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

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM

Date: 26-JAN-2018

SUBJECT: Reduced Residue Chemistry Data Requirements for Seed-Treatment Uses.

FROM: Dana M. Vogel, Division Director
Health Effects Division (HED; 7509P)

TO: Michael L. Goodis, P.E., Division Director
Registration Division (RD; 7505P)

And

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In the past, HED has received multiple waiver requests for seed-treatment field-trial residue data and has reviewed multiple field-trial datasets that indicated that there was the potential to reduce the number of field trials required to support the registration of seed-treatment uses. To evaluate this hypothesis, the HED Chemistry Science Advisory Council (ChemSAC), in collaboration with the Health Canada Pest Management Regulatory Agency (PMRA), has performed a retrospective analysis of all seed-treatment residue data that have been submitted to EPA/PMRA and has developed a tiered approach for determining if current crop-specific field trial data requirements are required to support new seed-treatment uses, or if a reduction in the number of required field trials is appropriate. Two decision trees were developed that detail the process for determining the residue chemistry field trial data requirements for seed-treatment uses, one for potato seed-treatments only and one for all remaining crops. The unique nature of potato seed-treatment requires separate considerations. To support the proposed reduction in field trials, a case study was also conducted using the available sedaxane data to demonstrate how the proposed seed-treatment decisions trees would affect the ultimate number of field trials required. That case study is included in this memo.

The outlined procedure for determining the number of field trials for seed-treatment uses, except for potato seed-treatment, differs from current HED guidance in that it:

1) Provides direction concerning data requirements in cases where the seed-treatment use is being proposed for a crop that has existing foliar uses of the same active ingredient. If the crop has an existing foliar use (or a foliar use is being requested concurrently with the seed-

treatment use), then the need for additional field trial data specific to the seed-treatment use can generally be reduced or eliminated. If there are no additional metabolites of concern from soil application and the total foliar plus seed-treatment rate does not exceed 125% of the registered (or proposed) maximum seasonal foliar application rate, then no additional seed-treatment field trial data will be required, assuming a complete residue chemistry database is available to support the foliar uses. The tolerances established in support of the foliar use will then cover the residues expected from the seed-treatment use.

2) In cases where field residue trials are required to support the seed-treatment use, allows for a 50% reduction in the number of trials for raw agricultural commodities (RACs) that are exclusively livestock feed items.

3) Allows for a significant reduction in residue data required in cases where the seed-treatment application rate is low (≤10 g ai/100 kg seed). Examination of the existing database indicated that residues are far more likely in livestock feed items than in RACs that are human food items. Therefore, for human foods, no field trial data are required and a limit of quantitation (LOQ)-level tolerance is set; for RACs that are only livestock feed items, a 50% reduction in the number of trials can be applied (however, a minimum of three trials are required).

For potato-seed piece treatment, the only situation in which residue chemistry data can be reduced is in cases where a radiotracer study has been performed in which potatoes are grown from seed-pieces treated at a 1X application rate and the residues of concern are <5 ppb in potato tubers. No further studies are required, and the use is considered non-food.

Case Study: Sedaxane

- For sedaxane, there were three separate petitions for seed-treatment of a variety of crops.
- If the seed-treatment decision tree were used, 109 field trials would have been waived, 40 field trials would have reduced data requirements, and five processing studies would have been waived.
- The same regulatory decision would have been made with a reduced dataset, as outlined in the seed-treatment decision tree. Through the submission of a reduced dataset, both the regulated community and the regulatory agency could have saved substantial resources while still providing a strong, health-protective regulatory position.
- Additionally, based on this new approach, waivers will no longer need to be submitted if the seed-treatment decision tree indicates that the data are not required.

Conclusions

The application of these decision trees will save both the petitioners and the Agency considerable resources in terms of conducting, submitting, and reviewing the studies while still obtaining the data necessary to support seed-treatment pesticide registrations that are health-protective. These changes are effective immediately upon dissemination.

Attachments:

Attachment 1: Seed-Treatment Focus Group (STFG) Guidance Document
Attachment 2: Sedaxane Case Study

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Date: 26-JAN-2018

SUBJECT: **Seed-Treatment Focus Group (STFG) Guidance Document**

FROM: George F. Kramer, Ph.D., Senior Chemist
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THROUGH: HED Management Team

TO: HED Chemistry Science Advisory Council (ChemSAC)

I. Executive Summary

HED's Management Team charged the STFG, in collaboration with PMRA, to perform a retrospective analysis of all seed-treatment residue data that have been submitted to EPA/PMRA and develop a tiered approach for determining if current data requirements are appropriate or if some streamlining is possible.

In response, the STFG developed a decision tree that details the process for determining the residue chemistry data requirements for seed-treatment use (see Appendix 1). The outlined procedure differs from current HED guidance in that it: 1) Provides direction concerning data requirements in cases where the seed-treatment use is being proposed for a crop that has existing foliar uses; 2) In cases where field residue trials are required to support the seed-treatment use, allows for a reduction in the number of trials for raw agricultural commodities (RACs) that are exclusively livestock feed items; and 3) Allows for a significant reduction in residue data required in cases where the seed-treatment application rate is low. The above discussion is not applicable to potato seed-piece (PSP) application, as the unique nature of this application requires separate considerations (see Appendix 2). Note that this document will supersede the previous ChemSAC guidance ("Classification of Seed Treatments as Food or Nonfood Uses," dated 10/28/99).

II. Detailed Considerations

The STFG, in collaboration with PMRA, performed a retrospective analysis of all seed-treatment residue data that have been submitted to EPA/PMRA, reviewed, and found acceptable. In addition, previous ChemSAC guidance ("Classification of Seed Treatments as Food or Nonfood Uses," dated 10/28/99) and subsequent ChemSAC decisions were consulted. Based on this information, a decision tree that details the process for determining the residue chemistry data requirements for seed-treatment use was developed (see Appendix 1). The following discussion is not applicable to PSP application, as the unique nature of this application requires separate considerations (see Appendix 2) and will be further discussed below.

A. Seed-treatment (excluding PSP Application)

Maximum Theoretical Residue in Harvested RACs

First, cases where the application rate was low enough to preclude the possibility of significant residues in the harvested crop were considered. As detailed in "Classification of Seed Treatments as Food or Nonfood Uses," if residues are <5 ppb (0.005 ppm) in all RACs of concern for the crop as delineated in Table 1 of Guideline 860.1000, then a non-food (NF) designation is appropriate. Using the maximum seeding rate and minimum yield per acre, the rates at which the maximum theoretical residue would equal 5 ppb (based solely on growth dilution of residues) were calculated for various crops (see Appendix 3). All treatments at or below these estimated rates will be considered NF uses. No additional data are required and no tolerances are needed.

Foliar Use Also Registered (or Proposed) for the Crop

The next consideration is whether the seed-treatment use is being proposed for a crop that has existing foliar uses. If the crop has an existing foliar use (or a foliar use is being requested concurrently with the seed-treatment use), then the need for additional residue chemistry data specific to the seed-treatment use can generally be reduced or eliminated. Consideration must be given as to whether the residues of concern (ROC) for tolerance enforcement are the same for foliar and soil treatments (including primary and rotational crop metabolism data). This decision is made by the HED Residues of Concern Knowledgebase Subcommittee (ROCKS) by comparing the foliar metabolism data with confined rotational crop data (or primary crop metabolism studies using soil application and any seed-treatment metabolism data, if available).

If there are no additional metabolites of concern from soil application and the total foliar plus seed rate does not exceed 125%[1] of the registered (or proposed) maximum seasonal foliar application rate, then no additional seed-treatment residue chemistry data will be required, assuming a complete residue chemistry database is available to support the foliar uses. The tolerances established in support of the foliar use will then cover the residues expected from the seed-treatment use.

If there are additional metabolites of concern from soil application, then additional residue data may be required to support the seed-treatment use (i.e., residue data for soil metabolites from seed-treatment field trials). This decision will be made on a case-by-case basis and will depend on the application rate and the applicability of any existing rotational crop data.

[1] As specified by the Organization for Economic Co-operation and Development (OECD) Guidelines (Test No. 509: Crop Field Trial), application rates within 25% are considered equivalent for tolerance setting.

When the seed-treatment rate is significant in comparison to the foliar rate (i.e., maximum per-acre seed-treatment rate ≥25% of the foliar rate) and residues from the seed-treatment are expected to be significant in comparison to the foliar treatment, the petitioner should generate field trial data representative of both use patterns combined, in order to ensure that the tolerance will be set at the proper level and will not be exceeded when a foliar use is applied to crops grown from treated seeds. In addition, in situations where higher residues are observed in the combined (seed + foliar) treatment in comparison to the foliar or seed-treatment alone, either a label restriction on the foliar end-use product specifying the foliar rate that can be applied to plants grown from treated seeds in order to limit the maximum seasonal application rate or an increased tolerance will be required.

Radiotracer Uptake Study

Seed-treatment uses that have no registered or applied-for foliar uses can often be classified as NF uses. This determination is made by performing a radiotracer uptake study in which the crop is grown from seed treated at a one-fold (1X) application rate with the radiolabeled active ingredient. If the ROC for tolerance enforcement are <5 ppb in all RACs of concern for the crop as delineated in Table 1 of Guideline 860.1000, then the use is considered NF. No additional data are required and no tolerances are needed. Note that if there is no characterization/identification of the TRR (total radioactive residues) in the radiotracer study, then it is assumed that the radioactivity consists of the parent molecule and as such, the ROC is parent (ROC = TRR).

If the ROC are ≥5 ppb in any of the RACs, then the use is considered a food use. A full set of field trial data (1X application rate) are required for all RACs in which the ROC are ≥5 ppb in the radiotracer study. Tolerances will be set based on the results of the field trial data (LOQ level for RACs in which ROC are <5 ppb). For RACs that are only livestock feed items, a 50% reduction in the number of trials can be applied (minimum of three trials). Note that all relevant residue chemistry data requirements must also be fulfilled (i.e., livestock metabolism and possibly feeding studies, plant metabolism studies, confined rotational crop studies, a validated enforcement method, etc.).

In situations where the ROC are slightly above 5 ppb in the radiotracer study, a significant reduction in data requirements is possible. The registrant has the option of performing three field trials with seed treated with unlabeled active ingredient at a five-fold (5X) rate. This option requires that adequate plant metabolism data to determine the ROC and a validated enforcement method are available. If the ROC are <LOQ in all RACs in the 5X trials, then no additional residue chemistry data are required and tolerances are set at the LOQ of the enforcement method for all RACs. If the ROC are >LOQ in any of the RACs in the 5X trials, then field trial data generated according to the proposed use pattern (1X application rate) are required for those RACs where residues were >LOQ. Processing studies, if applicable, may also be required. Tolerances will be set based on the results of the field trial data. For RACs that are only livestock feed items, a 50% reduction in the number of field trials can be applied (however, a minimum of three trials are required).

Seed-treatment Rate ≤10 g ai/100 kg seed

Situations may arise for seed-treatment uses that have no existing foliar use and a radiotracer study has not been performed. If adequate plant metabolism data are available to determine the ROC for tolerance enforcement and the application rate is ≤10 g ai/100 kg seed, then a significant reduction in data requirements is appropriate. This conclusion is based on the observation that the lowest seed-treatment rate at which residues have been found in edible RACs is ~50 g ai/100 kg

seed (see Appendix 4 for a full justification of 10 g ai/100 kg seed cut-off and for justification for requiring field trials on feedstuff only). For human foods, no field trial data are required and a LOQ-level tolerance is set; for RACs that are only livestock feed items, a 50% reduction in the number of trials can be applied (however, a minimum of three trials are required). If the application rate is >10 g ai/100 kg seed and adequate plant metabolism data available to determine the ROC, then the registrant has the option of performing a radiotracer study (and proceeding as described above) or performing a full set of field trials and processing studies (if applicable).

Additional Considerations: 1) For highly toxic chemicals, the 5 ppb ROC threshold value may be reduced; 2) If the ROC are <5 ppb in radiotracer studies conducted on five representative crops (small grain, radish or garden beets (analyze both root and tops), leaf lettuce, soybeans, and a short season fruiting or cucurbit vegetable), then seed-treatment uses on all crops will be considered NF; 3) If the ROC in wheat forage, hay, grain, and straw are all <5 ppb, then the seed-treatment can be considered NF for the following crops: wheat, barley, oats, rye, sorghum, triticale, buckwheat, rice, and millet. Also, if the ROC is <5 ppb in all wheat and corn RACs, then uses on all cereal grains can be classified as NF uses; 4) For uses on soybeans and peanuts (or other legumes that are not grown as livestock feeds) where ROC ≥5 ppb in forage/hay, but <5 ppb in seeds or nutmeats, the uses are classified as food uses and field trials are required unless the petitioner chooses to restrict feeding of the foliage parts of these crops. This restriction would eliminate the need for crop field trials on the foliage, but a LOQ-level tolerance would still be needed for the seeds or nutmeats. 5) If tolerances are needed, then a validated enforcement method will always be required; 6) A minimum of three trials are required for tolerance setting; 7) In cases where field trial data are waived for a human food RAC, a processing study will also not be required.

B. Potato Seed-Piece Application

Due to the unique nature of PSP application, a separate decision tree was developed (see Appendix 2) to detail the process for determining the residue chemistry data requirements for this use pattern.

When a registrant petitions for a PSP application, there are two possible scenarios with respect to the potato use: 1) either there are no registered potato uses; or 2) in-furrow and/or foliar uses are registered. Each scenario requires specific residue chemistry data requirements, which are described below.

<u>New Use for Potato</u>
Three different options are considered under this scenario:

Option 1: Radiotracer Uptake Study
A significant reduction in residue chemistry data requirements can be granted to a PSP application for an active ingredient that has no other registered potato uses. This determination is made by performing a radiotracer study in which potatoes are grown from seed-pieces treated at a 1X application rate with the radiolabeled active ingredient. If the ROC are <5 ppb in potato tubers, then no further data are required, and the use is considered NF. Note that if there is no characterization/identification of the TRR in the radiotracer study, then the ROC = TRR (as it is assumed that the radioactivity consists of the parent molecule and as such, the ROC is parent). If the ROC are ≥5 ppb in potato tubers in the radiotracer study, then PSP field trial data (1X

application rate) and potato processing data are required. Tolerances will be set based on the results of the PSP field trial data and all relevant residue chemistry data requirements must be fulfilled, unless other data are available (see Options 2 or 3 below).

Option 2: Foliar or Seed-treatments Registered in Other Crops
If there are existing foliar and/or seed-treatment uses registered in crops other than potatoes, then the need for additional residue chemistry data can generally be reduced. Consideration must be given as to whether the ROC are the same for foliar and soil treatments. This decision is made by comparing the foliar metabolism data (consisting of three dissimilar crops, including a root crop) with confined rotational crop data (or primary crop metabolism studies using soil application and any seed-treatment metabolism data, if available).

If there are no additional metabolites of concern from soil application, then no additional potato metabolism data will be required, assuming a complete residue chemistry database is available to support the foliar uses. A full complement of PSP field trials and potato processing data are required.

If there are additional metabolites of concern from soil application (thus the ROC is not the same for foliar and soil treatments), then a potato metabolism study (PSP or in-furrow treatment) may be required, in addition to the full complement of PSP field trials and potato processing data.

Option 3: No Other Uses Registered
All residue chemistry data requirements must be fulfilled.

<u>Potato Use Registered: In-furrow or Foliar</u>
If a potato in-furrow use is registered and assuming a complete residue chemistry database is available to support the in-furrow use, then only a full complement of PSP field trials is required. If the petitioner can demonstrate equivalency of residues between in-furrow and PSP applications by conducting bridging trials at similar application rates, then the full complement of PSP field trials can be waived and the in-furrow residue data will be considered sufficient to support the PSP use pattern. In order to demonstrate equivalency between in-furrow and PSP field trials, a minimum of three side-by-side trials in representative growing regions (including the region where the highest in-furrow residues were observed) must be conducted according to the proposed use.

If only a potato foliar use is registered, then the need for additional residue chemistry data can be reduced. Consideration must be given as to whether the ROC are the same for foliar and soil treatments. If there are no additional metabolites of concern from soil application, then no additional potato metabolism data will be required, assuming a complete residue chemistry database is available to support the foliar uses. A full complement of PSP field trials is required. If there are additional metabolites of concern from soil application (thus the ROC are not the same for foliar and soil treatment), then a potato metabolism study (PSP or in-furrow treatment) may be required in addition to the full complement of PSP field trials.

In summary, in all cases (except radiotracer study that shows no uptake in potato tubers), a full complement of PSP field trials is required. A tolerance will be calculated based on the results of the PSP trial data and will be compared to any existing potato tolerances. If a potato tolerance is not already established, then potato tolerance from the PSP application will be promulgated. On

the other hand, if a potato tolerance is already established, it will be compared to the PSP calculated tolerance and if the latter tolerance is higher, the tolerance will be revised accordingly.

III. Conclusions

Separate decision trees detailing the process for determining the residue chemistry data requirements for seed-treatment use (see Appendix 1) and the PSP application (see Appendix 2) were developed.

For seed-treatment (excluding PSP), the outlined procedure differs from current practice in that it:
1) Provides direction concerning data requirements in cases where the seed-treatment use is being proposed for a crop that has existing foliar uses. If the crop has an existing foliar use, then the need for additional data can generally be reduced or eliminated. Currently, these situations are addressed on a case-by-case basis and generally require ChemSAC review.

2) In cases where field residue trials are required to support the seed-treatment use, a 50% reduction in the number of trials for RACs that are exclusively livestock feed items is allowed. This decision was based on the retrospective analysis of currently available seed-treatment residue data that showed that residues in livestock feeds items from seed-treatment are generally low. However, a minimum of three trials is always required.

3) A significant reduction in residue data required is allowed in cases where the seed-treatment application rate is low. The rate at which the maximum theoretical residue = 5 ppb (based solely on growth dilution of residues) was calculated for various crops (see Appendix 3). All treatments at or below these rates will be automatically considered NF uses. No additional data are required and no tolerances are needed.

4) Situations may arise for seed-treatment uses that have no corresponding foliar use and a radiotracer study has not been performed. If adequate plant metabolism data (including primary and rotational crops) are available to determine the ROC and the application rate is ≤10 g ai/100 kg seed, then a significant reduction in data requirements is appropriate. For human foods, no field trial data are required and a LOQ-level tolerance is set; for RACs that are only livestock feed items, a 50% reduction in the number of trials can be applied (however, a minimum of three trials are required).

The above discussion is not applicable to PSP application, as the unique nature of this application requires separate considerations (see below for details).

For PSP treatment, the outlined procedure differs from current practice in that it:
1) Provides direction concerning data requirements in cases where the PSP treatment is being proposed for a crop that has existing foliar uses. If the crop has an existing foliar use, then the need for additional data can generally be reduced. Consideration must be given as to whether the ROC are the same for foliar and soil treatments. If there are no additional metabolites of concern from soil application, then no additional potato metabolism data will be required. A full complement of PSP field trials is required.

2) In cases where a potato in-furrow use is registered and assuming a complete residue chemistry database is available to support this use, then only a full complement of PSP field trials is required.

3) In cases where a radiotracer study has been performed in which potatoes are grown from seed-pieces treated at a 1X application rate and the ROC are <5 ppb in potato tubers, no further studies are required, and the use is considered NF.

IV. References

"Classification of Seed Treatments as Food or Nonfood Uses," ChemSAC guidance dated 10/28/99.

OECD Guidelines Test No. 509: Crop Field Trial.

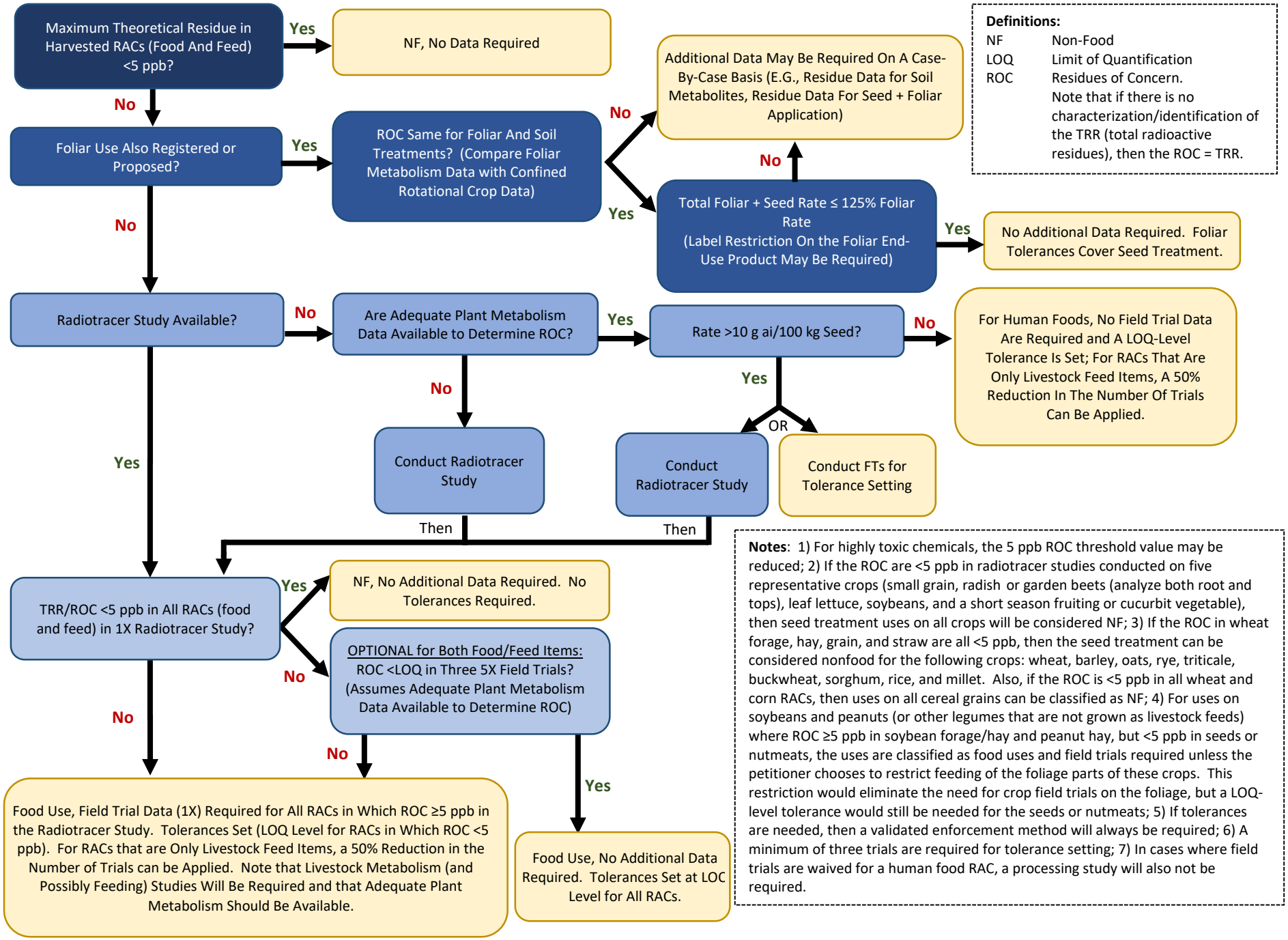
J. Becker and S. Ratnayake. "Acres Planted per Day and Seeding Rates of Crops Grown in the United States." USEPA Memo Dated 10 November 2010.

"Guidelines for Reduced Residue Field Trial Requirements to Support Joint Projects Between Canada and the United States" (https://www.canada.ca/en/health-canada/services/consumer-product-safety/reports-publications/pesticides-pest-management/policies-guidelines/science-policy-notes/2017/guidance-joint-canada-united-states-field-trial-requirements-spn2017-02.html)

Appendices

Appendix 1: Decision Tree for the Residue Chemistry Data Requirements of Seed-Treatment
Appendix 2: Decision Tree for the Residue Chemistry Data Requirements of PSP Treatment
Appendix 3: Seed-treatment Application Rates at Which the Maximum Theoretical Residue = 5 ppb Based on Growth Dilution of Residues
Appendix 4: Rationale Supporting Reduced Data Requirements for Application Rates at or Below 10 g ai/100 kg seed

Appendix 1: Decision Tree for Seed Treatment (Excluding Potato Seed-Piece Treatment)



Appendix 2: Decision Tree for the Residue Chemistry Data Requirements of Potato Seed-Piece (PSP) Treatments

LOQ = Limit of Quantification.
ROC = Residues of Concern.
[1] If in The Radiotracer Study There Is No Characterization/ Identification of The TRR (Total Radioactive Residues), Then The ROC = TRR.
Note That If Tolerances Are Needed, A Valid Enforcement Analytical Method Is Required.

Potato Seed-Piece Use

New Use
No Uses Registered on Potatoes

Choose One of The 3 Options

Option 1 — Is A Radiotracer Study Available?
- Yes → ROC[1] <5 ppb in Potato Tubers?
  - Yes → NF, No Additional Data Required. No Tolerances Required.
  - No → All Relevant Residue Chemistry Data Requirements Must Be Fulfilled, Unless Other Data Are Available (See Option 2 Or 3).

Option 2 — Foliar/Seed Uses Registered in Other Crops?
- Yes → Same ROC for Foliar and Soil Treatments ?
  - Yes → No Additional Potato Metabolism Study Required. → Full Complement of PSP Field Trials and Potato Processing Data Required.
  - No → Potato Metabolism Study May Be Required (PSP Or In-Furrow Treatments). → Full Complement of PSP Field Trials and Potato Processing Data Required.

Scientific Rationale: Similar Metabolic Pathways in 3 Dissimilar Crops, Including a Root Crop (Different Treatment Regime; Foliar/Seed/Soil) and Confined Crop Rotation.

Implies That There Are Adequate Ruminant Metabolism Data, Analytical Methods and Rotational Crop Data

Option 3 — No Other Uses Registered?
- Yes → All Relevant Residue Chemistry Data Requirements Must Be Fulfilled.

Potato Use Registered
Foliar or In-Furrow

In-Furrow Use?
- Yes → Full Complement of PSP Field Trials Required.

Implies Adequate Plant (Potato) Metabolism Data

Foliar Use ONLY?
- Yes → Same ROC for Foliar and Soil Treatments?
  - Yes → No Additional Potato Metabolism Study Required. → Full Complement of PSP Field Trials Required.
  - No → Potato Metabolism Study May Be Required (PSP Or In-Furrow Treatments). → Full Complement of PSP Field Trials Required.

Implies That There Are Adequate Ruminant Metabolism Data, Analytical Methods, Potato Processing Data and Rotational Crop Data

Scientific Rationale: Similar Metabolic Pathways in 3 Dissimilar Crops, Including A Root Crop (Different Treatment Regime; Foliar/Seed/Soil) And Confined Crop Rotation.

PSP Field Trials Are Required Even If The PSP Rate Is Similar to The In-Furrow Rate Unless Bridging Trials (Min 3 Field Trials) Demonstrating Equivalency of Residues Between In-Furrow and PSP Trials Are Provided.

Appendix 3: Seed-treatment Application Rates at Which the Maximum Theoretical Residue = 5 ppb Based on Growth Dilution of Residues

Crop Group / Subgroup	Crop	Maximum Planting Rate (lb/A) [kg/A]	Minimum Yield (lb/A) [kg/A]	Rate at Which Maximum Theoretical Residue= 5 ppb [g ai/100 kg seed]*
1A	Beet, Sugar	1.25 [0.57]	40,000 [18,144]	16
1A	Carrot	1 [0.454]	17,000 [7,711]	8.5
1B	Beet, garden	15 [6.8]	20,000 [9,072]	0.67
1C	Potato	3,000 lb seed pieces/A [1,361]	24,000 [10,886]	0.0040
3A	Onion, bulb	3 [1.361]	30,000 [13,608]	5.0
3B	Onion, green	5 [2.2.268]	16,000 [7,257]	1.6
4A	Lettuce, leaf	1 [0.454]	12,000 [5,443]	2.0
5A	Broccoli	2 [0.91]	5,000 [2,268]	1.2
5A	Cabbage	1.5 [0.68]	15,000 [6,804]	5.0
6A	Bean, snap	100 [45]	4,000 [1,814]	0.020
6B	Pea, succulent	150 [68]	2,800 [1,270]	0.0093
6C	Bean, dry	120 [54]	1,552 [704]	0.0065
7	Pea, field	20 [9.07]	2,242 [1,017]	0.056
8A	Tomato	2 [0.91]	10,000 [4,535]	2.5
8B	Pepper, bell	2 [0.91]	8,000 [3,628]	2.0
9A	Cantaloupe	2 [0.91]	8,000 [3,628]	2.0
9B	Cucumber	3 [1.361]	8,000 [3,628]	1.3
9B	Watermelon	4 [1.8]	18,000 [8,165]	2.3
15	Corn, Sweet	15 [6.8]	6,000 [2,722]	0.20
15	Corn, Field	16 [7.3]	7,840 [3,556]	0.24
15	Corn, Pop	5 [2.3]	2,846 [1,291]	0.28
15	Rice	100 [45]	7,000 [3,175]	0.035
15	Wheat, grain	150 [68]	4,980 [2,259]	0.017
16	Wheat, forage	150 [68]	4,400 [1,996]	0.015
17	Bluegrass, Kentucky	10 (4.5)	3,500 [1,588]	0.18
18	Alfalfa	20 [9.1]	5,000 [2,268]	0.13
18	Clover, red	10 [4.5]	6,600 [2,2,293]	0.33
20	Canola (Rapeseed)	6 [2.7]	1,500 [680]	0.13
20	Cotton	18 [8.2]	600 [272]	0.017
20	Soybean	65 [29]	2,700 [1,224]	0.021
20	Sorghum, Grain	15 [6.8]	2,800 [1,270]	0.093
20	Sunflower	8 [3.6]	1,000 [454]	0.063
Others	Peanut, runner	135 [61]	3,000 [1,361]	0.011

* = Min Yield/Max Planting Rate × 0.0005.

Appendix 4: Rationale Supporting Reduced Data Requirements for Application Rates at or Below 10 g ai/100 kg seed

Advantages of seed-treatment applications include the following: precise targeting of pesticide residues where they are most effective, reduced exposures to non-target organisms, lower pesticide residue levels at crop harvest, and cost efficiencies resulting from reduced needs for foliar applications during the crop-growing season. As a result of these advantages, seed-treatment use requests have increased and there is now a robust residue chemistry database available for seed-treatment uses.

Careful examination of this database shows that detectable residues are seldom found in the mature crops at harvest. When residues are found, they are typically low and more likely found in livestock feedstuffs (such as forage, hay, straw, etc.) than in human foods (such as grains, seeds, fruits, etc.). Potato seed pieces (PSPs) are considered a special case with only 5 - 11 seeds per pound; most seeds are considerably smaller. For example, celery has 1,000,000 - 1,152,000 seeds per pound (J. Becker and S. Ratnayake, Acres Planted per Day and Seeding Rates of Crops Grown in the United States, 10-NOV-2010). Because PSPs are much larger than other seeds (≥ ~100×), they are excluded from the considerations that follow.

When the seed-loading rate is expressed in grams of active ingredient per 100 kg of seed treated, the seed-treatment residue chemistry database has no examples of detectable residues in human foods at crop maturity following seed-treatment at a rate of 10 g ai/100 kg seed or less. The lowest seed-treatment rate at which residues have been found in edible RACs is 50 g ai/100 kg seed. The STFG agreed that because it is unlikely that detectable residues will be found in human foods at rates five times lower than the lowest rate at which residues in human foods have been reported in the current residue chemistry seed-treatment database, residue trials may not be necessary when proposed application rates are 10 g ai/100 kg seed or less.

While the current requirements for field trials for uses involving high seed-loading rates appear appropriate, the data support a modification of field trial requirements for uses where low seed-loading rates are proposed. Thus, when the target application rate is 10 g ai/100 kg seed or lower, no field trials are needed for crops that do not produce livestock feedstuffs, and tolerances should be set at the LOQ of the analytical method for the relevant human food RAC. In cases where crops do form livestock feedstuffs, a 50% reduction in the number of field trials is appropriate (with a minimum of three trials) so that tolerance levels may be set for these RACs. Refer to Appendix 1 for the complete decision tree developed for residue chemistry data requirements pertaining to seed-treatment uses.

Attachment 2: Sedaxane Case Study

Introduction

As part of its review of the available residue chemistry seed-treatment database, the STFG has put together a case study of the chemical sedaxane to illustrate how the application of the seed-treatment decision tree may result in savings. For sedaxane, three separate petitions were received for seed-treatment of a variety of crops. If the seed-treatment decision tree were used for these petitions, a total of 109 field trials would have been waived, 40 field trials would have reduced data requirements, and five processing studies would have been waived. The petitions and an explanation of the savings are outlined below. The STFG notes that depending on the use pattern, these types of savings may not apply to all chemicals; however, when chemicals do meet the criteria, both petitioners and the Agency would save a considerable amount of resources in terms of conducting, submitting, and reviewing the studies.

Case Study- Sedaxane

First petition: Application for Section 3 registration for seed-treatment use on canola, cereal grains (barley, oats, rye, triticale, and wheat), and soybean at 5.0 g ai/100 kg seed. As the submitted petition was a joint review with Canada (PMRA), the number of field trials required is based on the draft document "Guidelines for Reduced Residue Field Trial Requirements to support Joint Projects between Canada and the United States."

Acceptable metabolism/radiotracer studies to support seed-treatment uses were conducted in representative crops (wheat [40 g ai/100 kg], corn [110 g ai/100 kg], canola [7.5 g ai/100 kg], Swiss chard [40 g ai/100 kg], and soybean [110 g ai/100 kg]), in representative rotational crops at 100 g ai/ha (lettuce, turnips, and wheat), and in livestock (goats and hens). Based upon these metabolism studies HED determined that the residue of concern, and the residue for the tolerance expressions for all crops, including rotational crops, is parent only, determined as its trans and cis isomers (SYN508210 and SYN508211).

Twelve barley field trials were conducted in the U.S. in North American Free Trade Agreement (NAFTA) Growing Zones 1 (NY, 1 trial), 5 (IA and ND; 3 trials), 7 (ND; 4 trials), 9 (CO; 1 trial), 10 (CA; 1 trial), and 11 (OR and ND; 2 trials) during 2008 and 2009. Following seed-treatment at 5 g ai/100 kg seed, total sedaxane residues (SYN508210 and SYN508211) in/on barley hay at 45 days after planting (DAP) were <0.01 to <0.025 ppm with an average of 0.013 ppm. No sedaxane residues were found in barley straw and barley grains. Twelve barley field trials were conducted in Canada during the 2008 growing season in NAFTA Growing Zones 5 (MB; 1 trial), 5B (QC; 1 trial), 7 (SK; 2 trials), and 14 (MB, SK, and AB; 8 trials). Following a seed-treatment application of sedaxane at a total rate of 5 g ai/100 kg seed (1X application rate), total residues of sedaxane were all below the LOQ in/on barley (hay, grain, and straw) samples. Using the STFG Guidance Document, only 8 field trials would have been required (for hay and straw only), based on having adequate data to define the ROC and the proposed rate being <10 g ai/100 kg seed. **Total savings = 16 field trials for hay and straw and 24 field trials for grain. The submitted barley processing study would also not be required as field trials were waived for the RAC.**

Twenty wheat field trials were conducted during 2008 in NAFTA Growing Zones 2 (NC; 1 trial), 4 (LA; 1 trial), 5 (MO, KS, IA; 5 trials), 6 (TX; 1 trial), 7 (ND; 5 trials), 8 (TX; 6 trials), and 11

(OR; 1 trial). Following a seed-treatment application of sedaxane at a total rate of 5 g ai/100 kg seed (1X application rate), total sedaxane residues in/on wheat forage and wheat hay at 45 days after planting (DAP) were <0.01-0.015 ppm and <0.01-0.065 ppm, respectively. Average residues in/on wheat forage and wheat hay were 0.011 ppm and 0.017 ppm, respectively. Sedaxane residues in/on wheat straw and wheat grain at maturity were all below the LOQ. Sixteen wheat field trials were conducted in Canada during 2008 in NAFTA Growing Zones 5 (MB, 2 trials), 7 (SK, 6 trials), 7A (MB, 1 trial), and 14 (MB, SK, AB, 7 trials). Following a seed-treatment application of sedaxane at a total rate of 5 g ai/100 kg seed, residues of sedaxane were all below the LOQ in/on wheat (forage, hay, grain, and straw) samples. Using the STFG Guidance Document, only 10 trials would have been required (for forage, hay, and straw), based on having adequate data to define the ROC and the proposed rate being <10 g ai/100 kg seed. **Total savings = 26 field trials for forage, hay, and straw and 36 field trials for grain. The submitted wheat processing study would also not be required as field trials were waived for the RAC.**

Twenty soybean field trials were conducted during 2008 in Zones 2 (GA, 2 trials), 4 (LA, 3 trials), and 5 (MO, WI, ND, NE, IA, and MN, 15 trials). Following a seed-treatment application of sedaxane at a total rate of 40 g ai/100 kg seed (8X), total sedaxane residues in/on soybean forage and hay at 45 DAP were <0.01-0.065 ppm and <0.01 - 0.035 ppm, respectively. Sedaxane residues in/on soybean seed at maturity were never detected at or above 0.01 ppm. Using the STFG Guidance Document, only 10 trials would have been required (for forage and hay), based on having adequate data to define the ROC and the proposed rate being <10 g ai/100 kg seed. **Total savings = 10 field trials for hay and forage and 20 field trials for seed. The submitted soybean processing study would also not be required as field trials were waived for the RAC.**

Eight canola field trials were conducted in the United States during the 2008 growing season, encompassing Regions 2 (GA; 1 trial), 5 (WI; 2 trials), 7 (ND; 2 trials), and 11 (OR and ID; 3 trials). Following a seed-treatment application of sedaxane at a total rate of 7.5 g ai/100 kg seed, residue levels of sedaxane in/on canola seed harvested at maturity (84 to 232 days after planting) were below the LOQ (0.005 ppm for each isomer of SYN524464 and 0.01 ppm for the total). Sixteen canola field trials were conducted in Canada during the 2008 growing season in Regions 5 (MB; 1 trial), 7 (SK; 1 trial), and 14 (MB, SK, and AB; 14 trials). Following a seed-treatment application of sedaxane at a total rate of 5.87-5.95 g ai/100 kg seed or at an exaggerated rate of 17.6 g ai/100 kg seed, total residues of sedaxane in/on canola seed harvested at maturity (95 to 132 days after planting) were below the LOQ (0.01 ppm). Using the STFG Guidance Document, canola would have been considered a NF use, based on TRR less than 0.002 ppm in the canola radiotracer study. **Total savings = 24 field trials. The submitted canola processing study would also not be required as field trials were waived for the RAC.**

Second petition: Syngenta Crop Protection petitioned the EPA and PMRA to establish permanent tolerances for residues of sedaxane in/on corn [field, pop, and sweet], potato, crop subgroup 6C [pea and bean, dried shelled, except soybean, subgroup 6C], crop subgroup 20A [rapeseed subgroup 20A], and sorghum, following seed-treatment applications. The maximum proposed use rates were at 5.0 g ai/100 kg seed for pea and bean, dried shelled, except soybean, subgroup 6C; 40 g ai/100 kg seed for corn (field, pop, and sweet), rapeseed subgroup 20A, and sorghum; and 2.5 g ai/100 kg seed for potato. No new plant radiotracer/metabolism data were submitted.

Twenty trials with field corn were conducted in NAFTA Growing Zones 1 (PA, 1 trial), 2 (GA, 1 trial), 5 (KS, 1 trial; MO, 1 trial; MI, 1 trial; OH, 1 trial; IA, 7 trials; ND, 3 trials; and WI, 3 trials), and 6 (TX, 1 trial); at seven of these trials, samples were also collected at the milk stage to simulate sweet corn. Five separate trials were conducted with sweet corn in NAFTA Growing Zones 1 (PA), 3 (FL), 10 (CA), 11 (ID), and 12 (OR), and one trial with popcorn was conducted in Zone 8 (TX). In addition, three sweet corn field trials were conducted in Canada during the 2010 growing season in Zones 5 (ON), 7A (AB), and 12 (BC). Following seed-treatment at a rate of 40 g ai/100 kg seed, total residues of sedaxane were <0.005 ppm each in/on all samples of field corn [grain, forage and stover], sweet corn [K+CWHR, forage, and stover], and popcorn [grain and stover]. Using the STFG Guidance Document, as the corn metabolism study (conducted at ~3X) showed that the TRR in grain were <0.001 ppm, field trial data are only required for forage and stover, with 50% reduction being applicable. **Total savings = 14 field trials for forage and stover and 20 field trials for grain. The submitted corn processing study would also not be required as field trials were waived for the RAC.**

Five dry bean trials were conducted in NAFTA Growing Zones 7 (ND), 8 (CO), 9 (CO), 10 (CA), and 11 (OR) and five dry pea trials were conducted in NAFTA Growing Zones 5 (ND), 10 (CA), and 11 (OR; 2 trials, WA; 1 trial). In addition, five dry bean field trials were conducted in Canada during the 2010 growing season in Zones 5 (MB (1 trial), ON (2 trials), and QC (1 trial)) and 7A (AB (1 trial)); and eight dry pea field trials were conducted in Canada during the 2010 growing season in Zones 5 (MB; 2 trials) and 14 (MB; 3 trials, SK; 3 trials). Samples of dry bean forage and hay were harvested from three of the bean trials; samples of dry pea hay were harvested from three of the pea trials. Following seed-treatment at a rate of 5 g ai/100 kg seed, total residues of sedaxane were <0.005 ppm each in/on dry bean seed, hay, and forage harvested at 54-81 DAP, and in/on dry pea seed and hay harvested at maturity, 74-104 DAP. Similarly, following seed-treatment at a rate of 5 g ai/100 kg seed, residues of the cis- and trans-isomers of sedaxane were <0.005 ppm each in/on dry pea seed and hay harvested at maturity, 74-104 DAP. Using the STFG Guidance Document, only 10 trials would have been required (for forage and hay), based on having adequate data to define the ROC and the proposed rate being <10 g ai/100 kg seed. **Total savings = 23 field trials for seed.**

Sixteen potato field trials were conducted in the United States during the 2011 growing season in NAFTA Growing Zones 1 (NY; 1 trial, PA; 1 trial), 2 (NC; 1 trial), 3 (FL; 1 trial), 5 (MN; 3 trials, ND; 1 trial), 10 (CA; 1 trial), and 11 (ID; 5 trials, WA; 2 trials). In addition, thirteen field trials were completed in Canada during the 2011 growing season in Zones 1 (NB; 2 trials), 1A (PE; 5 trials), 5 (ON and QC; 2 trials each), and 7A (AB; 2 trials). Following treatment of potato seed pieces at a rate of 1.1-2.7 g ai/100 kg seed pieces, total sedaxane residues (and per-trial averages) were <0.010-<0.0184 ppm (<0.010-<0.0175 ppm) in/on potato tubers. Using the STFG Guidance Document, as no potato radiotracer study was performed, no reduction in the number of field trials is recommended. **Total savings = 0 field trials.**

Twelve field grain sorghum trials conducted in the United States during the 2010 growing season in NAFTA Growing Zones 2 (SC; 1 trial), 4 (LA; 1 trial), 5 (IA; 4 trials), 6 (TX; 2 trials), 7 (ND; 1 trial), and 8 (CO; 1 trial, and TX; 2 trials). Following seed-treatment at a rate of 40 g ai/100 kg, total residues of sedaxane were <0.005 ppm each in/on sorghum forage harvested at 54-81 DAP, as well as in/on stover and grain harvested at maturity, 107-168 DAP. Using the STFG Guidance Document, based on translation from the corn metabolism study, field trial data are only required for forage and stover, with 50% reduction being applicable. **Total savings = 6 field trials for forage and stover and 12 field trials for grain.**

Third petition: Syngenta Crop Protection petitioned the EPA to establish permanent tolerances for residues of sedaxane in/on cotton and sugar beet, following seed-treatment applications. The maximum proposed use rates were 20 g ai/100 kg seed for cotton and 660 g ai/100 kg seed sugar beet. No new plant radiotracer/metabolism data were submitted.

Twelve cotton field trials conducted in the United States during the 2012-2013 growing season in NAFTA Growing Zones 2 (SC, 1 trial), 4 (MO, 2 trials; AR, 1 trial), 6 (TX, 1 trial), 8 (OK, 1 trial; TX, 3 trials), and 10 (CA, 3 trials). Samples of gin byproducts were harvested at maturity from three trial sites. Following seed-treatment at a rate of 20 g ai/100 kg, total residues of sedaxane were <0.005 ppm each in/on all samples of cotton seed and cotton gin byproducts. As no cotton radiotracer study was performed, no reduction in the number of field trials is automatically recommended. **Total savings = 0 field trials.**

Twelve sugar beet field trials were conducted in the United States during the 2012 growing season in NAFTA Growing Zones 5 (ND, 2 trials; NE, 1 trial; MN, 2 trials), 7 (NE, 1 trial), 8 (CO, 1 trial), 9 (UT, 1 trial), 10 (CA, 2 trials) and 11 (ID, 2 trials). Following seed-treatment at a rate of 0.075 mg ai/seed (1X application rate), total residues of sedaxane were <0.005 ppm each in/on all samples of sugar beet roots and tops. As no sugar beet radiotracer study was performed, no reduction in the number of field trials is automatically recommended. **Total savings = 0 field trials.**