Tier-1 pesticide risk assessment for aquatic primary producers: A protectiveness check based on European Food Safety Authority endpoints

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INTRODUCTION

For several years now, there has been an ongoing debate in the scientific community regarding the validation of the chronic aquatic risk assessment for herbicides. The endpoints for algae and/or vascular plants usually drive the environmental risk assessment (ERA) in the aquatic Tier-1 effects assessment for plant protection products with a herbicidal mode of action. Tier-1 requires data from toxicity tests with at least two algae and one macrophyte species (e.g., *Lemna* sp.). Regulatory Acceptable Concentrations (RACs) are based on application of a conservative assessment factor (AF) of 10 to the lowest 50% effect concentration. If an unacceptable risk is concluded for algae and/or vascular plants in Tier-1 ERA, higher tiers should focus on primary producers. The topic of the debate narrows down to the response endpoints for primary producers used in the ERA and whether this has implications on the protectiveness of the Tier-1 effects assessment. These endpoints include biomass (*b*; measured at the end of a toxicity test, resulting in an E_bC_{50}), yield (y; gain in biomass over the test duration, resulting in an E_yC_{50}), and growth rate (*r*; a logarithmic function independent of test duration, resulting in an E_rC_{50}) for Tier-1. E_rC_{50} is recommended as the preferred endpoint by the Aquatic Guidance Document (AGD; European Food Safety Authority PPR Panel [EFSA Panel on Plant Protection Products and their Residues], 2013) because the $E_{b/y}C_{50}$ endpoint depends on the growth rate of the test species as well as the test duration and other elements of test design (EFSA, 2013). Moreover, the biomass without logarithmic transformation cannot be directly used in an analysis of results from a system in exponential growth (e.g., a Tier-1 algal test; European Chemicals Agency, 2008). For Tier-3, which is used as a reference tier with high ecological relevance, the endpoints are based on population- and ecosystem-level effects from micro-/mesocosm studies with primary producers. For these studies, the AF is determined during regulatory review(s). In recent years, several authors have compared Tier-1 versus Tier-3 RACs to check the protectiveness of Tier-1. These comparisons have resulted in contradictory conclusions concerning the protectiveness of Tier-1 in comparison with Tier-3, as presented during SETAC conferences (Arts & Van Wijngaarden, 2016; Duquesne et al., 2018; Swarowski et al., 2015) and published in a peerreviewed journal (Van Wijngaarden & Arts, 2018). Tier-2 is dealing with additional species in laboratory tests and/or refined exposure testing and was not relevant for the research question discussed in this article. In order to shed more light on the origin of these differences, we explored the following question: "Is the pesticide risk assessment for plant protection products still protective after replacing the $E_{b/y}C_{50}$ by the E_rC_{50}?" This question was addressed by using published EFSA ERA response endpoints.

This article contains online-only Supporting Information.

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EXPLORING THE AVAILABLE DATA

For 17 active substances (a.s.) with herbicidal modes of action, Tier-3 RACs were available from micro-/mesocosm studies with primary producers (see the Supporting Information). The RACs were derived from the EFSA List of Endpoints (LoEP), except for two a.s. (i.e., linuron and fenpropidin) for which EFSA did not provide an AF, and therefore did not result in an RAC. In these two cases, the RACs were derived from the guidance for AFs recommended in the AGD (EFSA, 2013). For lenacil, EFSA recommended a range of AFs of 3–5, so we used 3 and 5 as AFs in our approach. Tier-1 RAC values (using $E_{b/y}C_{50}$ and E_rC_{50}) were obtained from LoEP published in EFSA conclusions. Only for those cases in which EFSA did not provide the specific endpoint were the Tier-1 endpoints from the submitted dossiers used. The RACs were calculated as endpoint/AF. The ratio of Tier-3 RAC/Tier-1 RAC> 1 therefore indicated that the Tier-1 approach could be considered protective.

PROTECTIVENESS CHECK

The 17 a.s. comprised 14 herbicides and three fungicides with herbicidal modes of action. The number of compounds that could be used was limited by the availability of acceptable data pairs (i.e., both Tier-1 and Tier-3 results) provided in EFSA conclusions.

- Using the E_rC_{50}: 11 substances (65% of the cases) had a Tier-3 RAC/Tier-1 RAC ratio >1, indicating that Tier-1 ERA can be considered protective (Figure 1). Six substances (35% of the cases) had a ratio <1, indicating that in these cases, a Tier-1 ERA is not protective.
- Using the $E_{b/y}C_{50}$: 13 substances (76% of the cases) had a ratio >1 (therefore, protective), while four substances (24% of the cases) had a ratio <1 (therefore, not protective) (Figure 1).

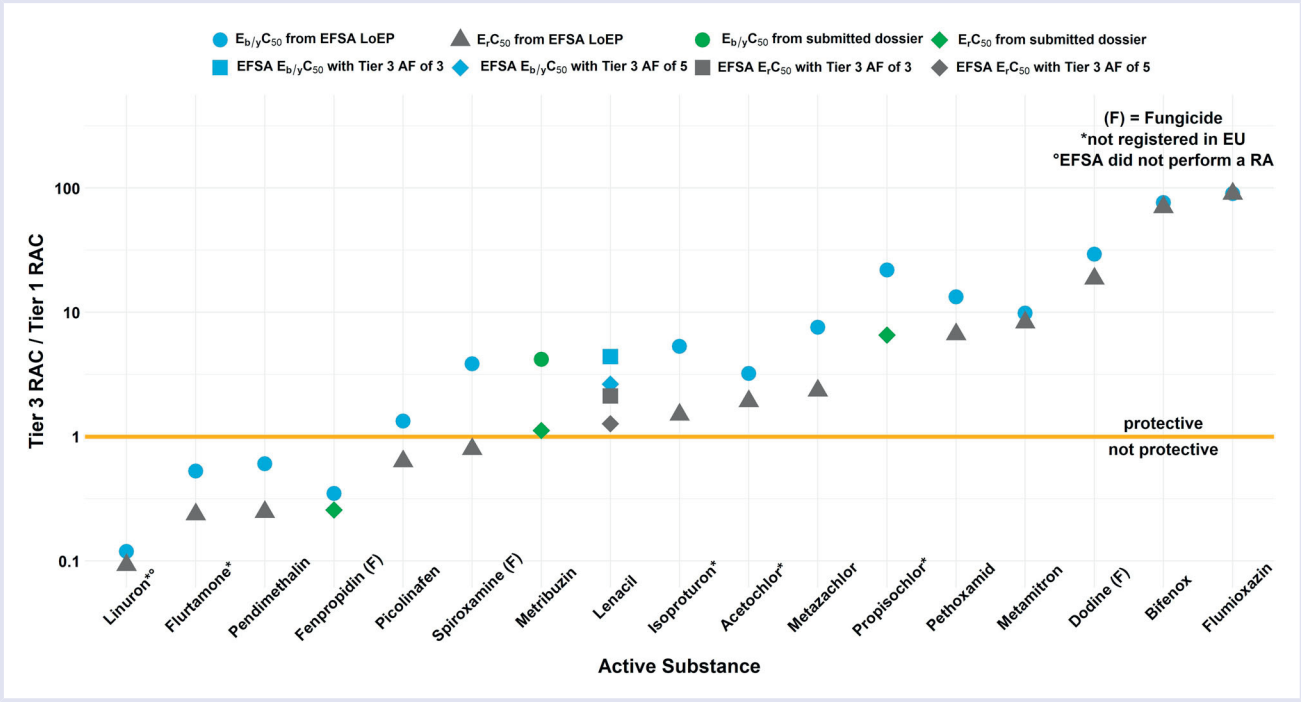

FIGURE 1 Protectiveness check for 17 active substances based on endpoints and assessment factors provided in European Food Safety Authority (EFSA) conclusions or submitted dossiers. Ratio >1 is considered protective. RA, risk assessment

For two of the substances (12% of the cases), the protectiveness changed to a ratio below the 1:1 line, when E_rC_{50} was used instead of $E_{b/y}C_{50}$.

DISCUSSION

The approach presented herein aimed to be as transparent and reproducible as possible. This is why the data selections are based on published endpoints in EFSA conclusions or submitted dossiers. By selecting data transparently, we aimed to limit the uncertainty surrounding the analysis. Van Wijngaarden and Arts (2018), Duquesne et al. (2018), and Swarowski et al. (2015) may have also used published literature not included in dossiers, which may not have been reviewed by the EFSA. The EFSA (2013) AGD recommends the use of E_rC_{50} over $E_{b/y}C_{50}$ for the scientific reasons described above.

When using an E_rC_{50}, our results show that in 65% of the cases, the Tier-1 ERA was protective compared with the Tier-3 ERA (Figure 1). These results are consistent with Van Wijngaarden and Arts (2018), who concluded that in their database, protectiveness was maintained when using an E_rC_{50} for either eight of the 10 herbicides (i.e., 80%) or nine of the 12 herbicides (i.e., 75%).

Our analysis indicates that about half of the compounds have a Tier-3/Tier-1 RAC ratio close to the 1:1 line (Figure 1, see the Supporting Information), consistent with Van Wijngaarden and Arts (2018). Consequently, a small change in the Tier-1 endpoint and/or the AF for Tier-3 can have implications for the protectiveness of the Tier-1 ERA.

A key factor influencing the datapoints in Figure 1 is the choice of the AF in Tier-3. For mesocosm studies, the AF lies between 2 and 5, according to the AGD (EFSA, 2013). The availability of the endpoint data is another issue. We noticed that—although required by EFSA (2013)—growth rate endpoints are not always available in the LoEP or in a dossier. We recommend amending this in the sequential updating of dossiers. Also, we noted that mesocosm data studying the effects of herbicides are limited. As Tier-3 is used as a reference tier, this data scarcity is problematic for the validation of the ERA. Our results demonstrate that using the E_rC_{50} as a Tier-1 ERA endpoint changes the overall protectiveness of the primary producer risk assessment from 76% to 65%.

AUTHOR CONTRIBUTION

Gertie H. P. Arts: Conceptualization; data curation; methodology; writing—original draft; writing—review and editing. **Eric Bruns:** Conceptualization; data curation; methodology; writing—review and editing. **Steven Droge:** Data curation; methodology; writing—review and editing. **Sarah Hartmann:** Data curation; methodology; visualization; writing—review and editing. **Ivo Roessink:** Methodology; writing—review and editing. **Andreas Solga:** Data curation; methodology; writing—review and editing.

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SUPPORTING INFORMATION

Seventeen active substances (a.s.) with herbicidal modes of action, Tier-1 Regulatory Acceptable Concentrations from standard tests with primary producers, and Tier-3 Regulatory Acceptable Concentrations from micro-/mesocosm studies with primary producers. $E_{b/y}C_{50}$, EC_{50} of the endpoint based on biomass/yield; E_rC50, endpoint based on growth rate; MoA, mode of action. The first column presents all EFSA references.

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