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Response from the authors of the article "Critical review of the role of personal protective Equipment (PPE) in the prevention of risks related to agricultural pesticide use" to the letter to the editor from the European crop protection association (ECPA) Occupational and bystander exposure expert group (OBEEG)

A. Garrigou [a], C. Laurent [b,*], I. Baldi [k], A. Berthet [c], C. Colosio [d], V. Daubas-Letourneux [e], L. Galey [a], F. Goutille [a], J.-M. Jackson Filho [f], N. Jas [g], J.-N. Jouzel [h], N. Judon [a], P. Lebailly [i], O. Samuel [j]

[a] University of Bordeaux, INSERM, Bordeaux Population Health Research Center, Team EPICENE, UMR 1219, 146 rue Leo Saignat, 33076 Bordeaux Cedex, France
[b] National Research Institute for Agriculture, Food and Environment (INRAE), UMR 1048 SAD-APT (INRAE, AgroParisTech), 16 rue Claude Bernard, 75231 Paris Cedex 5, France
[c] Center for Primary Care and Public Health (Unisanté), University of Lausanne (UNIL), Lausanne, Route de la Corniche 2, 1066 Epalinges, Switzerland
[d] Department of Health Sciences of the University of Milano, and Occupational Health Unit and International Centre for Rural Health of the SS. Paolo and Carlo Hospitals, Milano, Italy
[e] EHESP School of Public Health, Arene, UMR 6051 (CNRS, Inserm-Univ Rennes1, EHESP, Rennes Institute of Political studies), 15 avenue du Professeur Léon Bernard, CS 74312, 35043 Rennes Cedex, France
[f] Rua da Glória 91 ap. 701, 80030-060 Curitiba, PR, Brazil
[g] National Research Institute for Agriculture, Food and Environment (INRAE), UMR 7170-1427 IRISSO (Universite Paris-Dauphine, PSL University, CNRS, Place du Maréchal de Lattre de Tassigny), 75016 Paris, France
[h] French National Centre for Scientific Research & Sciences Po, Center for the Sociology of Organizations (CSO), 19 rue Amélie, 75007 Paris, France
[i] University of Caen-Normandy, INSERM, UMR 1086 ANTICIPE, Centre F Baclesse, avenue du General Harris, 14076 Caen Cedex 05, France
[j] Retired from Institut national de santé publique du Québec (INSPQ), Direction de la santé environnementales et de la toxicologie, & Consultant, 945 Avenue Wolfe, Québec, Québec G1V5B3, Canada
[k] University of Bordeaux, INSERM, Bordeaux Population Health Research Center, Team EPICENE, UMR 1219, University Hospital Center of Bordeaux, 146 rue Leo Saignat, 33076 Bordeaux Cedex, France

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ABSTRACT

In March 2020, Safety Science published the article "Critical review of the role of PPE in the prevention of risks related to agricultural pesticide use" by an international group of researchers working for public research organisations. An expert group from an association representing the interests of the agricultural pesticide industry at European level (the European Crop Protection Association -ECPA-) then published a letter challenging the relevance of the discussion and the conclusions of this article. The authors of the review have decided to use their right to reply.

In March 2020, we, a group of researchers working for public research organisations, published a review in *Safety Science*, titled "Critical review of the role of Personal Protective Equipment (PPE) in the prevention of risks related to agricultural pesticide use" (Garrigou et al. 2020)[1]. The European Crop Protection Association (ECPA) Occupational and Bystander Exposure Expert Group (OBEEG) subsequently

* Corresponding author.
E-mail addresses: alain.garrigou@u-bordeaux.fr (A. Garrigou), Catherine.laurent@inrae.fr (C. Laurent), isabelle.baldi@u-bordeaux.fr (I. Baldi), Aurelie.berthet@unisante.ch (A. Berthet), claudio.colosio@unimi.it (C. Colosio), veronique.daubas-letourneux@ehesp.fr (V. Daubas-Letourneux), louis.galey@u-bordeaux.fr (L. Galey), fabienne.goutille@gmail.com (F. Goutille), jmarcaljf@yahoo.com.br (J.-M. Jackson Filho), nathalie.jas@inrae.fr (N. Jas), jeannoel.jouzel@sciencespo.fr (J.-N. Jouzel), nathalie.judon@gmail.com (N. Judon), lebailly@baclesse.unicancer.fr (P. Lebailly), samuelonil@videotron.ca (O. Samuel).
[1] Published on line in December 2019.

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published a letter challenging the relevance of the discussion and conclusions of this review (Morgan et al. 2020). Three of the authors of the letter are also employees of organisations involved in agricultural chemical manufacturing[2]. The ECPA itself is an association representing the interests of the agricultural pesticide industry at European level.

Several points of this letter (hereinafter referred to as the "ECPA/OBEEG letter") are misrepresentations of our paper and provide misleading information. This is why we have decided to use our right of reply.

Our review published in March 2020 deals with the use of PPE and its expected protective role in occupational exposure to pesticides in agriculture. It is focused on the use of coveralls in OECD countries. Our analysis of available published data shows that the data measuring PPE effectiveness are still scarce and correspond to a limited number of exposure scenarios. These data show that recommending the wearing of PPE does not always result in effective protection.

Although the ECPA/OBEEG letter challenges only some of our arguments, it is questionable on many points. We do believe that dialogue between the pesticide industry and public research is necessary. We understand that two different cultures and origins are confronting each other, and that misinterpretation is possible. However, we regret that the ECPA/OBEEG letter contains so many misleading allegations about our work. We will discuss only the main ones.

1. The authors of the ECPA/OBEEG letter quote our text to denounce our "*alarming […] statement*" "*that PPPs would be banned if it were not for this assumption of protection*" (letter p.5). This quotation is not correct: our critical review of the literature indicates that "*Some*[3] *dangerous products only get marketing authorization because it is assumed that wearing PPE will considerably limit exposure. They*[4] *would be banned if it were not for this assumption of protection.*" This is one illustration of the way the authors of the ECPA/OBEEG letter distort our text to criticize it, which is very deceptive for the reader. In addition, the authors of the ECPA/OBEEG letter fail to explain why it would be misleading to link marketing authorization and PPE performance. It is precisely because the models may show that evaluation of exposure without PPE may exceed the AOEL, that new assessments are carried out with PPE whose performance will be decisive for delivering marketing authorizations. The premarketing modeling approach has to make assumptions regarding this level of performance. Hence, the questions we raise as to the capacity of the theoretical scenario of premarketing assessment to take into account all the variables of real-life situations. This is why it is so important to care about post-marketing risk assessment, carried out in the field.

2. The authors of the ECPA/OBEEG letter insist that "*it would be useful to know what the inclusion criteria were when selecting the papers to include*", as if the review had been completed with no specification of inclusion criteria (letter 2.10, p.4)**.** Actually, an entire section of our review (Section 2.2.) presents our selection criteria, which are based on standard academic principles, such as the exclusion of unpublished papers. We invite the authors of the ECPA/OBEEG letter to read this part of the article.

3. **The authors of the ECPA/OBEEG letter say that we have overlooked important information.** In particular we "*did not even cite ISO 18889: 2019 (*ISO, 2019*)*". We wish to point out that this norm concerns gloves, which were explicitly not included in our review (as explained in the methodology). They also claim that we have overlooked more than 30 "*modern studies*". Unfortunately, the authors of the letter fail to provide any evidence that these "*modern studies*" are available. Are they published? Are they accessible? The authors indicate only one additional paper that meets our selection criteria, Spaan et al. (2020), which was published when ours was already on line. The few other references (e.g. Spaan et al., 2011; Spaan et al., 2014; Wicke, 2010; ISO., 2019) are either unpublished studies or studies that do not meet the inclusion criteria of the review.

4. The ECPA/OBEEG letter emphasises in several places that the regulation is very conservative. We believe that individuals who make regulations are doing their best. However, it is widely acknowledged that, due to lack of data and complexity of field situations, the data used for regulatory purpose are not entirely without uncertainty. This is another reason why post-marketing risk assessment is so important. One example can be discussed briefly. The authors of the letter criticise our presentation of the AOEL (letter p.1). They consider that accurate and robust data are used to estimate NOAELs and AOELs. However, the European Commission reported in their guidelines on risk assessment for crop protection products that "*The majority of the mammalian toxicity data on plant protection products and active substances are obtained using the oral route, yet most exposures to operators, workers, bystanders and residents will be via dermal and / or inhalation routes. This will necessitate route-to-route extrapolation techniques, where appropriate*" (European Commission 2006). Ten years later the European Commission (2017) reported that "*As most of the studies submitted in pesticide dossiers are via the oral route, it is anticipated that AAOELs will be based on systemic effects seen in oral studies. Care should be taken in ensuring appropriate extrapolation when considering different routes of exposure*" (p.9). The extrapolation of toxicokinetic data from animal study NOAELs and AOELs are indeed determined by studies on animals exposed by oral route, while it is established that workers are mainly exposed via dermal route (Brouwer et al., 1994). The authors of the letter should have explained further to readers why this approach to extrapolate the oral route to other routes is to them so accurate and robust. They should have explained better the exact meaning of the statement "*the NOAELs is a no effect level*" (letter p.1).

5. The authors of the ECPA/OBEEG letter consider the questions regarding the variety of exposure scenarios taken into account in a particular field or in *in vitro* studies to be irrelevant. However, premarketing assessment modelling approaches rely on theoretical exposure scenarios which cannot reproduce the complexity of actual work situations where PPE wearing practices are not controlled. Studies of exposure conducted from various disciplinary stand points show that it is important to consider several parameters for risk prevention strategies, as they may influence results in the protection of workers: accidents during treatment, actual PPE wearing practices, workers' behaviour, specific farming systems, physical–chemical properties of PPPs as well as their formulation, and so on. These parameters are complex to test in *in vitro* studies and to include as parameters in exposure and risk assessment models. Regarding for instance the issue of formulation, each PPP formulation contains at least one active and several inert ingredients. An active ingredient is the biologically active substance that is designed to affect the pest, while an inert ingredient is responsible for enhancing the efficiency of the active ingredients or stabilizing the formulation (e.g. solvents, preservatives, surfactants) (US EPA O, 2012, Zacharia 2011: 16–17). Public information on inert ingredients is extremely limited, as they are considered confidential business information and therefore are not required to be listed in the formulation label. Yet inert ingredients may be as toxic as the active ones or contribute to increasing the permeation of the active ingredient through the skin (INSERM, 2013, Berthet et al. 2014). As testing involves a huge amount of work, the number of commercial PPPs that have been tested is still very limited compared with the number of pesticide formulations on the market, and workers are using the formulation and

[2] Syngenta, FMC Corporation (Food Machinery Corporation), UIPP. The UIPP ("Union des Industries de la Protection des Plantes") is itself "a professional association of 22 members that market phytopharmaceutical products for agricultural use and offer support solutions" (http://www.uipp.org/Qui-sommes-nous). The European Crop Protection Association (ECPA) is itself a Trade and Business association representing the interests of the crop protection industry at EU level (https://lobbyfacts.eu/representative/6ab5f09b55824f95b227c953b4097ceb/european-crop-protection-association).

[3] Our emphasis.

[4] Our emphasis.

not the active substance alone. The authors of the letter should have explained further to readers why extrapolation is not an issue and why "*there is no need for specific testing*" for each commercial formulation in spite of the heterogenicity of excipients (letter p.3).

6. The authors the ECPA/OBEEG letter state that "there is a lot of research available that shows good performance, not only for certified coveralls but for normal workwear". However, as with other statements in this letter, they fail to provide the references of these many research results**.** They put forward the article of Spaan et al. 2020 that was published after ours. Yet even if it had been included in our review, we cannot find evidence in this article that would challenge our main conclusions. Regarding the performance of PPE in general, Spaan et al. 2020 are quite cautious. They specify that *"measurements during application with high intensity contact between operator and treated plants were excluded"* (p.3). Yet, in their database, "*evaluation of exposure data showed that on average only 2.3–2.6% of the pesticides present on the outside of the clothing or gloves migrated through the garments, although there was a large variation with migration up to 99%*." (abstract). They insist a lot on the large variation of the levels of migration recorded in their database, with only 75% of the distribution below 9.3% for individual body parts (p.5 and Fig.2). Such variations concern all types of protective clothing, including normal workwear. They note that "*protective clothing does not always result in as much exposure reduction as is generally assumed based on, for instance, results of standard laboratory tests*" (p.9).

When prevention is at stake, not only the calculation of average values is important, but also the distribution of the data, and the estimate of the percentage of the population that will be outside the safety thresholds.

7. The authors of the ECPA/OBEEG letter are attributing to us an *"emotive stance"*, regarding the danger of agricultural pesticides for users. This statement sounds rather out of place especially as the authors of the letter fail to discuss the scientific data available today on this issue. For most of them, the danger of pesticides is inherent to their nature (destroying pests), and the risks for humans is supported by strong evidence largely documented by the epidemiological literature on various health endpoints. Better regulation is an issue that concerns all stakeholders. Existing regulations must continually be challenged by studies on post-marketing situations. This iterative process cannot ignore the evidence provided by different disciplinary perspectives, including the social sciences, or by different methodological perspectives, including observations of situations where PPE wearing practices are not controlled.

In conclusion, the statements in the ECPA/OBEEG letter are based on assertions which are not demonstrated, and the data to which they refer cannot be verified and are mainly unpublished. Throughout the letter, the authors use a number of terms and superlatives such as "increasingly protective of human health", "very highly protective", "high degree of conservatism" which are not substantiated by any published data. Furthermore, for many issues the authors of the ECPA/OBEEG letter have distorted our text. This is why **we strongly advise the readers to go back to the original paper**. We also do hope that in the future it will be possible for the various stakeholders to foster more discussion regarding PPE use in agriculture, in all transparency and fairness, with arguments based on reliable and relevant evidence.

Declaration of Competing Interest

This document is a **right of reply.** We did not receive any specific grant from funding agencies in the public, commercial, or not-for- profit sectors for writing it.

Individual declarations of interest statement were provided in March 2020 for the publication of the review. Only one author, Lebailly (p.12) was reporting links with commercial companies; those were described. No significant financial support that could have influenced the outcome of this work (the review and this answer) has been received.

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