Problem formulation

How is it used in environmental risk assessment of GMOs?

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EFSA involvement
-WGs of GMO, FEEDAP, CEP Panel
Topics: GMOs, synthetic biology, new genomic techniques, microorganisms, ERA
-FEEDAP Panel (Chair WG Microbiology), WG Microbial Pesticides

GMOs

- ✓ **Living** organisms that are genetically modified to introduce new trait(s)
- ✓ Different **organisms** (eg. plants, fish, insects, microorganisms)
- ✓ Range of **traits** that may be based on production of new active substances of low concern (e.g. metabolites, dsRNA)
- ✓ Range of **applications** (eg. field, aquatic, aerial)

Approaches in risk assessment of GMOs

Approaches for risk assessment of GMOs

- ✓ **One size fits all** approach (GM food and feed, non-living)
- ✓ Approaches **based on organism and/or traits** (contained use of GMOs)
- ✓ **Decision trees** (characterisation of microorganisms)
- ✓ **Case by case** approach (ERA of GMOs)

Problem formulation

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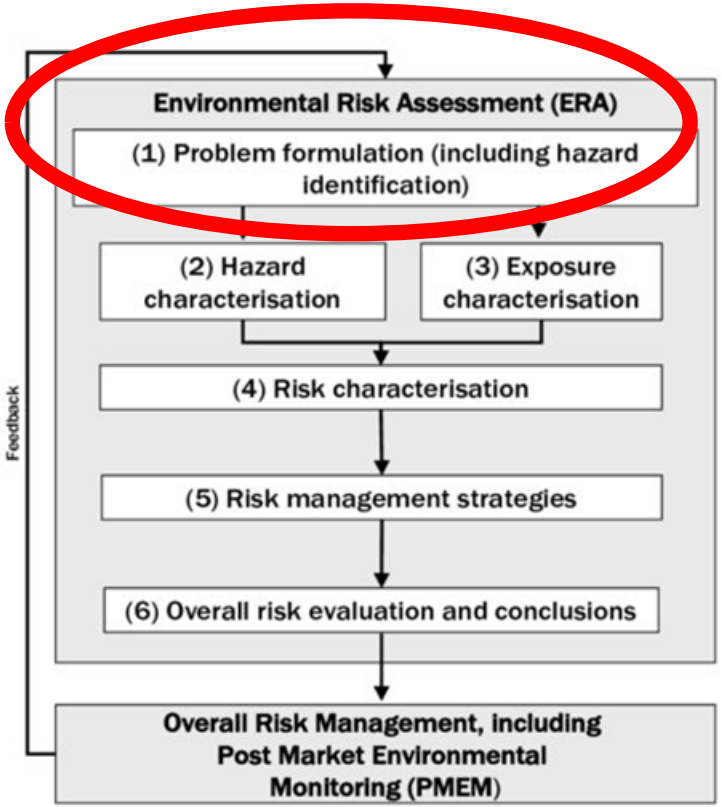
The first step in environmental risk assessment (since 1998, EPA)

Used by EFSA to ‘tailor’ ERA of GMOs

Worldwide use for fit for purpose ERA of GMOs

Steps in ERA

EFSA, 2010 Guidance on the risk assessment of GM plants



Problem formulation - questions

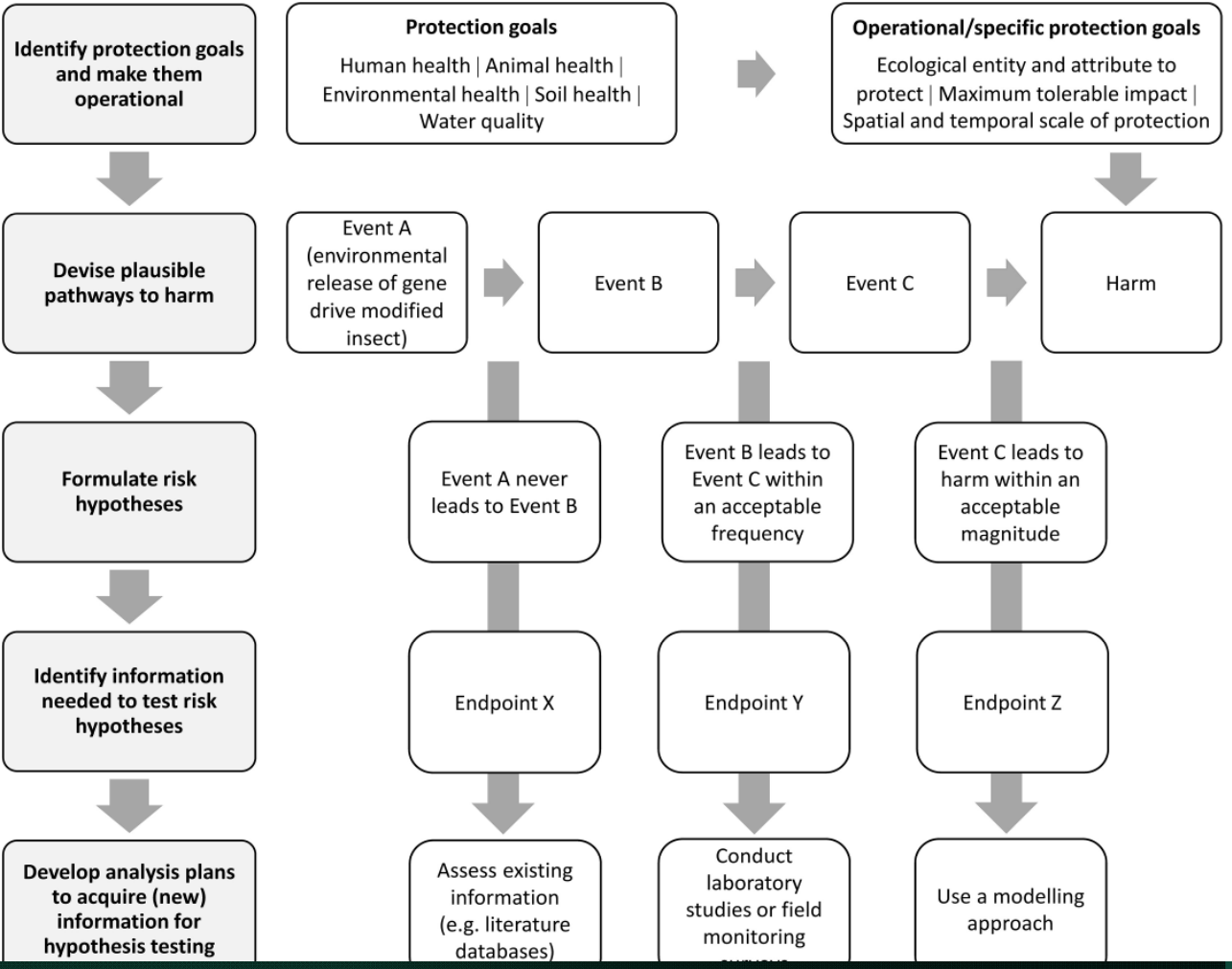
- ✓ What do we not want to see harmed? What must be protected?
- ✓ Can we envision a way in which they could be harmed?
- ✓ How can we assess whether they are likely to be harmed?
- ✓ Does it matter?

Gray, A, 2012 Problem Formulation in Environmental Risk Assessment for Genetically Modified Crops: A Practitioner's Approach. Collection of Biosafety reviews 6:10-65

Problem formulation - steps

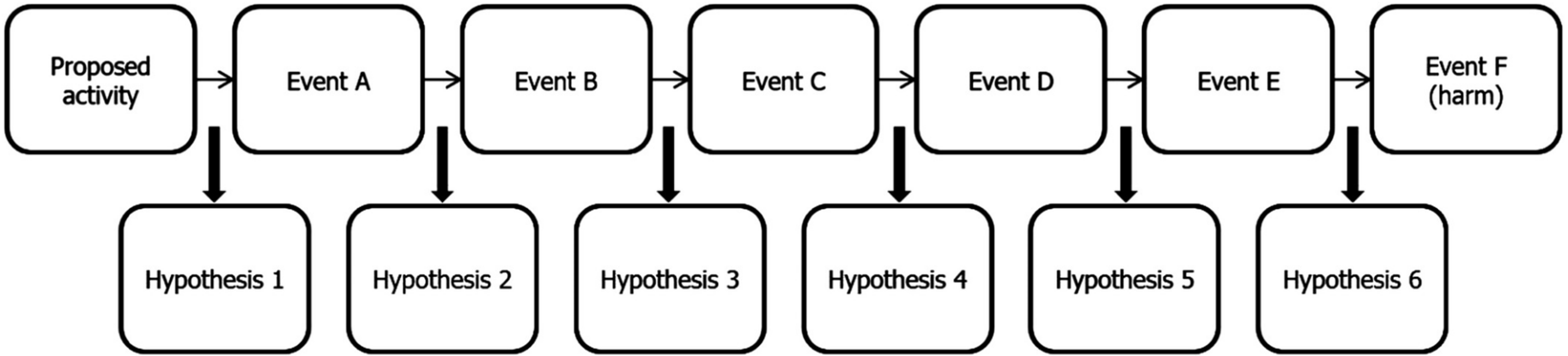
- ✓**Policy protection goals?** (in legislation)
- ✓Create a list of undesirable harms and devise plausible **pathways to harm** (or pathways to breach protection goals)
- ✓Formulate **risk hypotheses** to test steps in pathway to harm
- ✓Identify the information that is needed to **test these hypotheses**
- ✓Develop **analysis plans** to acquire information for hypothesis testing

Raybould, 2006 Problem formulation and hypothesis testing for environmental risk assessments of genetically modified crops. Environ. Biosafety Res. 5 (3) 119-125

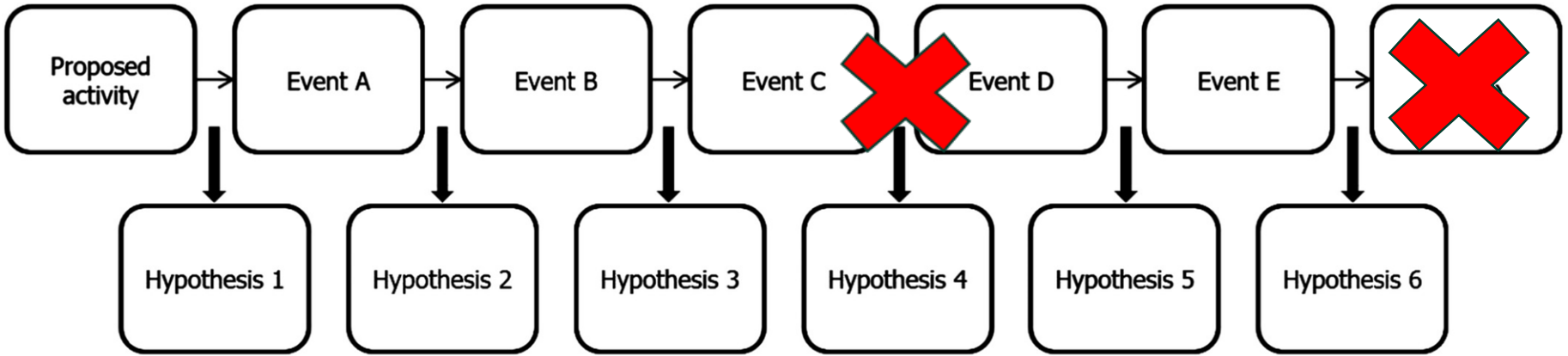


Devos et al., 2022
https://doi.org/10.1016/j.biotechadv.2021.107807

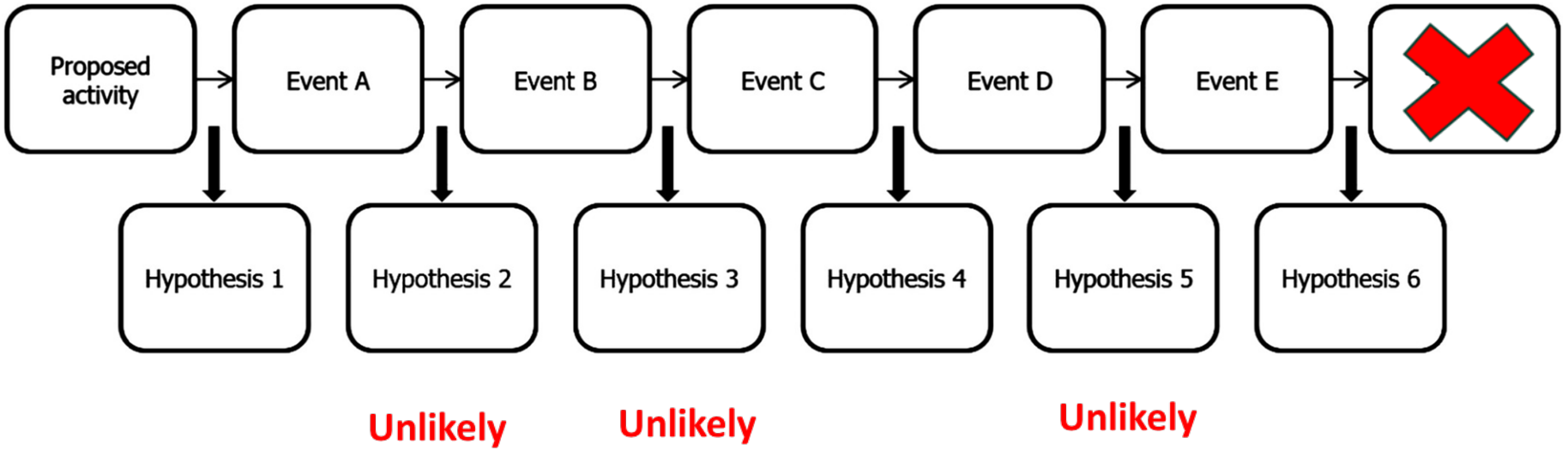
Use of pathway to harm (PTH)



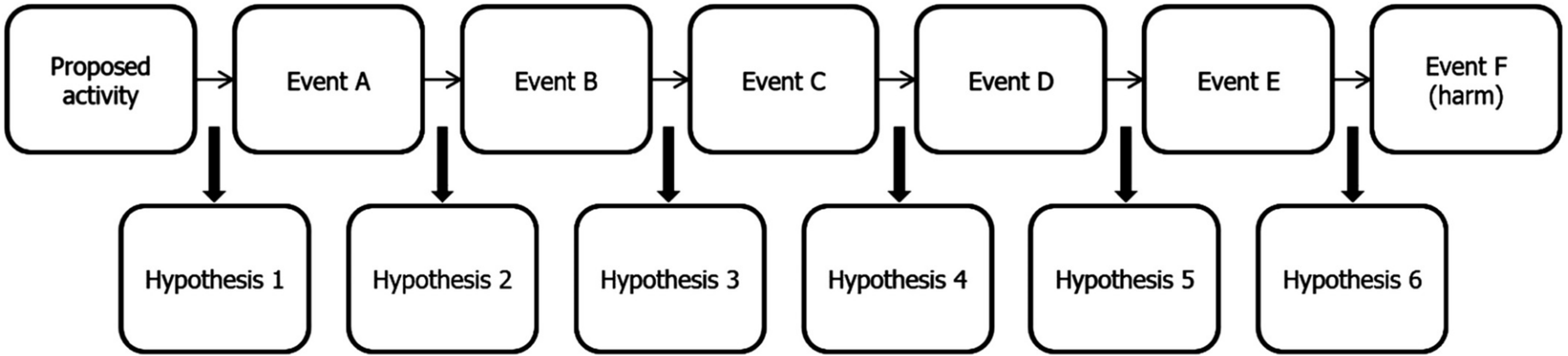
Use of PTH example 1



Use of PTH example 2

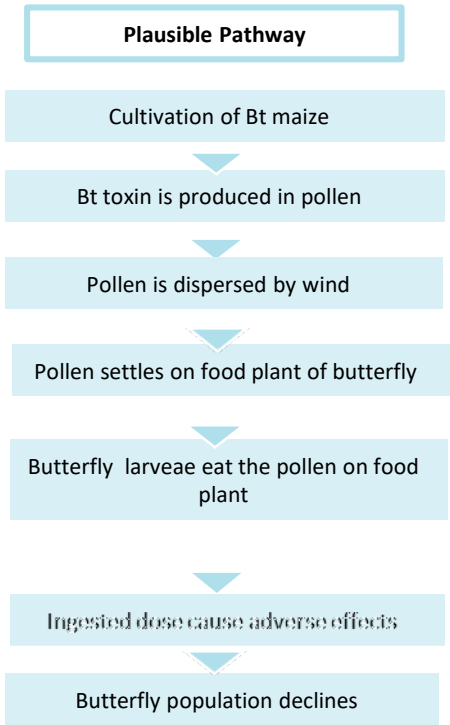


Use of PTH example 3



Likely ? Highly likely ?

Pathway 1. Population decline of butterflies by ingestion of pollen of Bt maize



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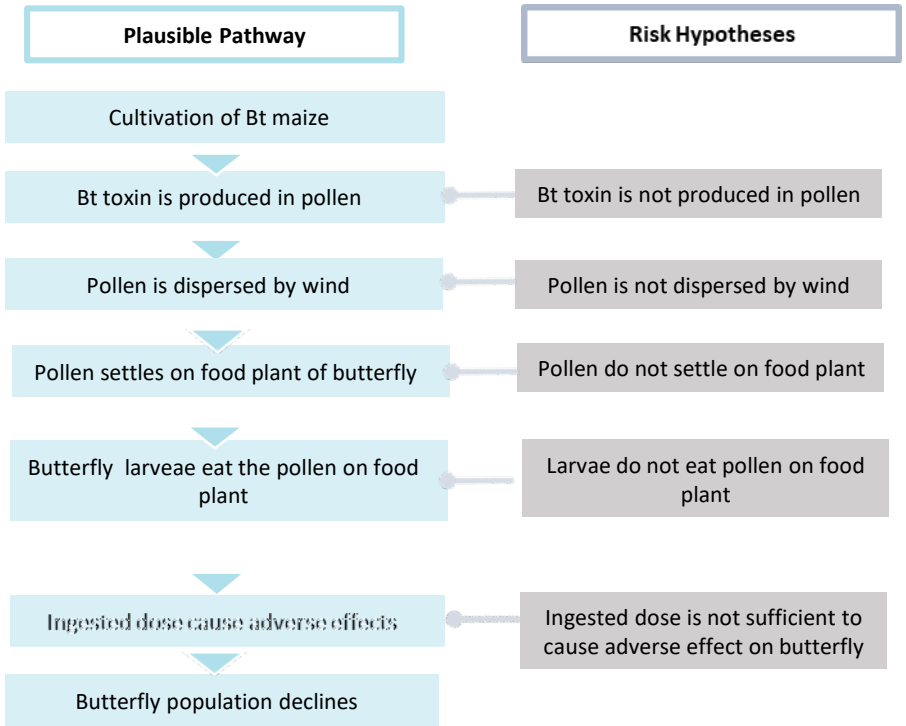

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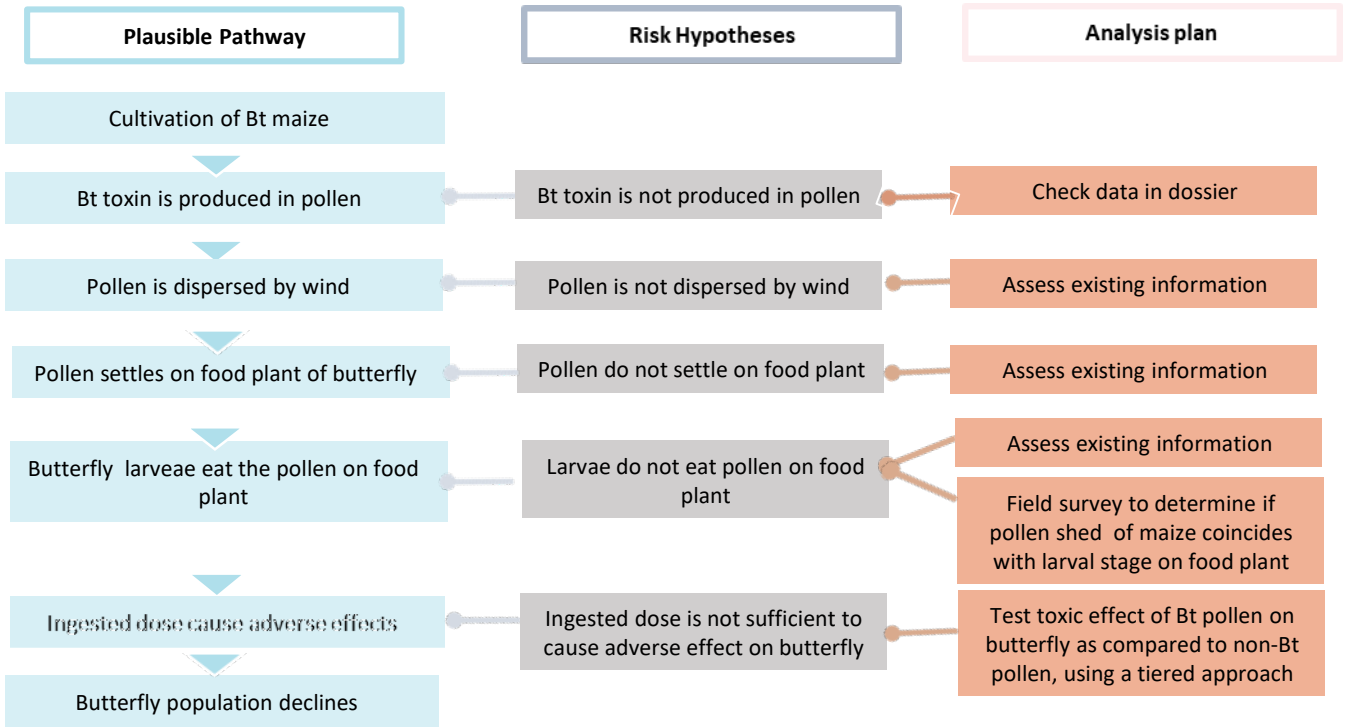

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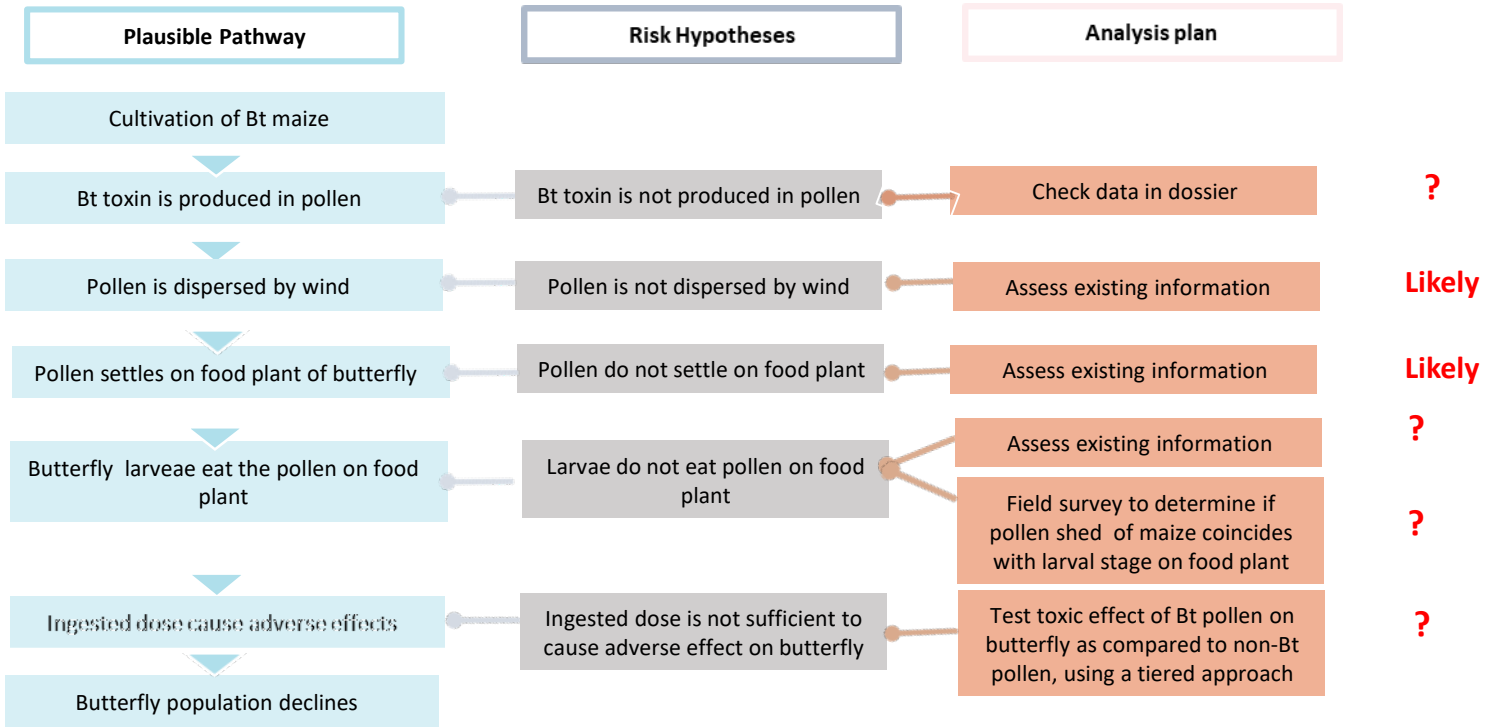
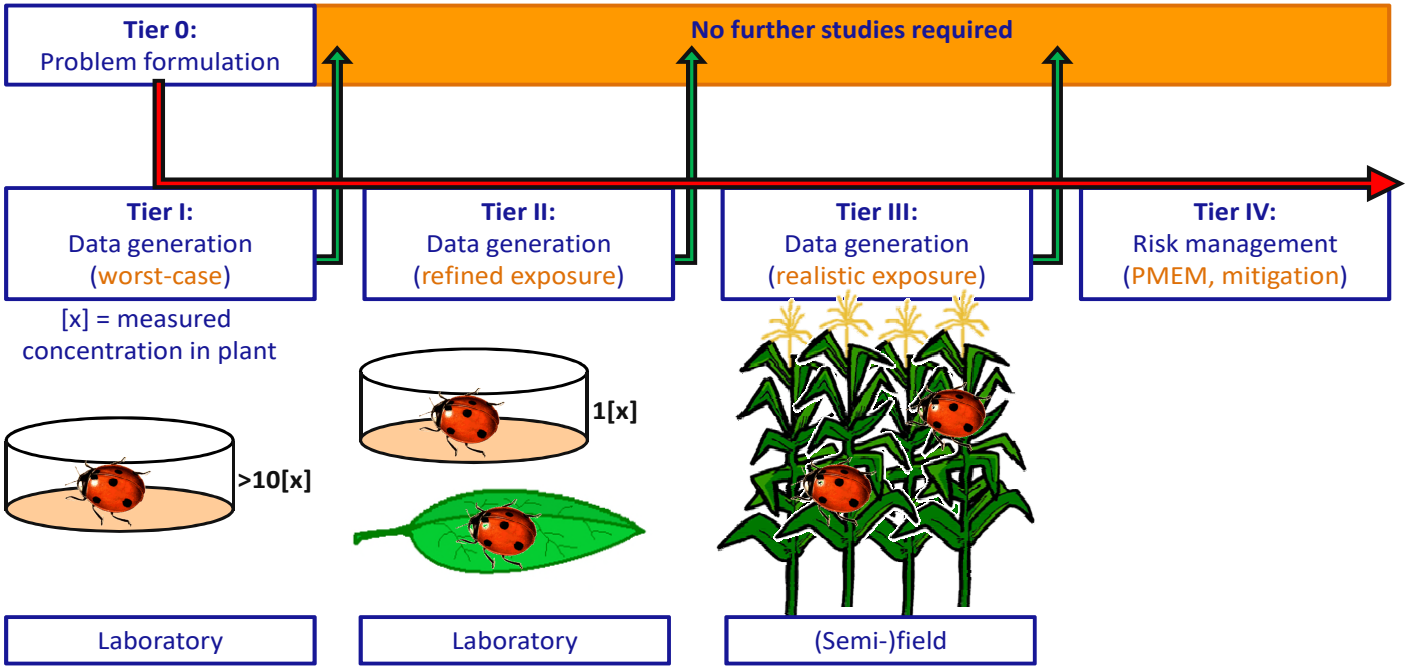


Tiered System

Example - Hazard Assessment Planning for NTOs



Adapted from Garcia-Alonso *et al.*, 2006. Environmental Biosafety Research 5:57-65

Multiple Pathways to Harm

Ingestion toxin → Decline pollinators

Indirect consumption toxin → Decline parasitoids

Suppression antagonist → Less disease control

Allergenic reaction to toxin → Decrease animal health

Allergenic reaction to toxin → Decrease human health

Horizontal gene transfer of antibiotic resistance gene → Decrease human health

Advantages of using Problem Formulation

- Flexible
- Can be used for a wide range of potential stressors (living or non-living)
- Focuses on most plausible pathways to harm
- Focuses on most critical steps in pathways to harm
- Results in clear analysis plan (if new data are needed)
- Transparent

Thanks for your attention!!