Differing criteria for setting crop group MRLs leads to non-harmonized MRLs - Current challenges and opportunities

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BASF Corporation

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What's the problem?

Crop Grouping

is a well accepted and cost effective approach that facilitates the establishment of pesticide tolerances for both major and minor crops.

Non-Harmonized MRLs

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Step 1 – Domestic Registration

Fungi-Blaster®

For effective treatment of Shot Hole disease in fruit trees

Cherry	6 field trials	**Apricot; apricot, Japanese; capulin; cherry, black; cherry, Nanking; cherry, sweet; cherry, tart; Jujube, Chinese; nectarine; peach; plum; plum, American; plum, beach; plum, Canada; plum, cherry; plum, Chickasaw; plum, Damson; plum, Japanese; plum, Klamath; plum, prune; plumcot; sloe; cultivars, varieties, and/or hybrids of these**
Peach	9 field trials	
Plum	6 field trials	

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Step 1 – Domestic Registration

Fungi-Res
Cherry
US
3x100g/ha 0 PHI

Total number of data (n)	6
Percentage of censored data	0%
Number of non-censored data	6
Lowest residue	1.200
Highest residue	2.900
Median residue	2.550
Mean	2.283
Standard deviation (SD)	0.624
Correction factor for censoring (CF)	1.000

Proposed MRL estimate

- Highest residue	2.900
- Mean + 4 SD	4.780
- CF x 3 Mean	6.850
Unrounded MRL	6.850
Rounded MRL	7

High uncertainty of MRL estimate.
[Small dataset]

Residues (mg/kg)	n
1.2	1
1.9	1
2.5	1
2.6	2
2.9	1

	US MRL
Cherry	7
Peach	
Plum	
Stone Fruit	

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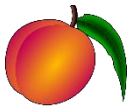
Step 1 – Domestic Registration



Fungi-Res
Peach
US
3x100g/ha 0 PHI

Total number of data (n)	9
Percentage of censored data	0%
Number of non-censored data	9
Lowest residue	0.500
Highest residue	2.700
Median residue	1.100
Mean	1.556
Standard deviation (SD)	0.872
Correction factor for censoring (CF)	1.000

Proposed MRL estimate

- Highest residue	2.700
- Mean + 4 SD	5.043
- CF x 3 Mean	4.667
Unrounded MRL	5.043
Rounded MRL	5

Residues (mg/kg)	n
0.5	1
0.8	1
0.9	2
1.1	1
2.2	1
2.4	1
2.5	1
2.7	1

	US MRL
Cherry	7
Peach	5
Plum	
Stone Fruit	

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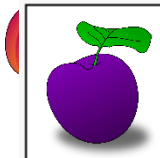
Step 1 – Domestic Registration



Fungi-Res
Peach
US
3x100g/ha 0 PHI

Total number of data (n)	6
Percentage of censored data	0%
Number of non-censored data	6
Lowest residue	0.800
Highest residue	2.200
Median residue	1.300
Mean	1.333
Standard deviation (SD)	0.516
Correction factor for censoring (CF)	1.000

Proposed MRL estimate

- Highest residue	2.200
- Mean + 4 SD	3.399
- CF x 3 Mean	4.000
Unrounded MRL	4.000
Rounded MRL	4

High uncertainty of MRL estimate.
[Small dataset]

Residues (mg/kg)	n
0.8	1
0.9	1
1.1	1
1.5	2
2.2	1

	US MRL
Cherry	7
Peach	5
Plum	4
Stone Fruit	**7**

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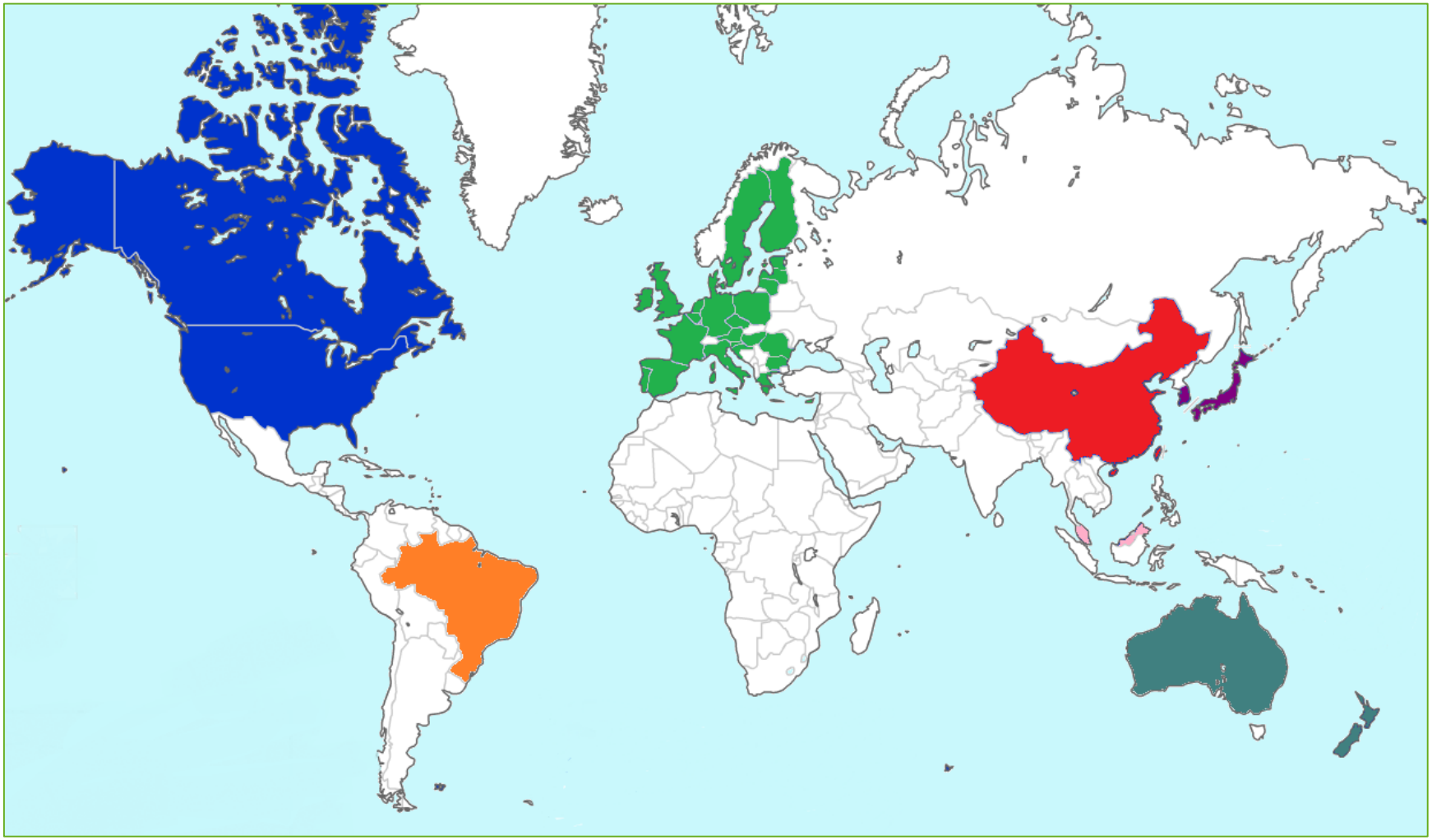
Step 2 – Import Tolerances

Crop Grouping Systems around the World



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Crop Grouping – EU and US

broccoli or cauliflower	broccoli and cauliflower
cabbage	head cabbage
mustard greens	kale

Brassica Vegetables

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Crop Grouping – EU and US

tomato	pepper

tomato	pepper
cucumber and melon	sweet corn

Fruiting Vegetables

EU: Guidelines on comparability, extrapolation, group tolerances and data requirements for setting MRLs

		nut"with the exception of coconuts (4 trials)	→	"Closed nuts"
(iii) Pome fruit	Apples Pears	Apple or pears (with a minimum of 4 apples trials)	→	Whole group
(iv) Stone fruit	Apricots Peaches (including nectarines and similar hybrids)	Peaches or apricots **(with a minimum of 4 trials on apricot)**	→	Nectarines, apricots, peaches
	Cherries	Sweet cherries	↔	Sour cherries
	Plums			
(v) Berries and small fruit				
(a) Table and wine grapes	Table grapes Wine grapes	Table grapes	↔	Wine grapes

Major crops
8 trials (each)

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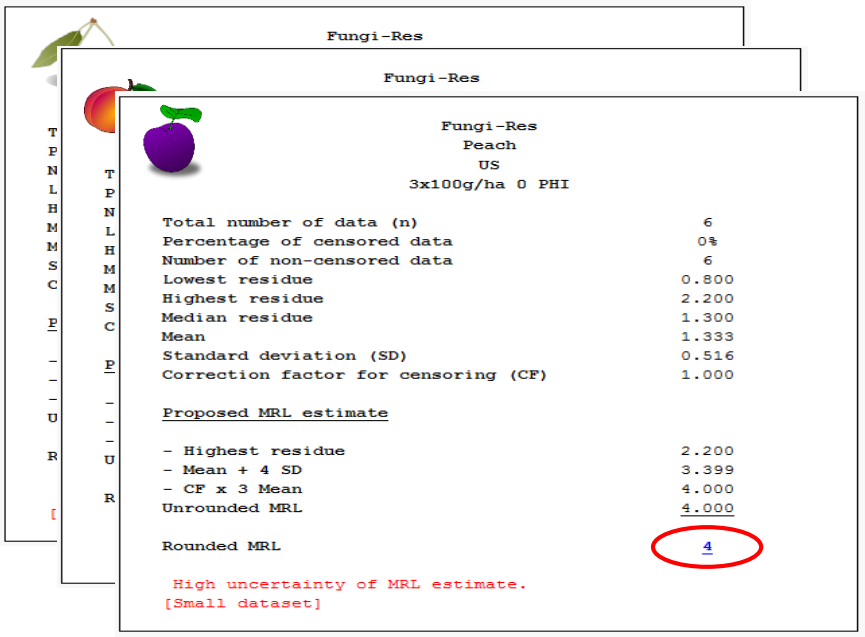
Challenge: different trial requirements in each country



Fungi-Res

Fungi-Res

Fungi-Res
Peach
US
3x100g/ha 0 PHI

Total number of data (n)	6
Percentage of censored data	0%
Number of non-censored data	6
Lowest residue	0.800
Highest residue	2.200
Median residue	1.300
Mean	1.333
Standard deviation (SD)	0.516
Correction factor for censoring (CF)	1.000
Proposed MRL estimate	
- Highest residue	2.200
- Mean + 4 SD	3.399
- CF x 3 Mean	4.000
Unrounded MRL	4.000
Rounded MRL	4

High uncertainty of MRL estimate.
[Small dataset]

…could lead to denial of MRLs

	EU MRL
Cherry	7
Peach	5
Plum	4
Stone Fruit	

Cherry	2+6 field trials
Peach	9 field trials
Plum	2+6 field trials

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Challenge: different crop group extrapolations in different countries

…leads to different MRLs

Fungi-Res MRLs

	US MRL	EU MRL
 Cherry	7	7
 Peach	7	5
 Plum	7	4

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Step 3 – Codex MRLs

Group 003 Stone fruits

Code No.	Commodity
FS 0012	**Stone fruits** *Prunus* spp.
FS 0013	**Cherries** *Prunus cerasus* L.; *P. avium* L.
FS 0014	**Plums (including Prunes)** *Prunus domestica* L.; other *Prunus* spp and ssp.
FS 0240	**Apricot** *Prunus armeniaca* L.; syn: *Armeniaca vulgaris* Lamarck
FS 0241	**Bullace** *Prunus insititia* L.; syn: *Prunus domestica* L., ssp. *insititia* (L.) Schneider
FS 0242	**Cherry plum** *Prunus cerasifera* Ehrhart, syn: *P. divaricata* Ledeboer *P. salicina* Lindl., var. Burbank
FS -	**Chickasaw plum**, see Plum, Chickasaw
FS 0243	**Cherry, Sour** *Prunus cerasus* L.
FS 0244	**Cherry, Sweet** *Prunus avium* L.
FS -	**Damsons (Damson plums)**, see Plum, Damson
FS -	**Greengages (Greengage plums)**, see Plum, Greengage
FS 0250	**Japanese apricot** *Prunus mume* Siebold & Zucc.
FS 0245	**Nectarine** *Prunus persica* (L.) Batch, var. *nectarina*
FS -	**Mirabelle**, see Plum, Mirabelle
FS 0246	**Morello** *Prunus cerasus* L., var. *austera* L.

Fungi-Res Residues

Residues (mg/kg)	n
1.2	1
1.9	1
2.5	1
2.6	2
2.9	1

Residues (mg/kg)	n
0.5	1
0.8	1
0.9	2
1.1	1
2.2	1
2.4	1
2.5	1
2.7	1

Residues (mg/kg)	n
0.8	1
0.9	1
1.1	1
1.5	2
2.2	1

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JMPR often uses statistical tests in their review process

Kruskal-Wallis Test

Cherry	Peach	Plum	Group 4	Group 5	Group 6	Group 7	Group 8
1.2	1.1	0.8					
2.5	2.7	1.5					
2.6	2.5	1.5					
1.9	2.4	2.2					
2.9	0.9	0.9					
2.6	0.5	1.1					
	2.2						
	0.8						
	0.9						

N Groups	Chi-Sq. Value	DF	p-value
3	5.47	2	0.065

Group	N	Median	Mean of Ranks
Cherry	6	2.550	15.92
Peach	9	1.100	9.56
Plum	6	1.300	8.25

Statistical test indicates that there is no evidence that the residues are from different distributions

Can combine datasets for MRL calculation

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Challenge: same MRL calculator – different result

Fungi-Res
Stonefruit
Region / Country
3 x 100g/ha 3D PHI

Total number of data (n)	21
Percentage of censored data	0%
Number of non-censored data	21
Lowest residue	0.500
Highest residue	2.900
Median residue	1.500
Mean	1.700
Standard deviation (SD)	0.787
Correction factor for censoring (CF)	1.000

Proposed MRL estimate

- Highest residue	2.900
- Mean + 4 SD	4.850
- CF x 3 Mean	5.100
Unrounded MRL	5.100
Rounded MRL	6

Residues (mg/kg)	n
0.5	1
0.8	2
0.9	3
1.1	2
1.2	1
1.5	2
1.9	1
2.2	2
2.4	1
2.5	2
2.6	2
2.7	1
2.9	1

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Challenge: different ways of combining residue data from representative crops

…leads to different MRLs

Fungi-Res MRLs

	US MRL	EU MRL	Codex CXL
 Cherry	7	7	6
 Peach	7	5	6
 Plum	7	4	6

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Opportunities

Projects and efforts that will make a difference
…to reduce the difference

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The International Crop Grouping Consulting Committee

The IR-4 Project

The ICGCC has been working to harmonize crop groups internationally for more than 10 years

Chaired by US and the Netherlands
Includes more than 200 crop experts and 35 countries

Argentina, Australia, Bangladesh, Belgium, Brazil, Burkina Faso, Canada, Chile, China, Columbia, France, Germany, Guatemala, Honduras, Hungary, India, Israel, Japan, Kenya, Lebanon, Mali, Mexico, Morocco, New Zealand, Nicaragua, Nigeria, S. Korea, Senegal, South Africa, St. Kitts, Taiwan, Thailand, Trinidad, United Kingdom, United States

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Develop harmonized crop groups that are considered by EPA and CCPR for revision of the Codex Committee on Pesticide Residues (CCPR) Classification of Food and Animal Feeds.

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"Principles and Guidance for the Selection of Representative Commodities for the Extrapolation of MRLs"

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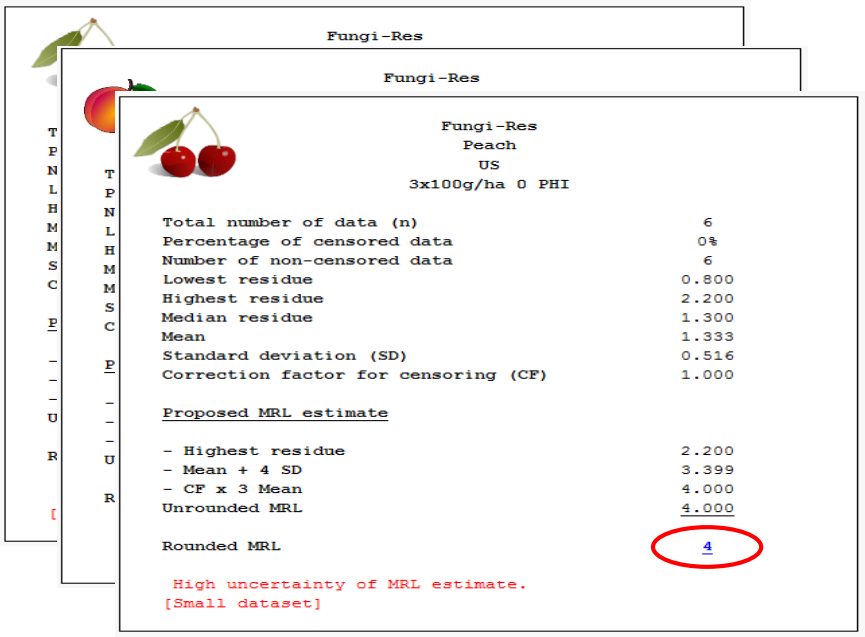
EPA 5X Rule - Current approach or…



Fungi-Res

Fungi-Res

Fungi-Res
Peach
US
3x100g/ha 0 PHI

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Rounded MRL	4

High uncertainty of MRL estimate.
[Small dataset]

	MRL
Cherry	7
Peach	5
Plum	4
Stone Fruit	**7**

EPA uses the “5X Rule” to determine if representative crops can support a crop group.

The MRL for each rep crop is calculated separately and the highest MRL is used for the whole group.

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… The statistical approach?

Kruskal-Wallis Test

Cherry	Peach	Plum	Group 4	Group 5	Group 6	Group 7	Group 8
1.2	1.1	0.8					
2.5	2.7	1.5					
2.6	2.5	1.5					
1.9	2.4	2.2					
2.9	0.9	0.9					
2.6	0.5	1.1					
	2.2						
	0.8						
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	MRL
Cherry	
Peach	
Plum	
Stone Fruit	**6**

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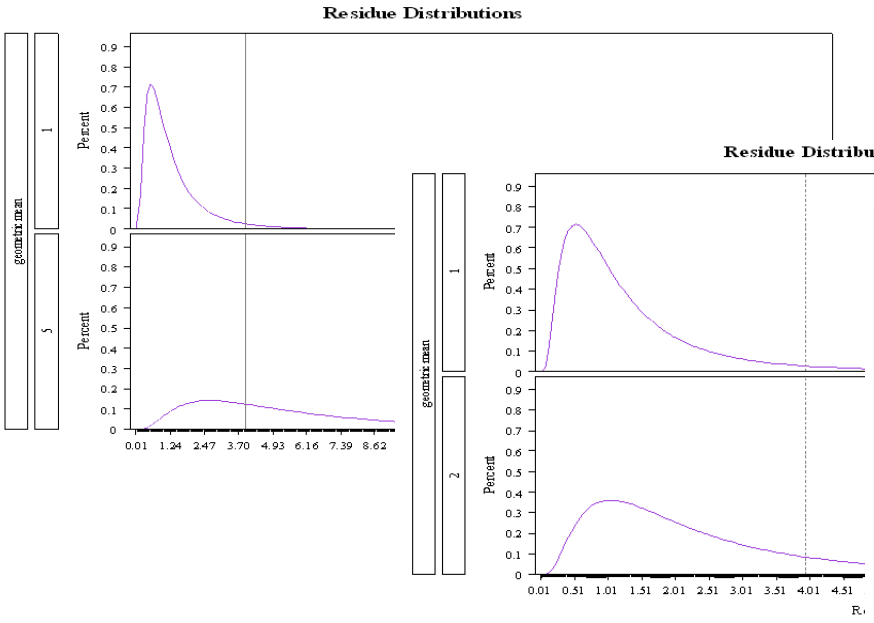
Possible harmonization of MRL calculation procedures

The EPA is currently testing the performance of the **Kruskal-Wallis** test against the current **5X Rule** to see which approach is better at distinguishing residue data sets that are statistically similar / different.

From a statistical viewpoint
Initial results look very promising in favor of the K-W test



Designed Max Ratio Factor (R)	Number of Groups (rep crops)	N Field Trials per group	Power to detect differences between groups when R=4		
			Kruskal Wallis	Max 5X	Med 5X
	2	5	0.63	0.38	0.36
		7	0.80	0.38	0.33
		10	0.93	0.36	0.31
5	2	5	0.75	0.49	0.50
		7	0.89	0.50	0.50
		10	0.98	0.49	0.50
	3	5	0.66	0.60	0.56
		7	0.86	0.61	0.59
		10	0.97	0.60	0.58
	4	5	0.65	0.69	0.66
		7	0.85	0.69	0.66
		10	0.97	0.68	0.63
	5	5	0.66	0.78	0.73
		7	0.87	0.75	0.70
		10	0.97	0.74	0.69

0.49	0.43
0.49	0.42
0.46	0.38
0.60	0.54
0.58	0.50
0.56	0.44
0.69	0.60
0.65	0.55
0.64	0.50

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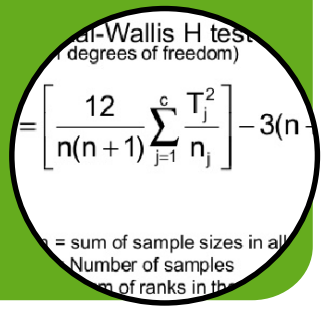
What's the answer?

International harmonized crop groups

Guidance on representative crops

Harmonized methods for calculating crop group MRLs



Harmonized MRLs allow greater commodity trade among countries and open more markets for growers

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