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

EU part

Plant Protection Products

Chapter 2 Physical and chemical properties

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Board for the authorisation of plant protection products and biocides

Chapter 2 Physical and chemical properties

Category: plant protection products

Changes in the Evaluation Manual

Evaluation manual PPP EU part Chapter 2 Physical and chemical properties			
Version	**Date**	**Paragraph**	**Changes**
2.0	January 2014	1.2.1 and 1.2.2	DPD classification and labelling was referred to
2.1	October 2016	1.2.1 and 1.2.2	Only CLP classification and labelling is referred to
2.2	January 2020	1.	Sentence included on the administrative EFSA guidance

GENERAL INTRODUCTION

This Evaluation manual describes the data requirements for the aspect physical-chemical properties and how these are evaluated in the EU framework under Regulation (EC) No 1107/2009.

1. EU FRAMEWORK

In this document, the procedures for the evaluation and re-evaluation of active substances (1.2.1) and plant protection products (1.2.2) as laid down in the EU are described; the NL procedure for evaluation is reverted to when no EU procedure has been laid down. This document aims to give procedures for the approval of active substances and inclusion in Commission Implementing Regulation (EU) No 540/2011

Notifiers preparing an assessment report for active substances need to comply with the relevant guidance, instructions and format laid down in the EFSA Administrative guidance on submission of dossiers and assessment reports for the peer-review of pesticide active substances

1.1. Introduction

The composition and physical-chemical properties of active substances and plant protection products are evaluated to prevent products being placed on the market which:

1. are of insufficient quality, resulting in reduced applicability or reduced efficacy
2. may cause risks to user, public health and environment.

Physical-chemical properties of a formulation are also important from a safety point of view. Aspects such as flammability of the product and the presence of undesirable impurities can be relevant for a safe use.

The most important guidance documents for this chapter are:

- SANCO/12638/2011 rev. 2, "Guidance document on significant and non-significant changes of the chemical composition of authorised plant protection products under Regulation (EC) No 1107/2009
- SANCO/10597/2003 rev. 10.1 "Guidance document on the assessment of the equivalence of technical materials of substances regulated under Regulation (EC) No 1107/2009."
- FAO/WHO November 2010 – second revision of the First "Manual on Development and Use of FAO and WHO Specifications for Pesticides"

1.2. Data requirements

In order to qualify for inclusion of an active substance in Commission Implementing Regulation (EU) No 540/2011 a dossier that meets the provisions laid down in Commission Regulation (EU) No 283/2013 and Commission Regulation (EU) No 284/2013 of Regulation (EC) No 1107/2009 must be submitted for the active substance as well as for the representative product.

Generally, EU and OECD guidelines for the protocol of experiments are mentioned in Commission Communications 2013/C 95/01 and 2013/C 95/02 (for (EU) No 283/2013 and (EU) No 284/2013 respectively)

When the applicant is of the opinion that a certain study is not necessary, a relevant scientific justification can be provided for the non-submission of the particular study.

Where GLP is required, studies carried out after 25 July 1993 should be performed to GLP.

There should be no doubt about the identity of the tested product or the purity of the tested substance or product for each study.

The data requirements and limits for physical properties, and the fact whether or not they are required for specific formulation types and the corresponding guidelines are summarised in the "Manual on Development and Use of FAO and WHO Specifications for Pesticides"

1.2.1. Data requirements for the active substance

The data requirements regarding the physical-chemical properties of the active substance are described in part A of Commission Regulation (EU) No 283/2013, points 1 (identity of the active substance), 2 (physical and chemical properties of the active substance), and 3 (further information on the active substance).
Generally, EU and OECD guidelines for the protocol of experiments are mentioned in Commission Communications 2013/C 95/01.

Any necessary additions to data requirements set in Commission Regulation (EU) No 283/2013 are described below.

Identity of the active substance
Producer (name, address, including location of plant) (283/2013; 1.2)
If the active substance is to be obtained from a different manufacturer or when there is a change of location of the manufacturing plant of the active substance, this should be notified. For guidance on data requirements related to changes of the producer, refer to the guidance document on the assessment of the equivalence of technical materials, Sanco/10597/2003.

CAS, EC and CIPAC numbers (283/2013; 1.6)
The CIPAC number of a substance can be obtained on the following website: http://www.cipac.org/.
The ESIS database (archived version), containing EC (EINECS and ELINCS) registered compounds has been discontinued 17 november 2014. Alternatively, ECHA has a database of all REACH registered substances and provisional and final classification and labelling information as included in annex VI of Regulation (EC) 1272/2008.

Method of manufacture (synthesis pathway) of the active substance (283/2013; 1.8)
For guidance on data requirements related to changes of the manufacturer, refer to the guidance document on the assessment of equivalence of technical materials, SANCO/10597/2003 rev. 10.1

Specification of purity of the active substance in g/kg (283/2013; 1.9)
The specification should at least meet the specification laid down by the FAO.
A non-isolated active substance in a solvent, including possible additives, is considered a technical concentrate (TK). This may be because the active substance is not stable in pure form, or for safety reasons. The technical material (TC) is the solvent-free material, including residual impurities, not isolated during manufacture of a TK. Specifications are mostly based on the TC, which is also known as a dry weight specification. Only a minimum specification has been laid down, without an upper limit. When the TC is not isolated, the relevant physical-chemical properties of the TK should be determined. Specifications for a TK can be derived from the specifications of a TC; in that case an upper limit should be specified (a concentration range). The conclusion of a discussion in EPCO 11 (2004) was: "if the TC is not transported, marketed and the TK is simply diluted to form the formulation, the data for the TC is not required. However, if the TC is also marketed, transported then data on both will be required. Or if the TK is dried down or converted to the TC then again the data will be

required". This concerns the flammability, explosive and oxidising properties of the active substance.

Identity and content of additives (such as stabilisers) and impurities (283/2013; 1.10)
The 'non-active isomers' of the active substance should according to the guidelines also be considered as impurities.
A detailed composition of the active substance should be provided by submitting a specification that is used for production. All impurities that could potentially exceed 0.1% w/w (or 1 g/kg) should be specified.

Significant impurities (283/2013; 1.10.2)
The specification should at least meet the FAO specification. Where relevant impurities are present, these should be included in the specification with a realistic maximum.
The specification should be a statistically based realistic reflection of the concentrations found in batch analyses (mean value found in the batch analysis+ three times standard deviation) and should be representative for the batches used for toxicological and ecotoxicological testing. According to the FAO/WHO manual the content of impurities must be given in g/kg *in comparison with* the active substance content. The absolute as well as the relative presentation of the specification are accepted.

Relevant impurities (283/2013; 1.10.3)
Relevant impurities may, e.g., be formed during the production process or by degradation of the active substance, but can also be process solvents or additives.
Examples of relevant impurities are hexachlorobenzene in chlorothalonil, ETU (ethylene thiourea) in dithiocarbamates, but also impurities that are not directly related to the active substance such as dioxins and nitrosamines. Where on the basis of the production process relevant impurities can be expected, analysis of the active substance for these impurities may be requested.
The applicant should indicate whether relevant impurities are present in the active substance; if this is the case, these should be included in the specification, even if below the cut-off criterium of 1g/kg.

Analytical profile of batches (283/2013; 1.11)
At least 5 representative batches should be analysed. These batches should be representative of the current production. The impurities content of the batches should meet the specification of the active substance as provided by the manufacturer and the FAO specification where available. The used analytical methods must meet the requirements laid down in Chapter 3 'Analytical methods'.
In addition to batch analysis data, quality control (QC) data can be used to support a proposed technical specification. The EFSA working document for PRAPeR meetings on section 1 mentions the following:

If quality control data are to be relied on in support of a technical specification what are the minimum requirements for the submission of this data.

- *Only a summary of the data is required, not the raw data, although this should be available on request. For the active substance and the impurities the mean, minimum, maximum values and standard deviation should be provided for each production year as well as for the total batch data submitted.*
- *The number of batches analysed, the year of their production and the total number of batches produced in the respective years should be provided.*
- *The site of manufacture (source) must be identified.*

Physical and chemical properties of the active substance
FAO specifications can be obtained via the internet. In addition, OECD test methods are available. A large number of test methods (EEC methods A1 - A21) are available on the internet as well although, in principle, the EEC methods are not valid for CLP labeling. CIPAC methods can be used without validation. The 'UN transport of dangerous goods, manual of tests and criteria' contains the testing methods required for classification and labelling.

The European guidelines and guidance documents do not clearly state what requirements apply in case a variant (ester, salt) of the active substance is used in the product. In principle, the (physical and chemical) properties of the substance that is applied in the product are required for the risk evaluation.

Melting point and boiling point (283/2013; 2.1)
There are no clear European agreements about the minimum temperature down to which the freezing point should be determined. Testing down to -20°C is generally considered to be adequate.

Spectra (UV/VIS, IR, NMR, MS), molecular extinction at relevant wavelengths, optical purity (283/2013; 2.4)
The spectra should be suitable for identification purposes.

Solubility in organic solvents (283/2013; 2.6)
CIPAC method MT 181 'solubility in organic solvents' can be used where solubility exceeds 10 g/L. CIPAC method MT 157 (water solubility) can be amended and used for lower concentrations.

Partition coefficient n-octanol/water (283/2013; 2.7)
According to the description the EC method (or in fact: the HPLC method as well as shake-flask method as described in EC method A8) cannot be used for surface active compounds (surface tension < 60mN/m tested at the appropriate concentration and temperature). During the EPCO 11 meeting (2004) the following was decided as regards the suitability of the method in case of a surface active compound: "It was thought that the shake-flask method could be used as long as there are no other problems encountered, e.g. phase separation. The column elution method cannot be used for surface active compounds". For surface active compounds the report on the determination of the octanol/water partition coefficient should contain information about a possible phase separation to enable evaluation.

Explosive properties (283/2013 ; 2.11)
In the case a theoretical estimation is insufficient, the requirements for explosive properties as laid down in Regulation (EC) 1272/2008 shall be followed.

Oxidising properties (283/2013; 2.13)
In the case a theoretical estimation is insufficient, the requirements for oxidising properties as laid down in Regulation (EC) 1272/2008 shall be followed.

Further information on the active substance
Methods and precautions concerning handling, storage, transport or fire (293/2013; 3.8)
Safety data sheets must be prepared according to Regulation (EC) No 1907/2006.

1.2.2. Data requirements for the plant protection product
The data requirements regarding the physical-chemical properties of the active substance

are described in part A of Commission Regulation (EU) No 284/2013, points 1 (identity of the plant protection product), 2 (physical-chemical and technical properties of the plant protection product), and 4 (further information on the plant protection product).

Generally, EU, CIPAC and OECD guidelines for the protocol of experiments are mentioned in Commission Communications 2013/C 95/02

Any necessary additions to data requirements set in Commission Regulation (EU) No 283/2013 are described below.

CIPAC standard water
The hardness of the water used in the test is relevant for a number of properties. From FAO guideline, revision 5, water types A and D are recommended as standard water, even if the CIPAC methods recommend a different water type. Standard water A and D must be used for the emulsion and dispersion tests because the properties may be affected by soft as well as by hard water. The type of water used must be clearly indicated for all tests.

Detailed quantitative and qualitative information on the composition of the plant protection product (284/2013; 1.4.1, 284/2013; 1.4.2, 284/2013; 1.4.3)
If the product contains a total of more than 10% 'aliphatic, alicyclic and aromatic hydrocarbons' the hazard statement H304 (1272/2008/EC) should be assigned, depending on viscosity and/or surface tension of the product. The term 'aliphatic, alicyclic and aromatic hydrocarbons' refers to solvents that consist only of carbon and hydrogen atoms.
The active substance is only included in the summation if it falls under this definition (e.g. mineral oils).

The laws, regulations and administrative provision relating to restrictions on the marketing and use of certain dangerous substances and preparations (and supplements) are set in the REACH Regulation (EC) No 1907/2006

Type and code of the plant protection product (284/2013; 1.5)
See also FAO/WHO manual for type and code.

Explosive and oxidizing properties (284/2013; 2.2)
Extrapolation of the test methods EC A14, EC A17 and EC A21 to the UN tests, as prescribed by Regulation (EC) 1272/2008 is problematic. It is advisable to use the screening procedures as much as possible.

Flammability and self-heating (284/2013; 2.3)
Extrapolation of the test methods EC A10, EC A15 and EC A16 to the UN tests, as prescribed by Regulation (EC) 1272/2008, is problematic. It is advisable to use the screening procedures as much as possible.

Viscosity and surface tension (284/2013; 2.5)
Only the rotational viscometer can be used for determination of the (dynamic) viscosity of non-newtonian liquids. CIPAC method MT 192, based op OECD114, is the preferred method. CIPAC MT192 requires two shear rates to be reported, covering the range of 20 to 100s^{-1}.
In case the viscosity is required for classification and labelling (assignment of H304), viscosity shall be determined at 40°C.

Storage stability and shelf-life: effects of temperature on technical characteristics of the plant

protection product (284/2013; 2.7)
Depending on the formulation type, physical properties need to be tested after storage. The requirements can be found in the specification guidelines in the Manual on Development and Use of FAO and WHO Specifications for Pesticides.

If the product shows a decrease of more than 10% of the active substance, it may be necessary to state the shelf-life of the product on the label(e.g. in months) if a shelf life of less than two years is assigned. This depends on the actual decrease, the fact whether or not the specifications are met after the decrease, and the efficacy of the product after storage.

For aerosols it should be demonstrated that the nozzle is not blocked after storage. No corrosion of the nozzle may be visible after storage. The aerosol must sometimes be opened for determination of the properties of its content.
This can, e.g., be done according to the method described in the Manual on Development and Use of FAO and WHO Specifications for Pesticides" under 8.11 (aerosol dispensers). More methods for determination of the physical properties of an aerosol can be obtained from the 'European Aerosol Federation'.

The suitability of the trade pack for its content should also be checked in the storage tests (e.g. by checking for: corrosion, leakage, malformation, closure). This means that the test must be carried out with the trade pack or a pack of the same material (or worst case). Where different packaging materials are applied for, these should all be investigated and described in the test, insofar as these show essential mutual differences (to be indicated by the applicant).

Technical characteristics of the plant protection product (284/2013; 2.8)
The requirements for determination of the technical characteristics of the plant protection product are formulation type specific. The Manual on Development and Use of FAO and WHO Specifications for Pesticides lists the specific requirements and preferred testing methods for frequently used formulation types.

FAO specifications are not yet available for new formulation types. In such cases, the criteria are derived from known formulation types, giving an explication of the choices that have been made.

Packaging
More information on packaging is given in the "UN transport of dangerous goods, manual of tests and criteria".

Controlled incineration (284/2103; 4.5.2.)
More information about incineration of dangerous substances is given in Directive 2000/76/EC.

1.2.3. Supplementary data requirements
In addition to the requirements described in Commission Regulation (EU) No 283/2013 and Commission Regulation (EU) No 284/2013 of Regulation (EC) No 1107/2009, there are supplementary requirements arising from overlap with other European guidelines or from the Uniform Principles Regulation (EU) 546/2011 (2.7.2).

Aerosols

For aerosols, the supplementary requirements as described in Directive (EU) 2008/47/EC are also applicable.

"Free" content active substance
For capsule suspensions (CS) and encapsulated granules intended as slow release formulations the content free, unbound, active substance should according to FAO also be determined. Methods are still under development. Requirements have not yet been laid down.

Water-soluble packaging
Where the formulation is used in water-soluble packaging, the relevant physical-chemical tests should be carried out with the water-soluble packaging because this may affect the physical properties.
The test must be carried out with the water-soluble packaging in the same ratio as for the use as proposed.

1.3. Assessment
The following guidance documents are relevant for the evaluation:

- SANCO/12638/2011 rev. 2, "Guidance document on significant and non-significant changes of the chemical composition of authorised plant protection products under Regulation (EC) No 1107/2009
- SANCO/10597/2003 rev. 10.1 "Guidance document on the assessment of the equivalence of technical materials of substances regulated under Regulation (EC) No 1107/2009."
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1.4. Approval
1.4.1. Approval of the active substace
Regulation (EC) No 1107/2009 Annex II (Point 3) provides the procedure and criteria for the approval of an active substances, safeners and synergists pursuant to Chapter II of Regulation (EC) No 1107/2009.

1.4.2. Decision making of plant protection products
The principles for the evaluation for decision making as regards physical and chemical properties are presented in Commission Regulation (EU) 546/2011.
These concern the relevant sections of the introductory principles, the general principles and the specific principles Physical and chemical properties.