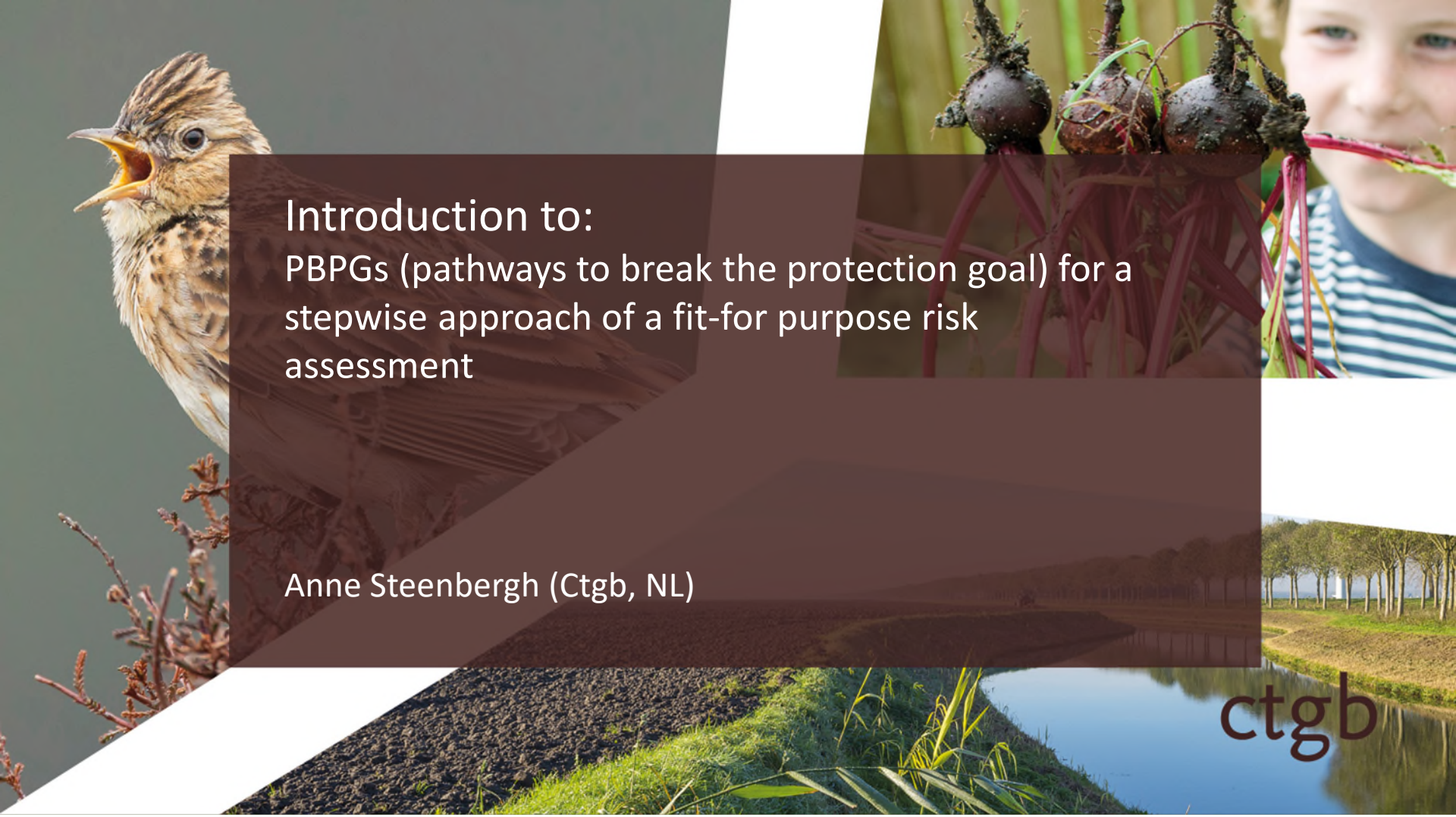


Introduction to:

PBPGs (pathways to break the protection goal) for a stepwise approach of a fit-for purpose risk assessment

Anne Steenbergh (Ctgb, NL)

ctgb

Contents

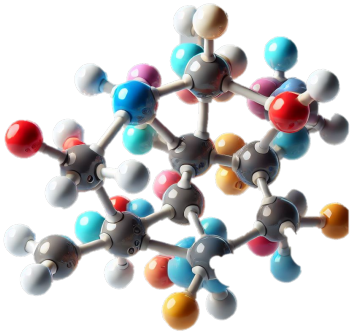
1. Why is a different approach needed for the risk assessment of low concern active substances (LCAS)?
2. Why do we need to develop something new if we've been assessing LCAS for years?
3. Introduction to problem formulation using pathways to breach the protection goal (PBPGs)
4. How to apply this method
5. Conclusions

ctgb

1. Why is a different approach needed for the risk assessment of low concern active substances (LCAS)?

ctgb

Risk assessment conventional substance



Toxicity testing

Exposure assessment

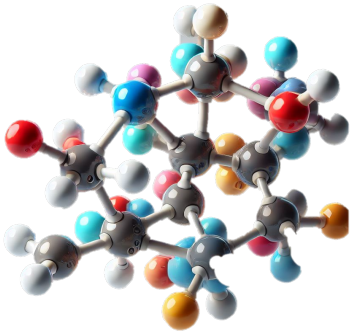
Quantitative risk assessment

ctgb

AI image (copilot)

Risk assessment conventional substance

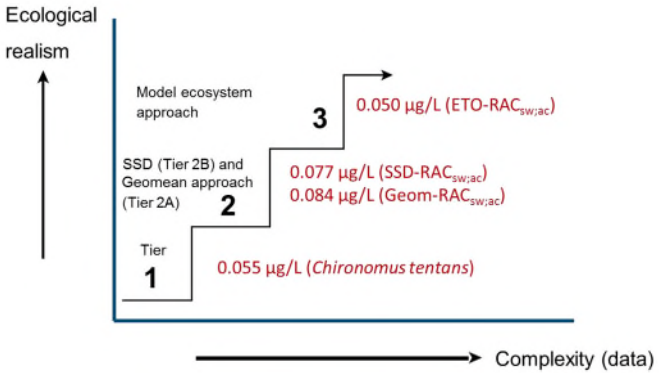
AI image (copilot)



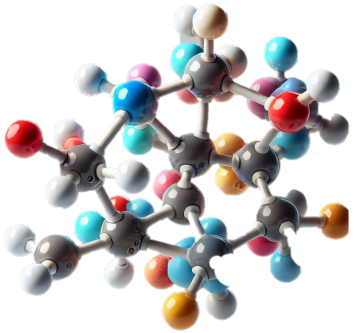
Toxicity testing

Exposure assessment

Quantitative risk assessment



Risk assessment conventional substance



Toxicity testing

Exposure assessment

Quantitative risk assessment

ctgb

AI image (molecule; copilot)

Risk assessment LCAS

Or other hazard?
And with which component?

Toxicity testing

Exposure assessment

Risk assessment

No thresholds in case of qualitative RA

Thresholds appropriate in case of other hazards?

Models relevant and appropriate?
Use information on natural exposure?

ctgb

AI image (copilot)

Risk assessment LCAS

Body of knowledge & targeted testing (for relevant hazard)

(Customized) modelling; targeted experimental data

(semi) qualitative risk assessment

AI image (copilot)

AI images (erlenmeyer and discussion table; copilot)

Approach for LCAS should be:

- More appropriate risk assessment fitting to properties of the substance
- Facilitate integration of all information relevant for the assessment of a protection goal (such as hazard, e-fate, effects)
- Fit for both quantitative and qualitative information
- Flexible approach (also suitable for new types of substances)
- NOT necessarily lighter assessment (only when this is fitting based on the properties of the substance)

ctgb

2. Why do we need to develop something new if we've been assessing LCAS for years?

ctgb

Current case-by-case approaches work

AI image (copilot)

ctgb

Current case-by-case approaches work, but

AI images (copilot)

Case-by-case approaches are possible, but

- currently not harmonized

applicant

RMS

MS & EFSA

ctgb

AI images (copilot)

Approach for LCAS should be:

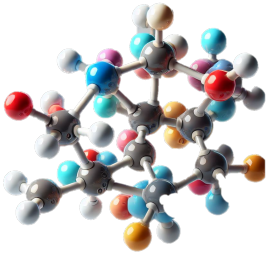
- More appropriate risk assessment fitting to properties of the substance
- Facilitate integration of all information relevant for the assessment of a protection goal (such as hazard, e-fate, effects)
- Fit for both quantitative and qualitative information
- Flexible approach (also suitable for new types of substances)
- NOT necessarily lighter assessment (only when this is fitting based on the properties of the substance)
- **Transparent approach for better communication**
- **Harmonised approach**

ctgb

3. Introduction to problem formulation using pathways to breach the protection goal (PBPGs)

ctgb

Method is used to assess the likelihood of breaching a protection goal



Quantitative threshold based on toxicity and exposure (e.g., RAC, TER)

- Agreement between risk assessors and risk managers
- Meeting threshold doesn't mean harm will never occur

Assessment of severity and likelihood of effects

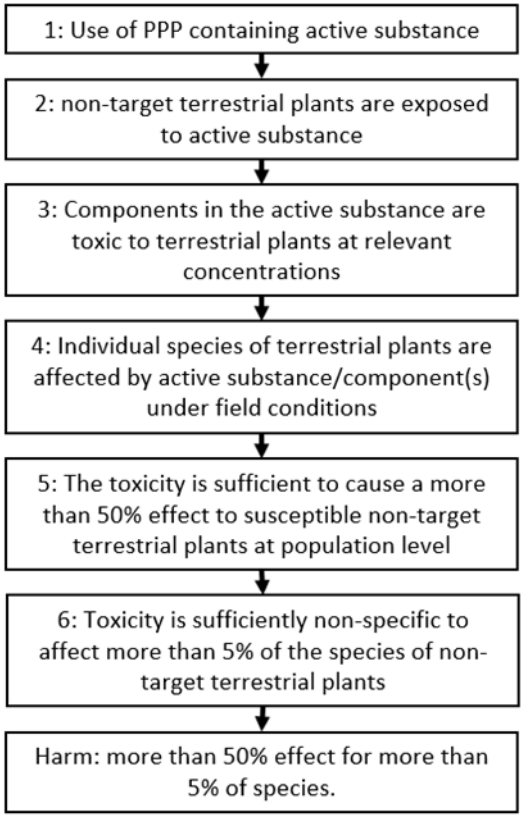
Assessment of the likelihood that effects are severe enough to breach the protection goal

ctgb

AI images (copilot)

Core: the generic PBPG

- Aim: to assess likelihood of breaching the protection goal
- 1 PBPG is for the combination of 1 hazard and 1 protection goal (such as toxicity to terrestrial plants)
- PBPG starts with use of the PPP
- PBPG ends with **'harm' which means breaching the protection goal** (important: not all adverse effects are thereby considered as 'harm')
- All events need to take place for harm to occur



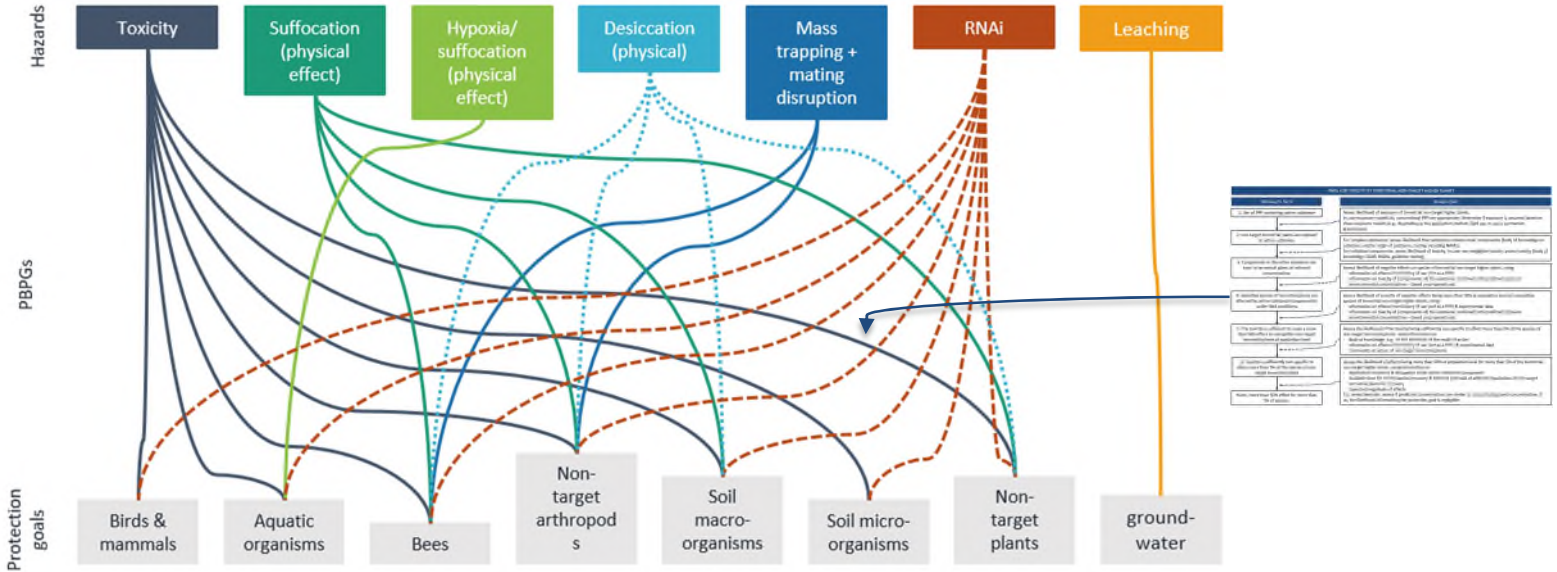
Generic PBPG & analysis plan

PBPG FOR TOXICITY TO TERRESTRIAL NON-TARGET HIGHER PLANTS

Pathway to harm	Analysis plan
1: Use of PPP containing active substance	Assess likelihood of exposure of terrestrial non-target higher plants. In case exposure models for conventional PPP are appropriate: Determine if exposure is assumed based on these exposure models (e.g., depending on the application method, field use vs use in permanent greenhouse).
2: non-target terrestrial plants are exposed to active substance	For complex substances: assess likelihood that substance contains toxic components (body of knowledge on substance and/or origin of substance, testing including NAMs). For individual components: assess likelihood of toxicity. In case non-negligible toxicity: assess toxicity (body of knowledge, QSAR, NAMs, guideline testing)
3: Components in the active substance are toxic to terrestrial plants at relevant concentrations	Assess likelihood of negative effects on species of terrestrial non-target higher plants, using: - Information on effects from history of use (not as a PPP) - Information on toxicity of (components of) the substance combined with predicted exposure (environmental concentrations – based on proposed use)
4: Individual species of terrestrial plants are affected by active substance/component(s) under field conditions	Assess likelihood of severity of negative effects being more than 50% at population level of susceptible species of terrestrial non-target higher plants, using: - Information on effects from history of use (not as a PPP) & experimental data - Information on toxicity of (components of) the substance combined with predicted exposure (environmental concentrations – based on proposed use)
5: The toxicity is sufficient to cause a more than 50% effect to susceptible non-target terrestrial plants at population level	Assess the likelihood of the toxicity being sufficiently non-specific to affect more than 5% of the species of non-target terrestrial plants, using information on: - Body of knowledge, e.g., on the specificity of the mode of action - Information on effects from history of use (not as a PPP) & experimental data - Community structure of non-target terrestrial plants
6: Toxicity is sufficiently non-specific to affect more than 5% of the species of non-target terrestrial plants	Assess the likelihood of effects being more than 50% at population level for more than 5% of the terrestrial non-target higher plants, using information on: - Application frequency & dissipation of the active substance/components - Available time for recolonization/recovery & inherent potential of affected populations of non-target terrestrial plants for recovery - Expected magnitude of effects For semiochemicals: assess if predicted concentrations are similar to natural background concentrations. If so, the likelihood of breaching the protection goal is negligible.
Harm: more than 50% effect for more than 5% of species.	

ctgb

PBPG for each combination of a hazard and a protection goal



ctgb

Why generic PBPGs and analysis plans?

- More appropriate risk assessment fitting to properties of the substance
- Facilitate integration of all information relevant for the assessment of a protection goal (such as hazard, e-fate, effects)
- Fit for both quantitative and qualitative information
- Flexible approach (also suitable for new types of substances)
- NOT necessarily lighter assessment (only when this is fitting based on the properties of the substance)
- Transparent approach for better communication
- **Harmonised approach**

ctgb

4. How to apply this method

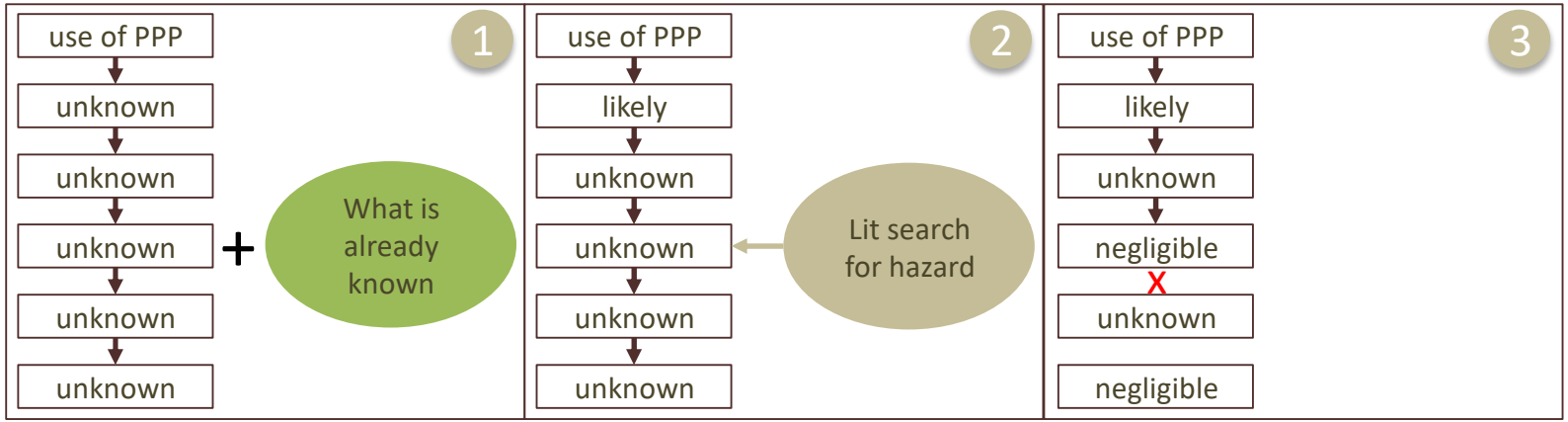
ctgb

Principles of using PBPGs

- No fixed order
- Process is repeated after new data has been generated
- In case one event can be demonstrated not to occur, the likelihood of breaching the protection goal is negligible and further information is not needed for this PBPG
- In case none of the events can be demonstrated not to occur, the assessment of the likelihood of the events in the PBPG are combined to assess the likelihood of breaching the protection goal

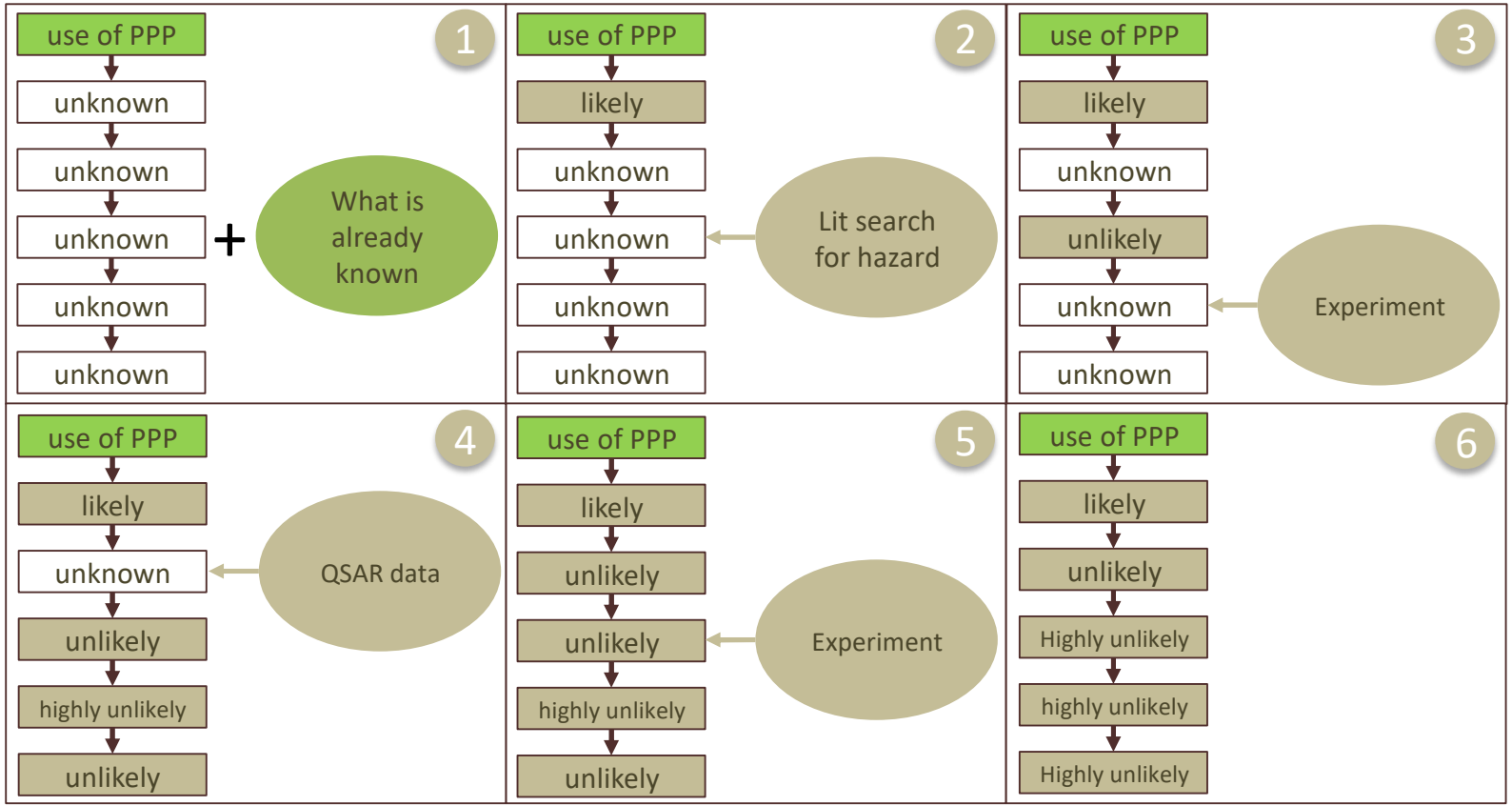
ctgb

Example: one event can be demonstrated not to occur



ctgb

Example: none of the events can be demonstrated not to occur



5. Conclusions

ctgb

Conclusions

- Case-by-case approach needed for many LCAS
- Need for harmonisation
- ➢ Generic PBPGs: harmonised & fit for purpose
- Problem formulation using PBPGs:
  - Explicitly includes hazards other than toxicity
  - Suitable for both qualitative and quantitative information
  - Combines all available information from different sections of the assessment
  - Transparent method; better communication

ctgb

AI image (copilot)

ctgb

PF vs decision trees

- Current decision trees:
  - Based on critical properties of biopesticides to shape risk assessment
  - Difficult to find right order of questions which is appropriate for all substances
  - Exceptions to rules in trees are not uncommon
- Problem formulation:
  - Based on causal pathways to harm
  - Analysis plan for individual biopesticides is derived from pathways to harm in a structured and transparent way
  - Flexible approach within structured framework: starting point of assessment depends on properties of the substance