Global Residues & MRL's Harmonization

A Registrant's Perspective

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Presentation Outline

1. Requirements for residues & MRLs

2. Harmonization opportunities

3. Global residue program - example

4. Challenges for MRLs harmonization

5. Conclusions & Recommendation

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1.Global Residues Requirements

Current regulatory framework set by OECD

- ✓ Crop Field Trials: OECD 509 + guidance
  - ✓ Comprehensive global packages
  - ✓ 40% fewer trials than nationally required
  - ✓ 50% data from overseas
- ✓ OECD global joint-reviews
- ✓ OECD MRL-calculator

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2.Harmonization Opportunities

Type of Data	US - OPPTS 860's	EU - Directive 91/414/EEC	Codex MRL (FAO-2009/OECD-509)	Import Tolerances
Chemical ID	1100	Annex II, 6.0	✓	✓
Directions for use (GAPs)	1200	Annex II, 6.0	✓	✓
NOR: plants, animals, livestock	1300	Appendix A, E	✓	✓
Analytical Methods	1340, 1360		✓	✓
Storage Stability	1380	Appendix H	✓	✓
Feeding studies	1480	Appendix F	✓	as needed
Crop Field trials (MOR)	1500	Appendix B	✓	✓ (else where)
Processed food/feed	1520	Appendix E	✓	as needed
Confined Accumulation Rotational crops	1850	Appendix C	✓	as needed
Tolerance/MRL Proposal/Review	1550	Appendix I, D	✓	✓
Supporting NOF, RA, residues at consumption	1560	Annex II, 6.0	✓	✓

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3. Global Residue Programs

- Harmonized GAP (or worst case critical-GAP)
- Similar number of trials as current national requirements, yet larger global packages
- More robust data representative of global climates, regions, soils, use patterns, pest intensity
- Enables harmonized MRL's globally
- Significant benefit on global trading of ag-commodities and reduction of food-chain issues

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Example of a global program

- New insecticide with wide spectrum of use
  - ➢ 600 trials in 4 continents
  - ➢ 39 crops (fruits, veggies, grains, oilseeds)
  - ➢ 8 – 44 trials/crop, in 2 - 4 geographies ★
  - ➢ Harmonized GAP's per crop @ c-GAP

Legend:
- Polar
- Temperate
- Arid
- Tropical
- Mediterranean
- Mountains

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Global residue program pre-OECD

- GAP's globalized (allowing proportionality for regional flexibility to account for pest spectrum & intensity)
- Number of trials based on contribution
  - Weighted (1-3 scale) from 3 variables (size of planted area, food consumption intensity, frequency of trading)
  - Location in countries/regions representative for each crop (one from each N and S-hemisphere, or from the tropical belt)
  - Minimum number trials per zone dictated by the relevance of statistical interpretation (6-8?)
- Crop grouping/extrapolation
  - As per ICGCC (25% reduction of # trials), or
  - Super-crop grouping, as supported by GAP's across crop-groups and countries (further reduction, as supported by statistical relevance of data)

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Ideal Global Residue Package (example)

Crops	Area	Consumption	Trading	Total Score	Min # trials	NAFTA	EU	BRAZIL	AUS&NZ	
* low	*	*	*		6 (*** , ****)	5-20	8-16	4	4-12	Total
** moderate	**	**	**		9 (*****, ******)					6 - 18
*** high	***	***	***		12 (*******, ********)					
					15 (*********)					
Head-lettuce	*	**	**	*****	9	6		6		12
Leaf-lettuce	*	***	*	*****	9	6	6		6	18
Broccoli/cauliflo	*	*	**	****	6	6		6		12
Cabbage	*	*	*	***	6		6			12
Tomatoes	**	***	**	*******	12		6		6	12
Cucumbers	*	*	**	****	6		6			6
Rice	***	**	**	*******	12			6		12
Wheat	***	***	***	*********	15	6	6		6	18

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Benefits from this Global Program

- Supported new regulation updates (OECD 509)

- Proved homogeneity of residue data produced in different regions at the same GAP
  - Variability of data across regions (avg12%) is much lower than within any particular region (avg 78%)

- Concurrent registration submissions & reviews
  - OECD joint review (EPA, PMRA, APVMA)
  - Codex (draft-MRL's available)
  - EU

- Cost optimization by crop, more MRLs proposed

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4.Challenges for MRL harmonization

A. GAP (Good Agricultural Practices)

– Rate, # applications and intervals, PHI

– Variety of use practices for same crop

– Variety of pests and their intensity

– Agencies' flexibility around 25% GAP variation

➢ Harmonization at critical GAP (cGAP) globally

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Challenges for MRL harmonization

B. Inputs for OECD-MRL calculator

- – Single vs. replicate samples

- – Average vs. highest across replicates

- – Treatment of outliers

- – Treatment of censored data (ND-non detects, LOD, LOQ)

- – Bundling data across regions

- – Bundling of data across crops (apricot, peach)

- ➢ Harmonized inputs for global data, average replicates (> 8 trials), data as reported, bundling & outliers as supported by statistics

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Challenges for MRL harmonization

C. Supporting Risk to Consumers

– Tiered approach for exposure

1. MRL/tolerances
2. Actual field data
3. Monitoring

– Acceptance of refinement factors

• Edibility, processing/cooking, % crop treated

– Agencies' policies to incorporate drinking water

➢Globalization of exposure refinement options

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Challenges for MRL harmonization

D. Other Challenges (just a few more…)

- Raw Agricultural Commodity description (fruits w/wo pits, peel, forage, etc)

- Crop groups differences (ICGCC, Codex, EPA)

- GLP global implementation

- Analytical data reports (LOQ/LOD,corrected/uncorrected)

- Statistical interpretation of results (mean/median, HR/HAFT, U-test similarity subsets, Dixon-outliers)

- Agencies' policies about residue definition, proportionality, zoning, bundling, extrapolation, mutual acceptance

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Conclusion & Recommendation

- Technically it is feasible to develop global residue packages following OECD guidelines recently updated with representative trials at global locations

- Faster availability MRLs and new technologies to more countries

- Minor crops need special consideration through regulating extrapolation and mutual acceptance

- Further guidelines updates is needed for harmonized criteria to use global datasets and mutual acceptance of reviews between countries.

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Let's go global!
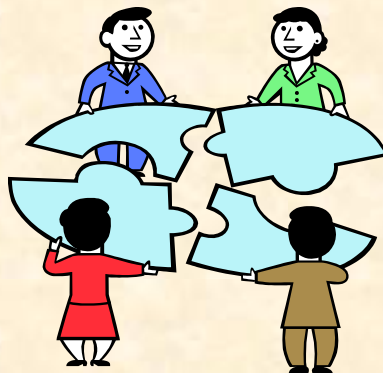
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