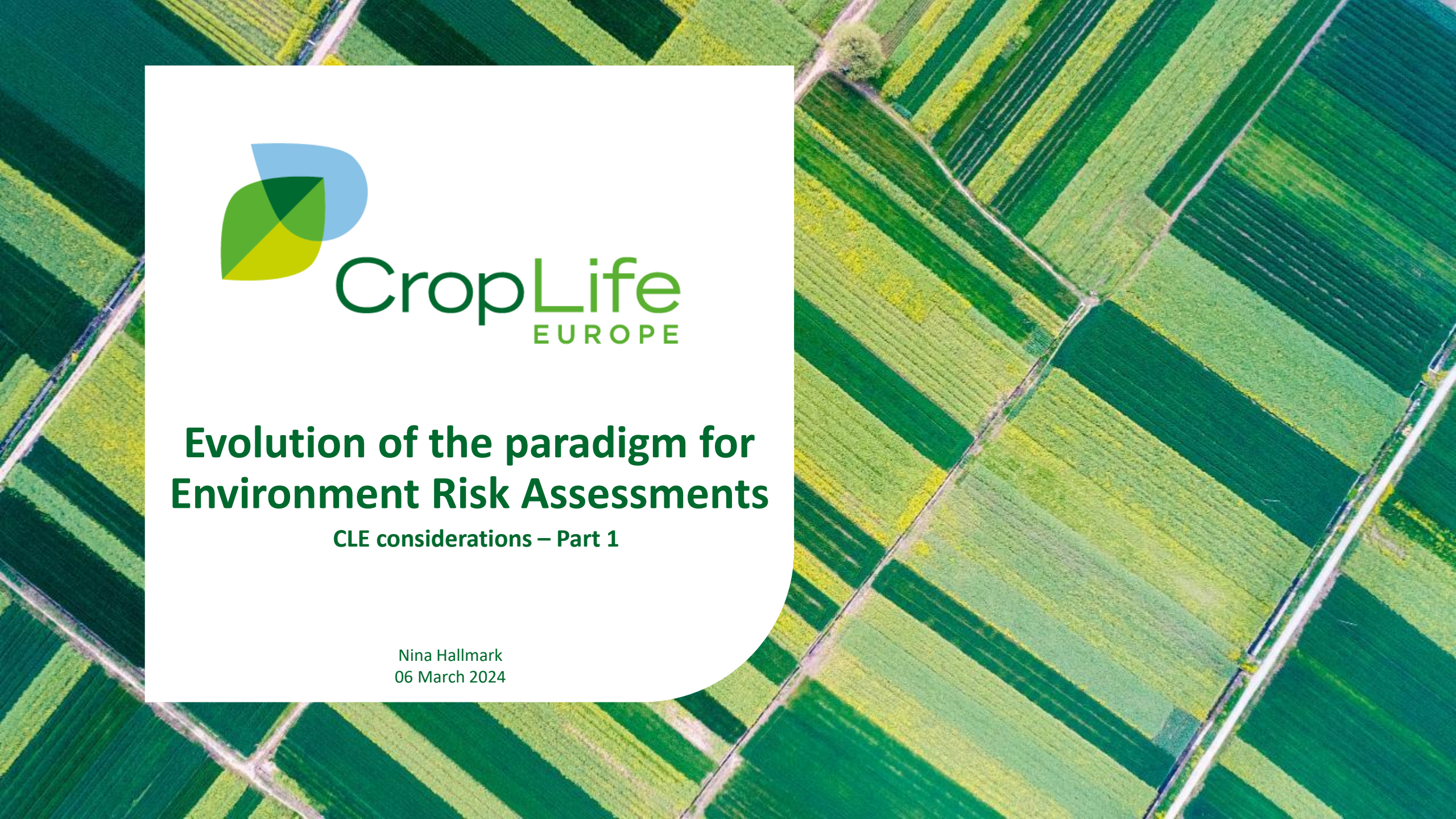
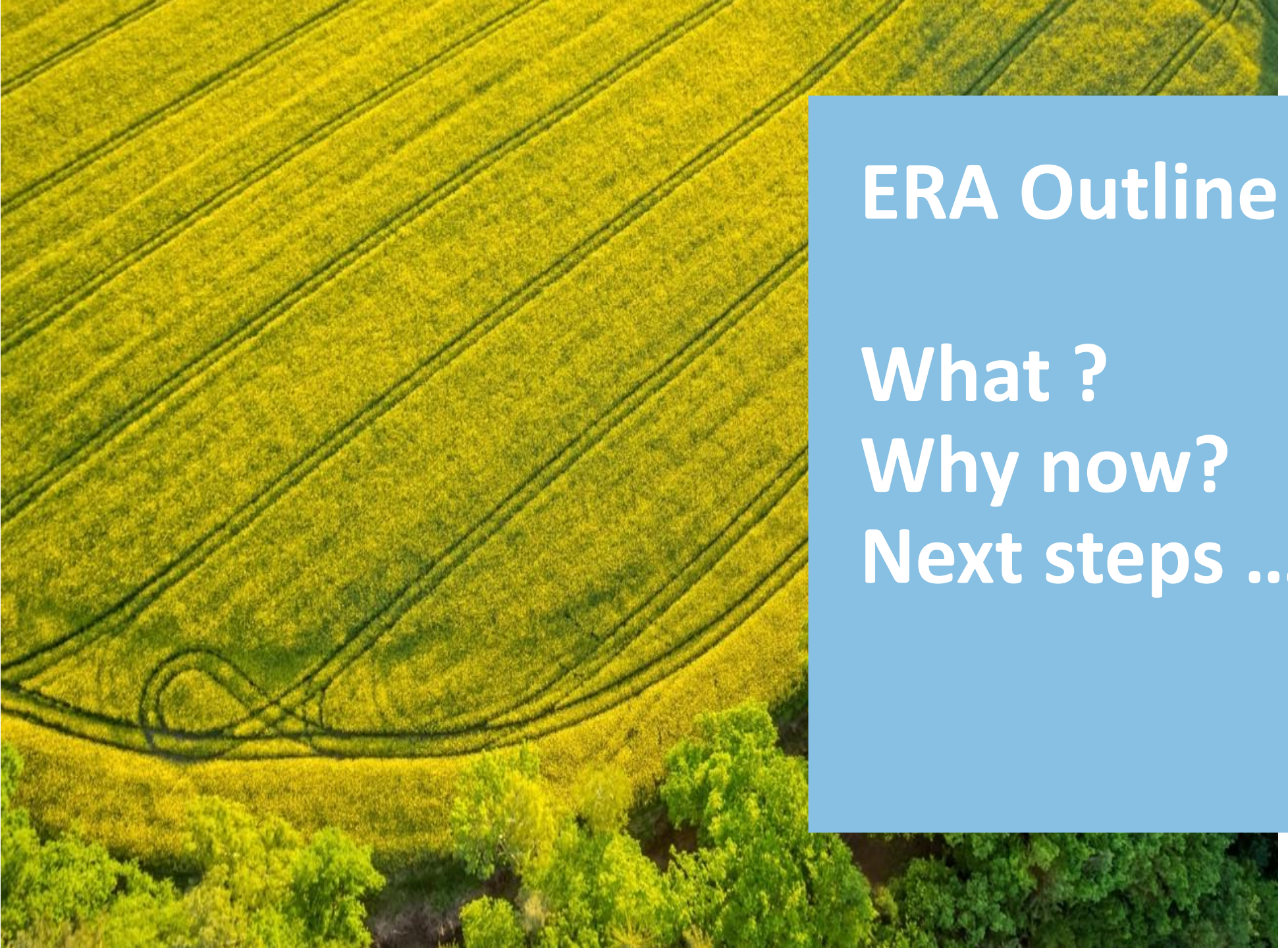


Evolution of the paradigm for Environment Risk Assessments

CLE considerations – Part 1

Nina Hallmark
06 March 2024



ERA Outline

What ?
Why now?
Next steps …

CropLife EUROPE

What: purpose of regulatory Risk Assessments is protection

EU REG (EC) No 1107/2009 - **Active substances authorisation and renewal**

(8) The purpose of this Regulation is to ensure a high level of protection of both human and animal health and the environment and at the same time to safeguard the competitiveness of Community agriculture. Particular attention should be paid to the protection of vulnerable groups of the population, including pregnant women, infants and children. The precautionary principle should be applied and this Regulation should ensure that industry demonstrates that substances or products produced or placed on the market do not have any harmful effect on human or animal health or any unacceptable effects on the environment.

General protection goal

CropLife EUROPE

What: Environment Risk Assessment (ERA) is required, usually…

EU REG (EC) No 1107/2009 - **Active substances authorisation and renewal - ANNEX II Procedure and criteria…**

1.3. During the process of evaluation and decision-making provided for in Articles 4 to 21, Member States and the Authority shall take into consideration any further guidance developed in the framework of the Standing Committee on the Food Chain and Animal Health for the purposes of refining, where relevant, the risk assessments.

SCOPAFF Guidance

3.8. Ecotoxicology

3.8.1. An active substance, safener or synergist shall only be approved if the risk assessment demonstrates risks to be acceptable in accordance with the criteria laid down in the uniform principles for evaluation and authorisation of plant protection products referred to in Article 29(6) under realistic proposed conditions of use of a plant protection product containing the active substance, safener or synergist. The assessment must take into account the severity of effects, the uncertainty of the data, and the number of organism groups which the active substance, safener or synergist is expected to affect adversely by the intended use.

Risk based protection

3.8.2. An active substance, safener or synergist shall only be approved if, on the basis of the assessment of Community or internationally agreed test guidelines, it is not considered to have endocrine disrupting properties that may cause adverse effects on non-target organisms unless the exposure of non-target organisms to that active substance in a plant protection product under realistic proposed conditions of use is negligible.

Hazard based precaution?

CropLife EUROPE

What: Environment Risk Assessment (ERA) method is protective

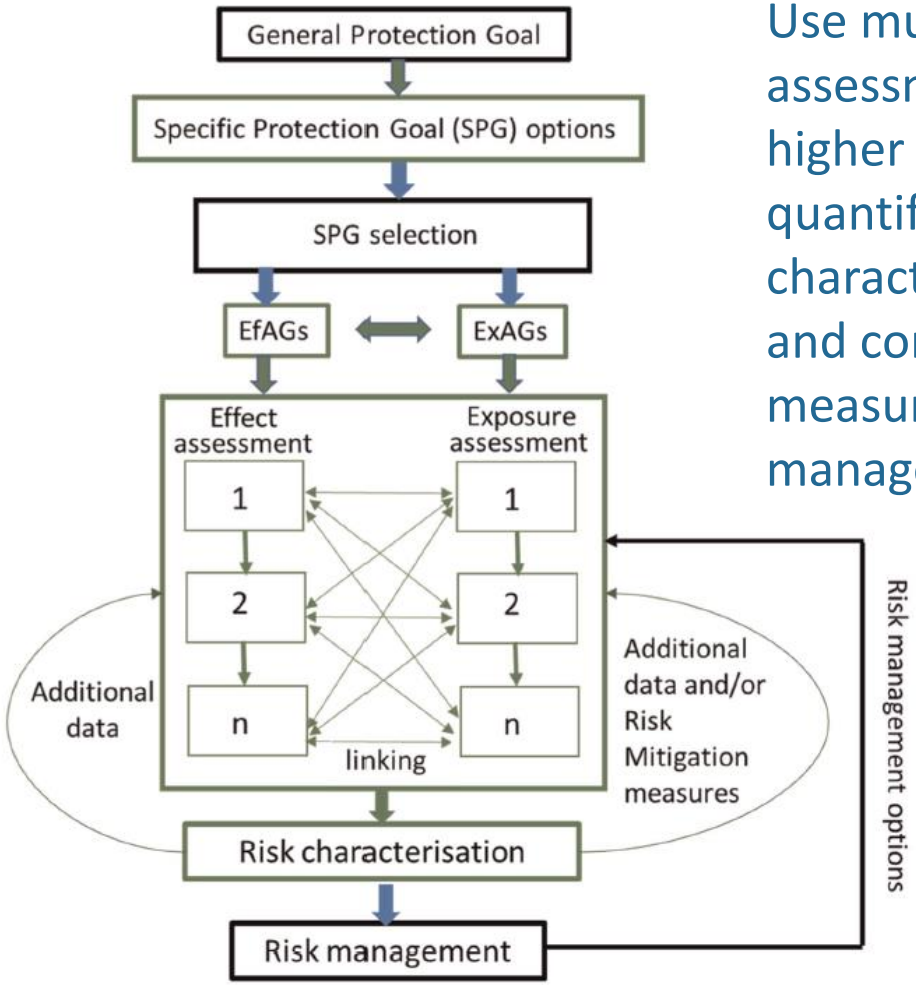
EU REG (EC) No 1107/2009 - **Active substances authorisation and renewal**

Start with the General Protection Goal, then become more specific e.g.,

Human safety SPG: individuals, including vulnerable populations

Environment safety SPG:

- Protecting populations e.g., normal operating ranges (NOR)
- Compartments (aquatic, terrestrial, soil wildlife)
- Complex exposure assessments e.g., direct vs. indirect, in-field vs. off-crop; biodiversity, etc…
- SPG rarely available (only some bees)



Use multi-tiered assessment, combine higher tier approaches to quantify risk, recognise and characterise uncertainties and consider mitigation measures and risk management options

Risk assessment scheme taken from EFSA Guidance on Risk Assessment for Birds and Mammals (2023)

- EfAGs = effect assessment goals
- ExAGs = exposure assessment goals

CropLife EUROPE

What: Environment Risk Assessment (ERA) – bird examples

Outcome = Toxicity / Exposure Ratio (TER)

Toxicity values

- derived experimentally from substance specific *in vivo* laboratory studies, with est. 5500 birds tested per AS
- priority for 3Rs and NAMs, expand from observation of what happened *in vivo* to understanding why (AOP)

Exposure values

- field studies are slow, expensive, low acceptance
- greater confidence in calculated values (reliability)
- substantial exposure modelling in use today
- no need for 3Rs, low priority for NAMs

Crop	Feeding guild	BBCH	Spray direction	Acute endpoint [mg a.s./kg bw]	Body weight [g]	Daily energy expenditure [kJ/day]	Food intake rate [g fresh weight/day]	Dietary dose [mg a.s./kg bw]	Toxicity exposure ratio
Vines	Small insectivorous	50-59	Crop	1000	8	43.9	8.16	25.3	39.55
Vines	Small omnivorous	50-59	Crop	1000	27	99.9	15.0	18.8	53.09
Vines	Granivorous	50-59	Crop	1000	11	54.4	3.48	11	90.8

Acute:
TER pass ≥ 10

Crop	Feeding guild	BBCH	Spray direction	Reproductive endpoint * [mg a.s./kg bw per day]	Body weight [g]	Daily energy expenditure [kJ/day]	Food intake rate [g fresh weight/day]	Daily dietary dose [mg a.s./kg bw per day]	Toxicity exposure ratio
Vines	Small insectivorous	50-59	Crop	100	8	43.9	8.16	8.56	11.7
Vines	Small omnivorous	50-59	Crop	100	27	99.9	15.0	7.3	13.7
Vines	Granivorous	50-59	Crop	100	11	54.4	3.48	5.09	19.6

Chronic (reproductive):
TER pass ≥ 5

TER calculations based on EFSA Guidance on Risk Assessment for Birds and Mammals (2023) * Reproductive endpoint can be determined using NOAEL or BMD10 approach

What: can EU regulatory risk assessment methods change? Yes!

EU REG (EC) No 1107/2009 - **Active substances authorisation and renewal**

(40) The use of non-animal test methods and other risk assessment strategies should be promoted. Animal testing for the purposes of this Regulation should be minimised and tests on vertebrates should be undertaken as a last resort. In accordance with Council Directive 86/609/EEC of 24 November 1986 on the approximation of laws, regulations and administrative provisions of the Member States regarding the protection of animals used for experimental and other scientific purposes (2), tests on vertebrate animals must be replaced, restricted or refined. Therefore, rules should be laid down to avoid duplicative testing and duplication of tests and studies on vertebrates should be prohibited. For the purpose of

NAMs and NGRA

3Rs

Not really new ideas.

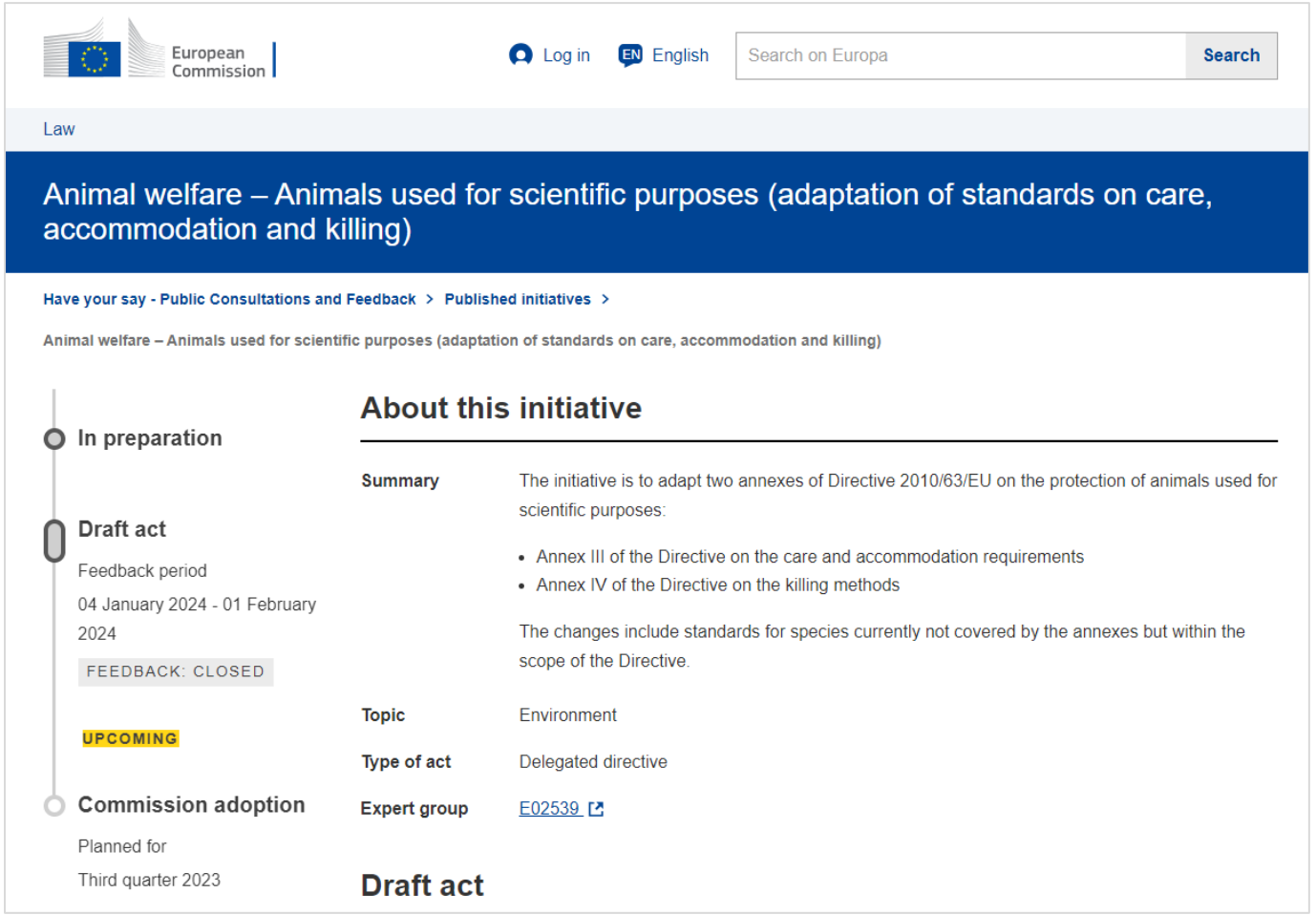
Possible since at least 2009, so why focus now?

Why now? Mix of new technology, opportunity and possibility…

e.g., scientific advances, societal / political push for 3Rs, regulatory drive, process in-efficiency, …

DIRECTIVE 2010/63/EU OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 22 September 2010
on the protection of animals used for scientific purposes

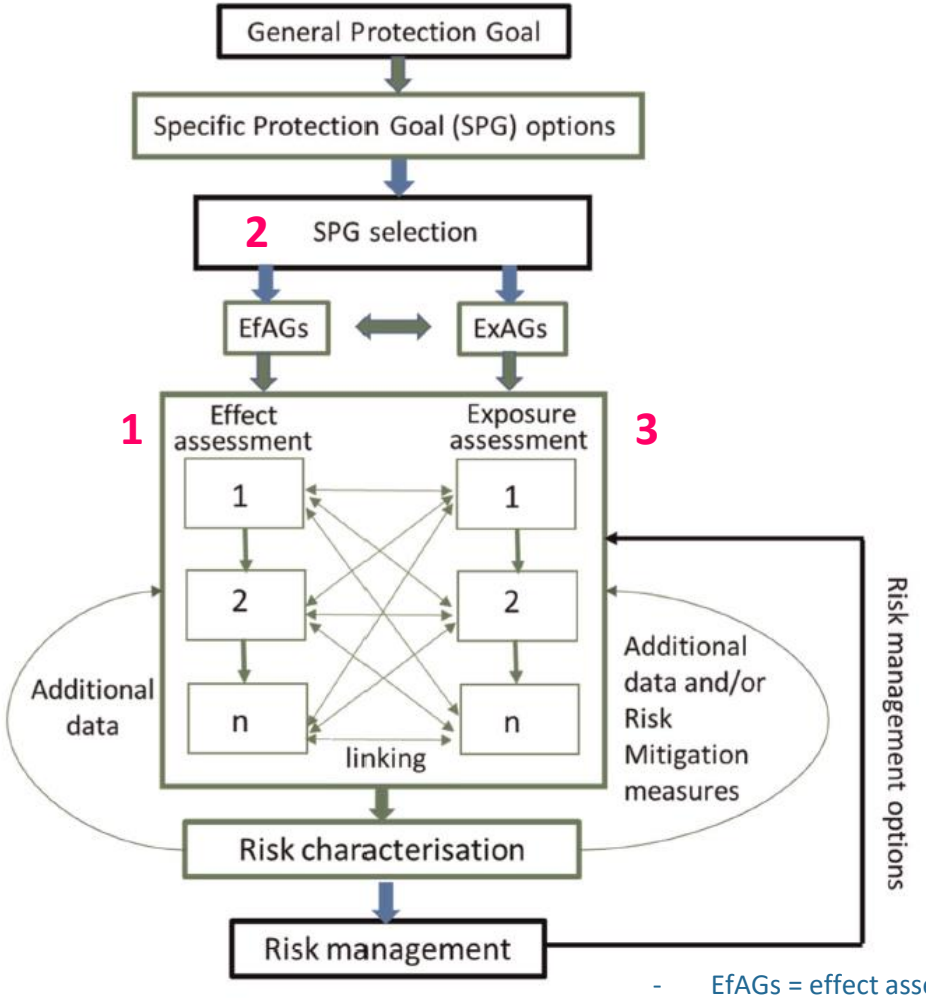
(11) The care and use of live animals for scientific purposes is governed by internationally established principles of replacement, reduction and refinement. To ensure that the way in which animals are bred, cared for and used in procedures within the Union is in line with that of the other international and national standards applicable outside the Union, the principles of replacement, reduction and refinement should be considered systematically when implementing this Directive. When choosing methods, the principles of replacement, reduction and refinement should be implemented through a strict hierarchy of the requirement to use alternative methods. Where no alternative method is recognised by the legislation of the Union, the numbers of animals used may be reduced by resorting to other methods and by implementing testing strategies, such as the use of *in vitro* and other methods that would reduce and refine the use of animals.



Next steps: risk assessment works today, however the data used for decision making can be optimised using advances in scientific technologies, to enable faster, more certain, protection of our environment

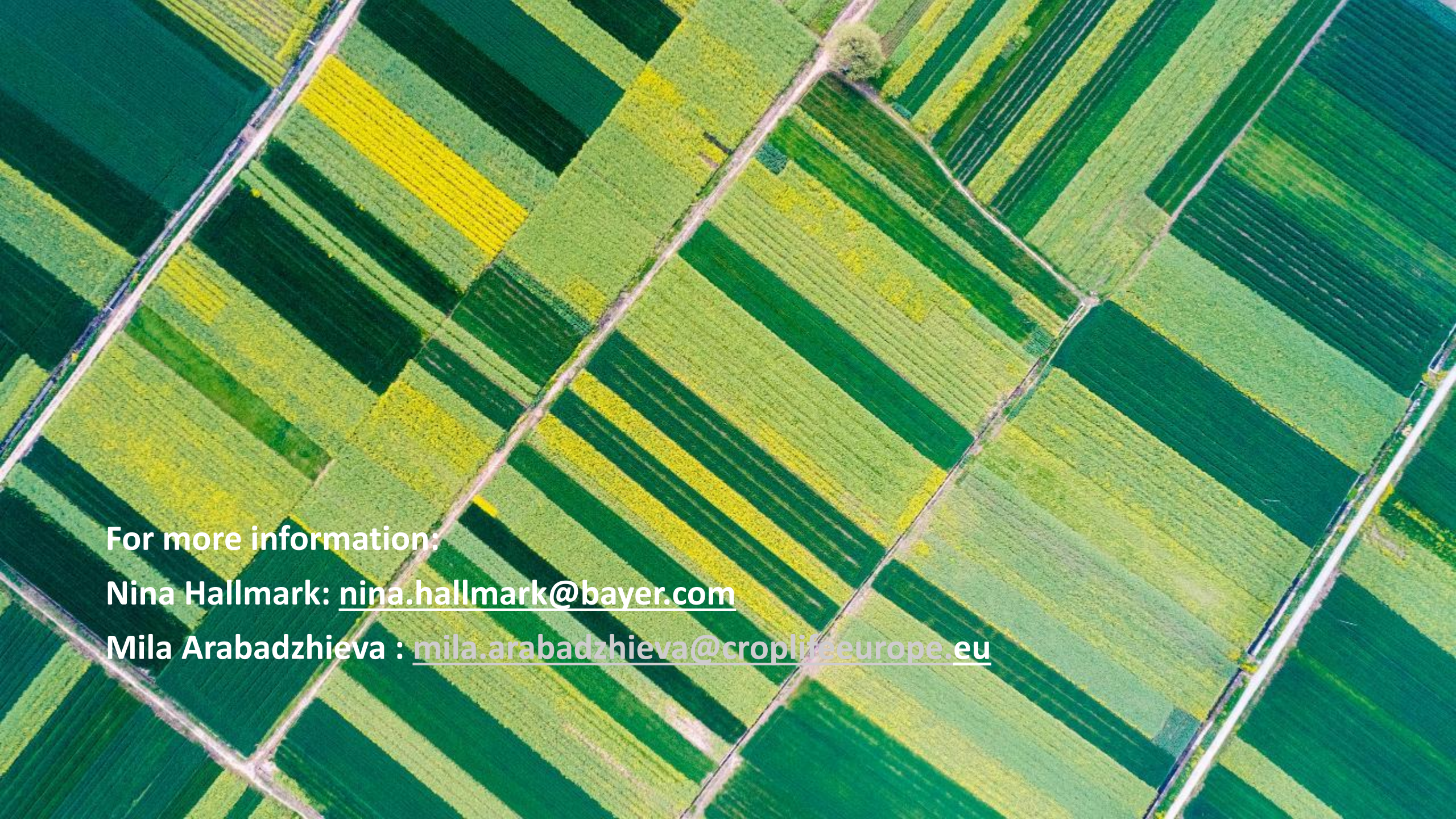
Proposed priorities:

1. Start with identifying and prioritising 3Rs and NAMs which can minimise *in vivo* testing and optimise effect assessment (toxicity), for relevant environmental species
   - Acute and Chronic / reproductive endpoint
   - Active substance / product
   - Identify relevant partners e.g., HESI NAMs https://hesiglobal.org/ecorisk/
2. Key data gaps include EU SPGs for relevant species and relevant models e.g., AOPs, PBK and NOR models
3. Move towards exposure-driven risk prioritisation and NGRA concept e.g., using predictive models and IATAs



Let's keep going!

- EfAGs = effect assessment goals
- ExAGs = exposure assessment goals



For more information:

Nina Hallmark: nina.hallmark@bayer.com

Mila Arabadzhieva : mila.arabadzhieva@croplifeeurope.eu