Science Policy Note SPN2018-01

Guidance on Streamlined Residue Chemistry Data Requirements for Seed Treatment Uses and Potato Seed-Piece Applications

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Background

Health Canada's Pest Management Regulatory Agency (PMRA), in collaboration with the Office of Pesticide Program's Health Effects Division of the United States Environmental Protection Agency (USEPA) have performed a retrospective analysis of all seed treatment residue data that have been submitted to EPA/PMRA for the purpose of determining whether current data requirements are appropriate, or if some streamlining or tiered approach was possible.

As a result of this analysis, a decision tree has been developed that details the process for determining the residue chemistry data requirements for seed treatment use (see Appendix I). The outlined procedure differs from current PMRA data requirements as per Regulatory Directives DIR98-02 and DIR2010-05 or Science Policy Note SPN2017-02 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;
2) In cases where field residue trials are required to support the seed treatment use, it allows for a reduction in the current number of residue trials required for the raw agricultural commodities (RACs) that are exclusively livestock feed items; and
3) It allows for a significant reduction in most of the current residue chemistry data requirements in cases where the seed treatment application rate is low.

The above conditions are not applicable to potato seed-piece (PSP) application, as the unique nature of this use pattern requires separate considerations (see Appendix II).

Detailed Considerations

Health Canada's PMRA in collaboration with the USEPA performed a retrospective analysis of all seed treatment residue data that have been submitted to EPA/PMRA, which had been previously reviewed and found acceptable. In addition, previous USEPA ChemSAC [Chemistry Science Advisory Council] 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 I). Note: Due to the unique nature of the PSP use pattern, separate considerations applicable to this type of application are discussed below (see Section 2 and Appendix II).

1.0 Outcome of Seed Treatment Data Analysis (excluding PSP Application)

1.1 Consideration of Maximum Theoretical Residue in Harvested RACs

Consideration was given to cases where the application rate for treated seed was sufficiently low to preclude the possibility of significant residues in the harvested crop. Using the maximum seeding rate and minimum yield per hectare, the rates at which the maximum theoretical residue would equal 5 ppb (i.e. 0.005 ppm, based solely on growth dilution of residues) were calculated for various crops (see Appendix III). It was concluded that, other than a valid enforcement

analytical method in the proposed plant commodities from treated seed, no residue chemistry data would be required for seed treatments at or below these estimated rates. In this situation, the maximum residue limits (MRLs) for the food commodities will be set at the limit of quantitation (LOQ) of the enforcement analytical method.

1.2 Consideration of Foliar Use Information for the same Crop as the Treated Seed

If the seed treatment 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 definition (RD) for enforcement purposes is the same for foliar and soil treatments (including primary and secondary crop metabolism data). This decision is made 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 treatment rate does not exceed 125%[1] 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 MRLs 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.

When the seed treatment rate is significantly greater in comparison to the foliar rate (i.e. maximum per hectare seed treatment rate $\geq$ 25% of the foliar rate) and residues from the seed treatment are expected to be significantly higher 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 MRL will be set at the proper level and will not be exceeded when crops are grown from treated seeds alone, or if 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, a label restriction on the foliar end-use product specifying the foliar rate that can be applied to plants grown from treated seeds (to limit the maximum seasonal application rate), or an increased MRL, will be required.

[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 MRL setting.

1.3 Consideration of Radiotracer Uptake

A significant reduction in current residue chemistry data requirements can often be granted to seed treatment uses that have no registered (or on-going submission) foliar uses. This determination is made by performing a radiotracer uptake study in which the crop is grown from seed treated at a one-fold (1×) application rate with the radiolabeled active ingredient. If the total radioactive residues (TRRs) are less than 5 ppb in all RACs of concern (aerial portion and root portion of the crop) as delineated in DIR2003-02 (page 7) "Harmonization of Regulation of Pesticide Seed Treatment in Canada and the United States" and DIR98-02 (page 9-13, number 14) "Residue Chemistry Guidelines", no further studies are required, other than a valid enforcement analytical method. Note that if there is no characterization/identification of the TRRs in the radiotracer study, then it is assumed that the radioactivity consists of the parent molecule and, as such, the RD is parent (RD = TRRs).

If the RD is ≥ 5 ppb in any of the RACs, then a full set of field trial data at 1× application rate (as outlined in DIR98-02 or DIR2010-05 or SPN2017-02) is required for these RACs. MRLs will be set based on the results of the field trial data for commodities showing uptake, and MRLs will be set at the LOQ of the enforcement analytical method for commodities in which the RD is <5 ppb in the radiotracer study. 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). 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 analytical method, etc.).

In situations where the RD is slightly above 5 ppb in the radiotracer study, a significant reduction in current 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 (5×) application rate. This option requires the availability of adequate plant metabolism data to determine the RD, and a validated enforcement analytical method. If the RD is < LOQ in all RACs in the 5× trials, then no additional residue chemistry data are required and MRLs are set at the LOQ of the enforcement analytical method for all human food RACs. If the RD is > LOQ in any of the RACs in the 5× trials, then field trial data generated according to the proposed use pattern (1× application rate) are required for those RACs (refer to DIR98-02 or DIR2010-05 or SPN2017-02). Processing studies, if applicable, may also be required. MRLs will be set based on the results of the field trial data. For RACs that are livestock feed items only, a 50% reduction in the number of field trials can be applied (however, a minimum of three trials are required).

Additional Considerations

1) If the RD is < 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 for all crops can be considered for registration without any additional residue data;

2) If the RD from radiotracer studies in wheat forage, hay, grain and straw are all < 5 ppb, then the seed treatment can be considered for registration for the following crops: wheat, barley, oats, rye, sorghum, triticale, buckwheat, rice and millet, without any additional residue data. Also, if the RD is < 5 ppb in all wheat and corn RACs, then uses on all cereal grains can be considered for registration without any additional residue data;

1.4 Consideration of 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 RD for enforcement purposes and the application rate is less than or equal to 10 g a.i./100 kg seed, then a significant reduction in current 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 a.i./100 kg seed (see Appendix IV for a full justification of the 10 g a.i./100 kg seed cut-off and justification for requiring field trials on feedstuff only). For human food commodities, no field trial data are required and the MRL is set at the LOQ of the enforcement analytical method; 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 greater than 10 g a.i./100 kg seed and adequate plant metabolism data are available to determine the RD, then the registrant has the option of performing a radiotracer study (and proceeding as described in Section 1.3 above) or performing a full set of field trials and processing studies (if applicable).

Additional Considerations
1) For highly toxic chemicals, the 5 ppb RD threshold value may be reduced;

2) For uses on soybeans and peanuts (or other legumes that are grown for livestock feeds) where the RD is ≥ 5 ppb in forage/hay, but is < 5 ppb in seed or nutmeat; 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 MRL would still be needed for the seed or nutmeat;

3) If MRLs are needed, a validated enforcement analytical method is required;

4) A minimum of three trials are required for MRL setting;

5) In cases where field trial data are waived for a human food RAC, a processing study will also not be required.

2.0 Outcome of Potato Seed-Piece Analysis

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

When an applicant petitions for a PSP application, there are two possible scenarios with respect to the status of the current potato use:

1) petition is a new use for the crop – i.e. there are no currently registered potato uses; or

2) in-furrow and/or foliar uses are already registered. Each scenario requires specific residue chemistry data requirements, which are described below.

2.1 Considerations when petition is a New Use for Potato

Three different options are considered under this scenario:

Option 1: Radiotracer Uptake Study

A significant reduction in current residue chemistry data requirements can be granted to a PSP application for an active ingredient that has no registered uses on other crops. This determination is made by performing a radiotracer study in which potatoes are grown from seed-pieces treated at a one-fold (1×) application rate with the radiolabeled active ingredient. If the total radioactive residues (TRRs) are less than 5 ppb in potato tubers, no further data are required, other than a valid enforcement analytical method. MRLs will be set at the LOQ of the enforcement analytical method for potato tubers in which the RD is <5 ppb in the radiotracer study. Note that if there is no characterization / identification of the TRRs in the radiotracer study, then the RD = TRRs (as it is assumed that the radioactivity consists of the parent molecule and, as such, the RD is the parent). If the RD is greater or equal to 5 ppb in potato tubers in the radiotracer study, then PSP field trial data (1× application rate) and potato processing data are required as per DIR98-02. MRLs will be set based on the results of the PSP field trial data. If the RD is ≥ 5 ppb, all relevant residue chemistry data requirements must be fulfilled as per DIR98-02, 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 RD is 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, as per DIR98-02 and DIR2010-05 or SPN2017-02.

If there are additional metabolites of concern from soil application (thus the RD 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 as per DIR98-02 and DIR2010-05 or SPN2017-02.

2.2 Considerations when Potato Use is Registered: In-furrow or Foliar

If a potato in-furrow use is registered, 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 demonstrates equivalency of residues between in-furrow and PSP applications by conducting bridging trials at similar application rate per hectare, 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 GAP.

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 RD is the same for foliar and soil treatments (including primary and secondary crop metabolism data). 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 is required as per DIR2010-05 or SPN2017-02.

If there are additional metabolites of concern from soil application (thus the RD 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 as per DIR2010-05 or SPN2017-02.

In summary, with the exception of radiotracer study results that shows no uptake in potato tubers, a full complement of PSP field trials is required as per DIR2010-05 or SPN2017-02. An MRL will be calculated based on the results of the PSP residue trial data and will be compared to any existing potato MRLs. If a potato MRL is not already established, then a potato MRL from the PSP application will be promulgated. On the other hand, if a potato MRL is already established, it will be compared to the PSP calculated MRL and if the latter MRL is higher, the MRL will be revised accordingly.

Conclusions

Separate decision trees detailing the process for determining the residue chemistry data requirements for seed treatment use (see Appendix I) and the potato seed-piece application (see Appendix II) 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.

2) In cases where field residue trials are required to support the seed treatment use, a 50% reduction in the number of trials required 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 feed items from seed treatment are generally low. However, a minimum of three trials is always required.

3) A significant reduction in most of the current residue chemistry data 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 III). All treatments at or below these estimated rates will not require residue chemistry data other than a valid enforcement analytical method in the proposed plant commodities to be treated as seed treatment. In this situation, the MRLs for the food commodities will be set at the LOQ of the enforcement analytical method.

4) 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 RD and the application rate is $\leq$ 10 g a.i./100 kg seed, then a significant reduction in data requirements is appropriate.

For human food commodities, no field trial data are required and the MRL is set at the LOQ of the enforcement analytical method; for RACs that are livestock feed items only, 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 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 RD is 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, assuming a complete residue chemistry database is available to support this use, 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 1× application rate and TRRs are less than 5 ppb in potato tubers, no further studies are required, except for a valid enforcement analytical method.

Appendices

Appendix I:	Decision Tree for the Residue Chemistry Data Requirements of Seed Treatment
Appendix II:	Decision Tree for the Residue Chemistry Data Requirements of Potato Seed-Piece (PSP) Treatment
Appendix III:	Seed Treatment Application Rates at Which the Maximum Theoretical Residue = 5 ppb Based on Growth Dilution of Residues
Appendix IV:	Rationale Supporting Reduced Data Requirements for Application Rates at or Below 10 g a.i./100 kg seed

References

Regulatory Directive DIR98-02: Residue Chemistry Guidelines
https://www.canada.ca/en/health-canada/services/consumer-product-safety/reports-publications/pesticides-pest-management/policies-guidelines/regulatory-directive/1998/residue-chemistry-guidelines-dir98-02.html

Regulatory Directive DIR2010-05: Revisions to the Residue Chemistry Crop Field Trial Requirements
https://www.canada.ca/en/health-canada/services/consumer-product-safety/reports-publications/pesticides-pest-management/policies-guidelines/regulatory-directive/2010/revisions-residue-chemistry-crop-field-trial-requirements-dir2010-05.html

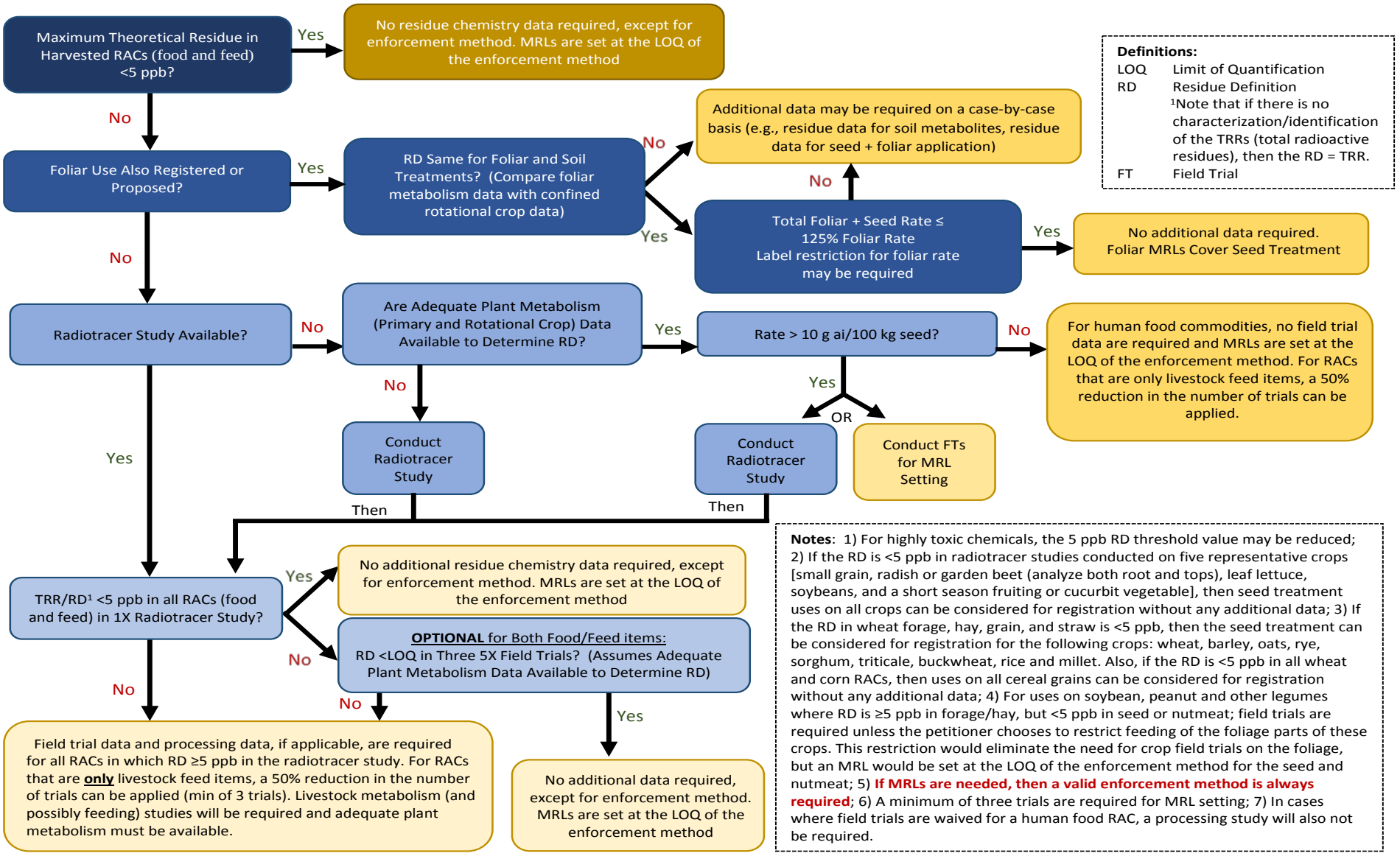
Science Policy Note SPN2017-02: Joint Canada/United States Field Trial Requirements
https://www.canada.ca/en/health-canada/services/consumer-product-safety/reports-publications/pesticides-pest-management/policies-guidelines/science-policy-notes/2017/guidance-joint-canada-united-states-field-trial-requirements-spn2017-02.html

Regulatory Directive DIR2003-02: Harmonization of Regulation of Pesticide Seed Treatment in Canada and the United States
https://www.canada.ca/en/health-canada/services/consumer-product-safety/reports-publications/pesticides-pest-management/policies-guidelines/regulatory-directive/2003/harmonization-regulation-pesticide-seed-treatment-canada-united-states-dir2003-02.html

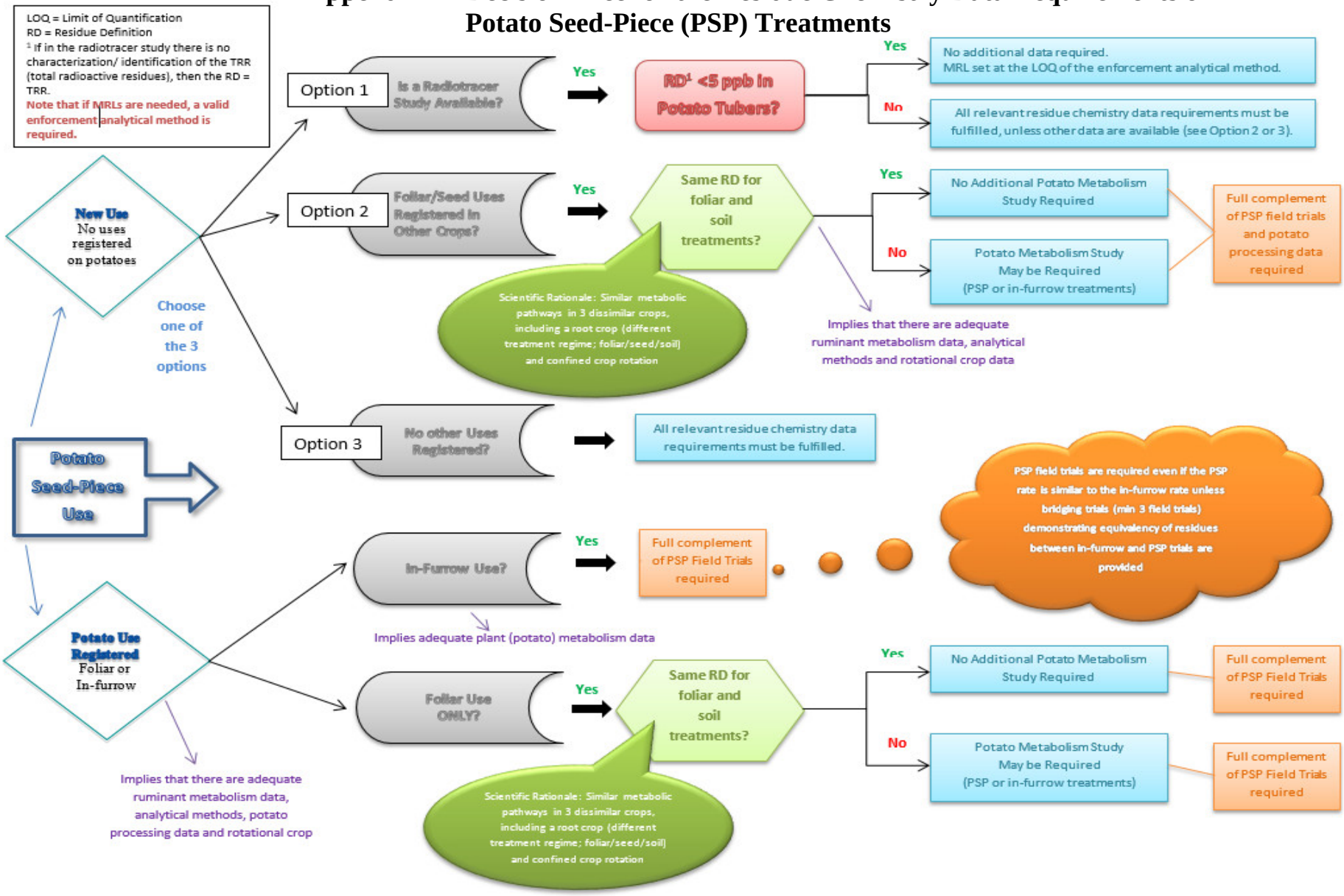
OECD Guidelines Test No. 509: Crop Field Trial
http://www.oecd-ilibrary.org/environment/oecd-guidelines-for-the-testing-of-chemicals-section-5-other-test-guidelines_20745796

OECD Guidance Document on Crop Field Trials
http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2011)50/REV1&doclanguage=en

Appendix I Decision Tree for the Residue Chemistry Data Requirements of Seed Treatment (excluding Potato Seed-Piece Treatment)



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



Appendix III Seed Treatment Application Rates at Which the Maximum Theoretical Residue = 5 ppb Based on Growth Dilution of Residues

Crop Group/ Subgroup	Crop	Maximum Canadian Planting Rate [kg/ha]	Minimum Yield [kg/ha]	Rate at Which Maximum Theoretical Residue = 5 ppb [g ai/100 kg seed]*
1A	Beet, Sugar	1.2	44,834	18.7
1A	Carrot	4.5	19,054	2.1
1B	Beet, garden	7.0	22,417	1.6
1C	Potato	4,035	26,899	0.003
3A	Onion, bulb	4.5	33,625	3.7
3B	Onion, green	7.0	17,932	1.3
4A	Lettuce, leaf	2.0	13,450	3.4
5A	Broccoli	0.35	5,604	8.0
5A	Cabbage	0.35	16,813	24.0
6A	Bean, snap	100	4,482	0.02
6B	Pea, succulent	300	3,138	0.005
6C	Bean, dry	83	1,740	0.01
7	Pea, field	277	2,513	0.005
8A	Tomato	1.1	11,206	5.1
8B	Pepper, bell	0.2	8,965	22.4
9A	Cantaloupe	0.28	8,965	16.0
9B	Cucumber	5.0	8,965	0.9
9B	Watermelon	0.62	20,176	16.3
15	Corn, Sweet	16.8	6,726	0.2
15	Corn, Field	31.5	8,787	0.1
15	Corn, Pop	14.6	3,190	0.1
15	Rice	Not grown	--	--
15	Wheat, grain	174.9	5,582	0.02
16	Wheat, forage	174.9	4,932	0.01
18	Alfalfa	13 (forage production) 1.0 (seed production)	5,604	0.2
18	Clover, red	11 (forage production) 2.2 (seed production)	7,396	0.3
20	Canola (Rapeseed)	8.0	1,680	0.1
20	Cotton	Not grown	--	--
20	Soybean	109	3,026	0.01
20	Sorghum, Grain	15	3,138	0.1
20	Sunflower	10.1 (confection type) 4.94 (oil type)	1,122	0.06
Others	Peanut, runner	Not available	--	--

* = Min Yield/Max Planting Rate × 0.0005.

Appendix IV Rationale Supporting Reduced Data Requirements for Application Rates at or Below 10 g a.i./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, use requests for seed treatment 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 present, 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 a.i./100 kg seed or less. The lowest seed treatment rate at which residues have been found in edible RACs is 50 g a.i./100 kg seed. As 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, it was concluded that residue trials are not necessary when proposed application rates are 10 g a.i./100 kg seed or less.

While current requirements for field trials appear appropriate for uses involving high seed loading rates, 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 a.i./100 kg seed or lower, no field trials are needed for crops that do not produce livestock feedstuffs, and MRLs will be set at the LOQ of the enforcement analytical method for the relevant human food RAC. In cases where crops do produce livestock feedstuffs, a 50% reduction in the number of field trials is appropriate (however, a minimum of three trials are required) so that appropriate levels may be estimated for these RACs and used in the calculation of the livestock dietary burdens. Refer to Appendix 1 for the complete decision tree developed for residue chemistry data requirements pertaining to seed treatment uses.