Comments in Response Consultation on Abamectin PMRL 2024-13

To: Pest Management Regulatory Agency September 13, 2024

Introduction

Safe Food Matters Inc. welcomes the opportunity to comment on "Consultation on abamectin, Proposed Maximum Residue Limit PMRL2024-13"**.** We have serious concerns with this pesticide and its assessment by PMRA, including:

1) The toxicology studies show serious harm to the brains of the young
2) Syngenta exerted influence on the assessments
3) The OECD Calculator shows most of the proposed MRL estimates are highly uncertain
4) PMRA did not employ a scientifically based approach

These concerns will become clear from the comments below.

The main regulatory documents referenced in these comments are:

Syngenta Evaluation Report or Canada 2016: *Evaluation Report for Category B, Subcategory 5.0 Application. New Maximum Residue Limits for Previously Assessed Abamectin Technical.* Registration Number 24484. Application Number 2013-4347 PMRA #2566198

2021 Integrated Assessment: October 28, 2021 Dietary Evaluation – Integrated Assessment : Import MRLs on various commodities, Submission: 2020-5848 Abamectin/ Syngenta Canada Inc. PMRA#3230165

PRVD = February 28, 2023 *Proposed Re-Evaluation Decision PRVD2023-01 Abamectin and Its Associated End-use Products, Consultation Document* Health Canada

PMRL or PMRL 2024-13: June 26, 2024 PMRA's *Proposed Maximum Residue Limit PMRL2024-13 Abamectin*

Vigilance OGM endorses these comments.

Unjustified lowering of PCPA Factor: Syngenta influence

The Proposed Re-evaluation Decision for Abamectin and its Associated End-Use Products PRVD2023-01 indicates under 3.0 Toxicology Summary and Pest Control Products Act Characterization that details can be found in "Canada 2016", which is the Syngenta Evaluation Report.

This 2016 Syngenta Evaluation Report 24484 concerned a 2013 application by Syngenta Canada Inc. to establish new import MRLs and amend existing ones. Notably, the Evaluation Report shows that Syngenta submitted a rationale to support a reduction in the uncertainty factor put in place to protect children (the "**PCPA Factor**") from 10 to 3, and PMRA accepted this rationale without justification.

However, the Pest Control Products Act(s.7(b)(iii)) does not allow for a reduction in the PCPA Factor without presentation of "reliable scientific data". The policy on such reductions, *Science Policy Note 2008-01: The Application of Uncertainty Factors and the Pest Control Products Act Factor in the Human Health Risk Assessment of Pesticides*, indicates that if there is a serious endpoint, this identifies a high degree of concern, and is clear that, "[i]f the level of concern is high, the 10 fold PCPA factor will be retained".

A serious toxicological effect for a pesticide is one that "causes congenital malformations, results in persistent or significant disability or incapacity, is life-threatening or results in the death of exposed animals". "Examples of serious endpoints of concern include, but are not limited to, reduced viability of offspring, the occurrence of malformations and changes in brain morphometrics (size or weight)."

The Syngenta Evaluation Report reveals that at least three of these serious toxicological effects occurred in the abamectin studies:

- There were congenital formations. "Malformations were a treatment-related finding in the fetuses of rabbits as well as CF-1 mice." "In the developmental toxicity studies, treatment resulted in fetal malformations, including cleft palate in rabbits, CF-1 mice, and possibly CD-1 mice. With the exception of the findings in the rabbit, these serious effects were observed in the absence of maternal toxicity."
- There was ample evidence that abamectin killed the infants quickly. "A key feature of the abamectin toxicity database was the **observation, in several studies, of pup mortality which typically began within the first week after birth".**
- There were "significant reductions in measurements of several regions of the brain of the young that were not present in the mothers." Equivocal brain morphometric findings in the follow-up DNT study were noted in the absence of maternal toxicity". (More on this study later)

Science Policy Note 2008-01 also indicates that the shape of the dose-response curve can influence the degree of concern, and "[a] steep dose response could heighten concern since a small increment in exposure could have a significant impact". Also Table 1 indicates a steep-dose response calls for a "high degree of concern".

The Syngenta Evaluation Report indicates: "A steep dose-response was demonstrated in many of the studies".

Thus, based upon the SPN2008-01 policy, there was a high degree of concern based upon both the seriousness of the endpoints and the dose-response, and therefore, based upon SPN2008-01, the PCPA Factor of 10 "will be retained." However, it appears PMRA lowered the PCPA Factor to 3, based upon the "rationales" presented by Syngenta. This was unjustified according to PMRA's own policies.

The rationales provided by Syngenta in essence provided explanations as to why the effects, considered serious by the policy, should not be considered serious. They said that rodent infants are more sensitive than humans with respect to abamectin toxicity because of differences in expression of a protein and development of the blood-brain barrier; and that it is unclear how abamectin would impact humans "during critical periods of fetal development".

PMRA concluded "[F]or these reasons, there **remains uncertainty with respect to sensitivity of the young**. This uncertainty was reflected through the use of a PCPA factor of 3-fold in the risk assessment".

However this reasoning is spurious and not science based. First, there was no uncertainty with respect to the findings of the studies, and these certain science findings are the basis for setting the PCPA

Factor. The standard of proof required of the Act is to provide "reliable scientific data" that shows otherwise, and no such data was presented.

Second, this "uncertainty" arising from differences between rodents and humans had already been accounted for. PMRA is clear in Table A1-1 of PMRL 2024-13 that it had already applied a factor to account for the uncertainty associated with the extrapolation of data from rodents to humans, which it described as a "10-fold safety factor for differences between animals and humans".

Thus PMRA did not follow its own policy when it decided to significantly reduce the legally mandated standard for protection to children, and it adopted rationales for same that were spurious and not scientifically justified. It is apparent PMRA ceded to the submissions presented by Syngenta, and thereby allowed a chemical that quickly causes infants deaths to maintain its registration.

Unscientific lowering of NOAEL: Syngenta influence

The Syngenta Evaluation Report also shows new data was submitted, presumably by Syngenta, that allowed for an eight-fold increase in the level for indicating an effect arising from exposure to abamectin. The new data allowed for an increase in No Observable Adverse Effect Level for **parental toxicity** in a development neurotoxicity study from 0.05 mg/kg bw/day to 0.4 mg/kg bw/day, allowing for higher levels of exposure.

The reason provided for the change was that there was a 20% reduction in body weight gain during lactation, but this was not considered to be adverse. PMRA Study #2334852 indicated that "Effects at the parental LOAEL included: ↓bwg (20%) during lactation (F1b♀)".

However, a decrease in body weight gain of 20% relative to controls is an adverse effect. No explanation as to why this finding should not have been considered adverse was provided in the Syngenta Evaluation Report or elsewhere.

High Uncertainty of almost all MRL estimates

There is high uncertainty of the MRLs set for most of the crops in PMRL2024-13. Only the estimates for apples and pears, grapes and plum can be considered set with any kind of certainty.

The commodities listed in the 2021 Integrated Assessment for which new residue data was submitted are carrots, papayas, sweet corn, lychees, pineapple, guava, dried chive leaves and tea. PMRA ran the calculations in the OECD Calculator on September 10, 2024, and for all except dried chive leaves and tea there was a warning message that stated "high uncertainty of the MRL estimate" - either "due to small dataset" or "due to high level of censoring", or both. The calculations from PMRA are here:

Compound	Abamectin	Abamectin	Abamectin	Abamectin	Abamectin	Abamectin	Abamectin	Abamectin
Crop	Carrots	Dried chive leaves	Papaya	Sweet corn	Lychee	Pineapple	Guava	Tea
Region / Country	US	Calculator not used	US	US	US	US	US	Calculator not used.
GAP	7 mg ai/seed; PHI: 7	ee PMRA# 3230165 p. 4	1.4 g ai/ha; PHI: 3-	9.0 g ai/ha; PHI: 6-	5.0 g ai/ha; PHI: 8-1	53.2 g ai/ha; PHI: 7	82.9 g ai/ha; PHI: 8	ee PMRA# 3230165 p. 4
Total number of data (n)	9	-	3	12	3	8	3	-
Percentage of censored data	67%	-	33%	100%	33%	100%	67%	-
Number of non-censored data	3	-	2	0	2	0	1	-
Lowest residue	0.006	-	0.005	0.001	0.002	0.004	0.004	-
Highest residue	0.019	-	0.131	0.001	0.003	0.004	0.005	-
Median residue	0.006	-	0.123	0.001	0.002	0.004	0.004	-
Mean	0.008	-	0.086	0.001	0.002	0.004	0.004	-
Standard deviation (SD)	0.004	-	0.070	0.000	0.000	0.000	0.001	-
Correction factor for censoring (CF)	0.556	-	0.778	0.333	0.778	0.333	0.556	-
Proposed MRL estimate								
- Highest residue	0.019	-	0.131	0.001	0.003	0.004	0.005	-
- Mean + 4 SD	0.024	-	0.368	0.001	0.004	0.004	0.007	-
- CF x 3 Mean	0.013	-	0.202	0.001	0.006	0.004	0.007	-
Unrounded MRL	0.024	-	0.368	0.001	0.006	0.004	0.007	-
Rounded MRL	0.03	-	0.4	0.01	0.01	0.01	0.01	-
	High uncertainty of MRL estimate due to high level of censoring.		High uncertainty of MRL estimate due to small dataset.	High uncertainty of MRL estimate due to high level of censoring.	High uncertainty of MRL estimate due to small dataset.	High uncertainty of MRL estimate due to high level of censoring.	High uncertainty of MRL estimate due to small dataset and high level of censoring.	

Residues (mg/kg)		Residues (mg/kg)		Residues (mg/kg)		Residues (mg/kg)		Residues (mg/kg)		Residues (mg/kg)		Residues (mg/kg)		Residues (mg/kg)	
0.0060	*			0.1310		0.0006	*	0.0024		0.004	*	0.005			
0.0060	*			0.0051	*	0.0006	*	0.0027		0.004	*	0.004	*		
0.0064				0.1230		0.0006	*	0.0020	*	0.004	*	0.004	*		
0.0060	*					0.0006	*			0.004	*				
0.0075						0.0006	*			0.004	*				
0.0187						0.0006	*			0.004	*				
0.0060	*					0.0006	*			0.004	*				
0.0060	*					0.0006	*			0.004	*				
0.0060	*					0.0006	*								
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						0.0006	*								
						0.0006	*								

The User Guide to the OECD Calculator provides guidance on what these warning messages mean. The explanations for these and other messages discussed later are set out here:

Explanatory messages displayed by the calculator

7. The warning "MRL calculation not possible. [Check data entry]" is displayed in case of implausible and most likely erroneous data entries such as non-numerical data, residue values ≤ 0 mg/kg or residue values > 10000 mg/kg. The same warning is also displayed if an asterisk is entered in the second column (to identify a result < LOQ) while the LOQ value was not entered in the left-hand adjacent cell.

8. If the dataset consists of less than 3 values the message "MRL calculation not possible. [Too small dataset]" is displayed at the bottom of the spreadsheet. The choice of 3 values was made based on the minimal requirement common among OECD countries. With a single residue value, it is impossible to compute an estimator for the standard deviation of the dataset, which is needed in the calculation procedure.

9. If the dataset consist of 3-7 residue values, the message "High uncertainty of MRL estimate. [Small dataset]" is displayed to remind the user of the considerable level of uncertainty surrounding the calculation of any statistical quantity for such small datasets. For a dataset with 8 residue values, the estimated failure rate, i.e. the probability that the MRL is below the 95th percentile of the residue distribution, reaches approximately 25 %.

10. Similarly, for the same reason the warning message "High uncertainty of MRL estimate. [High level of censoring]"is displayed if more than 50% of the dataset is censored (residues below the limit of quantification or LOQ). Although the methods selected for the MRL calculation are very robust to the presence of non-detected residues, uncertainty is considerable for residue datasets for which the majority of residues values are below the LOQ.

- With respect to tea, the Integrated Assessment indicates n=2. The OECD calculator is unable to calculate MRLs for sample sizes less than 3, based upon the White Paper para. 8. Nevertheless, , PMRA stated that "acceptable abamectin residue data were provided to calculate the recommended MRL on imported tea from Japan". The Integrated Assessment referenced a PMRA memo that states when n=2, the MRL is calculated as the mean residue value x 5, which produced an MRL of 1.4 ppm:

  > The OECD calculator is unable to calculate maximum residue limits for sample sizes <3. As per RCC memo (Y:\HC\PMRA\HED\DIETARY\X_REFERENCE\HEALTH RISK PROTECTION\PROCEDURES\RCC Memos\PMRA_HED Memo_MRL Methodology for n=2_signed.pdf), when n=2, the MRL is calculated as the mean residue value × 5. The mean residue value is 0.275 ppm × 5 = 1.4 ppm. Given that the HAFT is 0.477 ppm, the alignment of the MRL with that of the US tolerance and Japanese MRL of 1 ppm will cover potential residues of total abamectin in tea leaves.

  There is no scientific certainty of the MRL estimate when calculating an MRL based upon two datasets. The reasoning provided is the Integrated Assessment is not scientific and also does not accord with the approach iterated by PMRA in "*MRLs, human health, and food safety: How MRLs are set*" of setting MRLs by using the OECD Calculator.

- With respect to dried chive leaves, the MRL was set without scientific justification but only to align with the US tolerance. The Integrated Assessment indicated there was no residue data for dried chives, or a concentration factor. Even with this, the PMRA Indicated that the OECD would require an MRL of 0.015, but they recommend aligning with the US instead:

  > "A processing factor of 2.95 was derived for dried chive leaves. No theoretical concentration factors are available for dried herbs. Based on the HAFT (0.0043 ppm) from the three fresh chive residue trials, anticipated residues of the total abamectin residues would be 0.013 ppm. According to the OECD rounding classes, an MRL of 0.015 ppm would be recommended, however, to align with the US Tolerance and facilitate trade, an MRL of 0.02 ppm will be recommended".

The commodities listed in the 2021 Integrated Assessment for which no new residue data was submitted were:

- tomatoes, non-bell peppers, bell peppers (for Crop Group (CG)-09 fruiting vegetables)
- oranges, grapefruit and lemons (for CG10 citrus fruits)
- apples and pears
- sweet cherries, tart cherries, peaches and plums (for CG 12 stone fruits)
- Grapes

- Strawberries
- almonds and pecans (For CG14 tree nuts)

The details on the number of datasets ("**n**") for these commodities were not provided in PMRL 2024-13 or the Integrated Assessment or the Evaluation Report. On September 4, 2024, PMRA provided the number of field trials to determine the MRLs for the commodities set out in Table E.1 "Summary of Field Trial and Processing Data Used to Support Existing MRLs" of the Integrated Assessment, relating to the "no new residue data" commodities.

These data indicate that for all the commodities for which no new residue data was submitted, the "n" was less than 7 except for: oranges (n=12); apples (n=16); pears (n=18); peaches (n=8); plums (n=9) and grapes (n=13). The OECD calculations were not run or provided, but based upon the User Guide, there is a high uncertainty of the MRL estimate for all these commodities, but for the exceptions, based upon a small dataset.

In addition, the following concerns arise with the assessments set out in the Integrated Assessment:

- The "n" value for peaches (as well as pineapple) was 8. With respect to this data, the User Guide indicates in para that the probability that the MRL is below the 95th percentile of the residue distribution is approximately 25 %.

- With respect to papaya and lychee, the 2021 Integrated Assessment indicates the trials were conducted at the same location with the same varieties. With respect to guava, the three trials were separated by <30 km and two of them used the same variety. None of these trails can be considered independent trials. However, PMRA without justification indicated these data were acceptable. Even with this, there is a high uncertainty of the MRL estimates.

- With respect to lychee, PMRA allowed the extension of the MRL to all commodities within Crop Subgroup 24A. The establishment of an MRL for an entire crop group based upon 1 field trial is not reasonable or protective.

- PMRA employed unscientific and results-oriented reasoning when considering pineapple, guava and corn.
  - With respect to pineapple, the residues of abamectin were less than the limit of quantification, and the White Paper paragraph 7 warning indicates that the "MRL calculation is not possible". However PMRA in the 2021 Integrated Assessment unjustifiably concluded that the evidence was adequate, and that the higher MRL should be set, regardless of the lack of calculation, in order to align with higher residue levels:

    > "**While total residues of abamectin are less than LOQ, an MRL of 0.015 ppm is recommended to align with the US tolerance**". (p.38)

    This proposed MRL cannot be scientifically justified, and exhibits results-oriented reasoning.

  - This same unscientific reasoning applies to guava:

> "Although the OECD MRL calculator output was 0.01 ppm, the proposed MRL is 0.015 ppm to align with US Tolerance.

- Similarly, for corn, the residues were less than the LOQ. PMRA concluded:

> "As total residues of abamectin are less than LOQ, the MRL can be rounded up to 0.01
> ppm in order to align with the US EPA tolerance."

- With respect to the proposed extension of the proposed MRL to citrus fruits (CG10 – revised), such extension is not justified. The Integrated Assessment (pp 13-14) indicated adequate field trial was on file:

> "CG10-R: Orange or tangerine, lemon or lime and grapefruit are the representative crops for citrus fruits (CG10-R). Adequate field trial data are available reflecting the use of EC and SC formulations on oranges, lemons and grapefruits. Therefore, the established MRL of 0.02 ppm in/on CG10 can be extended to all commodities within CG10-Revised."

However, only the number of datasets reviewed by PMRA for oranges (n=12) were adequate for purposes of certainty of the MRL estimate. The datasets reviewed for grapefruit and lemon were both less than 7 and there was a high uncertainty of the MRL estimate associated with them. Thus the extension of the MRL to the full group is not justified.

Canada set original MRLs, now re-assessing them as "import": Syngenta influence

The Integrated Assessment indicates that over a decade ago, Syngenta had requested that MRLs be established on various crop groups, even though there were no residue levels (tolerances) in place in the US. The PMRA obliged, meaning Canada was the first to establish residue levels for these crops:

> "Under S2013-4347, Syngenta had requested that import MRLs be established on CG8-09, CG10-Revised, CG11-09, CG12-09, CSG13-07F (based on grapes), CSG13-07G (based on strawberries), and CG14-11. At the time, there were no US tolerances established for uses on these revised/updated crop groups/subgroups. Therefore, MRLs were set on crop groups listed under DIR98-02 (CG8, CG10, CG11, CG12, CG14, grapes and strawberries). Under S2016-7442, the MRL for CG8 was extended to all crops within CG8-09. The United States has since established tolerances on the relevant revised crop groups/subgroups. Previously reviewed residue data from field trials conducted on the representative commodities from each of the crop groups/subgroups were reassessed under the current submission"**.**

It is evident that, at the bequest of Syngenta, PMRA is both setting and increasing MRLs – in many cases without adequate scientific justification as described herein.

No scientific or factual evidence/rationale for extension to full crop groups

No rationale is provided for why these MRLs should be applied to entire crop groupings, nor is any evidence provided to show that growers even use or are contemplating use on all the commodities in the designated crop groups. Such evidence is required. If requests for MRLS on one commodity can extend to import MRLs for entire crop groups, it would not take long before the entire Canadian MRL system is comprised of the values for import MRLs.

Moreover, crop grouping is based on "botanical and taxonomic" criteria. These characteristics do not necessarily extend to the methods by which individual crops receive, process, translocate or transmit pesticides. PMRA has not provided evidence to prove that the criteria extend to the up-take of pesticides. Without such verification, there is no certainty that grouping one crop with the representative crops as they relate to accumulating pesticide residues is a sound methodology. Until such proof can be provided, a field trial study is required for each crop commodity in order for there to be reasonable scientific certainty that crop grouping for purposed of setting MRLs has a scientific basis.

PMRA not up to date on regulatory actions and abamectin concerns, or dismisses them

In Europe, the European Food Safety Authority (EFSA) reviewed abamectin in the July 27, 2022 "Peer review of the pesticide risk assessment of the active substance abamectin" (**2022 EFSA**). PMRA in the PRVD considered the 2020 EFSA peer review, but not the 2022 final review. The PMRA does not list this EFSA document as a review it considered in the Proposed Re-evaluation Decision for Abamectin, PRVD 2023-01, which means it has not taken into account the most up to date concerns of the EFSA. These concerns apply to the assessment of PMRA in PRVD 2023-01 and also PMRL 2024-13.

Syngenta's Influence: Unjustified dismissal of DNT for acute assessment

For the ARfd and the ADI, the EFSA has set a value of 0.0012 mg/kg bw per day. This was based on the rat developmental neurotoxicity study (**DNT**), which had originally not been provided by Syngenta to the EFSA. The previous references values for ADI were 0.0025 mg/kg bw per day based on short term dog studies, and he ARfd was 0.005 mg/kg bw per day based on the acute neurotoxicity study. Thus for both the ADI and ARfD, the EFSA lowered its values because of the newly submitted developmental neurotoxicity study.

In contrast, the PMRA in PMRL 2024-13 maintained its reliance on the acute neurotoxicity study and the dog studies, taken from calculations it made in the Syngenta Evaluation Report. It states in 3.2.1 of PMRL2024-13:

> "To estimate acute dietary risk (1 day), the **acute neurotoxicity study in rats** with a NOAEL of 0.5 mg/kg bw was selected for risk assessment. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied and a PCPA factor of threefold was considered appropriate. The composite assessment factor (CAF) is thus 300, resulting in an ARfD of 0.0017 mg/kg bw of abamectin. The ARfD is considered protective of all populations, including females of child-bearing age and nursing infants. Details on the derivation of the acute reference dose can be found in **Canada, 2016**."

The Syngenta Evaluation Report shows that PMRA did in fact consider the DNT study, and found pup mortality at the high dose, statistically significant reductions in the pup brain at mid-dose, and low values for almost all of the brain in the low dose group. Based on these findings, **the DNT study was relevant for purposes of setting the acute reference dose.** To quote:

> "At the mid dose, statistically significant reductions in measurements of several regions of the brain were noted in PND 12 and/or PND 63 animals. Consistently lower values for almost all brain region measurements were recorded for the low-dose group."

However PMRA chose to not consider the developmental neurotoxicity study as relevant for purposes of setting the Canadian ADI or ARfD, characterizing the findings as "equivocal". The statistically significant findings in the study, however, means these findings were not "equivocal".

In the Evaluation Report, for Sygenta's application, PMRA provided the "equivocal" reasoning: it provided the excuse that long term storage had some effect, and that they didn't look at all brain regions so it was hard to make comparisons. This rationale is not scientifically based, and cannot detract from statistically significant findings:

> "These consistently lower values were thought to result from longer storage time in wax blocks compared to that of the control and the mid-dose group. In an attempt to address this issue, additional tissues were cut and assessed from all groups after an extended storage period and demonstrated that there was some effect of storage time on tissue shrinkage. In addition to the confounding effect of storage time, not all brain regions were examined in the additional morphometric investigations, making it difficult to directly compare the measurements for the controls with those in the treated groups. Consequently, the low dose level findings were of limited utility in assisting in the interpretation of potential adverse effects. In view of this, the morphometric findings noted in PND 12 and/or PND 63 animals are considered equivocal, and endpoints for risk assessment take into account margins to these findings. In determining the overall level of concern, it is important to note that there were no treatment-related effects on neurobehavioural assessments or brain pathology in either DNT study. Decreased pup brain weights were only noted in the initial DNT study and only at the highest dose."

It is submitted that the findings of this DNT study are NOT equivocal, and the excuses provided are not scientifically based. Proffering alternative explanations and excuses in the face of statistically significant findings is not supportable. To be legitimate, evidence **disproving** the statistically significant finding is required.

Data gaps

The EFSA identified data gaps with respect to residue data on certain commodities, including almonds, papayas, apples and pears, strawberries, tomatoes and sweet peppers/bell peppers. The EFSA was seeking additional residue trials, including 4 additional residue trials for almonds, 6 additional residue trials for pome fruits, 4 specific residue trials for papayas, and 8 trials compliant with Good Agriculture Practice (GAP) for tomatoes.

Syngenta did not provide the data. Accordingly, many of the MRLs were either lowered to the limit of detection (**LOD**) or lowered (COMMISSION REGULATION (EU) 2023/198 of 30 January 2023 amending Annex II to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for abamectin in or on certain products):

- For almonds and papayas, residue information was not submitted by Syngenta, and the MRL was set at the LOD.
- For apples and pears, the EFSA found unacceptable risks, and the MRL was set at the LOD.

- For strawberries and tomatoes, the MRLS were lowered to 0.08 and 0.015 ppm respectively.
- For sweet peppers/bell peppers, the risks were unacceptable, and the MRL was set at 0.03.

In the end, the MRLs for which there were data gaps in Europe are lower than those being proposed in PMRL 2024-13 (except for almonds and strawberries):

Commodity	**Proposed MRL PMRL**	**Europe MRL**	**PMRA Difference**
Almond	0.01	0.01	Same
Papaya	0.4	0.01	Higher 40x
Pome Fruit (apples and pears)	0.02	0.006	Higher 3.3x
Strawberry	0.05	0.08	Lower 1.6
Sweet peppers/bell peppers	0.07	0.03	Higher 2.3x
Tomatoe	0.07	0.015	Higher 4.7x

PMRA has not reviewed data that the EFSA thinks shows unacceptable risks, or asked for the appropriate number of field trials from Syngenta. It is accordingly not in line with the international regulatory approach.

In addition, the other MRLs proposed in PMRL2024-13 are on balance higher than those in Europe, as shown here:

Commodity	**Proposed MRL PMRL**	**Europe MRL**	**Difference**
Tea (dried leaves)	1.0	0.05	Same
Carrot roots	0.03	No MRL	Higher
Citrus fruits CG 10	0.02	0.04	Lower
Small fruits CG13-07F	0.05	0.02	Higher
Dried chive leaves	0.02	-	Higher
Guava, pineapples	0.015	0.01	Higher
Tree nuts (CG14-11)	0.01	0.01	Same
Tropical and subtropical fruits; small fruits; inedible peel (CG 24A), sweet corn kernels plus cob	0.01	0.01	Same

Given that the proposed MRLs, which are being established to align with the tolerances in the US, differ from those in Europe, it is obvious that there will be trade concerns for foods imported from Europe, in particular those that have higher MRLs than the proposed MRLs. The PMRA has created a difficulty for

the Canada Food Inspection Agency (CFIA), because it has to inspect commodities being imported that have differing MRLs.

EFSA Data Gap on water so no consumer assessment

The EFSA identified a lack of "information on the effect of water treatment processes on the nature of residues of both the active substance and its identified metabolites potentially present in surface water, when surface water is abstracted for the production of drinking water. This gap leads to the consumer risk assessment from the consumption of drinking water being not finalised for all the representative uses". (Summary section)

As a result of this data gap, the consumer risk assessment concerning the consumption from drinking water was not finalized in Europe. In Europe, abamectin cannot be used on crops other than permanent greenhouse crops.

However, PMRA finalized its registration assessment, and the PMRL, notwithstanding the lack for Canadian watering monitoring data, as explained below. A science based approach is based on evidence, and requires that data on surface water be provided by the registrant, as stated above. The health risk assessments for both the PRVD and the PMRL are not evidence-based and do not accord with a science based approach.

Inadequate Health Risk Assessment

Section 11 of the Act requires that the health risks associated with specification of MRLs be acceptable:

> "Health risks to be considered acceptable
>
> **11** (1) The health risks associated with maximum residue limits specified by the Minister under sections 9 and 10 must be considered to be acceptable by the Minister.

However, the health risk assessment of PMRA consisted of only a dietary risk assessment. PMRA was of the view a dietary risk assessment "involved a thorough evaluation of health risks", as shown in Section 2.0 of PMRL 2024-13:

> "Health Canada conducted a thorough scientific assessment and found because that the health risk from eating food commodities treated with abamectin meets Health Canada's requirements for the protection of human health. **The main health assessment required for this consultation was the dietary risk assessment** and it was conducted in accordance with Sections 10 and 11 of the *Pest Control Products Act*. This assessment involves a thorough evaluation of health risks that considered the toxicity and dietary exposure of abamectin, and follows strict regulatory standards."

Inadequate and inconsistent evidence for Integrated Risk Assessment

A health assessment requires an aggregate assessment of intake through food and drinking water. There is no Canadian water monitoring data for abamectin (PRVD p. 14 and 30), so there can be no scientific certainty with respect to an aggregate/ integrated assessment.

PMRA resorted to inconsistent water data. Part F of the Integrated Assessment references a 2015 Dietary exposure assessment dated August 11, 2015 (PMRA #2532260) that was conducted under S2013-4347. It also states:

> "As the purpose of this submission is to specify MRLs for crops imported from the US,

> the EEC values on file for abamectin are adequate. A Level 1 EEC value is on file for abamectin (1.4 µg a.i./L, surface water; maximum application rate of 95 g a.i./ha/year) and are adequate to cover the proposed maximum use pattern

The PRVD used different EEC values for water, which is inconsistent with the Integrated Assessment. This provide no scientific certainty or consistency in approach.

No Review of Scientific Literature

PMRA did not conduct or consider the scientific peer-reviewed open literature on abamectin as part of its health risk assessment. No peer-reviewed open studies on health or toxicology, which were not from regulatory agencies or task forces, was listed in the PRVD or the PMRL. Europe recognized this as a data gap in the 2022 EFSA Peer Review, and requested of Syngenta the following (p.22):

> "A search of the scientific peer-reviewed open literature on the active substance and its relevant metabolites, dealing with side effects on health and published within the 10 years before the date of submission of the dossier, to be conducted and reported in accordance with EFSA guidance on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA, 2011; relevant for all representative uses evaluated)."

PMRA cannot purport to have conducted a thorough scientific risk assessment when it has not considered even one open-science literature on toxicology or health.

Current Scientific Literature Shows MRL assumption of PMRA Wrong

The premise of PMRA for allowing the allowable residue limits in Canada to align with the tolerances or legal residue levels in other countries is that such alignment will not increase the levels of pesticides in Canada, because it is against the law to spray in Canada except in accordance with the directions on the spray label. The premise is based on the assumption that when these directions are followed, the pesticide residues are safe. This premise and assumption are the basis for PMRA's position that a separate MRL for Canada is not needed – a "made in Canada" MRL that reflects the maximum levels of pesticide residue when sprayed in Canada according to Canadian labels.

However, two new studies from Agriculture Canada and the Barley Commission show that directions for preharvest spraying are not adequate to prevent high pesticide residue levels. The results on malting barley show that high levels, even extraordinarily high levels (95 ppm) can result even in controlled conditions, and that levels are exceeded even when the pesticide is sprayed "on-label" ie. according to label conditions. The studies are: *Effects of different timing and rate of glyphosate application on the residue level, grain quality, and processing performance of two Canadian malting barley varieties*, and The effects of pre-harvest glyphosate rate and timing on yield and pre-malt quality of malting barley.

This proves the assumption of PMRA is wrong, and justifies the need for setting "made in Canada" MRLs.

Current Scientific Literature shows MRL approach overstates safety

For your information, a commentary on this methodology that allows for assurances of safety for pesticides of concern, and an alternative approach, is set out in this article "Missing the mark - new methods needed to detect and address high-risk pesticide residues in the global food supply**".** The study references the US regulatory system, but the conclusions are applicable to Canada as well.

"Conclusions

Assurances to consumers that pesticide residues in food are safe because a small percentage of samples contains residues over applicable tolerances or MRLs are overstated for two reasons, especially in the US.

First, most of the high and very-high risk samples that regulators should be focused on contained residues below existing tolerances and MRLs. In the case of US-PDP testing, 95.7% of 1456 high and very-high-risk food samples over the last 10 years have contained residues below applicable tolerances, despite unambiguously exceeding EPA's "level of concern". In UK-FSA testing over the same 10 year period, 44% of high and very-high risk samples contained residues that did not exceed applicable MRLs.

Second, the majority of samples flagged by regulators for possible regulatory interventions because reported residues exceeded tolerances or MRLs actually pose little or essentially no dietary risk. Over the last 10 years, 66% of the samples of food with over-tolerance residues tested by the US-PDP posed low or very-low dietary risks, while 62% of samples with over-MLR residues also posed low or very-low risks in the case of UK-FSA testing.

Government pesticide testing and regulatory authorities need to adopt reforms that more effectively target risk-mitigation measures toward those foods associated with relatively high levels of dietary risk, while sparring those samples found to contain residues that do not warrant deeper scrutiny, and certainly not disposal in landfills. Tolerances or MRLs that allow residues in a single serving of food that exceed regulatory exposure benchmarks should be lowered across the board. Currently in the US, hundreds of tolerances are set at levels sanctioning residues in food at levels inconsistent with current law and EPA's pesticide dietary risk-assessment policies."

Conclusion

Based on the foregoing, the Minister cannot defend the proposal to increase maximum residue limits of abamectin. Syngenta clearly influenced the science reviewed by PMRA in the Syngenta Evaluation Report. The PMRA came to the unjustified conclusion (among others) that the PCPA Factor could be reduced. This factor was put in place to protect children, and PMRA was aware that the harmful effects of abamectin on the unborn and the young were pronounced and significant in the toxicological studies, including low values for the brain of the young at even the low dose.

There is high uncertainty with respect to almost all the MRL estimates. There are unresolved data gaps on field trials and water monitoring. Independent scientific literature, and the latest regulatory actions in Europe, were not canvassed.

This is far from a "thorough scientific assessment". The Minister of Health is mandated to apply a scientifically based approach. This did not happen.

The Minister of Health must ensure that the PMRA assessment provides a "reasonable certainty" of no harm to human health from abamectin. This standard is not met by the assessment outlined in PMRL2024-13.