

Workshop on the development of a fit-for-purpose approach for assessing the risk of low-concern active substances.

Agenda

15-16 January 2025

08:30-17:30 / 08:30-12:00



EUROPEAN
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Instituto Nacional de Investigación
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Example of application to LCAS: case studies presentations

A microbial metabolite with insecticidal activity



INTRODUCTION... ***BACKGROUND INFORMATION...***

- Secondary metabolites produced by living microorganisms are used for ppp. as active.
- Bioactive molecules: effectively control insect pests, nematodes, plant diseases and weeds.
- They fall under the same EU regulatory frame works as the chemical plant protection products and the data requirements for chemicals in the current Commission Regulations 283/2013 and 284/2013 (EU, 2013a, EU, 2013b).
- Different MoA: toxicity, induced resistance.

(Biological) properties of the active substance

- Active ingredient: Hypothetical BAM in purified fermentation broth.
- Production: fermentation of a naturally occurring soil microorganism. After the fermentation process is completed, the BAM is recovered from the fermentation broth by solvent extraction. The purity of the technical grade active substance is approximately 95%.
- Mode of action: affects the nervous system of insects.

MICROBIAL METABOLITES WITH INSECTICIDAL ACTIVITY

- Three scenarios are proposed for its use as insecticide:
 - Scenario 1: single **soil** application of a GR formulation at sowing (field use).
 - Scenario 2: multiple **foliar** applications of a SC formulation during the growing season (field use).
 - Scenario 3: multiple applications of a **bait** concentrate in orchards that is applied in patches (field use).
- Microbial metabolite is proposed to be used in **field crops**, the PBPGs potentially relevant are **toxicity** to all non-target organisms and **leaching** to groundwater (Figure 1 on the next slide).

GENERIC PBPGs FOR MICROBIAL METABOLITES

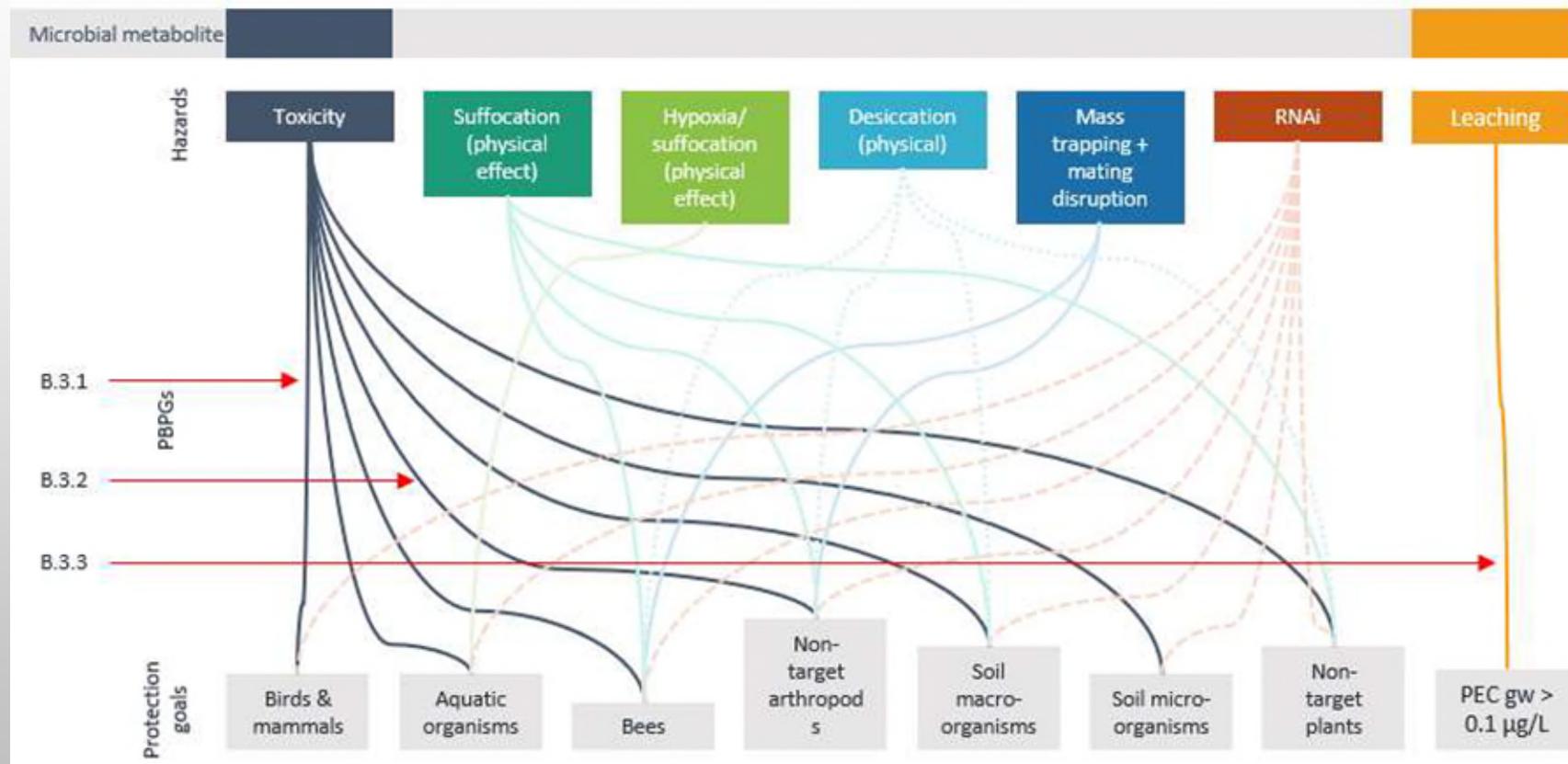


Figure 1: overview figure of all PBPGs for NTOs and groundwater. For microbial metabolites, the PBPGs as indicated in the grey bar at the top of the figure are in principle relevant. This case study focuses on the three PBPGs indicated with the red arrows.

SPECIFIC CASE STUDY FOR MICROBIAL METABOLITES

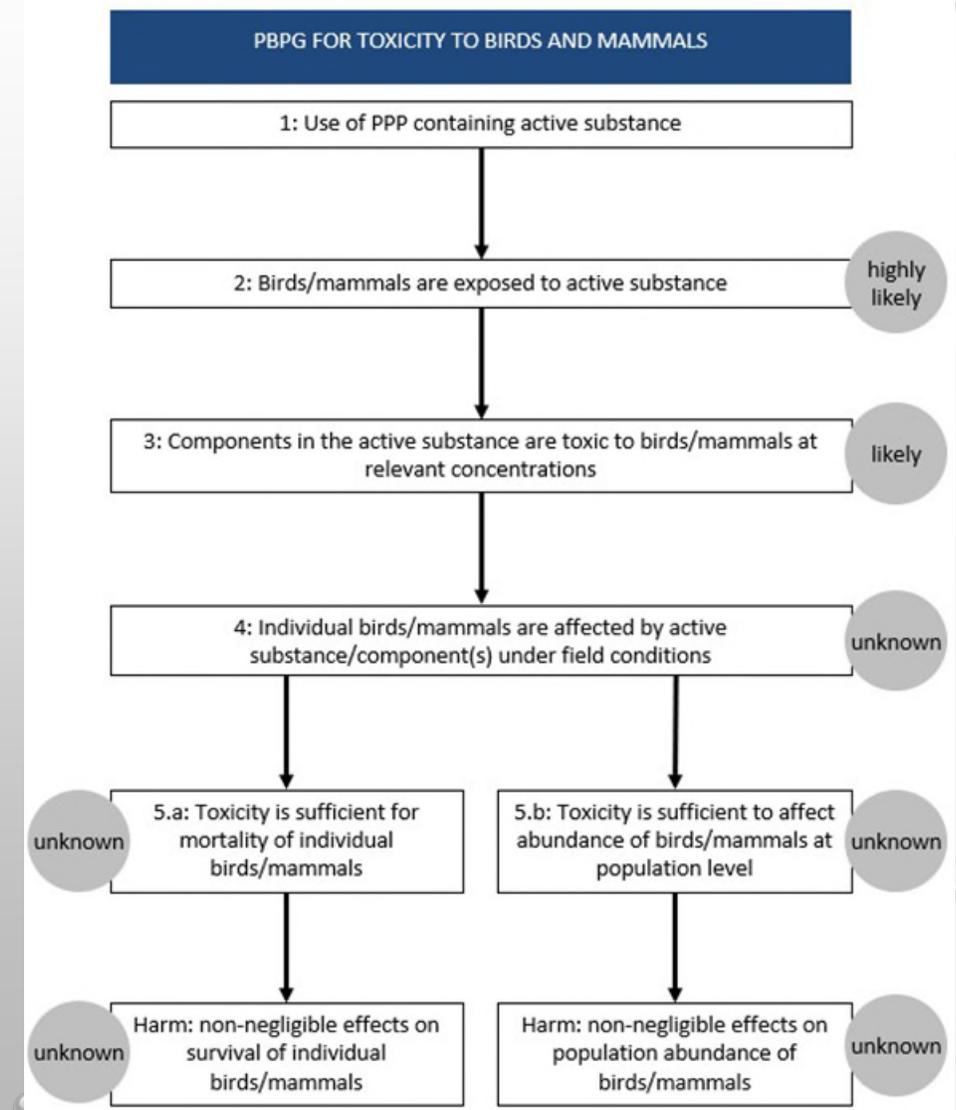
For this case study, we focus on three different generic **PBPGs**:

- PBPG for toxicity to **birds and mammals**
- PBPG for toxicity to **in-field non-target arthropods**
- PBPG for leaching to **groundwater**

PBPGs FOR TOXICITY TO BIRDS AND MAMMALS

For all proposed use scenarios of this substance:

- Natural concentrations of metabolite much lower than concentrations from use of purified metabolite
- Mode of action of technical grade a.i. (95% purity): **toxic**
- Exposure of birds and mammals to a.s. under natural conditions: **highly likely**
- Components in a.s. are toxic to birds and mammals at relevant concentrations: **likely**
- Individuals and populations of birds and mammals are affected by a.s./components: **unknown**
- Scenario 1 & 2: 'conventional' risk assessment; exposure models for granulated soil and foliar spray applications, respectively
- Scenario 3: to assess the effect of the presence of the bait substance in the PPP on the exposure of birds and mammals



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- **LIKELIHOOD OF BREACHING THE PROTECTION GOAL: UNKNOWN'**

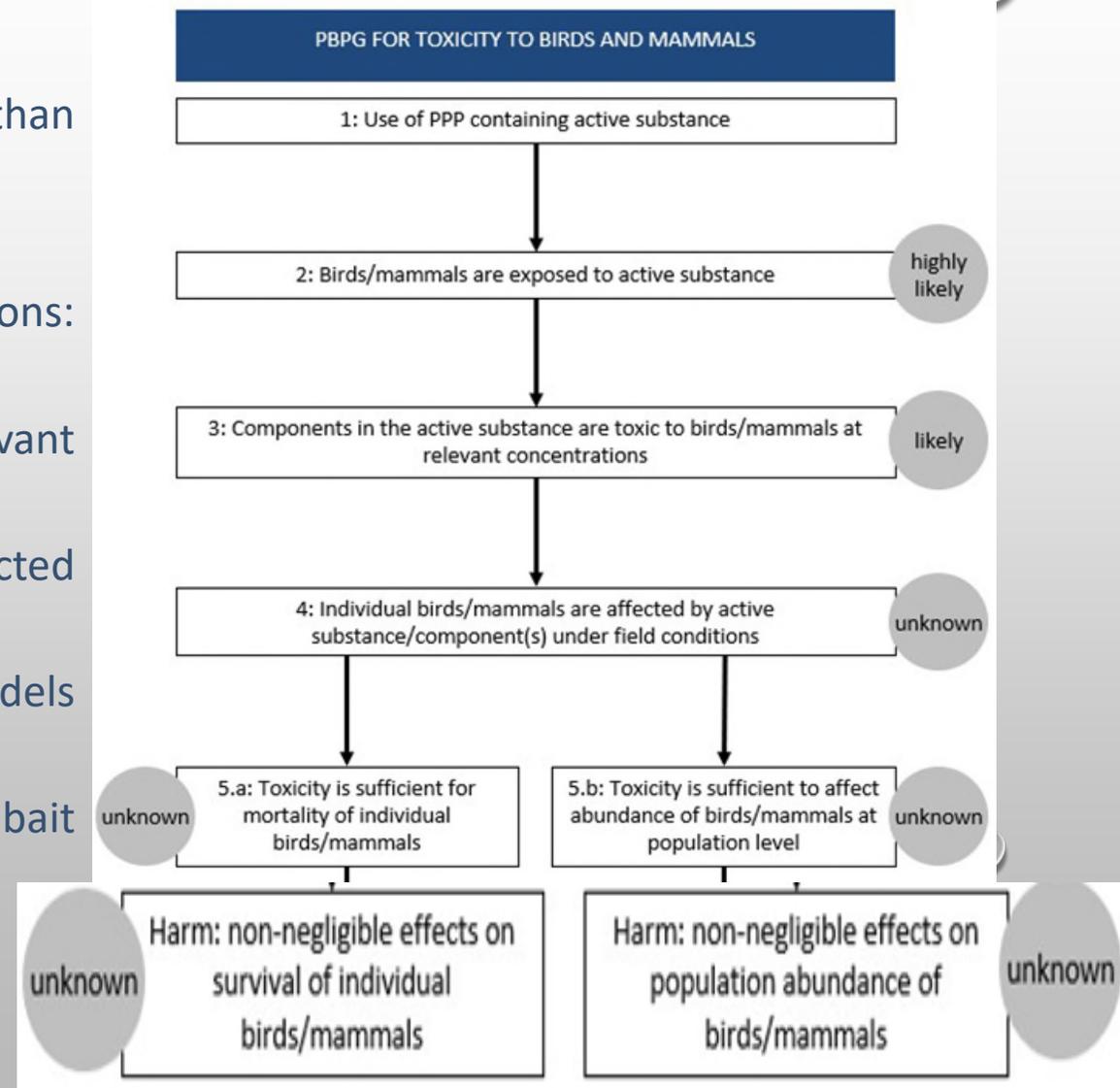
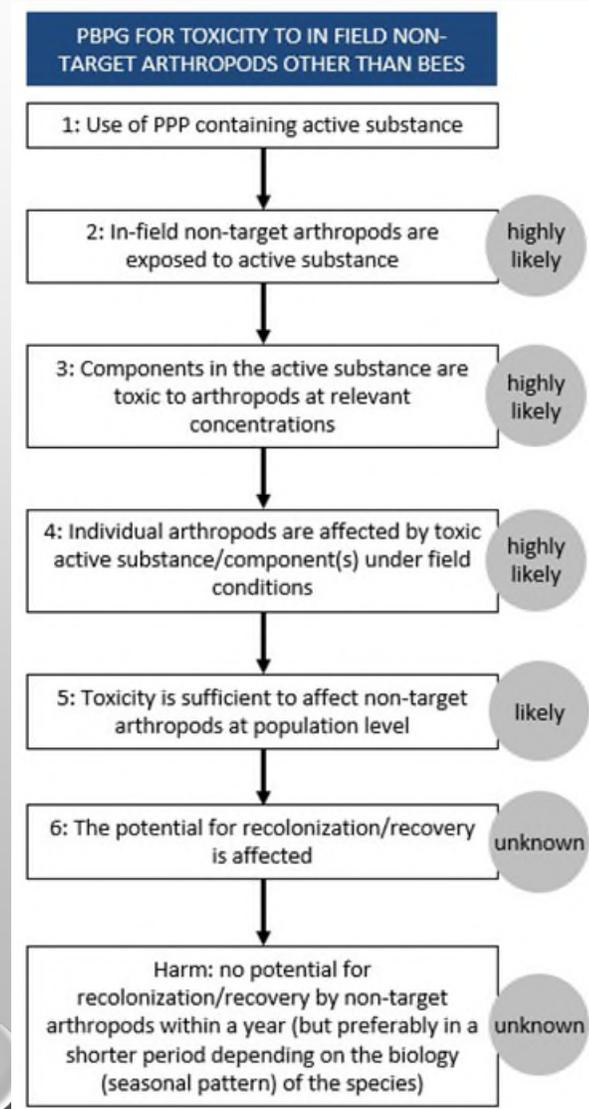


Figure 2. Generic PBPGs for toxicity to birds and mammals.

PBPGs FOR TOXICITY TO IN-FIELD NON-TARGET ARTHROPODS

For all proposed use scenarios of this substance:

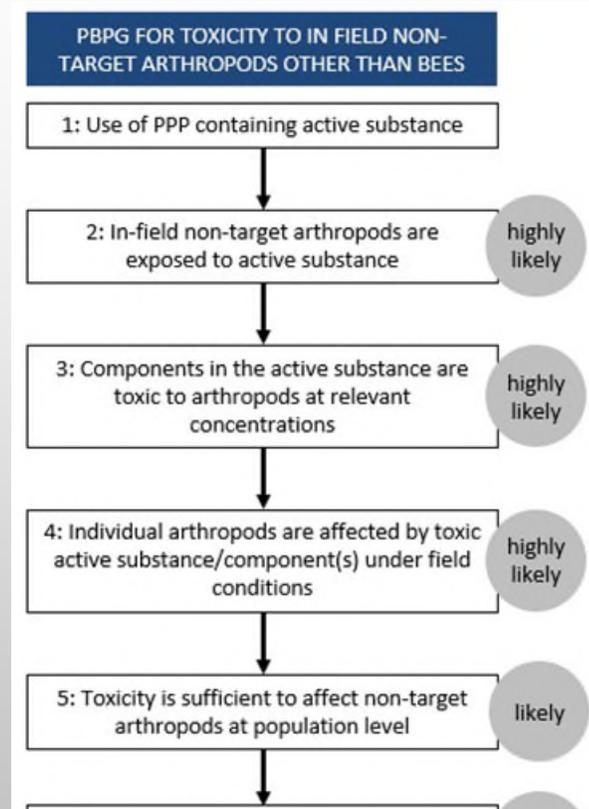
- Natural concentrations of metabolite much lower than concentrations from use of purified metabolite
- Mode of action of technical grade a.i. (95% purity): **toxic**
- Exposure of non-target arthropods to a.s. under natural conditions: **highly likely**
- Components in a.s. are toxic to non-target arthropods at relevant concentrations: **highly likely**
- Individuals and populations of non-target arthropods are affected by a.s./components: **highly likely** and **likely**, respectively
- Scenario 3: to assess the effect of the presence of the bait substance in the PPP on the exposure of non-target arthropods
- Effects on the potential for recolonization or recovery: **unknown**



PBPGs FOR TOXICITY TO IN-FIELD NON-TARGET ARTHROPODS

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- Scenario 3: to assess the effect of the presence of the bait substance in the PPP on the exposure of non-target arthropods
- Effects on the potential for recolonization or recovery: **unknown**
- Harm: **unknown**
- **LIKELIHOOD OF BREACHING THE PROTECTION GOAL: UNKNOWN'**



Harm: no potential for recolonization/recovery by non-target arthropods within a year (but preferably in a shorter period depending on the biology (seasonal pattern) of the species) **unknown**

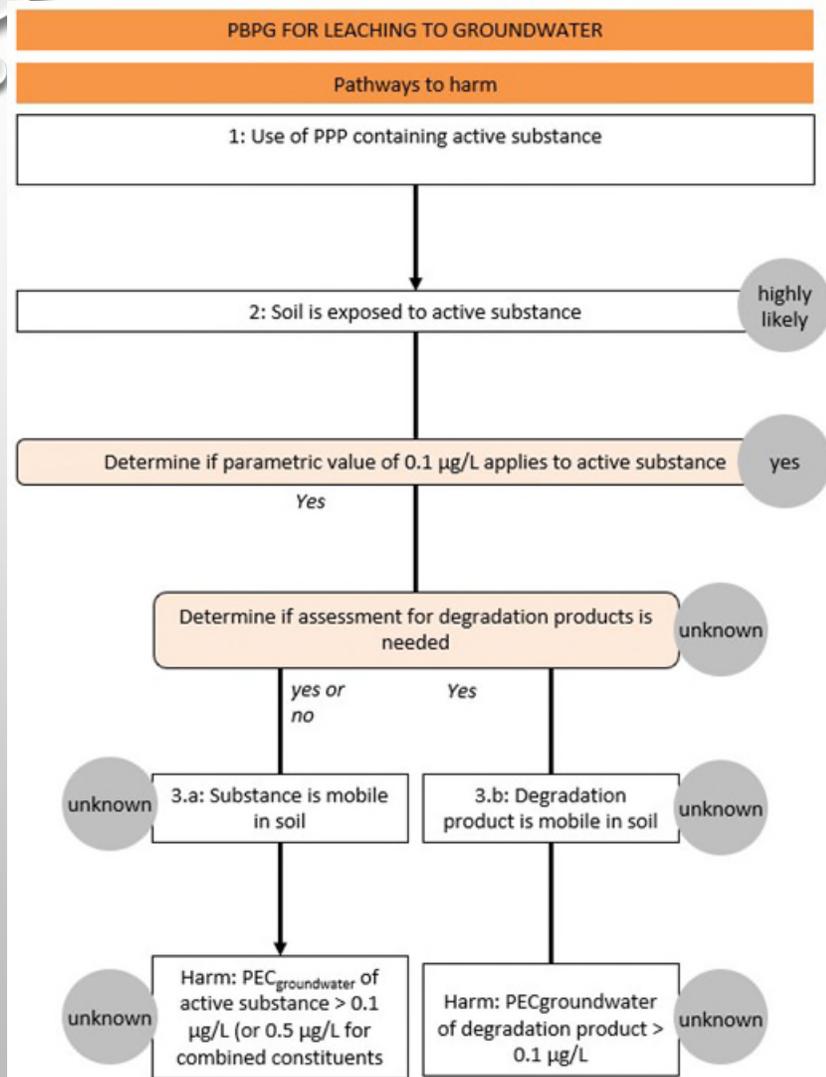


Figure 4. PBPG for leaching to groundwater.

PBPGS FOR LEACHING TO GROUNDWATER

For all proposed use scenarios of this substance:

- Natural concentrations of metabolite much lower than concentrations from use of purified metabolite
- Exposure of soil to a.s. under natural conditions: **highly likely**
- Persistency: **unlikely**
- Determine parametric limit of 0.1 µg/L to a.s.: **Yes**
- Conventional assessment: physical-chemical endpoints and rate of degradation in soil. **Unknown**
- **IT MAY BE POSSIBLE TO JUSTIFY'**

PBPGS FOR LEACHING TO GROUNDWATER

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- Natural concentrations of metabolite much lower than concentrations from use of purified metabolite
- Exposure of soil to a.s. under natural conditions: **highly likely**
- Persistency: **unlikely**
- Determine parametric limit of 0.1 µg/L to a.s.: **Yes**
- Conventional assessment: physical-chemical endpoints and rate of degradation in soil. **Unknown**
- Depending on structure and route of degradation, possible to justify that further information for the assessment of leaching of degradation products is not needed.
- **LIKELIHOOD OF BREACHING THE PROTECTION GOAL: UNKNOWN'**

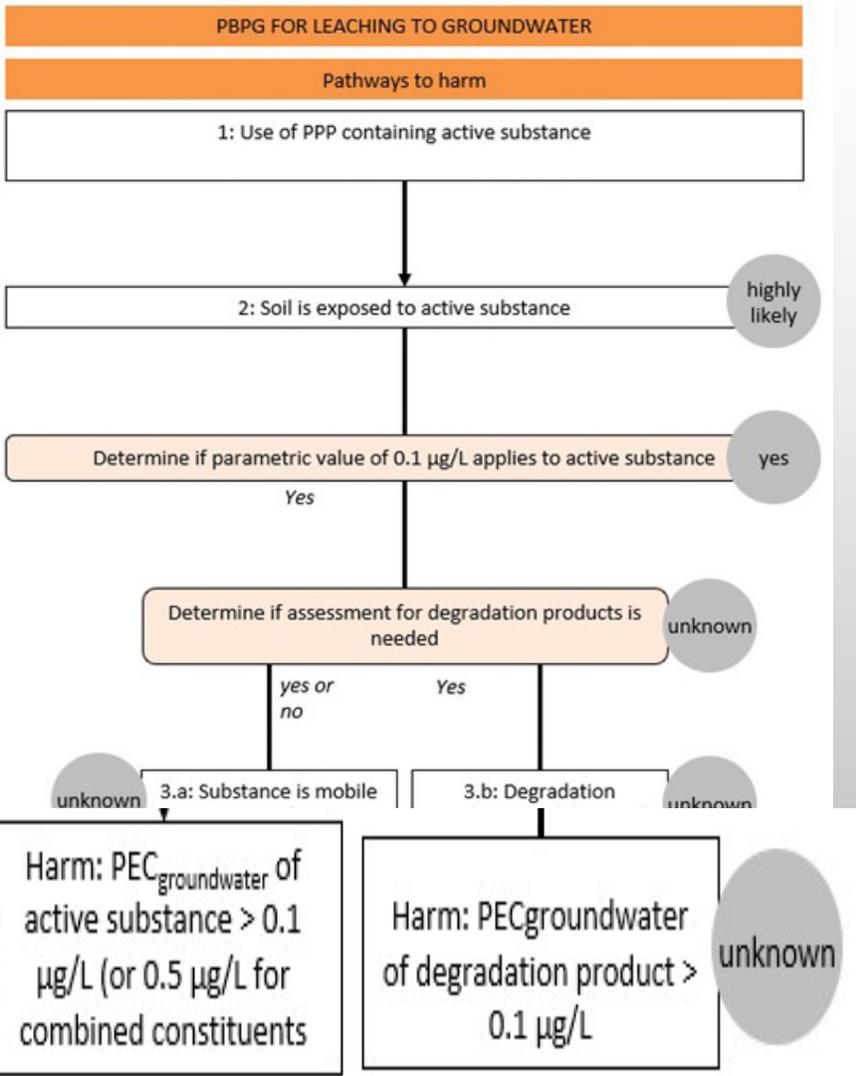


Figure 4. PBPG for leaching to groundwater.

CONCLUSIONS AND FUTURE PROSPECTS

- Microbial metabolites have highly **diverse properties**, and a **case-by-case approach** should be followed.
- It was assumed that metabolite is a **natural** substance produced by a common soil microorganisms and it has a **toxic** mode of action.
- PBPG approach **structures** and **harmonises** this approach and **communicates** the justification for the selected approach in a clear way.
- When applying generic PBPGs to this metabolite: it's not *a priori* possible to waive certain data because it is a natural substance.
- **Risk assessment** is needed due: the limited purity of the technical grade active substance and the bait spray applications.
- **Problem formulation approach using generic PBPGs helps to structure the overall approach for the risk assessment of this metabolite.**

CONCLUSIONS AND FUTURE PROSPECTS

- Microbial metabolite are naturally produced by a common soil microorganism **is not considered to be sufficient justification for waiving** of data requirements.
- PBPG approach was **applied** towards the **groundwater** protection goal and accessing **leaching potential** and had the **same outcome as a regular risk assessment**.
- PBPG is a general approach that can also be applied to conventional pesticides.

The fact that a substance is natural is not sufficient justification to waive data requirements; using the PBPG approach does not lead a 'lighter' assessment if this is not justified