

An international risk assessment and mitigation initiative on hand-held application commonly used in low- and middle-income countries (LMIC)

**Anugrah Shaw (ICPPE/UMES), Sabine Martin (BfR), Christian Kuester (Bayer Crop Science),
Neil Morgan (Syngenta)**

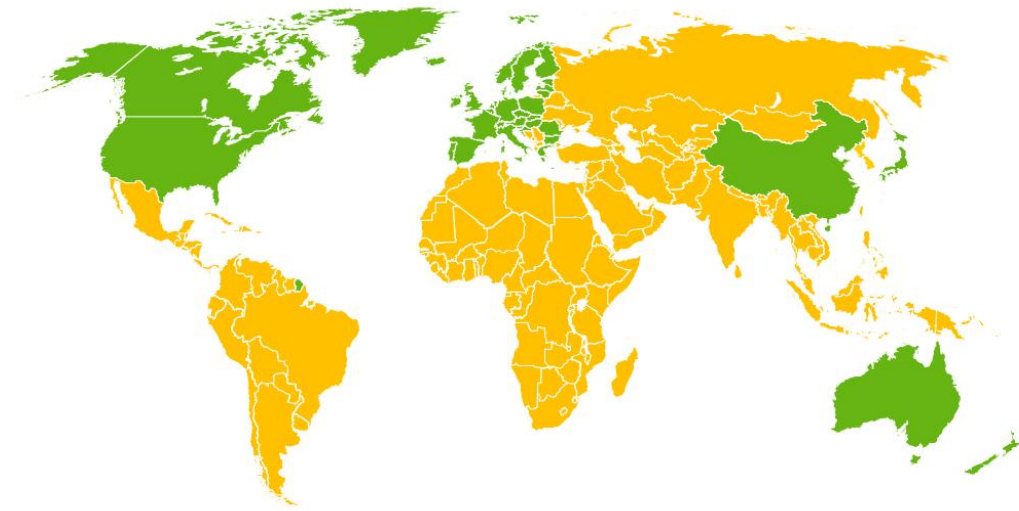
7th International Akademie Fresenius Conference Worker, Operator, Bystander and Resident Exposure and Risk Assessment / 13 and 14 December 2022 Cologne, Germany



International Center for PPE for Pesticide Operators and Reentry Workers (ICPPE)
University of Maryland Eastern Shore, Princess Anne, MD 21853. USA

Introduction

- Consideration of operator safety must be an important factor in pesticide registration processes.
- Regulatory process for pesticide registration is determined by regulations in the respective countries/regions.
 - Robust risk assessment process in countries colored green.
 - Some countries (e.g., Brazil and Kenya) are transitioning to a risk-based approach.



Global map of countries with the regulatory infrastructure to support complex process for risk assessment depicted in green

Introduction

- Operator exposure is often higher for hand-held applications when the operator is in contact with the foliage.
- Pesticide application using hand-held devices is still common in many LMICs.
- An international meeting held in September 2021 resulted in the risk assessment and mitigation initiative on hand-held applications commonly used in LMICs.
- The initiative, coordinated by ICPPE, is referred to as ICPPE LMIC Initiative.



Accuracy and Consistency

- **Accuracy** and **consistency** are important for operator safety assessments.
 - Relevant exposure scenarios and robust data set add to accuracy
 - Same approaches for derivation of endpoints (e.g. AOEL) and default values for dermal absorption add to the consistency



Significance of the ICPPE Initiative for LMIC

- Regional/country models and processes result in different requirements for the same hand-held scenarios.
 - Scenario based database for hand-held applications can build on international expertise to develop global model.
 - Number of studies underpinning the model if data is pooled allows for more robust analysis for model development.
 - Additionally, countries may not have the resources and expertise to develop their own models.



FAO and WHO as Observers

- FAO Pesticide Registration Toolkit used for training of regulators in many LMICs.
- The toolkit provides an option for LMIC's to transition to risk assessment and mitigation.
- FAO and WHO serve as observers on committees. Their comments focus on criteria FAO requires for databases/models for likely inclusion in the FAO toolkit to improve the occupational risk assessment.

The screenshot shows the 'Pesticide Registration Toolkit' website. At the top, there is a navigation bar with a home icon, 'Registration Tools' (highlighted in orange), 'Information Sources', 'Special Topics', 'News', 'About', and 'T'. Below the navigation bar is a sidebar menu with the following items: 'Registration strategies', 'Registration process', 'Data requirements and testing guidelines', 'Assessment methods' (highlighted in dark teal), 'Risk mitigation', 'Decision Making', 'Registration criteria', and 'Assessment of alternatives'. The main content area is titled 'Assessment method selection' and contains two dropdown menus. The first dropdown is labeled '- select pesticide group -' and the second is labeled '- select category -'. Below the second dropdown, a list of assessment categories is displayed, with 'Impact on human health' highlighted in light grey. The categories listed are: Identity & composition, Physical & chemical properties, Mode of action, handling, safety, Classification, packaging & labelling, Analytical methods, Impact on human health, Residues, Environmental fate, Environmental effects, Application & efficacy, and Overall conclusions.

Current Occupational Risk Evaluation in the FAO Toolkit

Assessment methods module

Justification for inclusion of operator/worker models

EFSA Calculator

- Based on Agricultural Operator Exposure Model (AOEM) & some USEPA Occupational Pesticide Handler Exposure Database
- Independently reviewed; adopted by EFSA

CropLife OPEX Tool

- Based on USEPA Occupational Pesticide Handler Exposure Database adopted by US-EPA & German model previously adopted by Germany/EU
- Independently reviewed
- CropLife contribution is providing a user-friendly calculation platform

- ✓ **FAO recognizes that current models may not include sufficient exposure data for pesticide application scenarios most relevant to LMICs (e.g. hand held applications)**
- ✓ **FAO welcomes the generation of such data and associated models/scenarios relevant to LMICs**

Source: FAO presentation at September 2021 meeting

Future Occupational Risk Evaluation in the FAO Toolkit

Assessment methods module

New/updated exposure models – required conditions

Likely inclusion if:

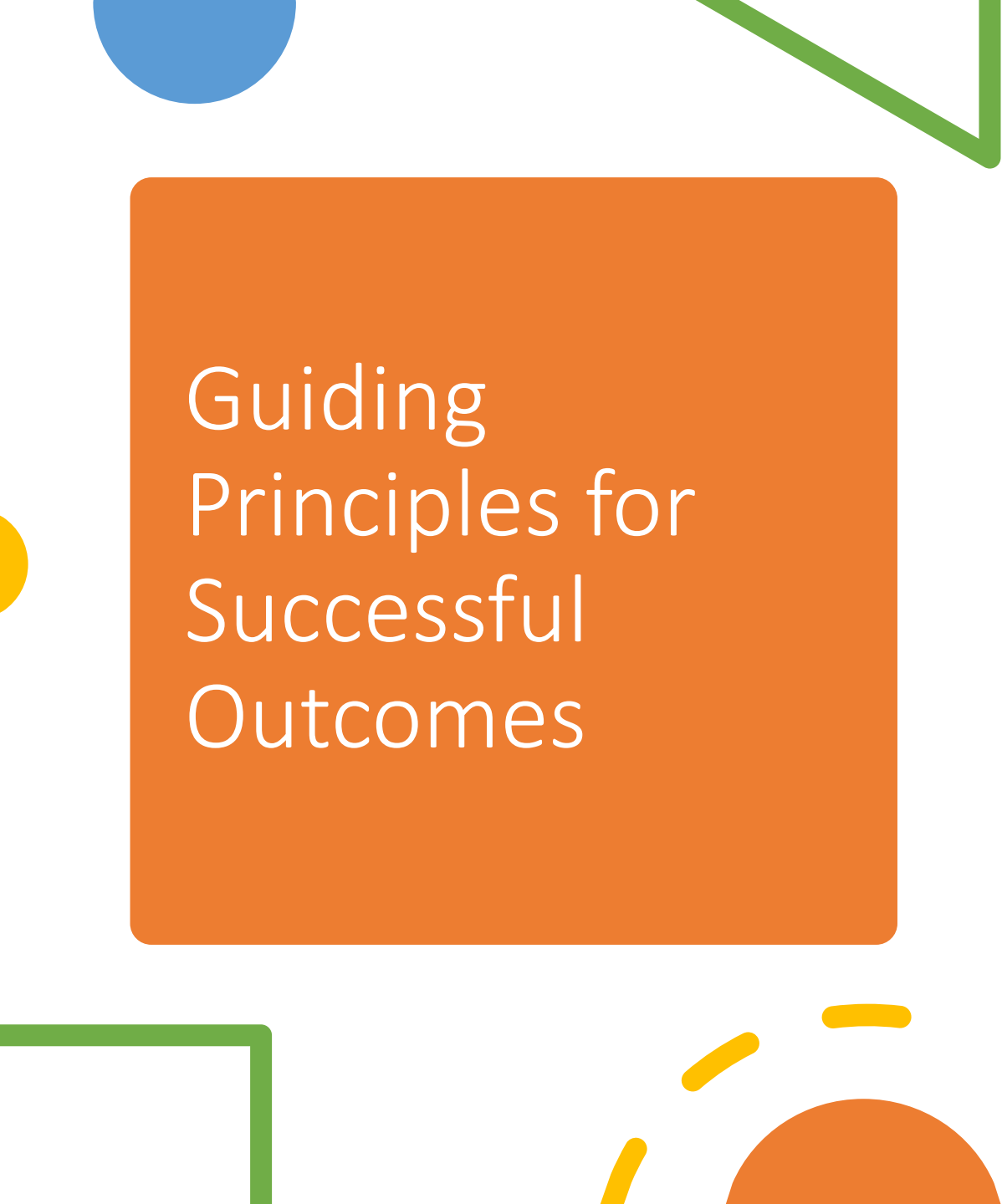
- relevant for pesticide application conditions in low and middle income countries
- both the underlying data and the model are considered scientifically sound after having gone through an independent review
- hosted by an independent and reputable institution / authority
- can be freely accessed by pesticide registration staff

Source: FAO presentation at September 2021 meeting



ICPPE LMIC Initiative

- Meeting FAO criteria for inclusion in Toolkit critical
- Guiding principles for successful outcomes –
September 2021 meeting
- Strategy to Improving Operator Safety in LMIC

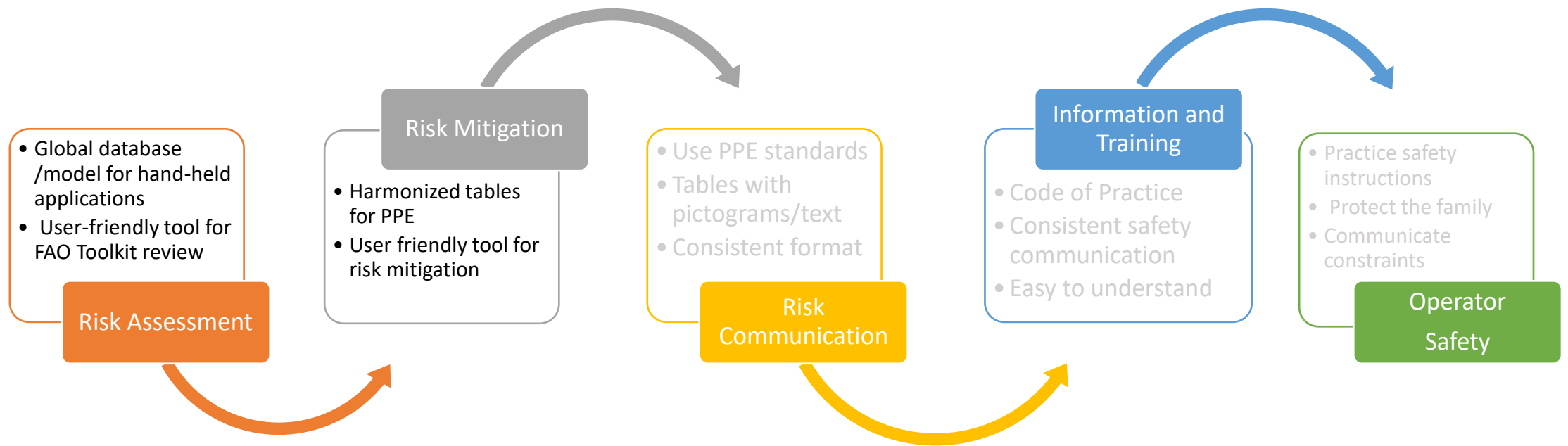


Guiding Principles for Successful Outcomes

- Acknowledge the “elephant in the room” that needs to be addressed: potential for conflict of interest.
- Build on the past accomplishments and international expertise.
- Establish four working groups of experts representing stakeholders including neutral entities as observers to avoid perceived or actual conflict of interest.
- Promote open candid technical discussions (including on topics with opposing views).
 - Work collectively to obtain and share information/data/resources to facilitate discussion.
 - Promote transparency by broadly circulating documents for comments and through publications.

Risk Assessment and Mitigation – The basis for operator safety

- Operator safety spans from product authorization to ability of operators to apply pesticides within acceptable risk
- Infrastructure - Four pillars to promote operator safety
- ICPPE LMIC Initiative for focuses on the first two pillars.



The ICPPE-LMIC Initiative: Strategy



Steering Committee

Strategy and scoping

WG1

Development of global database and operator exposure model for handheld applications relevant for LMIC.

WG2

Comparison of dermal absorption approaches with focus on default values.

WG3

PPE for risk mitigation based on exposure studies; partial body garments to balance protection and comfort

WG4

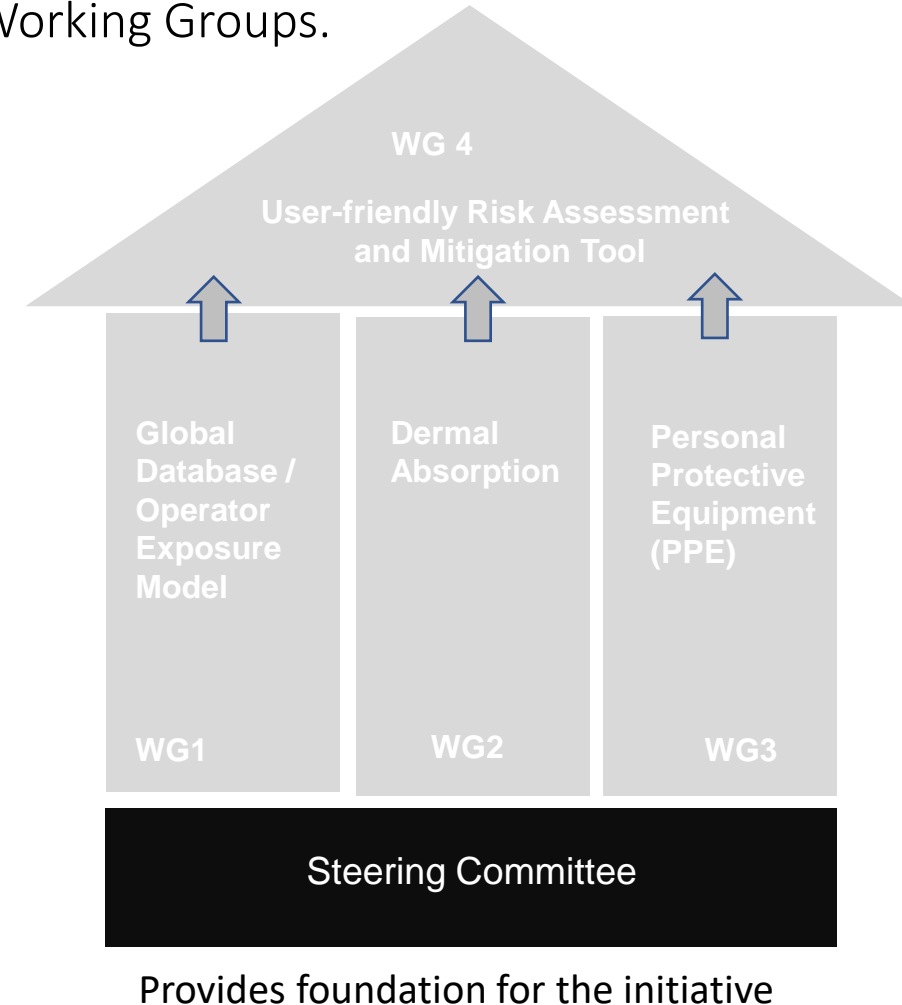
Based on outcome of WG1-3, development of a user-friendly risk assessment tool.

Steering Committee

Responsible for all administrative decisions, including approval of Working Groups.

- Beatrice Grenier/Harold van der Valk – Food and Agriculture Organization (FAO) - Observer
- Sabine Martin – German Federal Institute for Risk Assessment (BfR)
- Jurgen Schwarz – University of Maryland Eastern Shore (UMES)
- Tharacad Ramanarayanan – CropLife International (CLI) - OPEX Team Chair
- Christian Kuester* – Bayer AG Crop Science Division
- Markus Röver* – German Federal Office of Consumer Protection and Food Safety (BVL)
- Anugrah Shaw* – International Center for PPE for Pesticide Operators and Re-entry Workers (ICPPE)

* Operator safety discussion with perspectives based on their expertise and stakeholder group served as the basis for the September 2021 meeting.



Working Group 1

Coordinator – Sabine Martin

- Global Database Highlights
- Global Database Update

Global Database Update

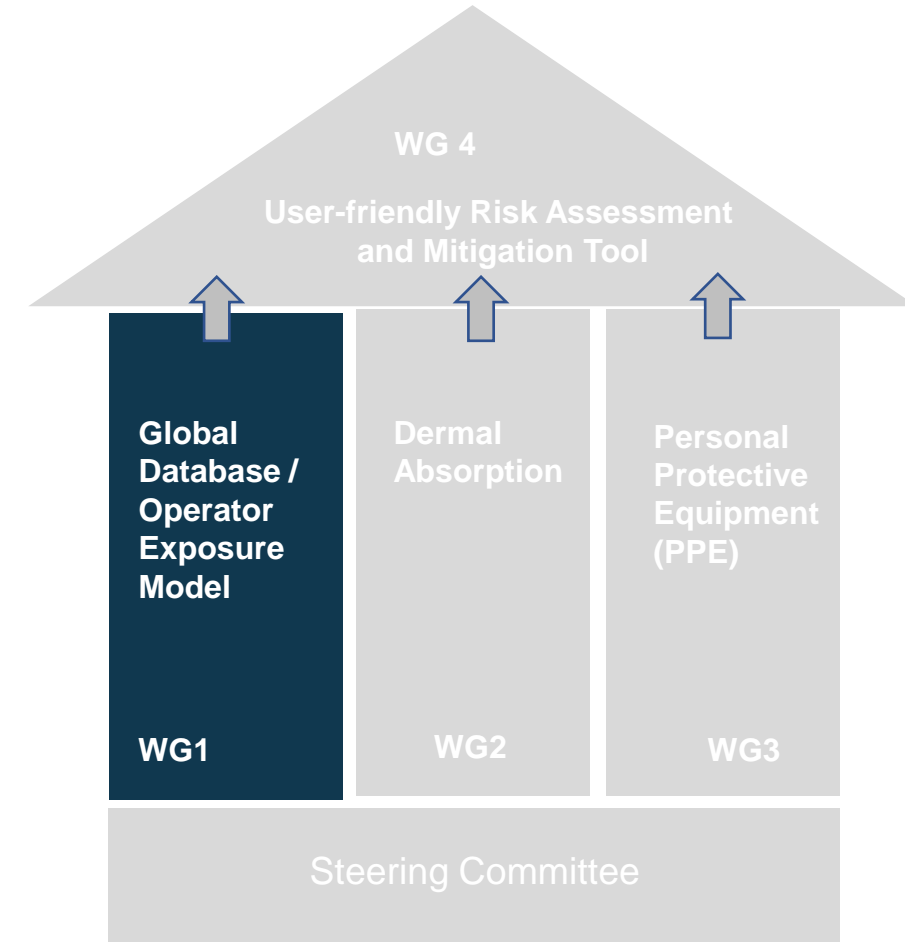
- Criteria for acceptance of studies discussed, agreed on list of criteria based on consensus
- AOEM data **template** modified for data entry
 - Garment details to support risk mitigation
 - Sub-group for hand-held application
- Images from studies and application in several LMICs
- Joint meeting -- CLI agrees to join the initiative
- In person meeting in Berlin to develop machine ready file.
- Statistical analysis and model development to be done by an independent consultant.

These criteria to be finalized at WG1 Virtual Meeting on 9 February 2022			Color coding - yellow and red cells to be discussed		
Topic	AOEM	Global database	Green	Yellow	Red
Guidance	Compliance with OECD Series No. 9	Procedure should be described properly. Guidance, which was followed to generate exposure data, should be mentioned (as a starting point).	Guidance Specified	Not specified or could not be determined.	
GLP	Full compliance with GLP	Full compliance with GLP preferred but not required. However, some sort of reliability criteria is important: Sound description of analytical method is needed and relevant information on the study design: application rates, crop structure, equipment, area treated.	GLP certified	Reliability criteria to be reviewed	
Data access	Only raw data in reports	Public availability of data is important to evaluate the data properly and to generate trust in the data and the model. Processed values from publications (e.g., mean values) are considered not sufficient. Individual exposure data from publication in peer-reviewed journals, where body and hand are separately measured could be acceptable (case by case).	Raw data available	Raw data not available. Individual exposure data included in the peer reviewed publication	Raw data not available. Only mean values in peer reviewed publication
Study participant	Monitoring of professional agricultural operators (e.g., farmers and contractors)	Professional participants are preferred, but not highest priority. Study details to include information on how participants were identified/recruited to rule out potential bias (e.g., 1. participants should not be employees of the pesticide company sponsoring the study. 2. higher exposure for inexperienced study participants).	Professional participants.		
Background information	Data recording and observations according to current scientific knowledge	A sound description for study is most important, photographic documentation preferred.	Study details available.		
Data structure	Suitable data form for model development (e.g., separately measured head, hand, and body exposure)	At least individual exposure data, where body and hand are separately measured. Differentiation of body parts (back/front torso, head and inhalation data is additionally helpful. Depending on the data, some higher flexibility in data acceptance and revision of criteria afterwards. Mean values can only be used for data validation.	separate measurements for hand and body.	for body only	
Dermal Dosimeters	Whole body dosimetry (WBD) for dermal exposure (exclusion of patch data)	For the inventory, both types of dosimeters (WBD + patch) were included in the Excel file in the shared drive. If, based on discussion there is a need to include patch study data, a statistician needs to be consulted.	Study garments for outer and inner WBD		WBD worn under personal clothing
Inhalation dosimeters	Inhalation exposure determined with appropriate inhalation fraction samplers	If inhalation exposure was measured, description on method should be given	Inhalation procedure provided		

Screen shot - Criteria for acceptance of studies

Global Database Highlights

- Diverse Working Group – regulators, industry experts, FAO and WHO Observers
- Robust dataset with exposure data for hand-held pesticide applications from existing models and “new data”:
 - Existing models - AOEM, AOEM Greenhouse, EPA Reviews
 - Twelve studies from Republic of Korea
 - Studies from CropLife International (CLI) member companies
 - Four additional studies from Greece, India and France



Exposure scenarios relevant for LMIC's

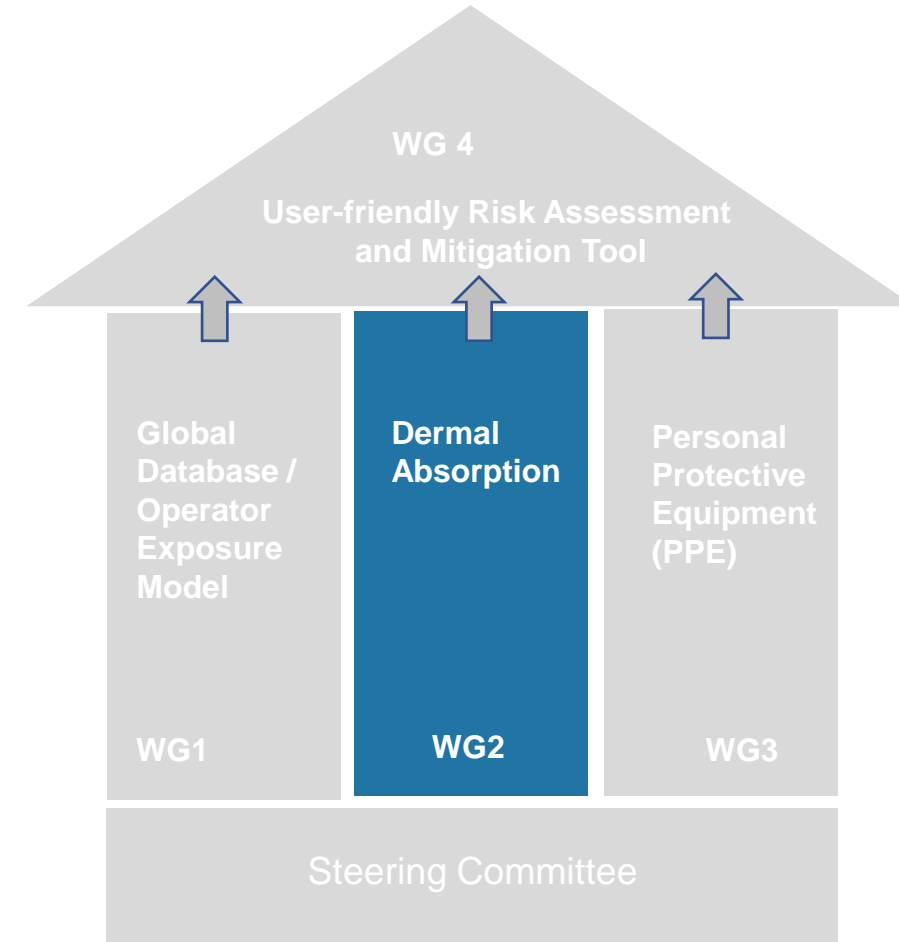
Working Group 2

Coordinator – Neil Morgan

- Smaller working group with expertise in dermal absorption
- Review default values for regulatory purpose
- Discussion on studies used for dermal absorption

Dermal Absorption – Default Factor Discussion

Complexity
Derivation of dermal absorption values from studies is complex. Studies and calculation methods used can vary considerably.
Limited resources
Default values will be important in developing a robust but user-friendly risk assessment tool for countries with limited resources.
Global understanding
Understanding the basis for different default values used by respective countries/models is important.
Document
Requires development of document that explains the similarity and differences in data sets and statistical analysis that result in very different default values.



Major factor for risk assessment

Dermal Absorption – Default Factor Discussion

Goal

- The goal is to propose scientifically justified principles for default values. A scientific publication could add to the body of knowledge.

Disclaimer

- Important: Engaging in scientific discussions does not imply endorsement of the information by the expert's organization.



Dermal Absorption Studies

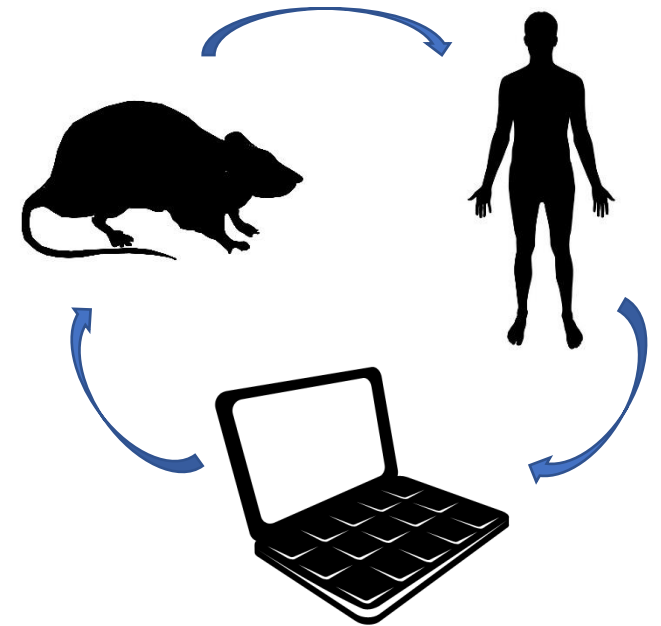
Specific studies

Discussion on approach to derive product/ or substance-specific dermal absorption values from experimental studies

Study methodology

Discussion on merits of different approaches

- *in vitro* (human/rat skin)
- *in vivo* (rat)
- Newer *in silico* methods for estimation of dermal absorption



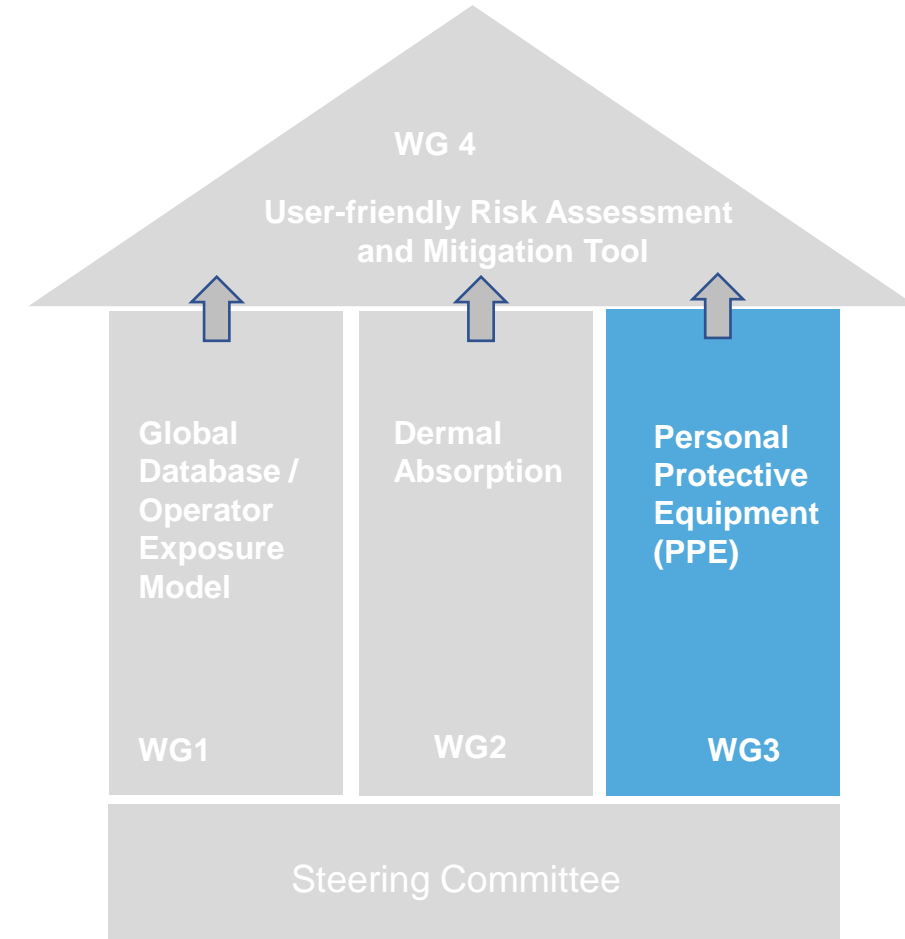
Working Group 3

Coordinator – Anugrah Shaw

- Risk assessors, risk managers, and PPE experts to work collectively
- Operator exposure studies as basis for risk mitigation
- Partial body garments for additional protection
- “Locally” manufactured garments to address Availability

PPE for Risk Mitigation

- Risk mitigation the bridge between risk assessment and risk management.
- PPE for risk mitigation requires PPE expertise (including certification)
- WG 3 includes experts in risk assessment, risk management and PPE/PPE Certification.
 - Risk assessors - data analysis of global database
 - PPE experts – work with risk assessors on equivalencies
 - Risk managers – work with PPE experts on availability and user acceptance.



Equivalencies based on OPEX studies

PPE for Risk Mitigation

Potential and actual exposure data in operator exposure studies provide data to determine protection provided by garments and gloves.

- Certified gloves used for operator exposure studies.
 - Determining equivalencies not required.
- Certified garments not used for most studies.
 - Global database provides data to determine equivalencies for ISO 27065 a global standard specifically for protection against pesticides.
 - C1 for basic requirement and C3 for additional protection.

Respiratory protection, when needed, requires certified respirators/facemasks.



Study garment meets C1 requirements

Constraints – Comfort, Availability, Cost, User Acceptance

- C3 partial-body garments provide a balance between protection and comfort.
- Cost and availability, based on demand, addressed at the country/region level.
 - “Locally” manufactured garments could address availability and possibly cost.
- PPE style and colors, based on user preferences addressed at the “local” level.
 - Brazil is an example of easily available, locally made and certified ISO 27065 garments.



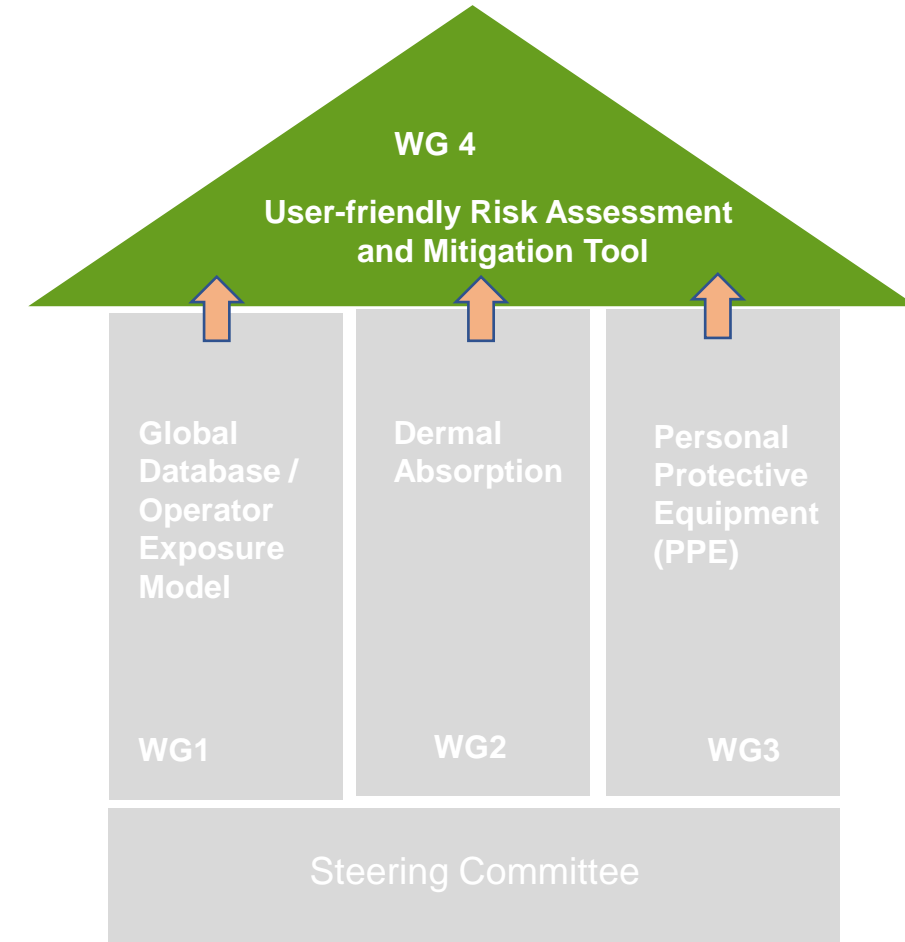
Working Group 4

Coordinator – Christian Kuester

- International expertise in risk assessment
- LMIC input to develop a tool that meets their needs
- Comments/input from FAO trainers
- Flexibility, consistency and accuracy

User-friendly Risk Assessment and Mitigation Tool

- A web-based tool developed with “global” data and expertise to address “local” needs of LMIC’s.
- Builds on outcomes of Working Groups 1, 2, and 3.
 - Global database/model for hand-held applications developed by WG1.
 - Principles for default values for dermal protection proposed by WG2
 - PPE for risk mitigation proposed by WG3, in consultation with WG1
- Input from the users is critical - LMIC transitioning to risk assessment and FAO toolkit trainers



Builds on WG1, 2, and 3 outcomes

Flexibility, Consistency, Accuracy

A user-friendly tool that balances flexibility with consistency and accuracy.

- Flexibility
 - Default values for factors such as area treated and body weight with flexibility to enter country specific values.
 - Flexibility also in terms of available technology.

- Consistency
 - Access to AOEL values
 - Principles for default values/ guidelines for dermal absorption

- Accuracy
 - Based on robust global database for hand-held applications
 - Model based on factors agreed by international experts, many engaged in the development of models currently in use.