Evaluation Manual for the Authorisation of plant protection products according to Regulation (EC) No 1107/2009

EU part

Plant Protection Products

Chapter 4 Human toxicology; risk operator, worker bystander and resident

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ctgb

Board for the authorisation of plant protection products and biocides

Chapter 4 Human toxicology; risk operator, worker, bystander and resident

Category: Plant protection products

Changes in the Evaluation Manual

Evaluation manual PPP EU part Chapter 4 Human toxicology; risk operator, worker, bystander and resident			
Version	**Date**	**Paragraph**	**Changes**
2.0	Janaury 2014	1.3	Section 1.3 included the former exposure models.
2.1	October 2016	1.3	Updated to include the EFSA Opex model.
2.2	March 2017	1.3 and 1.4	Updated to take into account the revised Guidance document on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products (SANTE-10832-2015 rev. 1.7)

GENERAL INTRODUCTION

This chapter describes the methodology for estimation of the risk of the application of plant protection products to operator, worker, bystander and resident for the EU framework (§1 - §1.5) under Regulation (EC) No 1107/2009.The described risk assessment in this chapter can be used for both the approval procedure for active substances as well as for zonal applications for the authorization of plant protection products (i.e. core registration reports).

1. EU FRAMEWORK

In this document, the procedures for the evaluation and re-evaluation of active substances and products as laid down in the EU are described; the NL procedure for evaluation of a substance and product is reverted to when no EU procedure has been laid down. The NL-procedure for the evaluation of a product is described the NL part of the Evaluation Manual (plant protection products) chapter 4 human toxicology; risk operator, worker and bystander..

1.1. Introduction

The purpose of the risk assessment for operator, worker, bystander or resident is to establish whether the application of a plant protection product has no adverse consequences for these groups of people. For this purpose the endpoints as described in Chapter 4 Human toxicology; mammalian toxicity dossier are compared with the expected exposure.

1.2. Data requirements

The data requirements regarding operator, worker, bystander and resident exposure are described in the Chapter Human toxicology; mammalian toxicity dossier, §1.2.2.

1.3. Risk assessment

To assess whether the application of a plant protection product has no adverse consequences for operator, worker, bystander and resident, the endpoints from the toxicological dossier and the corresponding reference value (e.g. AOEL) (see Chapter 4 Human toxicology; mammalian toxicity dossier) must be compared with the expected semi-chronic exposure.

With the adoption of the revised Guidance document on the assessment of exposure of operator, workers, residents and bystanders in risk assessment for plant protection products (SANTE-10832-2015 rev. 1.7) an acute risk assessment should also be carried out for active substances for which an Acute AOEL has been derived. An acute risk assessment is only required for operators and bystanders. The revised Guidance document applies to all 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.
This chapter describes the EU-methodology for the exposure estimation.

1.3.1 Estimation of operator exposure

From January 1st 2016 the EFSA Opex model will be used for all exposure scenarios included in this model (EFSA Journal 2014: 12(10):3874).

Exposure is first estimated for the unprotected operator in normal working clothes.
Where necessary, a further estimation shall be made with the assumption that the operator is using effective and readily obtainable protective equipment, which is feasible to be used in practice.

At the moment only field application are included in the EFSA OPEX model although the model is expected to be updated for greenhouse uses. The NL greenhouse model is

specifically developed for estimation of exposure for various activities in greenhouses. In the EU framework, modules available in the DE model (manual upward spraying) or the UK model (manual downward spraying) which are not specific for applications in greenhouses are sometimes also used for applications in greenhouses. Recently a new greenhouse model has been developed, especially for greenhouses in the Mediterranean countries (ECPA greenhouse model).

Suitable models are not available for a number of exposure scenarios. While awaiting further research, a qualitative exposure estimation based on expert judgement is made for these applications. Where induced by this risk assessment, supplementary data on actual exposure are requested.

For plant protection products in spray cans no harmonized model is available. However, the exposure of operators could be estimated with the model CONSEXPO.

Calculation of the systemic exposure
External exposure is adjusted for route-specific absorption to calculate systemic exposure.

Uptake after dermal exposure
Insight in the extent to which the skin absorbs a substance and/or formulation after exposure to a relevant level is important for calculation of systemic exposure.
A description of the method used to determine dermal absorption is given in the Chapter Human toxicology; mammalian toxicity dossier, §1.3.6 (EU part of the Evaluation Manual).

Uptake after respiratory exposure
The level of systemic exposure requires insight in the extent to which a substance and/or formulation is taken up in the body via inhalation after exposure to a relevant level.
A default value of 100% is applied where no suitable data on respiratory absorption at the respiratory NOAEL are available.

1.3.2 Estimation of worker exposure (re-entry)
From January 1st 2016 the EFSA Opex model will be used for all exposure scenarios included in this guidance.

Exposure is first estimated for the unprotected worker in normal working clothes. Where necessary, a further estimation shall be made with the assumption that the worker is using effective and readily obtainable protective equipment, which is feasible to be used in practice. Other possible refinements include a DFR study or refinement of the DT50 value used in the worker exposure assessment.

1.3.3 Estimation of bystander and resident exposure
From January 1st 2016 the EFSA Opex model will be used for all exposure scenarios included in this guidance.

Exposure is first estimated for the unprotected bystander and resident. If no safe use has been shown refinement may be possible, e.g. with a specific DT50 value or refined dermal absorption values. Every proposed higher tier refinement should be scientifically justified. The German model (Martin et al. 2008) and the UK method are not accepted as refinements.

Adults and children who recreate or sport on lawns or sports fields, treated with PPPs, can be exposed to these compounds. The EFSA model provides an assessment for recreational

exposure for the crop types golf course, turf and other sport lawns.

1.4. Approval

This section describes the approval criteria for active substances (section 1.4.1) and plant protection products (section 1.4.2 and 1.4.3). For the EU approval procedure of active substances a representative formulation has to be included in the dossier. Therefore section 1.4.1 to 1.4.3 apply. For the zonal applications of plant protection products only section 1.4.2 and 1.4.3 apply.

1.4.1 Approval of the active substance

Regulation (EC) No 1107/2009 Annex II provides the procedure and criteria for the approval of active substances, safeners and synergists pursuant to Chapter II of Regulation (EC) No 1107/2009.
Point 3 of Annex II of Regulation (EC) No 1107/2009 defines the criteria that have to be met for the approval of an active substance. The texts specifically applicable to the aspect human toxicology and operator risk are presented below.

3.1. Dossier
The dossiers submitted pursuant to Article 7(1) shall contain the information needed to establish, where relevant, Acceptable Daily Intake (ADI), Acceptable Operator Exposure Level (AOEL) and Acute Reference Dose (ARfD).

With the adoption of the revised Guidance document on the assessment of exposure of operator, workers, residents and bystanders in risk assessment for plant protection products (SANTE-10832-2015 rev. 1.7) an Acute AOEL (AAOEL) also has to be derived. This should only be done at EU level for approvals of new active substance and renewal evaluations of active substances. No AAOEL will be derived at a national level for product approvals. The Guidance document provides more information on how to derive an AAOEL.

3.3. Relevance of metabolites
Where applicable the documentation submitted shall be sufficient to permit the establishment of the toxicological, ecotoxicological or environmental relevance of metabolites.

3.6. Impact on human health

3.6.1. Where relevant, an ADI, AOEL and ARfD shall be established. When establishing such values an appropriate safety margin of at least 100 shall be ensured taking into account the type and severity of effects and the vulnerability of specific groups of the population. When the critical effect is judged of particular significance, such as developmental neurotoxic or immunotoxic effects, an increased margin of safety shall be considered, and applied if necessary.

3.6.2. An active substance, safener or synergist shall only be approved if, on the basis of assessment of higher tier genotoxicity testing carried out in accordance with the data requirements for the active substances, safeners or synergists and other available data and information, including a review of the scientific literature, reviewed by the Authority, it is not or has not to be classified, in accordance with the provisions of Regulation EC) No 1272/2008, as mutagen category 1A or 1B.

3.6.3. An active substance, safener or synergist shall only be approved, if, on the basis of assessment of carcinogenicity testing carried out in accordance with the data requirements

for the active substances, safener or synergist and other available data and information, including a review of the scientific literature, reviewed by the Authority, it is not or has not to be classified, in accordance with the provisions of Regulation (EC) No 1272/2008, as carcinogen category 1A or 1B, unless the exposure of humans to that active substance, safener or synergist in a plant protection product, under realistic proposed conditions of use, is negligible, that is, the product is used in closed systems or in other conditions excluding contact with humans and where residues of the active substance, safener or synergist concerned on food and feed do not exceed the default value set in accordance with Article 18(1)(b) of Regulation (EC) No 396/2005.

3.6.4. An active substance, safener or synergist shall only be approved if, on the basis of assessment of reproductive toxicity testing carried out in accordance with the data requirements for the active substances, safeners or synergists and other available data and information, including a review of the scientific literature, reviewed by the Authority, it is not or has not to be classified, in accordance with the provisions of Regulation (EC) No 1272/2008, as toxic for reproduction category 1A or 1B, unless the exposure of humans to that active substance, safener or synergist in a plant protection product, under realistic proposed conditions of use, is negligible, that is, the product is used in closed systems or in other conditions excluding contact with humans and where residues of the active substance, safener or synergist concerned on food and feed do not exceed the default value set in accordance with point (b) of Article 18(1) of Regulation (EC) No 396/2005.

3.6.5. An active substance, safener or synergist shall only be approved if, on the basis of the assessment of Community or internationally agreed test guidelines or other available data and information, including a review of the scientific literature, reviewed by the Authority, it is not considered to have endocrine disrupting properties that may cause adverse effect in humans, unless the exposure of humans to that active substance, safener or synergist in a plant protection product, under realistic proposed conditions of use, is negligible, that is, the product is used in closed systems or in other conditions excluding contact with humans and where residues of the active substance, safener or synergist concerned on food and feed do not exceed the default value set in accordance with point (b) of Article 18(1) of Regulation (EC) No 396/2005.

By 14 December 2013, the Commission shall present to the Standing Committee on the Food Chain and Animal Health a draft of the measures concerning specific scientific criteria for the determination of endocrine disrupting properties to be adopted in accordance with the regulatory procedure with scrutiny referred to in Article 79(4).

Pending the adoption of these criteria, substances that are or have to be classified, in accordance with the provisions of Regulation (EC) No 1272/2008, as carcinogenic category 2 and toxic for reproduction category 2, shall be considered to have endocrine disrupting properties.

In addition, substances such as those that are or have to be classified, in accordance with the provisions of Regulation (EC) No 1272/2008, as toxic for reproduction category 2 and which have toxic effects on the endocrine organs, may be considered to have such endocrine disrupting properties.

Point 4 of Annex II of Regulation (EC) No 1107/2009 gives criteria for substitution. The texts specifically applicable to the aspect human toxicology and operator risk are presented below. In the chapter “Generic aspects” of this Evaluation Manual, more information is provided on criteria for substitution and on how Ctgb will carry out the comparative assessment at a

national level.

Point 5 of Annex II of Regulation (EC) No 1107/2009 gives information on low risk substances. The texts specifically applicable to the aspect human toxicology and operator risk are presented below. In the chapter “Generic aspects” of this Evaluation Manual, more information is provided on low risk substances. The criteria for low risk substances are currently under discussion and are likely to change in the near future.

1.4.2 Evaluation of plant protection products

The principles for the evaluation (the Uniform Principles) regarding mammalian toxicology are presented in the Annex to Commission Regulation (EU) No 546/2011 section B Evaluation. These concern the relevant sections of the introductory principles, the general principles and the specific principles Impact on human or animal health (section 2.4.1).

1.4.3 Decision making for plant protection products

The principles for the evaluation for decision making are presented in Commission Regulation (EU) No 546/2011 section C Decision-making.
These concern the relevant sections of the introductory principles, the general principles and the specific principles Impact on human or animal health (section 2.4.1).

1.5. Developments

- The EFSA model is expected to undergo further development to include e.g. an exposure assessment for greenhouse uses.