodity highest residue result/feeding level.

² MBD – More Balanced Diet

³ Anticipated Residue = TF x MBD

Conclusions. Based on the determination of anticipated residues, there is no reasonable expectation of finite residues of afidopyropen in ruminant or poultry commodities. For swine, the calculated dietary burden of 0.0008 ppm is sufficiently low that tolerances for residues of afidopyropen in hogs are not needed. As a result, the proposed uses of afidopyropen will fall under category 3 of 40 CFR 180.6(a) for livestock.

5.3.5. Food Handling (860.1460)

There are no proposed uses of afidopyropen relevant to this guideline topic.

5.3.6 Water, Fish, and Irrigated Crops (860.1400)

There are no proposed uses of afidopyropen relevant to this guideline topic.

5.4 Food Residue Profile

The submitted residue chemistry studies are adequate for supporting regulatory conclusions, establishing appropriate tolerance levels for enforcement, and for purposes of risk assessment. The analysis of afidopyropen can be accomplished through standard analytical techniques with residues showing limited dissipation during the employed frozen storage intervals. The nature of the residue is adequately understood based plant and livestock metabolism studies conducted with afidopyropen. Translocation and metabolism in plants (tomato, cabbage, and soybean) is minimal with some variation on the nature and extent of conjugations between crops. In livestock, metabolism studies found the metabolic pathways of afidopyropen to be similar in

ruminants and poultry. Parent afidopyropen is concluded to be the only residue of concern for tolerance enforcement and risk assessment in both plants and livestock.

Adequate residue chemistry data have been provided for afidopyropen. Field trial studies are of an adequate number and geographic representation. The magnitude of the residue data show that when following the proposed patterns of use, detectable residues of afidopyropen are expected in crops. HAFT residues of afidopyropen found in the matrices of target crops ranged from <0.01 ppm in/on potatoes, soybean seed, and tree nuts to 1.275 ppm in/on celery. The crop field trial data were generated using validated data-collection methods and are adequately supported by frozen storage stability data. Sufficient processing study data were submitted for potatoes, tomatoes, soybeans, oranges, apples, plums, and cotton to determine if residues concentrate in processed commodities derived from these crops. These data indicate that residues of afidopyropen may concentrate in dried tomatoes, soybean AGF, apple wet pomace and dried pomace, and citrus peel and oil.

The submitted rotational crop data indicate that no residues of concern are expected to be present in rotational crops. Because no residues are evident in the confined study at the 30-day PBI (i.e.; shortest PBI studied), field rotational crop studies are not needed to set plant-back restrictions. These data are adequate to demonstrate that a 30-day plant-back interval is appropriate for non-labeled crops.

Afidopyropen is proposed for use on a number of commodities that are significant livestock feedstuffs. As a result, dietary burdens were calculated to determine the potential for secondary transfer of residues to livestock. The cattle feeding study results and dietary burden calculations indicate that afidopyropen residues of concern are not expected tissues or milk of ruminants. Anticipated residues for poultry based on the results of the metabolism study and dietary burden calculations indicate there are no expectation of finite residues in tissue or eggs. Given these results, tolerances for ruminant and poultry commodities are not needed. For swine, there is also no expected secondary transfer of afidopyropen residues based on the significantly low MBD calculated for hogs. As a result, livestock will fall under category 3 of 40 CFR 180.6(a); there is negligible expectation of finite afidopyropen residues of concern in these commodities.

6.0 Tolerance Derivation

The recommended tolerances for the residues of afidopyropen in/on the requested crops were obtained using the OECD calculation procedures. The residue data and calculation procedure outputs are included in Appendix E. All relevant crop group tolerances were established following guideline requirements. However, for cucurbit vegetables, a group tolerance would not be ordinarily established because the MRLs of the representative crops differ by more than a factor of 5x. In consideration of this requested registration, the ChemSAC looked at this issue and recommended in favor of establishing a group tolerance in this instance (ChemSAC Meeting Minutes, 11/22/2017). ChemSAC agreed in recommending that a group tolerance set at the highest MRL of 0.70 ppm obtained for cucumbers will cover the variability of residues in these crops caused by the photo-degradation effects reported by the registrant. For the determination of processed commodity tolerances, the HAFT residue for afidopyropen was multiplied by the empirical processing factor that was obtained to get an anticipated residue value (see section 5.3.3). Because afidopyropen is a new active ingredient, no MRLs have yet been established by Codex, Canada, or Mexico. For this joint review being conducted with PMRA, all of the recommended MRLs for this petition are harmonized between Canada and the U.S.

7.0 ChemSAC Reference

This memorandum was reviewed by the Chemistry Science Advisory Council (ChemSAC) on 01/17/2018 and was revised to reflect the recommendations of that group.

Appendix A. Summary of Metabolites.

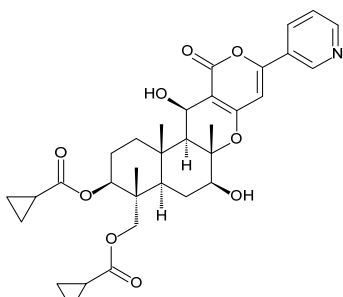
Table A.1. Summary of Metabolites and Degradates			
Chemical Name	Matrix	Percent TRR (PPM) ¹	
		Matrices - Major Residue (>10%TRR)	Matrices - Minor Residue (<10%TRR)
Afidopyropen Reg. No.: 5599022 (BAS 440 I, ME5343, M440I0000) 	Tomato Fruit	32% (0.1079) NCA- ¹⁴ C - 7 DALA 16% (0.0484) NCA- ¹⁴ C - 14 DALA 61% (0.033) pyranone-4- ¹⁴ C - 1 DALA	--
	Tomato Leaves	25% (1.0443) NCA- ¹⁴ C - 14 DALA 27% (0.627) pyranone-4- ¹⁴ C - 1 DALA	--
	Cabbage	143% (0.202) NCA- ¹⁴ C - 7 DALA 23% (0.398) pyranone-4- ¹⁴ C - 1 DALA, outer leaves 22% (0.094) pyranone-4- ¹⁴ C - 1 DALA, inner leaves	6.9% (0.073) NCA- ¹⁴ C - 14 DALA
	Soybean Leaves	18% (2.944) NCA- ¹⁴ C 32% (1.572) CPCA- ¹⁴ C 19% (3.8) pyranone-4- ¹⁴ C	--
	Soybean Seed	--	--
	Soybean Hulls	13% (0.189) NCA- ¹⁴ C 17% (0.441) CPCA- ¹⁴ C - pods 18% (0.031) CPCA- ¹⁴ C - green pods	--
	Soybean Plant		8.2% (0.033) NCA- ¹⁴ C
	Rotational Crops	--	--
	Rat	23% - 39% in feces both sexes (3 ppm/bw) 10% - 37% in feces both sexes (300 ppm/bw)	<0.10% - <0.84% in urine both sexes (3 & 300 ppm/day)
	Milk	--	6.8% (<0.001) pyranone-4-C ¹⁴
Ruminant Muscle	26% (0.002) pyranone-4- ¹⁴ C	--	
Ruminant Fat	49% (0.002) pyranone-4- ¹⁴ C	--	
Ruminant Kidney	17% (0.006) pyranone-4- ¹⁴ C	--	
Ruminant Liver	35% (0.068) pyranone-4- ¹⁴ C 18% (0.038) CPCA- ¹⁴ C	--	
Poultry Muscle	46% (0.021) CPCA- ¹⁴ C	--	
Poultry Skin and Fat	96% (0.097) CPCA- ¹⁴ C	--	
Poultry Liver	59% (0.241) CPCA- ¹⁴ C	--	
Egg Yolk	97% (0.355) CPCA- ¹⁴ C	--	
Egg White	919% (0.125) CPCA- ¹⁴ C	--	
Water	Maximum % Applied (day)		Final % Applied (day)
	Aerobic soil	Not Reported	13% (121 d)
	Anaerobic soil	Not Reported	23% (134 d)
	Soil photolysis, light	Not Reported	92% (14 d)
	Soil photolysis, dark	Not Reported	35% (15 d)
	Aqueous photolysis	Not Reported	pH 7; 55% (8 d)
			Natural water; 34% (13 d)
			pH 9, 10; 98% (30 d)
	Hydrolysis	Not Reported	pH 9, 25; 85% (30 d)
			pH 9, 50; 15% (30 d)
Aerobic aquatic	Not Reported	51% (100 d)	
Anaerobic aquatic	Not Reported	27% (100 d)	
Terrestrial field dissipation	Not Reported	6.4 (450 d)	

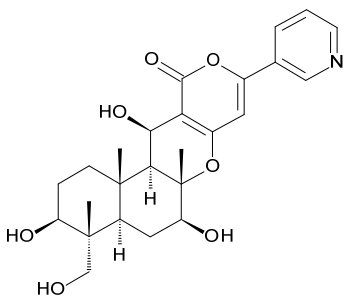
Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) ¹		
		Matrices - Major Residue (>10%TRR)	Matrices - Minor Residue (<10%TRR)	
M440I001 Reg. No.: 5741530 (ME5343-T1) 	Tomato Fruit	--	--	
	Tomato Leaves	--	2.3% (0.053) pyranone-4-C ¹⁴ - 1 DALA	
	Cabbage	--	--	
	Soybean Leaves	--	--	
	Soybean Seed	--	--	
	Soybean Hulls	--	--	
	Soybean Plant	--	--	
	Rotational Crops	--	--	
	Milk	45% (0.002) pyranone-4-C ¹⁴	--	
	Ruminant Muscle	24% (0.002) pyranone-4-C ¹⁴	--	
	Ruminant Fat	--	4.6% (<0.001) pyranone-4-C ¹⁴	
	Ruminant Kidney	66% (0.025) pyranone-4-C ¹⁴	--	
	Ruminant Liver	46% (0.089) pyranone-4-C ¹⁴	--	
	Poultry Muscle	--	--	
	Poultry Skin and Fat	--	--	
	Poultry Liver	--	--	
	Egg Yolk	--	--	
	Egg White	--	--	
	Rat	14% - 24% in feces both sexes (3 ppm/bw) 14% - 19% in feces both sexes (300 ppm/bw) 10% in urine in males (300 ppm/bw)	1.96% - 8.17% in urine both sexes (3 & 300 ppm/day) 3.43% - 4.11% in bile both sexes (3 & 300 ppm/bw)	
	Water	Maximum % Applied (day)		Final % Applied (day)
		Aerobic soil	Not Reported	Not Reported
		Anaerobic soil	37% (134 d)	37% (134 d)
		Soil photolysis, light	Not Reported	Not Reported
		Soil photolysis, dark	3.7% (15 d)	3.7% (15 d)
		Aqueous photolysis	Not Reported	Not Reported
		Hydrolysis	pH 4; Not Reported	pH 4; Not Reported
			pH 7; Not Reported	pH 7; Not Reported
pH 9; 47% (50, 30 d)			pH 9; 47% (50, 30 d)	
Aerobic aquatic		Not Reported	Not Reported	
Anaerobic aquatic		46% (100 d)	46% (100 d)	
Terrestrial field dissipation	2.7% (24 d)	Not Reported (450 d)		

Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) ¹		
		Matrices - Major Residue (>10%TRR)	Matrices - Minor Residue (<10%TRR)	
M440I002 Reg. No.: 5741532 (ME5354-T2)	Tomato Fruit	--	--	
	Tomato Leaves	--	3.6% (0.082) pyranone-4-C ¹⁴ - 1 DALA	
	Cabbage	--	--	
	Soybean Leaves	--	--	
	Soybean Seed	--	--	
	Soybean Hulls	--	--	
	Soybean Plant	--	--	
	Rotational Crops	--	--	
	Milk	--	--	
	Ruminant Muscle	--	--	
	Ruminant Fat	--	--	
	Ruminant Kidney	--	--	
	Ruminant Liver	--	2.1% (0.004) pyranone-4-C ¹⁴ 1.5% (0.003) CPCA- ¹⁴ C	
	Poultry Muscle	--	--	
	Poultry Skin and Fat	--	--	
	Poultry Liver	--	--	
	Egg Yolk	--	--	
	Egg White	--	--	
	Rat	11% males in feces (300 ppm/bw)	0.58% - 9% in urine and feces both sexes (3 and 300 ppm/bw)	
	Water	Maximum % Applied (day)		Final % Applied (day)
		Aerobic soil	12% (7 d)	1.1% (120 d)
		Anaerobic soil	20% (14 d)	13% (150 d)
		Soil photolysis, light	2.5% (10 d)	2.3% (15 d)
		Soil photolysis, dark	8.7% (10 d)	7.2% (15 d)
		Aqueous photolysis	pH 7 Buffer; 1.2% (10 d)	pH 7 Buffer; Not Reported
			Natural water; 3.4% (7 d)	Natural water; 1.7% (14 d)
		Hydrolysis	pH 4; Not Reported	pH 4; Not Reported
pH 7; Not Reported			pH 7; Not Reported	
pH 9; 9.3% (15 d)			pH 9; 5.6% (30 d)	
Aerobic aquatic		6.1% (56 d)	5.3% (100 d)	
Anaerobic aquatic	18% (30 d)	11% (100 d)		
Terrestrial field dissipation	19% (22 d)	Not Reported (450 d)		
N-oxide of ME5343-T2	Rat	10% in bile both sexes (300 ppm/bw)	0.29% - 2.10% in urine both sexes (3 & 300 ppm/bw) 6% - 9% in bile both sexes (3 & 300 ppm/bw)	

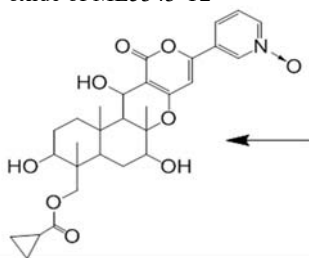


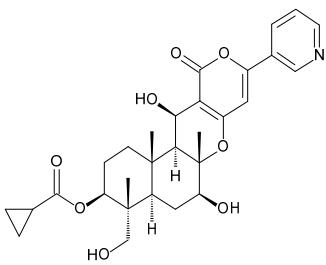
Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) ¹		
		Matrices - Major Residue (>10%TRR)	Matrices - Minor Residue (<10%TRR)	
M440I003 Reg. No.: 5741533 (ME5343-T3) 	Tomato Fruit	--	--	
	Tomato Leaves	--	--	
	Cabbage	--	--	
	Soybean Leaves	--	--	
	Soybean Seed	--	--	
	Soybean Hulls	--	--	
	Soybean Plant	--	--	
	Rotational Crops	--	Wheat Straw 0.9% (0.001) NCA-¹⁴C - 31 day PBI	
	Milk	--	3.6% (<0.001) pyranone-4-C ¹⁴	
	Ruminant Muscle	22% (0.002) pyranone-4-C ¹⁴	0.2% (0.001) CPCA- ¹⁴ C	
	Ruminant Fat	--	8.1% (<0.001) pyranone-4-C ¹⁴	
	Ruminant Kidney	12% (0.005) pyranone-4-C ¹⁴	1.4% (0.007) CPCA- ¹⁴ C	
	Ruminant Liver	12% (0.026) CPCA- ¹⁴ C	4.4% (0.009) pyranone-4-C ¹⁴	
	Poultry Muscle	--	--	
	Poultry Skin and Fat	--	--	
	Poultry Liver	--	--	
	Egg Yolk	--	--	
	Egg White	--	--	
	Rat	--	<0.06% – 4.01% both sexes in urine and feces (3 & 300 ppm/bw)	
	Water	Maximum % Applied (day)		Final % Applied (day)
		Aerobic soil	8.0% (7 d)	3.3% (121 d)
		Anaerobic soil	17% (21 d)	5.2% (134 d)
		Soil photolysis, light	3.2% (7 d)	2.7% (15 d)
		Soil photolysis, dark	14% (15 d)	14% (15 d)
		Aqueous photolysis	pH 7: 2.9% (4 d)	pH 7: 1.6% (14 d)
			Natural water; 3.6% (7 d)	Natural water; 3.4% (14 d)
		Hydrolysis	pH 4; Not Reported	pH 4; Not Reported
			pH 7; Not Reported	pH 7; Not Reported
pH 9; 3.7% (6 d)			pH 9; 1.6% (30 d)	
Aerobic aquatic		6.5% (78 d)	5.7% (100 d)	
Anaerobic aquatic		6.5% (30 d)	5.1% (100 d)	
Terrestrial field dissipation		9.3% (31 d)	0.18% (450 d)	

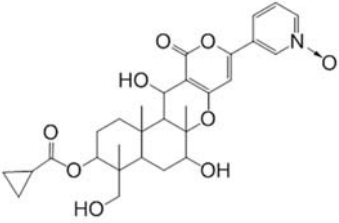
Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) ¹		
		Matrices - Major Residue (>10%TRR)	Matrices - Minor Residue (<10%TRR)	
N-oxide of ME5343-T3 	Rat	--	1.48% -5% both sexes in bile (3 & 300 ppm/bw)	
M440I004 Reg. No.: 5824381 (ME5343-T4)	Tomato Fruit	--	--	
	Tomato Leaves	--	--	
	Cabbage	--	--	
	Soybean Leaves	--	--	
	Soybean Seed	--	--	
	Soybean Hulls	--	--	
	Soybean Plant	--	--	
	Rotational Crops	--	--	
	Milk	--	--	
	Ruminant Muscle	--	--	
	Ruminant Fat	--	--	
	Ruminant Kidney	--	--	
	Ruminant Liver	--	2.9% (0.006) pyranone-4-C ¹⁴	
	Poultry Muscle	--	--	
	Poultry Skin and Fat	--	--	
	Poultry Liver	--	--	
	Egg Yolk	--	--	
	Egg White	--	--	
	Rat	--	--	
	Water	Maximum % Applied (day)		Final % Applied (day)
		Aerobic soil	--	--
Anaerobic soil		--	--	
Soil photolysis, light		--	--	
Soil photolysis, dark		--	--	
Aqueous photolysis		--	--	
Hydrolysis		--	--	
Aerobic aquatic		--	--	
Anaerobic aquatic		--	--	
Terrestrial field dissipation	--	--		

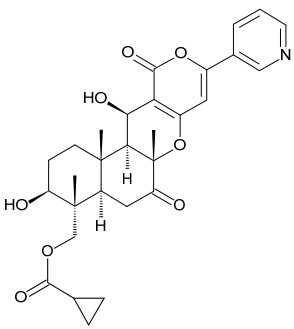
Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) ¹		
		Matrices - Major Residue (>10%TRR)	Matrices - Minor Residue (<10%TRR)	
M440I005 Reg. No.: 5824382 (ME5343-T5) 	Tomato Fruit	--	--	
	Tomato Leaves	--	--	
	Cabbage	--	--	
	Soybean Leaves	--	--	
	Soybean Seed	--	--	
	Soybean Hulls	--	--	
	Soybean Plant	--	--	
	Rotational Crops	--	--	
	Milk	17% (0.001) pyranone-4-C ¹⁴	--	
	Ruminant Muscle	--	--	
	Ruminant Fat	--	--	
	Ruminant Kidney	--	--	
	Ruminant Liver	--	--	
	Poultry Muscle	--	--	
	Poultry Skin and Fat	--	--	
	Poultry Liver	--	--	
	Egg Yolk	--	--	
	Egg White	--	--	
	Rat	--	--	
	Water (Minor Transformation; <10%)	Maximum % Applied (day)		Final % Applied (day)
		Aerobic soil	Not Reported	Not Reported
		Anaerobic soil	Not Reported	Not Reported
		Soil photolysis, light	Not Reported	Not Reported
		Soil photolysis, dark	3.2% (15 d)	3.2% (15 d)
		Aqueous photolysis	Not Reported	Not Reported
		Hydrolysis	pH 4; Not Reported	pH 4; Not Reported
			pH 7; Not Reported	pH 7; Not Reported
			pH 9; Not Reported	pH 9; Not Reported
Aerobic aquatic		6.0% (56 d)	5.0% (100 d)	
Anaerobic aquatic	Not Reported	Not Reported		
Terrestrial field dissipation	Not Reported	Not Reported		

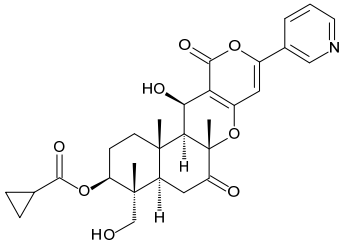
Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) ¹		
		Matrices - Major Residue (>10%TRR)	Matrices - Minor Residue (<10%TRR)	
M440I006 Reg. No.: 5824383 (ME5343-T6) 	Tomato Fruit	--	--	
	Tomato Leaves	--	--	
	Cabbage	--	--	
	Soybean Leaves	--	--	
	Soybean Seed	--	--	
	Soybean Hulls	--	--	
	Soybean Plant	--	--	
	Rotational Crops	--	--	
	Milk	--	5.4% (<0.001) pyranone-4- ¹⁴ C	
	Ruminant Muscle	--	5.3% (<0.001) pyranone-4- ¹⁴ C	
	Ruminant Fat	--	5.2% (<0.001) pyranone-4- ¹⁴ C	
	Ruminant Kidney	--	--	
	Ruminant Liver	--	--	
	Poultry Muscle	--	--	
	Poultry Skin and Fat	--	--	
	Poultry Liver	--	--	
	Egg Yolk	--	--	
	Egg White	--	--	
	Rat	--	--	
	Water (Minor Transformation; <10%)	Maximum % Applied (day)		Final % Applied (day)
		Aerobic soil	Not Reported	Not Reported
		Anaerobic soil	Not Reported	Not Reported
		Soil photolysis, light	Not Reported	Not Reported
		Soil photolysis, dark	Not Reported	Not Reported
		Aqueous photolysis	Not Reported	Not Reported
		Hydrolysis	pH 4; Not Reported	pH 4; Not Reported
			pH 7; Not Reported	pH 7; Not Reported
pH 9; Not Reported			pH 9; Not Reported	
Aerobic aquatic		0.5% (100 d)	0.5% (100 d)	
Anaerobic aquatic	Not Reported	Not Reported		
Terrestrial field dissipation	Not Reported	Not Reported		

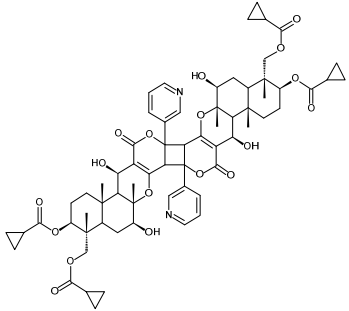
Table A.1. Summary of Metabolites and Degradates			
Chemical Name	Matrix	Percent TRR (PPM) ¹	
		Matrices - Major Residue (>10%TRR)	Matrices - Minor Residue (<10%TRR)
M440I007 Reg. No.: 5824749 (ME5343-T7) 	Tomato Fruit	10% (0.0344) NCA- ¹⁴ C – 7 DALA	6.7% (0.0201) NCA- ¹⁴ C – 14 DALA
	Tomato Leaves	15% (0.6277) NCA- ¹⁴ C – 14 DALA	2.1% (0.048) pyranone-4- ¹⁴ C - 1 DALA
	Cabbage	17% (0.244) NCA- ¹⁴ C - 7 DALA 17% (0.302) pyranone-4- ¹⁴ C – 1 DALA, outer leaves 14 (0.060) pyranone-4- ¹⁴ C – 1 DALA, inner leaves	9.9% (0.105) NCA- ¹⁴ C – 14 DALA
	Soybean Leaves	15% (2.566) NCA- ¹⁴ C 18% (3.532) pyranone-4- ¹⁴ C	9.2% (0.457) CPCA- ¹⁴ C
	Soybean Seed	12% (0.002) CPCA- ¹⁴ C	1% (0.002) pyranone-4- ¹⁴ C
	Soybean Hulls	26% (0.397) NCA- ¹⁴ C 24% (0.614) CPCA- ¹⁴ C – pods 32% (0.056) CPCA- ¹⁴ C – green pods 50% (0.782) pyranone-4- ¹⁴ C	--
	Soybean Plant	14% (0.055) NCA- ¹⁴ C 38% (0.136) pyranone-4- ¹⁴ C	--
	Rotational Crops	--	--
	Milk	--	--
	Ruminant Muscle	--	--
	Ruminant Fat	--	--
	Ruminant Kidney	--	--
	Ruminant Liver	--	--
	Poultry Muscle	--	--
	Poultry Skin and Fat	--	--
	Poultry Liver	--	--
	Egg Yolk	--	--
	Egg White	--	--
	Rat	--	--
	Water (Minor Transformation; <10%)	Maximum % Applied (day)	
Aerobic soil		Not Reported	Not Reported
Anaerobic soil		Not Reported	Not Reported
Soil photolysis, light		Not Reported	Not Reported
Soil photolysis, dark		Not Reported	Not Reported
Hydrolysis		pH 4; Not Reported	pH 4; Not Reported
		pH 7; Not Reported	pH 7; Not Reported
		pH 9; 3.7% (6 d)	pH 9; 1.6% (30 d)
Aerobic aquatic		Not Reported	Not Reported
Anaerobic aquatic		Not Reported	Not Reported
Terrestrial field dissipation	Not Reported	Not Reported	

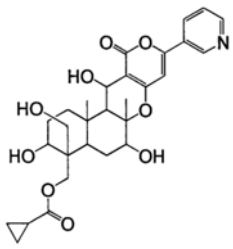
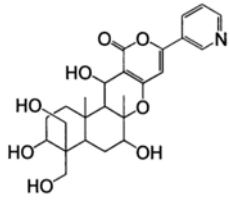
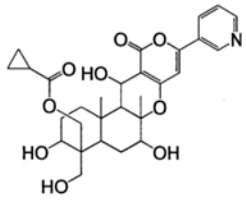
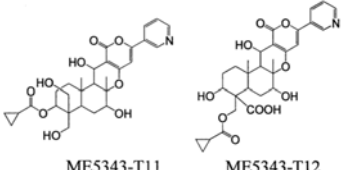
Table A.1. Summary of Metabolites and Degradates			
Chemical Name	Matrix	Percent TRR (PPM) ¹	
		Matrices - Major Residue (>10%TRR)	Matrices - Minor Residue (<10%TRR)
ME5343-T8 	Rat	10% in feces males (300 ppm/bw)	0.10% - 8% urine and feces both sexes (3 & 300 ppm/bw)
ME5343-T9 	Rat	--	<0.12% - 4% urine and feces both sexes (3 & 300 ppm/day)
ME5343-T10 	Rat	--	<0.58% - 7% urine and feces both sexes (3 & 300 ppm/day)
ME5343-T11/ ME5343-T12 (co-eluted under 1 peak; HPLC) 	Rat	--	<0.10% - 5.07% urine and feces both sexes (3 & 300 ppm/day)

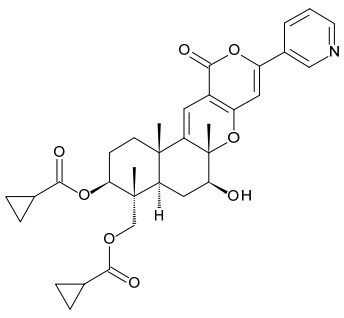
Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) ¹		
		Matrices - Major Residue (>10%TRR)	Matrices - Minor Residue (<10%TRR)	
M440I014 Reg. No.: 5741536 	Tomato Fruit	--	--	
	Tomato Leaves	--	--	
	Cabbage	--	--	
	Soybean Leaves	--	2.5% (0.421) NCA- ¹⁴ C 3.9% (0.193) CPCA- ¹⁴ C	
	Soybean Seed	--	--	
	Soybean Hulls	3.9% (0.193) CPCA- ¹⁴ C - pods	--	
	Soybean Plant	--	--	
	Rotational Crops	--	--	
	Milk	--	--	
	Ruminant Muscle	--	--	
	Ruminant Fat	--	--	
	Ruminant Kidney	--	--	
	Ruminant Liver	--	--	
	Poultry Muscle	--	--	
	Poultry Skin and Fat	--	--	
	Poultry Liver	--	--	
	Egg Yolk	--	--	
	Egg White	--	--	
	Rat	--	--	
	Water (Minor Transformation; <10%)	Maximum % Applied (day)		Final % Applied (day)
		Aerobic soil	6.5% (7 d)	4.5% (120 d)
		Anaerobic soil	Not Reported	Not Reported
		Soil photolysis, light	Not Reported	Not Reported
		Soil photolysis, dark	Not Reported	Not Reported
		Aqueous photolysis	Not Reported	Not Reported
		Hydrolysis	pH 4; Not Reported	pH 4; Not Reported
			pH 7; Not Reported	pH 7; Not Reported
pH 9; Not Reported			pH 9; Not Reported	
Aerobic aquatic		Not Reported	Not Reported	
Anaerobic aquatic	Not Reported	Not Reported		
Terrestrial field dissipation	Not Reported	Not Reported		

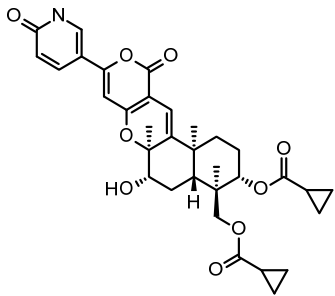
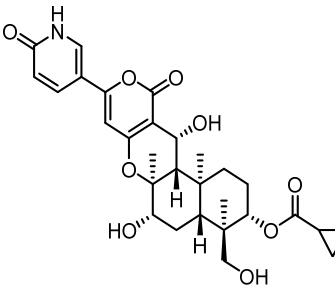
Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) ¹		
		Matrices - Major Residue (>10%TRR)	Matrices - Major Residue (>10%TRR)	
M440I015 	Water (Minor Transformation; <10%)	Maximum % Applied (day)		
		Aerobic soil	8.9% (10 d)	6.0% (120 d)
		Anaerobic soil	Not Reported	Not Reported
		Soil photolysis, light	Not Reported	Not Reported
		Soil photolysis, dark	Not Reported	Not Reported
		Aqueous photolysis	Not Reported	Not Reported
		Hydrolysis	pH 4: Not Reported	pH 4: Not Reported
			pH 7: Not Reported	pH 7: Not Reported
			pH 9: Not Reported	pH 9: Not Reported
		Aerobic aquatic	Not Reported	Not Reported
		Anaerobic aquatic	Not Reported	Not Reported
		Terrestrial field dissipation	Not Reported	Not Reported
M440I016 	Water (Minor Transformation; <10%)	Maximum % Applied (day)		
		Aerobic soil	2.0% (10 d)	0.6% (120 d)
		Anaerobic soil	Not Reported	Not Reported
		Soil photolysis, light	Not Reported	Not Reported
		Soil photolysis, dark	8.5% (15 d)	8.5% (15 d)
		Aqueous photolysis	Not Reported	Not Reported
		Hydrolysis	pH 4: Not Reported	pH 4: Not Reported
			pH 7: Not Reported	pH 7: Not Reported
			pH 9: Not Reported	pH 9: Not Reported
		Aerobic aquatic	Not Reported	Not Reported
		Anaerobic aquatic	Not Reported	Not Reported
		Terrestrial field dissipation	Not Reported	Not Reported

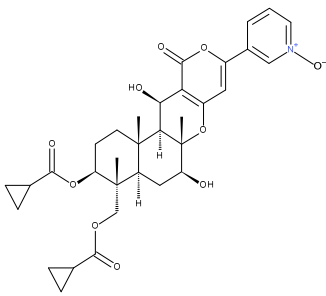
Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) ¹		
		Matrices - Major Residue (>10%TRR)	Matrices - Major Residue (>10%TRR)	
M440I017 Reg. No.: 6045738 	Tomato Fruit	--	--	
	Tomato Leaves	--	8.4% (0.193) pyranone-4- ¹⁴ C - 1 DALA	
	Cabbage	--	2.1% (0.037) pyranone-4- ¹⁴ C - 1 DALA, outer leaves 2.8% (0.012) pyranone-4- ¹⁴ C - 1 DALA, inner leaves	
	Soybean Leaves	--	--	
	Soybean Seed	--	--	
	Soybean Hulls	--	--	
	Soybean Plant	--	--	
	Rotational Crops	--	--	
	Milk	--	--	
	Ruminant Muscle	--	--	
	Ruminant Fat	--	--	
	Ruminant Kidney	--	--	
	Ruminant Liver	--	3.7% (.008) CPCA- ¹⁴ C	
	Poultry Muscle	--	--	
	Poultry Skin and Fat	--	--	
	Poultry Liver	21% (0.085) CPCA- ¹⁴ C	--	
	Egg Yolk	--	--	
	Egg White	--	5.4% (.007) CPCA- ¹⁴ C	
	Rat	20% - 32% in bile both sexes (3 ppm/bw)	<0.38 - 1.46 urine and feces both sexes (3 and 300 ppm/bw) 5% - 6% in bile both sexes (300 ppm/bw)	
	Water	Maximum % Applied (day)		Final % Applied (day)
		Aerobic soil	--	--
Anaerobic soil		--	--	
Soil photolysis, light		--	--	
Soil photolysis, dark		--	--	
Aqueous photolysis		--	--	
Hydrolysis		--	--	
Aerobic aquatic		--	--	
Anaerobic aquatic		--	--	
Terrestrial field dissipation	--	--		

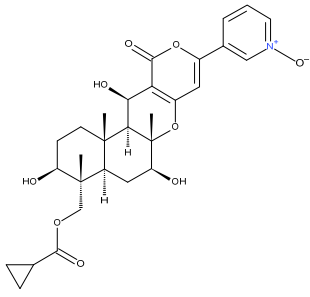
Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) ¹		
		Matrices - Major Residue (>10%TRR)	Matrices - Minor Residue (<10%TRR)	
<p>M440I019</p> 	Tomato Fruit	--	--	
	Tomato Leaves	--	3.1% (0.071) pyranone-4- ¹⁴ C - 1 DALA	
	Cabbage	--	--	
	Soybean Leaves	--	--	
	Soybean Seed	--	--	
	Soybean Hulls	--	--	
	Soybean Plant	--	--	
	Rotational Crops	--	--	
	Milk	--	--	
	Ruminant Muscle	--	--	
	Ruminant Fat	--	--	
	Ruminant Kidney	--	--	
	Ruminant Liver	--	--	
	Poultry Muscle	--	--	
	Poultry Skin and Fat	--	--	
	Poultry Liver	--	--	
	Egg Yolk	--	--	
	Egg White	--	--	
	Rat	--	--	
	Water	Maximum % Applied (day)		Final % Applied (day)
		Aerobic soil	--	--
		Anaerobic soil	--	--
		Soil photolysis, light	--	--
		Soil photolysis, dark	--	--
		Aqueous photolysis	--	--
		Hydrolysis	--	--
		Aerobic aquatic	--	--
Anaerobic aquatic		--	--	
Terrestrial field dissipation		--	--	

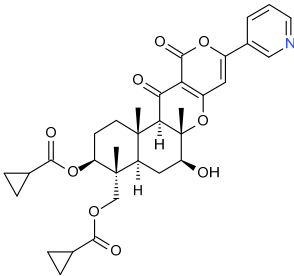
Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) ¹		
		Matrices - Major Residue (>10%TRR)	Matrices - Minor Residue (<10%TRR)	
M440I020 Reg. No.: 5881593 	Tomato Fruit	--	--	
	Tomato Leaves	--	3.0% (0.070) pyranone-4- ¹⁴ C - 1 DALA	
	Cabbage	--	1.6% (0.029) pyranone-4- ¹⁴ C - 1 DALA, outer leaves 2.6 (0.011) pyranone-4- ¹⁴ C - 1 DALA, inner leaves	
	Soybean Leaves	--	--	
	Soybean Seed	--	--	
	Soybean Hulls	--	--	
	Soybean Plant	--	--	
	Rotational Crops	--	--	
	Milk	--	--	
	Ruminant Muscle	--	--	
	Ruminant Fat	--	--	
	Ruminant Kidney	--	--	
	Ruminant Liver	--	--	
	Poultry Muscle	--	--	
	Poultry Skin and Fat	--	--	
	Poultry Liver	--	--	
	Egg Yolk	--	--	
	Egg White	--	--	
	Rat	--	--	
	Water	Maximum % Applied (day)		Final % Applied (day)
		Aerobic soil	--	--
		Anaerobic soil	--	--
		Soil photolysis, light	--	--
Soil photolysis, dark		--	--	
Aqueous photolysis		--	--	
Hydrolysis		--	--	
Aerobic aquatic		--	--	
Anaerobic aquatic		--	--	
Terrestrial field dissipation	--	--		

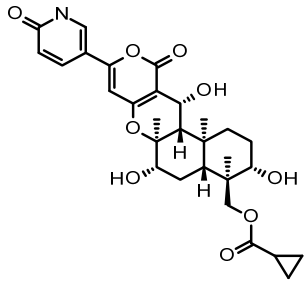
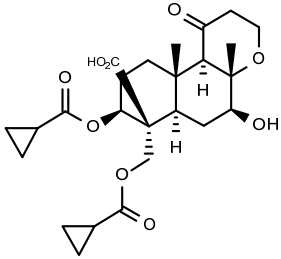
Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) ¹		
		Matrices - Major Residue (>10%TRR)	Matrices - Major Residue (>10%TRR)	
M440I021 	Water (Minor Transformation; <10%)	Maximum % Applied (day)		
		Aerobic soil	5.7% (88 d)	3.1% (120 d)
		Anaerobic soil	Not Reported	Not Reported
		Soil photolysis, light	Not Reported	Not Reported
		Soil photolysis, dark	Not Reported	Not Reported
		Aqueous photolysis	Not Reported	Not Reported
		Hydrolysis	pH 4: Not Reported	pH 4: Not Reported
			pH 7: Not Reported	pH 7: Not Reported
			pH 9: Not Reported	pH 9: Not Reported
		Aerobic aquatic	Not Reported	Not Reported
		Anaerobic aquatic	Not Reported	Not Reported
Terrestrial field dissipation	Not Reported	Not Reported		
M440I022 	Tomato Fruit	--	--	
	Tomato Leaves	--	--	
	Cabbage	--	--	
	Soybean Leaves	--	--	
	Soybean Seed	--	--	
	Soybean Hulls	--	--	
	Soybean Plant	--	--	
	Rotational Crops	--	--	
	Milk	--	--	
	Ruminant Muscle	--	--	
	Ruminant Fat	--	--	
	Ruminant Kidney	--	--	
	Ruminant Liver	--	--	
	Poultry Muscle	--	--	
	Poultry Skin and Fat	--	--	
	Poultry Liver	--	--	
	Egg Yolk	--	--	
	Egg White	--	--	
	Rat	--	--	
	Water	Maximum % Applied (day)		Final % Applied (day)
		Aerobic soil	--	--
		Anaerobic soil	--	--
		Soil photolysis, light	--	--
		Soil photolysis, dark	--	--
		Aqueous photolysis	--	--
Hydrolysis		--	--	
Aerobic aquatic		--	--	
Anaerobic aquatic		--	--	
Terrestrial field dissipation		--	--	

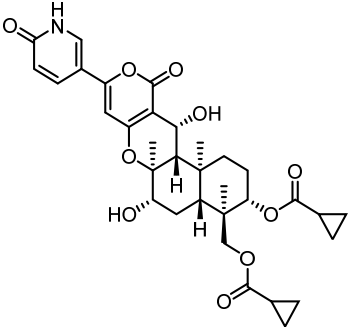
Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) ¹		
		Matrices - Major Residue (>10%TRR)	Matrices - Major Residue (>10%TRR)	
	Tomato Fruit	--	--	
	Tomato Leaves	--	--	
	Cabbage	--	--	
	Soybean Leaves	--	--	
	Soybean Seed	--	--	
	Soybean Hulls	--	--	
	Soybean Plant	--	--	
	Rotational Crops	--	--	
	Milk	--	--	
	Ruminant Muscle	--	--	
	Ruminant Fat	--	--	
	Ruminant Kidney	--	--	
	Ruminant Liver	--	--	
	Poultry Muscle	--	--	
	Poultry Skin and Fat	--	--	
	Poultry Liver	--	--	
	Egg Yolk	--	--	
	Egg White	--	--	
	Rat	--	--	
	Water	Maximum % Applied (day)		Final % Applied (day)
		Aerobic soil	6.5% (7 d)	1.4% (120 d)
		Anaerobic soil	Not Reported	Not Reported
		Soil photolysis, light	Not Reported	Not Reported
		Soil photolysis, dark	9.0% (15 d)	9.0% (15 d)
		Aqueous photolysis	Not Reported	Not Reported
		Hydrolysis	pH 4; Not Reported	pH 4; Not Reported
			pH 7; Not Reported	pH 7; Not Reported
			pH 9; Not Reported	pH 9; Not Reported
Aerobic aquatic		12% (78 d)	11% (100 d)	
Anaerobic aquatic	Not Reported	Not Reported		
Terrestrial field dissipation	8.6% (42 d)	0.27% (450 d)		

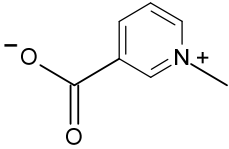
Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) ¹		
		Matrices - Major Residue (>10%TRR)	Matrices - Major Residue (>10%TRR)	
M440I031 Reg. No.: 68482 (trigonelline) 	Tomato Fruit	--	--	
	Tomato Leaves	--	--	
	Cabbage	--	--	
	Soybean Leaves	--	2.6% (0.432) NCA- ¹⁴ C	
	Soybean Seed	47% (0.179) NCA- ¹⁴ C	--	
	Soybean Hulls	--	--	
	Soybean Plant	--	--	
	Rotational Crops	--	--	
	Milk	--	--	
	Ruminant Muscle	--	--	
	Ruminant Fat	--	--	
	Ruminant Kidney	--	--	
	Ruminant Liver	--	--	
	Poultry Muscle	--	--	
	Poultry Skin and Fat	--	--	
	Poultry Liver	--	--	
	Egg Yolk	--	--	
	Egg White	--	--	
	Rat	--	--	
	Water	Maximum % Applied (day)		Final % Applied (day)
		Aerobic soil	--	--
		Anaerobic soil	--	--
		Soil photolysis, light	--	--
		Soil photolysis, dark	--	--
		Aqueous photolysis	--	--
		Hydrolysis	--	--
		Aerobic aquatic	--	--
		Anaerobic aquatic	--	--
Terrestrial field dissipation	--	--		

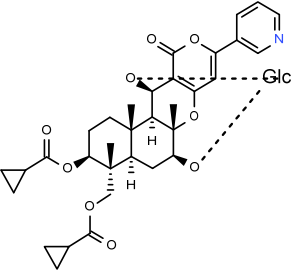
Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) ¹		
		Matrices - Major Residue (>10%TRR)	Matrices - Major Residue (>10%TRR)	
	Tomato Fruit	--	--	
	Tomato Leaves	--	--	
	Cabbage	--	--	
	Soybean Leaves	--	1.3% (0.216) NCA- ¹⁴ C 1.5% (0.074) CPCA- ¹⁴ C	
	Soybean Seed	47% (0.179) NCA- ¹⁴ C	--	
	Soybean Hulls	--	--	
	Soybean Plant	--	--	
	Rotational Crops	--	--	
	Milk	--	--	
	Ruminant Muscle	--	--	
	Ruminant Fat	--	--	
	Ruminant Kidney	--	--	
	Ruminant Liver	--	--	
	Poultry Muscle	--	--	
	Poultry Skin and Fat	--	--	
	Poultry Liver	--	--	
	Egg Yolk	--	--	
	Egg White	--	--	
	Rat	--	--	
	Water	Maximum % Applied (day)		Final % Applied (day)
		Aerobic soil	--	--
		Anaerobic soil	--	--
		Soil photolysis, light	--	--
		Soil photolysis, dark	--	--
		Aqueous photolysis	--	--
Hydrolysis		--	--	
Aerobic aquatic		--	--	
Anaerobic aquatic		--	--	
Terrestrial field dissipation		--	--	

Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) ¹		
		Matrices - Major Residue (>10%TRR)	Matrices - Major Residue (>10%TRR)	
M440I044 Reg. No.: 59878 (nicotinamide)	Tomato Fruit	--	--	
	Tomato Leaves	--	--	
	Cabbage	--	9.8% (0.143) NCA- ¹⁴ C – 7 DALA 8.1% (0.087) NCA- ¹⁴ C – 14 DALA	
	Soybean Leaves	--	--	
	Soybean Seed	--	--	
	Soybean Hulls	--	--	
	Soybean Plant	--	--	
	Rotational Crops	--	--	
	Milk	--	--	
	Ruminant Muscle	--	--	
	Ruminant Fat	--	--	
	Ruminant Kidney	--	--	
	Ruminant Liver	--	--	
	Poultry Muscle	--	--	
	Poultry Skin and Fat	--	--	
	Poultry Liver	--	--	
	Egg Yolk	--	--	
	Egg White	--	--	
	Rat	--	--	
	Water	Maximum % Applied (day)		Final % Applied (day)
		Aerobic soil	--	--
		Anaerobic soil	--	--
		Soil photolysis, light	--	--
		Soil photolysis, dark	--	--
		Aqueous photolysis	--	--
		Hydrolysis	--	--
		Aerobic aquatic	--	--
Anaerobic aquatic		--	--	
Terrestrial field dissipation		--	--	

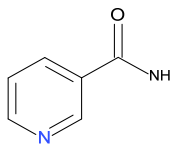


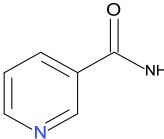
Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) ¹		
		Matrices - Major Residue (>10%TRR)	Matrices - Major Residue (>10%TRR)	
M440I045 Reg. No.: 14673 (nicotinic acid) 	Tomato Fruit	--	Trace NCA- ¹⁴ C – 7 DALA Trace NCA- ¹⁴ C – 14 DALA	
	Tomato Leaves	--	--	
	Cabbage	--	3.7% (0.053) NCA- ¹⁴ C – 7 DALA 2.5% (0.027) NCA- ¹⁴ C – 14 DALA	
	Soybean Leaves	--	--	
	Soybean Seed	--	--	
	Soybean Hulls	--	--	
	Soybean Plant	--	--	
	Rotational Crops	--	--	
	Milk	--	--	
	Ruminant Muscle	--	--	
	Ruminant Fat	--	--	
	Ruminant Kidney	--	--	
	Ruminant Liver	--	--	
	Poultry Muscle	--	--	
	Poultry Skin and Fat	--	--	
	Poultry Liver	--	--	
	Egg Yolk	--	--	
	Egg White	--	--	
	Rat	--	--	
	Water	Maximum % Applied (day)		Final % Applied (day)
		Aerobic soil	Not Reported	Not Reported
		Anaerobic soil	Not Reported	Not Reported
		Soil photolysis, light	Not Reported	Not Reported
		Soil photolysis, dark	Not Reported	Not Reported
		Aqueous photolysis	pH 7; 8.4% (8 d)	pH 7; 8.4% (8 d)
			Natural water; 26% (6 d)	Natural water; 20% (8 d)
		Hydrolysis	pH 4; Not Reported	pH 4; Not Reported
			pH 7; Not Reported	pH 7; Not Reported
pH 9; Not Reported			pH 9; Not Reported	
Aerobic aquatic		Not Reported	Not Reported	
Anaerobic aquatic		Not Reported	Not Reported	
Terrestrial field dissipation	Not Reported	Not Reported		

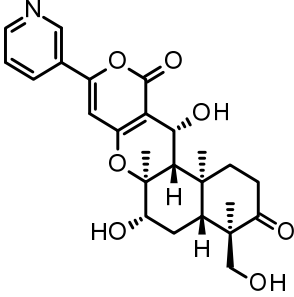
Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) ¹		
		Matrices - Major Residue (>10%TRR)	Matrices - Major Residue (>10%TRR)	
	Tomato Fruit	--	--	
	Tomato Leaves	--	--	
	Cabbage	--	--	
	Soybean Leaves	--	--	
	Soybean Seed	--	--	
	Soybean Hulls	--	--	
	Soybean Plant	--	--	
	Rotational Crops	--	--	
	Milk	--	--	
	Ruminant Muscle	--	--	
	Ruminant Fat	--	--	
	Ruminant Kidney	--	--	
	Ruminant Liver	--	--	
	Poultry Muscle	--	--	
	Poultry Skin and Fat	--	--	
	Poultry Liver	--	--	
	Egg Yolk	--	--	
	Egg White	--	--	
	Rat	--	--	
	Water	Maximum % Applied (day)		Final % Applied (day)
		Aerobic soil	Not Reported	Not Reported
		Anaerobic soil	18% (105 d)	14% (134 d)
		Soil photolysis, light	Not Reported	Not Reported
		Soil photolysis, dark	Not Reported	Not Reported
		Aqueous photolysis	Not Reported	Not Reported
		Hydrolysis	pH 4; Not Reported	pH 4; Not Reported
			pH 7; Not Reported	pH 7; Not Reported
			pH 9; Not Reported	pH 9; Not Reported
		Aerobic aquatic	Not Reported	Not Reported
	Anaerobic aquatic	Not Reported	Not Reported	
	Terrestrial field dissipation	Not Reported	Not Reported	

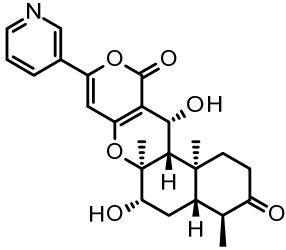
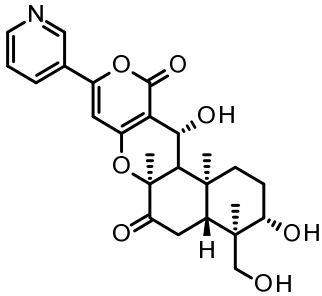
Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) ¹		
		Matrices - Major Residue (>10%TRR)	Matrices - Major Residue (>10%TRR)	
M440I047 	Tomato Fruit	--	--	
	Tomato Leaves	--	--	
	Cabbage	--	--	
	Soybean Leaves	--	--	
	Soybean Seed	--	--	
	Soybean Hulls	--	--	
	Soybean Plant	--	--	
	Rotational Crops	--	--	
	Milk	--	--	
	Ruminant Muscle	--	--	
	Ruminant Fat	--	--	
	Ruminant Kidney	--	--	
	Ruminant Liver	--	--	
	Poultry Muscle	--	--	
	Poultry Skin and Fat	--	--	
	Poultry Liver	--	--	
	Egg Yolk	--	--	
	Egg White	--	--	
	Rat	--	--	
	Water	Maximum % Applied (day)		Final % Applied (day)
		Aerobic soil	Not Reported	Not Reported
		Anaerobic soil	18% (105 d)	17% (134 d)
		Soil photolysis, light	Not Reported	Not Reported
		Soil photolysis, dark	Not Reported	Not Reported
		Aqueous photolysis	Not Reported	Not Reported
		Hydrolysis	pH 4; Not Reported	pH 4; Not Reported
			pH 7; Not Reported	pH 7; Not Reported
			pH 9; Not Reported	pH 9; Not Reported
Aerobic aquatic		Not Reported	Not Reported	
Anaerobic aquatic	Not Reported	Not Reported		
Terrestrial field dissipation	Not Reported	Not Reported		
M440I048 	Water (Minor Transformation; <10%)	Maximum % Applied (day)		Final % Applied (day)
		Aerobic soil	Not Reported	Not Reported
		Anaerobic soil	Not Reported	Not Reported
		Soil photolysis, light	Not Reported	Not Reported
		Soil photolysis, dark	Not Reported	Not Reported
		Aqueous photolysis	Not Reported	Not Reported
		Hydrolysis	pH 4; Not Reported	pH 4; Not Reported
			pH 7; Not Reported	pH 7; Not Reported
			pH 9; Not Reported	pH 9; Not Reported
		Aerobic aquatic	Not Reported	Not Reported
		Anaerobic aquatic	Not Reported	Not Reported
		Terrestrial field dissipation	Not Reported	Not Reported

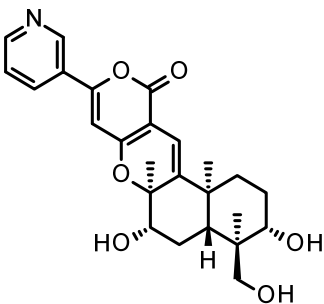
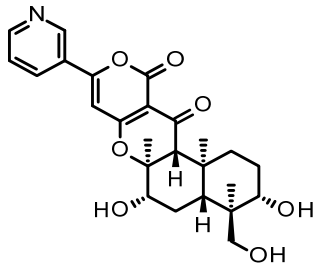
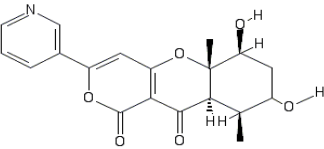
Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) ¹		
		Matrices - Major Residue (>10%TRR)	Matrices - Major Residue (>10%TRR)	
M440I049 	Water (Minor Transformation; <10%)	Maximum % Applied (day)		
		Aerobic soil	7.2% (29 d)	2.4% (120 d)
		Anaerobic soil	Not Reported	Not Reported
		Soil photolysis, light	Not Reported	Not Reported
		Soil photolysis, dark	Not Reported	Not Reported
		Aqueous photolysis	Not Reported	Not Reported
		Hydrolysis	pH 4; Not Reported	pH 4; Not Reported
			pH 7; Not Reported	pH 7; Not Reported
			pH 9; Not Reported	pH 9; Not Reported
		Aerobic aquatic	Not Reported	Not Reported
		Anaerobic aquatic	Not Reported	Not Reported
		Terrestrial field dissipation	Not Reported	Not Reported
M440I050  +unidentified contaminant	Water (Minor Transformation; <10%)	Maximum % Applied (day)		
		Aerobic soil	Not Reported	Not Reported
		Anaerobic soil	Not Reported	Not Reported
		Soil photolysis, light	Not Reported	Not Reported
		Soil photolysis, dark	Not Reported	Not Reported
		Aqueous photolysis	Not Reported	Not Reported
		Hydrolysis	pH 4; Not Reported	pH 4; Not Reported
			pH 7; Not Reported	pH 7; Not Reported
			pH 9; Not Reported	pH 9; Not Reported
		Aerobic aquatic	Not Reported	Not Reported
		Anaerobic aquatic	Not Reported	Not Reported
		Terrestrial field dissipation	Not Reported	Not Reported
M440I052 	Water (Minor Transformation; <10%)	Maximum % Applied (day)		
		Aerobic soil	4.6% (62 d)	3.4% (120 d)
		Anaerobic soil	Not Reported	Not Reported
		Soil photolysis, light	Not Reported	Not Reported
		Soil photolysis, dark	Not Reported	Not Reported
		Aqueous photolysis	Not Reported	Not Reported
		Hydrolysis	pH 4; Not Reported	pH 4; Not Reported
			pH 7; Not Reported	pH 7; Not Reported
			pH 9; Not Reported	pH 9; Not Reported
		Aerobic aquatic	Not Reported	Not Reported
		Anaerobic aquatic	Not Reported	Not Reported
		Terrestrial field dissipation	Not Reported	Not Reported

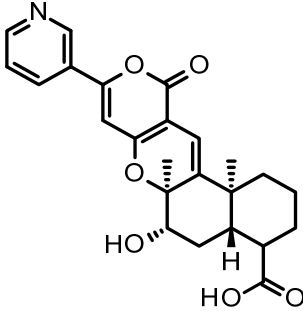
Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) ¹		
		Matrices - Major Residue (>10%TRR)	Matrices - Major Residue (>10%TRR)	
M440I053 	Water (Minor Transformation; <10%)	Maximum % Applied (day)		
		Aerobic soil	7.2% (29 d)	2.4% (120 d)
		Anaerobic soil	Not Reported	Not Reported
		Soil photolysis, light	Not Reported	Not Reported
		Soil photolysis, dark	Not Reported	Not Reported
		Aqueous photolysis	Not Reported	Not Reported
		Hydrolysis	pH 4; Not Reported	pH 4; Not Reported
			pH 7; Not Reported	pH 7; Not Reported
			pH 9; Not Reported	pH 9; Not Reported
		Aerobic aquatic	Not Reported	Not Reported
		Anaerobic aquatic	Not Reported	Not Reported
		Terrestrial field dissipation	Not Reported	Not Reported

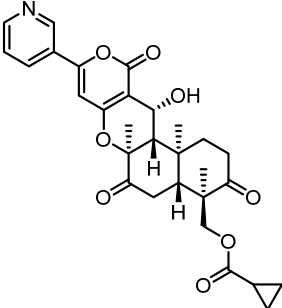
Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) ¹		
		Matrices - Major Residue (>10%TRR)	Matrices - Major Residue (>10%TRR)	
M4401057 	Tomato Fruit	--	--	
	Tomato Leaves	--	--	
	Cabbage	--	--	
	Soybean Leaves	--	--	
	Soybean Seed	--	--	
	Soybean Hulls	--	--	
	Soybean Plant	--	--	
	Rotational Crops	--	--	
	Milk	--	--	
	Ruminant Muscle	--	--	
	Ruminant Fat	--	--	
	Ruminant Kidney	--	--	
	Ruminant Liver	--	--	
	Poultry Muscle	--	--	
	Poultry Skin and Fat	--	--	
	Poultry Liver	--	--	
	Egg Yolk	--	--	
	Egg White	--	--	
	Rat	--	--	
	Water	Maximum % Applied (day)		Final % Applied (day)
		Aerobic soil	38% (7 d)	4.7% (120 d)
		Anaerobic soil	40% (29 d)	11% (134 d)
		Soil photolysis, light	Not Reported	Not Reported
		Soil photolysis, dark	Not Reported	Not Reported
		Aqueous photolysis	Not Reported	Not Reported
		Hydrolysis	pH 4; Not Reported	pH 4; Not Reported
			pH 7; Not Reported	pH 7; Not Reported
			pH 9; Not Reported	pH 9; Not Reported
Aerobic aquatic		Not Reported	Not Reported	
Anaerobic aquatic		Not Reported	Not Reported	
Terrestrial field dissipation		Not Reported	Not Reported	

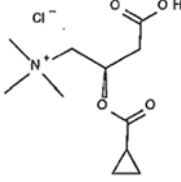
Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) ¹		
		Matrices - Major Residue (>10%TRR)	Matrices - Major Residue (>10%TRR)	
M440I060 Reg. No.: 6009307 CPCA-carnitine 	Tomato Fruit	--	--	
	Tomato Leaves	--	--	
	Cabbage	--	--	
	Soybean Leaves	--	--	
	Soybean Seed	--	--	
	Soybean Hulls	--	--	
	Soybean Plant	--	--	
	Rotational Crops	--	--	
	Milk	--	--	
	Ruminant Muscle	91% (0.283) CPCA- ¹⁴ C	--	
	Ruminant Fat	--	--	
	Ruminant Kidney	--	5.8% (0.028) CPCA- ¹⁴ C	
	Ruminant Liver	--	6.9% (0.014) CPCA- ¹⁴ C	
	Poultry Muscle	38% (0.017) CPCA- ¹⁴ C	--	
	Poultry Skin and Fat	--	--	
	Poultry Liver	--	--	
	Egg Yolk	--	--	
	Egg White	--	--	
	Rat	--	--	
	Water	Maximum % Applied (day)		Final % Applied (day)
		Aerobic soil	--	--
		Anaerobic soil	--	--
		Soil photolysis, light	--	--
		Soil photolysis, dark	--	--
		Aqueous photolysis	--	--
		Hydrolysis	--	--
		Aerobic aquatic	--	--
Anaerobic aquatic		--	--	
Terrestrial field dissipation		--	--	

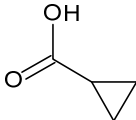
Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) ¹		
		Matrices - Major Residue (>10%TRR)	Matrices - Major Residue (>10%TRR)	
M440I061 Reg. No.: 53128 (CPCA) 	Tomato Fruit	--	--	
	Tomato Leaves	--	--	
	Cabbage	--	--	
	Soybean Leaves	--	--	
	Soybean Seed	--	--	
	Soybean Hulls	--	--	
	Soybean Plant	--	--	
	Rotational Crops	--	--	
	Milk	--	--	
	Ruminant Muscle	--	2.3% (0.007) CPCA- ¹⁴ C	
	Ruminant Fat	--	--	
	Ruminant Kidney	64% (0.307) CPCA- ¹⁴ C	--	
	Ruminant Liver	28% (0.057) CPCA- ¹⁴ C	--	
	Poultry Muscle	--	--	
	Poultry Skin and Fat	--	--	
	Poultry Liver	--	4.1% (0.017) CPCA- ¹⁴ C	
	Egg Yolk	--	--	
	Egg White	--	--	
	Rat	--	--	
	Water	Maximum % Applied (day)		Final % Applied (day)
		Aerobic soil	Not Reported	14% (28 d)
		Anaerobic soil	Not Reported	Not Reported
		Soil photolysis, light	Not Reported	Not Reported
Soil photolysis, dark		Not Reported	Not Reported	
Aqueous photolysis		Not Reported	Not Reported	
Hydrolysis		Not Reported	Not Reported	
Aerobic aquatic		Not Reported	Not Reported	
Anaerobic aquatic		Not Reported	Not Reported	
Terrestrial field dissipation		Not Reported	Not Reported	
Carbon Dioxide $O=C=O$	Water	Maximum % Applied (day)		Final % Applied (day)
		Aerobic soil	28% (120 d)	28% (120 d)
		Anaerobic soil	2.6% (120 d)	2.6% (120 d)
		Soil photolysis, light	0.7% (15 d)	0.7% (15 d)
		Soil photolysis, dark	Not Reported	Not Reported
		Aqueous photolysis	0.8% (8 d)	0.8% (8 d)
			21% (14 d)	21% (14 d)
		Hydrolysis	pH 4; Not Reported	pH 4; Not Reported
			pH 7; Not Reported	pH 7; Not Reported
			pH 9; Not Reported	pH 9; Not Reported
		Aerobic aquatic	5.3% (100 d)	5.3% (100 d)
		Anaerobic aquatic	0.5% (100 d)	0.5% (100 d)
		Terrestrial field dissipation	Not Reported	Not Reported

Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) ¹		
		Matrices - Major Residue (>10%TRR)	Matrices - Major Residue (>10%TRR)	
Unextracted Residues	Water	Maximum % Applied (day)		Final % Applied (day)
		Aerobic soil	51% (120 d)	51% (120 d)
		Anaerobic soil	55% (120 d)	55% (120 d)
		Soil photolysis, light	13% (15 d)	13% (15 d)
		Soil photolysis, dark	Not Reported	Not Reported
		Aqueous photolysis	Not Reported	Not Reported
		Hydrolysis	pH 4; Not Reported	pH 4; Not Reported
			pH 7; Not Reported	pH 7; Not Reported
			pH 9; Not Reported	pH 9; Not Reported
		Aerobic aquatic	25% (100 d)	25% (100 d)
		Anaerobic aquatic	40% (100 d)	40% (100 d)
		Terrestrial field dissipation	Not Reported	Not Reported
Total Unidentified Residues	Water	Maximum % Applied (day)		Final % Applied (day)
		Aerobic soil	24% (120 d)	24% (120 d)
		Anaerobic soil	23% (73 d)	13% (120 d)
		Soil photolysis,	7.8% (10 d)	6.0% (15 d)
		Aqueous photolysis	34% (8 d)	34% (8 d)
			39% (14 d)	39% (14 d)
		Hydrolysis	pH 4; Not Reported	pH 4; Not Reported
			pH 7; Not Reported	pH 7; Not Reported
			pH 9; 7.3% (10 d)	pH 9; 7.3% (10 d)
		Aerobic aquatic	9.4% (100 d)	9.4% (100 d)
		Anaerobic aquatic	13% (100 d)	13% (100 d)
		Terrestrial field dissipation	Not Reported	Not Reported
Tomato Metabolism Study; MRID No. 49689019/PMRA No. 2627938; approximately 0.707 kg ai/ha (0.631 lbs ai/A) total; NCA- ¹⁴ C labeled. Tomato Metabolism Study; MRID No. 49689020/PMRA No. 2627934; approximately 125.0 g ai/ha (0.112 lbs ai/A) total; pyranone-4- ¹⁴ C labeled. Cabbage Metabolism Study; MRID No. 49689021/PMRA No. 2627939; approximately 1.14 kg ai/ha (1.02 lbs ai/A) total; NCA- ¹⁴ C labeled. Cabbage Metabolism Study; MRID No. 49689022/PMRA No. 2627932; approximately 125.0 g ai/ha (0.112 lbs ai/A) total; pyranone-4- ¹⁴ C labeled. Cabbage Metabolism Study; MRID No. 49689023/PMRA No. 2627937; approximately 1.14 kg ai/ha (1.02 lbs ai/A) total; pyranone-6- ¹⁴ C labeled. Soybean Metabolism Study; MRID No. 49689024/PMRA No. 2627930; approximately 125.0 g ai/ha (0.112 lbs ai/A) total; NCA- ¹⁴ C labeled. Soybean Metabolism Study; MRID No. 49689025/PMRA No. 2627936; approximately 125.0 g ai/ha (0.112 lbs ai/A) total; CPCA- ¹⁴ C labeled. Poultry Metabolism Study; MRID No. 49689026/PMRA No. 2627941; approximately 12 ppm; CPCA- ¹⁴ C labeled. Lactating Goat Metabolism Study; MRID No. 49689027; PMRA No. 2627940; approximately 17.3 ppm; pyranone-4- ¹⁴ C labeled. Lactating Goat Metabolism Study; MRID No. 49689028; PMRA No. 2627942; approximately 12 ppm; CPCA- ¹⁴ C labeled. Confined Rotational Crop Study; MRID No. 49689050/PMRA No. 2627963; approximately 125.0 g ai/ha (0.112 lbs ai/A) total; NCA- ¹⁴ C and pyranone-4- ¹⁴ C labeled. Confined Rotational Crop Study; MRID No. 49689051/PMRA No. 2627965; approximately 19.9 g ai/ha (0.02 lbs ai/A) total; NCA- ¹⁴ C labeled. Confined Rotational Crop Study; MRID No. 49689052/PMRA No. 2627964; approximately 125.0 g ai/ha (0.112 lbs ai/A) total for radish and spinach, and 19.9 g ai/ha (0.02 lbs ai/A) total for wheat; CPCA- ¹⁴ C labeled. Rat Metabolism Studies; MRID 49688952 and MRID 49688953; single gavage dose (3 or 300 ppm/bw) Mouse Metabolism Study; MRID 49557917; multiple radiolabeled dose at 10 and 100 ppm				

Appendix B. Metabolic Pathways.

Figure B.1; Proposed Metabolic Pathway of Afidopyropen in Tomato (NCA-¹⁴C Label)

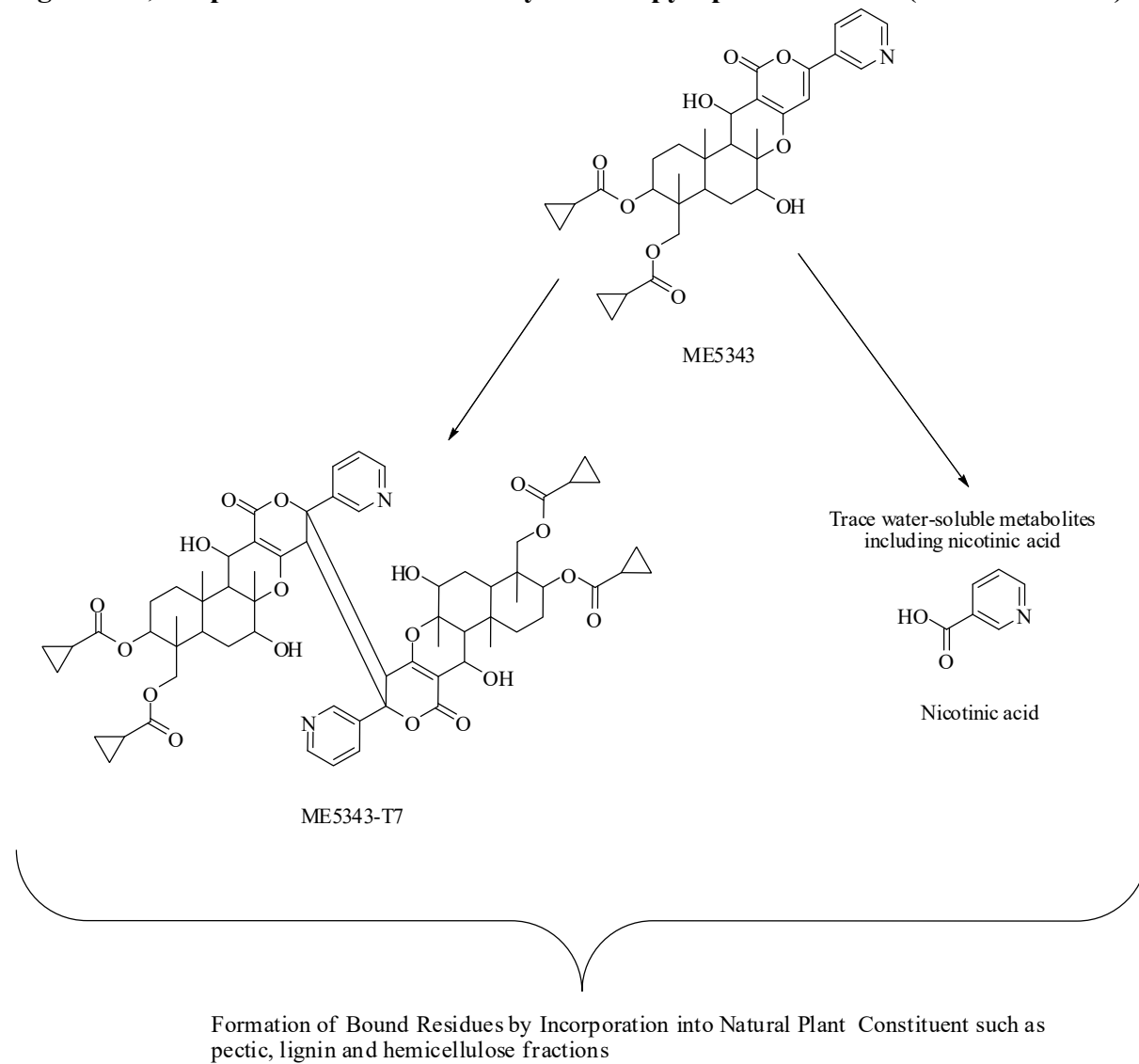


Figure B.2; Proposed Metabolic Pathway of Afidopyropen in Tomato (Pyranone-4-¹⁴C Label)

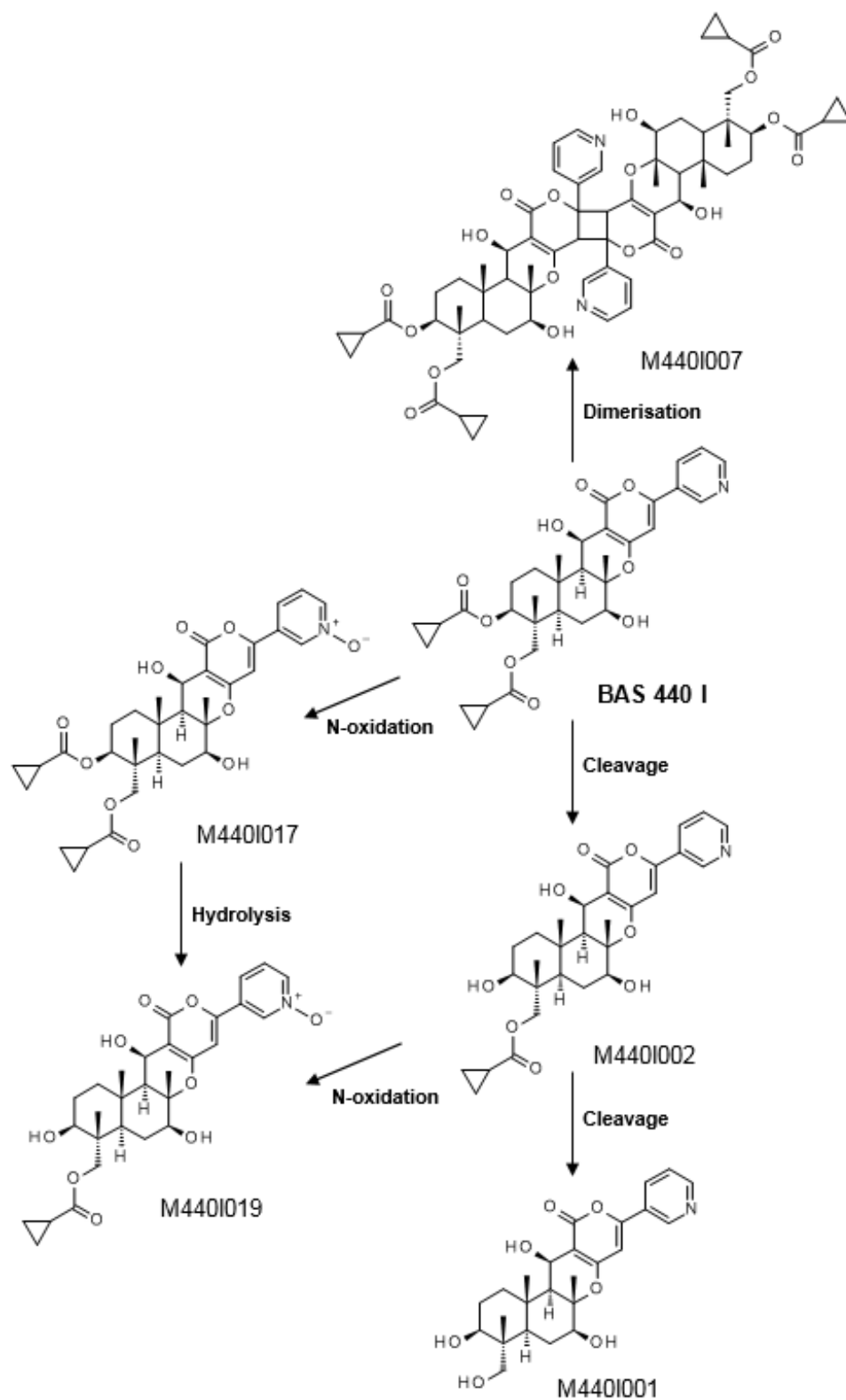


Figure B.3; Proposed Metabolic Pathway of Afidopyropen in Cabbage (NCA-¹⁴C Label)

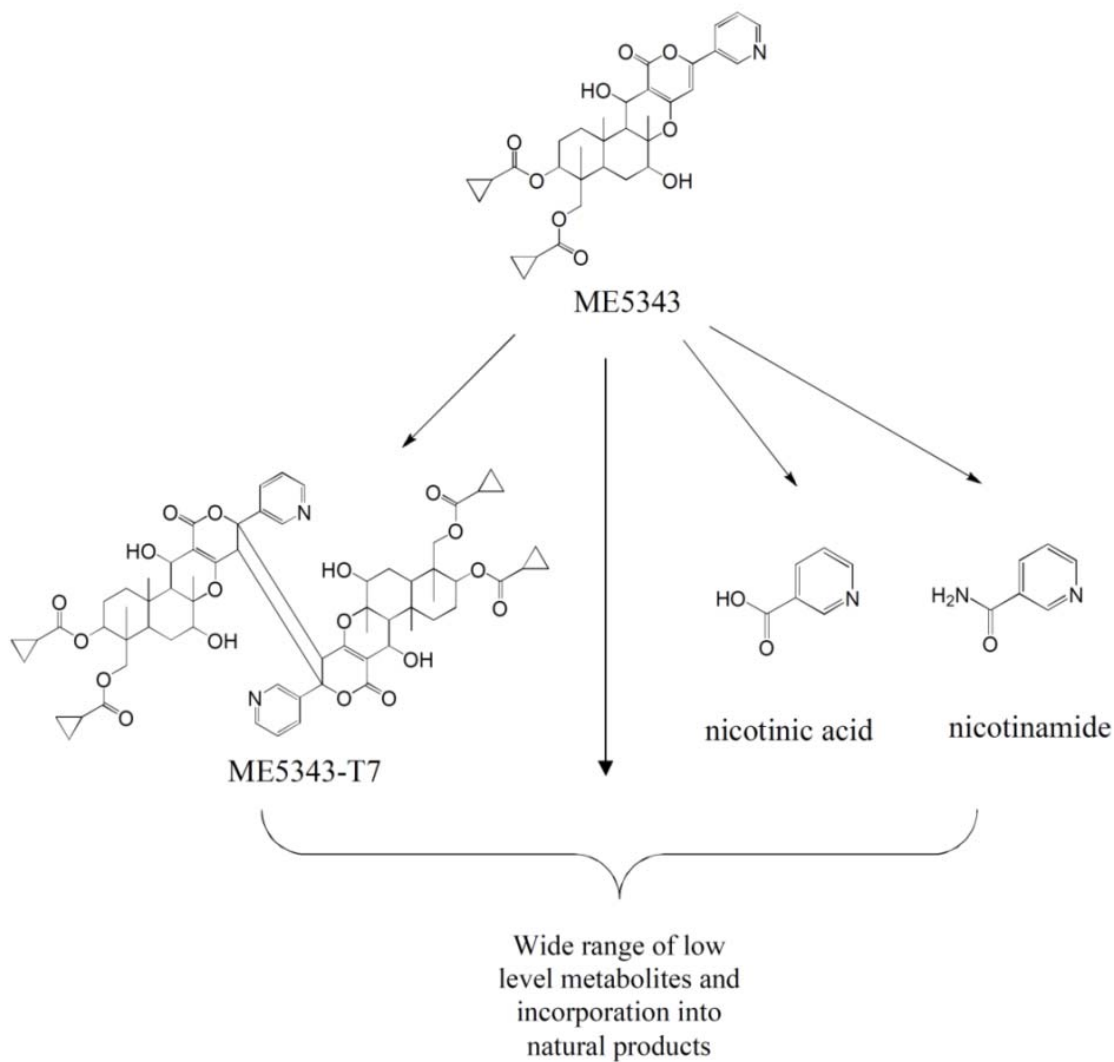


Figure B.4; Proposed Metabolic Pathway of Afidopyropen in Cabbage (Pyranone-4-¹⁴C Label)

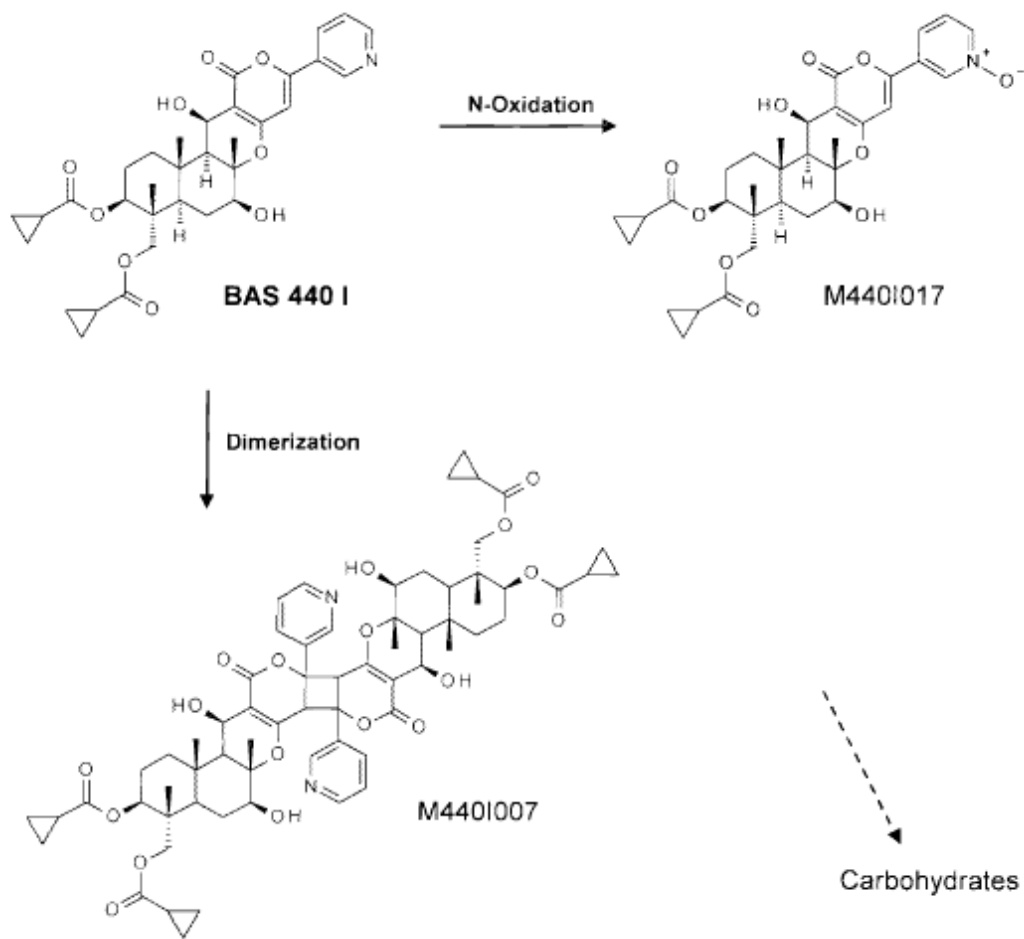


Figure B.5; Proposed Metabolic Pathway of Afidopyropen in Soybean (NCA-¹⁴C Label)

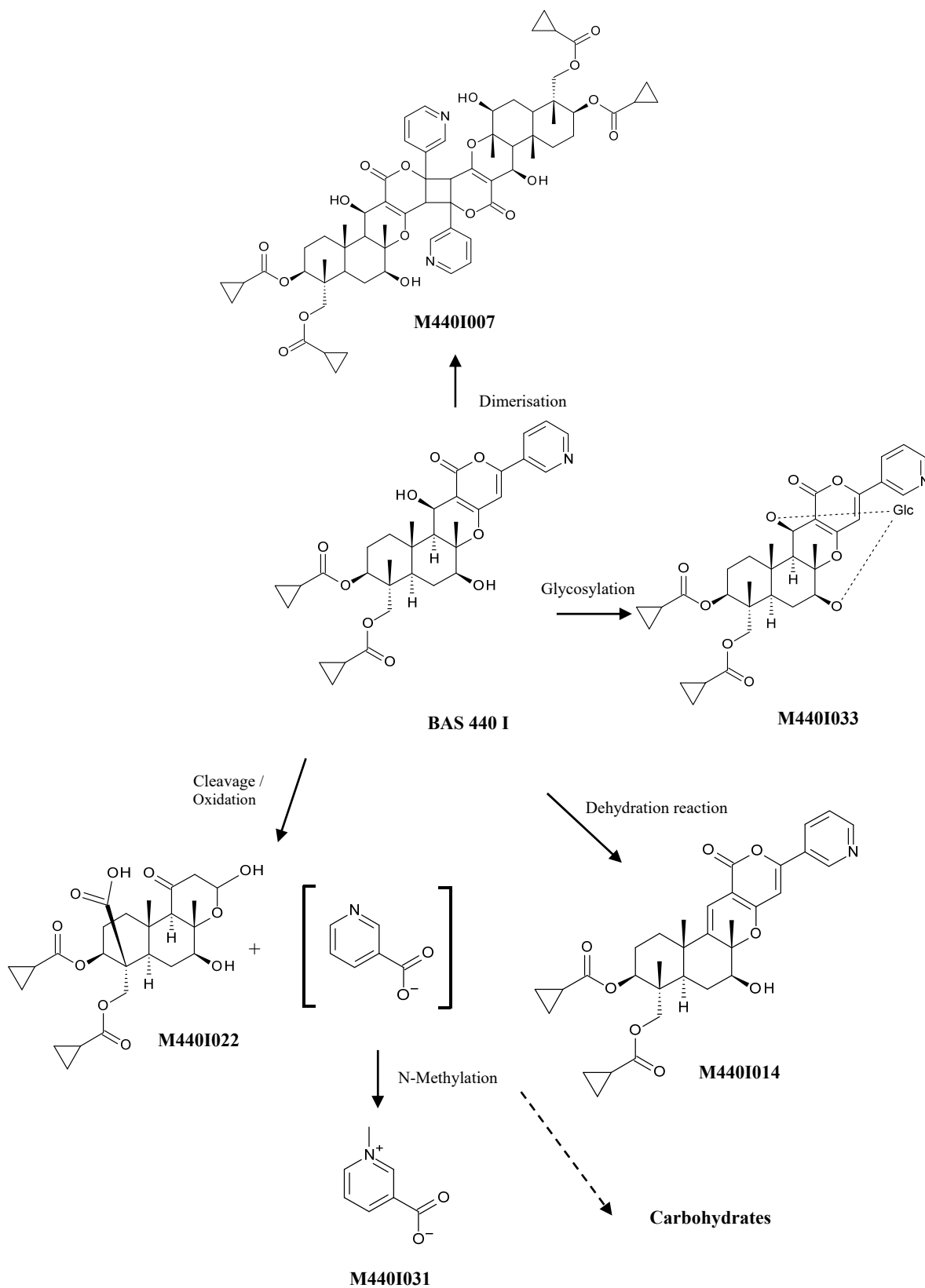


Figure B.6; Proposed Metabolic Pathway of Afidopyropen in Soybean (CPCA-¹⁴C Label)

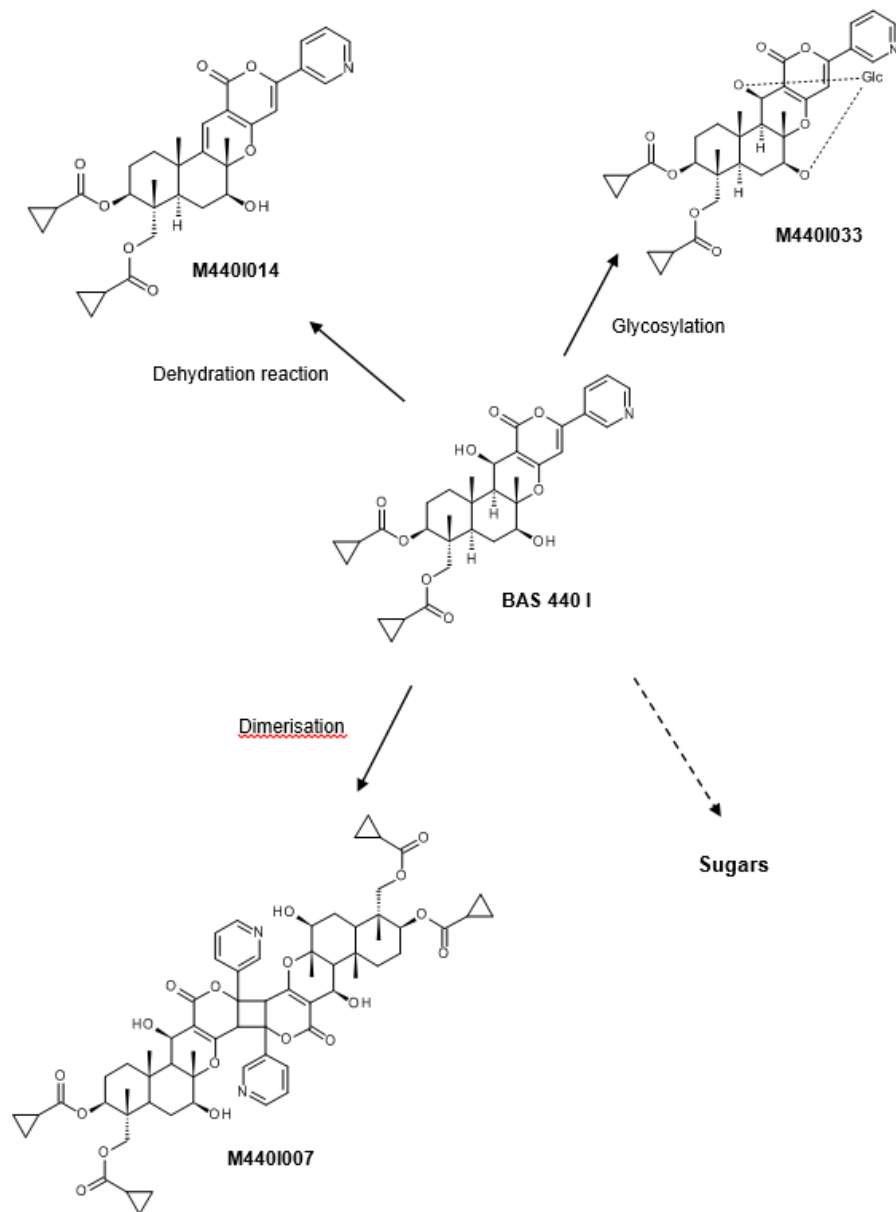


Figure B.7; Proposed Metabolic Pathway of Afidopyropen in Poultry (CPCA-¹⁴C Label)

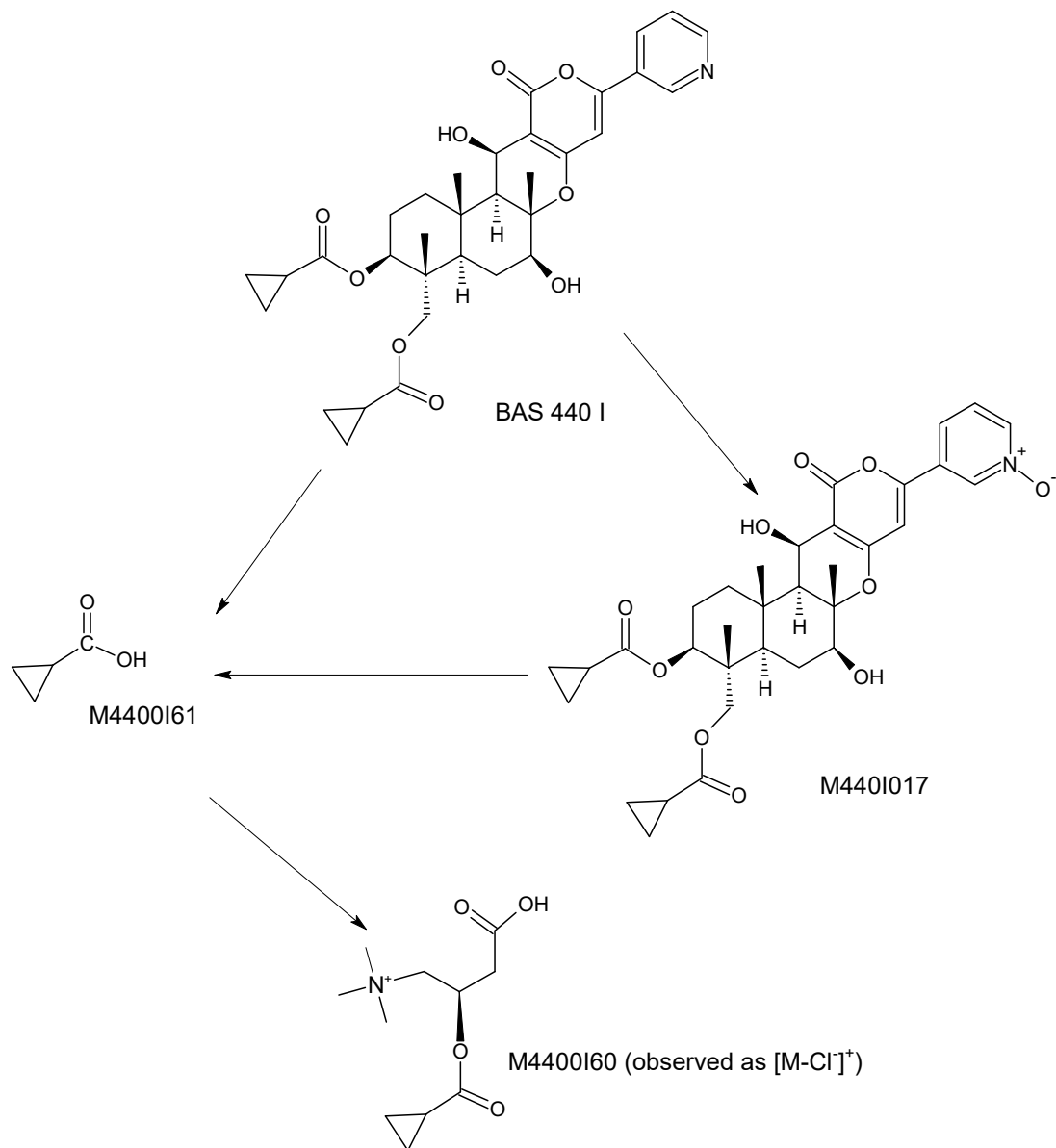


Figure B.8; Proposed Metabolic Pathway of Afidopyropen in Ruminants (Pyranone-4-¹⁴C Label)

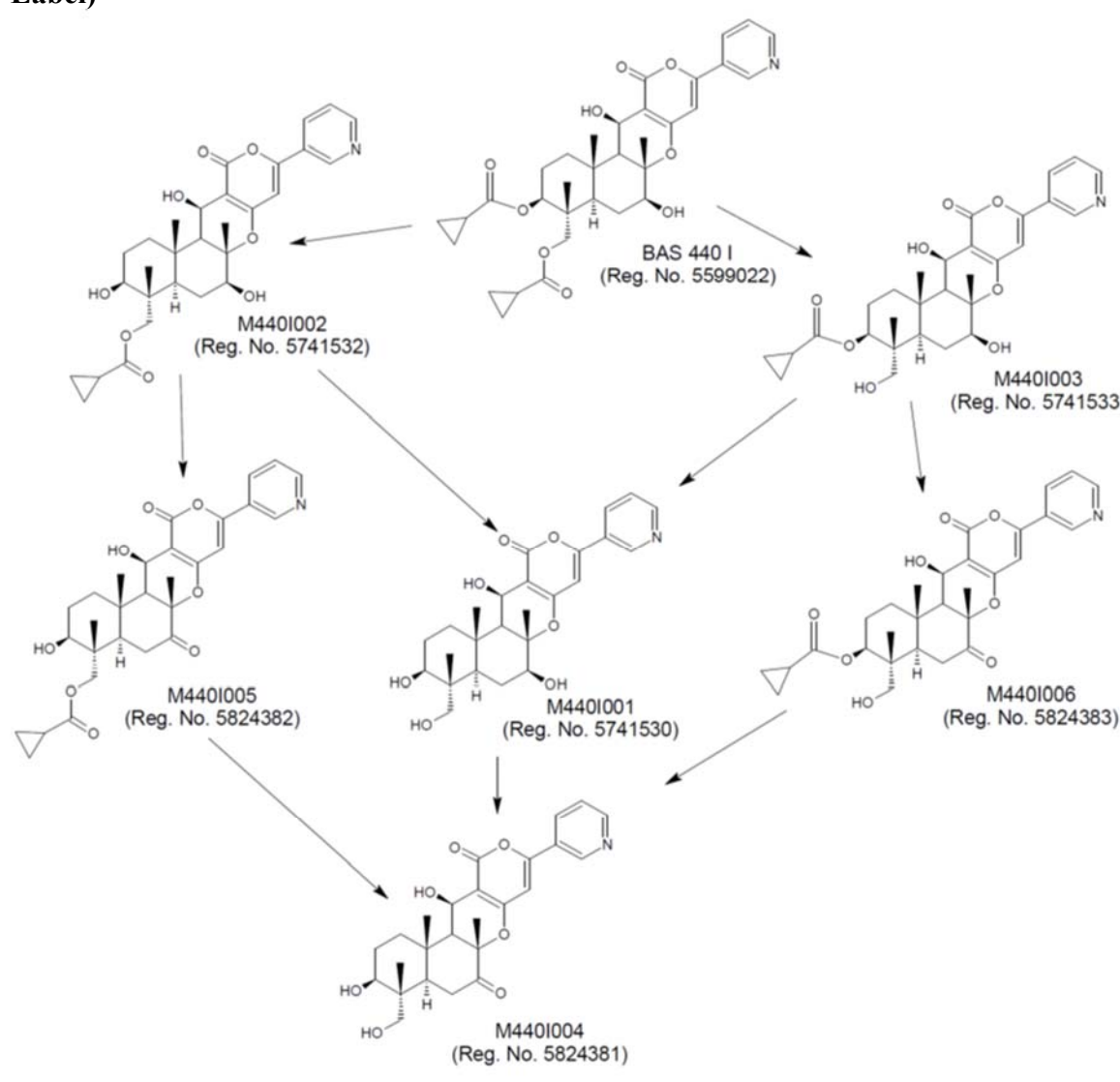


Figure B.9; Proposed Metabolic Pathway of Afidopyropen in Ruminants (CPA-¹⁴C Label)

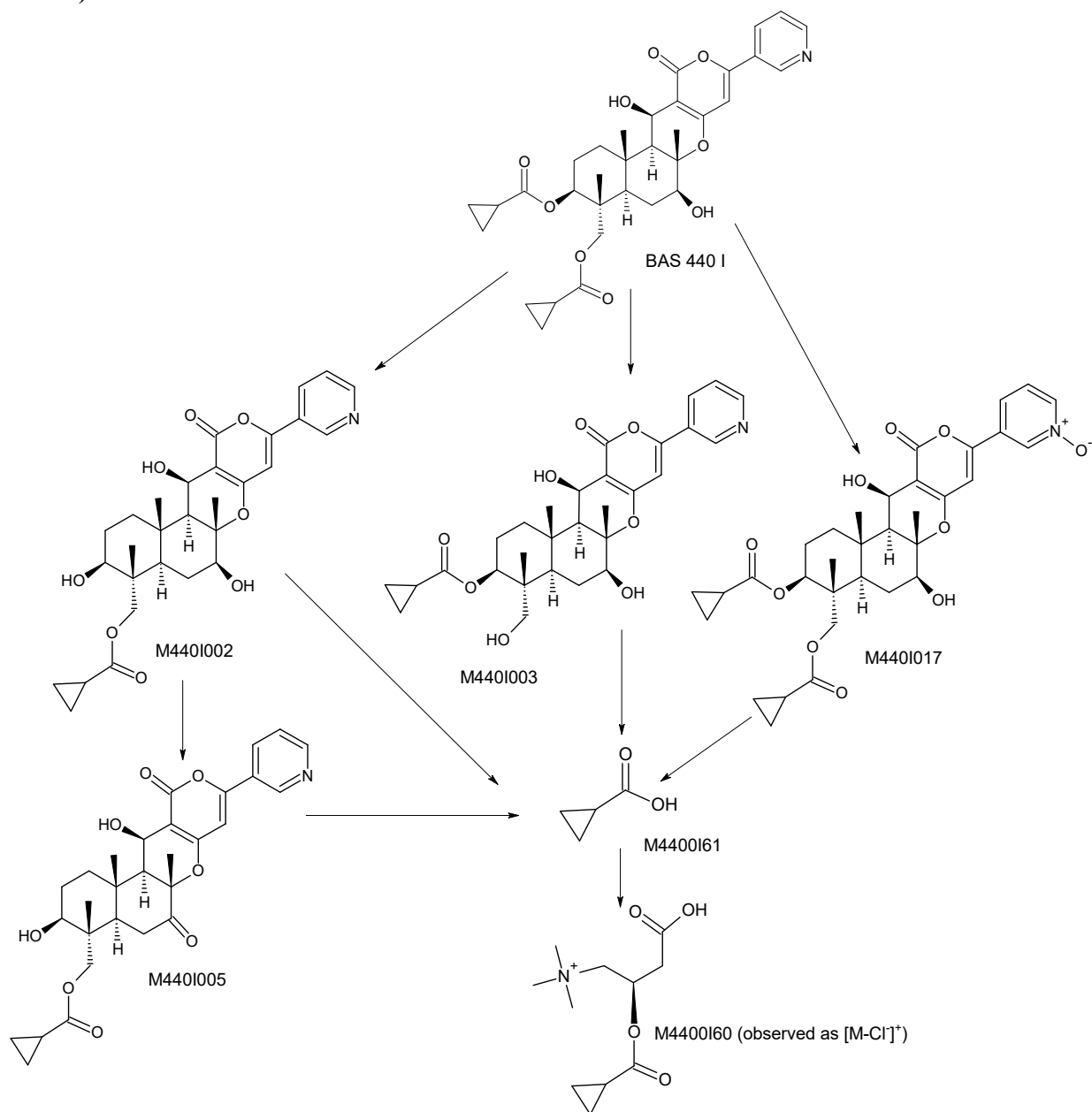


Figure B.10; Proposed Metabolic Pathway of Afidopyropen in the Rat

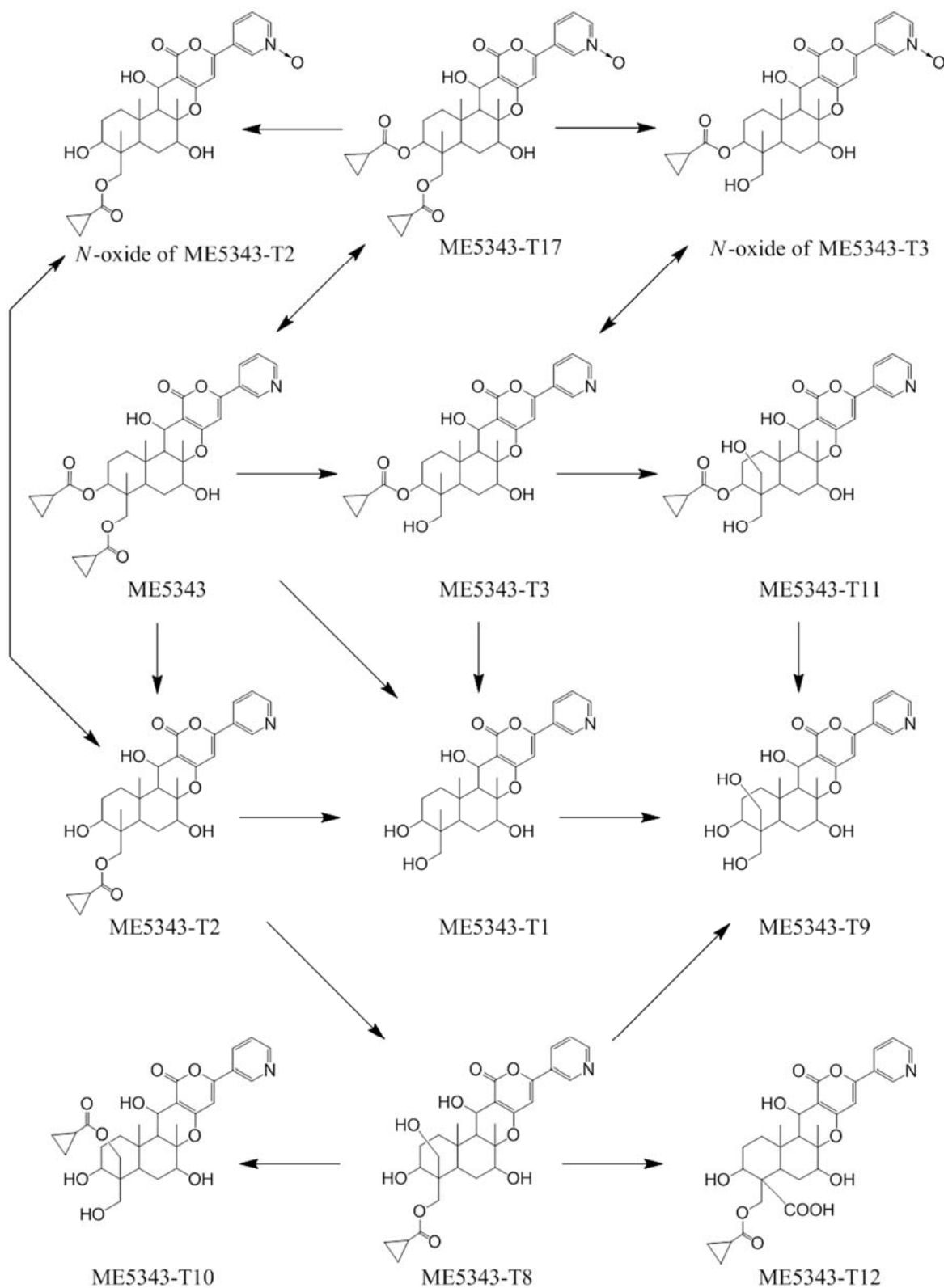
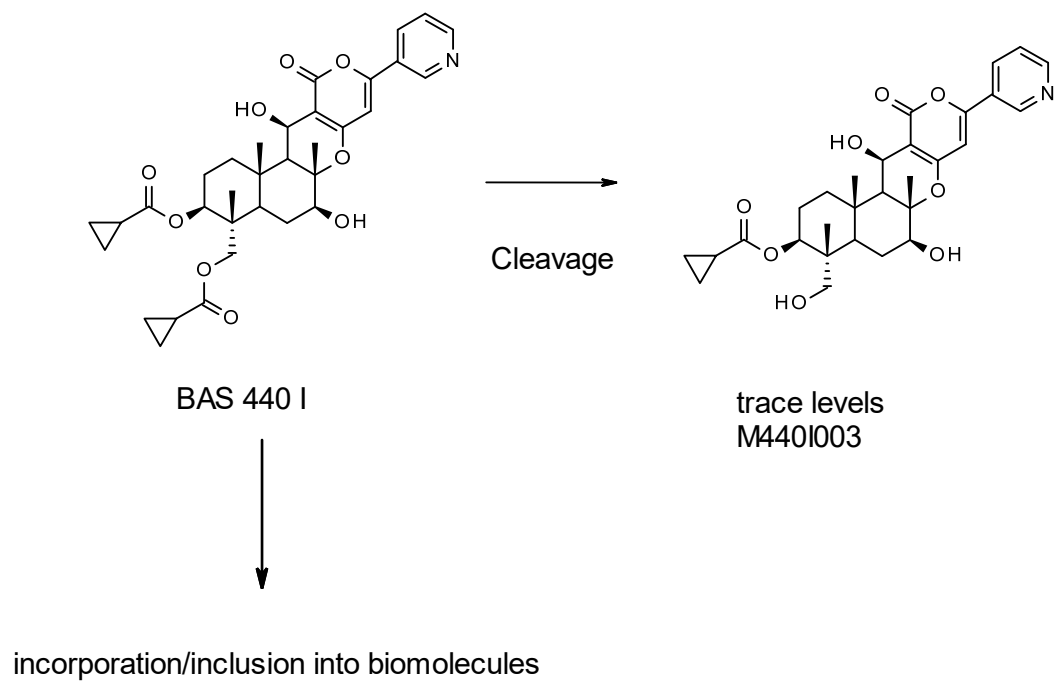


Figure B.11; Metabolic Pathway of Afidopyropen in Confined Rotational Crops



Appendix C. Guidance for Submitted Analytical Standards to NPSR.



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF PESTICIDE PROGRAMS
NATIONAL PESTICIDE STANDARD REPOSITORY
ENVIRONMENTAL SCIENCE CENTER
701 MAPES ROAD
FORT MEADE, MARYLAND 20755-5350

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

Dear Sir/Madam,

The U.S. EPA National Pesticide Standard Repository (NPSR) will be adopting a new guideline for registrants to follow when submitting analytical standards. Currently, the NPSR requests 1 to 5 grams of material in a bulk bottle for each requested standard. Starting on April 01, 2016, instead of the material being submitted in a bulk bottle, the NPSR is requesting that each gram of material be submitted in 10 aliquot vials of 100 mg each. Each aliquot vial must be sealed, and labeled with the name of the analytical standard, percent purity, lot number and expiration date. It will not be necessary to provide an exact weight or a tare weight since this aliquot vial is only being used as a transfer container. The end user at the laboratory will weigh out the amount of material needed.

This new guideline will be beneficial for registrants as well as the NPSR. It will eliminate the possibility of cross contamination between standards and/or mislabeling of standards during the transfer of over 60 individual standards per day from bulk bottle to aliquots in the NPSR. In addition it may lower the frequency of the NPSR requesting standards from the registrants. Registrants will now be asked to send only 3 grams of analytical standard for parent compounds and 1 gram of analytical standard for metabolites, degradates and related compounds.

Your continued support of the U.S. EPA National Pesticide Standard Repository is greatly appreciated. If you have any questions, please contact me by telephone (410-305-2907) or email (cole.theresa@epa.gov).

Sincerely,

Theresa M. Cole

Theresa M. Cole
U.S. Environmental Protection Agency
National Pesticide Standard Repository
Office of Pesticide Programs

Appendix D. Field Trial Geographic Distribution.

Table D.1. Trial Numbers and Geographical Locations of Tuberous and Corm Subgroup 1C Vegetables.																		
No. Trials	NAFTA Growing Zone														Total			
	1	1A	2	3	4	5	5A	5B	6	7	7A	8	9	10		11	12	14
Potato																		
Sub.	4		2	1		4					1		1	1	4		2	20
Req. U.S. ¹	2/2		1/1	1/1		4/2							1/1	1/1	6/4			16/12
Req. Can. ²	3	4				3	1	1			2						2	16

¹ As per Table 5 of 860.1500; the second number reflects a 25% reduction in the number of field trials allowed for the crop as a representative commodity in support of a crop group/subgroup tolerance or when application results in no quantifiable residues.

² As per Table 1.2 of PMRA Regulatory Directive DIR2010-05.

Table D.2. Trial Numbers and Geographical Locations of Leafy Greens Subgroup 4-16A Vegetables.																		
No. Trials	NAFTA Growing Zone														Total			
	1	2	3	4	5	5B	6	7	8	9	10	11	12					
Celery																		
Sub.			1		2 ¹							4						7
Req. U.S. ²			2/1		1/1							5/4						8/6
Req. Can. ³					2	3												5
Head Lettuce																		
Sub.	1		1		2							4						8
Req. U.S. ²	1/1 ⁴		1/1									6/4						8/6
Req. Can. ³					1	4												5
Leaf Lettuce																		
Sub.		1	1		2							4						8
Req. U.S. ²	1/1 ⁴		1/1									6/4						8/6
Req. Can. ³					1	4												5
Spinach																		
Sub.	1	1			2		1				1	2						8
Req. U.S. ²	1/1	2/1					2/1				1/1	2/2						8/6
Req. Can. ³					2	1												3

¹ HED has determined that two pairs of celery trials conducted in Zone 5 are replicate trials.

² As per Table 5 of 860.1500; the second number reflects a 25% reduction in the number of field trials allowed for the crop as a representative commodity in support of a crop group/subgroup tolerance or when application results in no quantifiable residues.

³ As per Table 1.2 of PMRA Regulatory Directive DIR2010-05. As Table 1.2 does not specify separate requirements for head and leaf lettuce, the same requirements are listed here for each crop.

⁴ Either zone is acceptable.

Table D.3. Trial Numbers and Geographical Locations for Brassica Leafy Greens Subgroup 4-16B Vegetables.																		
No. Trials	NAFTA Growing Zone														Total			
	1	2	3	4	5	5A	5B	6	7	8	9	10	11	12				
Broccoli																		
Sub.					3	1		1				4			1			10
Req. U.S. ¹								1/1				6/4			1/1			8/6
Req. Can. ²					2		2								1			5
Cabbage																		
Sub.	1	1	1		3	1		1		1		1						10
Req. U.S. ¹	2/1	1/1	1/1		1/1			1/1		1/0		1/1						8/6
Req. Can. ²					2	1	2											5

Table D.3. Trial Numbers and Geographical Locations for Brassica Leafy Greens Subgroup 4-16B Vegetables.

No. Trials	NAFTA Growing Zone														Total
	1	2	3	4	5	5A	5B	6	7	8	9	10	11	12	
Mustard Greens															
Sub.		2	1	1	1			1				2			8
Req. U.S. ¹		2/1	1/0	1/1	1/1			1/1				2/1			8/5
Req. Can. ²					2									1	3

¹ As per Table 5 of 860.1500; the second number reflects a 25% reduction in the number of field trials allowed for the crop as a representative commodity in support of a crop group/subgroup tolerance or when application results in no quantifiable residues.

² As per Table 1.2 of PMRA Regulatory Directive DIR2010-05.

Table D.4. Trial Numbers and Geographical Locations for Soybeans.

No. Trials	NAFTA Growing Zone														Total
	1	2	3	4	5	5B	6	7	8	9	10	11	12		
Soybean															
Sub.		2		3	15										20
Req. U.S. ¹		2/2		3/2	15/11										20/15
Req. Can. ²					13	3									16

¹ As per Table 5 of 860.1500 for soybean; the second number reflects a 25% reduction in the number of field trials allowed for the crop as a representative commodity in support of a crop group/subgroup tolerance as applicable (refer to Tables 2 and 3) or when application results in no quantifiable residues.

² As per Table 1.2 of PMRA Regulatory Directive DIR2010-05.

Table D.5. Trial Numbers and Geographical Locations for Fruiting Vegetables Group 8-10..

No. Trials	NAFTA Growing Zone														Total
	1	2	3	4	5	5B	6	7	8	9	10	11	12		
Bell Pepper															
Sub.		1	1		3						2				7
Req. U.S. ¹		2/1	2/1		1/1		1/1				2/2				8/6
Req. Can. ²					3	2									5
Non-Bell Pepper															
Sub.		1	1				1								3
Req. U.S. ³															3
Req. Can. ²					3	2									5
Tomato															
Sub.	1	1	1		8 ⁴						8				19
Req. U.S. ¹	1/1	1/1	2/2		1/1						11/7				16/12
Req. Can. ⁵					11	1									12

¹ As per Table 5 of 860.1500; the second number reflects a 25% reduction in the number of field trials allowed for the crop as a representative commodity in support of a crop group/subgroup tolerance or when application results in no quantifiable residues.

² As per Table 1.2 of PMRA Regulatory Directive DIR2010-05 for peppers. As Table 1.2 does not specify separate requirements for bell and non-bell pepper, the same requirements are listed here for each crop.

³ As per Table 1 of 860.1500 for non-bell peppers; trial locations are not specified for crops requiring ≤3 field trials. According to Table 6 of 860.1500, non-bell pepper production occurs in Zones 2 (4%), 3 (3%), 5 (4%), 8 (50%), 9 (15%), and 10 (18%).

⁴ HED has determined that one pair of tomato trials conducted in Zone 5 are replicate trials.

⁵ As per Table 1.2 of PMRA Regulatory Directive DIR2010-05 for field tomatoes.

Table D.6. Trial Numbers and Geographical Locations of Cucurbit Vegetables Group 9.															
No. Trials	NAFTA Growing Zone													Total	
	1	2	3	4	5	5A	5B	6	7	8	9	10	11		12
Cucumber															
Sub.		2	1		4			1				1			9
Req. U.S. ¹		3/2	1/1		2/2			1/1				1/0			8/6
Req. Can. ²					3		2								5
Melon (Cantaloupe)															
Sub.		1			3			1				3			8
Req. U.S. ¹		1/1			1/1			2/1				4/3			8/6
Req. Can. ³					3		2								5
Summer Squash															
Sub.			1		2								1	1	5
Req. U.S. ⁴	1/1	2/1	1/1		1/1			1/0				1/1	1/0		8/5
Req. Can. ⁵					3		1							1	5
Winter Squash															
Sub.	1	1	1		1							1			5
Req. U.S. ⁴	1	1	1		1							1			5
Req. Can. ⁵					3		1							1	5

¹ As per Table 5 of 860.1500; the second number reflects a 25% reduction in the number of field trials allowed for the crop as a representative commodity in support of a crop group/subgroup tolerance or when application results in no quantifiable residues.

² As per Table 1.2 of PMRA Regulatory Directive DIR2010-05 for field cucumbers.

³ As per Table 1.2 of PMRA Regulatory Directive DIR2010-05 for melons.

⁴ As per Table 5 of 860.1500 for summer and winter squash. A minimum of five trials is required for a tolerance on “summer squash”. If a tolerance is sought on “squash”, at least 8 trials are required on summer squash as a representative commodity; alternatively, five trials each could be conducted on summer squash and winter squash to obtain a tolerance on “squash”.

⁵ As per Table 1.2 of PMRA Regulatory Directive DIR2010-05 for squash, pumpkins, and zucchini. As Table 1.2 does not identify separate requirements for summer and winter squash, the same requirements are listed here for each crop.

Table D.7. Trial Numbers and Geographical Locations for Citrus Fruit Group 10-10.															
No. Trials	NAFTA Growing Zone													Total	
	1	2	3	4	5	6	7	8	9	10	11	12			
Grapefruit															
Sub.			3			1					2				6
Req. U.S. ¹			5/3			1/1					2/2				8/6
Lemon															
Sub.			2								6				8
Req. U.S. ¹			1								4				5
Orange															
Sub.			8			1					3				12
Req. U.S. ¹			11/8			1/1					4/3				16/12

¹ As per Table 5 of 860.1500; the second number reflects a 25% reduction in the number of field trials allowed for the crop as a representative commodity in support of a crop group/subgroup tolerance or when application results in no quantifiable residues.

Table D.8. Trial Numbers and Geographical Locations for Pome Fruit Group 11-10.															
No. Trials	NAFTA Growing Zone													Total	
	1	1A	2	3	4	5	5B	6	7	8	9	10	11		12
Apple															
Sub.	3		1			5					1	1	3 ¹		14
Req. U.S. ²	4/3		2/1			3/2					1/1	1/1	5/4		16/12
Req. Can. ³	1	2				4	3						2		12
Pear															
Sub.	1					3						2	2 ¹		8
Req. U.S. ²	1/1											3/2	4/3		8/6
Req. Can. ³						4							1		5

¹ HED has determined that one pair of apple trials and one pair of pear trials conducted in Zone 11 are replicate trials.

² As per Table 5 of 860.1500; the second number reflects a 25% reduction in the number of field trials allowed for the crop as a representative commodity in support of a crop group/subgroup tolerance or when application results in no quantifiable residues.

³ As per Table 1.2 of PMRA Regulatory Directive DIR2010-05.

Table D.9. Trial Numbers and Geographical Locations Stone Fruit Group 12-12.															
No. Trials	NAFTA Growing Zone													Total	
	1	2	3	4	5	6	7	8	9	10	11	12	14		
Cherry, sweet															
Sub.										3	1				4
Req. U.S. ¹					2/2					2/2	3/2	1/0			8/6
Req. Can. ²					1				1		3				5
Cherry, tart															
Sub.					3						1				4
Req. U.S. ¹	1/1				5/4				1/1			1 ³ /0			8/6
Req. Can. ²					4									1	5
Peach															
Sub.	1	3			4	1				3	1				13
Req. U.S. ¹	1/1	4/3		1/0	1/1	1/1				4/3					12/9
Req. Can. ²					4						1				5
Plum															
Sub.	1				3					4	1	1			10
Req. U.S. ²					1/1					5/4	1/0	1/1			8/6
Req. Can. ²					2						1				3

¹ As per Table 5 of 860.1500; the second number reflects a 25% reduction in the number of field trials allowed for the crop as a representative commodity in support of a crop group/subgroup tolerance or when application results in no quantifiable residues. Sweet and/or tart cherry is acceptable as a representative crop of the Stone Fruit Group 12-12/U.S.; 12-09/Canada.

² As per Table 1.2 of PMRA Regulatory Directive DIR2010-05.

³ Either zone is acceptable.

Table D.10. Trial Numbers and Geographical Locations for Tree Nuts Group 14-12.													
No. Trials	NAFTA Growing Zone												Total
	1	2	3	4	5	6	7	8	9	10	11	12	
Almond													
Sub.										5			5
Req. U.S. ¹										5			5
Pecan													
Sub.		2		1		1		1					5
Req. U.S. ¹		2		1		1		1					5
Pistachio													
Sub.										3			3
Req. U.S. ¹													3 ²

¹ As per Table 5 of 860.1500; the same number of trials is required for almond and pecan for individual crop tolerances and for the crop as a representative commodity in support of a crop group/subgroup tolerance.

² As per Table 1 of 860.1500 for pistachio; trial locations are not specified for crops requiring ≤3 field trials. According to Table 6 of 860.1500, 100% of pistachio production occurs in Zone 10.

Table D.11. Trial Numbers and Geographical Locations for Cotton.														
Crop	No. Trials	NAFTA Growing Zone												Total
		1	2	3	4	5	6	7	8	9	10	11	12	
Cotton	Sub.		1		3		1		4		3			12
	Req. ¹		1/1		3/2		1/1		4/3		3/2			12/9

¹ As per Table 5 of 860.1500 for cotton; the second number reflects a 25% reduction in the number of field trials allowed for the crop as a representative commodity in support of a crop group/subgroup tolerance or when application results in no quantifiable residues. Per OCSPP 860.1000 Supplement (6/30/08), for cotton gin byproducts, cotton must be harvested by commercial equipment to provide an adequate representation of plant residue for the ginning process; three field trials for harvesting of stripper cotton are needed (no data are needed for picker cotton).

Appendix E. OECD MRL Calculation Procedure Inputs/Outputs**Almond, Hulls**

Compound	Afidopyropen	Afidopyropen
Crop	Almond Hulls (Concentrated Spray Application)	Almond Hulls (Dilute Spray Application)
Analytes	Parent only	Parent only
GAP	0.018 lb ai/A	0.018 lb ai/A
Total number of data (n)	5	5
Percentage of censored data	0%	0%
Number of non-censored data	5	5
Lowest residue	0.019	0.016
Highest residue	0.058	0.056
Median residue	0.025	0.039
Mean	0.030	0.037
Standard deviation (SD)	0.016	0.015
Correction factor for censoring (CF)	1.000	1.000
<u>Proposed MRL estimate</u>		
- Highest residue	0.058	0.056
- Mean + 4 SD	0.095	0.098
- CF x 3 Mean	0.091	0.110
Unrounded MRL	<u>0.095</u>	<u>0.110</u>
Rounded MRL	<u>0.10</u>	<u>0.15</u>
	High uncertainty of MRL estimate due to small dataset.	High uncertainty of MRL estimate due to small dataset.
	Residues (ppm)	Residues (ppm)
	0.025	0.016
	0.020	0.056
	0.058	0.044
	0.019	0.039
	0.030	0.028

Brassica, Head and Stem, Group 5-16

Compound Crop	Afidopyropen	Afidopyropen
	Broccoli (Head)	Cabbage (Head w/Wrapper)
Analytes	Parent only	Parent only
GAP	0.11 lb ai/A	0.11 lb ai/A
Total number of data (n)	10	10
Percentage of censored data	0%	10%
Number of non-censored data	10	9
Lowest residue	0.043	0.010
Highest residue	0.205	0.276
Median residue	0.105	0.042
Mean	0.112	0.091
Standard deviation (SD)	0.054	0.101
Correction factor for censoring (CF)	1.000	0.933

Proposed MRL estimate

- Highest residue	0.205	0.276
- Mean + 4 SD	0.327	0.496
- CF x 3 Mean	0.336	0.254
Unrounded MRL	<u>0.336</u>	<u>0.496</u>
Rounded MRL	<u>0.40</u>	<u>0.50</u>

Residues (ppm)		Residues (ppm)	
0.046		0.049	
0.205		0.034	
0.122		0.276	
0.170		0.039	
0.164		0.136	
0.103		0.010	*
0.043		0.043	
0.078		0.012	
0.084		0.041	
0.106		0.267	

Brassica, Leafy Greens, Subgroup 4-16B

Compound	Afidopyropen
Crop	Mustard Greens (Leaves)
Analytes	Parent only
GAP	0.11 lb ai/A

Total number of data (n)	8
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Percentage of censored data	13%
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Number of non-censored data	7
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Lowest residue	0.010
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Highest residue	2.733
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Median residue	1.196
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Mean	1.315
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Standard deviation (SD)	0.825
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Correction factor for censoring (CF)	0.917
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Proposed MRL estimate

- Highest residue	2.733
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- Mean + 4 SD	4.616
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- CF x 3 Mean	3.617
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Unrounded MRL	4.616
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Rounded MRL	5.0
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Residues (ppm)	
1.301	
2.733	
1.822	
1.829	
0.668	
1.067	
1.091	
0.010	*

Cotton, Gin Byproducts

Compound	Afidopyropen
Crop	Cotton Gin Byproducts (Harvested as Stripper Cotton)
Analytes	Parent only
GAP	0.11 lb ai/A
Total number of data (n)	3
Percentage of censored data	0%
Number of non-censored data	3
Lowest residue	0.460
Highest residue	0.600
Median residue	0.540
Mean	0.460
Standard deviation (SD)	0.600
Correction factor for censoring (CF)	0.540
<u>Proposed MRL estimate</u>	
- Highest residue	0.600
- Mean + 4 SD	0.814
- CF x 3 Mean	1.600
Unrounded MRL	<u>1.600</u>
Rounded MRL	<u>2.0</u>

High uncertainty of MRL estimate due to small dataset.

Residues (ppm)	
0.600	
0.540	
0.460	

Cotton, Undelinted Seed

Compound	Afidopyropen
Crop	Cotton Undelinted Seed
Analytes	Parent only
GAP	0.11 lb ai/A

Total number of data (n)	12
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Percentage of censored data	67%
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Number of non-censored data	4
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Lowest residue	0.010
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Highest residue	0.059
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Median residue	0.010
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Mean	0.010
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Standard deviation (SD)	0.059
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Correction factor for censoring (CF)	0.010
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Proposed MRL estimate

- Highest residue	0.059
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- Mean + 4 SD	0.077
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- CF x 3 Mean	0.030
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Unrounded MRL	<u>0.077</u>
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Rounded MRL	<u>0.08</u>
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High uncertainty of MRL estimate (High level of censoring).

Residues (ppm)	
0.010	*
0.010	*
0.029	
0.018	
0.010	*
0.010	*
0.011	*
0.028	
0.059	
0.010	*
0.010	*
0.010	*

Fruit, Citrus, Group 10-10 (Concentrated Spray Application)

Compound	Afidopyropen	Afidopyropen	Afidopyropen
Crop	Grapefruit (Concentrated Spray Application)	Lemon (Concentrated Spray Application)	Orange (Concentrated Spray Application)
Analytes	Parent only	Parent only	Parent only
GAP	0.11 lb ai/A	0.11 lb ai/A	0.11 lb ai/A
Total number of data (n)	6	8	12
Percentage of censored data	17%	25%	8%
Number of non-censored data	5	6	11
Lowest residue	0.010	0.010	0.010
Highest residue	0.062	0.070	0.069
Median residue	0.025	0.025	0.049
Mean	0.031	0.030	0.045
Standard deviation (SD)	0.022	0.022	0.021
Correction factor for censoring (CF)	0.889	0.833	0.944
<u>Proposed MRL estimate</u>			
- Highest residue	0.062	0.070	0.069
- Mean + 4 SD	0.121	0.116	0.130
- CF x 3 Mean	0.083	0.074	0.128
Unrounded MRL	<u>0.121</u>	<u>0.116</u>	<u>0.130</u>
Rounded MRL	0.15	0.15	0.15

High uncertainty of MRL estimate due to small dataset.

Residues (ppm)	Residues (ppm)	Residues (ppm)
0.054	0.696	0.027
0.033	0.467	0.047
0.062	0.525	0.064
0.010 *	0.254	0.051
0.011	0.170	0.019
0.017	0.944	0.064
	0.760	0.063
	0.042	0.069
		0.069
		0.032
		0.010 *
		0.028

Fruit, Citrus, Group 10-10 (Dilute Spray Application)

Compound	Afidopyropen	Afidopyropen	Afidopyropen
Crop	Grapefruit (Dilute Spray Application)	Lemon (Dilute Spray Application)	Orange (Dilute Spray Application)
Analytes	Parent only	Parent only	Parent only
GAP	0.11 lb ai/A	0.11 lb ai/A	0.11 lb ai/A
Total number of data (n)	6	8	12
Percentage of censored data	17%	25%	8%
Number of non-censored data	5	6	11
Lowest residue	0.010	0.010	0.010
Highest residue	0.041	0.055	0.072
Median residue	0.026	0.038	0.043
Mean	0.025	0.032	0.044
Standard deviation (SD)	0.012	0.016	0.020
Correction factor for censoring (CF)	0.889	0.833	0.944
<u>Proposed MRL estimate</u>			
- Highest residue	0.041	0.055	0.072
- Mean + 4 SD	0.075	0.097	0.125
- CF x 3 Mean	0.067	0.080	0.125
Unrounded MRL	<u>0.075</u>	<u>0.097</u>	<u>0.125</u>
Rounded MRL	<u>0.08</u>	<u>0.10</u>	<u>0.15</u>

High uncertainty of MRL estimate due to small dataset.

Residues (ppm)	Residues (ppm)	Residues (ppm)	Residues (ppm)	Residues (ppm)
0.031	0.023		0.036	
0.035	0.055		0.070	
0.041	0.010	*	0.072	
0.010	0.035		0.023	
0.014	0.041		0.025	
0.020	0.010	*	0.052	
	0.041		0.034	
	0.041		0.048	
			0.072	
			0.046	
			0.010	*
			0.040	

Fruit, Pome, Group 11-10 (Concentrated Spray Application)

Compound Crop	Afidopyropen	Afidopyropen
	Apple (Concentrated Spray Application)	Pear (Concentrated Spray Application)
Analytes	Parent only	Parent only
GAP	0.044 lb ai/A	0.044 lb ai/A
Total number of data (n)	14	8
Percentage of censored data	93%	75%
Number of non-censored data	1	2
Lowest residue	0.010	0.010
Highest residue	0.011	0.014
Median residue	0.010	0.010
Mean	0.010	0.011
Standard deviation (SD)	0.000	0.001
Correction factor for censoring (CF)	0.381	0.500
<u>Proposed MRL estimate</u>		
- Highest residue	0.011	0.014
- Mean + 4 SD	0.011	0.016
- CF x 3 Mean	0.012	0.016
Unrounded MRL	<u>0.012</u>	<u>0.016</u>
Rounded MRL	<u>0.015</u>	<u>0.02</u>
	High uncertainty of MRL estimate (High level of censoring).	High uncertainty of MRL estimate (High level of censoring).
	Residues (ppm)	Residues (ppm)
	0.010 *	0.010 *
	0.010 *	0.010 *
	0.011	0.010 *
	0.010 *	0.014
	0.010 *	0.010 *
	0.010 *	0.011
	0.010 *	0.010 *
	0.010 *	0.010 *
	0.010 *	
	0.010 *	
	0.010 *	
	0.010 *	
	0.010 *	
	0.0.10 *	

Fruit, Pome, Group 11-10 (Diluted Spray Application)

Compound Crop	Afidopyropen	Afidopyropen
	Apple (Diluted Spray Application)	Pear (Diluted Spray Application)
Analytes	Parent only	Parent only
GAP	0.044 lb ai/A	0.044 lb ai/A
Total number of data (n)	14	8
Percentage of censored data	NA	88%
Number of non-censored data	NA	1
Lowest residue	NA	0.010
Highest residue	NA	0.012
Median residue	NA	0.010
Mean	NA	0.011
Standard deviation (SD)	NA	0.001
Correction factor for censoring (CF)	NA	0.417
<u>Proposed MRL estimate</u>		
- Highest residue	NA	0.012
- Mean + 4 SD	NA	0.014
- CF x 3 Mean	NA	0.013
Unrounded MRL	<u>NA</u>	<u>0.014</u>
Rounded MRL	<u>0.010</u>	<u>0.015</u>

LOQ MRL, no measurable field trial results. High uncertainty of MRL estimate (High level of censoring).

Residues (ppm)		Residues (ppm)	
0.010	*	0.010	*
0.010	*	0.010	*
0.010	*	0.010	*
0.010	*	0.012	
0.010	*	0.010	*
0.010	*	0.010	*
0.010	*	0.012	*
0.010	*	0.011	*
0.010	*		
0.010	*		
0.010	*		
0.010	*		
0.010	*		
0.010	*		

Fruit, Stone, Group 12-10 (Concentrated Spray Application)

Compound	Afidopyropen	Afidopyropen	Afidopyropen
Crop	Cherry (Concentrated Spray Application)	Peach (Concentrated Spray Application)	Plum (Concentrated Spray Application)
Analytes	Parent only	Parent only	Parent only
GAP	0.018 lb ai/A	0.018 lb ai/A	0.018 lb ai/A
Total number of data (n)	8	13	10
Percentage of censored data	88%	NA	NA
Number of non-censored data	1	NA	NA
Lowest residue	0.010	NA	NA
Highest residue	0.014	NA	NA
Median residue	0.010	NA	NA
Mean	0.011	NA	NA
Standard deviation (SD)	0.001	NA	NA
Correction factor for censoring (CF)	0.417	NA	NA
<u>Proposed MRL estimate</u>			
- Highest residue	0.014	NA	NA
- Mean + 4 SD	0.016	NA	NA
- CF x 3 Mean	0.013	NA	NA
Unrounded MRL	<u>0.016</u>	<u>NA</u>	<u>NA</u>
Rounded MRL	<u>0.02</u>	<u>0.010</u>	<u>0.010</u>

High uncertainty of MRL estimate (High level of censoring). LOQ MRL, no measurable field trial results. LOQ MRL, no measurable field trial results.

Residues (ppm)		Residues (ppm)		Residues (ppm)	
0.014		0.010	*	0.010	*
0.010	*	0.010	*	0.010	*
0.010	*	0.010	*	0.010	*
0.010	*	0.010	*	0.010	*
0.010	*	0.010	*	0.010	*
0.010	*	0.010	*	0.010	*
0.010	*	0.010	*	0.010	*
0.010	*	0.010	*	0.010	*
		0.010	*	0.010	*
		0.010	*	0.010	*
		0.010	*		
		0.010	*		

Fruit, Stone, Group 12-10 (Dilute Spray Application)

Compound	Afidopyropen	Afidopyropen	Afidopyropen
Crop	Cherry (Dilute Spray Application)	Peach (Dilute Spray Application)	Plum (Dilute Spray Application)
Analytes	Parent only	Parent only	Parent only
GAP	0.018 lb ai/A	0.018 lb ai/A	0.018 lb ai/A
Total number of data (n)	8	13	10
Percentage of censored data	63%	100%	NA
Number of non-censored data	3	0	NA
Lowest residue	0.010	0.010	NA
Highest residue	0.021	0.011	NA
Median residue	0.010	0.010	NA
Mean	0.012	0.010	NA
Standard deviation (SD)	0.004	0.000	NA
Correction factor for censoring (CF)	0.583	0.333	NA
<u>Proposed MRL estimate</u>			
- Highest residue	0.021	0.011	NA
- Mean + 4 SD	0.027	0.011	NA
- CF x 3 Mean	0.021	0.010	NA
Unrounded MRL	<u>0.027</u>	<u>0.011</u>	<u>NA</u>
Rounded MRL	<u>0.03</u>	<u>0.015</u>	<u>0.010</u>

High uncertainty of MRL estimate (High level of censoring). High uncertainty of MRL estimate (High level of censoring). LOQ MRL, no measurable field trial results.

Residues (ppm)		Residues (ppm)		Residues (ppm)	
0.011		0.010	*	0.010	*
0.021		0.010	*	0.010	*
0.010	*	0.010	*	0.010	*
0.010	*	0.010	*	0.010	*
0.010	*	0.010	*	0.010	*
0.010	*	0.010	*	0.010	*
0.010	*	0.010	*	0.010	*
0.013		0.010	*	0.010	*
		0.010	*	0.010	*
		0.010	*		
		0.010	*		
		0.011	*		

Leafy Greens Subgroup 4-16B

Compound	Afidopyropen	Afidopyropen	Afidopyropen
Crop	Head Lettuce (Head w/Wrapper)	Leaf Lettuce	Spinach
Analytes	Parent only	Parent only	Parent only
GAP	0.11 lb ai/A	0.11 lb ai/A	0.11 lb ai/A
Total number of data (n)	8	8	8
Percentage of censored data	0%	0%	0%
Number of non-censored data	8	8	8
Lowest residue	0.014	0.042	0.042
Highest residue	0.278	0.944	1.074
Median residue	0.165	0.496	0.629
Mean	0.149	0.482	0.651
Standard deviation (SD)	0.078	0.312	0.337
Correction factor for censoring (CF)	1.000	1.000	1.000
<u>Proposed MRL estimate</u>			
- Highest residue	0.278	0.944	1.074
- Mean + 4 SD	0.463	1.730	2.000
- CF x 3 Mean	0.448	1.447	1.954
Unrounded MRL	<u>0.463</u>	<u>1.730</u>	<u>2.000</u>
Rounded MRL	<u>0.50</u>	<u>2.0</u>	<u>2.0</u>

Residues (ppm)	Residues (ppm)	Residues (ppm)
0.170	0.696	0.423
0.164	0.467	0.042
0.119	0.525	1.074
0.278	0.254	1.043
0.198	0.170	0.550
0.086	0.944	0.616
0.165	0.760	0.642
0.014	0.042	0.821

Leaf Petiole Vegetable Subgroup 22B

Compound	Afidopyropen
Crop	Celery
Analytes	Parent only
GAP	0.11 lb ai/A
Total number of data (n)	7
Percentage of censored data	0%
Number of non-censored data	7
Lowest residue	0.027
Highest residue	1.275
Median residue	0.283
Mean	0.434
Standard deviation (SD)	0.447
Correction factor for censoring (CF)	1.000
<u>Proposed MRL estimate</u>	
- Highest residue	1.275
- Mean + 4 SD	2.220
- CF x 3 Mean	1.302
Unrounded MRL	<u>2.220</u>
Rounded MRL	<u>3.0</u>

Residues (ppm)	
0.128	
0.774	
1.275	
0.418	
0.027	
0.283	
0.132	

Nut, Tree, Group 14-12 (Dilute Spray Application)

Compound	Afidopyropen	Afidopyropen	Afidopyropen
Crop	Almond, Nutmeat (Dilute Spray Application)	Pecan, Nutmeat (Dilute Spray Application)	Pistachio, Nutmeat (Dilute Spray Application)
Analytes	Parent only	Parent only	Parent only
GAP	0.018 lb ai/A	0.018 lb ai/A	0.018 lb ai/A
Total number of data (n)	5	5	3
Percentage of censored data	NA	NA	NA
Number of non-censored data	NA	NA	NA
Lowest residue	NA	NA	NA
Highest residue	NA	NA	NA
Median residue	NA	NA	NA
Mean	NA	NA	NA
Standard deviation (SD)	NA	NA	NA
Correction factor for censoring (CF)	NA	NA	NA
<u>Proposed MRL estimate</u>			
- Highest residue	NA	NA	NA
- Mean + 4 SD	NA	NA	NA
- CF x 3 Mean	NA	NA	NA
Unrounded MRL	<u>NA</u>	<u>NA</u>	<u>NA</u>
Rounded MRL	<u>0.010</u>	<u>0.010</u>	<u>0.010</u>
	LOQ MRL, no measurable field trial results.	LOQ MRL, no measurable field trial results.	LOQ MRL, no measurable field trial results.
	Residues (ppm)	Residues (ppm)	Residues (ppm)
	0.010 *	0.010 *	0.010 *
	0.010 *	0.010 *	0.010 *
	0.010 *	0.010 *	0.010 *
	0.010 *	0.010 *	
	0.010 *	0.010 *	

Soybean, Seed

Compound	Afidopyropen
Crop	Soybean Seed
Analytes	Parent only
GAP	0.018 lb ai/A

Total number of data (n)	20
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Percentage of censored data	NA
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Number of non-censored data	NA
-----------------------------	----

Lowest residue	NA
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Highest residue	NA
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Median residue	NA
----------------	----

Mean	NA
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Standard deviation (SD)	NA
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Correction factor for censoring (CF)	NA
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Proposed MRL estimate

- Highest residue	NA
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- Mean + 4 SD	NA
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- CF x 3 Mean	NA
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Unrounded MRL	<u>NA</u>
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Rounded MRL	<u>0.010</u>
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LOQ MRL, no measurable field trial results.

Residues (ppm)	
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*

Vegetable, Cucurbit, Group 9

Compound	Afidopyropen	Afidopyropen	Afidopyropen	Afidopyropen
Crop	Cucumber (Fruit)	Cantaloupe (Fruit)	Squash, Summer (Fruit)	Squash, Winter (Fruit)
Analytes	Parent only	Parent only	Parent only	Parent only
GAP	0.11 lb ai/A	0.11 lb ai/A	0.11 lb ai/A	0.11 lb ai/A

Total number of data (n)	9	8	5	5
Percentage of censored data	0%	13%	20%	60%
Number of non-censored data	9	7	4	2
Lowest residue	0.053	0.010	0.010	0.010
Highest residue	0.406	0.023	0.033	0.037
Median residue	0.112	0.018	0.018	0.011
Mean	0.162	0.018	0.021	0.018
Standard deviation (SD)	0.120	0.005	0.010	0.012
Correction factor for censoring (CF)	1.000	0.917	0.867	0.600

Proposed MRL estimate

- Highest residue	0.406	0.023	0.033	0.037
- Mean + 4 SD	0.642	0.036	0.061	0.064
- CF x 3 Mean	0.486	0.048	0.054	0.032
Unrounded MRL	<u>0.642</u>	<u>0.048</u>	<u>0.061</u>	<u>0.064</u>
Rounded MRL	<u>0.70</u>	<u>0.05</u>	<u>0.06</u>	<u>0.07</u>

High uncertainty of MRL estimate (Small dataset). High uncertainty of MRL estimate (Small dataset and high level of censoring).

Residues (ppm)	Residues (ppm)	Residues (ppm)	Residues (ppm)
0.112	0.022	0.033	0.010 *
0.154	0.021	0.018	0.022
0.406	0.019	0.029	0.037
0.081	0.017	0.010 *	0.010 *
0.110	0.023	0.014	0.011 *
0.149	0.010 *		
0.318	0.017		
0.053	0.012		
0.076			

Vegetable, Fruiting, Group 8-10

Compound	Afidopyropen	Afidopyropen	Afidopyropen
Crop	Bell Pepper (Fruit)	Non-Bell Pepper (Fruit)	Tomato (Fruit)
Analytes	Parent only	Parent only	Parent only
GAP	0.11 lb ai/A	0.11 lb ai/A	0.11 lb ai/A

Total number of data (n)	7	3	19
Percentage of censored data	29%	0%	26%
Number of non-censored data	5	3	14
Lowest residue	0.010	0.046	0.010
Highest residue	0.046	0.059	0.097
Median residue	0.022	0.055	0.019
Mean	0.023	0.053	0.030
Standard deviation (SD)	0.012	0.007	0.025
Correction factor for censoring (CF)	0.810	1.000	0.825

Proposed MRL estimate

- Highest residue	0.046	0.059	0.097
- Mean + 4 SD	0.073	0.080	0.128
- CF x 3 Mean	0.056	0.160	0.073
Unrounded MRL	<u>0.073</u>	<u>0.160</u>	<u>0.128</u>
Rounded MRL	0.08	0.20	0.15

High uncertainty of MRL estimate due to small dataset. High uncertainty of MRL estimate due to small dataset.

Residues (ppm)	Residues (ppm)	Residues (ppm)
0.046	0.059	0.040
0.026	0.046	0.071
0.022	0.055	0.018
0.016		0.019
0.011	*	0.019
0.029		0.010
0.010	*	0.011
		0.042
		0.097
		0.015
		0.014
		0.020
		0.012
		0.014
		0.068
		0.040
		0.024
		0.019
		0.010

Appendix F. Bibliographic Listing of Submitted Residue Chemistry Studies

MRID/ Accession No.	OCSP Guideline No.	Title	GLP	Suitable for Review	Comments
49689019	860.1300	Hayashi, O. (2015) [NCA-(Carbon 14)]ME5343. Metabolic Fate in Tomato. Project Number: 2015/8000184, IET/09/8006. Unpublished study prepared by the Institute of Environmental Toxicology. 153p. MRID No. 49689019/PMRA No. 2627938.	Yes	Yes	--
49689020	860.1300	Lutz, T.; Udo, R. (2015) Metabolism of (Carbon 14) BAS 440 I in Tomato. Project Number: 394612, 2015/117/1144. Unpublished study prepared by BASF SE. 147p. MRID No. 49689020/PMRA No. 2627934 & 2627935.	Yes	Yes	--
49689021	860.1300	Penketh, S. (2015) Amended Report – [NCA- ¹⁴ C]ME5343 – Metabolism in Cabbages. Study Identification Number(s) Envigo Project Identity JHW0002, BASF Registration Document Number 2015/8000406. Unpublished study prepared by BASF SE. 87p. MRID No. 49689021/PMRA No. 2627939.	Yes	Yes	This study was not specified as part of the D433606 bean-sheet for review.
49689022	860.1300	Rabe, U. (2015) Metabolism of (Carbon 14) BAS 440 I in Cabbage. Project Number: 394616, 2015/1171143, 2015/1171144. Unpublished study prepared by BASF SE. 101p. MRID No. 49689022/PMRA No. 2627932 & 2627933.	Yes	Yes	--
49689023	860.1300	Schaffert, D.; Kemper, C. (2016) Investigation of BAS M440I031 (Trigoneline) in (Carbon 14)-BAS 440 I Treated Cabbage. Project Number: 2015/1252661, 788690, JHW0002. Unpublished study prepared by BASF SE. 55p. MRID No. 49689023/PMRA No. 2627937.	Yes	Yes	--
49689024	860.1300	Schweda, Z.; Kaylon, B.; Possienke, M.; et al. (2015) Metabolism of (Carbon 14)-BAS 440 I in Soybean. Project Number: 2013/1395580, 394611, 2010/1007833. Unpublished study prepared by BASF SE. 287p. MRID No. 49689024/PMRA No. 2627930 & 2627931.	Yes	Yes	--
49689025	860.1300	Schweda, Z.; Lutz, T. (2015) Metabolism of (Carbon 14)-BAS 440 I in Soybean. Project Number: 727301, 2015/1191862, 2013/1395580. Unpublished study prepared by BASF SE. 130p. MRID No. 49689025/PMRA No. 2627936.	Yes	Yes	--
49689026	860.1300	Blair, K.; Wicksted, G. (2016) The Metabolism of [(Carbon 14)-CPCA]-BAS 440 I in the Laying Hen: Final Report. Project Number: 394772, 812248, 2015/1237954. Unpublished study prepared by Charles River Laboratories Edinburgh Ltd. 213p. MRID No. 49689026/PMRA No. 2627941.	Yes	Yes	--
49689027	860.1300	Vance, C; Lowrie, C.; Young, L. (2013) The Metabolism of (Carbon 14)-BAS 440 I in the Lactating Goat. Project Number: 2012/1002483, 286390, 394700. Unpublished study prepared by Charles River. 127p. MRID No. 49689027/PMRA No. 2627940.	Yes	Yes	--
49689028	860.1300	Wicksted, G.; White, J. (2016) The Metabolism of [(Carbon 14)-CPCA]-BAS 440 I in the Lactating Goat: (Including Amendment No. 1). Project Number: 394716, 812515, 2016/7001920. Unpublished study prepared by Charles River Laboratories Edinburgh Ltd. 377p. MRID No. 49689028/PMRA No. 2627942.	Yes	Yes	--

MRID/ Accession No.	OCSPP Guideline No.	Title	GLP	Suitable for Review	Comments
49688938	860.1340	Perez, R. (2015) Independent Laboratory Validation of BASF Analytical Method D1103/01: Determination of Residues of BAS 440 I and its Metabolite M440I007 in Plant Matrices using LC-MS/MS. Project Number: 394761, 2015/7005948, 2K15/394761. Unpublished study prepared by ADPEN Laboratories, Inc. 183p. MRID No. 49688938/PMRA No. 2627725.	Yes	Yes	--
49688941	860.1340	Schweda, Z. (2015) Investigation of the Extractability of BAS 440 I and its Metabolite M440I007 in Samples from [Carbon 14] Plant Metabolism Studies. Project Number: 733252, 2015/1204968. Unpublished study prepared by BASF SE. 43p. MRID No. 49688941/PMRA No. 2627723.	Yes	Yes	--
49688942	860.1340	Jose, W. (2015) Validation of BASF Method D1103 in Cotton Seed (Seed), Beans (Seed), Tomato (Whole Fruit), Citrus (Whole Fruit) and Potato (Tuber): Determination of Residues of BAS 440 I and its Metabolite M440I007 in Plant Matrices using LC-MS/MS. Project Number: 699187, 2015/3000324. Unpublished study prepared by Global Environmental and Consumer Safety Laboratory – GENCS. 347p. MRID No. 49688942/PMRA No. 2627724.	Yes	Yes	--
49688943	860.1340	Jose, W. (2016) Validation of BASF Method D1103/01 for the Determination of Residues of BAS 440 I and its Metabolite M440I007 in Cotton (Seed), Dry Bean (Seed), Tomato (Whole Fruit), Citrus (Whole Fruit) and Rice (Grain with Hulls) using LC-MS/MS. Project Number: 699187/1, 2016/7001980. Unpublished study prepared by Global Environmental and Consumer Safety Laboratory – GENCS. 347p. MRID No. 49688943/PMRA No. 2627729.	Yes	Yes	--
49688939	860.1340	Xu, A. (2016) Independent Laboratory Validation of Residue Method D1507/01: Method for the Determination of Residues of Afidopyropen and its Metabolites M440I001, M440I003, M440I005 and CPCA Carnitine in Animal Matrices by LC-MS/MS. Project Number: 394765, 053/1201, PASC/REP/0670. Unpublished study prepared by Primera Analytical Solutions Corporation. 275p. MRID No. 49688939/PMRA No. 2627726.	Yes	Yes	--
49688944	860.1340	Gooding, R. (2016) Validation of BASF Analytical Method D1507/01: Method for the Determination of Residues of Afidopyropen and its Metabolites M440I001, M440I003, M440I005, and CPCA Carnitine in Animal Matrices by LC-MS/MS. Unpublished study prepared by BASF Corporation. 303p. MRID No. 49688944/PMRA No. 2627727.	Yes	Yes	--
49688940	860.1360	Gooding, R. (2016) Validation of BASF Analytical Method D1514/01: “Multi-Residue Method using modified AOAC Official Method 2007.01 for the Determination of Residues of Afidopyropen (BAS 440 I, Reg No. 5599022) and its Metabolite M440I007 (Reg No. 5824749) in Plant Matrices using LC-MS/MS. Project Number: 2015/7006136, BASF Study Number 394762. Unpublished study prepared by BASF Corporation. 30p. MRID No. 49688940/PMRA No. 2627728.			No MRM Test Data for Plant Matrices

MRID/ Accession No.	OCSPP Guideline No.	Title	GLP	Suitable for Review	Comments
49689017	860.1380	Fang, M.; Black, M. (2016) 18 Month Freezer Stability Report: Determination of Residues of Afidopyropen (BAS 440 I) and its Metabolites M4401007 in Plant Matrices using LC-MS/MS. Project Number: 2016/7001836, 715903, 2015/3002646. Unpublished study prepared by Alliance Pharma, Inc. 135p. MRID No. 49689017/PMRA No. 2627927.	Yes	Yes	18-month Storage Stability of Plant Matrices
50157201	860.1380	Fang, M.; Black, M. (2016) 24 Month Freezer Stability Report: Determination of Residues of Afidopyropen (BAS 440 I) and its Metabolites M4401007 in Plant Matrices using LC-MS/MS. Project Number: 2016/7006470, BASF Study No. 715903, Alliance Pharma Study No. 140420. Unpublished study prepared by Alliance Pharma, Inc. 141p. MRID No. 50157201/PMRA No. 2715858.	Yes	Yes	Final 24-month Storage Stability of Plant Matrices
49688951	860.1380	Panek, M. (2016) Afidopyropen (BAS 440 I): Request to Waive Requirement for Additional Freezer Storage Stability Data for Afidopyropen and its Metabolites in Animal Matrices. Project Number: 2016/7001958. Unpublished study prepared by BASF Corporation. 12p. MRID No. 49688951/PMRA No. 2627929.	NA	Yes	Livestock Storage Stability Waiver Request
49689041	860.1480	Panek, M. (2016) Afidopyropen (BAS 440 I) Request Waiver of a Feeding Study in Poultry: Final Report. Project Number: 2016/7001324, 2015/1237954. Unpublished study prepared by BASF Corporation. 10p. MRID No. 49689041/PMRA No. 2627956.	NA	Yes	Poultry Feeding Study Waiver Request
49689042	860.1480	Malinsky, D. (2016) A Meat and Milk Magnitude of the Residue Study with BAS 440 I in Lactating Cows: Final Report. Project Number: 394770, 053/1204, 210/007/10. Unpublished study prepared by BASF Corporation, Genesis Midwest Laboratories, Primera Analytical Solutions Corporation, Dairyland Laboratories, Inc., and Agsource Food and Environmental Lab. 404p. MRID No. 49689042/PMRA No. 2627957.	Yes	Yes	Dairy Cattle Feeding Study
49689030	860.1500	Csinos, A. (2016) Magnitude of BAS 440 I and Metabolite Residues in Potato Following Applications of BAS 440 001 DC in North America: Final Report. Project Number: 697858, S14/01622, 2015/7001496. Unpublished study prepared by Eurofins Agrosience Services, Inc., A.C.D.S. Research, Inc., Crop Management Strategies, Inc., Reality Research, AGVISE Research, Inc., Ag-Quest Inc., Bennett Agricultural Research Consulting, AgraServ, Inc., Research for Hire, Qualls Agricultural Laboratory, Inc., Smith Biological Services, and Varco, Inc. 249p. MRID No. 49686030/PMRA No. 2627949.	Yes	Yes	--
49689031	860.1500	Brungardt, J. (2015) Magnitude of the Residues of BAS 440 I in/on Leafy Vegetables Following Applications of BAS 440 00 I: Final Report. Project Number: 698878, 2015/7000084, 05SRLS14R/05. Unpublished study prepared by SynTech Research, Inc., Glades Crop Care, Easton Agri-Consulting, Inc., Coastal Research Services, Inc., Research for Hire, A.C.D.S. Research Inc., Research 2000, Crop Guard Research, Inc., VARCO, Inc., and EPL Bio Analytical Services. 355p. MRID No. 49689031/PMRA No. 2627944.	Yes	Yes	--

MRID/ Accession No.	OCSPP Guideline No.	Title	GLP	Suitable for Review	Comments
49689032	860.1500	Greenland, R. (2016) Magnitude of the Residues of BAS 440 I in Brassica Leafy Vegetables Following Applications of BAS 440 00 I: Final Report. Project Number: 698872, BASF/698872, 137G854. Unpublished study prepared by Tewart Agricultural Research Services, Inc., Agricultural Research of Wisconsin, LLC, Cropwise Research LLC, Crow River Research, Inc., Bennett Agricultural Research Corporation, Coastal Ag Research, Inc., EXCEL Research Services, Inc., Lange research and Consulting, Research 2000, California Agricultural Research, Inc., Collins Agricultural Consultants, Reality Research, Crop Management Strategies, Inc., Florida Pesticide Research, Inc., Ripple Agricultural Research, Inc., Carolina Ag Research Services, Inc., Agricultural Systems Associates, and MOARK Agricultural Research, LLC. 360p. MRID No. 49689032/PMRA No. 2627946.	Yes	Yes	--
49689033	860.1500	Csinos, A. (2016) Magnitude of BAS 440 I and Metabolite Residues in Soybean Following Applications of BAS 440 01 I in North America: Final Report. Project Number: 394707, S14/01629, 2015/7006063. Unpublished study prepared by Crop Management Strategies, Inc., Eurofins Agrosience Services, Inc., Mid-South Ag Research, Inc., AgPro Partners Midwest, LLC, AGVISE Research, Inc., Crow River Research, Easton Agri-Consulting, Inc., South Dakota Ag Research, Inc., Stewart Agr. Research Services, Inc., Northern Plains Ag Research, Bennett Agricultural Research Consulting, Ag-Quest, Inc., Pest Management Enterprises, LLC, MOARK Agricultural Research, LLC, and CMS, Inc. 409p. MRID No. 49686033/PMRA No. 2627950.	Yes	Yes	--
49689034	860.1500	Woodward, D. (2016) Magnitude of the Residues of BAS 440 I in Fruiting Vegetables Following Applications of BAS 440 00 I: Final Report. Project Number: 698873, 054SRLS14R/03, S14/04781. Unpublished study prepared by SynTech Research, Inc., Coastal Research Services, Inc., CMS, Inc., Harris Farms and Research, Easton Agri-Consulting, Inc., Northern Plains Ag Research, Bennett Ag Research Corporation, Heartland Ag Research, LLC, Research 2000, Research for Hire, and Crop Guard Research, Inc. 240p. MRID No. 49686034/PMRA No. 2627943.	Yes	Yes	--
49689035	860.1500	Woodward, D. (2016) Magnitude of the Residues of BAS 440 I in/on Cucurbit Vegetables Following Applications of BAS 440 00 I: Final Report. Project Number: 394665, 054SRLS14R/04, S14/047776. Unpublished study prepared by BASF Corporation, SynTech Research, Inc., Bennett Ag Research, Inc., Northern Plains Agricultural Research, Crop Guard Research, Inc., Research 2000, Coastal Research Services, Qualls Agricultural Laboratory, Collins Agricultural Consultants, Inc., And Crop Management Strategies, Inc. 246p. MRID No. 49686035/PMRA No. 2627945.	Yes	Yes	--

MRID/ Accession No.	OCSPP Guideline No.	Title	GLP	Suitable for Review	Comments
49689036	860.1500	Greenland, R. (2016) Magnitude of the Residues of Afidopyropen in Citrus Fruits Following Foliar Applications of BAS 440 00 I. Final Report. Project Number: BASF/698793, 698793, 053/1019B. Unpublished study prepared by Stewart Agricultural Research Services, Inc., Primera Analytical Solutions Corporation, Florida Pesticide Research, Inc., Research 2000, Eurofins Agrosience Services, Inc., Southeast Ag Research, Inc., South Texas Ag Research-RGV, Inc., Coastal Research Services, and California Agricultural, Inc. 303p. MRID No. 49686036/PMRA No. 2627113.	Yes	Yes	--
49689037	860.1500	Hummel, R. (2016) Magnitude of the Residue of BAS 440 I in Pome Fruits (Crop Group 11): Final Report. Project Number: 394660, S14/04625, 2015/7000095. Unpublished study prepared by Eurofins Agrosience Services, Inc., Landis International, Inc., ACDS Research, Crow Rivers Research, Research 2000, Qualls Agricultural laboratory, Ron Britt & Associates, Agricultural Systems Associates, Illinois Ag Research, AgraServ, and Vaughn Agricultural Research. 219p. MRID No. 49689037/PMRA No. 2627948.	Yes	Yes	--
49689038	860.1500	Hummel, R. (2016) Magnitude of the Residue of BAS 440 I in Stone Fruits (Crop Group 12): Final Report. Project Number: 697856, S14/04780, 2015/7000090. Unpublished study prepared by Landis International, Inc., Eurofins Lancaster Laboratories, Vaughn Agricultural Research Services, Ltd., Crow Rivers Research, Research 2000, Qualls Agricultural laboratory, ACDS Research, ICMS, Southeast Agricultural Research, Agricultural Systems Associates, MOARK Ag Research, Crop Guard Research, and Research for Hire. 247p. MRID No. 49689038/PMRA No. 2627947.	Yes	Yes	--
49689039	860.1500	Wyatt, D. (2016) Magnitude of the Residues of BAS 440 I in Tree Nut Raw Agricultural Commodities: Amended Final Report. Project Number: 394673, 2016/7001262, 053/1050A. Unpublished study prepared by BASF Crop Protection, Primera Analytical Solutions Corporation, Agricultural Systems Associates, Southeast Ag Research, Inc., Pest Management Enterprises, LLC, South Texas Ag Research, Research 2000, and Research for Hire. 216p. MRID No. 49686039/PMRA No. 2627955.	Yes	Yes	--
49689040	860.1500	Csinos, A. (2016) Magnitude and Decline of BAS 440 I and Metabolite Residues in Cotton Following Applications of BAS 440 00 I DC: Final Report. Project Number: 697857, S14/01616, 2015/7000081. Unpublished study prepared by Eurofins Agrosience Services, Inc., Mid-South Ag Research, Inc., Pest Management Enterprises, LLC, Crop Guard Research, Inc., Great Plains Crop Research, MOARK Agricultural Research, LLC, South Texas Ag Research-High Plains, Coastal Ag Research, Inc., Coastal Research Services, Inc., and Research for Hire. 226p. MRID No. 49686040/PMRA No. 2627112.	Yes	Yes	--

MRID/ Accession No.	OCSPP Guideline No.	Title	GLP	Suitable for Review	Comments
49689121	860.1500	Bower, M. (2015) Determination of Residues of BAS440 00I in Cotton Following Four (4) Applications of BAS 440 00I. Project Number: BAS14405, 2015/8000481. Unpublished study prepared by Peracto Pty Ltd. 72p. MRID No. 49689121/PMRA No. 2627115.	Yes	Yes	--
49689122	860.1500	Bower, M. (2015) Determination of Residues of BAS440 00I in Potatoes Following Four (4) Applications of BAS 440 00I. Project Number: BAS14406, 2015/8000482. Unpublished study prepared by Peracto Pty Ltd. 58p. MRID No. 49689122/PMRA No. 2627951.	Yes	Yes	--
49689123	860.1500	Bower, M. (2015) Determination of Residues of BAS440 00I in Fruiting Vegetables Following Four (4) Applications of BAS 440 00I. Project Number: 2015/8000483, BAS14407, 15/0007. Unpublished study prepared by Peracto Pty Ltd. 56p. MRID No. 49689123/PMRA No. 2627952.	Yes	Yes	--
49689124	860.1500	Bower, M. (2015) Determination of Residues of BAS440 00I in Brassica and Leafy Vegetables Following Four (4) Applications of BAS 440 00I. Project Number: BAS14409, 2015/8000484, 14/0962A. Unpublished study prepared by Peracto Pty Ltd. 88p. MRID No. 49689124/PMRA No. 2627953.	Yes	Yes	--
49689043	860.1520	Csinos, A. (2016) Magnitude of the Residues of BAS 440 I in Potato Processed Fractions Following Applications of BAS 440 00 I DC: Final Report. Project Number: 698322, S14/01626, 2014/7003953. Unpublished study prepared by Crop Management Strategies, Inc., Bennett Agricultural Research & Consulting, Smith Biological Services, and Eurofins Agrosience Services, Inc. 177p. MRID No. 49689043/PMRA No. 2627958.	Yes	Yes	Potato Processing Study
49689044	860.1520	Woodward, D. (2015) Magnitude of the Residues of BAS 440 I in Tomato Processing Fractions Following Applications of BAS 440 00 I DC: Final Report. Project Number: 697852, 05SRLS14R/02, S14/04779. Unpublished study prepared by SynTech Research Laboratory Services, LLC, and Coastal Research Services. 294p. MRID No. 49689044/PMRA No. 2627959.	Yes	Yes	Tomato Processing Study
49689045	860.1520	Csinos, A. (2016) Magnitude of the Residues of BAS 440 I in Soybean Processed Fractions: Final Report. Project Number: 394742, S14/01632, 2015/7000097. Unpublished study prepared by Bennett Agricultural Research & Consulting, Agvise Research, MOARK Agricultural Research, LLC, and Eurofins Agrosience Services, Inc. 217p. MRID No. 49689045/PMRA No. 2627962.	Yes	Yes	Soybean Processing Study
49689046	860.1520	Greenland, R. (2016) Magnitude of Afidopyropen Residues in Orange Processed Fractions Following Foliar Applications of BAS 440 00 I: Final Report. Project Number: BASF/394753, 394753, 053/1019A. Unpublished study prepared by Stewart Agricultural Research Services, Inc., Primera Analytical Solutions Corporation, and University of Idaho, Cooperative Extension. 274p. MRID No. 49686046/PMRA No. 2627114.	Yes	Yes	Orange Processing Study

MRID/ Accession No.	OCSPP Guideline No.	Title	GLP	Suitable for Review	Comments
49689047	860.1520	Hummel, R. (2016) Evaluation of Processed Food/Feed (PF) Residues of BAS 440 I in Apple: Final Report. Project Number: 394754, S14/04778, 2015/7000096. Unpublished study prepared by Landis International, Inc., Eurofins Agrosience Services, Inc., ACDS Research, Research 2000, and Qualls Agricultural laboratory. 261p. MRID No. 49689047/PMRA No. 2627961.	Yes	Yes	Apple Processing Study
49689048	860.1520	Hummel, R. (2016) Evaluation of Processed Food/Feed (PF) Residues of BAS 440 I in Plums: Final Report. Project Number: 394697, S14/04777, 2015/7000091. Unpublished study prepared by Landis International, Inc., Eurofins Agrosience Services, Inc., ACDS Research, Qualls Agricultural laboratory, and Research for Hire. 220p. MRID No. 49689048/PMRA No. 2627960.	Yes	Yes	Plum Processing Study
49689049	860.1520	Csinos, A. (2016) Magnitude of the Residues of BAS 440 I in Cotton Processed Fractions Following Applications of BAS 440 00 IDC: Final Report. Project Number: 394669, S14/01620, 2014/7003954. Unpublished study prepared by Eurofins Agrosience Services, Inc. 226p. MRID No. 49689049/PMRA No. 2627110.	Yes	Yes	Cotton Processing Study
49689050	860.1850	Funk, D.; Doebbe, A. (2015) Confined Rotational Crop Study with (Carbon 14) BAS 440 I: Final Report. Project Number: 2015/1020129, 2013/1395580. Unpublished Study prepared by BASF SE. 267p. MRID No. 49689050/PMRA No. 2627963.	Yes	Yes	
49689051	860.1850	Rabe, U.; Bogen, C. (2016) Confined Rotational Crop Study with (Carbon 14) BAS 440 I: Final Report. Project Number: 2015/1231132, 743798, 2015/1231131. Unpublished Study prepared by BASF SE. 267p. MRID No. 49689051/PMRA No. 2627965.	Yes	Yes	--
49689052	860.1850	Rabe, U.; Possienke, M. (2016) Confined Rotational Crop Study with (Carbon 14)-BAS 440 I: Final Report. Project Number: 743662, 2015/1231131, 2013/1395580. Unpublished Study prepared by BASF SE. 108p. MRID No. 49689052/PMRA No. 2627964.	Yes	Yes	--
49689133	860.1900	Panek, M. (2016) Afidopyropen (BAS 440 I) Request to Waive Requirement for Field Accumulation in Rotational Crops. Project Number: 2016/7002060, 2015/1020129, 2015/1231131. Unpublished study prepared by BASF Corporation. 7p. MRID No. 49689133/PMRA No. 2627966.	NA	Yes	Request to waive Field Accumulation Studies