Robust Regulatory Tools for European Non-dietary Risk Assessment: Plant Protection Industry's Data Collection Initiative

Christiane Wiemann on behalf of CropLife Europe Occupational and Bystander Exposure Technical SubGroup

CLE OBE TSG

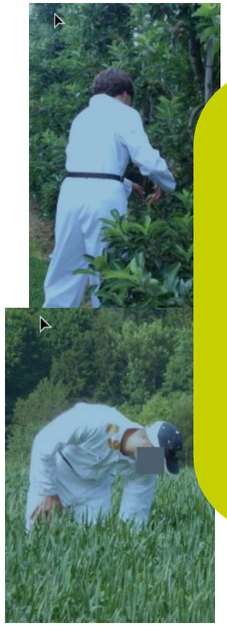
ISES Europe Chapter Workshop 19-21.03.2023

Background

- Product use related (occupational) non-dietary exposure is predominantly by dermal contact and inhalation, excluding exposure via residues in the diet.
- Risk assessment models in place are deterministic models relying on measured field/greenhouse exposure data under real life conditions.
- Historically and continuingly data of the crop protection industry form the backbone of the model developments and improvements thereof.
- To close data-gaps and to provide data driven model improvements industry continues efforts to conduct studies, collect and evaluate data.

Exposure related data generation for plant protection product (PPP) use

Operator exposure
(Work-related during use)



Re-entry worker exposure
(Work-related after use)

Bystander and resident exposure
(General population during and after use)

Dermal Exposure
(Dermal absorption)

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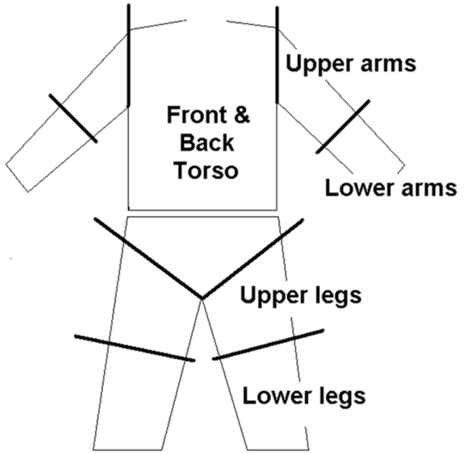
Exposure measurement: Dermal by whole body dosimetry and inhalation by personal air sampling

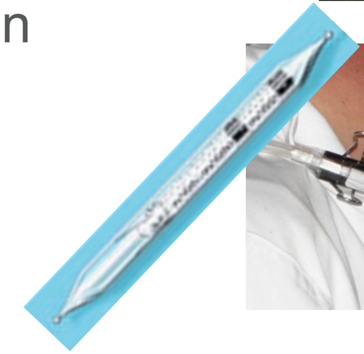
Dermal

- Outer and inner dosimeters
- <u>Outer dosimeter</u>
    - Body: Regular work clothing
    - Hand: Protective gloves
- <u>Inner dosimeter</u>
    - Body: long sleeved shirt and long johns (cotton)
    - Hand: Hand-wash (or cotton glove)
    - Head: Face/neck wipe or cap
- Inner dosimeters = surrogate of skin



Inhalation:

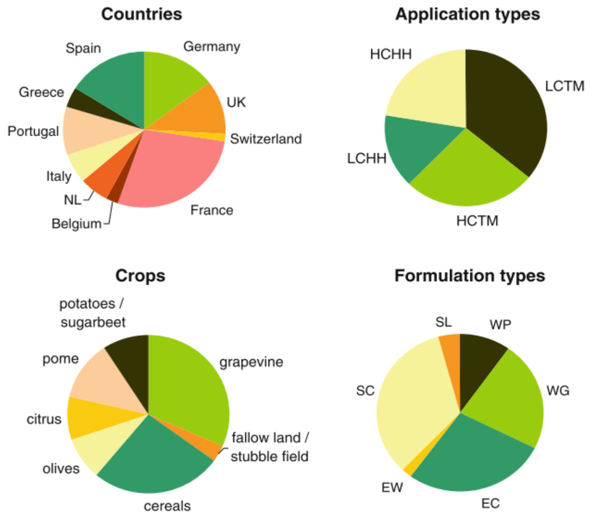
- Air sampling pump: colleting air in breathing zone through a sampling device (filter tube)



Operator Exposure: Agricultural Operator Exposure Model (AOEM) – Basis of current EU risk assessment

- AOEM 2013: Joint effort from EU authorities and industry
- **34 industry whole body dosimeter exposure studies** selected based on high quality criteria
- Allowing model development covering different scenario
- Followed by AOEM Greenhouse model 2016/2020 based on **10 studies** generated particularly for model purpose

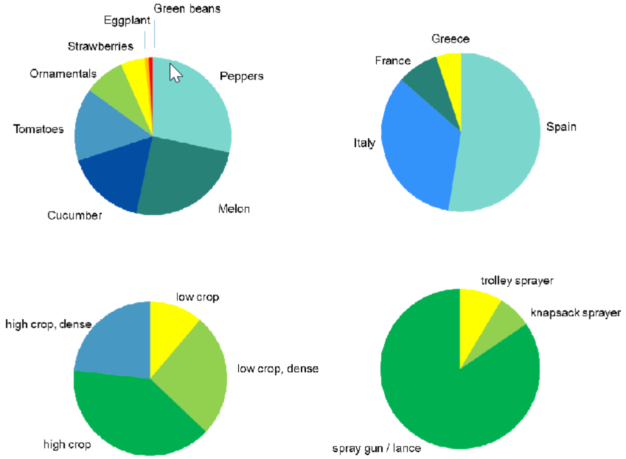
AOEM



AOEM: Number of data points for modelling

	Mixing/loading						Application					
	Inhalation	Hands	Gloves	$Body^{inner}$	$Body^{outer}$	Head	Inhalation	Hands	Gloves	$Body^{inner}$	$Body^{outer}$	Head
LCTM	77	96	108	56	57	57	66	85	74	45	46	46
HCTM	52	66	77	41	41	40	83	97	92	72	72	71
LCHH	40	49	49	40	40	40	39	48	20	39	39	39
HCHH	32	44	44	32	32	32	90	90	90	90	90	90
All	201	255	278	169	170	169	278	320	276	246	247	246

Greenhouse AOEM



J. Verbr. Lebensm.
DOI 10.1007/s00003-013-0836-x
Journal für Verbraucherschutz und Lebensmittelsicherheit
Journal of Consumer Protection and Food Safety

RESEARCH ARTICLE

A new model for the prediction of agricultural operator exposure during professional application of plant protection products in outdoor crops

Claudia Großkopf · Hans Mielke · Dieter Westphal · Martina Erdtmann-Vourliotis · Paul Hamey · Francoise Bouneb · Dirk Rautmann · Franz Stauber · Heinrich Wicke · Wolfgang Maasfeld · Jose Domingo Salazar · Graham Chester · Sabine Martin

Joint development of a new Greenhouse Agricultural Operator Exposure Model for hand-held application

Project Report

Bundesinstitut für Risikobewertung

Update of the Greenhouse Agricultural Operator Exposure Model

Amendment to Project Report 01/2016

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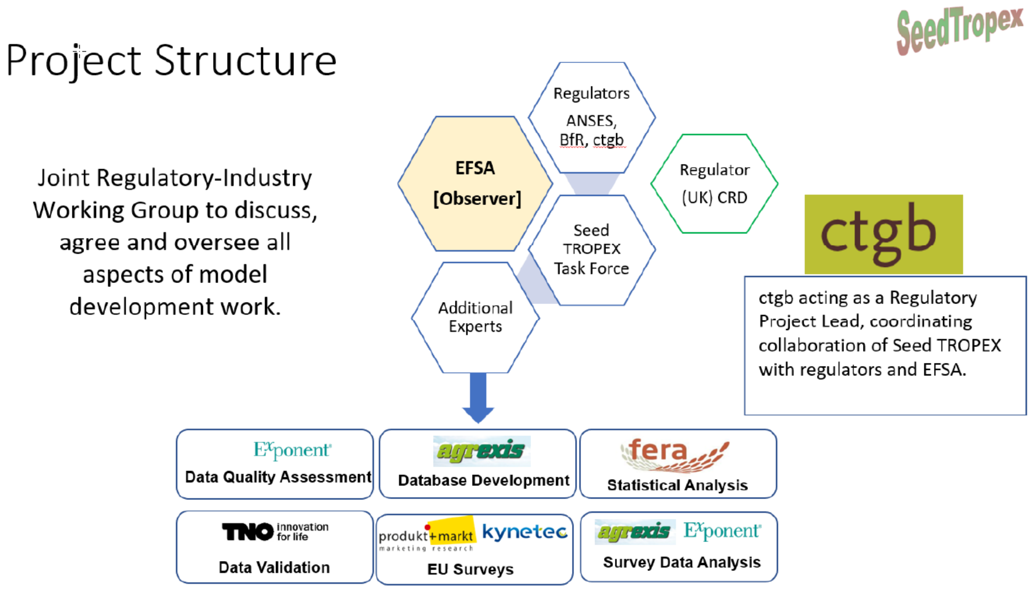
Operator Exposure: Seed treatment a different exposure scenario requiring separate exposure models to be brought to EU acceptance

- Currently, no harmonized model at EU level for seed treatment risk assessment,
- Tier 1 model = Seed TROPEX model, not publicly available.
- The Seed TROPEX Task Force, recognized need fo a new regulatory model and provided studies and knowledge to populate model development.
- **31 exposure studies**, reflecting changes in technology and work practices accompanied by **survey on EU use conditions**
- Predictive models for seed treatment and sowing of treated seed developed by independent specialists.
- Model and data submitted to EFSA for peer review



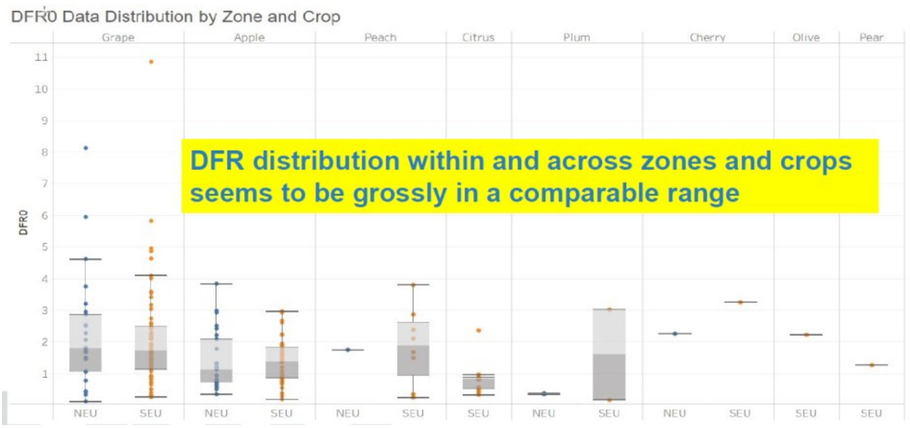
Re-entry exposure: DFR database

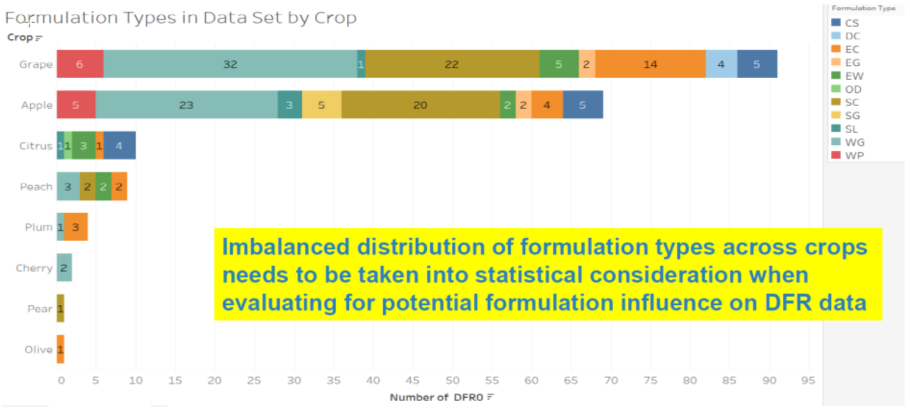
Generic risk equation for dermal exposure during re-entry activities:

PDE = (**DFR** x TC x T) / 1,000

- **DFR play a significant role in worker exposure assessments**
- **Re-entry assessments are now required for bystanders and residents following similar principles as those for workers.**
- **EFSA default DFR value is 3 µg/cm² / kg of active ingredient applied per hectare, based on a database of 55 studies.**
- **CLE is conducting <u>an ongoing project</u> to evaluate a larger database of DFR data and investigate how various parameters, such as crop type and product type, can influence DFR magnitude**
- **Database collected comprises of > 1250 data sets**

Part 1 EU DFR data on vineyard and orchard crops



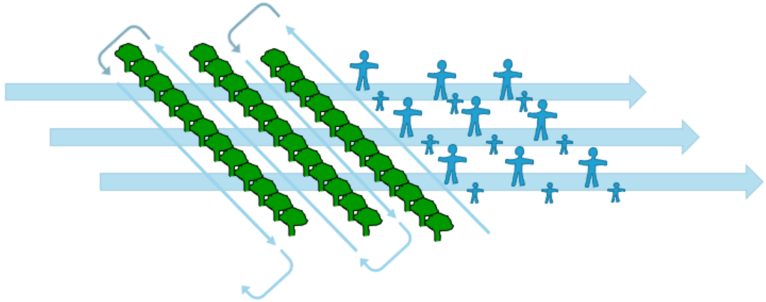


Bystander and resident exposure: BROV Project Spray Drift Exposure

- EFSA: Current spray drift study data for high crop scenarios are limited, also acknowledged by EFSA.
- BROV research program: **16 new studies in 4 EU countries: 8 trials in orchards and 8 in vineyards**.
- Clear differentiation
  - adult vs. child, crop type, leaf cover, distance from the sprayer,
- Significantly lower dermal and inhalation exposure levels in vineyards compared to orchards.
- Data evaluated by UK-HSE and submitted to EFSA in 2020 but not considered for guidance update 2022 for formal reasons

Bystander 95th percentile exposure (mL spray /person)

Time of application	Distance	Orchards		Vineyards	
		Adults	Children	Adults	Children
Early application	5 m	0.0136	0.0114	0.0020	0.0042
	10 m	0.0089	0.0102	0.0017	0.0017
	15 m	0.0053	0.0067	0.0015	0.0014
Late application	5 m	0.0052	0.0055	0.0042	0.0028
	10 m	0.0042	0.0038	0.0034	0.0029
	15 m	0.0040	0.0024	0.0026	0.0016
EFSA	5+10 m	0.00440	0.00350	0.00440	0.00350



Aspects of Applied Biology 148, 2024
International Advances in Pesticide Application

Proposals for new spray drift exposure values in orchard and vineyards for residents and bystanders

By UDO BLASCHKE[1], EDGARS FELKERS[2], NICOLA J HEWITT[3], FELIX M KLUXEN[4], NEIL MORGAN[5] and CHRISTIANE WIEMANN [6]

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Dermal Absorption: Converting externally measured / estimated dermal exposure into systemic exposure for risk assessment

- CLE database: **295 studies, 152 agrochemicals, 19 product types** proposed default values thereof **(+ Brazil Prohuma database 486 studies)**
- CLE sponsored studies and analysis
  - Improved understanding of methodology capabilities and data interpretation
  - New exposure scenarios e.g. Dried residues or extended exposure under in vitro conditions
  - New data driven evaluation strategies for relevant exposure scenarios challenging the EFSA approach

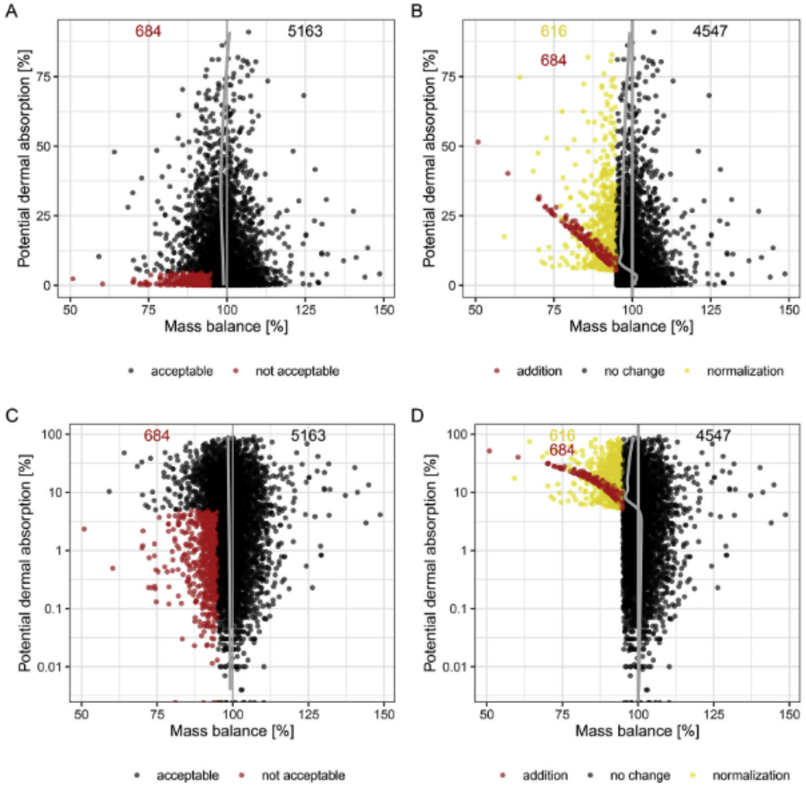
Selected descriptive statistics of dermal absorption values for concentrates grouped by formulation type for the new and the combined datasets (% dermal absorption).

	Number of values	% Dermal absorption 95th percentile	75th percentile	Median
New dataset				
EC + EW + SE	61	6.2	2.3	1.1
SL + SC + OD + FS	79	2.3	0.8	0.4
WP + WG + SG	29	1.6	0.8	0.2
Combined dataset				
EC + EW + SE	107	6.2	3.0	1.2
SL + SC + OD + FS	135	2.9	0.8	0.4
WP + WG + SG	48	1.7	0.7	0.3

Dermal absorption (%) for diluted PPPs.

Percentile	Receptor fluid + receptor chamber wash + skin sample excluding tape strips No. 1 + 2 (Definition 1)		
	All (n = 167)	Liquids (n = 136)	Solids (n = 31)
25th	3.56	3.73	3.29
Median	6.93	7.13	5.04
75th	14.1	14.6	10.5
95th	28.0	27.7	29.3

n = Number of dermal absorption values.



Aggarwal, M., et al., 2014. Assessment of in vitro human dermal absorption studies on pesticides to determine default values, opportunities for read-across and influence of dilution on absorption. Regul Toxicol Pharmacol. 68, 412-23.

Aggarwal, M., et al., 2015. Assessment of an extended dataset of in vitro human dermal absorption studies on pesticides to determine default values, opportunities for read-across and influence of dilution on absorption. Regul Toxicol Pharmacol. 72, 58-70.

Aggarwal, M., P. Fisher, F. M. Kluxen, W. Maas, N. Morgan, R. Parr-Dobrzanski, C. Strupp and C. Wiemann (2019). "Assessing in vitro dermal absorption of dry residues of agrochemical sprays using human skin within OECD TG 428." Regul Toxicol Pharmacol **106**: 55-67.

Kluxen, F. M., E. Felkers, S. M. Jensen, J. Domoradzki, C. Lorez, P. Fisher and C. Wiemann (2023). "Practical guidance to evaluate in vitro dermal absorption studies for pesticide registration: An industry perspective." Regulatory Toxicology and Pharmacology **142**: 105432.

Kluxen, F. M., E. Felkers, S. McEuen, P. Fisher, C. Strupp, C. Lorez, J. Y. Domoradzki and C. Wiemann (2022). "A new conceptional model for deriving average dermal absorption estimates from studies with multiple tested concentrations for non-dietary risk assessment of pesticides." Arch Toxicol **96**(9): 2429-2445.

Kluxen, F. M., S. Gregoire, A. Schepky, N. J. Hewitt, M. Klaric, J. Y. Domoradzki, E. Felkers, J. Fernandes, P. Fisher, S. F. McEuen, R. Parr-Dobrzanski and C. Wiemann (2019). "Dermal absorption study OECD TG 428 mass balance recommendations based on the EFSA database." Regul Toxicol Pharmacol **108**: 104475.

Kluxen, F. M., S. Totti, W. Maas, F. Toner, L. Page, K. Webbley, R. Nagane, R. Mingoia, C. Whitfield, J. Kendrick, C. Valentine, J. B. Dorange, C. Egron, C. Imart, J. Y. Domoradzki, P. Fisher, C. Lorez, S. McEuen, E. Felkers, T. Chen and C. Wiemann (2022). "An OECD TG 428 study ring trial with (14)C-Caffeine demonstrating repeatability and robustness of the dermal absorption in vitro method." Regul Toxicol Pharmacol **132**: 105184.

Morgan, N., N. J. Hewitt, E. Felkers, C. Wiemann, F. M. Kluxen and C. J. Kuster (2021). "Dose Setting for Dermal Absorption Studies on Dried Foliar Residues." Ann Work Expo Health **65**(4): 397-405.

The complete? list…

Operator Exposure related:

- AOEM model database
- GH AOEM model database
- SeedTropex database
- SeedTropex Survey
- Closed transfer system studies (technical exposure reduction solution for spray tank loading)
  Sasturain et al. 2024
  10.1007/s00003-023-01472-7
- PPE protection factors are suitable
  Morgan et al. 2022
  10.1016/j.ssci.2020.104940

Re-entry worker exposure related:

- BROV Re-entry worker project
  UK-HSE et al. 2020
  https://croplifeeurope.eu/our-contribution/human-health/protecting-farmers/workers/
- CLE DFR Database collection (ongoing project)

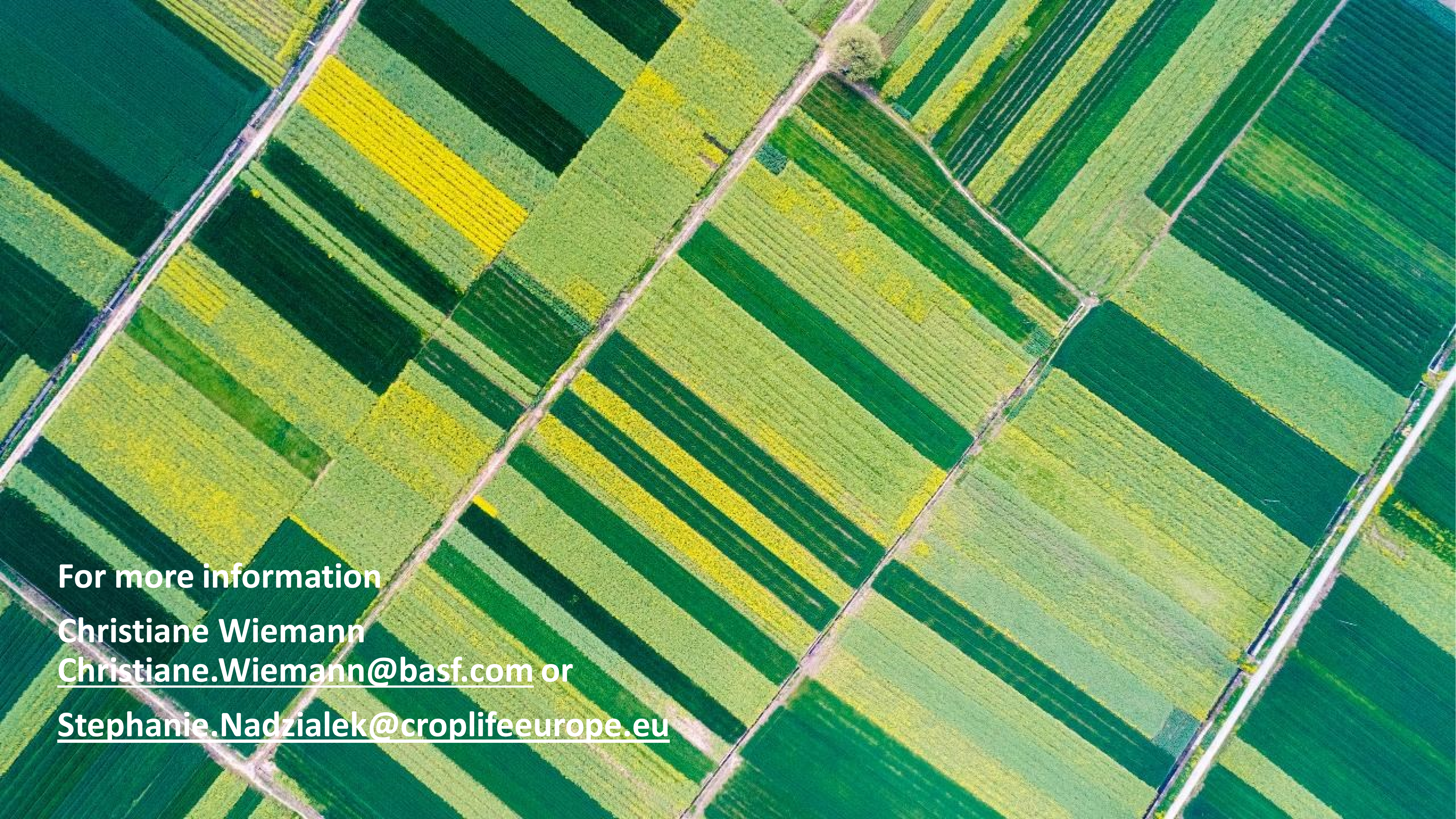
Bystander / resident exposure related:

- BROV Spray Drift Project
  UK-HSE et al 2021
  https://croplifeeurope.eu/our-contribution/human-health/protecting-farmers/bystanders/
- Impact of drift reducing nozzles
  Kuster et al 2021
  10.1111/aab.12686
- BREAM version 2 development
  Butler-Ellis et al 2018
  10.1093/annweh/wxy017
- Protection factors for light clothing
  Felkers et al 2023
  10.1007/s00003-023-01430-3
- Pesticides in air
  Felkers et al. 2022a, b
  10.1016/j.yrtph.2022.105285
  10.1016/j.yrtph.2022.105172
  Butler-Ellis et al. 2023
  10.1016/j.yrtph.2023.105504
  Vinck et al (submitted manuscript)

Conclusions

- Appropriate high-quality databases and profound data analysis form the basis for high quality and reliable risk assessments
- Data generation efforts by industry form the backbone of regulatory model developments and improvements thereof
- Joint projects of data-generators and data evaluators improve the transparency and trust into data generation and data interpretation
- Regulatory use of data-driven evidence will improve the risk assessment
- Regulatory adoption of improved risk assessments needs to speed up

Acknowledgement:
Thank you to all current and former scientific experts contributing to the in here presented work and underlying data generation



For more information

Christiane Wiemann
Christiane.Wiemann@basf.com or
Stephanie.Nadzialek@croplifeeurope.eu

Bystander and resident exposure: Pesticides in Air

- EFSA guidance: Exposure to volatilized pesticides relies on limited data assigning default air concentrations based on vapour pressure: No accurate reflection of associated risk?
- CLE conducted studies and collated field data to compare
  - Current approach is hyper-conservative
  - Refinement proposal: normalizing air concentrations to application rate.
  - Use BROV and other field data and BROWSE models which allow refined risk assessments by incorporating risk mitigation measures and probabilistic features.
- Additional evidence by literature reviews and monitoring campaigns provided

Ambient air concentrations of Plant Protection Products: data collection for the Combined Air Concentration Database and associated risk assessment

Anne-Kim Vinck [a], Edgars Felkers [b], Michel Urtizberea [c], Nicola J. Hewitt [d], Kathrin Bürling [e], Alistair Morriss [f]

Manuscript submitted to Regulatory Toxicology and Pharmacology

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Measured air concentrations of pesticides for the estimation of exposure to vapour in European risk assessments

Edgars Felkers [a,1,*], Felix M. Kluxen [a], Sarah Adham [b], Anne-Kim Vinck [c], Nicola J. Hewitt [d], Neil Morgan [e]

Regulatory Toxicology and Pharmacology 145 (2023) 105504

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A comparison between field measurements of vapour concentrations of plant protection products and predictions by the BROWSE model

M. Clare Butler Ellis [a,*], Edgars Felkers [b], Sarah Adham [c], Anne-Kim Vinck [d], Kathrin Bürling [e], Neil Morgan [f]

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