

European Conference on Safe Use of Plant Protection Products

Conference Report, 18 June 2014

In June 2014, the Federal Institute for Risk Assessment in Germany (BfR) and the European Commission hosted the “European Conference on Safe Use of Plant Protection Products” in Berlin, Germany. The expert conference was attended by representatives of the European Commission (Directorate-General for Health and Consumers), the European Food Safety Authority (EFSA), Member States Competent Authorities, the European Crop Protection Association (ECPA) and the Committee of Professional Agricultural Organisations and the General Committee for Agricultural Cooperation in the European Union (COPA-COGECA). Central topics were the new EFSA draft „*Guidance on the Assessment of Exposure for Operators, Workers, Residents and Bystanders in Risk Assessment of Plant Protection Products*” and the further harmonisation of derivation of dermal absorption values and allocation of risk mitigation measures.

1 Introduction

The “European Conference on Safe Use of Plant Protection Products” held in Berlin, Germany, was the first conference of its kind to address harmonisation of zonal risk assessment. Issues which are crucial for better harmonisation of the risk assessment with a focus on safe use and in the context of the zonal authorisation of plant protection products (PPP) were discussed among experts from the national competent authorities, European institutions, and stakeholders.

Since the implementation of the Regulation (EC) No. 1107/2009 concerning the placing of plant protection products on the market, many questions have been raised within the scope of zonal authorisation and mutual recognition. Both procedures require a high level of harmonisation between the Member States (MS). Hence, further harmonisation of non-dietary exposure models and risk assessment procedures was the overall objective of this conference. In particular, the conference focused on the EFSA draft „*Guidance on the Assessment of Exposure for Operators, Workers, Residents and Bystanders in Risk Assessment of Plant Protection Products*” and on further harmonisation of derivation of dermal absorption values and allocation of risk mitigation measures. The main benefits of such a harmonised approach have been identified as: (1) the same level of protection in all MS, (2) the predictability of evaluations by applying the same methodology, (3) the improved confidence in zonal authorisation and (4) more efficient procedures for zonal authorisation.

The transparency of data, the traceability of information and the reproducibility and mutual understanding of the outcomes were highlighted during the discussions as key principles of a harmonised risk assessment. It was pointed out that risk assessment is based on a tiered approach starting with ‘worst case’ assumptions, allowing a subsequent refinement. Scenarios could be more realistic (less “worst case”) if suitable and representative data are avail-

able. There was a broad consensus that the development of more realistic models is inevitably linked with increasing data availability.

2 Conference Results

2.1 Risk Assessment and Safe Use of PPP in the EU

The conference started with a plenary lecture session introducing the regulatory framework of risk assessment and safe use of PPP in the European Union. The presentations were given by European Commission and EFSA.

In the first presentation an overview over the legal frame of zonal evaluation and mutual recognition within the European Union according to Regulation (EC) No 1107/2009 was given. The European Commission is dedicated to support the functioning of mutual recognition. New tools for information exchange between the MS of the European Union could be developed if desired by MS. The communication and document sharing tool "CIRCA BC" is available to all registered CIRCA BC members in the working area of PPP's and residues. The European Commission is supportive with regards to further harmonisation of risk assessment and welcomes the organisation of subsequent conferences.

In accordance with Article 31 of Regulation (EC) No 178/2002 EFSA was asked to proceed with the preparation of a Guidance Document on the Pesticide Exposure Assessment for Workers, Operators, Bystanders and Residents. In the second presentation EFSA's activities on non-dietary exposure to PPP's were presented focussing on the new EFSA guidance document. The guidance provides a quality assessment of existing data bases made available to EFSA and gives recommendations for models and default parameters. An outlook was given on the further steps for finalisation of the document. It is expected that the final guidance document will be forwarded to the European Commission in the autumn of this year and noted by the Standing Committee afterwards. Further EFSA projects in this field, namely the field data collection for non-dietary cumulative exposure assessment and the developed database on operator exposure assessment scenarios, were presented as well. Setting up a database for bystanders and residents was discussed as a future perspective.

In the concluding discussion on this session, it was pointed out that a common understanding of the tiered approach in the draft of the EFSA guidance document is essential for further harmonisation. It was noted that more guidance in the EFSA document is needed especially for risk refinement (e.g. which scenarios are covered by first tier assessments, the evaluation of additional studies, and the use of risk mitigation measures). There was a broad agreement that the EFSA draft document "*Guidance on the Assessment of Exposure for Operators, Workers, Residents and Bystanders in Risk Assessment of Plant Protection Products*" shall be applied by applicants and authorities to further harmonise the zonal risk assessment procedure of PPP. EFSA will offer presentation and training in early 2015 after the adoption of the guidance. It is intended to update the guidance document as soon as possible if new data become available.

2.2 Exposure Estimation and Risk Assessment

In this plenary lecture session the exposure assessments for the different exposed groups (operator, worker, bystander and resident) were discussed. Presentations were given by HSE, BfR and ECPA.

The exposure assessment for bystanders and residents was presented by HSE. Based on the definition of bystander and resident the differences between these groups and operators and workers were highlighted. In the EFSA draft guidance document four exposure pathways (spray drift, vapour, surface deposits, and entry into adjacent treated crops) are now considered for bystanders and residents. With respect to differences in exposure frequency and duration a short-term exposure assessment is proposed for each of these individual pathways for the bystander based on the 95th percentile of the exposure estimations. Long-term exposure assessment is proposed for each individual exposure pathway for residents based on the 75th percentile of the exposure estimates. An addition of all four exposure pathways is considered to be realistic for residents only; in this case the mean exposure estimates would be calculated. The Bystander and Resident Exposure Model (BREAM) database for spray drift exposure was presented. Exposure estimation based on these data is one integral part of the risk assessment for bystanders and residents according to the draft EFSA guidance.

In the following discussion the participants agreed that the EFSA Guidance is a starting point for further harmonisation of bystander and resident exposure. Ongoing efforts are needed to close the data gap for several pathways and to increase the level of information on realistic worst case exposure scenarios. All experts appreciated the fact that more data for relevant exposure routes will be provided soon within the framework of the BROWSE project (Bystanders, Residents, Operators and WorkerS Exposure models for plant protection products). In addition, European Crop Protection Association (ECPA) will also provide more data related to exposure routes for bystander and residents.

The recently finalised “Agricultural Operator Exposure Model” (AOEM) was presented by the BfR which led the project. The AOEM is based on a statistical evaluation of new operator exposure data, which have not been used in exposure models before. The new operator exposure model is recommended in the draft EFSA guidance as first tier approach for exposure assessments of typical outdoor application scenarios. The database and the development of the model were described in detail in this presentation.

Following the same approach as for the AOEM a new greenhouse model is under development which was presented by the BfR. First results of the re-evaluation of the available greenhouse data from the southern greenhouse project were shown. It is the aim to consider the new greenhouse model after finalisation and adoption by the MS in an amended EFSA guidance.

The following discussion highlighted that the AOEM is currently the best available database model for operator exposure estimation and is included in the draft EFSA guidance docu-

ment. Participants expressed that this draft should be noted by the Standing Committee and the Member States as soon as possible because it will include the first harmonised exposure model for the procedure of zonal evaluation.

It was noted that an *ad hoc* approach can be followed (e.g. other application techniques) when the model does not cover specific scenarios. For taking into account national characteristics, national addenda will be still necessary in the authorisation procedure. Proposals for the exposure assessments of missing application scenarios such as greenhouse applications, seed treatments or post-harvest applications should be implemented in the EFSA guidance document as well. The participants would welcome more guidance in the EFSA document for the allocation of risk mitigation measures (e.g. definition of working clothing vs. certified coveralls).

ECPA's view on the draft EFSA guidance document was also presented. Results of exposure estimations for operators, workers, bystanders and residents prior to and according to the new EFSA guidance were compared. In the discussion afterwards, it was pointed out that the conservatism of certain scenarios is related to the limited data availability. With respect to worker transfer coefficient values ECPA signalled their willingness to check the possibility of providing data used by the US Environmental Protection Agency (Office of Pesticide Programs). Regarding worker exposure the EFSA guidance addresses exposure assessments for repeated applications. The consideration of GAP specifications (e.g. re-entry intervals) could be a possibility for a refinement of worker exposure. The experts expressed their wish for more guidance on the allocation of risk mitigation measures for workers as well (e.g. definition of working clothing vs. certified coverall).

2.3 Dermal Absorption

The third session dealt with the estimation of values derived from dermal absorption studies, which is an integral part of risk assessment and closely linked to exposure estimations. Presentations were given by BfR and ECPA.

This session provided an overview about different databases that include information on dermal absorption studies. First results from these data evaluation were shown. Furthermore, a proposal for a harmonised procedure estimating dermal absorption was presented.

The BfR has developed a database in order to evaluate available data, to check the applicability of the new default values and to derive proposals for further harmonisation of the risk assessment. The BfR database comprises information from 1553 experiments with 131 active substances and 231 formulations. Moreover, it includes a large number of dermal absorption studies, of which 379 studies are rat *in vivo*, 212 studies are rat *in vitro* and 387 studies are human *in vitro*. Data from *in vitro* studies on human skin have been derived from both dermatomed skin and isolated epidermis. The results support the proposed default values (EFSA 2012) of 25 % for concentrates and 75 % for dilutions of pesticide formulations. A refinement of these default values was not intended by BfR. These default values may be used for the risk assessment of PPP's when experimental data have not been submitted. A comparison of the relative permeability of rat skin vs. human skin using the BfR database

has proven its consistency with the current state of knowledge: For the majority of the tests, rat skin had higher permeability than human skin. Moreover, the hypothesis was verified that the dermal absorption rate according to a “Triple pack” is lower compared to the stand-alone test using human skin *in vitro* (a “Triple pack” is the combination of *in vivo* animal, *in vitro* animal and *in vitro* human dermal absorption studies, OECD 2011). For studies on isolated epidermis, 53 experiments with 19 active substances and 19 formulations were analysed. In 81 % of the cases the dermal absorption rates were lower when “Triple packs” were used. In contrast, 19 % of the experimental data showed a decreased dermal absorption rate when *in vitro* human skin studies were considered.

The database developed by the European Crop Protection Association (ECPA) is based on an initiative evaluating the reliability and possible reduction of default values and opportunities for “read-across” that were proposed in the EFSA “*Scientific opinion: Guidance on Dermal Absorption*”. ECPA’s database includes 360 human *in vitro* skin studies. With regard to default values for the concentrate, ECPA proposes a decrease of default values of liquids (6%) and for solids (2 %). For the dilution an overall reduction to 30% is proposed. Moreover, for the “read across” approach ECPA proposes that solvent-based data shall be considered as “worst case-read across”. Dermal absorption values derived from water-based formulations may function as “read across” for solids. In contrast, the EFSA guidance document states that a “read across” between formulation types is largely not acceptable. With respect to the *pro rata* analysis ECPA concluded that dermal absorption does not increase linearly with the dilution, which again is contrary to EFSA’s guidance (EFSA 2012). Therefore, ECPA proposes a *pro rata* correction with a maximum of 5-fold increase or a default value of 30 %.

In the last presentation of this session the BfR proposed a procedure for estimating dermal absorption in the risk assessment. In terms of interpretation and use of experimental data BfR recommends the use of *in vitro* human skin data according to OECD guideline 428 as a starting point for the assessment. If further refinement is necessary the tiered approach is possible using the above mentioned “Triple pack” analysis. For the estimation BfR recommends the use of the EFSA “*Scientific opinion: Guidance on Dermal Absorption*” (EFSA 2012) to further improve the harmonised procedure. Regarding the *pro rata* analysis, BfR will perform additional analyses of its database. In the absence of product-specific data BfR recommends three options for the estimation of dermal absorption in the following order:

- (1) default values are used for the estimation,
- (2) the “one-to-one” transfer of experimental data from dermal absorption studies to a similar formulation with the identical active substance may be used. Regarding the similarity of a formulation, BfR recommends to strictly follow the criteria stated by EFSA (EFSA 2012), and
- (3) the “many-to-one” approach is envisaged as described in the OECD guidance (OECD 2011). This approach includes the rough estimation of dermal absorption values derived from experimental data of different compounds from the same chemical class or group.

For the estimation of dermal absorption values, BfR would not support consideration of oral absorption and oral or dermal toxicological studies with the active substance since in these

studies only the active substance was tested and not the possible effects of e.g. co-formulants.

The following plenary discussion addressed the different goals and outcomes of the databases of the BfR and ECPA. Importantly, it was clarified that these databases were established with different aims and therefore complement each other. The focus of the BfR was the evaluation of available data whereas ECPA's intention was the refinement of already existing values. The experts then explained the differences of the data sets in more detail. BfR included all available data from *in vitro* human skin studies in the database (e.g. isolated epidermis and dermatomed skin, up to 24 hours of exposure) while on the other hand a restricted scope of selection criteria is characteristic for ECPA's data sets (e.g. only dermatomed skin, 6-10 hours of exposure). The participants agreed that further evaluation of existing data is needed to proceed with the harmonisation in the derivation of dermal absorption. It was proposed that clearly defined evaluation rules and a similar evaluation of both databases would benefit the process of harmonisation. In addition, further guidance for a harmonised procedure for estimating the dermal absorption shall be implemented. At first, exchange of experience between experts from the MS will be required in regard of the harmonisation of single study evaluation results. The results of this exchange will be included in the already existing and updated EFSA document "*Scientific opinion: Guidance on Dermal Absorption*".

2.4 Allocation of Risk Mitigation Measures

In the last plenary lecture session the Member State's perspectives regarding risk mitigation measures (RMM) were presented and discussed. In this framework the perspectives from France (ANSES), United Kingdom (HSE) and Germany (BfR) were presented.

In France recommendations for personal protective equipment (PPE) are provided by the applicant and have to be verified by the agency in order to advise authorities. Such proposals for PPE or working clothes are based on hazard identification and risk assessment. Working coveralls are used in most cases if they are effective for intended uses. However, these coveralls are currently not regarded as PPE, and certified PPE is needed for specific uses. It was mentioned, that ISO 27065 could be applied for the certification of working coveralls to harmonise the requirements.

Also in the United Kingdom the PPE recommendations are based on hazard identification and risk assessment. Operators are assumed to wear coveralls as standard working clothes. No PPE is assumed for amateur use. Outdoor workers are generally assumed to have arms, body and legs covered, but for indoor workers minimal protection is assumed. Gloves are not currently considered for worker risk mitigation, but this will change provided employers agree to necessary measures like training including risk awareness, safety signs and regular checks. Risk mitigation measures are limited for bystanders and residents.

In Germany PPE recommendations are based on hazard identification and risk assessment as stated by the other MS before. The assessment of operators (certified PPE recommenda-

tions according to the Directive “Personal protective equipment for handling plant protection products”, 2006), workers (RMM, e.g. PPE, re-entry restriction), bystander and residents (allocation of RMM, e.g. drift reducing nozzles, safety distances) were summarised.

Within the following plenary discussion the need for a consistent definition, mutual understanding and allocation of “general” RMM (e.g. certified gloves and coveralls, working clothes) became clear. To further improve harmonisation, sharing of information and training as well as voluntary stewardship (e.g. consider lack of compliance for workers) are essential. Moreover, the allocation of safety distances for bystander and residents and the consistency of common approaches (e.g. certain PPE for specific exposure groups, assessment of specific uses – home and garden uses, assessment of public areas) are topics requiring further harmonisation.

3 Conclusions

According to the experts, holding a first conference on topics of harmonisation of zonal non-dietary risk assessment was long-awaited. It is an important step towards information exchange and improvement of harmonisation of the safe use of plant protection products.

There was consensus among the participants that the EFSA draft *„Guidance on the Assessment of Exposure for Operators, Workers, Residents and Bystanders in Risk Assessment of Plant Protection Products”* is a major step towards harmonised risk assessment. The guidance should become mandatory for first tier assessments in the zonal authorisation procedure for applicants and should be the basis for the risk assessment of the Member States Competent Authorities. It was suggested, that further development of an amended EFSA guidance is essential and missing scenarios such as greenhouse applications have to be implemented as soon as possible.

With respect to derivation of dermal absorption there is a great interest among all participants in ongoing harmonisation of the procedure. To further develop current assessment approaches, actual results from dermal absorption studies will also be taken into account. The participants agreed that further evaluation of existing data is needed to proceed with the harmonisation in the derivation of dermal absorption.

All experts agreed that there is a high need in harmonisation regarding the consistency of definition, mutual understanding and allocation of ‘general’ risk mitigation measures.

Lastly, it became clear that the participants would greatly welcome subsequent meetings in order to share experiences and discuss new and updated information. This is also important for other fields of risk assessment relevant for zonal authorisation.

The presentations given in the plenary session are also available in full on the BfR website: http://www.bfr.bund.de/en/event/european_conference_on_safe_use_of_plant_protection_products-190862.html