



EUROPEAN COMMISSION
DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY
Safety of the Food Chain
Pesticides and Biocides

COMMISSION GUIDANCE DOCUMENT¹

SANTE-10832-2015 rev. 1.7
24 January 2017

Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products

¹ Does not necessarily represent the views of the Commission.

Introduction

European Food Safety Authority (EFSA), following its standard procedures for development of guidance documents, including consultation of stakeholders and general public, has published the following guidance document:

EFSA, 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, 55pp., doi:10.2903/j.efsa.2014.3874.

The document has been presented and discussed at the Standing Committee on Plants, Animals, Food and Feed between December 2014 and May 2015. This document has been adopted in the Standing Committee on Plants, Animals, Food and Feed on 29 May 2015.

The guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products, as noted at the Standing Committee on Plants, Animals, Food and Feed in May 2015, states that [guidance on] the derivation of acute acceptable operator exposure values (AAOELs) is unresolved. Similarly, no complete higher tier risk assessment schemes (i.e. refined, more realistic- and less worst-case exposure scenario) are available for residents and bystanders scenarios.

That is still the situation. However, AAOELs have been established during the substance approval or renewal evaluation for a small number of substances. The Standing Committee developed an outline to set AAOELs (see Appendix). The Standing Committee also considered that the Guidance Document from EFSA should be updated considering recent scientific/technological progress, such as the BROWSE project.

Furthermore, the May 2015 implementation schedule of the guidance referred to the approval of active substances but did not explicitly mention authorisation of PPPs.

Implementation schedule

When this document was adopted in the Standing Committee on Plants, Animals, Food and Feed on 29 May 2015, it was decided it should be applied since 1 January 2016 for the approval of active substances and the applications to authorise or renew authorisations for plant protection products, with exception of the unresolved issues mentioned above. These issues are further clarified below:

1. Consideration of acute exposure should only be made where an AAOEL has been established during an approval, review or renewal evaluation of an active substance, i.e. no acute operator, worker and bystander exposure assessments can be performed with the OPEX model where no AAOEL has been set;
2. The guidance is well-developed in respect of operators and should be fully applied for the corresponding risk assessments, including the acute risk assessment where an AAOEL has been set;
3. The guidance does not set out fully detailed higher-tier risk assessment schemes for bystanders or residents. However several risk management options are available for ad-hoc approaches for controlling risk or conducting a more refined

assessment (note the EUROPOEM, old DE and UK models are not considered refinements) so there is no justification for a delay in implementation of bystander or resident assessments when it comes to chronic risk assessment;

4. Bystander risk assessments, when not covered by the resident risk assessment, require an AAOEL to be set. So it is not possible to perform such assessments where an AAOEL value has not been established;
5. The guidance does not contain suitable information to estimate acute worker exposure so without further development worker risks should only consider the longer risk assessment, using the AOEL.

The Standing Committee on Plants, Animals, Food and Feed agreed on 24 January 2017 to revise the implementation schedule for this guidance. In order to improve harmonisation, rev. 1.7 of this GD will apply, to applications for the approval or renewal of approval of active substances and the applications to authorise or renew authorisations for plant protection products submitted from the 1st March 2017 as follows:

6. Where necessary, an AAOEL should be proposed during the EU peer-review taking into account the Annex to this Commission guidance document.

Annex

CRD thought-starter paper – Draft 3 (September 2015)

DERIVATION OF ACUTE ACCEPTABLE OPERATOR EXPOSURE LEVEL ('AAOEL')

Background

In October 2014, EFSA published *Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products*². It recognised, however, the lack of an appropriate methodology to derive an Acute Acceptable Operator Exposure Level ('AAOEL') for active substances with the potential to induce acute systemic toxicity.

This paper was produced at the request of the Commission, to explore ways in which the 'AAOEL' might be derived. This paper is not the formal view of CRD or the UK; it is a rough draft intended to initiate debate on the concept and associated assessments. It does not go into the fine detail of the derivation of an 'AAOEL', as this is seen as a subsequent step in the process. It has **not** been subjected to full internal peer review.

This third draft has been produced following comments on the second draft received from some AT and HU. A summary of these comments and the responses is available as a separate document.

The paper is based on the extensive experience of the development and use of the Acute Reference Dose (ARfD) concept; the 'AAOEL' equivalent for dietary exposures. The ideas behind the proposals are to develop a scheme that is simple to use and understand, and will require a minimum of additional data from vertebrate studies.

The scheme is based on a tiered approach making extensive use of pre-existing data and reference values in the initial phase. It is envisaged that in the fullness of time an 'AAOEL' will be considered for all active substances.

Nomenclature

The term 'Acute Acceptable Operator Exposure Level' has been criticised³ as the exposure assessments relate to workers, bystanders and residents in addition. The

² EFSA Journal 2014, 12(10), 3874

³ The term Acute Acceptable Operator Exposure Level ('AAOEL') has been used initially, but the recently published EFSA guidance noted that the public consultation on the draft identified some issues with the term. The final guidance therefore avoided it and referred to appropriate reference values. This concern echoed the earlier EFSA PPR Panel Opinion on the same subject (EFSA Journal, 2010;8(2);1501) which adopted the term 'AAOEL' to be consistent with the terminology that is already in use for assessment of risks from non-dietary exposures to PPPs. It recognised, however, that the usage is unsatisfactory insofar

term proposed by CRD is '**acute non-dietary acceptable exposure level (ANDAEEL)**'. EFSA (20/4/2015) have proposed the term RVAAS (Reference value acutely toxic active substance), but this does not differentiate it clearly from the ARfD.

Local Effects

The issue of local effects is not specific to an acute non-dietary assessment but has been raised as a concern during the commenting phase. Local effects are related to the product rather than the active substance and require a different approach to the formal derivation of an 'AAOEL'.

EU biocide assessments include local effects and a guidance document has been produced (see section 4.3.2 of https://echa.europa.eu/documents/10162/15623299/biocides_guidance_human_health_ra_iii_partb_en.pdf). The approach is qualitative and is therefore distinct from the approach to systemic effects. Some pesticide active substances and formulations are also used as biocides. Developing a common approach based on the existing biocide approach would be logical and an effective use of resources. The initial trigger for a consideration of local effects is the classification of the product for one or more of the following effects: corrosion, irritation or sensitisation. The biocides guidance refers to exposures to both the product and any in-use-dilutions.

Most classified pesticide products are diluted with typical water volumes of 1 + 100 or more. In most cases, the only consideration for local effects related to exposure to the in-use-dilution will be for products classified as strong or extreme sensitisers. Application rates and water volumes are frequently member State-specific and the final decision should be taken at member State level. However, generic guidance will enhance harmonisation of approaches.

Should this be addressed within the 'AAOEL' guidance or as a separate element of the non-dietary exposure assessment?

New Active Substance (NAS) evaluations

An 'AAOEL' should be considered during the EFSA evaluation of all NAS. An 'AAOEL' should be derived based on the toxicological profile of the active substance (see below).

Renewal of active substances

An 'AAOEL' should be considered during the EFSA review of all existing active substances. An 'AAOEL' should be derived based on the toxicological profile of the active substance (see below).

as the reference value is applied to exposure groups other than just operators and suggested the nomenclature be considered further.

Active substance not in the NAS or Review programmes

In order to prioritise formal derivation of 'AAOEL's and make the best use of resources, it is proposed that a Tiered approach is used if acute non-dietary risk assessments are to be performed.

Tier 1 Assessment without a specific 'AAOEL' being set

1. Comparison with AOEL

- a. The existing evaluation process for plant protection products in the EU includes the derivation of an acceptable operator exposure level (AOEL). This value is typically based on repeat dose toxicity studies of durations up to 90 days. The value of the AOEL will always be the same as or lower than an 'AAOEL', i.e. the same or more precautionary. Therefore an initial comparison can be made between the acute exposure estimates and the existing AOEL. If the exposure estimates are below the AOEL, the exposures are acceptable and no further evaluation is required.

In addition a consideration of local effects should be performed based on the biocide guidance document.

2. Comparison with ARfD

- a. If the AOEL is exceeded by the exposure estimate in point 1, a comparison can be done against the ARfD for the active substance, corrected for the extent of oral absorption used in the derivation of the AOEL. If the exposure estimates are below the corrected ARfD, the systemic exposure is acceptable and no further evaluation is required.

In addition a consideration of local effects should be performed based on the biocide guidance document.

- b. If it was concluded that an ARfD was not required for the active substance, there is no reason for a specific consideration of acute non-dietary systemic exposures.

A consideration of local effects should be performed based on the biocide guidance document.

3. Comparison with biocide Acute Exposure Level (AEL) (if available)

If an active substance is used in the EU and an AEL has been agreed, this can be used as a surrogate for an 'AAOEL'. The AEL is used in biocide evaluations and a consistent approach with biocides would be a benefit, since a number of active substances are used in both plant protection products and biocides.

Potential issues

- *Are agreed biocide AELs readily available? If not, this option should be deleted. It will apply to only a relatively small number of active substances.*
- *Is it possible to use this approach if the biocide data holder is different from the pesticide data holder?*

Tier 2 – Derivation of an ‘AAOEL’

If the exposure estimates are above the AOEL, corrected ARfD and biocide AEL consideration is needed regarding the derivation of an ‘AAOEL’.

1. Review of ARfD derivation

- a. If an ARfD has been set, it is possible that the route of exposure used in the critical study is not appropriate to non-dietary exposures. For example, the dosing by gavage (stomach tube) of a locally acting compound could produce effects that are not relevant to non-dietary exposures. This is particularly applicable to the dermal route, where systemic effects related to high concentrations produced by gavage dosing might not be relevant. If the basis of the ARfD is considered of questionable relevance to non-dietary exposures, a more appropriate basis could be sought and a specific ‘AAOEL’ derived.
- b. Effects that have been used to derive ARfDs but might be of no relevance to an ‘AAOEL’ could include:
 - i. reduced food consumption and body weight from gavage dosing, especially of irritant compounds;
 - ii. gastrointestinal effects, such as vomiting and diarrhoea;
 - iii. effects on the liver. The liver receives orally absorbed chemicals before they are circulated round the majority of the body and therefore receives a relatively high dose in a short space of time. Dermal and inhalation exposures do not go directly to the liver.

Does a more extensive list of end-points not relevant for ‘AAOEL’ need to be produced?

- c. Effects that have been used to derive ARfDs that should be considered relevant to an ‘AAOEL’ in the absence of specific contrary information include:
 - i. overt developmental effects e.g. malformations;
 - ii. clinical signs seen in dietary studies;
 - iii. effects on blood and organs other than the liver.

- d. If the ARfD is relevant to the acute non-dietary assessment, the specific use of the product would appear to be unacceptable as a comparison with a corrected ARfD was performed at Tier 1.
- e. If the effects used to derive the ARfD are considered not relevant to the acute non-dietary assessment, an 'AAOEL' needs to be derived.

2. Derivation of specific 'AAOEL'

- a. The process for derivation of an 'AAOEL' is basically the same as for an AOEL: only the effect and study most relevant to acute exposures should be used. All potentially exposed sub-groups should be protected. A safety factor of 100 (or more, if appropriate) should be applied to the NOAEL for the critical effect. If necessary, a correction for the extent of oral absorption should be applied.
- b. As most of the studies submitted in pesticide dossiers are via the oral routes, it is anticipated that 'AAOEL's will be based on **systemic** effects seen in oral studies. Care should be taken in ensuring appropriate extrapolation when considering different routes of exposure. Local effects will be addressed separately.
- c. If the exposure scenarios are predominantly via a particular route and an appropriate study is available, a route-specific 'AAOEL' can be derived.

Other aspects for consideration

1. If an 'AAOEL' is based on fetal effects, this is not applicable to exposure scenarios for infants, toddlers and young children. If the exposure estimates for these groups exceeds the 'AAOEL', scientifically a second 'AAOEL' specific to infants, toddlers and young children could be derived. This raises policy and presentational issues – do member States support the derivation of sub-group specific 'AAOEL's? In the EU there is normally only one ARfD set to cover all sub-populations for acute dietary exposure.

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September 2015



Proposal for Flow Chart for 'AAOEL' considerations for active substances not under full evaluation.

