

# ***Digest* of Dietary Exposure Methodologies in Support of Global MRLS**

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Global Consumer Safety  
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**BASF**

We create chemistry



**Consumer Safety**  
safe use — safe food

# World of MRLs

## Why MRLs?

Grower's  
Production

International  
Stewardship

Food Trade

Public Health

## Data for MRL values

Field trials and  
GAPs

Crop grouping

OECD calculator

Proportionality

Crop Zones

## Dietary Risk Assessment

Regulatory  
Endpoint

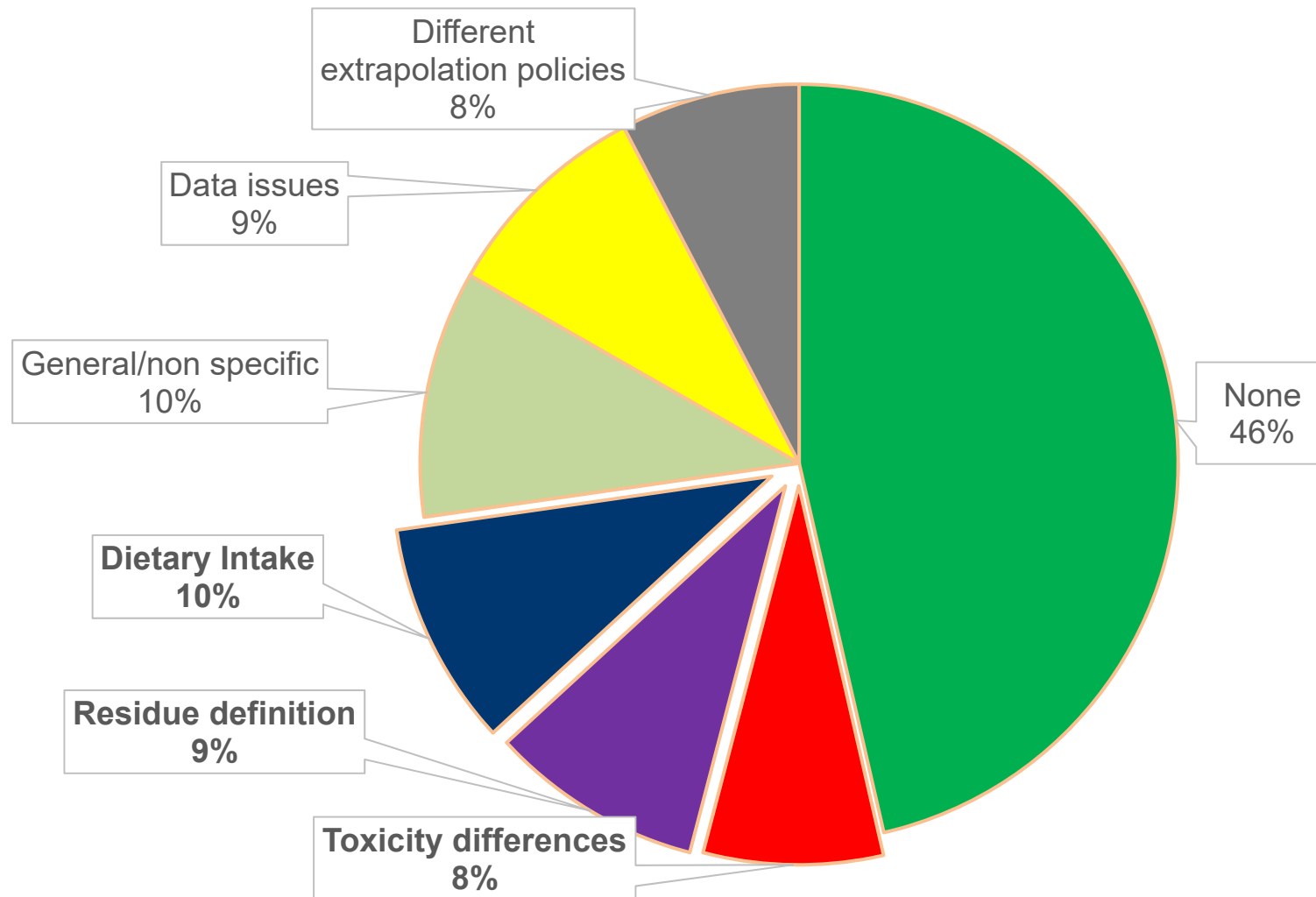
Residue  
Definition

Consumption

Dietary  
Residue  
Estimates

Protection  
Goals &  
Models

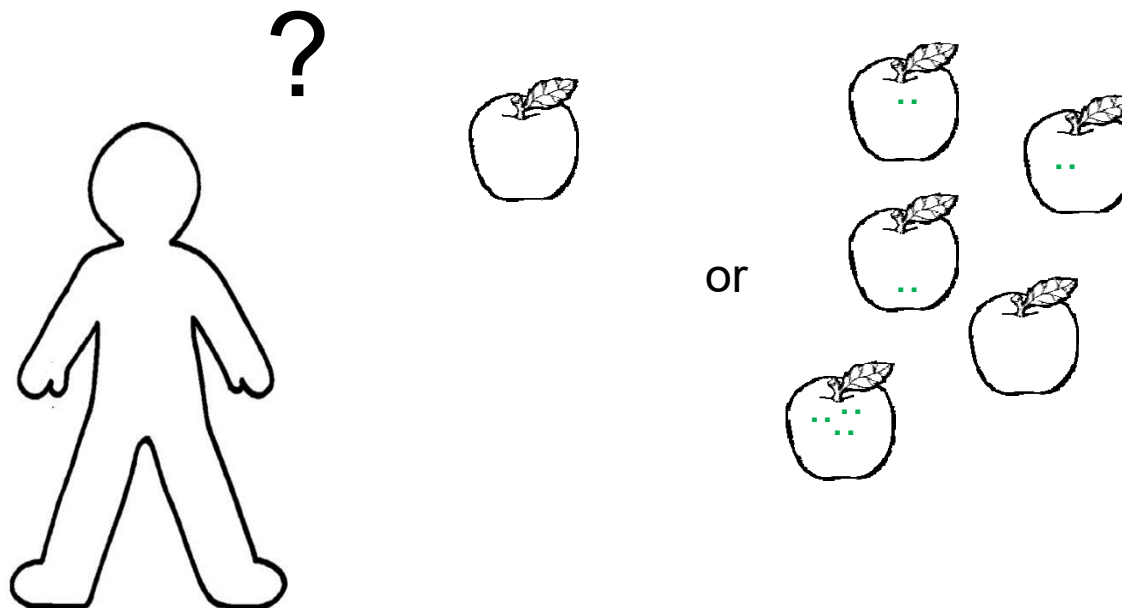
# Disharmony of MRLs at CCPR



# Dietary Risk Assessment for Pesticides

$$\text{Risk} = f(\text{Exposure}, \text{Hazard})$$

$$\text{Exposure} = \text{Consumption} \times \text{Residue in Food}$$



# Overview – Exposure Components and Acute Dietary Model OPTIONS

Level	Consumption	Residue Estimates	Model
Unrefined Less Resources	<ul style="list-style-type: none"> <li>• Food Balance Sheets</li> </ul>		
Intermediate	<ul style="list-style-type: none"> <li>• House Hold Surveys</li> <li>• Recipes for RACs</li> </ul>	<ul style="list-style-type: none"> <li>• Field Trials (HR and STMR)</li> <li>• Worst Case Scenario</li> <li>• Variability for HR</li> <li>• AI-specific processing</li> </ul>	
Refined Data intensive	<ul style="list-style-type: none"> <li>• Individual Diet Surveys</li> <li>• Recipes for RACs and processed products</li> </ul>	<ul style="list-style-type: none"> <li>• Percent Crop Treated</li> <li>• Dietary Monitoring Data</li> <li>• Washing and Cooking Factors</li> <li>• Duplicate Dinner Plates</li> </ul>	

# Overview – Exposure Components and Acute Dietary Model OPTIONS

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# Overview – Exposure Components and Acute Dietary Model OPTIONS

Level	Consumption	Residue Estimates	Model
Unrefined Less Resources			<ul style="list-style-type: none"> <li>• Deterministic (single values)</li> <li>• Single foods assessments</li> </ul>
Intermediate		<p>Food Use Categories (FUCs)</p> <p>Food Use Categories (FUCs)</p> <p>Food Use Categories (FUCs)</p> <p>Food Use Categories (FUCs)</p> <p>Food Use Categories (FUCs)</p>	<ul style="list-style-type: none"> <li>• Probabilistic consumption with deterministic residue estimates</li> </ul>
Refined Data intensive	<ul style="list-style-type: none"> <li>• Individual Diet Surveys</li> <li>• Recipes for RACs and processed products</li> </ul>		<ul style="list-style-type: none"> <li>• Probabilistic consumption with residue distributions for individual foods</li> </ul>

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Refined Data intensive	<ul style="list-style-type: none"> <li>• Individual Diet Surveys</li> <li>• Recipes for RACs and processed products</li> </ul>	<ul style="list-style-type: none"> <li>• Percent Crop Treated</li> <li>• Dietary Monitoring Data</li> <li>• Washing and Cooking Factors</li> <li>• <i>Duplicate Dinner Plates</i></li> </ul>	<ul style="list-style-type: none"> <li>• Probabilistic consumption with residue distributions for individual foods</li> </ul>



# Acute US Processes

Level	Consumption <b>WWEIA</b>	Residue <b>Tiered</b> Estimates	Model <b>DEEM FCID</b>
Unrefined Less Resources		<ul style="list-style-type: none"> <li>MRL and 100% CT</li> </ul>	
Intermediate		<ul style="list-style-type: none"> <li>Field Trial (<b>HAFT and averages</b>)</li> <li>AI-specific processing</li> </ul>	<ul style="list-style-type: none"> <li>Probabilistic consumption with deterministic residue estimates (<b>95%th</b>)</li> </ul>
Refined Data intensive	<ul style="list-style-type: none"> <li>Individual Diet Surveys</li> <li>Recipes for RACs and processed products</li> </ul>	<ul style="list-style-type: none"> <li>Percent Crop Treated (<b>BEAD</b>)</li> <li>Dietary Monitoring Data (<b>USDA PDP</b>)</li> <li>Washing and Cooking Factors</li> <li><b>TOTAL DIET STUDY</b></li> </ul>	<ul style="list-style-type: none"> <li>Probabilistic consumption with residue distributions for individual foods (<b>99.9%th</b>)</li> </ul>

# Acute EU Process

Level	Consumption EU National Diets	Residue Estimates	Model PRIMo - IESTI
Unrefined Less Resources		<ul style="list-style-type: none"> <li>MRL and 100% CT</li> </ul>	<ul style="list-style-type: none"> <li>Deterministic (single values)</li> <li>Single foods assessments</li> </ul>
Intermediate	<ul style="list-style-type: none"> <li><i>House Hold Surveys</i></li> <li>Recipes for RACs</li> </ul>	<ul style="list-style-type: none"> <li>Field Trial (HR and STMR)</li> <li><i>Variability for HR (3,5,7)</i></li> <li>AI-specific processing</li> </ul>	
Refined Data intensive	<ul style="list-style-type: none"> <li>Individual Diet Surveys</li> <li>Recipes for RACs and <b>limited</b> processed products</li> </ul>	<ul style="list-style-type: none"> <li>Percent Crop Treated</li> <li>Dietary Monitoring Data</li> <li>Washing and Cooking Factors</li> <li>Duplicate Dinner Plates</li> </ul>	

# Acute CODEX process

Level	Consumption <b>WHO GEMS</b>	Residue Estimates	Model
Unrefined Less Resources		<ul style="list-style-type: none"> <li>• 100% CT</li> </ul>	<ul style="list-style-type: none"> <li>• Deterministic (single values)</li> <li>• Single foods assessments</li> </ul>
Intermediate	<ul style="list-style-type: none"> <li>• House Hold Surveys</li> <li>• Recipes for RACs</li> </ul>	<ul style="list-style-type: none"> <li>• Field Trial (HR and STMR)</li> <li>• <i>Variability for HR</i></li> <li>• <b><math>vF = 3</math></b></li> <li>• AI-specific processing</li> </ul>	
Refined Data intensive	<ul style="list-style-type: none"> <li>• Individual Diet Surveys (<b>14 countries</b>)</li> <li>• Recipes for RACs and processed products</li> </ul>	<ul style="list-style-type: none"> <li>• Percent Crop Treated</li> <li>• Dietary Monitoring Data</li> <li>• Washing and Cooking Factors</li> <li>• (<b>Case by Case</b>)</li> </ul>	

# Comparison of Driver Foods in acute assessments

## US Children

- milk , Juices (*apple and grape*) ,
- Orange juice, wheat flour, banana, **apple**, corn syrup, soymilk, wheat flour, potato

## EU Children

- Potatoes, melons, oranges, milk
- Watermelons, pineapple, **apples**, pear, grapefruit, cauliflower and pears

EPA Code	Crop Grp	Commodity Name	NFF
1100009000	11	Apple, dried	4
1100009001	11	Apple, dried-babyfood	1
1100007000	11	Apple, fruit with peel	4
		110-Uncooked; Fresh or N/S; Cook Meth N/S	
		150-Uncooked; Cured, etc; Cook Meth N/S	
		211-Cooked; Fresh or N/S; Baked	
		213-Cooked; Fresh or N/S; Fried	
1100010000	11	Apple, juice	10
		110-Uncooked; Fresh or N/S; Cook Meth N/S	
		120-Uncooked; Frozen; Cook Meth N/S	
		130-Uncooked; Dried; Cook Meth N/S	
		210-Cooked; Fresh or N/S; Cook Meth N/S	
		211-Cooked; Fresh or N/S; Baked	
		212-Cooked; Fresh or N/S; Boiled	
		213-Cooked; Fresh or N/S; Fried	
		214-Cooked; Fresh or N/S; Fried/baked	
		230-Cooked; Dried; Cook Meth N/S	
		240-Cooked; Canned; Cook Meth N/S	
1100010001	11	Apple, juice-babyfood	2
1100008000	11	Apple, peeled fruit	8
1100008001	11	Apple, peeled fruit-babyfood	3
1100011000	11	Apple, sauce	5
1100011001	11	Apple, sauce-babyfood	1
1100129000	11	Crabapple	0
1100210000	11	Loquat	0

# Dietary Risk Assessment for Pesticides

$$\text{Risk} = f(\text{Exposure}, \text{Hazard})$$

$$\text{Exposure} = \text{Consumption} \times \text{Residue in Food}$$

$$\text{Hazard} = f(\text{Toxicological Endpoint}, \text{Residue Definition})$$



# Divergence in Toxicological Interpretation Impacts Risk Cup

$$RfD = \text{NOAEL} / (10X * 10X * 3X)$$



$$RfD = \text{NOAEL} / (10X * 10X)$$



*RfD for parent*  
*RfD for metabolite*



$$RfD = \text{alternate NOAEL} / (10X * 10X)$$

- Different UF
- Different POD
- Different residue definition

# Generalized Process for RA Residue Definition

## Conduct $^{14}\text{C}$ Metabolism

- Goat, hen, 3 crops, rotational crop

## Determine Metabolic Pathway(s)

- $A \rightarrow B + C \rightarrow D + E$

## Establish Residue Definition List

- A, B, C most *significant* metabolites (prevalence and toxicity expertise)

## Is Toxicology Covered?

- Review of rat metabolism and PK studies

## Conduct Field Trials

- Collect field data on metabolite levels to confirm the final definition

## Conduct Dietary Assessment

- For RA residue definition

# Planned EU Process for Residue Definition

## Conduct <sup>14</sup>C Metabolism

- Goat, hen, 3 crops, rotational crop, **high temp hydrolysis, stereo chemical metabolism considerations**

## Determine Metabolic Pathways

- $A \rightarrow B + C \rightarrow D + E$  **+???** more **ID**

## Review ALL Metabolites

- Conduct deeper toxicity evaluations

## Is Toxicology Covered?

- **Focus on >10% dose urine/bile/organs** of rat metabolism
- Larger toxicology data set for metabolites

## Mathematically Sum for Residue Definition

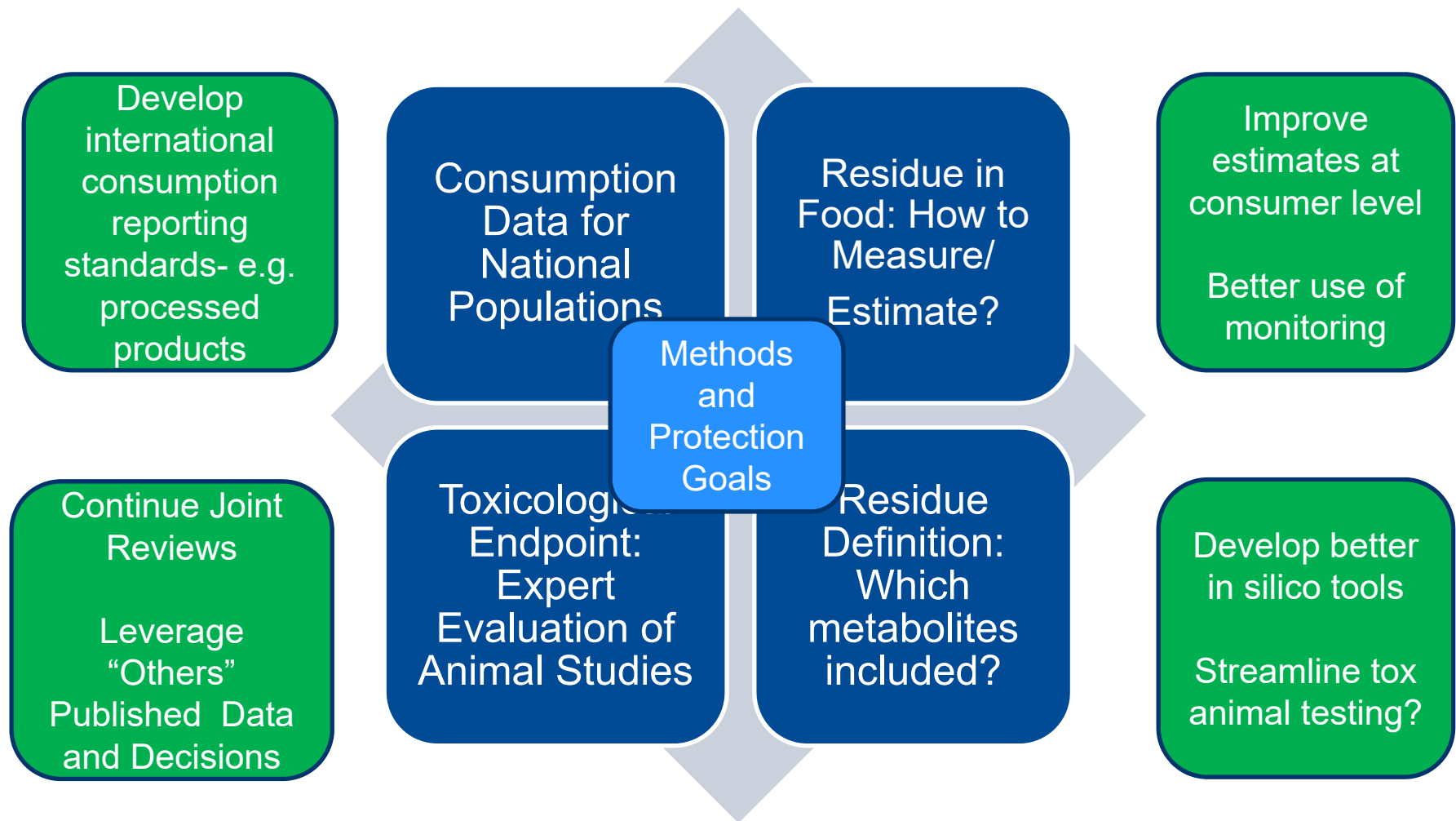
- Derive total toxicological burden (sum of parent + metabolites)
- Add metabolites into residue definition (RD) to **reach  $\geq 75\%$  toxicological burden**

## Apply to Field Trials . . .

- **with increased # analytes in trials**



# Key Areas Where Dietary Risk Assessments May Differ Globally





# Toxicology Trends Impact Risk Cup

## NA Focus

New studies at various lifestages to address **FQPA 10X** -> *different subpopulation endpoints*

Acute Neurotox study -> *more AIs with ARfDs*

## EU Focus

Hazard **Cut Offs**-> *less emphasis on exposure and risk assessment*

Metabolite Toxicity -> *diverging residue definitions or metabolite endpoints for risk assessment*

*Use of early repeat dose for acute: different ARfDs*

## Asia Focus

Independent Reivew of Global Data  
-> *different subpopulation endpoints;*  
-> *new emphasis on ARfDs*

## LA Focus

Seeking balance between Hazard focus and Risk assessment

*Typical RfD = NOAEL/(10X\*10X)*

Global Divergence of Final Endpoint  
either from **POD** or **Safety Factor**