Influence of including uncertainty on species sensitivity distribution (SSD) analyses – A case study with non-target terrestrial plants (NTTP)

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Introduction

Species Sensitivity Distribution (SSD):

- is a key tool at higher tiers of the environmental risk assessment (ERA) for chemicals;
- describes the sensitivity of a set of species to a chemical substance as a probability distribution of toxicity values;
- allows to estimate the HR_5 that is the Hazard Rate prone to affect 5% of the species.

Toxicity values as input for SSD: namely 50% Effective Rates (ER_{50}), usually provided as estimates deriving from dose-response models fitted on toxicity test data. The uncertainty associated to toxicity values is currently ignored, due to a lack of clear recommendations on the way to proceed.

Objective of our project: Account for the uncertainty on toxicity values in SSD analyses and study how this uncertainty may influence the HR_5 estimate. We used Non-Target Terrestrial Plants (NTTP) exposed to herbicides as a case study.

Material and methods

Data: Standard toxicity test data on NTTP provided by BAYER for 11 compounds, collected in seedling emergence (SE) and vegetative vigour (VV) tests.

- Species: a set of 10 different species were exposed to a range of five tested rates plus a control;
- Endpoints: emergence (SE), survival (SE and VV) and shoot dry weight (SE and VV) at day 21.

Step 1

Dose-response modelling

- A three-parameter log-logistic model was fitted to toxicity test data under a Bayesian framework.
- The R-packages 'morse' and "rjags" were used.
- A marginal posterior probability distribution of the ER_{50} is returned, which can be summarized with a median and a 95% credible interval (CI95).

Step 2

Accounting for the uncertainty on the ER_{50}

➡ Always use the CI95 of the ER_{50}?

- The highest tested rate (max_rate) in NTTP test equals the maximum field application rate for agronomical relevance. For some species, this rate might be too low to generate more than 50% effects, leading to an unreasonable estimate of the ER_{50}. In this case, can the information still be included in the SSD as a right-censored probability distribution of the ER_{50}? If yes, how?
- Need for a decision criterion that we built as a probability-based overlapping ratio:

$$ratio = \frac{P(LCI95 \leq ER_{50} \leq max\_rate)}{P(LCI95 \leq ER_{50} \leq UCI95)}$$

LCI95 (UCI95): lower (upper) bound of the CI95

- Given a decision threshold T initially ranging from 0 to 1, we propose to censor the ER_{50} as follows:

$$\begin{cases} [LCI95, UCI95] & if\ ratio > T \\ [\min(\mathrm{LCI95}, \max\_rate), +\infty[& if\ ratio \leq T \end{cases}$$

- Ultimately, we chose T = 0.5 as the best compromise.

Step 3

SSD analyses

- A log-normal probability distribution was fitted to input ER_{50} values under a frequentist framework in two ways:
  1) only point estimates (ER_{50} medians), that is the current practice. The obtained HR_5 is denoted $HR_{5,1}$.
  2) censored ER_{50} obtained from Step 2. The obtained HR_5 is denoted $HR_{5,2}$.
- The R-package 'fitdistrplus' dealing with censored data in a mathematically sound way was used. An alternative is the MOSAIC web platform https://mosaic.univ-lyon1.fr/ssd.

Results

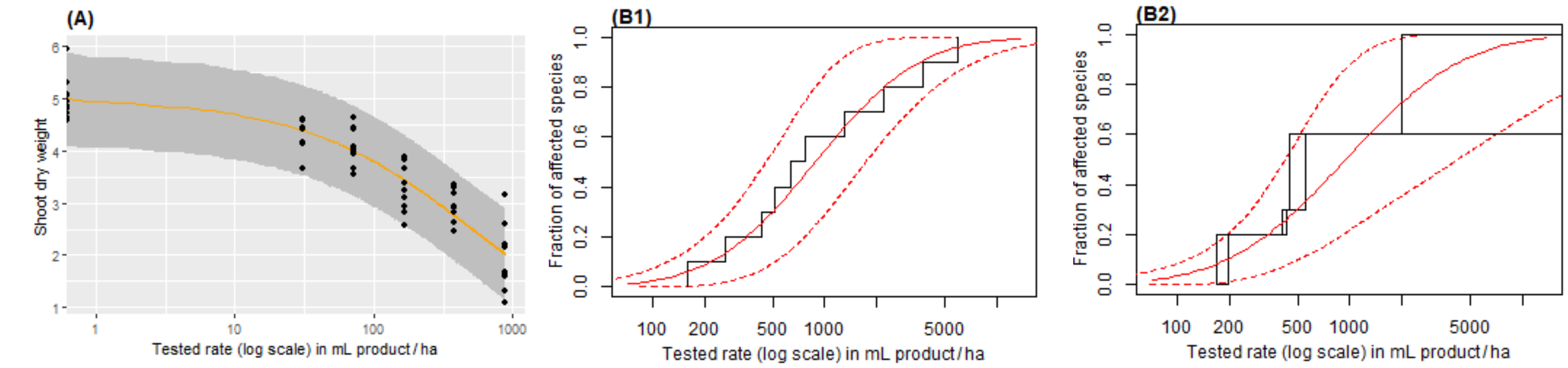

Figure 1: Example fits of dose-response (A) and SSD based on either ER_{50} medians (B1) or censored ER_{50} (B2) for the shoot dry weight endpoint

Comments

- The orange curve above with 95% confidence interval in grey credible band describes the effect of the tested compound on the shoot dry weight for the sugar beet.
- The SSD curve in Figure B2 has a much larger confidence band (red dotted curves) than the one in Figure B1.
- Table 1 shows that the $HR_{5,2}$ is smaller than the $HR_{5,1}$, the same for the lower bounds of their 95% confidence interval.

In the present study, for the five studied endpoints and by comparing $HR_{5,2}$ to $HR_{5,1}$, accounting for the uncertainty on the ER_{50} provides :

- a lower HR_5 value for survival (SE) and shoot dry weight (SE and VV) endpoints;
- a higher HR_5 value for emergence (SE) and survival (VV) endpoints (based on respectively only 5 and 3 distinct ER_{50} values because of lots of right-censored ER_{50} values).

Table 1: HR_5 based on either ER_{50} medians ($HR_{5,1}$) or censored ER_{50} ($HR_{5,2}$)

	Method (1)	Method (2)
Nb. ER_{50} values (right-censored)	10 (0)	10 (4)
HR_5 [95% confidence interval]	145.8 [79.6; 378.7]	123.1 [65.5; 337.1]

Conclusion

Based on our preliminary results of NTTP exposed to an herbicide, we are confident in the fact that accounting for the uncertainty on ER_{50} values is the way to move forward in the future for ERA.

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