Title: Authors' response to the letter to the editor by Jowsey et al.

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Response to the letter to the editor by Jowsey et al. (Manuscript Number: RTP-18-461

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We would like to thank Dr. Jowsey and his co-authors for their valuable contribution to our recent article describing a novel approach for a quantitative risk assessment (QRA) for skin sensitizing plant protection products (Sanvido et al., 2018). As the authors of the letter to the editor correctly point out, an important component of the QRA is to determine which sensitization assessment factor (SAF) are to be used and what value is to be assigned to each of the different SAFs. SAFs take into account uncertainties when extrapolating from the experimental test conditions used for identifying the sensitizing potency of a given chemical to its actual in-use exposure conditions (Kimber et al., 2017). Dr. Jowsey and his co-authors emphasize in their letter to the editor that there is a key source of divergence in terms of how SAF values are deployed in our article and in a recent article published by Basketter and Safford (2016). Indeed, as we mention in the discussion section of our article, the number of SAFs to be assigned can be debated. The same is of course true for their assigned numerical values. As Basketter and Safford (2016) correctly cautioned that, “In setting these values it is recognised that, given the uncertainty in the supporting data, exact values cannot be derived, and a certain amount of expert judgement is required”.

We would also like to emphasize here, as we already did in our original article, that the question regarding which SAF to assign, is primarily relevant for ***moderate*** skin sensitizers. To illustrate this, we assigned the SAF of 900 proposed by Dr. Jowsey and colleagues (based on Basketter and Safford (2016)) to our dataset (shown in Table 4 of our article). The QRA outcomes (i.e. whether additional protective measures for at least one part of the body are needed to avoid sensitization) were the same for four of the six products assessed. The QRA outcomes for two moderate skin sensitizers (i.e., products D and E) (Table 1) changed. Independently of whether a SAF of 900 or 7500 is assigned, the ***exposure to strong sensitizers exceeds the Derived No-Effect Levels (DNELs)*** (i.e., products A, B, and C). **Weak sensitizers remain below the DNEL** (i.e., product F).

Our intention was to propose a novel approach for QRA of skin sensitizing plant protection products (PPPs) because such an approach is currently lacking. Within this remit, we followed

the classical approach to QRA for skin sensitizing chemicals advocated by Kimber et al. (2017), which incorporates the following features:

1. A no effect level is derived from the predictive toxicology work
2. Appropriate safety factors are used to adjust the no effect level
3. The adjusted level is compared with the human exposure level

Our article should be regarded as a proof of concept that DNELs can be derived for skin sensitizing PPPs. These can subsequently be used together with an agricultural operator exposure model (AOEM) to predict exposure exceedance. We firmly believe that this approach will lead to an appropriate risk assessment for skin sensitizing PPPs and eventually reduce work-related skin diseases among PPP exposed workers. Nevertheless, we are fully aware that each newly proposed methodology needs discussions among experts and re-adjustments before it can be implemented to serve as a fully operational new risk assessment methodology, especially if to be used in a regulatory framework. Hence, the assigned total SAF of 7500 was never intended to be seen as the only possible SAF to be used in QRA of skin sensitizing PPPs. We strongly support further discussions on the selection of appropriate SAFs with the aim to define scientifically sound SAFs for PPPs that represent a reasonable worst-case. We therefore welcome the offer of Dr. Jowsey and his co-authors to further collaborate in evolving this approach in the field of pesticide risk assessment.

Table 1

Exposure calculation for two different SAFs of 900 and 7’500, respectively. The comparison shows that the outcome whether the DNEL is exceeded for at least one part of the body or not (i.e. % of DNEL > 100) remains the same for four of the six products assessed. The QRA differs only for products D and E depending on the SAF assigned.

	SAF 900 Basketter and Safford (2016)	SAF 7’500 Sanvido et al. (2018)

	DNEL	Exposure no PPE scenario [% of DNEL]		DNEL	Exposure no PPE scenario [% of DNEL]	
Product A	0.87	Hands Body Head	814 613 22	0.11	Hands Body Head	6’780 5’112 183
Product B	0.01	Hands Body Head	26’183 43’959 1’291	0.001	Hands Body Head	218’195 366’326 10’761
Product C	1.43	Hands Body Head	74 261 6	0.171	Hands Body Head	619 2’171 54
Product D	4.0	Hands Body Head	8 74 2	0.48	Hands Body Head	70 619 13
Product E	24.57	Hands Body Head	17 20 1	2.95	Hands Body Head	143 164 5
Product F	26.92	Hands Body Head	1 11 0	3.23	Hands Body Head	12 95 2

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