

APPROVED: 6 July 2018

doi: 10.2903/j.efsa.2018.e16087

Assessment of occupational and dietary exposure to pesticide residues

National Institute for Public Health and the Environment (RIVM)

The Netherlands

Chemical Food Safety Department, Centre for Nutrition, Prevention and Health Services

M Markantonis, T van der Velde-Koerts, C Graven, JD te Biesebeek, M Zeilmaker,
AG Rietveld and BC Ossendorp

Abstract

Plant protection products (PPPs) are pesticides containing at least one active substance that drives specific actions against pests (diseases). PPPs are regulated in the EU and cannot be placed on the market or used without prior authorisation. EFSA assesses the possible risks of the use of active substances to humans and environment. Member States decide whether or not to approve their use at EU level. Furthermore, Member States decide at national level on the authorisation of PPPs containing approved substances. In agriculture, exposure to PPPs and their residues during occupational tasks is estimated prior to product authorisation, using models fed with study-specific (e.g. absorption, dissipation) and default values. Exposure of workers to pesticide residues reduces with the pesticide's dissipation time during crop-related tasks. However, the current risk assessment gap is that no methodology is available to calculate the re-entry interval (REI) for workers, which specifies how long they should wear personal protective clothing during their first entry into pesticide-sprayed crops. Protective clothing (such as gloves) can reduce pesticide residue exposure to an acceptable level of worker safety. Within the European Food Risk Assessment Fellowship Programme (EU-FORA) assignment, a methodology was developed to calculate agricultural-use-specific and pesticide-specific REIs for which period workers should wear gloves. This was an assignment of the Dutch Ministry of Social Affairs and Employment. Another important aspect of risk assessment to ensure consumer safety is dietary risk assessment. A critical evaluation of residue studies and metabolism of the pesticide in question in crops results in a residue definition for dietary risk assessment and for enforcement and monitoring to define maximum residue limits allowed legally on or in raw agricultural commodities when applying pesticides according to good agricultural practices. This work was assigned by the Dutch Ministry of Health, Welfare and Sport and contributes to the work of the Joint FAO/WHO Meeting on Pesticide Residues.

© 2018 European Food Safety Authority. *EFSA Journal* published by John Wiley and Sons Ltd on behalf of European Food Safety Authority.

Keywords: plant protection products, residue exposure, re-entry interval, dermal absorption, dietary risk assessment, maximum residue level

Correspondence: eu-fora@efsa.europa.eu

Acknowledgements: This report is funded by EFSA as part of the EU-FORA programme.

Suggested citation: National Institute for Public Health and the Environment (RIVM) The Netherlands, Chemical Food Safety Department, Centre for Nutrition, Prevention and Health Services, Markantonis M, van der Velde-Koerts T, Graven C, te Biesebeek JD, Zeilmaker M, Rietveld AG and Ossendorp BC, 2018. Assessment of occupational and dietary exposure to pesticide residues. *EFSA Journal* 2018;16(S1):e16087, 8 pp. <https://doi.org/10.2903/j.efsa.2018.e16087>

ISSN: 1831-4732

© 2018 European Food Safety Authority. *EFSA Journal* published by John Wiley and Sons Ltd on behalf of European Food Safety Authority.

This is an open access article under the terms of the [Creative Commons Attribution-NoDerivs](https://creativecommons.org/licenses/by/4.0/) License, which permits use and distribution in any medium, provided the original work is properly cited and no modifications or adaptations are made.



The EFSA Journal is a publication of the European Food Safety Authority, an agency of the European Union.



Table of contents

Abstract.....	1
1. Introduction.....	4
1.1. Regulation of Plant protection products.....	4
1.2. Risk assessment of occupational exposure of agricultural workers to PPP residues.....	5
1.3. Assessment of dietary exposure to PPP residues.....	5
2. Description of work programme.....	6
2.1. Aims.....	6
2.2. Activities/methods.....	6
2.2.1. Exposure of workers upon entry into pesticide-treated crops.....	6
2.2.2. Dietary exposure to pesticide residues.....	7
3. Conclusions.....	7
References.....	8
Abbreviations.....	8

1. Introduction

The principal focus of the European Food Risk Assessment Fellowship Programme (EU-FORA) is to provide hands-on skills in chemical and microbiological risk assessment for food safety. This individual work programme focused on two aspects of exposure assessment for plant protection product (PPP) residues: non-dietary and dietary exposure.

The work was performed at the Dutch National Institute for Public Health and the Environment (RIVM) in the Chemical Food Safety Department. The department works on the safety of food by contributing nationally, at the European Union (EU) level and globally to the development and harmonisation of risk assessment methodology, carrying out risk assessments and advising policy-makers and scrutinising decision-making. Chemical substances in food include pesticides, biocides, and veterinary drug residues, food and feed additives, contaminants, substances in food contact materials and botanicals. The department contributes to the evaluation of substances in biocides and PPPs prior to their registration based on manufacturers' applications and focuses on method and model development for use in exposure and risk assessment.

The following paragraphs give background information on the non-dietary and dietary exposure assessment. To start with, PPPs and their current regulation in the EU are briefly described. Second, a short overview of the risk assessment of PPPs in an occupational setting is given, focusing on exposure assessment of residues for crop workers. A gap in the current risk assessment methodology and in the regulation of PPPs is identified. At present, there is no methodology available to calculate product-specific re-entry intervals (REI) for workers entering pesticide-sprayed crops, which specify the period of wearing personal protective clothing. The final paragraph briefly presents the purpose of setting maximum residue limits (MRLs) for PPPs in or on raw agricultural commodities, as a result of the extensive evaluation of residue studies as a basis for the dietary exposure assessment and the relevance of the work of the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) for the EU authorisation system.

1.1. Regulation of plant protection products

PPPs are mainly used to keep crops healthy and prevent them from being destroyed by disease and infestation. They include herbicides, fungicides, insecticides, acaricides, plant growth regulators and repellents. PPPs contain at least one active substance (chemicals or microorganisms) that enables the product to perform its action. Before an active substance can be used in a PPP in the EU, it must be approved by the European Commission. Active substances undergo an intensive evaluation process before a decision can be made as to approval. PPPs are regulated by Regulation EC 1107/2009 concerning the placing of PPPs on the market including basic substances¹ (art. 23).

A large body of EU legislation regulates the marketing and use of PPPs and their residues in food. PPPs cannot be placed on the market or used without prior authorisation. A system was established whereby: (1) Member State competent authorities peer review the application, and after discussion between the competent authorities, the European Food Safety Authority (EFSA) comes to a conclusion; (2) Member State risk managers decide in Brussels, together with the European Commission, on the approval of the active substances; and (3) Member States decide at national level on the approval of products.

Regulation (EC) No 396/2005² covers compliance with legal limits for pesticide residues in food and feed, including provisions on official controls of pesticide residues in food (plant or animal origin).

Meeting current and future food safety demands, an optimal food safety assessment (risk assessment) requires scientific understanding and measurement of chemical hazards, estimating or modelling exposures, and ultimately concluding on risks associated with them.

¹ Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309, 24.11.2009, p. 1–50.

² Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC. OJ L 70, 16.3.2005, p. 1–16.

1.2. Risk assessment of occupational exposure of agricultural workers to PPP residues

During occupational tasks, operators and workers may be exposed to pesticides either directly through contact with spray drift (via dermal or inhalation routes) or indirectly through contact with drift deposits (dermal or ingestion) or vapour drift arising from volatilisation of deposits. Exposure is expected to decline over time from the initial value at, or close to, the time of application.

Therefore, the total exposure from the application of PPPs results from different exposure routes (dermal, inhalation, ingestion). The Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products (EFSA, 2014) provides a model for assessing the major exposure pathways. Nevertheless, the EFSA working group on pesticides recommends that further research must be carried out to perform a more representative exposure assessment. However, for non-dietary exposure pathways, other than dermal or inhalation, in most cases few data are available to provide quantification of their impact on the overall exposure assessment.

Agricultural workers are potentially exposed to pesticide residues when they enter pesticide-treated fields to perform a variety of hand-labour tasks, such as pruning, thinning, scouting and harvesting of agricultural crops. These exposures can occur in different crops throughout the growing season and can be of similar magnitude to the exposure of operators, who mix, load and apply pesticides. For authorisation of PPPs, risk assessments must be carried out for all scenarios of exposure of operators, workers, residents and bystanders that can be expected to occur as a consequence of the proposed uses of a PPP. The risk assessment methodology focuses on scenarios for workers, and specifically assesses the period for safe re-entry of workers into a treated crop area after application of a PPP (e.g. risk-based restricted entry interval).

The practical options for managing exposures through the use of personal protective equipment, or other measures such as technical solutions, are considerably more limited for re-entry workers performing crop-related tasks, than for operators during mixing, loading and application.

Establishment of a period for safe re-entry, the REI, is a risk mitigation option although currently not used in the EU for active substance approval and PPP authorisation. The REI is intended to provide sufficient time for pesticide residues to degrade to a safe level, after which workers can safely enter a field.

Currently, risks for workers are mitigated by prescribing gloves for re-entry tasks on the PPP label. However, at present, there is no harmonised methodology available to estimate the pesticide-specific and agricultural-use-related interval for which these gloves should be worn for each intended use. A methodology has been developed to determine the REI (in this report framed as the period during which workers must wear protective clothing, e.g. gloves).

Additionally, current exposure assessment methodology takes into account principal parameters such as the dissipation time of the active substance in the PPP (DT_{50}), the transfer coefficient (from crop to worker) and the dermal absorption (DA) factor. However, current approaches take into account the DA of the spray dilution of the PPP, but not of its dried residues to which a worker is exposed. At present, there is no harmonised methodology to determine the DA factor for dried residues.

1.3. Assessment of dietary exposure to PPP residues

If PPPs are used in accordance with the regulations, residues are expected to remain in or on the harvested commodities, especially when applications are close to harvest or post-harvest. PPP residues are defined as residues of active substances and their (toxicologically) relevant degradation products that remain on or in food or feed. MRLs are stipulated for residues of PPPs in food and feed.

The Codex Alimentarius, or 'Food Code', is a collection of standards, guidelines and codes of practice adopted by the Codex Alimentarius Commission. The Commission is the central part of the Joint FAO/WHO Food Standards Programme and was established by the FAO and WHO to protect consumer health and promote fair practices in food trade. The 188 Codex members have negotiated science-based recommendations in all areas related to food safety and quality, including in the area of pesticide residues (FAO, online-a). The JMPR is an expert ad hoc body governed jointly by the FAO and WHO that proposes MRLs that can be used as Codex maximum residue limits. Furthermore, the JMPR produces guidance on the applicable risk assessment methodology. It consists of experts who act in a personal capacity and not as Member State representatives, and has performed annual

evaluations of pesticide residues in food since 1963, advising on the acceptable levels of pesticide residues, namely MRLs in food (FAO, online-b).

The current JMPR comprises the WHO Core Assessment Group and the FAO Panel of Experts on Pesticide Residues in Food and the Environment. The WHO Core Assessment Group is responsible for reviewing pesticide toxicological data and estimating acceptable daily intakes, acute reference doses and characterises other toxicological criteria. The FAO Panel reviews pesticide residue data for estimated MRLs, supervised trials median residue values and highest residues in food and feed (FAO, online-b; WHO, online). Combining the efforts of both panels, a dietary risk assessment is performed to evaluate the toxicological acceptability of the proposed MRLs. The MRLs are recommended to the Codex Committee on Pesticide Residues (CCPR) for consideration for adoption by the Codex Alimentarius Commission as Codex MRLs. Harmonised MRLs benefit trade.

2. Description of work programme

2.1. Aims

The objective of the work programme was to work on two aspects of exposure to PPP residues: (i) exposure of workers upon entry into pesticide-treated crops; and (ii) dietary exposure to residues. The first part of the project involved the use of exposure models for pesticides and identifies the information required to develop a methodology to calculate a safe REI for crop workers. The second part of the project aimed to gain a thorough understanding of critical evaluations of residue field trials, metabolism studies, and other residue studies for PPPs that were submitted by the product applicant, in order to provide an MRL for the respective food commodities and to perform a dietary risk assessment for these food commodities in the context of the JMPR.

Overall, the objective was to be involved in all aspects of daily routine work and ad hoc projects at the Department of Chemical Food Safety at the RIVM.

2.2. Activities/methods

2.2.1. Exposure of workers upon entry into pesticide-treated crops

A report was prepared that provides a methodology to determine a safe REI, during which workers must wear protective clothing (such as gloves) during entry into previously pesticide-treated crops as an exposure mitigation option for authorised PPPs. Moreover, the report contains a discussion of the parameters that have an impact on the exposure to residues, such as DA and product properties, like acute toxicity, skin irritation or sensibilisation of spray dilutions and foliar dry residues.

The drafting of the report provided an in-depth understanding of the process of legal authorisation of PPPs and the assessment requirements of the exposure risk of workers during crop entry after treatment. Moreover, information was collected through a literature search (e.g. scientific publications and EU guidance documents (Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products (EFSA, 2014) and Guidance on Dermal Absorption (EFSA, 2017)), EU Regulation (EC) No 1272/2008³ (Regulation on Classification and Labelling) and up-to-date modelling techniques (e.g. EFSA OPEX) were applied and a new methodology developed to calculate the REI. A visit was made to the Dutch competent authority for authorisation of PPPs and biocides, namely the Dutch Board for the Authorisation of Plant Protection Products and Biocides (College voor de toelating van gewasbeschermingsmiddelen en biociden). This offered the opportunity to discuss which mathematical models were previously and currently used for the preregistration exposure risk assessment (for operators, workers, residents and bystanders) for the respective agrochemicals to be authorised in the Netherlands. On another occasion, a representative of STIGAS (the certified occupational health and safety service in the Netherlands) was invited by RIVM to give a presentation on agricultural practices in the Netherlands in terms of occupational safety for farmers, operators and farm workers. Moreover, STIGAS presented their mode of communication with farmers, including training for the workers, and provided leaflets that were handed out to farmers and workers advising on the 'dos and don'ts' for workers performing hand-labour tasks in crops previously treated with agrochemicals (in fields and greenhouses).

³ Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006. OJ L 353, 31.12.2008, p. 1–1355.

The output of this work programme is foreseen to be made publically available as a report on the RIVM website in 2018.

2.2.2. Dietary exposure to pesticide residues

The evaluation of pesticide residue studies for the purpose of setting MRLs in plant and animal commodities for a new PPP (mandestrobin) and its dietary risk assessment was performed in the period January–August 2018. This part of the work programme gave an insight into the practices of the JMPR and the CCPR. As the European Commission and EFSA represent the EU Member States at the CCPR, the work programme facilitates worldwide trade in agricultural commodities.

The work consisted of drafting a summary of evaluations based on residue studies conducted by the manufacturer of the pesticide in question. Numerous studies were evaluated including the physical chemical properties of the pesticide, its metabolism in plant and animal commodities, its degradation in soil and water, the validity of analytical methods, the magnitude of pesticide residues in raw agricultural commodities following application according to good agricultural practices, the stability of pesticide residues during freezer storage, the degradation of pesticide residues during food processing and the magnitude of pesticide residues in animal commodities following livestock feeding. The rationale for methodologies for long- and short-term dietary risk assessments are described in detail in the FAO manual on the submission and evaluation of pesticide residue data for the estimation of MRLs in food and feed (FAO, 2012).

Participation at the international Fresenius conference (Mainz, April 2018) on cumulative risk assessment and dietary risk assessment (MRL setting) offered the opportunity to have a dialogue with EU and national food safety authorities and representatives of the industrial sector to discuss new advances in the EU and worldwide (including the US Environmental Protection Agency).

This work package will provide two written outputs to which the EU-FORA work programme contributed. The detailed evaluation report and the appraisal document, proposing MRLs for the respective food plant commodities, will be finalised for submission to the FAO secretariat (due date August 2018). These reports will be discussed (and adapted) at the JMPR meeting in September 2018 and will then be published in the JMPR 2018 report and JMPR 2018 evaluation on the FAO website (due dates December 2018 and January 2019).

3. Conclusions

The work programme at the RIVM in the Chemical Food Safety Department provided the opportunity to get a thorough insight into the EU Member States' responsibility in risk assessment for the authorisation of PPPs. The preparation of a report on exposure assessment of pesticide residues focused on risk mitigation measures for workers during re-entry into sprayed crops, with consideration of the EU guidance (Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products (EFSA, 2014) and Guidance on dermal absorption (EFSA, 2017)), EU Regulation (EC) No 1272/2008 and exposure assessment models (EFSA OPEX). The development of a new methodology to calculate a safe REI indicates the period during which workers should wear personal protective clothing to reduce the risk of residue exposure to a safe level. The initial report may serve as a basis for developing a guidance document on the estimation of safe REIs for workers during first crop entry post application.

The preparation of the critical in-depth evaluation of the manufacturer-submitted residue studies of the pesticide in question was based on numerous studies (See Section 2.2.2). The final summary document will contain the proposed MRLs for different food commodities and a dietary risk assessment. The document will serve as the starting point for the discussion by the FAO and WHO panels in the JMPR, resulting in agreed MRLs for the pesticide in question and the respective food commodities. The MRLs are evaluated for food safety and help to accommodate the world trade of goods. However, MRLs are not health-based safety levels.

The EU-FORA training on chemical and microbiological risk assessment gave a broad overview of the European and global risk assessment practices. The projects performed in the Chemical Food Safety Department at the RIVM perfectly complemented the previously gained knowledge in the theory-based training programmes at EFSA. Newly acquired knowledge was immediately applied in the exposure evaluations of PPPs in an occupational and dietary setting.

In a pleasant working atmosphere in the department, the daily exchange with experts of different chemical food safety aspects through flexible working places, group meetings and the opportunity to

participate in international congresses enabled the fellow to learn new methodologies, gain more expertise and start building a network in the European food safety community.

References

- EFSA (European Food Safety Authority), 2014. Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products. EFSA Journal 2014;12(10):3874, 55 pp. <https://doi.org/10.2903/j.efsa.2014.3874>
- EFSA (European Food Safety Authority), Buist H, Craig P, Dewhurst I, Hougaard Bennekou S, Kneuer C, Machera K, Pieper C, Court Marques D, Guillot G, Ruffo F and Chiusolo A, 2017. Guidance on dermal absorption. EFSA Journal 2017;15(6):4873, 60 pp. <https://doi.org/10.2903/j.efsa.2017.4873>
- FAO (Food and Agriculture Organization), 2012. Submission and evaluation of pesticide residues data for the estimation of maximum residue levels in food and feed. (FAO plant production and protection paper 225). FAO, Rome, 298 pp.
- FAO (Food and Agriculture Organization), online-a. Codex Alimentarius. Available online: <http://www.fao.org/fao-who-codexalimentarius/en/> [Accessed: 30 May 2018]
- FAO (Food and Agriculture Organization), online-b. AGP - JMPR Guidance and related documents. Available online: <http://www.fao.org/agriculture/crops/thematic-sitemap/theme/pests/jmpr/jmpr-docs/en/> [Accessed: 30 May 2018]
- WHO (World Health Organization), online. Food safety. Joint FAO/WHO Meeting on Pesticide Residues (JMPR). Available online: http://www.who.int/foodsafety/areas_work/chemical-risks/jmpr/en/ [Accessed: 30 May 2018]

Abbreviations

CCPR	Codex Committee on Pesticide Residues
DA	dermal absorption
DT ₅₀	50% dissipation time of the active substance in the PPP
EU-FORA	The European Food Risk Assessment Fellowship Programme
FAO	Food and Agriculture Organization of the United Nations
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
MRL	maximum residue level
PPP	plant protection product
REI	re-entry interval
RIVM	National Institute for Public Health and the Environment (the Netherlands)
WHO	World Health Organization