International Discussions of the IESTI and Implications for Global MRLs

Cheryl Cleveland
Global Consumer Safety
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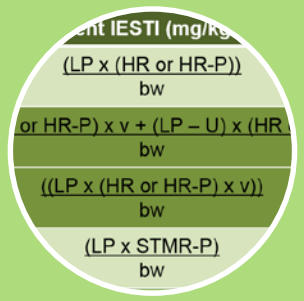
Overview of Talk

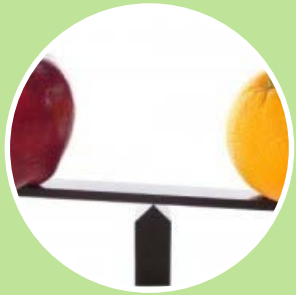
IESTI:

What is it? Why it matters?

Basics of Dietary Risk Assessment and MRLs



Current IESTI and Proposed Changes and Impact



Benchmarking

Continued Discussion

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IESTI:

What is it? Why it matters?

What is the Issue Around IESTI?

Many concerned that proposed change to the IESTI equation may lead to a loss of CODEX MRLs without international justification.

There is also concern the proposal leads to inflated dietary estimates for all commodities at international level.

There is confusion for many relative to EU versus CODEX versions of IESTI equations.

IESTI = International Estimated Short-Term Intake

- Set of 4 deterministic equations
- For single day exposures
- Conservative/protective
- One commodity at a time

- **JMPR, EU,** Australia, Japan, *Brazil?*
- Inputs differ such as variability factor = v

- Spreadsheet with Large Portion consumption data

- Final step in the approval of MRL
- Acceptable Intake <100% ARfD

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Recent Timeline of Key IESTI CODEX Activities

- GMUS 3 & CLI Case Studies
- EU “Impact” Publications
- EU PRIMo 3; Brazil Notice

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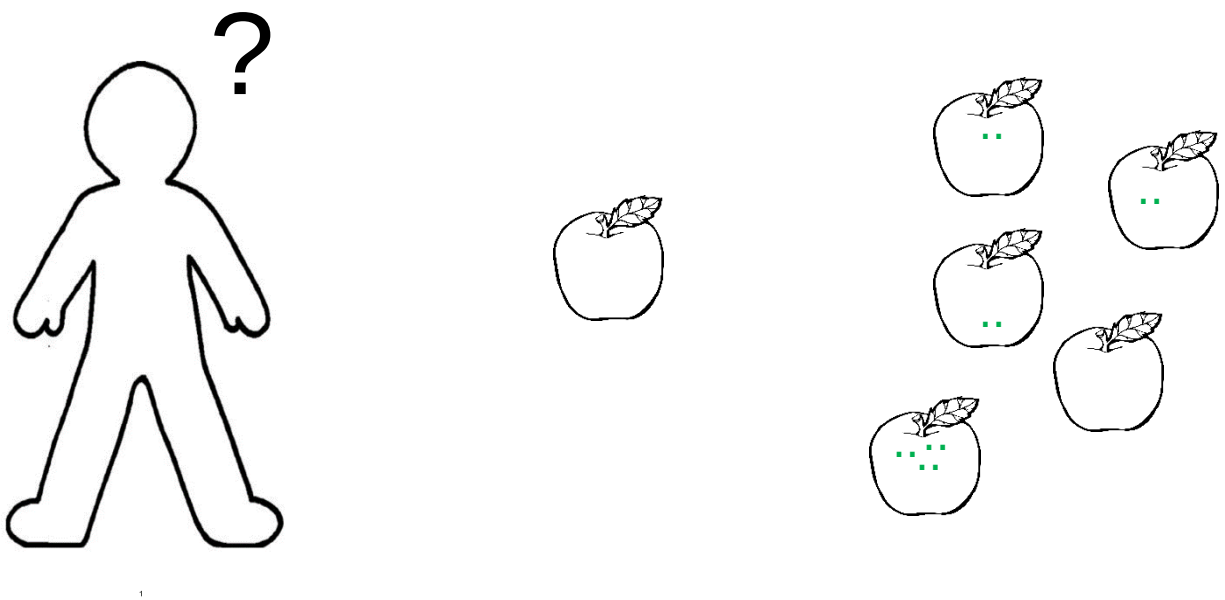
Basics of Dietary Risk Assessment and MRLs

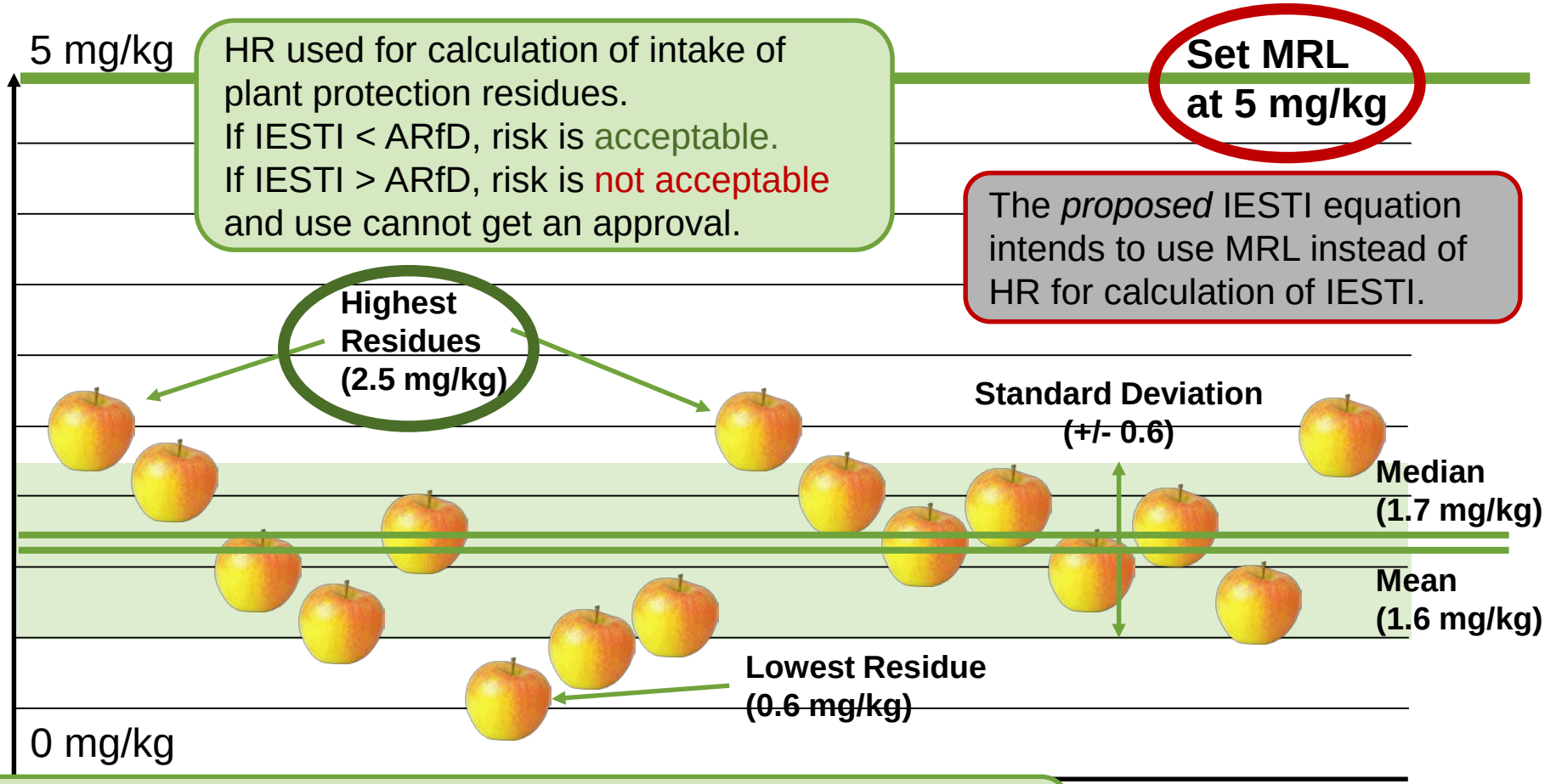
Generalized Dietary Risk Assessment

Risk = f (Exposure, Hazard)

Exposure = Consumption X Residue in Food



How is the value of an MRL set?



These residues are the result of regulatory supervised field trials, needed for a registration of an active substance in e.g. apples.

Trials are conducted at the maximum application rates, application numbers, shortest interval between applications and to harvest to leave highest possible residues.

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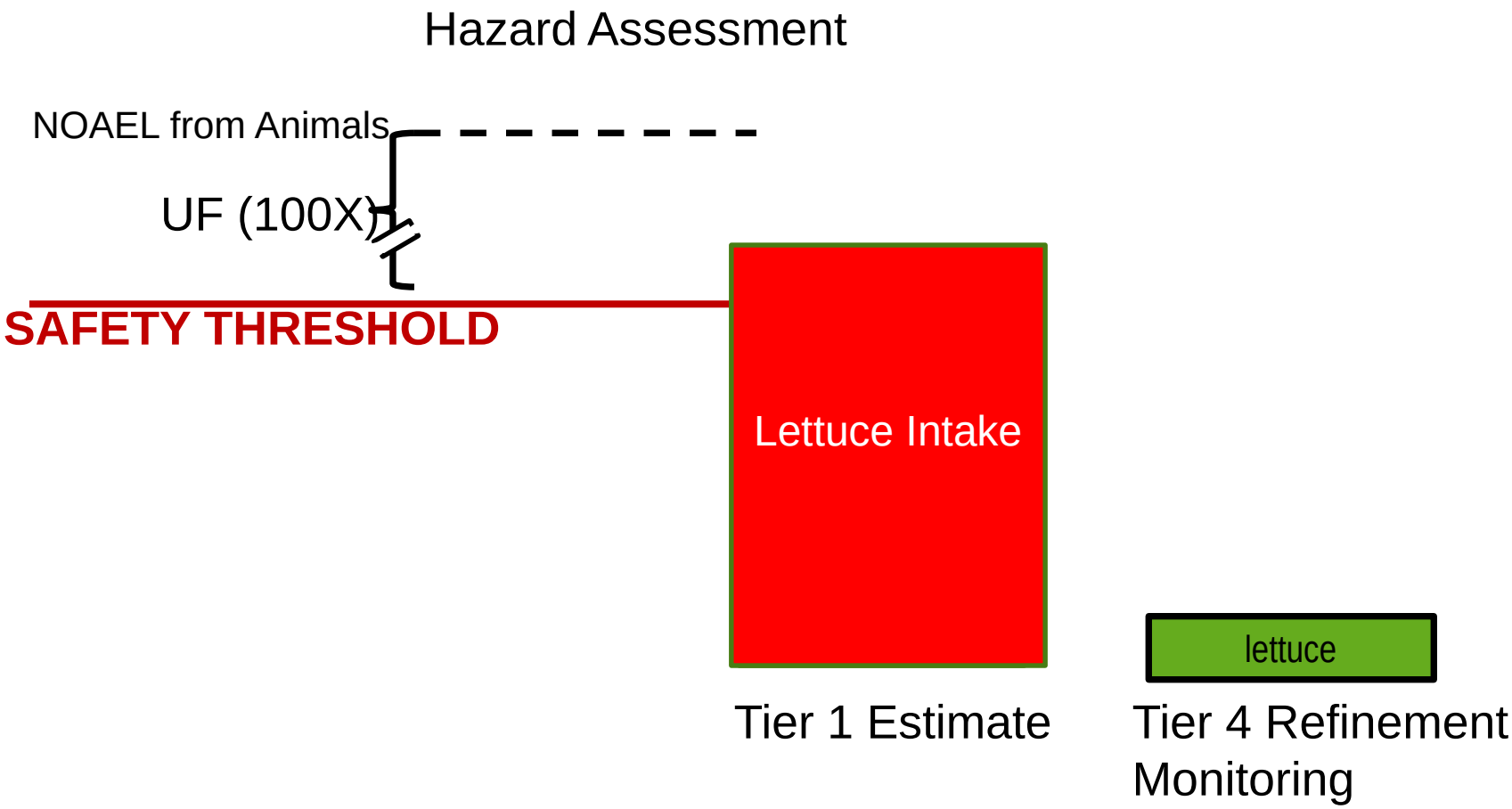
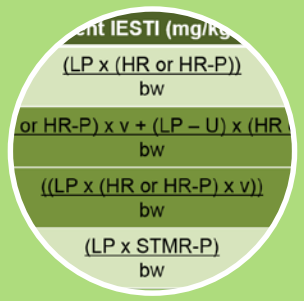
Dietary Risk/Safety Assessments





Current IESTI and Proposed Changes and Impact

IESTI Equations: Proposal from EFSA / WHO workshop, 2015

Dietary exposure = consumption X residues

Case	Current IESTI (mg/kg bw)	*Proposed IESTI (mg/kg bw)*
1	$\frac{(LP \times (HR \text{ or } HR-P))}{bw}$	$LP_{bw} \times MRL \times CF \times PF$
2a	$\frac{((Ue \times (HR \text{ or } HR-P) \times v + (LP-Ue) \times (HR \text{ or } HR-P))}{bw}$	$LP_{bw} \times MRL \times v \times CF \times PF$
2b	$\frac{((LP \times (HR \text{ or } HR-P) \times v))}{bw}$	$LP_{bw} \times MRL \times v \times CF \times PF$
3	$\frac{(LP * STMR-P)}{bw}$	$LP_{bw} \times MRL \times CF \times PF$

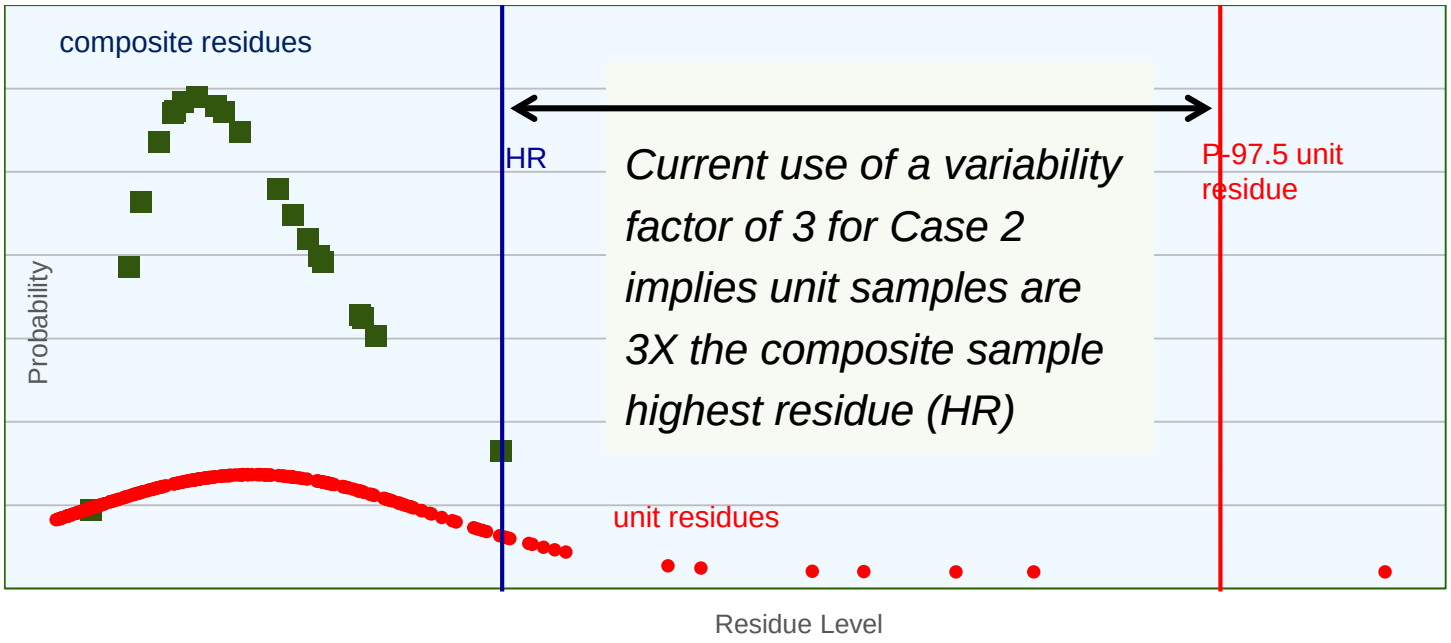
The proposal . . .

- Replaces all field data (HR and STMR) with MRL as exposure
- Keeps variability factor 3, but applies it to the MRL
- Removes unit weight from Case 2a
- Introduces new CF in order to use MRL
- Projects use of LP_{bw} data not yet available

The Varability Factor in CASE 2

The variability factor is an upper percentile estimate of the ratio between the pesticide residue in the unit samples and the residue in the composite samples

$$V = \frac{\text{97.5th percentile Unit Residue}}{\text{Composite Residue}}$$



Current use of a variability factor of 3 for Case 2 implies unit samples are 3X the composite sample highest residue (HR)

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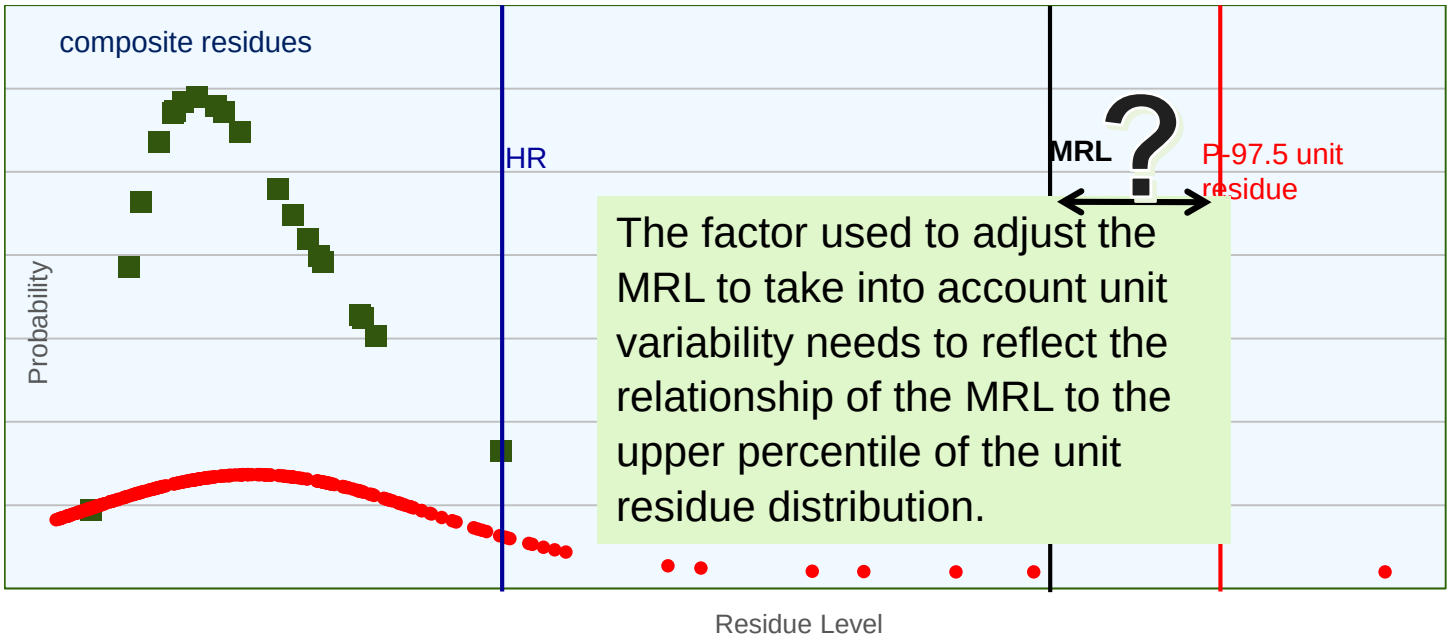
The Varability Factor in CASE 2

Proposed Acute Exp (mg/kg-bw/day) = MRL x **V** x LP

The variability factor is an upper percentile estimate of the ratio between the pesticide residue in the unit samples and the residue in the composite samples

V = 97.5th percentile Unit Residue / Composite Residue



The factor used to adjust the MRL to take into account unit variability needs to reflect the relationship of the MRL to the upper percentile of the unit residue distribution.

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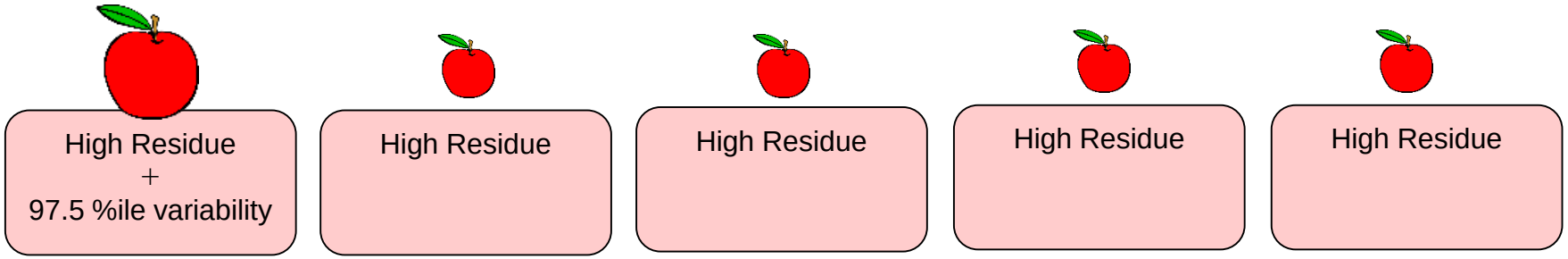
The Varability Factor in CASE 2a

Current

LP for children age 1-6: 5 127g apples

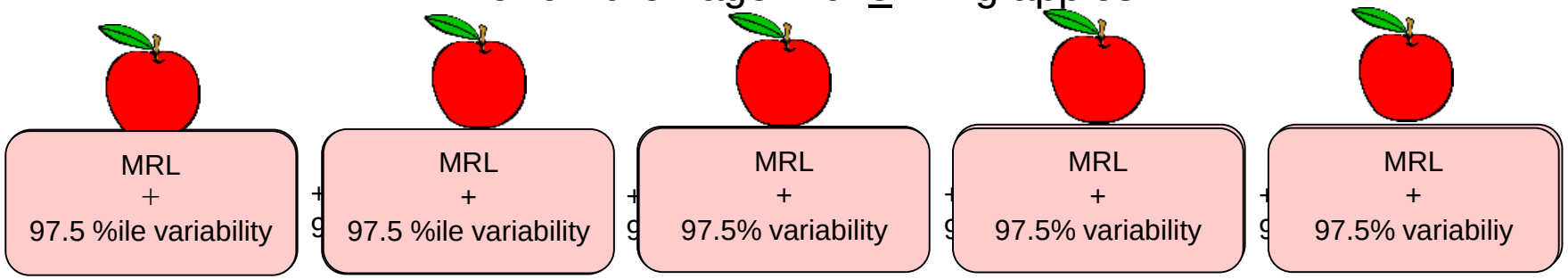


Smaller case 2a commodities like apricots, kiwi, fig, garlic, carrot, mandarin are even more affected by this compounded conservatism.

The Varability Factor in CASE 2a

Proposed IESTI = MRL x **V** x LP

LP for children age 1-6: 5 127g apples



Smaller case 2a commodities like apricots, kiwi, fig, garlic, carrot, mandarin are even more affected by this compounded conservatism.

➔ **The variability factor is SIGNIFICANTLY over conservative for case 2a commodities**

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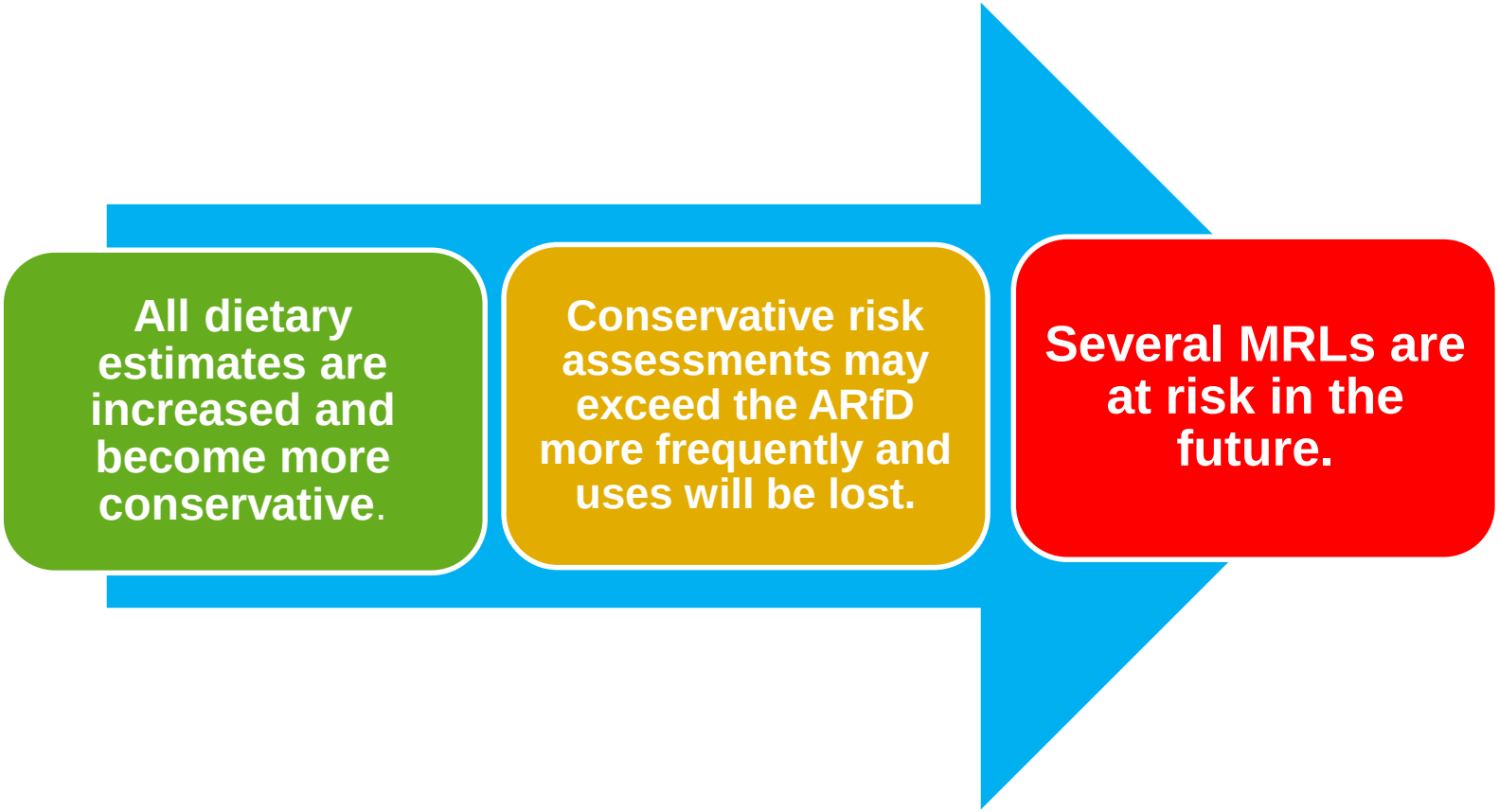
What is the Impact at JMPR?



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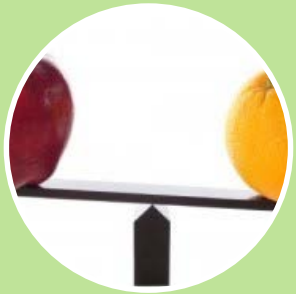
ECPA 2016 Preliminary impact - Revision of the IESTI equation

Case	Crops / commodities	Increase of Calculated exposure
1	  **Meal portion < 0.025 kg** *including meat, eggs*	1.7X
2a	  **Meal portion > 0.025 kg** Ue<LP *Use of 3 x MRL for all food*	3.5X
2b	  Ue>LP	2.3X
3	   **Bulked and blended**	5.2X

Contrast of EU and CODEX versions of the IESTI equation

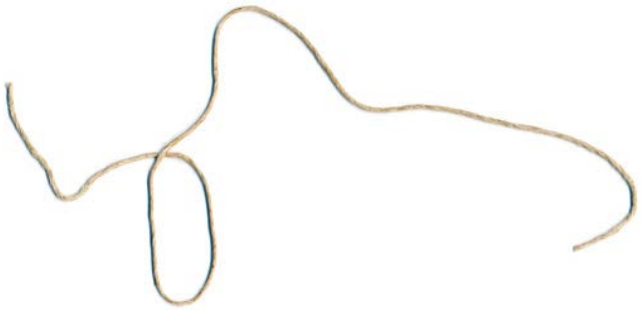
	CODEX	EU
Current Residue INPUTs for Dietary	HR, STMR, v= 1, 3	HR, STMR, v= 1, 3, **5, 7**
Food Inspection Use	Not done	MRL with v= 1, **3, 5, 7**
Proposed INPUTs	MRL ↑, v = 1, 3	MRL ↑ v= 1, 3 ↓
Resulting Impact of Proposal	Intake ↑	Intake ↑↓ = →
2018 Side Event Publications Impact Loss of MRLs	**4%** CODEX 12% Australia targeted	1.2% (crops & animal matrices)
Alternate "Harmonization"	HR, STMR, v= 1 3	***HR, STMR, v= 1 3***

Ball park assuming 5% impact. . .
Total CXLs at group level = ~ 5900
Extrapolated to individual CXLs ~34,000
Adjusted for projections w/ARfD - ~1000 CXLs



Benchmarking

Why Benchmarking?



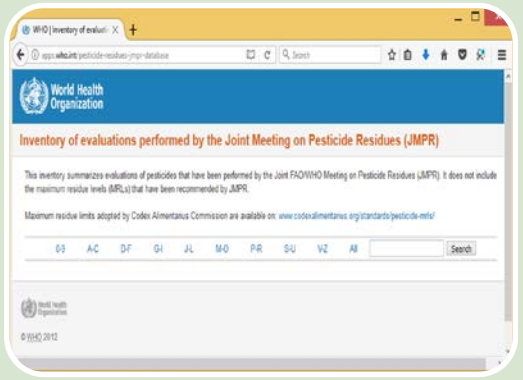
General IESTI spreadsheets are valuable

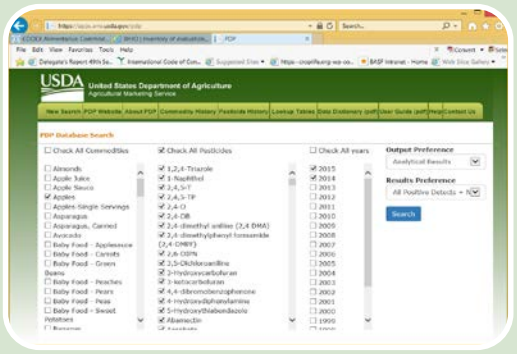
- enable the adoption of many new Codex MRLs (CXL) each year

Probabilistic Models envisioned as a calibration

- aid for risk communication discussions,
- not replacement for routine assessments

AI Criteria for US Benchmarking





CODEX MRL

- apple
- pome

ARfD

- Children
- General population

USDA PDP

- 2014-15
- >5% detects

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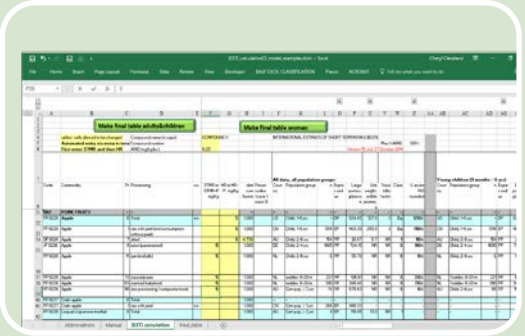
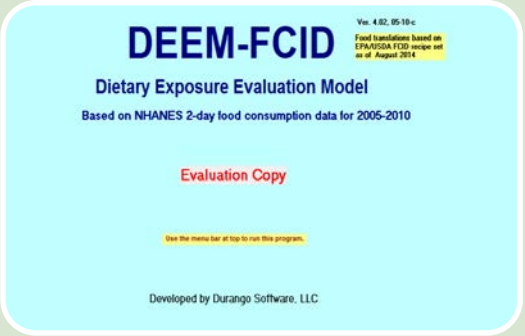
US Case Studies for Benchmarking





Deterministic

- IESTI
  1. Current HR
  2. Proposed MRL
  - 97.5th consumption

Quasi-Probabilistic

1. MRL
   - Consumption distribution

Probabilistic

1. Field Distribution
2. Monitoring Distribution

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US Apple Case Study: Intakes (ug/kg bw/day)

Active Ingredient	IESTI Deterministic	IESTI Deterministic	Quasi Probabilistic	Probabilistic	Probabilistic
	Current	*Proposed*	*Acute w/MRL* 97.5th %ile User Only	*Field Trial Data* 95th %ile Per Capita	*PDP Data* 99.9th %ile Per Capita
A	**33.4**	**60** (+ 1.8x)	**13** (- 2.6x)	**1.7** (- 20.2x)	**1.3** (- 25.5x)
B	**50.9**	**225** (+ 4.4x)	**48.9** (- 1x)	**4.5** (- 11.3x)	**0.9** (- 54.4x)
C	**5.66**	**15** (+ 2.7x)	**3.3** (- 1.7x)	**0.6** (- 8.7x)	**0.2** (- 34.9x)
D	**13.6**	**22.5** (+ 1.7x)	**4.9** (- 2.8x)	**0.4** (- 30.8x)	**0.2** (- 69.7x)
E	**13.0**	**37** (+ 2.8x)	**8.1** (- 1.6x)	**0.7** (- 18.2x)	**0.2** (- 74.3x)
F	**413**	**750** (+ 1.8x)	**163** (- 2.5x)	**26** (- 15.9x)	**1.6** (- 256x)
G	**16.4**	**37.5** (+ 2.3x)	**8.2** (- 2x)	**1** (- 16.6x)	**0.6** (- 26.2x)
H	**113**	**225** (+ 2x)	**48.9** (- 2.3x)	**14.8** (- 7.6x)	**23.2** (- 4.9x)
J	**21.5**	**52.5** (+ 2.4x)	**11.4** (- 1.9x)	**1** (- 20.6x)	0.2 (- 128.7x)

Comparison with Current IESTI Intake (Fold Increase+/Decrease-)

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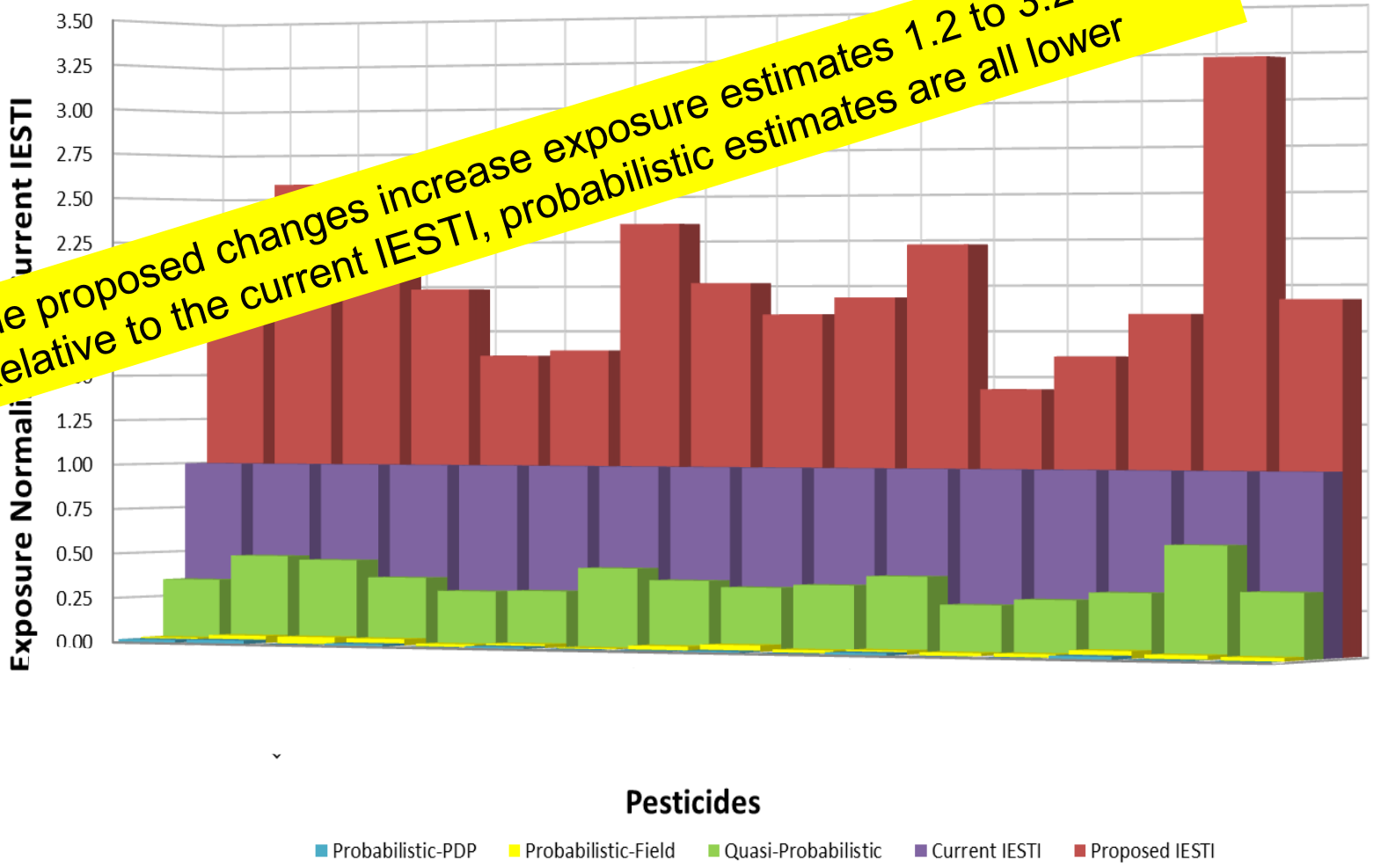
Tomato Case Study: Intakes (ug/kg bw/day)

- The proposed changes increase exposure estimates 1.2 to 3.2-fold.
- Relative to the current IESTI, probabilistic estimates are all lower



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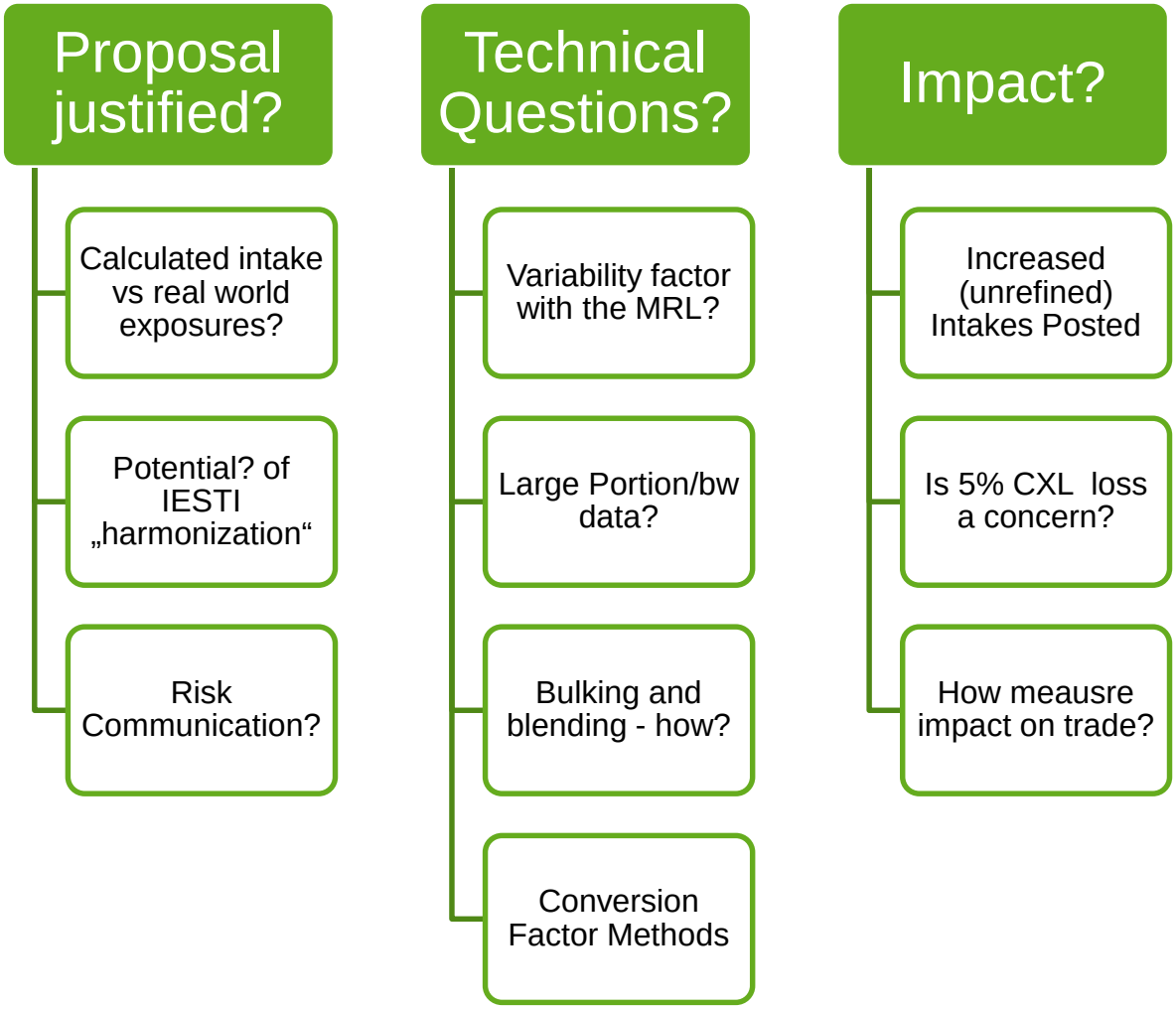
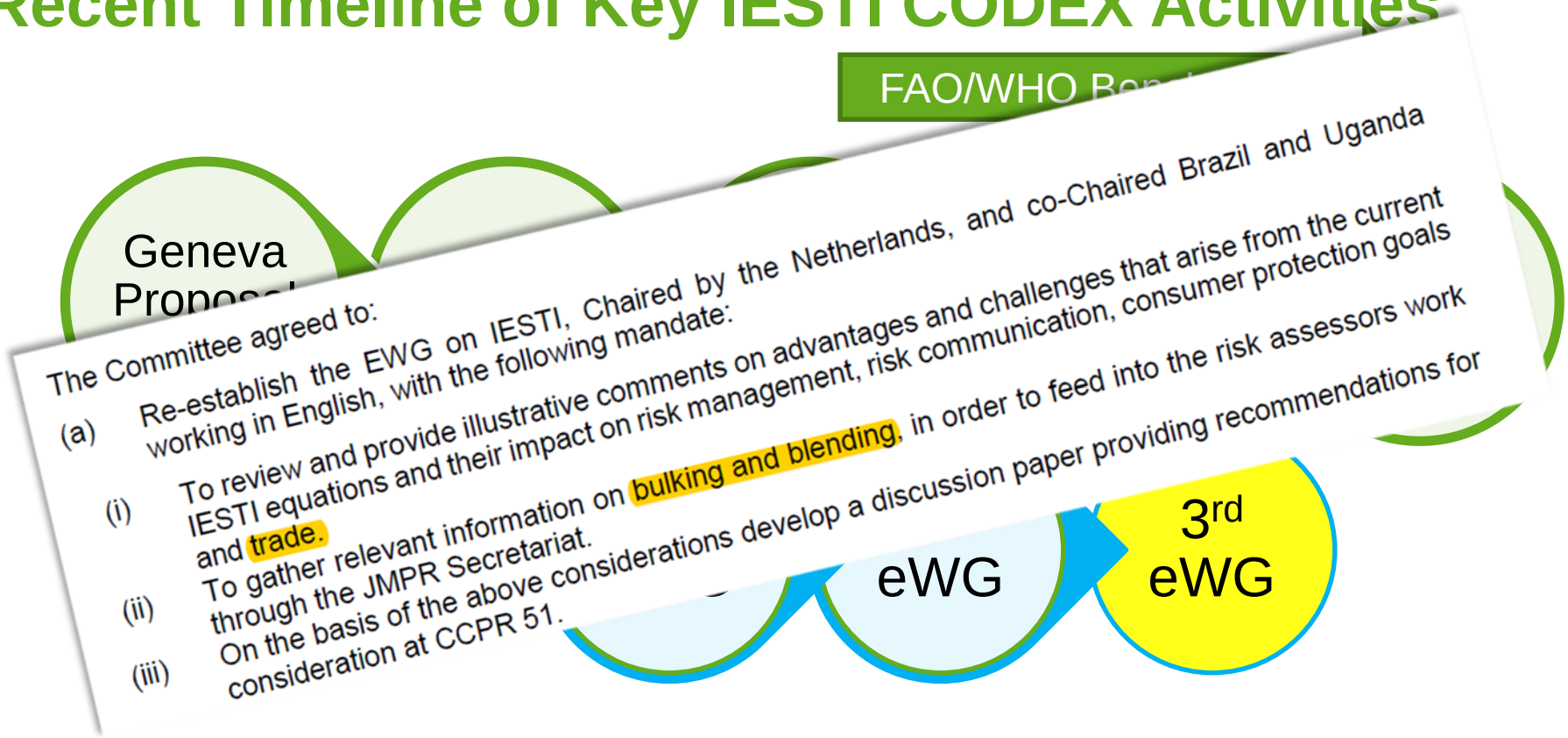
Continued Discussion

Many Levels of Debate on IESTI Proposal . . .



Recent Timeline of Key IESTI CODEX Activities



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Benchmarking exercise reflects EPA tiered approaches for dietary risk assessment

cheryl.cleveland@basf.com

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