CLEs technical and scientific response to an article published in Le Monde, "Pesticides: the grand illusion of farmers' protective equipment."

Answer prepared by OBE technical subgroup of CLE

On February 16th, 2022, an article by Stephane Horel was published in Le Monde which was an indictment of the use and performance of personal protective equipment and its role in risk assessments for plant protection products. CropLife Europe, an Industry body which represents sustainable, innovative and science-based crop protection solutions that contribute to providing Europeans with a safe, affordable, healthy, and sustainable food supply, would like to respond to this article. We feel that it does not give a balanced view and contains several misleading pieces of information.

The article describes the use of patch dosimetry by the Pestexpo researchers. This is, according to the OECD guidance on operator exposure studies, still a valid method, although the revised EFSA guidance on non-dietary exposure assessment[1], which is globally viewed as very protective, states that "Patch data should not be considered unless uniform exposure can be demonstrated" and the inclusion criteria for the agricultural operator exposure model (AOEM) which forms the basis of the EFSA operator exposure model dictate that data should come from whole body dosimetry studies. Nevertheless, the researchers have clearly carried out the studies in an appropriate manner for the method and the comment that "the aluminum will act as a barrier between the farmer's job and his body" needs addressing. The intention of placing an impermeable layer at the bottom of a patch dosimeter is to ensure that any material captured on the patch will not penetrate either to the clothing or skin beneath, ensuring that all the material is accounted for and exposure is not underestimated. It is not there to protect the operator.

There is also a statement that the Pestexpo team have discovered that operators may be more exposed than previously thought. However, the use of patch dosimetry, which depending on whether splash or drip lands on the patch or not can over- or underestimate exposure, does not give a more robust prediction of exposure than the AOEM, which is based on over 30 studies which satisfy the following rigorous inclusion criteria:

- Compliance with OECD Series No. 9 1)
- Full compliance with GLP
- Monitoring of real-life professional agricultural operators (e.g. farmers and contractors) working in accordance with GAP (Good Agricultural Practice), but with their own "natural work behaviour and habits"
- Data recording and observations according to current scientific knowledge
- Consistent field recovery (any outlying data must be reported and in case such data are not used to derive exposure results, appropriate argumentation must be provided on a scientific basis)
- Suitable data form for model development (e.g. separately measured head, hand and body exposure)
- Whole body dosimetry for dermal exposure (exclusion of patch data)
- Inhalation exposure determined with appropriate inhalation fraction samplers
- Representative application methods and application techniques reflecting current agricultural application practices in Europe

[1] https://www.efsa.europa.eu/en/efsajournal/pub/7032

The final report and model were developed by the German BfR (German Federal Institute for risk assessment), observed by EFSA. These are studies carried out by members companies of CLE, but are scientifically robust and satisfactory according to the regulatory authorities involved. The comment that exposure data owned by companies are kept away from scientific scrutiny is no longer valid, as full access to the data underpinning the AOEM was given to the regulatory authorities in the working group. Like the Pestexpo researchers, the company experts responsible for the studies are experienced scientists who have a duty to generate the data needed for registration in a responsible and professional way. Were this not the case, the studies would not be accepted by European regulators. The CLE member companies have rigorous internal safety standards, and the European review process must be recognised as protective. If a PPP does not have an acceptable risk profile according to the national and regional regulators, it will not be authorised and will not be used.

In the article, it is reported that the Pestexpo project identified instances where in some cases, wearing coveralls or gloves might even increase exposure. We would be very interested in seeing the evidence for this which is not reported in the article. In the referenced publication, PPE led to an overall exposure reduction of >90%.

It is stated that the concept of a “safe use” of pesticides is “pure fiction”. On the contrary, countless plant protection products have been used for a considerable period of time under real conditions without any evidence of harm. Risk assessments for operators necessarily take into account exposure which is expected under “normal” conditions as “unexpected use/misuse” cannot sensibly be accounted for in any regulatory scheme. Nevertheless, the safety endpoints against which this exposure is assessed are not “regulatory jargon” as implied in the article, but precautionary, health-based limits which take into account uncertainty. The acceptable operator exposure level (AOEL) is defined as "the maximum amount of active substance to which the operator may be exposed without any adverse health effects," but this does not reflect the true nature of the endpoint. From the relevant animal studies, the endpoint is based on a dose level at which no adverse effects were observed. A safety factor of at least 100 is then applied to derive the AOEL. In other words, the AOEL represents a level which limits the exposure to a maximum of 1% of an exposure which did not cause the test species any observable harm. Additionally, regulatory models have demonstrable levels of conservatism built into them which generally overpredict exposures which are compared with these precautionary endpoints.

It is true that certain types of PPE may be stipulated in the risk assessment and on the product label to mitigate risk. However, some of these mentioned in the article, like goggles, are to protect the operator against local effects like eye irritation and have nothing to do with systemic exposure and the AOEL. It should also be noted that operator exposure assessments carried out using the AOEM do not consider the use of protective coveralls as a means of reducing systemic exposure. Whether they comply with the assigned protection factors given in the EFSA guidance or not is therefore a moot point. Exposure data in the AOEM were gathered for operators wearing a single layer of workwear and in many instances protective gloves. In this way, the actual performance of the garments was measured under field conditions and there is no need to make any assumptions about protection factors. The AOEM is based on studies where real operators applied real products under real field conditions. The operator is not instructed to behave in a particular way but asked to follow their normal working practice. Technical problems like those mentioned in the article, such as splashes during mixing and loading the product, nozzles getting blocked, mixtures foaming do occur, but these are captured in the exposure measurements from the study.

Reference to occurrences like operators blowing into nozzles to unblock them are unfortunate, but it must be recognised that this is completely against good practice and common sense and the kind of thing CropLife Europe companies would target through stewardship activities and education rather than expect such misuse to prevent the registration of products. The press article, however, tends to suggest that such situations of bad practice (mixing the product by hand...) are generalized and typical situations, which is of course fortunately not the case.

In relation to the comment about re-entry tasks like harvesting "while the fruits and leaves are still soaked with the product applied a few days earlier," good practice would dictate that the crop is not entered until the spray has dried, but moreover, a satisfactory risk assessment for this scenario is also required for registration and the worst case first tier assumption is that exposure may occur before any dissipation of foliar residues has occurred. In general, Industry studies to monitor re-entry exposure are typically performed a short time after the last application to reflect this worst case exposure scenario. The EFSA approach to compounding high percentiles for the parameters in the re-entry risk assessment has been highlighted as being very precautionary (Kluxen *et al*., 2021[2]).

There is reference to the exclusion of outliers, this is not specific to pesticide exposure assessment, but is a valid scientific process based on observations, considering whether incidents are out of the ordinary. Sometimes, anomalous points do occur in datasets, which may give higher or lower exposures than the trend without an obvious explanation. Even with supporting statistical evaluation, it is rare for regulators to exclude these data points. The exclusion of outliers may not have a dramatic effect on the overall outcome of a risk assessment where large datasets are available. The AOEM represents such a large dataset and after the modelling process an internal model validation (cross validation) was performed by analysing the model prediction when different sets of data or complete studies were excluded from the database. The exposures predicted by the model were in good agreement with those measured.

The concept that the human adult body can be considered just in terms of its surface area seems to be ridiculed. However, the default body areas only have a part to play when patch dosimetry studies, like those favoured by the Pestexpo researchers, are carried out. The surface areas have no part to play in risk assessments based on whole body dosimetry and this applies to those performed for operators using the AOEM. The article goes on to criticise the use of predictive models, namely the German Model, UK POEM and EUROPOEM, which use assigned protection factors to adjust exposures for the use of PPE. The article is rather out of date in this respect, as these models have not been used since the implementation of the EFSA guidance on 1st January, 2016 in favour of the AOEM which makes no assumptions about protection factors for coveralls and gloves etc., but uses measured data. Assigned protection factors are used for respiratory protective equipment (RPE), but this is necessary as it is not possible to measure inhalation exposure in a passive way inside a mask. In any case, the protection factors chosen by EFSA are in line or even more precautionary than for other sectors of occupational health and the chemicals industry. Jean-Noël Jouzel is quoted as data are considered good when the operators "who have done everything right as it says on the label." The operators in studies are, of course given access to the product with a label, but these are real operators, not selected to be superior or more likely to comply with the label and minor deviations may well occur. Where an event occurs which is obviously a one-off accident leading to gross contamination, this cannot be seen to be reflective of typical practice. The AOEL for an active substance is typically set on the outcome of a study where test animals are dosed for at least 90 days and is therefore protective of operators repeatedly applying the product for a period of 3

[2] Kluxen FM, Felkers E, Baumann J, Morgan N, Wiemann C, Stauber F, Strupp C, Adham S, Kuster CJ. Compounded conservatism in European re-entry worker risk assessment of pesticides. Regul Toxicol Pharmacol. 2021 Apr;121:104864.

months, an unlikely and very precautionary assumption for most PPPs. Acute events have to be accounted for, but gross contamination events (like spillage of undiluted product on the arm) would normally be followed by decontamination, the nature of which would depend on the severity of contamination.

Some consideration is given to the comfort of the operator or worker who is expected to wear PPE, and this is agreed to be vitally important. The Pestexpo researchers have also observed operators not wearing PPE. What is not clear from the article is whether there are any risk assessment based requirements for wearing PPE on these occasions and this also applies to the observation on wearing of coveralls. The cost of protective coveralls is significant, but the suggestion that seasonal and illegal workers need these for re-entry or harvesting tasks should be questioned. Exposure assessments for re-entry workers according to the EFSA guidance consider a body covered by normal workwear. Moreover, it seems that the researchers and the press article are critical of the new PPE standards, which is precisely very paradoxical, since the new clothing standards allow the use of protective, but more comfortable, breathable and reusable PPE, which also leads at lower protection costs over one year.

The performance of PVC aprons is called into question. Whilst these garments have been recommended to minimise exposure, it is recognised that PPPs and active substances differ greatly in physicochemical properties and permeation may differ. This is also the case for skin (despite the fact that active substances may target pests and diseases at a cellular level, some pesticides are very poorly absorbed by skin, so it is not a given that formulating a pesticide to achieve optimum efficacy always leads to high dermal absorption). However, such garments whilst they can help with avoidance of local effects are not routinely considered in estimation of systemic exposure according to the EFSA guidance. In fact, the word apron is not even mentioned in the EFSA guidance in its 2014 first edition or in the recently published revision. It should also be noted that the new clothing PPE standards require testing the levels of protection by using a validated test product whose characteristics are those of the most penetrating pesticide formulations, and not standard chemical products, as in the previous standards.

The article refers to the fact that representatives of the working group that helped to develop the AOEM included employees of CropLife Europe member companies. The integrity of these representatives is without question, and it needs to be recognised that a great deal of the experience in this area is to be found within the Industry. The article says that greenhouse spraying was not included in the 2014 guidance, but other models were available at the time and this has been addressed in the current revision of the guidance with a model which include empirical data for additional types of dermal protection. The fact that the word “permeation” was not mentioned in the 2014 guidance may be due to the fact that is not considered as an isolated parameter and is dealt with in relation to systemic exposure by considering measured actual dermal exposures.

The statements that “EFSA’s old model, dressed up as new, still assumes that coveralls and gloves offer protection” and “…PPE factor in the equation still allows an automatic reduction in 90-95% exposure discount” are not accurate. In the AOEM, no such assumptions are made for gloves and coveralls. Actual dermal exposure was measured *in situ* beneath standard workwear and gloves and there is no “PPE factor” in the equation.

CropLife Europe stands by its comments on the Garrigou paper of 2020 which is mentioned. CropLife Europe also still feel that the ISO standards are a step in the right direction. The fact that ISO is a private organisation (but open to all stakeholders interested) demonstrates that industries are

prepared to put resources and expertise into proactively developing continuous improved safety standards.

In conclusion, CropLife believes that the article presents a one-sided argument, often supported by misleading argumentation. In summary, the performance of clothing, certified protective or otherwise, is important to the Industry but the reliance on assumed protection factors in European non-dietary risk assessment is limited and largely irrelevant for coveralls and gloves. The EFSA guidance does give a table of protection factors for PPE, but in the revision goes on to explain that these should not be used to adjust exposures from the predictive operator exposure models allied to the guidance, i.e. additional PPE cannot be used to refine the values from the AOEM which are based on empirical exposure data. Registration of plant protection products in Europe largely relies on risk-based assessments and the apparent concept that exposure equals danger is not helpful in understanding risk where both exposure and hazard need to be taken into account. This not only applies to PPPs, but also to industrial and household chemical to which we may be exposed. We hope that these comments will be taken in good faith and will to redress the balance.