COMMISSION DU CODEX ALIMENTARIUS

Organisation des Nations Unies pour l'alimentation et l'agriculture

Organisation mondiale de la Santé

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Point 6 de l'ordre du jour **CX/PR 21/52/5-Add.1**
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PROGRAMME CONJOINT FAO/OMS SUR LES NORMES ALIMENTAIRES

COMITÉ DU CODEX SUR LES RÉSIDUS DE PESTICIDES

Cinquante-deuxième session
(en ligne)
26-30 juillet et 3 août 2021

LIMITES MAXIMALES PROPOSEES DE RÉSIDUS POUR LES PESTICIDES DANS L'ALIMENTATION HUMAINE ET DANS L'ALIMENTATION ANIMALE

Commentaires à l'étape 3 en réponse à la lettre circulaire CL 2020/6-PR soumise par l'Australie, le Brésil, le Canada, le Chili, l'Égypte, Union européenne
et les États-Unis d'Amérique.

Étapes de la procédure CCPR-Codex

Étape 1	Recommandation des composés prioritaires par le CCPR, avec la participation du groupe de travail *ad hoc* sur les priorités.
Étape 2	Première évaluation du composé par la réunion conjointe FAO/OMS sur les résidus de pesticides ; estimation d'une DJA et de LMR (projets de LMR ou LMR Codex proposées).
Étape 3	Soumission des LMR Codex proposées aux gouvernements pour une première série de commentaires.
Étape 4	Première discussion des LMR proposées par le CCPR à la lumière des commentaires reçus
Étape 5	Soumission des LMR Codex proposées à la Commission du Codex Alimentarius à la lumière de la discussion du CCPR, pour examen.
Étape 6	Soumission des LMR Codex proposées aux gouvernements pour une deuxième série de commentaires
Étape 7	Discussion finale des LMR Codex proposées par le CCPR à la lumière des commentaires reçus
Étape 8	Examen par la CAC en vue de l'adoption de la proposition en tant que LMR Codex (CXL)
Étape 5/8	La LMR Codex proposée est soumise à la Commission à l'étape 5 ; comme il ne semble pas y avoir de controverse et qu'il n'est pas nécessaire de poursuivre la discussion aux étapes 6 et 7, l'omission de ces étapes est recommandée à la Commission.

La partie I du document contient des commentaires sur les LMR à examiner par le CCPR52.

La partie II de ce document contient des formulaires de notification de réserve à examiner par le CCPR52.

PARTIE I : COMMENTAIRES SUR LES LMR

COMMENTAIRES GÉNÉRAUX

Chili

Le Chili soutient toutes les recommandations faites par la JMPR, en tant qu'organe consultatif scientifique de ce Comité du Codex, et donc l'avancement de l'étape correspondante pour leur adoption rapide.

Justification : Il est important que le Codex avance dans l'étude et la détermination des LMR des substances actives qui sont largement utilisées.

Égypte

L'Égypte approuve les avant-projets de LMR qui correspondent à l'étape 3 de la procédure du Codex, tels que proposés par les réunions extraordinaire et ordinaire de la JMPR 2019.

Union européenne

L'UE souhaite **faire remarquer** que les LMR ainsi que les positions actuelles pour le thiabendazole, le tébuconazole et le metconazole pourraient être révisées à l'avenir, en attendant une évaluation des métabolites dérivés du triazole dans l'UE.

Une stratégie d'évaluation des métabolites dérivés du triazole a récemment été adoptée dans l'UE et est applicable depuis septembre 2019. Des valeurs toxicologiques de référence ont été approuvées pour ces métabolites.

OBSERVATIONS SPÉCIFIQUES

Diméthoate (027)

Australie

L'Australie note que les données n'ont pas permis d'établir une définition du résidu pour l'évaluation du risque alimentaire. L'Australie suggère que le CCPR demande conseil au fabricant afin de déterminer si de nouvelles données seront soumises pour résoudre les problèmes toxicologiques.

Canada

Le Canada reconnaît la recommandation de la JMPR de retirer toutes les LMR en l'absence de données pour l'ométhoate, le principal métabolite. Le diméthoate a été récemment réévalué par le Canada. Voir PRVD2011-12 et RVD2015-04 pour plus de détails.

Égypte

L'Égypte n'est pas d'accord pour retirer la limite maximale de résidus précédemment établie pour le "Diméthoate (027)" dans (Blé) et propose de maintenir la limite fixée (0,05 mg/kg).

Ométhoate (055)

Australie

L'Australie note que les CXL actuelles pour l'ométhoate sur les épices sont basées sur les résidus de l'utilisation du diméthoate. Si le fabricant ne s'engage pas à fournir de nouvelles données pour résoudre les problèmes toxicologiques du diméthoate, l'Australie soutient le retrait des LMR pour l'ométhoate sur les épices.

Thiabendazole (065)

Australie

L'Australie soutient l'avancement des LMR à l'étape 5/8.

Canada

Le Canada soutient les LMR recommandées par la JMPR pour les nouvelles utilisations sur les légumes secs et les légumes légumineuses.

Union européenne

L'UE émet une **réserve quant à l'avancement de l'**avant-projet de LMR pour les produits suivants, en attendant le résultat des demandes de tolérance à l'importation en cours dans l'UE :

- **Mangue**
- **Patate douce**

L'UE **note** que pour les haricots avec gousses, la description du produit liée au code VP 2060 devrait être corrigée (pour inclure le suffixe "(comprend tous les produits de ce sous-groupe)".

Carbendazime (072)

Australie

L'Australie soutient l'avancement à l'étape 5/8 pour les LMR du carbendazime sur les épices (graines).

Union européenne

L'UE émet une **réserve quant à l'avancement des** avant-projets de LMR pour les produits suivants, dans l'attente des résultats d'une évaluation en cours du bénomyl, du carbendazime et du thiophanate-méthyl dans l'UE :

- **Épices, graines, Sous-groupe de**

En outre, l'UE invite à clarifier le statut du bénomyl, du carbendazime et du thiophanate-méthyl, tel qu'il est décrit dans le formulaire de notification de réserve soumis par l'UE.

Chlorothalonil (081)

Australie

L'Australie soutient l'avancement de la LMR à l'étape 5/8.

Canada

Le Canada n'a aucune objection à la LMR recommandée par la JMPR pour la nouvelle utilisation de la canneberge. Le chlorothalonil a récemment été réévalué au Canada. Voir PRVD2011-14 et RVD2018-11 pour plus de détails.

Union européenne

L'UE émet une **réserve quant à l'avancement** de l'avant-projet de LMR pour les produits suivants :

-Cranberry

Dans une évaluation récente de l'UE, un problème de génotoxicité n'a pu être exclu pour les résidus auxquels les consommateurs seront exposés. En l'absence de valeurs toxicologiques de référence de l'UE pour le métabolite SDS-3701 (R182281), même une évaluation indicative des risques pour le consommateur utilisant des définitions préliminaires des résidus n'a pu être réalisée.

Iprodione (111)

Union européenne

L'UE a identifié une préoccupation concernant la sécurité des résidus d'iprodione. L'UE remercie la JMPR pour son examen de la préoccupation de l'UE et soutient la forte recommandation de la JMPR que l'iprodione soit prioritaire pour une réévaluation périodique.

Cyperméthrine (118)

Australie

L'Australie soutient l'avancement de la LMR à l'étape 5/8.

Canada

Le Canada n'a pas d'objection aux LMR recommandées par la JMPR. Le cyperméthrine a été récemment réévalué par le Canada. Voir PRVD2016-18 et RVD2018-22 pour plus de détails.

Union européenne

L'UE émet une **réserve quant à l'avancement de l'**avant-projet de LMR pour les produits suivants, en attendant le résultat de la réévaluation périodique en cours dans l'UE :

- **Ginseng, séché, y compris le ginseng rouge**

Diflubenzuron (130)

Union européenne

L'UE a identifié une préoccupation concernant un métabolite végétal du diflubenzuron, la 4-chloroaniline. L'UE prend note de l'évaluation récemment menée par le JECFA.

Méthoprène (147)

Australie

L'Australie soutient l'avancement des LMR à l'étape 5/8.

Canada

Le Canada n'a aucune objection à la LMR recommandée par la JMPR pour la nouvelle utilisation sur les arachides.

Union européenne

L'UE émet une **réserve quant à l'avancement** de l'avant-projet de LMR pour les produits suivants :

- **Cacahuète, entière**

Un risque chronique pour les consommateurs européens n'a pu être exclu. Compte tenu de l'exposition de fond significative résultant des LMR européennes existantes, il n'y a pas de possibilité d'augmenter les LMR. Il est possible d'affiner le calcul de l'exposition chronique, mais les données pertinentes n'ont pas encore été évaluées dans l'UE.

Les études portant sur le comportement métabolique après le traitement post-récolte et sur la nature et l'ampleur des résidus dans les produits transformés font défaut.

Glyphosate (158)

Australie

L'Australie soutient l'avancement des LMR à l'étape 5/8.

Canada

Le Canada n'a pas d'objection aux LMR recommandées par la JMPR pour les nouvelles utilisations. Le glyphosate a récemment fait l'objet d'une évaluation électronique au Canada. Voir PRVD2015-01 et RVD2017-01 pour plus de détails.

Union européenne

L'UE émet une **réserve quant à l'avancement** de l'avant-projet de LMR pour les produits suivants, en attendant le résultat de la réévaluation périodique en cours dans l'UE :

- **Haricots secs, sous-groupe de (sauf soja)**
- **Pois secs, sous-groupe de**

Propiconazole (160)

Australie

L'Australie soutient l'avancement des LMR à l'étape 5/8.

Canada

Le Canada n'a aucune objection à la LMR recommandée par la JMPR pour le sous-groupe des pêches.

Union européenne

L'UE émet une **réserve quant à l'avancement de l'**avant-projet de LMR pour les produits suivants :

- **Pêche**

Suite à une évaluation récente de l'UE, la substance active n'a pas été approuvée dans l'UE. Dans ce cadre, l'évaluation du risque pour le consommateur n'a pas pu être finalisée en raison de lacunes dans les données, et aucune conclusion n'a pu être tirée sur la génotoxicité et la toxicité générale de plusieurs métabolites.

En ce qui concerne spécifiquement les pêches, un risque aigu pour les consommateurs européens a été identifié. En outre, la LMR proposée par le Codex n'est pas acceptable car le nombre d'essais sur les résidus est insuffisant selon le document d'information sur l'application des directives visant à faciliter l'établissement de LMR pour les pesticides destinés aux cultures mineures (mentionné à l'annexe D des Principes d'analyse des risques appliqués par le Comité du Codex sur les résidus de pesticides, Manuel de procédure du Codex).

Buprofézine (173)

Australie

L'Australie soutient l'avancement des LMR à l'étape 5/8.

Canada

Le Canada n'a pas d'objection à la DJA et à la DARf recommandées par la JMPR pour le métabolite de l'aniline et aux LMR recommandées par la JMPR pour la buprofézine dans les différentes nouvelles utilisations.

Union européenne

L'UE émet une **réserve quant à l'avancement** de l'avant-projet de LMR pour les produits suivants :

- **Groupe de fruits à coque**
- **Œufs**
- **Graisses de mammifères, à l'exception des graisses du lait**
- **Volaille, abats comestibles de**
- **Graisses de volaille**
- **Viande de volaille**

L'UE a identifié une préoccupation concernant le potentiel de formation d'aniline à partir de résidus de buprofézine dans les produits soumis à une transformation. L'UE remercie la JMPR pour son examen de la préoccupation de l'UE et note que la JMPR a pris en considération de nouvelles données y compris une nouvelle étude de génotoxicité in vivo sur l'aniline non encore évaluée dans l'UE.

L'UE note que la JMPR a dérivé une proposition de LMR Codex pour l'huile d'olive brute, bien qu'aucune proposition de LMR ne soit faite pour les olives non transformées destinées à la production d'huile (SO 0305). L'UE comprend qu'une LMR Codex pour le produit agricole brut correspondant doit être établie avant qu'une LMR Codex pour un produit transformé puisse être fixée. Toutefois, la préoccupation concernant le potentiel de formation d'aniline à partir de résidus de buprofézine reste valable ~~pour le produit agricole brut que sont les olives destinées à la production d'huile.~~

Bifenthrine (178)

Australie

L'Australie note que la JMPR a identifié un risque d'exposition aiguë associé à la fraise et ne soutient pas l'avancement de cette LMR. L'Australie soutient l'avancement de la LMR pour la paille et le fourrage sec de céréales à l'étape 5/8.

Brésil

Le Brésil souhaite informer que l'Agence brésilienne de réglementation de la santé (ANVISA) a réalisé une évaluation du risque alimentaire à court terme pour les composés et les produits signalés dans la lettre circulaire CL 2020/06-PR.

La méthodologie d'évaluation des risques était basée sur les directives de l'OMS/FAO. La consommation alimentaire individuelle et le poids corporel des personnes âgées de plus de 10 ans ont été établis sur la base du rapport d'enquête sur le budget des ménages brésiliens publié en 2009.

D'après les résultats de l'évaluation du risque alimentaire à court terme, le Brésil est préoccupé par la LMR proposée pour les fraises sur le composé Bifenthrine (178). Dans ce cas, l'exposition alimentaire aiguë aux résidus lors de la consommation de fraises présente un problème de santé publique pour les consommateurs brésiliens. Il convient de mentionner que l'ANVISA a considéré que 0,01 mg/kg pc était la DARf.

Canada

Le Canada reconnaît le risque alimentaire aigu préoccupant identifié par la JMPR en raison de l'exposition aux résidus de bifenthrine dans les fraises.

Union européenne

L'UE **s'oppose à l'avancement** de l'avant-projet de LMR pour les produits suivants :

- **Fraise**

La JMPR a conclu que l'exposition alimentaire aiguë estimée aux résidus de bifenthrine pour la consommation de fraises peut présenter un problème de santé publique.

L'UE **note que** :

Pour les fraises, la CXL de 1 mg/kg, adoptée en 1995, peut également poser un problème de santé publique. Par conséquent, l'UE considère que la CXL existante pour les fraises devrait être révoquée.

Pour le céleri et la laitue, les LMR proposées ont été retenues à l'étape 4 par le CCPR 2016 selon la règle des quatre ans. Aucune donnée supplémentaire n'ayant été soumise, l'UE considère que les projets de LMR proposés pour le céleri et la laitue doivent être retirés.

Cléthodime (187)

Australie

L'Australie note que les données n'ont pas permis d'établir une définition du résidu pour l'évaluation du risque alimentaire. L'Australie suggère que le CCPR demande conseil au fabricant afin de déterminer si de nouvelles données seront soumises pour résoudre les problèmes toxicologiques.

Canada

La cléthodime a récemment été réévalué par le Canada. Voir PRVD2016-11 et RVD2017-10 pour plus de détails.

Bien que le Canada n'ait pas d'objection à la DJA recommandée par la JMPR, il est préoccupé par le retrait de la limite maximale de résidus pour le colza/canola en raison du nombre insuffisant d'essais sur le terrain réalisés conformément au GGAP.

Le Canada demande respectueusement que la CXL existante soit maintenue pour une période maximale de quatre ans en attendant qu'un titulaire s'engage à effectuer des essais supplémentaires sur le colza/canola. Si cet engagement n'est pas respecté avant la CCPR52, le Canada retirera sa demande.

Tébuconazole (189)

Australie

L'Australie soutient l'avancement des LMR à l'étape 5/8.

Canada

Le Canada n'a aucune objection aux LMR recommandées par la JMPR pour les différentes cultures d'agrumes.

Union européenne

L'UE émet une **réserve quant à l'avancement** de l'avant-projet de LMR pour les produits suivants, en attendant le résultat de la réévaluation périodique en cours dans l'UE :

- **Mandarines (y compris les hybrides de type mandarine) Sous-groupe de**
- **Oranges, sucrées, acides, sous-groupe de**

Tolclofos-méthyle (191)

Australie

L'Australie soutient l'avancement de la LMR à l'étape 5/8.

Canada

Le Canada n'a aucune objection à la DJA et aux LMR recommandées par la JMPR. Le tolclofos-méthyle n'est pas enregistré pour une utilisation au Canada et aucune LMR d'importation n'a été établie.

Union européenne

L'UE émet une **réserve quant à l'avancement de l'**avant-projet de LMR pour les produits suivants :

- **Pommes de terre**

Un risque aigu a été identifié pour les consommateurs européens. L'UE a fixé une dose de référence aiguë, basée sur une étude de 9 mois chez la souris et un facteur d'incertitude de 100.

Kresoxim-méthyle (199)

Australie

L'Australie soutient l'avancement des LMR à l'étape 5/8.

Canada

Le Canada n'a pas d'objection aux LMR recommandées par la JMPR.

Pyriproxyfène (200)

Australie

L'Australie soutient l'avancement des LMR à l'étape 5/8.

Cyprodinile (207)

Australie

L'Australie soutient l'avancement de la LMR à l'étape 5/8.

Canada

Le Canada n'a aucune objection à la LMR recommandée par la JMPR pour la nouvelle utilisation du soja (sec).

Union européenne

- **Fève de soja (sèche)**

L'UE **note** que l'approche adoptée par la JMPR n'est pas conforme au point 4 de l'annexe C des Principes d'analyse des risques appliqués par le Comité du Codex sur les résidus de pesticides (Commission du Codex Alimentarius, Manuel de procédure). L'approche de la proportionnalité a été appliquée en dépit d'un écart de plus d'un paramètre par rapport aux BPAc.

Pyraclostrobine (210)

Australie

L'Australie soutient l'avancement de la LMR à l'étape 5/8

Boscalide (221)

Australie

L'Australie soutient l'avancement des LMR à l'étape 5/8.

Canada

Le Canada n'a pas d'objection aux LMR recommandées par la JMPR pour les nouvelles utilisations.

Union européenne

L'UE émet une **réserve quant à l'avancement de l'**avant-projet de LMR pour les produits suivants :

- **Fruits à pépins (sous-groupe)**

Le calculateur de LMR de l'OCDE donne une LMR inférieure de 1,5 mg/kg.

Azoxystrobine (229)

Australie

L'Australie soutient l'avancement des LMR à l'étape 5/8.

Canada

Le Canada n'a aucune objection à la LMR recommandée par la JMPR pour la nouvelle utilisation sur le goyavier.

Chlorantraniliprole (230)

Australie

L'Australie soutient l'avancement des LMR à l'étape 5/8.

Canada

Le Canada reconnaît que les LMR recommandées pour les nouveaux sous-groupes de pois secs et de haricots sont inférieures à la LMR canadienne pour les légumes légumineux, selon des données d'essais sur le terrain différentes.

Union européenne

- Fruit du palmier (palmier à huile africain)

L'**UE note** que, conformément au document d'information sur l'application de la directive visant à faciliter l'établissement de LMR de pesticides pour les cultures mineures (mentionné à l'annexe D des Principes d'analyse des risques appliqués par le Comité du Codex sur les résidus de pesticides, Manuel de procédure du Codex), le fruit (huile) de palmier est une culture majeure. L'UE estime que l'établissement de LMR Codex pour les amandes et les fruits de palmier devrait faire l'objet de discussions plus approfondies.

Spirotetramat (234)

Australie

L'Australie soutient l'avancement des LMR à l'étape 5/8.

Canada

Le Canada reconnaît que les LMR recommandées par la JMPR sont inférieures aux LMR canadiennes pour les mêmes cultures, sur la base de définitions de résidus différentes pour la mise en application.

Métaflumizone (236)

Australie

L'Australie soutient l'avancement des LMR à l'étape 5/8.

Canada

Le Canada n'a pas d'objection aux LMR recommandées par la JMPR pour les nouvelles utilisations. La métaflumizone n'est pas enregistrée pour une utilisation au Canada, et aucune LMR d'importation n'a été établie.

Union européenne

L'UE émet une **réserve quant à l'avancement de l'**avant-projet de LMR pour les produits suivants :

- **Raisin**

Pour le raisin, un risque aigu a été identifié pour les consommateurs européens. L'UE a fixé une dose de référence aiguë (ARfD) basée sur la réduction de la prise de poids corporel observée dans une étude de développement chez le rat.

Dicamba (240)

Australie

L'Australie soutient l'avancement des LMR à l'étape 5/8.

Canada

Le Canada n'a pas d'objection aux LMR recommandées par la JMPR pour les nouvelles utilisations.

Union européenne

L'UE émet une **réserve quant à l'avancement de l'**avant-projet de LMR pour les produits suivants, dans l'attente des résultats de la réévaluation périodique en cours dans l'UE :

- **Graines de coton**
- **Maïs**
- **Fèves de soja**

L'UE **note** que pour les **coques** et la **farine de soja,** le facteur de transformation dérivé des BPA dans le soja tolérant au dicamba a été utilisé pour proposer des projets de LMR, qui reflètent les différentes utilisations dans les cultures conventionnelles.

Acétamipride (246)

Australie

L'Australie soutient l'avancement à l'étape 5/8 pour les LMR de l'acétamipride sur les épices (graines).

Penthiopyrad (253)

Australie

L'Australie soutient l'avancement des LMR à l'étape 5/8.

Canada

Le Canada n'a pas d'objection aux LMR recommandées par la JMPR pour les différentes cultures ou groupes de cultures de baies.

Union européenne

L'UE émet une **réserve quant à l'avancement de l'**avant-projet de LMR pour les produits suivants :

- **Baies de buisson, sous-groupe de**

- **Baies de canne, Sous-groupe de**

Dans l'UE, une définition de résidu distincte pour l'évaluation des risques s'applique au métabolite 1-méthyl-3-trifluorométhyl-1H-pyrazole-4-carboxamide (PAM). Les niveaux individuels de penthiopyrad et de PAM n'ont pas été rapportés séparément dans le rapport de la JMPR.

- **Baies de sureau**

Une extrapolation des myrtilles aux baies de sureau n'est pas prévue dans les règles d'extrapolation du Codex. L'UE comprend que la JMPR a dérivé l'avant-projet de CXL pour les baies de sureau sur la base de la portée de l'autorisation sous-jacente. Cependant, l'UE considère que l'extrapolation des myrtilles aux baies de sureau et à la rose guilder devrait être discutée par le groupe de travail électronique sur la classification afin de déterminer si une telle extrapolation est appropriée.

Fluxapyroxade (256)

Australie

L'Australie soutient l'avancement des LMR à l'étape 5/8.

Canada

Le Canada n'a pas d'objection aux LMR recommandées par la JMPR pour les sous-groupes de cultures d'agrumes.

Union européenne

L'UE **note** que l'extrapolation proposée des citrons aux mandarines n'est pas conforme aux règles d'extrapolation convenues du Codex.

Picoxystrobine (258)

Australie

L'Australie soutient l'avancement des LMR à l'étape 5/8.

Canada

Le Canada n'a aucune objection aux LMR recommandées par la JMPR pour les différentes cultures.

Union européenne

L'UE **émet une réserve** quant à l'avancement de l'avant-projet de LMR pour les produits suivants, en raison de plusieurs problèmes de santé identifiés dans l'examen par les pairs de l'EFSA, notamment la génotoxicité possible de la picoxystrobine et de ses principaux métabolites végétaux :

- **Grain de café**
- **Graine de coton**
- **Abats comestibles (Mammifères)**
- **Graisses de mammifères (sauf les graisses du lait)**
- **Viande (de mammifères autres que les mammifères marins)**
- **Laits**
- **Grain de sorgho**
- **Thé, vert, noir (noir, fermenté et séché)**

Benzovindiflupyr (261)

Australie

L'Australie soutient l'avancement de la LMR à l'étape 5/8.

Canada

Le Canada n'a aucune objection aux LMR recommandées par la JMPR pour les nouvelles utilisations de l'oignon bulbeux et de la canne à sucre.

Fluensulfone (265)

Australie

L'Australie soutient l'avancement des LMR à l'étape 5/8.

Canada

Le Canada n'a pas d'objection aux LMR recommandées par la JMPR pour les différentes cultures/groupes de cultures.

Union européenne

L'UE émet une **réserve quant à l'avancement des** avant-projets de LMR pour les produits suivants :

- **Orge, grains similaires et pseudo-céréales à enveloppe, Sous-groupe de**
- **Agrumes, Groupe des**
- **Grain de café**
- **Céréales de maïs, sous-groupe de**
- **Fruits à pépins, groupe de (sauf kaki du Japon)**
- **Céréales de riz, sous-groupe de**
- **Vigne à petits fruits grimpants, sous-groupe de**
- **Sorgho à grain et millet, Sous-groupe de**
- **Fruits à noyau, groupe de**
- **Canne à sucre**
- **Maïs doux, sous-groupe de**
- **Noix d'arbre, Groupe de**
- **Blé, céréales similaires et pseudo-céréales non décortiquées, Sous-groupe des**

Les études sur le métabolisme ne sont pas représentatives du comportement des résidus observé dans les essais sur les résidus. En outre, l'UE est d'avis que le potentiel génotoxique du MeS ne peut être exclu et que d'autres tests de génotoxicité seraient nécessaires pour donner suite aux résultats positifs obtenus in vitro.

Tolfenpyrade (269)

Australie

À l'exception des tomates et des aubergines pour lesquelles un problème d'exposition aiguë a été identifié par la JMPR, l'Australie soutient l'avancement de la LMR à l'étape 5/8.

Canada

Le Canada n'a aucune objection aux LMR recommandées par la JMPR pour les sous-groupes de cultures d'agrumes et de légumes-fruits et les produits animaux.

Union européenne

L'UE émet une **réserve quant à l'avancement** de l'avant-projet de LMR pour les produits suivants, en attendant le résultat des demandes de tolérance à l'importation en cours dans l'UE :

- **Abats comestibles (mammifères)**
- **Œufs**
- **Citrons et limes, Sous-groupe de**
- **Graisses de mammifères, à l'exception des graisses du lait**
- **Mandarines, sous-groupe de**
- **Viande (de mammifères autres que les mammifères marins)**
- **Laits**
- **Oranges, douces, amères, sous-groupe de**
- **Poivrons, sous-groupe de (sauf gombo, martynia et roselle)**
- **Pomelo et pamplemousses, Sous-groupe de**
- **Volaille, abats comestibles de**
- **Graisses de volaille**
- **Viande de volaille**

Pour les mandarines, les oranges et les poivrons, sur la base des valeurs toxicologiques de référence dérivées par la JMPR, un risque aigu pour les consommateurs européens a été identifié.

L'UE **s'oppose à l'avancement de l'**avant-projet de LMR pour les produits suivants :

- **Aubergines, sous-groupe des**
- **Tomates, sous-groupe de**

La JMPR a conclu que l'exposition alimentaire aiguë estimée aux résidus de tolfenpyrade pour la consommation de tomates et d'aubergines peut présenter un problème de santé publique.

Mésotrione (277)

Australie

L'Australie soutient l'avancement des LMR à l'étape 5/8.

Canada

Le Canada n'a pas d'objection aux LMR recommandées par la JMPR pour les nouvelles utilisations sur les cultures de vergers.

Acétochlore (280)

Australie

L'Australie soutient l'avancement des LMR à l'étape 5/8.

Canada

Le Canada n'a pas d'objection aux LMR recommandées par la JMPR pour les nouvelles utilisations. L'acétochlore n'est pas enregistré pour une utilisation au Canada, et aucune LMR d'importation n'a été établie.

Union européenne

L'UE émet une **réserve quant à l'avancement** de l'avant-projet de LMR pour les produits suivants :

- **Abats comestibles (mammifères)**
- **Fève de soja (sèche)**

Les définitions des résidus d'application pour les produits végétaux et animaux dans l'UE diffèrent des définitions appliquées par la JMPR.

Flonicamide (282)

Australie

L'Australie soutient l'avancement des LMR à l'étape 5/8.

Canada

Le Canada n'a pas d'objection aux LMR recommandées par la JMPR pour les nouvelles utilisations.

Union européenne

L'UE émet une **réserve quant à l'avancement** de l'avant-projet de LMR pour les produits suivants :

- **Citrons et Limes (sous-groupe)**
- **Oranges, douces, amères (sous-groupe)**
- **Pomelo et pamplemousse (y compris les hybrides de type Shaddock) (sous-groupe)**

La définition des résidus d'application de la loi pour les produits végétaux dans l'UE diffère de la définition appliquée par la JMPR.

Pour les oranges, un risque aigu a été identifié pour les consommateurs européens. L'UE a fixé une DAR basée sur une étude du développement des lapins.

Fluazifop-p-butyl (283)

Australie

L'Australie note que la décision du CCPR 2017 de retirer les projets de LMR pour la patate douce et l'igname a résolu le problème d'exposition alimentaire à long terme.

L'Australie soutient l'avancement de la LMR à l'étape 5/8.

Canada

Le Canada n'a pas d'objection aux LMR recommandées par la JMPR pour les différentes cultures ou groupes de cultures de baies.

Union européenne

L'UE émet une **réserve quant à l'avancement de l'**avant-projet de LMR pour les produits suivants :

- **Baies de sureau**

Une extrapolation des myrtilles aux baies de sureau n'est pas prévue dans les règles d'extrapolation du Codex. L'UE comprend que la JMPR a dérivé l'avant-projet de CXL pour les baies de sureau sur la base de la portée de l'autorisation sous-jacente. Cependant, l'UE considère que l'extrapolation des myrtilles aux baies de sureau et à la rose guilder devrait être discutée par le groupe de travail électronique sur la classification afin de déterminer si une telle extrapolation est appropriée.

- **Fraise**

Un risque aigu pour les consommateurs européens a été identifié.

En outre, un risque chronique a été identifié pour les consommateurs européens, les fraises étant le principal contributeur parmi les cultures considérées.

Flupyradifurone (285)

Australie

L'Australie soutient l'avancement des LMR à l'étape 5/8.

Canada

Le Canada n'a pas d'objection aux LMR recommandées par la JMPR pour les nouvelles utilisations.

Isofétamide (290)

Australie

L'Australie soutient l'avancement des LMR à l'étape 5/8.

Canada

Le Canada reconnaît que les LMR recommandées par la JMPR sont inférieures aux LMR canadiennes pour les mêmes cultures, en raison de définitions de résidus différentes pour l'application et la mise à l'échelle des résidus effectuée par la JMPR.

Pendiméthaline (292)

Australie

L'Australie soutient l'avancement des LMR à l'étape 5/8.

Canada

Le Canada n'a pas d'objection aux LMR recommandées par la JMPR pour les nouvelles utilisations sur les différents sous-groupes de baies de canne et de buisson, y compris les fraises.

Cyclaniliprole (296)

Canada

Le Canada soutient les LMR recommandées par la JMPR.

Union européenne

L'UE émet une **réserve quant à l'avancement de l'**avant-projet de LMR pour les produits suivants :

- **Amandes**
- **Baies de buisson, sous-groupe de**
- **Choux, tête**
- **Baies de canne, Sous-groupe de**
- **Cerises, sous-groupe des**
- **Agrumes, Groupe des**
- **Concombres et courges d'été, Sous-groupe des**
- **Œufs**
- **Aubergines, sous-groupe des**
- **Brassicas à tête fleurie, sous-groupe de**
- **Raisins**
- **Feuilles de Brassicacées, sous-groupe de,**
- **Baies à faible croissance, sous-groupe des (sauf canneberges)**
- **Melons, citrouilles et courges d'hiver, Sous-groupe de**
- **Pêches (y compris les abricots et les nectarines), Sous-groupe des**
- **Poivrons, sous-groupe des (sauf Martynia, Okra et Roselle)**
- **Prunes, sous-groupe de**
- **Fruits à pépins, groupe de (à l'exception des kakis japonais)**

- **Thé, vert, noir (noir, fermenté et séché)**
- **Tomates, sous-groupe de**
- **Légumes-tubercules et légumes-maïs, Sous-groupe des**

Dans une évaluation récente de l'UE, l'évaluation des risques pour le consommateur n'a pas pu être finalisée en raison de lacunes dans les données, et aucune conclusion n'a pu être tirée sur la génotoxicité et la toxicité générale de plusieurs métabolites.

L'UE note que pour le sous-groupe des feuilles de Brassicaceae ~~et du thé~~, les LMR proposées par le Codex ne sont pas acceptables car le nombre d'essais sur les résidus est insuffisant.

Fénazaquin (297)

Australie

L'Australie soutient l'avancement des LMR à l'étape 5/8.

Canada

Le Canada n'a pas d'objection aux LMR recommandées par la JMPR pour les nouvelles utilisations. Le Fénazaquin est en cours de révision au Canada pour soutenir un enregistrement national.

Fosétyl-Al (302)

Australie

L'Australie soutient l'avancement des LMR à l'étape 5/8.

Canada

Le Canada n'a pas d'objection aux LMR recommandées par la JMPR pour les nouvelles utilisations. Le fosétyl-aluminium a récemment été réévalué au Canada. Voir PRVD2017-19 et RVD2019-08 pour plus de détails.

Union européenne

L'UE émet une **réserve quant à l'avancement** de l'avant-projet de LMR pour les produits suivants :

- **Grains de café**

Conformément au document d'information sur l'application de la directive visant à faciliter l'établissement de LMR pour les pesticides destinés aux cultures mineures (mentionné à l'annexe D des Principes d'analyse des risques appliqués par le Comité du Codex sur les résidus de pesticides, Manuel de procédure du Codex), les grains de café sont une culture majeure. Par conséquent, le nombre d'essais de résidus soumis est insuffisant.

Mandestrobine (307)

Australie

L'Australie soutient l'avancement des LMR à l'étape 5/8.

Canada

Le Canada n'a aucune objection à la DJA et à la DAR recommandée par la JMPR mais reconnaît que la LMR recommandée par la JMPR pour le colza est inférieure à la LMR canadienne basée sur une interprétation différente des données de résidus. Le Canada a reçu une demande du sponsor pour réévaluer sa LMR afin de l'aligner sur celle recommandée par la JMPR.

Union européenne

L'UE émet une **réserve quant à l'avancement** de l'avant-projet de LMR pour les produits suivants :

- **Graines de colza**

Dans l'UE, une définition différente des résidus pour l'évaluation des risques s'applique, qui inclut également les métabolites De-Xy-S-2200, 4-OH-S-2200 conjugué, et 2-CH2OH-S-2200 conjugué. Un facteur de conversion pour recalculer les résidus selon la définition de résidu pour la surveillance à la définition de résidu de l'UE pour l'évaluation des risques n'est pas disponible pour les graines de colza.

Pydiflumetofèn (309)

Australie

À l'exception des légumes verts à feuilles pour lesquels un problème d'exposition aiguë a été identifié par la JMPR, l'Australie soutient l'avancement de la LMR à l'étape 5/8.

Canada

Le Canada reconnaît que plusieurs des LMR recommandées par la JMPR sont inférieures aux LMR canadiennes en raison de l'interprétation et de l'application différentes de l'absorption des résidus par le sol, comme le montrent les études d'accumulation en champ.

Union européenne

L'UE émet une **réserve quant à l'avancement** de l'avant-projet de LMR pour les produits suivants, dans l'attente du résultat de la procédure d'approbation en cours dans l'UE :

- **Orge, céréales similaires et pseudo-céréales à cosse, Sous-groupe des**
- **Légumes du genre Brassica (sauf légumes à feuilles du genre Brassica), Groupe de**
- **Graines de coton**
- **Haricots secs, sous-groupe de**
- **Pois secs, sous-groupe de**
- **Abats comestibles (Mammifères)**
- **Œufs**
- **Légumes-fruits, cucurbitacées, Groupe des**
- **Légumes-fruits, autres que les cucurbitacées, groupe de (sauf Martynia, Okra et Roselle)**
- **Feuilles de Brassicaceae, sous-groupe des**
- **Feuilles de légumes-racines et de légumes-tubercules, sous-groupe de (sauf feuilles de légumes-tubercules)**
- **Légumes-légumes, Groupe de**
- **Céréales de maïs, sous-groupe de**
- **Graisses de mammifères (sauf les graisses du lait)**
- **Viande (de mammifères autres que les mammifères marins)**
- **Laits**
- **Gombo**
- **Cacahuète**
- **Volaille, abats comestibles de**
- **Graisses de volaille**
- **Viande de volaille**
- **Céréales de riz, sous-groupe de**
- **Légumes-racines, sous-groupe des**
- **Graines oléagineuses à petites graines, Sous-groupe des**
- **Sorgho grain et Millet, sous-groupe du**
- **Tiges et pétioles, sous-groupe de**
- **Graines de tournesol, sous-groupe de**
- **Maïs doux, sous-groupe de**
- **Légumes-tubercules et légumes-cormes, Sous-groupe des**
- **Blé, céréales similaires et pseudo-céréales non décortiquées, Sous-groupe des**

L'UE note que pour le sous-groupe des tiges et des pétioles, un risque aigu pour les consommateurs européens a été identifié.

L'UE **s'oppose à l'avancement** de l'avant-projet de LMR pour les produits suivants :

- **Légumes-feuilles, sous-groupe de**

La JMPR a conclu que l'exposition alimentaire aiguë estimée aux résidus de pydiflumetofen pour la consommation de légumes verts à feuilles peut présenter un problème de santé publique. Un risque aigu pour le consommateur a été identifié pour les consommateurs européens.

Pyriofénone (310)

Australie

L'Australie soutient l'avancement de la LMR à l'étape 5/8.

Canada

Le Canada n'a aucune objection aux LMR recommandées par la JMPR pour les produits d'origine animale.

Afidopyropenz (312)

Australie

L'Australie soutient l'avancement de la LMR à l'étape 5/8.

Canada

Le Canada n'a aucune objection à la DJA, aux DARf et aux LMR recommandées par la JMPR. L'afidopyropen a été récemment enregistré au Canada. Voir PRD2018-15 et RVD2018-18 pour plus de détails.

Union européenne

L'UE émet une **réserve quant à l'avancement** de l'avant-projet de LMR pour les produits suivants, en attendant le résultat des demandes de tolérance à l'importation en cours dans l'UE :

- **Choux, tête**
- **Cerises, sous-groupe des**
- **Agrumes, groupe des**
- **Coriandre, feuilles**
- **Graines de coton**
- **Concombre**
- **Aneth, feuilles**
- **Abats comestibles (mammifères)**
- **Œufs**
- **Aubergines, sous-groupe des**
- **Brassicas à tête fleurie, sous-groupe de**
- **Légumes-fruits, cucurbitacées - melon, citrouilles et courges d'hiver, sous-groupe de**
- **Gingembre, rhizome (frais)**
- **Légumes-feuilles, sous-groupe de**
- **Feuilles de Brassicaceae, sous-groupe des**
- **Graisses de mammifères (sauf les graisses du lait)**
- **Viande (de mammifères autres que les mammifères marins)**
- **Laits**
- **Persil, feuilles**
- **Pêches, sous-groupe de**
- **Poivrons, sous-groupe de, à l'exclusion du gombo, de la martynie et de la roselle**
- **Fruits à pépins, groupe de, à l'exception du kaki**
- **Prunes, sous-groupe de**
- **Volaille, abats comestibles de**
- **Volaille, graisses**
- **Volaille, viande**
- **Fève de soja (sèche)**
- **Tige et pétioles, sous-groupe de**
- **Courge d'été**
- **Tomates, sous-groupe de**
- **Noix d'arbre, Groupe de**
- **Légumes-tubercules et légumes-cormes, Sous-groupe des**
- **Curcuma, racine (fraîche)**

L'UE note que :

Pour les feuilles de Brassicacée, sur la base des valeurs toxicologiques de référence dérivées par la JMPR, un risque aigu pour les consommateurs européens a été identifié.

Pour les feuilles de coriandre, d'aneth et de persil, la JMPR a considéré que les feuilles de moutarde étaient plus représentatives pour les herbes que la laitue à feuilles ou les épinards. Cependant, les règles d'extrapolations convenues (Annexe VIII de REP18/PR) spécifient que les essais sur le basilic, la menthe, la laitue à feuilles ou les épinards doivent être utilisés pour dériver une LMR pour les herbes. En considérant les essais de résidus dans la laitue et les épinards, une proposition de LMR inférieure de 2 mg/kg est dérivée.

Metconazole (313)

Australie

L'Australie soutient l'avancement des LMR à l'étape 5/8.

Canada

Le Canada n'a pas d'objection à la DJA et à la DARf recommandées par la JMPR mais reconnaît que les LMR recommandées par la JMPR pour le sous-groupe des pois secs et du soja sec sont inférieures à la LMR canadienne basée sur une approche différente du regroupement des cultures et de l'interprétation des données de résidus.

Union européenne

L'UE émet une **<u>réserve quant à l'avancement</u>** de l'avant-projet de LMR pour les produits suivants, en attendant le résultat de la réévaluation périodique en cours dans l'UE :

- **Banane**
- **Haricots à gousses (Phaseolus spp.) gousses immatures et graines succulentes)**
- **Myrtilles**
- **Cerises, sous-groupe des**
- **Graines de coton**
- **Haricots secs, sous-groupe de (sauf soja)**
- **Pois secs, sous-groupe de**
- **Abats comestibles (mammifères)**
- **Œufs**
- **Ail**
- **Maïs**
- **Graisses de mammifères (sauf les graisses du lait)**
- **Viande (de mammifères autres que les mammifères marins)**
- **Laits**
- **Oignon, bulbe**
- **Pêches, sous-groupe de**
- **Cacahuète**
- **Prunes, sous-groupe de**
- **Volaille, abats comestibles de**
- **Graisses de volaille**
- **Viande de volaille**
- **Graines de colza**
- **Fève de soja (sèche)**
- **Betterave sucrière**
- **Canne à sucre**
- **Graines de tournesol, sous-groupe de**
- **Maïs doux (maïs en épi)**
- **Noix d'arbre, Groupe de**
- **Légumes-tubercules et légumes-cormes, Sous-groupe des**

L'UE <u>note que</u> :

<u>Pour les pêches</u>, une LMR de 0,15 mg/kg est suffisante selon le calculateur de l'OCDE.

<u>Pour le maïs doux</u> (maïs en épi), l'astérisque doit être supprimé, car une LMR de 0,015 mg/kg est dérivée avec le calculateur de l'OCDE.

<u>Pour les prunes</u>, sous-groupe de, le nombre d'essais de résidus soumis est insuffisant. Conformément au document d'information sur l'application de la directive visant à faciliter l'établissement de LMR pour les pesticides destinés aux cultures mineures (mentionné à l'annexe D des Principes d'analyse des risques appliqués par le Comité du Codex sur les résidus de pesticides, Manuel de procédure du Codex), les prunes sont une culture majeure.

<u>Pour les cerises</u>, le tournesol et la betterave à sucre, moins d'essais de résidus ont été soumis à la JMPR qu'à l'UE pour les demandes de tolérance à l'importation pour les mêmes produits. L'UE considère que la JMPR doit fonder ses recommandations sur l'ensemble de données le plus complet possible, et que la soumission d'un ensemble de données réduit, intentionnellement ou non, n'est pas acceptable. L'UE appelle tous les sponsors à s'assurer que toutes les études disponibles sont soumises à la JMPR.

Pyflubumide (314)

Australie

L'Australie note que la JMPR a identifié un problème d'exposition aiguë pour la consommation de pommes et de thé. L'Australie ne soutient pas l'avancement des LMR.

Canada

Le Canada reconnaît le risque alimentaire aigu préoccupant lié à l'exposition aux résidus de pyflubumide dans les pommes et le thé. L'utilisation du pyflubumide n'est pas homologuée au Canada, et aucune LMR d'importation n'a été établie.

Union européenne

L'UE **s'oppose à l'avancement** de l'avant-projet de LMR pour les produits suivants :

- **Apple**
- **Thé, vert, noir (noir, fermenté et séché)**

La JMPR a conclu que l'exposition alimentaire aiguë estimée aux résidus de pyflubumide pour la consommation de pommes et de thé peut présenter un problème de santé publique.

L'UE **note** que l'utilisation dans les pommes déclencherait un calcul de la charge alimentaire pour le bétail et une évaluation des résidus dans les produits animaux, qui n'ont pas été signalés dans le rapport de la JMPR.

Pyridate (315)

Canada

Le Canada n'a pas d'objection aux LMR recommandées par la JMPR pour les nouvelles utilisations. Le pyridate est en cours de révision au Canada pour soutenir un enregistrement national.

Union européenne

L'UE note des différences dans les valeurs toxicologiques de référence dérivées de la JMPR. Les études choisies comme point de départ (étude multi-générationnelle et étude de toxicité sur le développement du rat) et l'application de l'UF (appliquée en raison de la gravité de l'effet) conduiraient à une VTR plus faible.

L'UE est d'accord avec les informations fournies par la JMPR considérant que la toxicité des métabolites pyridafol CL 9673-N-glucoside (pyridafol-N-glucoside) et pyridafol-O-méthyle (CL 9869) pourrait être couverte par la molécule mère.

Pyrifluquinazon (316)

Canada

Le Canada n'a pas d'objection à la DJA et aux DRf recommandées par la JMPR et reconnaît que la JMPR n'a pas pu recommander de LMR car la réunion n'a pas été en mesure de parvenir à une conclusion sur la définition du résidu pour l'évaluation des risques pour les produits d'origine animale. Le pyrifluquinazon n'est pas enregistré pour une utilisation au Canada, et aucune LMR d'importation n'a été établie.

Triflumuron (317)

Canada

Le Canada reconnaît que la JMPR n'a pas pu recommander de LMR car la réunion n'a pas été en mesure de parvenir à une conclusion sur la définition du résidu pour l'évaluation des risques. Le triflumuron n'est pas homologué pour une utilisation au Canada, et aucune LMR d'importation n'a été établie.

Valifenalate (318)

Australie

L'Australie soutient l'avancement de la LMR à l'étape 5/8.

Canada

Le Canada n'a aucune objection à la DJA et aux LMR recommandées par la JMPR. Le valifénalate n'est pas enregistré pour une utilisation au Canada, et aucune LMR d'importation n'a été établie.

PARTIE II : CLARIFICATION / FORMULAIRES POUR EXPRIMER DES PREOCCUPATIONS SUR LES LMR

Union européenne

FORMULAIRE POUR EXPRIMER DES PRÉOCCUPATIONS CONCERNANT L'AVANCEMENT D'UNE LMR OU DEMANDE DE CLARIFICATION DE PRÉOCCUPATIONS Bénomyl (69), Carbendazime (72) et Thiophanate-méthyl (77)

Soumis par : *Union européenne*			
Date : *Mars 2021*			
Pesticide/ Numéro de code du pesticide :	***Aliment(s) / Numéro(s) de code alimentaire***	***LMR (mg/kg)***	***Présent Étape***
Benomyl (69) Carbendazim (72) Thiophanate-méthyle (77)	*Tous les produits de base*	*Toutes les LMR*	*CXL*

S'agit-il d'une demande de clarification ?

Oui

Demande d'éclaircissement (énoncé précis de l'éclaircissement demandé)

Le bénomyl a été initialement évalué par la JMPR avant 1995 et révisé à quelques reprises pour la toxicologie et les résidus (dernière révision en 1998 pour les résidus ; en 1995 pour la toxicologie).

Le carbendazime a été initialement évalué par la JMPR avant 1973 et revu plusieurs fois pour la toxicologie et les résidus (dernière révision en 2005). Une révision périodique toxicologique a eu lieu en 1995 ; en 2005, seule une évaluation concernant une DAR a été faite.

Le thiophanate-méthyle a été initialement évalué par la JMPR en 1973 et revu plusieurs fois pour la toxicologie et les résidus (dernière révision périodique en 1998 pour les résidus ; en 2017 pour la toxicologie). La JMPR en 2017 a noté qu'elle n'avait reçu aucune information sur la toxicologie du carbendazime. La réunion n'a pas été en mesure de terminer son évaluation pour les résidus.

En 2003, il a été décidé de combiner les définitions des résidus pour le bénomyl, le carbendazime et le thiophanate-méthyle en "Somme du bénomyl, du carbendazime et du thiophanate-méthyle, exprimée en carbendazime". À ce moment-là, l'Allemagne a noté "que le bénomyl n'est plus soutenu dans l'UE et aux États-Unis, mais elle a également été informée que le bénomyl avait encore des utilisations en Australie. La délégation allemande a également souligné que la majorité des LMR provenaient de l'utilisation du bénomyl et qu'à son avis, toutes les LMR devraient être réexaminées". (ALINORM 03/24A).

En même temps, le bénomyl et le thiophanate-méthyl ont été transférés au tableau 1 "LISTE DES PESTICIDES DONT LES **LMRS(CXLS) OU GLS ONT ÉTÉ SUPPRIMÉS** PAR LA COMMISSION DU CODEX ALIMENTARIUS **ET POUR LESQUELS AUCUNE LMRS N'A ÉTÉ PROPOSÉE**" avec la **note "voir Carbendazime"** dans le document sur les PROJETS ET AVANT-PROJETS DE LIMITES MAXIMALES DE RÉSIDUS DANS LES DENRÉES ALIMENTAIRES ET LES ALIMENTS POUR ANIMAUX AUX ÉTAPES 7 ET 4. Ceci est trompeur en raison de l'intitulé du tableau mais correct puisque les **CXL n'ont pas encore été supprimées**. En conséquence, les **deux substances ne font plus partie du tableau 3 dans les listes prioritaires** !

L'UE souhaite obtenir des conseils sur les questions suivantes :

- Si les entrées du tableau 1 des PROJETS ET AVANT-PROJETS de LIMITES MAXIMALES DE RÉSIDUS DANS LES ALIMENTS ET LES ALIMENTS POUR ANIMAUX AUX ÉTAPES 7 ET 4 sont correctes, pourquoi avons-nous des qualificatifs pour le bénomyl et le thiophanate-méthyl dans la liste des CXL pour le carbendazime ?
- Dans le cas où les entrées du tableau 1 des PROJETS ET AVANT-PROJETS DE LIMITES MAXIMALES DE RÉSIDUS DANS LES DENRÉES ALIMENTAIRES ET LES ALIMENTS POUR ANIMAUX AUX ÉTAPES 7 ET 4 ne sont pas correctes, comment est-il possible d'effectuer une réévaluation périodique de la toxicologie et des résidus pour le bénomyl puisque la substance ne fait plus partie des listes prioritaires ? Comment a-t-il été possible d'effectuer une réévaluation périodique de la toxicologie pour le thiophanate-méthyle en 2017, car cette substance ne figure plus sur les listes prioritaires ?

Est-ce un problème ?

Oui

Est-ce une préoccupation constante ? Non
Préoccupation (déclaration spécifique de la raison de la préoccupation concernant l'avancement de la LMR proposée) Comme indiqué ci-dessus, il a été mentionné en 2003 que le bénomyl n'est plus autorisé dans l'UE et aux États-Unis. L'UE prend note du fait que l'évaluation toxicologique du thiophanate-méthyle n'a pu être finalisée en raison de l'absence d'une évaluation réelle de la toxicologie du carbendenzime. L'UE reconnaît que la révision périodique du carbendazime est prévue en 2022. Cette substance n'est plus approuvée dans l'UE depuis 2014. Il est également noté que jusqu'à présent, aucune information n'a été rendue disponible sur la manière dont les résultats de la réévaluation toxicologique du carbendazime s'intégreront dans l'examen toxicologique du thiophanate-méthyle et du bénomyl. Le processus de réévaluation du thiophanate-méthyle dans l'UE a pris fin en 2020, suite au retrait de la demande de renouvellement d'approbation par le demandeur. La substance n'est donc plus approuvée dans l'UE. Une réévaluation des propriétés toxicologiques et des LMR du carbendazime et du thiophanate-méthyle dans l'UE est en cours, en tenant compte des informations disponibles dans différents cadres juridiques et pour les deux substances. L'avis de l'Autorité européenne de sécurité des aliments devrait être publié au troisième trimestre de 2021.
Souhaitez-vous que cette préoccupation soit notée dans le rapport du CCPR ? Oui
Données/informations (description de chaque élément distinct de données/informations qui sera fourni au secrétaire compétent de la JMPR dans un délai d'un mois après la réunion du CCPR).

États-Unis d'Amérique

Cher Secrétariat du CCPR :

Les États-Unis apprécient l'opportunité qui leur est offerte et souhaitent fournir les commentaires suivants en réponse à la lettre circulaire CL 2020/6(REV2)-PR --Demande de commentaires sur les recommandations des réunions conjointes FAO/OMS de 2019 sur les résidus de pesticides (JMPR).

Commentaires spécifiques

Les Etats-Unis ont reçu un total de quatre formulaires de notification de réserve de la part de déclarants/sponsors de pesticides. Après un examen minutieux, nous pensons que trois d'entre eux étaient fondés et devraient être examinés plus avant par la JMPR. Conformément à la pratique, nous avons limité les formulaires de notification de réserve soumis à ceux qui traitent des questions techniques spécifiques et des corrections qui ont été soulevées à la délégation américaine par les promoteurs ; le simple fait d'être en désaccord avec une décision ou un jugement de la JMPR n'est pas une raison valable pour soumettre un formulaire de notification de réserve.

Compte tenu de ce qui précède et en réponse à la lettre circulaire CL 2020/6(REV2)-PR, les États-Unis soumettent les formulaires de notification de réserve suivants à l'examen du secrétariat de la JMPR:

1. Flensulfone-Pommes et jus d'agrumes (265)
2. Métaconazole-Blé (313)
3. Afidopyropen (312)

Nous espérons que les formulaires de notification de réserve fournissent suffisamment d'informations pour être pleinement pris en compte par le secrétariat de la JMPR et nous sommes ouverts à toute question de clarification avant la CCPR52. Si vous avez des questions ou des problèmes, n'hésitez pas à contacter directement le délégué américain David Miller (miller.davidj@epa.gov) et Aaron Niman (niman.aaron@epa.gov).

FORMULAIRE POUR EXPRIMER DES PRÉOCCUPATIONS CONCERNANT L'AVANCEMENT D'UNE LMR OU DEMANDE DE CLARIFICATION DE PRÉOCCUPATIONS
FLUENSULFONE
(265)

Soumis par :

Délégation américaine

Date :

28 février 2021

Pesticide/ Numéro de code du pesticide	**Produits de base/ Numéro de code de produit**	**LMR (mg/kg)**	**Étape actuelle**
Fluensulfone (265)	Fruits à pépins (FB 0272)	N/A	Nouvelles utilisations

S'agit-il d'une demande d'éclaircissement ? **Non**

Est-ce un problème ? **Oui**

S'agit-il d'une préoccupation constante ? **Non**

Préoccupation *(*déclaration *spécifique* de la raison de la préoccupation concernant l'avancement de la LMR proposée).

Cette préoccupation concerne la valeur de la LMR de 0,2 ppm proposée pour les fruits à pépins ainsi que les propositions de calcul des LMR/facteurs de transformation pour le jus d'orange/agrumes.

Demande d'éclaircissement *(*énoncé *précis de* l'éclaircissement demandé).

Souhaitez-vous que cette préoccupation soit notée dans le rapport du CCPR ? **Oui**

Données/Informations (Description de chaque élément distinct de données/informations qui est joint ou sera fourni au secrétaire compétent de la JMPR dans un délai d'un mois après la réunion du CCPR).

Fruits à pépins

Dans l'évaluation, les valeurs de résidus pour la poire dans l'étude de déclin étaient incorrectes (Hoi et Jones, 2016, R-35572, essai PR-WA). Au PHI de 128 jours, les résidus de BSA étaient de 0,138 et 0,140 mg/kg, ce qui donne une somme de fluensulfone + BSA exprimée en fluensulfone de 0,22 mg/kg au lieu de la valeur rapportée dans l'évaluation de la JMPR de <0,025 mg/kg.

En utilisant les valeurs corrigées ci-dessus, les données relatives aux pommes et aux poires seraient toujours considérées comme provenant de la même population et pourraient être combinées en un seul ensemble de données communes et utilisées pour calculer la LMR.

Pommes : < 0,025 (10), 0,028 (3), 0,031, 0,037 et 0,16 mg/kg (n = 16) ;

Poires : < 0,025 (4), 0,026, 0,11 0,17 et 0,22 mg/kg (n = 8).

En utilisant les valeurs corrigées ci-dessus, le calculateur de l'OCDE prévoit une LMR de 0,3 mg/kg de fluensulfone (résidus totaux). La HR et la STMR restent inchangées à 0 mg/kg de fluensulfone.

Jus d'agrumes

Les LMR pour le jus d'agrumes n'ont pas été calculées pour le jus d'orange car il n'y avait pas de niveaux détectables dans le RAC d'agrumes. Ceci est vrai pour le parent fluensulfone mais des résidus détectables du métabolite BSA étaient présents. Par conséquent, un facteur de transformation basé sur les résidus totaux dans les agrumes pourrait être calculé, mais la JMPR ne l'a pas fait. Avec un ensemble de données comparables, l'approche consistant à utiliser un facteur de transformation basé sur les résidus totaux a été adoptée par la JMPR lors du calcul des facteurs de transformation pour les fruits à pépins/jus de pomme. Deux facteurs de transformation ont été calculés dans les deux études de transformation effectuées pour le jus d'agrumes : 0,44 et 1,8 ; cependant, la valeur la plus élevée est très similaire à celle du jus de pomme (1,7) et devrait être considérée comme le facteur de transformation approprié pour calculer la LMR pour le jus d'agrumes/orange.

FORMULAIRE POUR EXPRIMER DES PRÉOCCUPATIONS CONCERNANT L'AVANCEMENT D'UNE LMR OU DEMANDE DE CLARIFICATION DES PRÉOCCUPATIONS
METCONAZOLE (313)

<table>
<tr><td colspan="4">Soumis par :
Délégation américaine au CCPR</td></tr>
<tr><td colspan="4">Date :
28 février 2021</td></tr>
<tr><td>Pesticide/
Numéro de code du pesticide</td><td>Produits de base/
Numéro de code de produit</td><td>LMR
(mg/kg)</td><td>Étape actuelle</td></tr>
<tr><td>Metconazole / 313</td><td>Blé / GC 0654</td><td>-</td><td>-</td></tr>
<tr><td colspan="4">S'agit-il d'une demande d'éclaircissement ?</td></tr>
<tr><td colspan="4">Est-ce un problème ?
Oui</td></tr>
<tr><td colspan="4">S'agit-il d'une préoccupation constante ?
Non</td></tr>
<tr><td colspan="4">Préoccupation (déclaration spécifique de la raison de la préoccupation concernant l'avancement de la LMR proposée).
La JMPR 2019 a conclu qu'aucune LMR ne pouvait être proposée pour le metconazole sur les grains de blé en raison du nombre insuffisant d'essais correspondant aux paramètres d'application de l'étiquette américaine (à moins de 25%).
Plus spécifiquement : La JMPR n'a pris en compte que les 4 essais de résidus dont le délai avant récolte (DAR) était supérieur à 21 jours, car ce sont les seuls qui ont été considérés comme se situant dans les 25% du DAR de 30 jours de l'étiquette, malgré le fait que la plupart des essais avaient des DAR de 20-22 jours. Toutefois, selon le manuel actuel de la FAO, les tolérances sur les paramètres d'application doivent être celles qui entraîneraient une variation de 25 % de la <u>concentration de résidus</u>, et non pas des variations de 25 % des <u>paramètres eux-mêmes</u>.
Il est demandé à la JMPR de réévaluer sa détermination qu'une LMR n'a pas pu être établie et de considérer les onze autres essais de blé américains avec un PHI de 20-22 jours. Ces essais doivent être pris en compte car le comportement de diminution des résidus pour les grains de blé entre les PHI 14 et 35/36 jours mesuré dans les deux essais de diminution démontre clairement que les essais de résidus avec PHI 20-22 jours résulteront en une déviation des résidus de moins de 25% par rapport au niveau de résidu attendu à un PHI 30 jours.</td></tr>
<tr><td colspan="4">Demande d'éclaircissement (énoncé précis de l'éclaircissement demandé).</td></tr>
<tr><td colspan="4">Souhaitez-vous que cette préoccupation soit notée dans le rapport du CCPR ?
Oui</td></tr>
<tr><td colspan="4">Données/Informations (Description de chaque élément distinct de données/informations qui est joint ou sera fourni au secrétaire compétent de la JMPR dans un délai d'un mois après la réunion du CCPR).
BASF a soumis à la JMPR 2019 des données de résidus et des étiquettes provenant d'essais américains sur les résidus de metconazole sur plusieurs céréales (blé, seigle, avoine, orge et maïs). La demande de LMR Codex dans ces céréales visait principalement à soutenir les producteurs américains. La BPA critique pour le blé, l'orge, l'avoine, le seigle et le triticale aux États-Unis autorise deux applications foliaires extérieures de metconazole à 112 g ai/ha chacune avec un intervalle de retraitement de 6 jours et un PHI de 30 jours. La tolérance américaine actuelle pour le metconazole sur le grain de blé est de 0,15 ppm (somme des isomères cis et trans) et est basée sur les données de résidus de blé incluses dans le dossier de la JMPR.
La JMPR 2019 a conclu qu'aucune limite maximale de résidus ne pouvait être proposée pour le metconazole sur le grain de blé, en raison d'un nombre insuffisant d'essais correspondant aux paramètres d'application de l'étiquette américaine (dans les 25%). Seuls les essais sur les résidus avec des délais avant récolte (DAR) supérieurs à 21 jours (4 essais) ont été considérés comme se situant dans les 25% du DAR de 30 jours de l'étiquette, malgré le fait que la plupart des essais avaient des DAR de 20-22 jours. Cependant,</td></tr>
</table>

selon le manuel actuel de la FAO, les tolérances sur les paramètres d'application doivent être celles qui entraîneraient une variation de 25 % de la concentration de résidus, et non des variations de 25 % des paramètres eux-mêmes. L'application de la "règle des 25 %" au délai avant récolte est expliquée en détail dans le manuel de la FAO de 2016. Au chapitre 5.2.3 du manuel, il est indiqué : " *La latitude des intervalles acceptables autour du délai d'attente avant récolte dépend du taux de diminution des résidus du composé évalué. La latitude admissible doit se rapporter à une variation de ±25% du niveau de résidus et peut être estimée à partir d'études sur le déclin des résidus."*

Ce qui suit dans le chapitre du Manuel de la FAO 2016 est une approche mathématique pour calculer les intervalles acceptables pour le délai avant récolte qui conduira à un écart maximal de 25% dans les valeurs finales de résidus dans le produit récolté.

BASF demande à la JMPR de prendre également en considération les onze autres essais sur le blé aux Etats-Unis et au Canada avec un PHI de 20-22 jours, car le comportement de diminution des résidus pour les grains de blé entre les PHI 14 et 35/36 jours mesuré dans les deux essais de diminution démontre clairement que les essais sur les résidus avec un PHI de 20-22 jours aboutiront à un écart de moins de 25% par rapport au niveau de résidus attendu au PHI de 30 jours de l'étiquette.

Culture / produit de base	Refuser le procès	Valeurs résiduelles mg/kg (total *cis+trans* metconazole)	Demi-vie calculée (jours)
Grain de blé d'hiver	R05047 (IL)	Résidu PHI 14 0.034, 0.045 21 0.077, 0.062 28 0.051, 0.051 35 0.036, 0.048	387 (R^2 = 0.0041)
Grain de blé de printemps	R05050 (ND)	Résidu PHI 14 0.018, 0.022 22 0.014, 0.016 28 0.013, 0.013 36 0.012, 0.013	32 (R^2 = 0.886)

L'essai de blé d'hiver de l'État de l'Illinois (IL) n'a pas montré un comportement typique de diminution des résidus. Les résidus ont en fait augmenté entre la première et la deuxième date d'échantillonnage, ce qui a donné lieu à une très longue demi-vie et à une mauvaise correspondance avec la décroissance de premier ordre prévue. Cependant, l'essai de décroissance mené sur le blé de printemps dans l'État du Dakota du Nord (ND) a présenté un ajustement acceptable à la décroissance de premier ordre et a donné lieu à une demi-vie calculée de 32 jours. En se basant sur une demi-vie estimée de 32 jours pour le metconazole dans le grain de blé, la variance acceptable autour d'un DAI de 30 jours figurant sur l'étiquette est de 20 à 43 jours (voir les calculs ci-dessous). En supposant que les autres paramètres d'application correspondent à l'étiquette enregistrée, les valeurs de résidus des échantillons prélevés à l'intérieur de cette plage de DSP de 20 à 43 jours se situeront à moins de 25 % des valeurs de résidus attendues à partir du DSP de 30 jours de l'étiquette.

Extrait du manuel de la FAO (2016), page 86 :

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

Où t_1 - t_2 est le temps (jours) entre le PHI enregistré (t1) et le PHI de l'essai sur les résidus (t2).

C_1 est le niveau de résidu attendu du PHI enregistré

C_2 est le niveau de résidus mesuré dans les essais sur le terrain.

$t_{1/2}$ est la demi-vie (jours)

Lorsque C_2 est supérieur de 25 % à C_1, alors C_2 = 1,25 x C_1.

Et lorsque C_2 est inférieur de 25% à C_1, alors C_2 = 0,75 x C_1.

Avec ces contraintes, l'équation donne les intervalles suivants pour le temps entre le PHI enregistré et le PHI d'essai :

t_1 - t_2 = 0,32 x $t_{1/2}$ (lorsque le PHI d'essai est plus court que le PHI enregistré)

$t_2 - t_1 = 0{,}42 \times t_{1/2}$ (lorsque le PHI d'essai est plus long que le PHI enregistré)

Ainsi, pour le metconazole sur le grain de blé où la demi-vie observée était d'au moins 32 jours, la fourchette de DSP acceptable qui mènera à des résidus se situant à moins de 25 % du résidu prévu au DSP de l'étiquette est de 20 à 43 jours.

En résumé, BASF demande à la JMPR de prendre en compte l'ensemble des 15 essais de résidus soumis par les Etats-Unis et le Canada pour soutenir l'étiquette Caramba® car ils entrent dans le cadre de l'interprétation de la FAO de la "règle des 25%" en ce qui concerne les niveaux de résidus attendus dans le grain de blé lorsqu'ils sont calculés selon la pratique dirigée par le manuel de la FAO.

FORMULAIRE POUR EXPRIMER DES PRÉOCCUPATIONS CONCERNANT L'AVANCEMENT D'UNE LMR OU DEMANDE DE CLARIFICATION DES PRÉOCCUPATIONS
AFIDOPYROPEN (312)

Soumis par : Délégation américaine au CCPR			
Date : 28 février 2021			
Pesticide/ **Numéro de code du pesticide**	**Produits de base/** **Numéro de code de produit**	**LMR** **(mg/kg)**	**Étape actuelle**
Afidopyropen/ 312	Tous les produits de base	Toutes les LMR	Première demande
S'agit-il d'une demande d'éclaircissement ? *Oui*			
Est-ce un problème ? Oui, c'est surtout une préoccupation			
S'agit-il d'une préoccupation constante ? Non, mais cela a un impact sur les CXL examinés précédemment et sur une nouvelle demande faite en 2020.			

Préoccupation *(*déclaration *spécifique* de la raison de la préoccupation concernant l'avancement de la LMR proposée).

Préoccupation n° 1 :

BASF est préoccupé par les calculs numériques utilisés pour mettre en œuvre la définition de résidu d'évaluation des risques proposée par la JMPR pour les plantes pour l'Afidopyropène.

- La JMPR a établi la définition du résidu pour l'évaluation du risque alimentaire pour les produits végétaux : somme de l'afidopyropène + M440I007, *exprimée en afidopyropène.*
- Pour exprimer M440I007 en tant que parent, le rapport des poids moléculaires doit être utilisé comme facteur d'ajustement ; l'expression de M440I007 en tant que parent **nécessite une mise à l'échelle de 0,5 X sur la base des poids moléculaires mis à l'échelle** = MW où afidopyropen / M440I007 = (593,7/1187,3).
- Cependant, le rapport final de la JMPR montre clairement que les résidus du parent et de M440I007 ont été simplement additionnés ; l'addition implique qu'ils appliquent une règle spéciale de dimère pour compter M440I007 = 2 molécules du parent.
- BASF a fourni à la JMPR trois sources de preuves différentes (une étude ADME chez le rat avec le ^{14C} M440I007, un argument de ratio tox comparatif et un calcul de chimie quantique sur la force du pont dimère) pour expliquer pourquoi le M440I007 ne reformera pas 2 molécules de la molécule mère en tant que résidu.
- Enfin, nous pensons que sans l'ajustement des MW, les **valeurs de HR et de STMR dans le projet de document sont actuellement incorrectement trop élevées pour** tous les produits végétaux. À titre d'exemple, veuillez vous référer au document HED de l'US EPA ci-joint. Un extrait du tableau 5.3.1 du résumé analytique de l'US EPA (correctement) décrit les calculs utilisant le facteur de conversion MW déjà résumé pour M440I007. (Et bien que le document présente également un ensemble "combiné" avec M440I007 ; nous notons que la décision finale de l'US EPA n'a pas inclus M440I007). Le document complet de l'EPA sur la chimie des résidus est fourni comme référence supplémentaire pratique et est joint à ce formulaire de notification de réserve.
- Nous demandons que les valeurs de HR et STMR dans le projet de document de la JMPR soient recalculées en utilisant le facteur d'échelle approprié basé sur les MWs plutôt que la simple addition incorrecte de l'Afidopyropène parent et du métabolite M440I007.

Préoccupation n° 2

Il est également demandé à la réunion de reconsidérer la très faible LMR rédigée pour le lait à 0,001 ppm. Bien que cette valeur soit soutenue par les méthodes actuelles, elle est très faible pour une surveillance pratique dans le commerce. Une valeur par défaut de 0,01* ppm serait mieux harmonisée avec les pratiques d'application et plus utile pour la communauté commerciale internationale et nous recommandons que cette valeur de 0,01 ppm* CXL soit utilisée à la place.

Demande d'éclaircissement (énoncé *précis de* l'éclaircissement demandé).

BASF accueille favorablement toute clarification supplémentaire de la part de la JMPR lors de la révision de l'automne 2021 qui n'a pas été incluse dans le rapport final concernant l'inclusion de M440I007 dans la définition de l'évaluation des risques. Des informations supplémentaires de BASF sont fournies ci-dessous sur la demande de clarification.

- Dans notre dossier et dans la correspondance ultérieure, nous avons noté que l'ajout du M440I007 dans la définition de l'évaluation des risques ne reflète pas la toxicité significativement plus faible connue du métabolite M440I007 ; il est très conservateur d'ajouter la mère et le métabolite M440I007 et ensuite d'évaluer par rapport aux doses de référence de la mère (en particulier pour l'ARfD, où il n'y a aucune preuve de toxicité aiguë). Une explication plus claire sur ce point devrait être fournie par la JMPR.

Souhaitez-vous que cette préoccupation soit notée dans le rapport du CCPR ?

Données/Informations (Description de chaque élément distinct de données/informations qui est joint ou sera fourni au secrétaire compétent de la JMPR dans un délai d'un mois après la réunion du CCPR).

Pièces jointes :

- Annexe 1. Réponse de BASF du 23 septembre 2019 concernant le projet d'évaluation des résidus de l'afidopyropène par la JMPR

  Veuillez vous référer aux pgs. 3-4 de l'annexe 1 pour un exemple détaillé des calculs utilisant le facteur de conversion MW correct pour M440I007.

  PDF
  Attachment 1_Appendix BASF Re

- Annexe 2. U.S. EPA (D439679). Afidopyropène. Résumé des données sur la chimie analytique et les résidus. 3 avril 2018.

  PDF
  Attachment 2_U.S. EPA_Afidopyropen_

Pièces jointes 1 et 2 comme suit.

BASF Sept 23, 2019 Response for Afidopyropen JMPR Residue Appraisal Draft
Doc ID: 2019/2051490

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 rational 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 defintion.
   - 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 Summary[1]

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:
  Total afidopyropen = afidopyropen + 0.1 X 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 Afidopyrpopen 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

From: Peter Savoia, Chemist
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Through: Michael S. Metzger, Chief
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and
Julie L. Van Alstine, Co-Chair
George F. Kramer/ Tom Bloem, Detailed Reviewers
Chemistry Science Advisory Council
Health Effects Division (7509P)

To: Danette Drew, Chemist, Risk Assessor
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Richard Gebken, Risk Manager
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Invertebrate and Vertebrate Branch II
Registration Division (7505P)

Table of Contents

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 VersysTM 100 g ai/L and SefinaTM 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*,4a*R*,6*S*,6a*S*,12*R*,12a*S*,12b*S*)-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)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	*Brassica, head and stem, group 5-16*
Vegetable, leafy, subgroup 4-13B	5	5.0	*Brassica, leafy greens, subgroup 4-16B*
Citrus, oil	0.3	0.40	*Tolerance is harmonized to the Canadian MRL*
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	*Leafy Greens, subgroup 4-16A*
Vegetable, leaf petioles, subgroup 22B	3	3.0	*Leaf petiole vegetable subgroup 22B*
Nut, tree, group 14-12	0.01	0.01	
Plum, prune	0.06	Not Recommended	
Soybean, aspirated grain fractions	0.4	0.15	*Grain, aspirated fractions*
Soybean, seed	0.01	0.01	
Tomato, dried	None Requested	0.50	*Tolerance is harmonized to the Canadian MRL*
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.

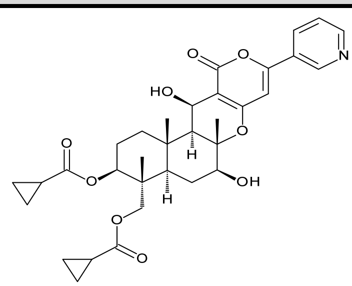
Table 3.1. Afidopyropen Nomenclature.	
Compound Afidopyropen	
Common name	Afidopyropen

Table 3.1. Afidopyropen Nomenclature.	
Company experimental name	BAS 440 I
IUPAC name	[(3*S*,4*R*,4a*R*,6*S*,6a*S*,12*R*,12a*S*,12b*S*)-3-(cyclopropylcarbonyloxy)-1,2,3,4,4a,5,6,6a,12,12a,12b-decahydro-6,12-dihydroxy-4,6a,12b-trimethyl-11-oxo-9-(3-pyridyl)-11*H*,12*H*-benzo[*f*]pyrano[4,3-*b*]chromen-4-yl]methyl cyclopropanecarboxylate
CAS name	[(3*S*,4*R*,4a*R*,6*S*,6a*S*,12*R*,12a*S*,12b*S*)-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)2*H*,11*H*-naphtho[2,1-*b*]pyrano[3,4-*e*]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 ℃	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 ℃ <1.13x10^{-7} at 50 ℃	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: € = 20900 L mol^{-1}cm^{-1} 321 nm: € = 13200 L mol^{-1}cm^{-1} In Aqueous Solution (pH 7.44): 231 nm: € = 20900 L mol^{-1}cm^{-1} 317 nm: € = 14100 L mol^{-1}cm^{-1} In Acidic Solution (pH 1.03): 231 nm: € = 19100 L mol^{-1}cm^{-1} 330 nm: € = 10700 L mol^{-1}cm^{-1} In Basic Solution (pH 13.36): 231 nm: € = 21400 L mol^{-1}cm^{-1} 320 nm: € = 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 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
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 Versys™ 100 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

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.

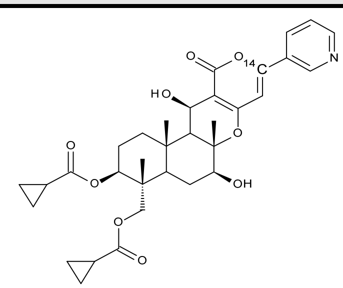
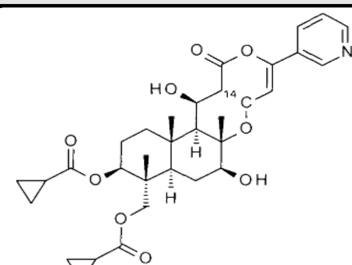
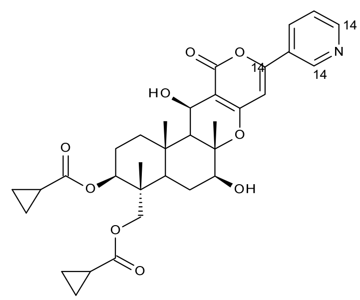
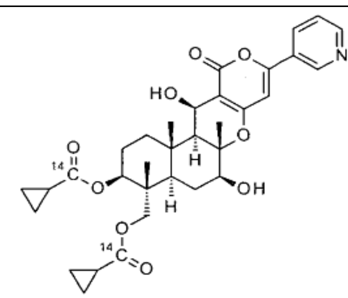
4.0 Metabolite/Degradate Residue Profile

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

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 ≤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.

Table 4.1.1.1. Summary of characterization and identification of radioactive residues in tomato harvested 7 or 14 days after the last application of NCA-^{14}C-Afidopyropen.

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-^{14}C Label)

The metabolism of afidopyropen was investigated in tomato using radiolabeled afidopyropen at position 4 of the pyranone ring (pyranone-4-^{14}C 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 ≤ -18°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.

Table 4.1.1.2. Summary of characterization and identification of radioactive residues in tomato harvested 1 day after the last application of Pyranone-4-^{14}C-Afidopyropen.

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 (^{14}C-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 ^{14}C-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 ^{14}C-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-^{14}C-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-^{14}C Label)

The metabolism of afidopyropen was investigated in greenhouse cabbage using radiolabeled afidopyropen at position 4 of the pyranone ring (pyranone-4-^{14}C 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 M4401007, 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 ^{14}C- 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-^{14}C-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-^{14}C Label)

The metabolism of afidopyropen was previously investigated in cabbage with the ^{14}C-NCA radiolabel (also described as pyranone-6-^{14}C) 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 ^{14}C-afidopyropen labeled at position 6 of the pyranone ring (pyranone-6-^{14}C 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 (^{14}C-NCA) & Pyranone-4-^{14}C 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, afidpoyropen was either ^{14}C-labeled in the pyranone and pyridine ring (pyranone-6-^{14}C, pyridine-2,6-^{14}C, Nicotinic Acid label) or only in the pyranone ring (pyranone-4-^{14}C, 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 afodpyropen 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-^{14}C and Pyranone-4-^{14}C-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-^{14}C 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**	

n.d. = not detected; n.a. = not applicable
**Accountability = Sum of identified + characterized + PES (all in ppm)/overall TRR (ppm) x 100*

4.1.1.7 Soybean (CPCA-^{14}C Label)

The metabolism of afidopyropen was investigated in soybean using a radiolabeled CPCA-^{14}C-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-^{14}C.

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**	

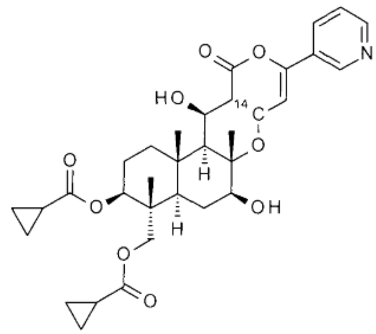
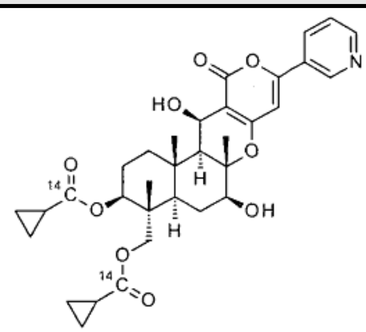
n.d. not detected
*Accountability = Identified (ppm) + Characterized (ppm) + PES (ppm)/Overall TRR (ppm) * 100

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).

Table 4.1.2.1.1. Summary of identified and characterized ^{14}C-residues extracted from tissues (liver, muscle and fat) after 14 daily doses of [^{14}C-CPCA]-Afidopyropen at 12 ppm (12000x).

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_2O Extracts (liver, muscle) *DCM:MeOH, MeOH:H_2O 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 ^{14}C-residues extracted from egg yolk and egg white after 14 daily doses of [^{14}C-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 ^{14}C-Residues Extracted from Excreta after 14 Daily Doses of [^{14}C-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-^{14}C 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-^{14}C label). The lactating goat was dosed for seven consecutive days at an average of 17.3 mg [^{14}C]-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-^{14}C]-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.

Table 4.1.2.2.1. Pyranone-4-^{14}C Labeled Afidopyropen Residues Identified and Characterized in Goat Tissues and Milk.

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	

[1]The 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-^{14}C 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-^{14}C Label)

The metabolism of afidopyropen was investigated in ruminants by dosing a single lactating goat with radiolabeled CPCA-^{14}C-afidopyropen **(**CPCA-^{14}C 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 [^{14}C]-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 [^{14}C-CPCA]-Afidopyropen.

Matrix [1]	Liver		Kidney		Composite Muscle		Whole Milk	
Metabolite[2]	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 [^{14}C-CPCA]-Afidopyropen.

Matrix	Urine	Feces
Metabolite[1]	% of the TRRs	% of the TRRs
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;

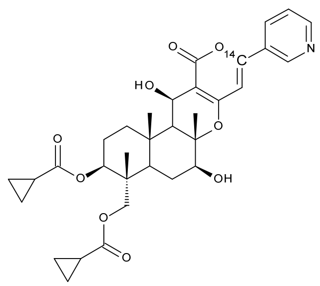
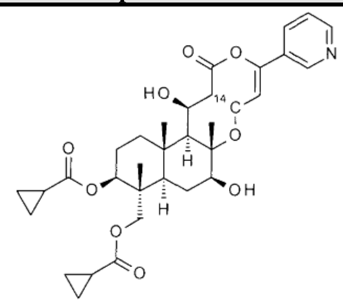
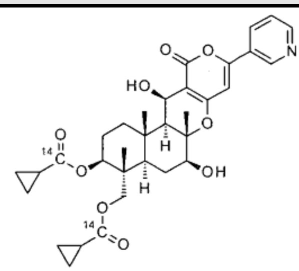
[1] The presence of the metabolite M440I001, produced by the loss of both ester groups, could not be detected with radiometric detection due to the location of the label in the CPCA moiety.

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.

Table 4.1.3.1. Summary of characterization and identification of radioactive residues in rotational crop matrices following an application of NCA-^{14}C Radiolabeled Afidopyropen at 125 g ai/ha.

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-^{14}C 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 ppm[2]**		**TRR= 0.001 ppm[2]**	
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 ppm[2]**		**TRR= 0.003 ppm[2]**	
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**	
M440I003	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 (^{14}C-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 ^{14}C-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-^{14}C 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-^{14}C-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-^{14}C radiolabel.

Table 4.1.3.3. Summary of characterization and identification of radioactive residues in rotational crop matrices following an application of Pyranone-4-^{14}C 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 ppm[3]**		**TRR= 0.001 ppm[3]**	
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 ppm[3]**		**TRR= 0.001 ppm[3]**	
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-^{14}C 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.

Table 4.3. Summary of Metabolites and Degradates to be included in the Afidopyropen Risk Assessment and Tolerance Expression.[1]

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 $MgSO_4$ 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.		
	Ion Transitions Monitored	
Analyte	**Quantitation**	**Confirmation**
Afidopyropen	*m/z* 594→148	*m/z* 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

<u>Plants</u>

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 ($MgSO_4$, 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.		
	Ion Transitions Monitored	
Analyte	Quantitation	Confirmation
Afidopyropen	*m/z* 594→202	*m/z* 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.		
	Ion Transitions Monitored	
Analyte	Quantitation	Confirmation
Afidopyropen	*m/z* 594→148	*m/z* 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

<u>Plants</u>

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 ≤-20°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).

Table 5.2.1. Summary Storage Durations for Crop Commodities Collected from the Field Trial Studies Conducted for Afidopyropen Held in Frozen Storage at ≈-20°C.

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 M44I007 (%)														
Day	**A: Corrected mean in stored samples, % of nominal** B: mean procedural, in freshly spiked sample													
	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 ≤-20°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		0.0157-0.0184 [17.7-20.6]	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		0.0157-0.0184 [17.7-20.6]	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		0.0157-0.0184 [17.7-20.6]	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		0.107-0.109 (120-122)	0	3	0.040	0.061	0.046	0.059	0.055	0.053	0.007
Tomato		0.104-0.115 (116-129)	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		0.107-0.109 (120-122)	0	3	<0.005	0.026	<0.005	0.024	0.007	0.012	0.010
Tomato		0.104-0.115 (116-129)	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		0.107-0.109 (120-122)	0	3	<0.045	0.087	<0.051	0.079	0.066	0.065	0.014
Tomato		0.104-0.115 (116-129)	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 apploication 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* - M440I007
	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.

<u>Cattle</u>

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.

Table 5.3.4.1. Summary of Residues in Cattle Matrices after Dosing with Afidopyropen.[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

Table 5.3.4.1. Summary of Residues in Cattle Matrices after Dosing with Afidopyropen.[1]								
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
M440I001[3] 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).

Table 5.3.4.2. Summary of Residues of Afidopyropen in Whole Milk From the Depuration Study.						
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
	Whole Milk / Day 38		<0.001	<0.001	<0.001	< 0.005
	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	input			ppm
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 is 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

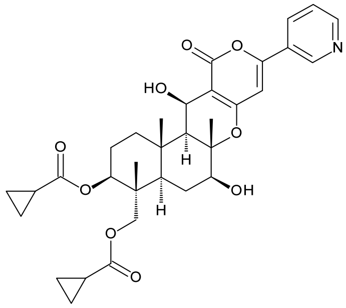
Chemical Name	Matrix	Percent TRR (PPM) [1]		
		Matrices - Major Residue (>10%TRR)		Matrices - Minor Residue (<10%TRR)
Afidopyropen Reg. No.: 5599022 (BAS 440 I, ME5343, M440I0000) 	Tomato Fruit	32% (0.1079) NCA-^{14}C - 7 DALA 16% (0.0484) NCA-^{14}C – 14 DALA 61% (0.033) pyranone-4-^{14}C - 1 DALA		--
	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)
		Hydrolysis	Not Reported	pH 9, 10; 98% (30 d)
				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

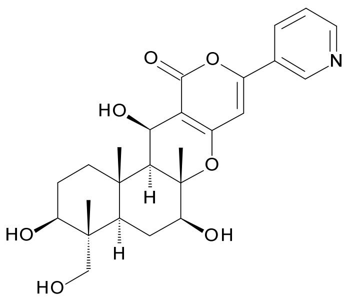
Chemical Name	Matrix	Percent TRR (PPM) [1]		
		Matrices - Major Residue (>10%TRR)		Matrices - Minor Residue (<10%TRR)
M440I001 Reg. No.: 5741530 (ME5343-T1) 	Tomato Fruit	--		--
	Tomato Leaves	--		2.3% (0.053) pyranone-4-C^{14} - 1 DALA
	Cabbage	--		--
	Soybean Leaves	--		--
	Soybean Seed	--		--
	Soybean 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)

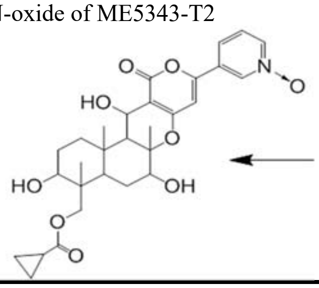
Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) [1]		
		Matrices - Major Residue (>10%TRR)		Matrices - Minor Residue (<10%TRR)
M440I002 Reg. No.: 5741532 (ME5354-T2)	Tomato Fruit	--		--
	Tomato Leaves	--		3.6% (0.082) pyranone-4-C^{14} - 1 DALA
	Cabbage	--		--
	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

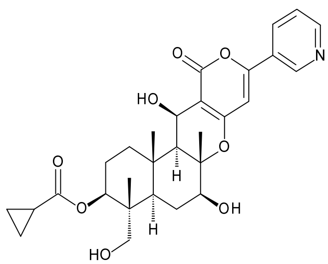
Chemical Name	Matrix	Percent TRR (PPM) [1]		
		Matrices - Major Residue (>10%TRR)		Matrices - Minor Residue (<10%TRR)
M440I003 Reg. No.: 5741533 (ME5343-T3) 	Tomato Fruit	--		--
	Tomato Leaves	--		--
	Cabbage	--		--
	Soybean Leaves	--		--
	Soybean Seed	--		--
	Soybean Hulls	--		--
	Soybean Plant	--		--
	Rotational Crops	--		**Wheat Straw** 0.9% (0.001) NCA-^{14}C - 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

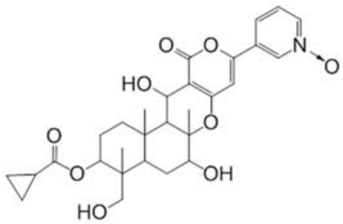
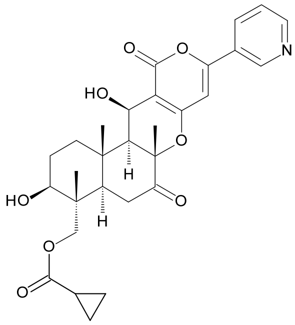
Chemical Name	Matrix	Percent TRR (PPM) [1]		
		Matrices - Major Residue (>10%TRR)		Matrices - Minor Residue (<10%TRR)
N-oxide of ME5343-T3 	Rat	--		1.48% -5% both sexes in bile (3 & 300 ppm/bw)
M440I004 Reg. No.: 5824381 (ME5343-T4)	Tomato Fruit	--		--
	Tomato Leaves	--		--
	Cabbage	--		--
	Soybean Leaves	--		--
	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

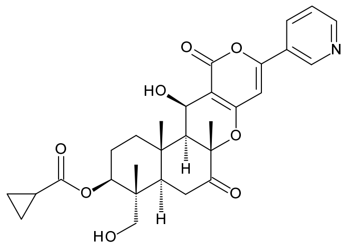
<table>
<tr><th colspan="5">Table A.1. Summary of Metabolites and Degradates</th></tr>
<tr><th rowspan="2">Chemical Name</th><th rowspan="2">Matrix</th><th colspan="3">Percent TRR (PPM) [1]</th></tr>
<tr><th colspan="2">Matrices - Major Residue (>10%TRR)</th><th>Matrices - Minor Residue (<10%TRR)</th></tr>
<tr><td rowspan="30">M440I006
Reg. No.: 5824383
(ME5343-T6)
</td><td>Tomato Fruit</td><td colspan="2">--</td><td>--</td></tr>
<tr><td>Tomato Leaves</td><td colspan="2">--</td><td>--</td></tr>
<tr><td>Cabbage</td><td colspan="2">--</td><td>--</td></tr>
<tr><td>Soybean Leaves</td><td colspan="2">--</td><td>--</td></tr>
<tr><td>Soybean Seed</td><td colspan="2">--</td><td>--</td></tr>
<tr><td>Soybean Hulls</td><td colspan="2">--</td><td>--</td></tr>
<tr><td>Soybean Plant</td><td colspan="2">--</td><td>--</td></tr>
<tr><td>Rotational Crops</td><td colspan="2">--</td><td>--</td></tr>
<tr><td>Milk</td><td colspan="2">--</td><td>5.4% (<0.001)
pyranone-4-^{14}C</td></tr>
<tr><td>Ruminant Muscle</td><td colspan="2">--</td><td>5.3% (<0.001)
pyranone-4-^{14}C</td></tr>
<tr><td>Ruminant Fat</td><td colspan="2">--</td><td>5.2% (<0.001)
pyranone-4-^{14}C</td></tr>
<tr><td>Ruminant Kidney</td><td colspan="2">--</td><td>--</td></tr>
<tr><td>Ruminant Liver</td><td colspan="2">--</td><td>--</td></tr>
<tr><td>Poultry Muscle</td><td colspan="2">--</td><td>--</td></tr>
<tr><td>Poultry Skin and Fat</td><td colspan="2">--</td><td>--</td></tr>
<tr><td>Poultry Liver</td><td colspan="2">--</td><td>--</td></tr>
<tr><td>Egg Yolk</td><td colspan="2">--</td><td>--</td></tr>
<tr><td>Egg White</td><td colspan="2">--</td><td>--</td></tr>
<tr><td>Rat</td><td colspan="2">--</td><td>--</td></tr>
<tr><td rowspan="12">Water
(Minor Transformation; <10%)</td><td colspan="2">Maximum % Applied (day)</td><td>Final % Applied (day)</td></tr>
<tr><td>Aerobic soil</td><td>Not Reported</td><td>Not Reported</td></tr>
<tr><td>Anaerobic soil</td><td>Not Reported</td><td>Not Reported</td></tr>
<tr><td>Soil photolysis, light</td><td>Not Reported</td><td>Not Reported</td></tr>
<tr><td>Soil photolysis, dark</td><td>Not Reported</td><td>Not Reported</td></tr>
<tr><td>Aqueous photolysis</td><td>Not Reported</td><td>Not Reported</td></tr>
<tr><td rowspan="3">Hydrolysis</td><td>pH 4; Not Reported</td><td>pH 4; Not Reported</td></tr>
<tr><td>pH 7; Not Reported</td><td>pH 7; Not Reported</td></tr>
<tr><td>pH 9; Not Reported</td><td>pH 9; Not Reported</td></tr>
<tr><td>Aerobic aquatic</td><td>0.5% (100 d)</td><td>0.5% (100 d)</td></tr>
<tr><td>Anaerobic aquatic</td><td>Not Reported</td><td>Not Reported</td></tr>
<tr><td>Terrestrial field dissipation</td><td>Not Reported</td><td>Not Reported</td></tr>
</table>

Table A.1. Summary of Metabolites and Degradates

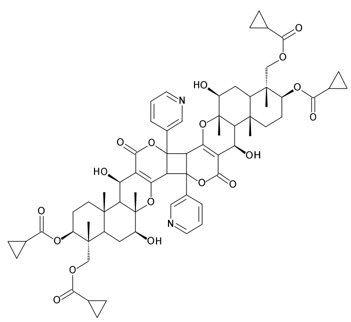
Chemical Name	Matrix	Percent TRR (PPM) [1]		
		Matrices - Major Residue (>10%TRR)		Matrices - Minor Residue (<10%TRR)
M440I007 Reg. No.: 5824749 (ME5343-T7) 	Tomato Fruit	10% (0.0344) NCA-^{14}C – 7 DALA		6.7% (0.0201) NCA-^{14}C – 14 DALA
	Tomato Leaves	15% (0.6277) NCA-^{14}C – 14 DALA		2.1% (0.048) 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)		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
		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

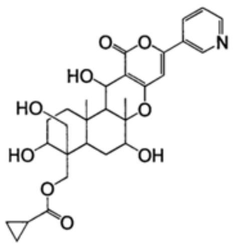
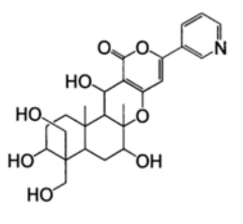
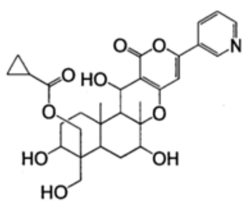
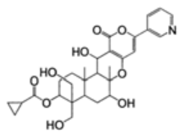
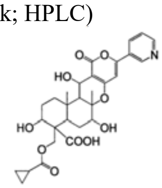
Chemical Name	Matrix	Percent TRR (PPM) [1]	
		Matrices - Major Residue (>10%TRR)	Matrices - Minor Residue (<10%TRR)
ME5343-T8 	Rat	10% in feces males (300 ppm/bw)	0.10% - 8% urine and feces both sexes (3 & 300 ppm/bw)
ME5343-T9 	Rat	--	<0.12% - 4% urine and feces both sexes (3 & 300 ppm/day)
ME5343-T10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

Table A.1. Summary of Metabolites and Degradates

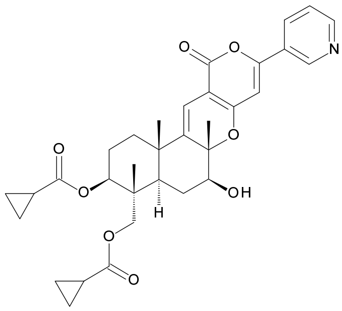
Chemical Name	Matrix	Percent TRR (PPM) [1]		
		Matrices - Major Residue (>10%TRR)		Matrices - Minor Residue (<10%TRR)
M440I014 Reg. No.: 5741536 	Tomato Fruit	--		--
	Tomato Leaves	--		--
	Cabbage	--		--
	Soybean Leaves	--		2.5% (0.421) NCA-^{14}C 3.9% (0.193) CPCA-^{14}C
	Soybean Seed	--		--
	Soybean 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

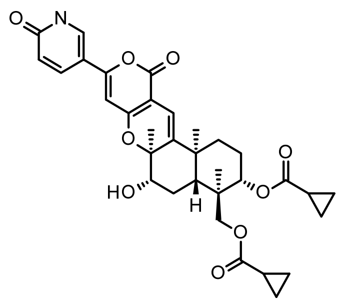
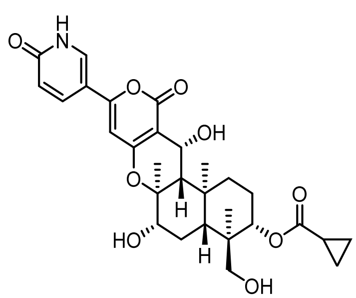
Chemical Name	Matrix	Percent TRR (PPM) [1]		
		Matrices - Major Residue (>10%TRR)		Matrices - Major Residue (>10%TRR)
M440I015 	Water (Minor Transformation; <10%)	Maximum % Applied (day)		Final % Applied (day)
		Aerobic soil	8.9% (10 d)	6.0% (120 d)
		Anaerobic soil	Not Reported	Not Reported
		Soil photolysis, 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

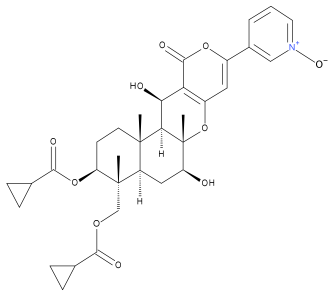
Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) [1]		
		Matrices - Major Residue (>10%TRR)		Matrices - Major Residue (>10%TRR)
M440I017 Reg. No.: 6045738 	Tomato Fruit	--		--
	Tomato Leaves	--		8.4% (0.193) pyranone-4-^{14}C - 1 DALA
	Cabbage	--		2.1% (0.037) 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

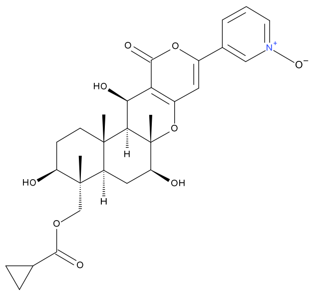
Chemical Name	Matrix	Percent TRR (PPM) [1]		
		Matrices - Major Residue (>10%TRR)		Matrices - Minor Residue (<10%TRR)
M440I019 	Tomato Fruit	--		--
	Tomato Leaves	--		3.1% (0.071) pyranone-4-^{14}C - 1 DALA
	Cabbage	--		--
	Soybean Leaves	--		--
	Soybean Seed	--		--
	Soybean Hulls	--		--
	Soybean Plant	--		--
	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

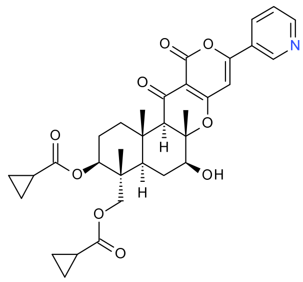
Chemical Name	Matrix	Percent TRR (PPM) [1]		
		Matrices - Major Residue (>10%TRR)		Matrices - Minor Residue (<10%TRR)
M440I020 Reg. No.: 5881593 	Tomato Fruit	--		--
	Tomato Leaves	--		3.0% (0.070) pyranone-4-^{14}C - 1 DALA
	Cabbage	--		1.6% (0.029) pyranone-4-^{14}C – 1 DALA, outer leaves 2.6 (0.011) 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

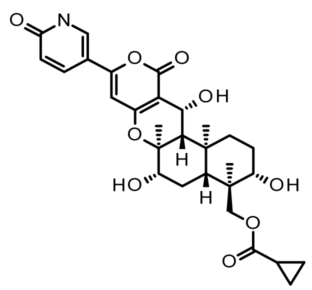
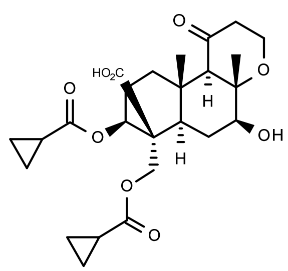
Chemical Name	Matrix	Percent TRR (PPM) [1]		
		Matrices - Major Residue (>10%TRR)		Matrices - Major Residue (>10%TRR)
M440I021 	Water (Minor Transformation; <10%)	Maximum % Applied (day)		
		Aerobic soil	5.7% (88 d)	3.1% (120 d)
		Anaerobic soil	Not Reported	Not Reported
		Soil photolysis, light	Not 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

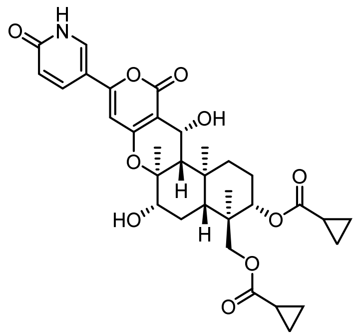
Chemical Name	Matrix	Percent TRR (PPM) [1]		
		Matrices - Major Residue (>10%TRR)		Matrices - Major Residue (>10%TRR)
M440I024 	Tomato Fruit	--		--
	Tomato Leaves	--		--
	Cabbage	--		--
	Soybean Leaves	--		--
	Soybean Seed	--		--
	Soybean Hulls	--		--
	Soybean Plant	--		--
	Rotational Crops	--		--
	Milk	--		--
	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

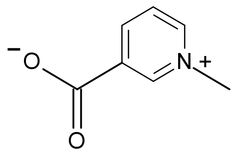
Chemical Name	Matrix	Percent TRR (PPM) [1]		
		Matrices - Major Residue (>10%TRR)		Matrices - Major Residue (>10%TRR)
M440I031 Reg. No.: 68482 (trigonelline) 	Tomato Fruit	--		--
	Tomato Leaves	--		--
	Cabbage	--		--
	Soybean Leaves	--		2.6% (0.432) NCA-^{14}C
	Soybean Seed	47% (0.179) NCA-^{14}C		--
	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	--	--

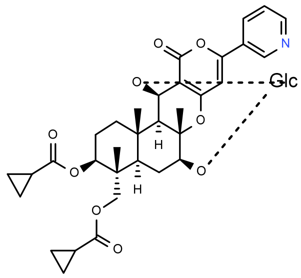
Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) [1]		
		Matrices - Major Residue (>10%TRR)		Matrices - Major Residue (>10%TRR)
M440I033 	Tomato Fruit	--		--
	Tomato Leaves	--		--
	Cabbage	--		--
	Soybean Leaves	--		1.3% (0.216) NCA-^{14}C 1.5% (0.074) CPCA-^{14}C
	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

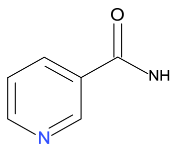
Chemical Name	Matrix		Percent TRR (PPM) [1]	
			Matrices - Major Residue (>10%TRR)	Matrices - Major Residue (>10%TRR)
M440I044 Reg. No.: 59878 (nicotinamide)  	Tomato Fruit		--	--
	Tomato Leaves		--	--
	Cabbage		--	9.8% (0.143) NCA-^{14}C – 7 DALA 8.1% (0.087) NCA-^{14}C – 14 DALA
	Soybean Leaves		--	--
	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	--	--

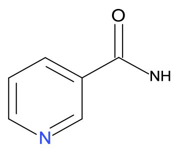
Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) [1]		
		Matrices - Major Residue (>10%TRR)		Matrices - Major Residue (>10%TRR)
M440I045 Reg. No.: 14673 (nicotinic acid) 	Tomato Fruit	--		Trace NCA-^{14}C – 7 DALA Trace NCA-^{14}C – 14 DALA
	Tomato Leaves	--		--
	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

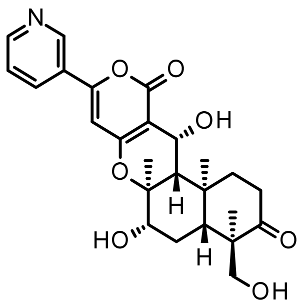
Chemical Name	Matrix	Percent TRR (PPM) [1]		
		Matrices - Major Residue (>10%TRR)		Matrices - Major Residue (>10%TRR)
M440I046 	Tomato Fruit	--		--
	Tomato Leaves	--		--
	Cabbage	--		--
	Soybean Leaves	--		--
	Soybean Seed	--		--
	Soybean Hulls	--		--
	Soybean Plant	--		--
	Rotational Crops	--		--
	Milk	--		--
	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

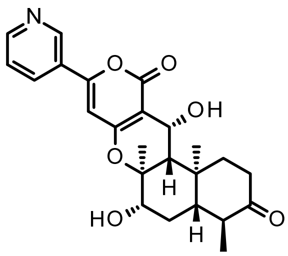
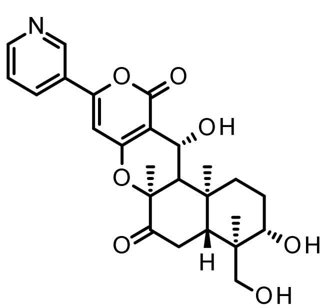
Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) [1]		
		Matrices - Major Residue (>10%TRR)		Matrices - Major Residue (>10%TRR)
M440I047	Tomato Fruit	--		--
	Tomato Leaves	--		--
	Cabbage	--		--
	Soybean Leaves	--		--
	Soybean Seed	--		--
	Soybean Hulls	--		--
	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

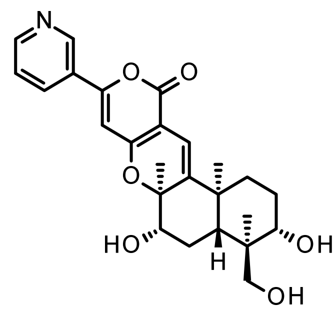
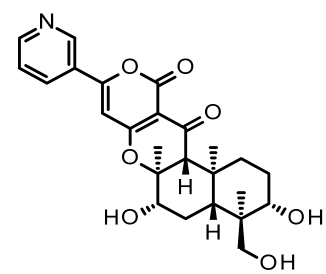
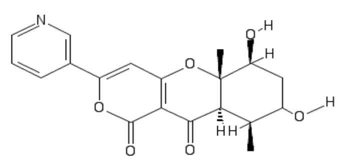
Chemical Name	Matrix	Percent TRR (PPM) [1]		
		Matrices - Major Residue (>10%TRR)		Matrices - Major Residue (>10%TRR)
M440I049 	Water (Minor Transformation; <10%)	Maximum % Applied (day)		Final % Applied (day)
		Aerobic soil	7.2% (29 d)	2.4% (120 d)
		Anaerobic soil	Not Reported	Not Reported
		Soil photolysis, 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)		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
M440I052 	Water (Minor Transformation; <10%)	Maximum % Applied (day)		Final % 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

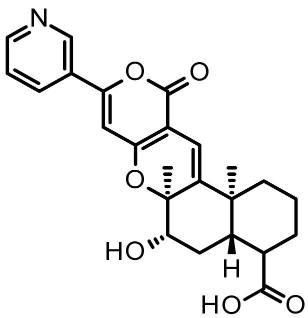
Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) [1]		
		Matrices - Major Residue (>10%TRR)		Matrices - Major Residue (>10%TRR)
M440I053 	Water (Minor Transformation; <10%)	Maximum % Applied (day)		Final % Applied (day)
		Aerobic soil	7.2% (29 d)	2.4% (120 d)
		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

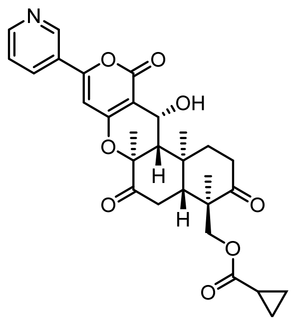
Table A.1. Summary of Metabolites and Degradates				
Chemical Name	Matrix	Percent TRR (PPM) [1]		
		Matrices - Major Residue (>10%TRR)		Matrices - Major Residue (>10%TRR)
M440I057 	Tomato Fruit	--		--
	Tomato Leaves	--		--
	Cabbage	--		--
	Soybean Leaves	--		--
	Soybean Seed	--		--
	Soybean Hulls	--		--
	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

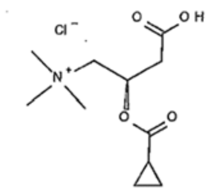
Chemical Name	Matrix	Percent TRR (PPM) [1]		
		Matrices - Major Residue (>10%TRR)		Matrices - Major Residue (>10%TRR)
M440I060 Reg. No.: 6009307 CPCA-carnitine 	Tomato Fruit	--		--
	Tomato Leaves	--		--
	Cabbage	--		--
	Soybean Leaves	--		--
	Soybean Seed	--		--
	Soybean Hulls	--		--
	Soybean Plant	--		--
	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

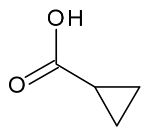
Chemical Name	Matrix	Percent TRR (PPM) [1]		
		Matrices - Major Residue (>10%TRR)		Matrices - Major Residue (>10%TRR)
M440I061 Reg. No.: 53128 (CPCA) 	Tomato Fruit	--		--
	Tomato Leaves	--		--
	Cabbage	--		--
	Soybean Leaves	--		--
	Soybean Seed	--		--
	Soybean Hulls	--		--
	Soybean Plant	--		--
	Rotational 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-^{14}C Label)

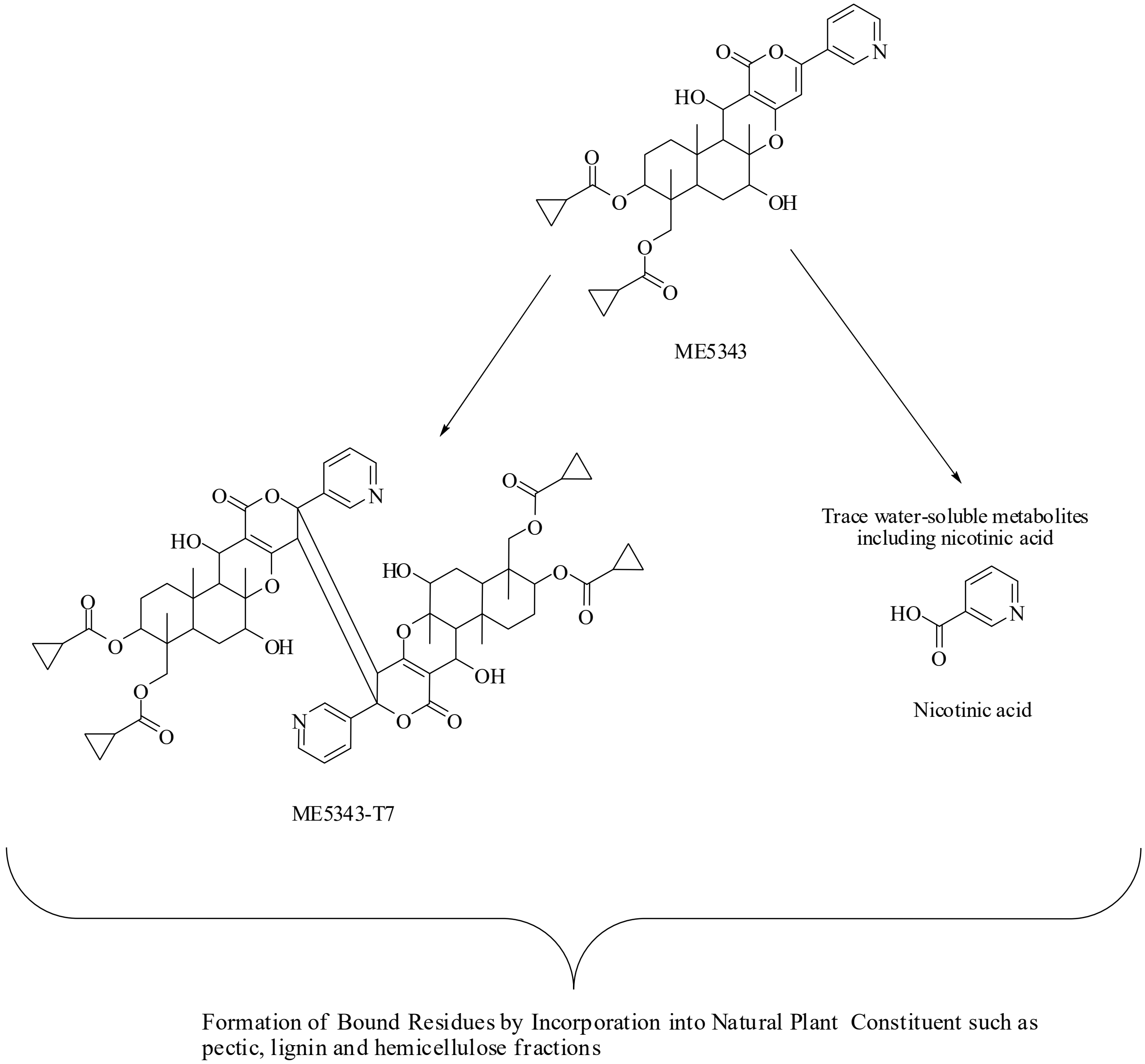


Figure B.2; Proposed Metabolic Pathway of Afidopyropen in Tomato (Pyranone-4-^{14}C Label)

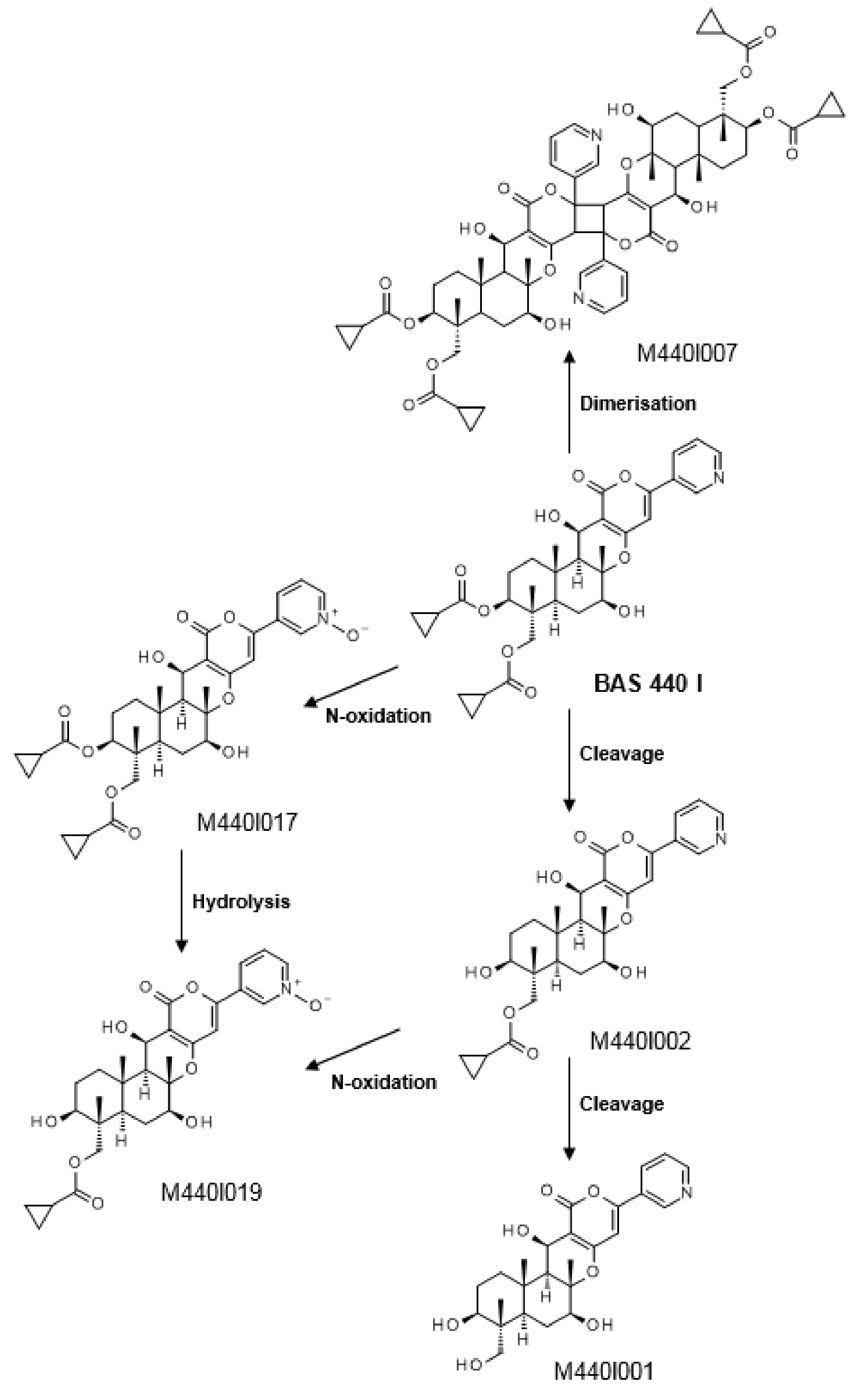


Figure B.3; Proposed Metabolic Pathway of Afidopyropen in Cabbage (NCA-[14]C Label)

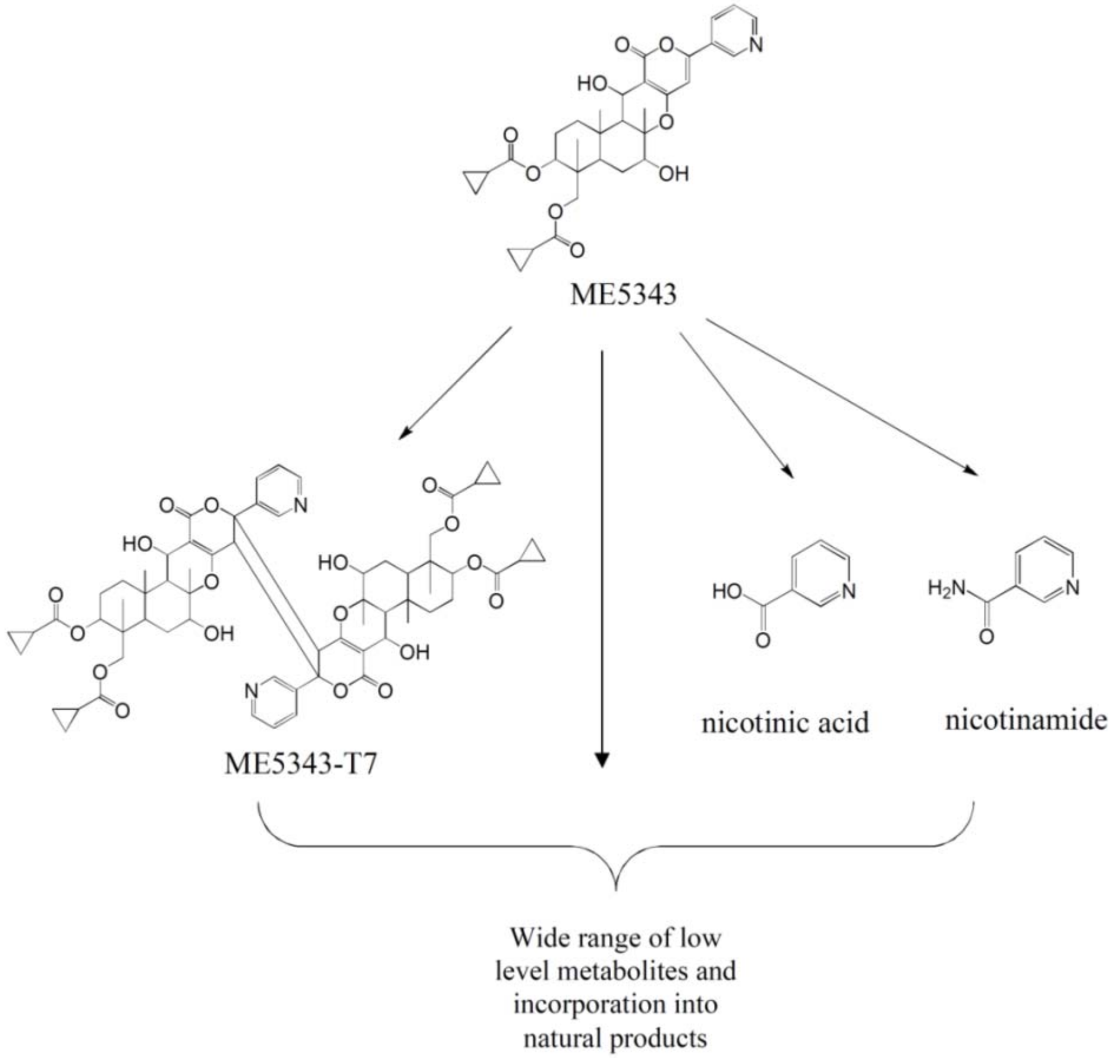


Figure B.4; Proposed Metabolic Pathway of Afidopyropen in Cabbage (Pyranone-4-^{14}C Label)

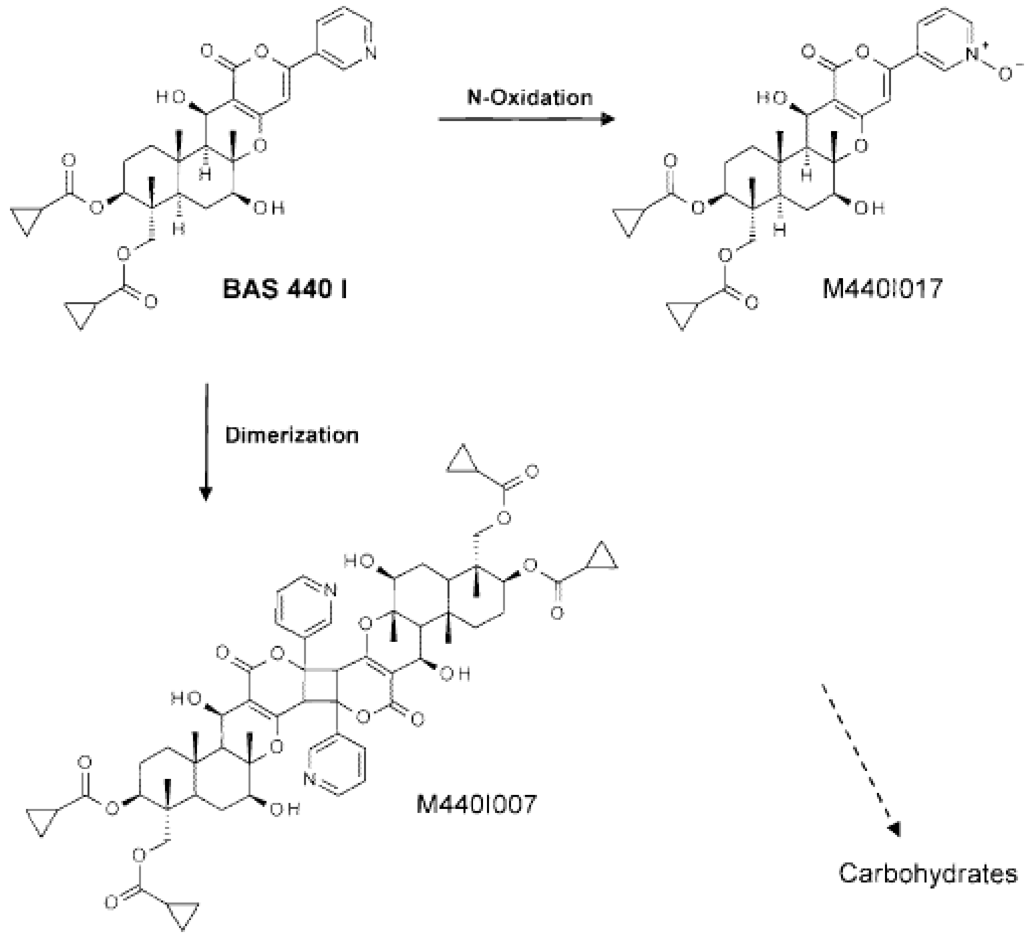


Figure B.5; Proposed Metabolic Pathway of Afidopyropen in Soybean (NCA-^{14}C Label)

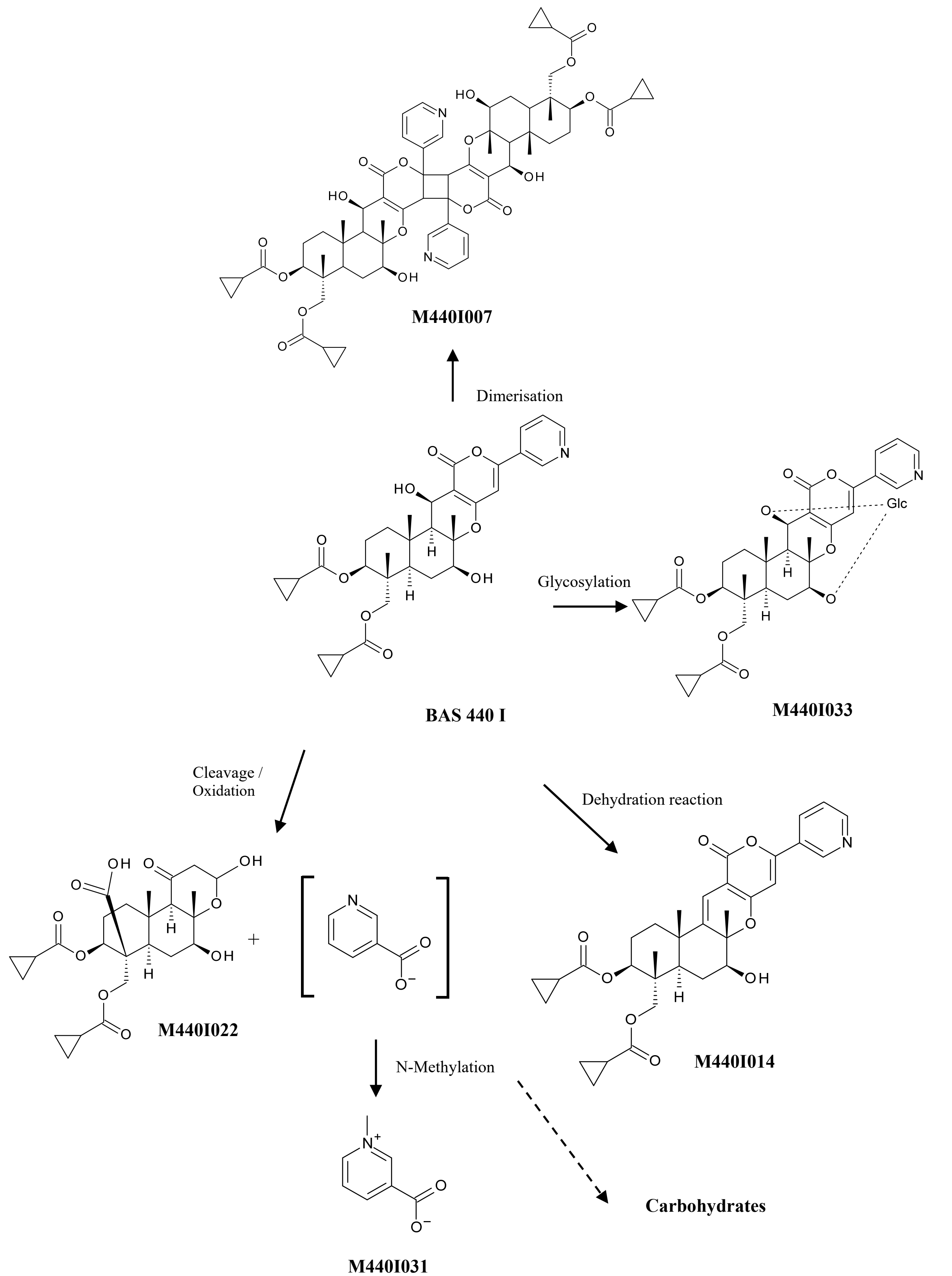


Figure B.6; Proposed Metabolic Pathway of Afidopyropen in Soybean (CPCA-^{14}C Label)

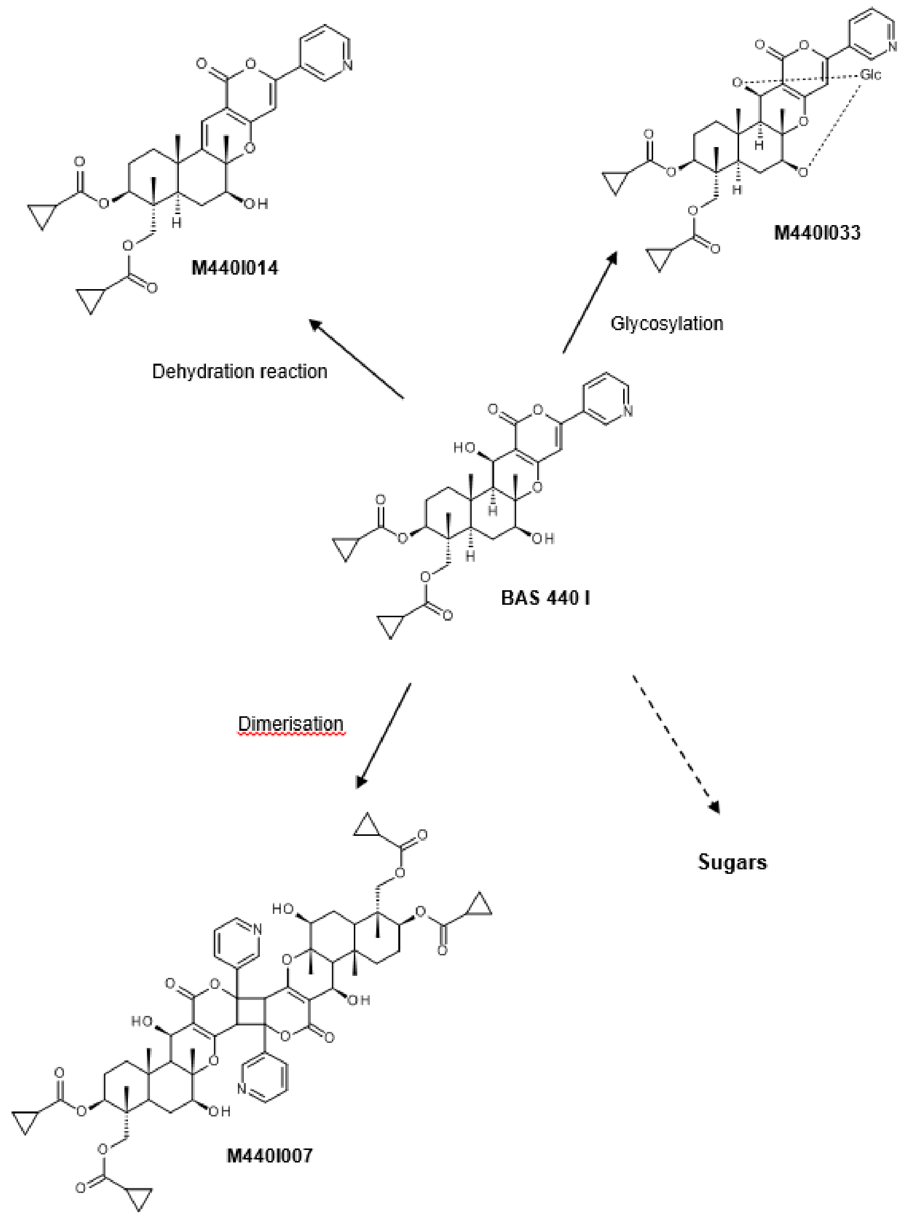


Figure B.7; Proposed Metabolic Pathway of Afidopyropen in Poultry (CPCA-^{14}C Label)

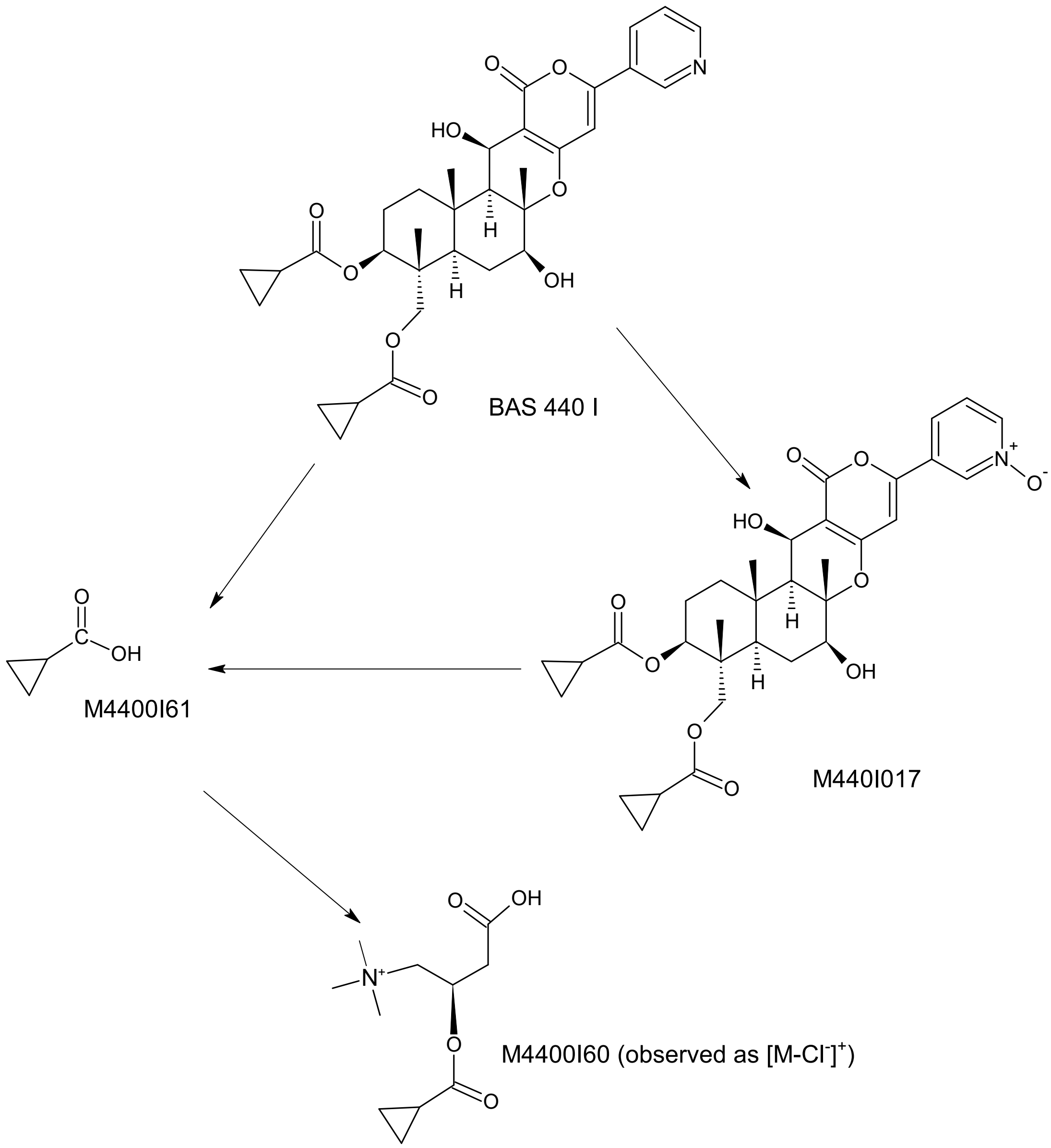


Figure B.8; Proposed Metabolic Pathway of Afidopyropen in Ruminants (Pyranone-4-^{14}C Label)

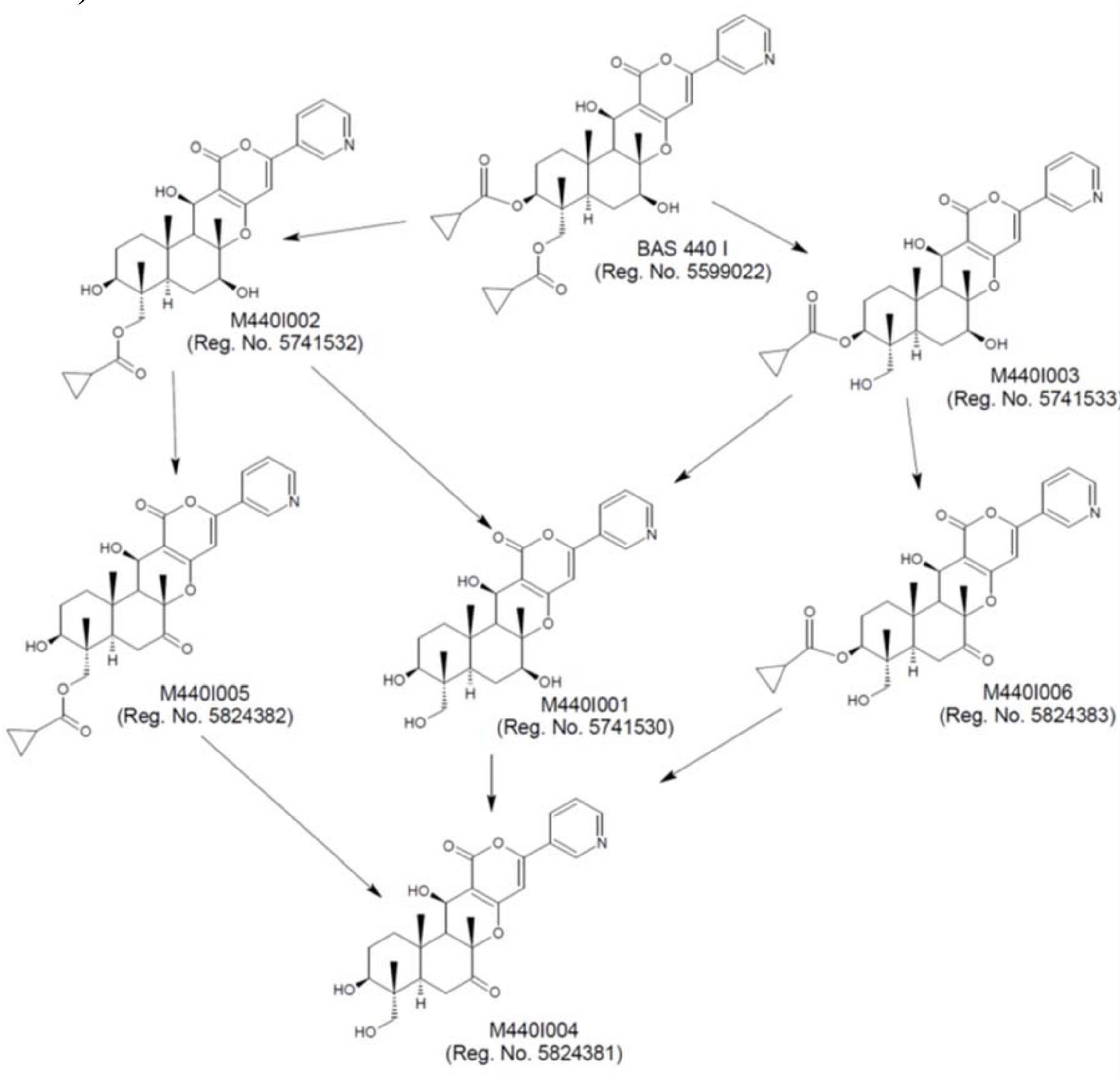


Figure B.9; Proposed Metabolic Pathway of Afidopyropen in Ruminants (CPCA-^{14}C Label)

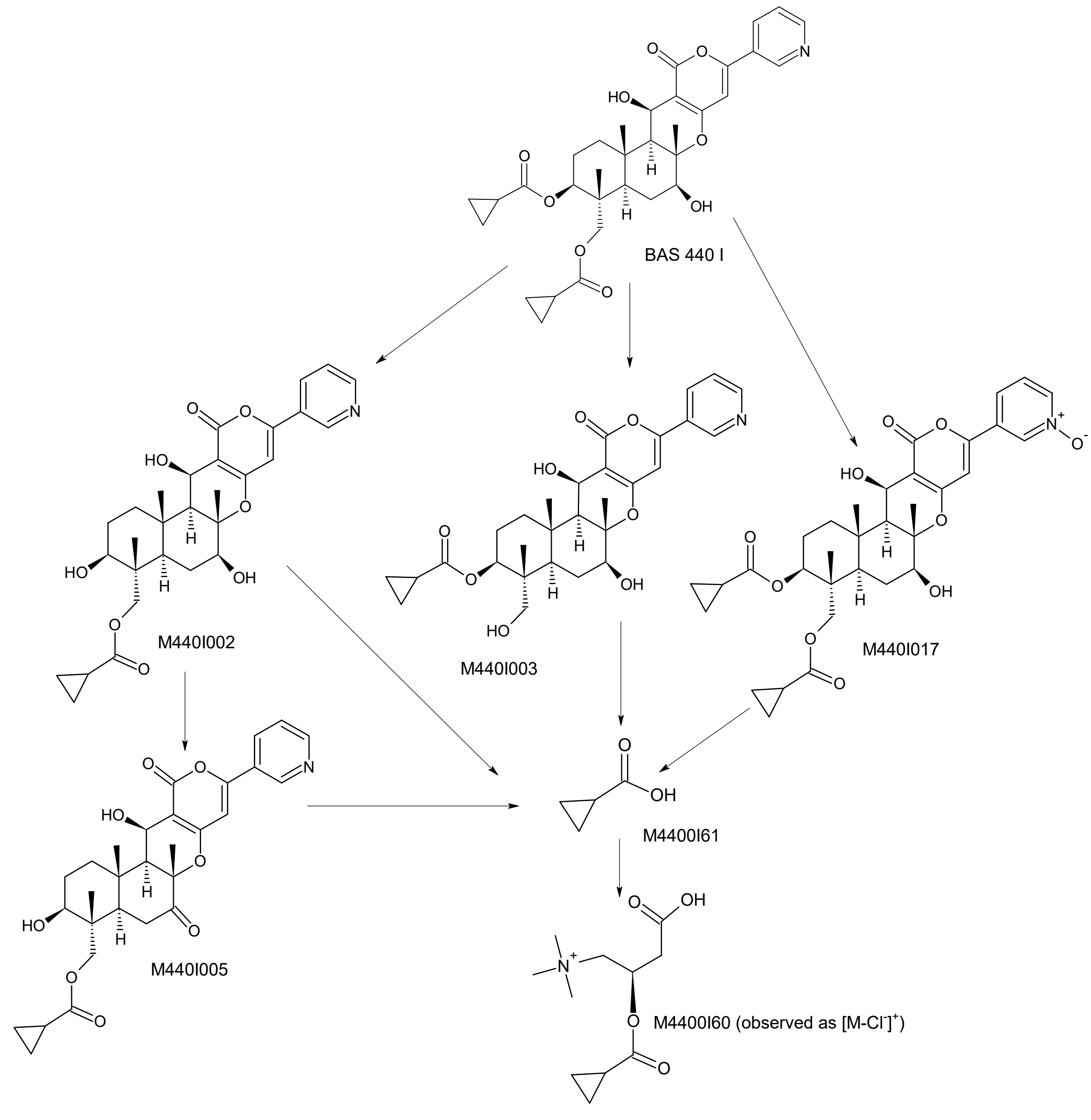


Figure B.10; Proposed Metabolic Pathway of Afidopyropen in the Rat

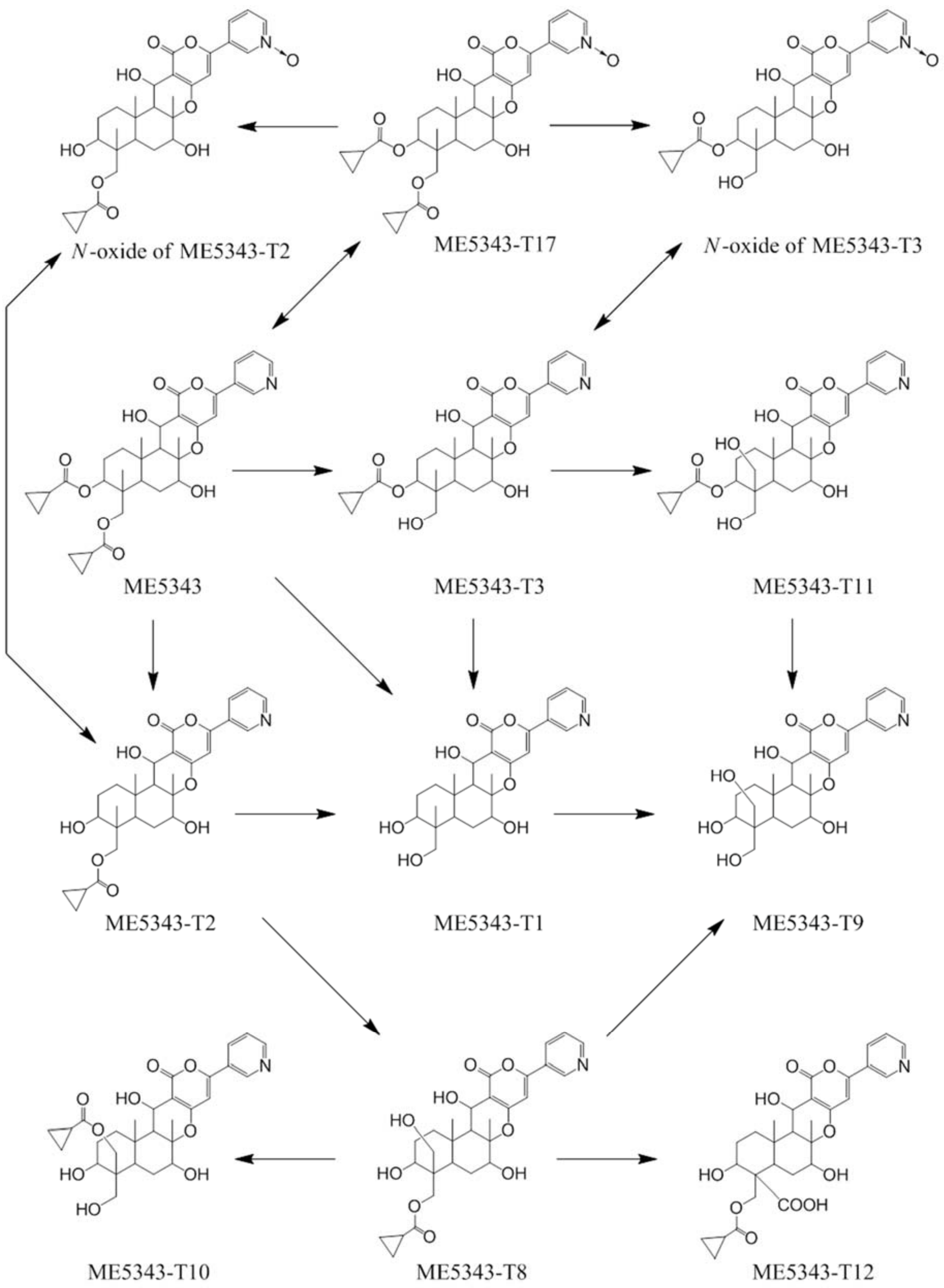
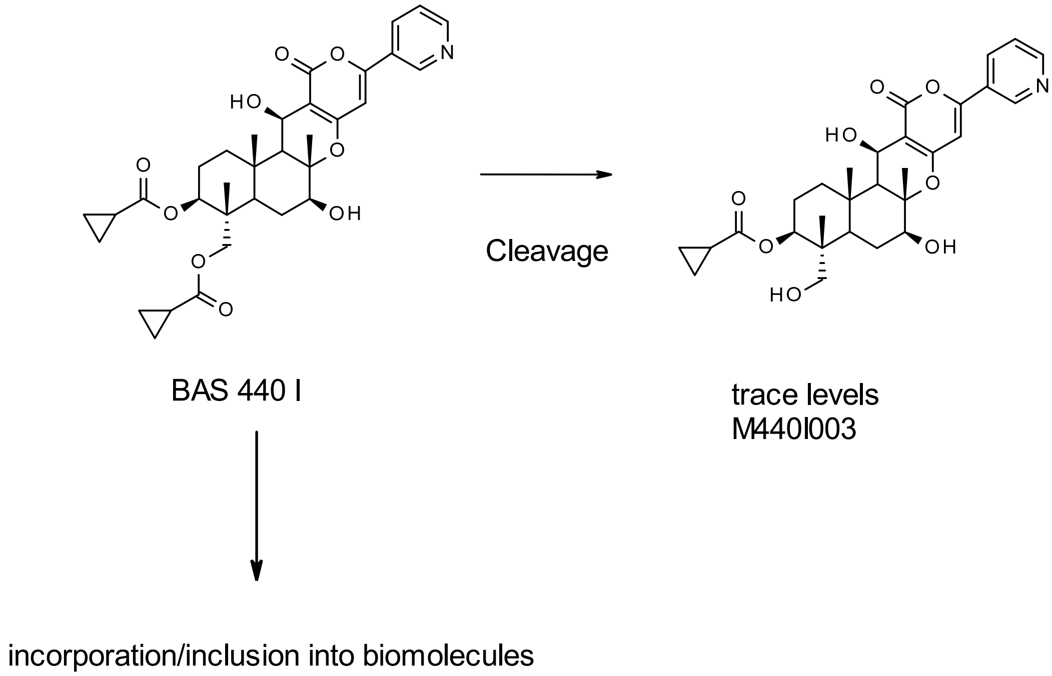


Figure B.11; Metabolic Pathway of Afidopyropen in Confined Rotational Crops



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
Proposed MRL estimate		
- Highest residue	0.058	0.056
- Mean + 4 SD	0.095	0.098
- CF x 3 Mean	0.091	0.110
Unrounded MRL	0.095	0.110
Rounded MRL	**0.10**	**0.15**
	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	**Afidopyropen**	**Afidopyropen**
Crop	**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

<u>Proposed MRL estimate</u>

- 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
Percentage of censored data	13%
Number of non-censored data	7
Lowest residue	0.010
Highest residue	2.733
Median residue	1.196
Mean	1.315
Standard deviation (SD)	0.825
Correction factor for censoring (CF)	0.917
<u>Proposed MRL estimate</u>	
- Highest residue	2.733
- Mean + 4 SD	4.616
- CF x 3 Mean	3.617
Unrounded MRL	<u>4.616</u>
Rounded MRL	**<u>5.0</u>**

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

Proposed MRL estimate

- Highest residue	0.600
- Mean + 4 SD	0.814
- CF x 3 Mean	1.600
Unrounded MRL	1.600
Rounded MRL	**2.0**

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
Percentage of censored data	67%
Number of non-censored data	4
Lowest residue	0.010
Highest residue	0.059
Median residue	0.010
Mean	0.010
Standard deviation (SD)	0.059
Correction factor for censoring (CF)	0.010
Proposed MRL estimate	
- Highest residue	0.059
- Mean + 4 SD	0.077
- CF x 3 Mean	0.030
Unrounded MRL	0.077
Rounded MRL	0.08

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
Proposed MRL estimate			
- 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	0.121	0.116	0.130
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
Proposed MRL estimate			
- 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	0.075	0.097	0.125
Rounded MRL	**0.08**	**0.10**	**0.15**

High uncertainty of MRL estimate due to small dataset.

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	**Afidopyropen**	**Afidopyropen**
Crop	**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	Afidopyropen	Afidopyropen
Crop	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
Proposed MRL estimate		
- Highest residue	NA	0.012
- Mean + 4 SD	NA	0.014
- CF x 3 Mean	NA	0.013
Unrounded MRL	NA	0.014
Rounded MRL	0.010	0.015
	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	*		
		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
Proposed MRL estimate			
- 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	0.027	0.011	NA
Rounded MRL	**0.03**	**0.015**	**0.010**
	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	*
		0.010	*		
		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
Proposed MRL estimate			
- 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	0.463	1.730	2.000
Rounded MRL	**0.50**	**2.0**	**2.0**

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	2.220
Rounded MRL	**3.0**

Residues (ppm)	
0.128	
0.774	
1.275	
0.418	
0.027	
0.283	
0.132	

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

Compound	**Afidopyropen**	**Afidopyropen**	**Afidopyropen**
Crop	**Almond, Nutmeat (Concentrated Spray Application)**	**Pecan, Nutmeat (Concentrated Spray Application)**	**Pistachio, Nutmeat (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)	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
Proposed MRL estimate			
- Highest residue	NA	NA	NA
- Mean + 4 SD	NA	NA	NA
- CF x 3 Mean	NA	NA	NA
Unrounded MRL	NA	NA	NA
Rounded MRL	**0.010**	**0.010**	**0.010**
	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	*		

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
Proposed MRL estimate			
- Highest residue	NA	NA	NA
- Mean + 4 SD	NA	NA	NA
- CF x 3 Mean	NA	NA	NA
Unrounded MRL	NA	NA	NA
Rounded MRL	**0.010**	**0.010**	**0.010**
	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
Percentage of censored data	NA
Number of non-censored data	NA
Lowest residue	NA
Highest residue	NA
Median residue	NA
Mean	NA
Standard deviation (SD)	NA
Correction factor for censoring (CF)	NA

Proposed MRL estimate

- Highest residue	NA
- Mean + 4 SD	NA
- CF x 3 Mean	NA
Unrounded MRL	NA
Rounded MRL	**0.010**

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	*

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	0.642	0.048	0.061	0.064
Rounded MRL	**0.70**	**0.05**	**0.06**	**0.07**
	.		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	0.073	0.160	0.128
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.	OCSPP 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 Agroscience 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 Agroscience Services, Inc., Mid-South Ag Research, Inc., AgPro Partners Midwest, LLC, AGVISE Reasearch, 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 Agroscience Services, Inc., Southeast Ag Research, Inc., South Texas Ag Research-RGV, Inc., Coastal Rsearch 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 Agroscience 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 Agroscience 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 Agroscience 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 Agroscience 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 Agroscience 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 Agroscience 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 Agroscience 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