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Contents

II *Non-legislative acts*

REGULATIONS

- ★ **Commission Regulation (EU) No 283/2013 of 1 March 2013 setting out the data requirements for active substances, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market ⁽¹⁾** 1
- ★ **Commission Regulation (EU) No 284/2013 of 1 March 2013 setting out the data requirements for plant protection products, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market ⁽¹⁾** 85

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⁽¹⁾ Text with EEA relevance

EN

Acts whose titles are printed in light type are those relating to day-to-day management of agricultural matters, and are generally valid for a limited period.

The titles of all other acts are printed in bold type and preceded by an asterisk.

II

(Non-legislative acts)

REGULATIONS

COMMISSION REGULATION (EU) No 283/2013

of 1 March 2013

setting out the data requirements for active substances, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market

(Text with EEA relevance)

THE EUROPEAN COMMISSION,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to 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 ⁽¹⁾, and in particular Article 78(1)(b) thereof,

Whereas:

(1) In accordance with Article 8(4) of Regulation (EC) No 1107/2009, Commission Regulation (EU) No 544/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the data requirements for active substances ⁽²⁾ was adopted. It contains the requirements for the dossiers to be submitted for the approval of active substances, as set out in Annex II to Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market ⁽³⁾.

(2) It is necessary to modify the data requirements concerning chemical substances in order to take into account current scientific and technical knowledge.

(3) More detailed information for the implementation of the data requirements is laid down in relevant guidance documents.

(4) Regulation (EU) No 544/2011 should therefore be repealed.

(5) A reasonable period should be allowed to elapse before the modified data requirements become applicable in order to permit applicants to prepare themselves to meet those requirements.

(6) In order to permit Member States and the interested parties to prepare themselves to meet the new requirements, it is appropriate to lay down transitional measures concerning data submitted for applications for the approval, renewal of approval or amendment to the conditions of approval of active substances and data submitted for applications for authorisation, renewal of authorisation and amendment to the authorisation of plant protection products.

(7) These transitional measures are without prejudice to Article 80 of Regulation (EC) No 1107/2009.

(8) The measures provided for in this Regulation are in accordance with the opinion of the Standing Committee on the Food Chain and Animal Health and neither the European Parliament nor the Council has opposed them,

HAS ADOPTED THIS REGULATION:

Article 1

Data requirements for active substances

The data requirements for the active substance provided for in Article 8(1)(b) of Regulation (EC) No 1107/2009 shall be as set out in the Annex to this Regulation.

Article 2

Repeal

Regulation (EU) No 544/2011 is repealed.

⁽¹⁾ OJ L 309, 24.11.2009, p. 1.

⁽²⁾ OJ L 155, 11.6.2011, p. 1.

⁽³⁾ OJ L 230, 19.8.1991, p. 1.

References to the repealed Regulation shall be construed as references to this Regulation

*Article 3***Transitional measures as regards procedures concerning active substances**

With respect to active substances, Regulation (EU) No 544/2011 shall continue to apply as regards the following:

- (a) procedures concerning the approval of an active substance or an amendment to the approval of such a substance pursuant to Article 13 of Regulation (EC) No 1107/2009 for which the dossiers provided for in Article 8(1) and (2) thereof have been submitted by 31 December 2013;
- (b) procedures concerning the renewal of approval of an active substance pursuant to Article 20 of Regulation (EC) No 1107/2009 for which the supplementary dossiers referred to in Article 9 of Commission Regulation (EU) No 1141/2010 ⁽¹⁾ have been submitted by 31 December 2013.

*Article 4***Transitional measures as regards procedures concerning plant protection products**

1. Regulation (EU) No 544/2011 shall continue to apply as regards procedures concerning the authorisation of a plant protection product, as referred to in Article 28 of Regulation

(EC) No 1107/2009, provided that the respective application has been submitted by 31 December 2015 and that the plant protection product contains at least one active substance for which the dossiers or supplementary dossiers have been submitted in compliance with Article 3.

2. By way of derogation from paragraph 1, from 1 January 2014 applicants may choose to apply the data requirements, as set out in the Annex to this Regulation. This choice shall be made in writing when submitting the application and shall be irrevocable.

*Article 5***Entry into force and date of application**

1. This Regulation shall enter into force on the twentieth day following that of its publication in the *Official Journal of the European Union*.

2. For procedures concerning the renewal of approval of active substances whose approval expires on 1 January 2016 or later, this Regulation shall apply as of entry into force.

As regards all other procedures, it shall apply from 1 January 2014.

This Regulation shall be binding in its entirety and directly applicable in all Member States.

Done at Brussels, 1 March 2013.

For the Commission
The President
José Manuel BARROSO

⁽¹⁾ OJ L 322, 8.12.2010, p. 10.

ANNEX

INTRODUCTION

Information to be submitted, its generation and its presentation

1. The information submitted shall meet the following requirements.
 - 1.1. The information shall be sufficient to evaluate the foreseeable risks, whether immediate or delayed, which the active substance may entail for humans, including vulnerable groups, animals and the environment and contain at least the information and results of the studies referred to in this Annex.
 - 1.2. Any information on potentially harmful effects of the active substance, its metabolites and impurities on human and animal health or on groundwater shall be included.
 - 1.3. Any information on potentially unacceptable effects of the active substance, its metabolites and impurities on the environment, on plants and plant products shall be included.
 - 1.4. The information shall include all relevant data from the scientific peer reviewed open literature on the active substance, metabolites and breakdown or reaction products and plant protection products containing the active substance and dealing with side-effects on health, the environment and non-target species. A summary of this data shall be provided.
 - 1.5. The information shall include a full and unbiased report of the studies conducted as well as a full description of them. Such information shall not be required, where one of the following conditions is fulfilled:
 - (a) it is not necessary owing to the nature of the product or its proposed uses, or it is not scientifically necessary;
 - (b) it is technically not possible to supply.In such a case a justification shall be provided.
 - 1.6. The simultaneous use of the active substance as a biocide or in veterinary medicine shall be reported.

If the applicant for the active substance in the plant protection product is identical to the one responsible for the notification of the active substance as a biocide or as a veterinary medicine, a summary of all relevant data submitted for approval of the biocide or the veterinary medicine, shall be submitted. This summary shall include toxicological reference values and MRL proposals, taking into account any possible cumulative exposure due to different uses of the same substance based on scientific methods accepted by the European competent authorities, together with a summary of the residues and toxicology data and information on the use of the product.

If the applicant for the active substance in the plant protection product is not identical to the one responsible for the notification of the active substance as a biocide or in veterinary medicine, a summary of all available data shall be submitted.
 - 1.7. Where relevant, the information shall be generated using test methods, which are included in the list referred to in point 6. In the absence of suitable internationally or nationally validated test guidelines, test guidelines accepted by the European competent authority shall be used. Any deviations shall be described and justified.
 - 1.8. The information shall include a full description of the test methods used.
 - 1.9. The information shall include a list of endpoints for the active substance.
 - 1.10. Where relevant, the information shall be generated in accordance with Directive 2010/63/EU of the European Parliament and of the Council ⁽¹⁾.
 - 1.11. The information on the active substance, taken together with the information concerning one or more plant protection products containing the active substance and together, if appropriate, with the information concerning safeners and synergists and other components of the plant protection product, shall be sufficient to:
 - (a) permit an assessment of the risks for humans, associated with handling and use of plant protection products containing the active substance;
 - (b) permit an assessment of the risks for human and animal health, arising from residues of the active substance and its metabolites, impurities, breakdown and reaction products remaining in water, air, food and feed;

⁽¹⁾ OL L 276, 20.10.2010, p. 33.

- (c) predict the distribution, fate and behaviour in the environment of the active substance and metabolites, breakdown and reaction products, where they are of toxicological or environmental significance, as well as the time courses involved;
- (d) permit an assessment of the impact on non-target species (flora and fauna), including the impact on their behaviour, which are likely to be exposed to the active substance, its metabolites, breakdown and reaction products, where they are of toxicological or environmental significance. Impact can result from single, prolonged or repeated exposure and can be direct or indirect, reversible or irreversible;
- (e) evaluate the impact on biodiversity and the ecosystem;
- (f) identify non-target species and populations for which hazards arise because of potential exposure;
- (g) permit an evaluation of short and long-term risks for non-target species, populations, communities and processes;
- (h) classify the active substance as to hazard in accordance with Regulation (EC) No 1272/2008 of the European Parliament and of the Council ⁽¹⁾;
- (i) specify the pictograms, the signal words, and relevant hazard and precautionary statements for the protection of man, non-target species and the environment, which are to be used for labelling purposes;
- (j) establish, where relevant, an acceptable daily intake (ADI) level for humans;
- (k) establish acceptable operator exposure levels (AOEL);
- (l) establish, where relevant, an acute reference dose, (ARfD) for humans;
- (m) identify relevant first aid measures as well as appropriate diagnostic and therapeutic measures to be followed in the event of poisoning in humans;
- (n) establish the isomeric composition and the possible metabolic conversion of the isomers, when relevant;
- (o) establish residues definitions appropriate for risk assessment;
- (p) establish residues definitions appropriate for monitoring and enforcement purposes;
- (q) permit a risk assessment of consumer exposure, including, where relevant, a cumulative risk assessment deriving from exposure to more than one active substance;
- (r) permit an estimation of the exposure to operators, workers, residents and bystanders including, where relevant, the cumulative exposure to more than one active substance;
- (s) establish maximum residue levels and concentration/dilution factors in accordance with Regulation (EC) No 396/2005 of the European Parliament and of the Council ⁽²⁾;
- (t) permit an evaluation to be made as to the nature and extent of the risks for man, animals (species normally fed and kept by humans or food producing animals) and of the risks for other non-target vertebrate species;
- (u) identify measures necessary to minimise contamination of the environment and impact on non-target species;
- (v) decide whether or not the active substance has to be considered as persistent organic pollutant (POP), persistent, bio accumulative and toxic (PBT) or very persistent and very bio accumulative (vPvB) in accordance with the criteria laid down in Annex II to Regulation (EC) No 1107/2009;
- (w) decide whether or not the active substance has to be considered as a candidate for substitution in accordance with the criteria laid down in Annex II to Regulation (EC) No 1107/2009;
- (x) decide whether or not the active substance has to be considered as a low-risk active substance in accordance with the criteria laid down in Annex II to Regulation (EC) No 1107/2009;
- (y) decide whether, or not, the active substance is to be approved;
- (z) specify conditions or restrictions to be associated with any approval.

1.12. Where relevant, tests shall be designed and data analysed using appropriate statistical methods.

1.13. Exposure calculations shall refer to scientific methods accepted by the European Food Safety Authority, (the Authority), when available. Additional methods, when used, shall be justified.

⁽¹⁾ OJ L 353, 31.12.2008, p. 1.

⁽²⁾ OJ L 70, 16.3.2005, p. 1.

- 1.14. For each section of the data requirements, a summary of all data, information and evaluation made shall be submitted. This shall include a detailed and critical assessment according to the provisions of Article 4 of Regulation (EC) No 1107/2009.
2. The requirements set out in this Regulation shall represent the minimum data to be submitted. Additional requirements at national level may be necessary in specific circumstances, that is to say specific scenarios, patterns of use other than those taken into account for approval. Careful attention shall be given to environmental, climatic and agronomic conditions when tests are set up and approved by the competent authorities.
3. **Good laboratory practice (GLP)**
- 3.1. Tests and analyses shall be conducted in accordance with the principles laid down in Directive 2004/10/EC of the European Parliament and of the Council ⁽¹⁾ where testing is done to obtain data on the properties or safety with respect to human or animal health or the environment.
- 3.2. By way of derogation from point 3.1:
- 3.2.1. For active substances consisting of micro-organisms or viruses, tests and analyses done to obtain data on the properties and safety with respect to other aspects than human health, may be conducted by official or officially recognised testing facilities or organisations which satisfy at least the requirements under points 3.2 and 3.3 of the introduction of the Annex to Commission Regulation (EU) No 284/2013 ⁽²⁾.
- 3.2.2. For tests and analyses made to obtain data for minor crops required under points 6.3 and 6.5.2 of Part A:
- the field phase may have been conducted by official or officially recognised testing facilities or organisations which satisfy at least the requirements as laid down in points 3.2 and 3.3 of the introduction of the Annex to Regulation (EU) No 284/2013;
 - the analytical phase, if not done in accordance with the GLP requirements, shall be conducted by laboratories accredited for the relevant method in accordance with the European standard EN ISO/IEC 17025 'General requirements for the competence of testing and calibration laboratories'.
- 3.2.3. Studies conducted before the application of this Regulation, although not fully compliant with GLP requirements or with current test methods, may be integrated into the assessment, when accepted by the competent authorities as scientifically valid, thereby removing the need for repeating animal tests, especially for carcinogenicity and reprotoxicity studies. This derogation applies to studies on all vertebrate species.
4. **Test material**
- 4.1. A detailed description (specification) of the material used shall be provided. Where tests are done using the active substance, the material used shall comply with the specification that will be used in the manufacture of plant protection products to be authorised, except where radio-labelled material or the purified active substance is used.
- 4.2. Where studies are conducted using an active substance produced in the laboratory or in a pilot plant production system, the studies shall be repeated using the active substance as manufactured, unless the applicant shows that the test material used is essentially the same, for the purposes of toxicological, ecotoxicological, environmental and residue testing and assessment. In cases of uncertainty, bridging studies shall be submitted to serve as a basis for a decision as to the possible need for repetition of the studies.
- 4.3. Where studies are conducted using an active substance of different purity or which contains different impurities or different levels of impurities to the technical specification or where the active substance is a mixture of components, the significance of the differences shall be addressed either by data or scientific case. In cases of uncertainty, appropriate studies using the active substance as manufactured for commercial production shall be submitted to serve as a basis for a decision.
- 4.4. In the case of studies in which dosing extends over a period (for example repeated dose studies), dosing shall be done using a single batch of active substance if stability permits. Whenever a study implies the use of different doses, the relationship between dose and adverse effect shall be reported.

⁽¹⁾ OJ L 50, 20.2.2004, p. 44.

⁽²⁾ See page 85 of his Official Journal.

- 4.5. When tests shall be conducted using purified active substance (≥ 980 g/kg) of stated specification, the purity of such test material shall be as high as can be achieved using the best available technology and shall be reported. A justification shall be provided in cases where the degree of purity achieved is less than 980 g/kg. Such justification shall demonstrate that all technically feasible and reasonable possibilities for the production of the purified active substance have been exhausted.
- 4.6. Where radio-labelled test material is used, radio-labels shall be positioned at sites (one or more as necessary), to facilitate elucidation of metabolic and transformation pathways and to facilitate investigation of the distribution of the active substance and of its metabolites, reaction and breakdown products.
5. **Tests on vertebrate animals**
- 5.1. Tests on vertebrate animals shall be undertaken only where no other validated methods are available. Alternative methods to be considered shall include *in vitro* methods and *in silico* methods. Reduction and refinement methods for *in vivo* testing shall also be encouraged to keep the number of animals used in testing to a minimum.
- 5.2. The principles of replacement, reduction and refinement of the use of animals shall be taken into account in the design of the test methods, in particular when appropriate validated methods become available to replace, reduce or refine animal testing.
- 5.3. Tests involving the deliberate administration of the active substance or the plant protection product to humans and non-human primates shall not be performed for the purpose of this Regulation.
- 5.4. For ethical reasons, study designs shall be carefully considered, taking into account the scope for reduction, refinement and replacement of animal tests. For example, by including one or more additional dose groups or time points for blood sampling in one study, it may be possible to avoid the need for another study.
6. For purposes of information and of harmonisation the list of test methods and guidance documents relevant to the implementation of this Regulation shall be published in the *Official Journal of the European Union*. This list shall be regularly updated.

PART A

CHEMICAL ACTIVE SUBSTANCES

TABLE OF CONTENTS

SECTION 1. **Identity of the active substance**

- 1.1. Applicant
- 1.2. Producer
- 1.3. Common name proposed or ISO-accepted and synonyms
- 1.4. Chemical name (IUPAC and CA nomenclature)
- 1.5. Producer's development code numbers
- 1.6. CAS, EC and CIPAC numbers
- 1.7. Molecular and structural formula, molar mass
- 1.8. Method of manufacture (synthesis pathway) of the active substance
- 1.9. Specification of purity of the active substance in g/kg
- 1.10. Identity and content of additives (such as stabilisers) and impurities
- 1.10.1. Additives
- 1.10.2. Significant impurities
- 1.10.3. Relevant impurities
- 1.11. Analytical profile of batches

SECTION 2. **Physical and chemical properties of the active substance**

- 2.1. Melting point and boiling point
- 2.2. Vapour pressure, volatility

- 2.3. Appearance (physical state, colour)
- 2.4. Spectra (UV/VIS, IR, NMR, MS), molar extinction at relevant wavelengths, optical purity
- 2.5. Solubility in water
- 2.6. Solubility in organic solvents
- 2.7. Partition coefficient n-octanol/water
- 2.8. Dissociation in water
- 2.9. Flammability and self-heating
- 2.10. Flash point
- 2.11. Explosive properties
- 2.12. Surface tension
- 2.13. Oxidising properties
- 2.14. Other studies

SECTION 3. Further information on the active substance

- 3.1. Use of the active substance
- 3.2. Function
- 3.3. Effects on harmful organisms
- 3.4. Field of use envisaged
- 3.5. Harmful organisms controlled and crops or products protected or treated
- 3.6. Mode of action
- 3.7. Information on the occurrence or possible occurrence of the development of resistance and appropriate management strategies
- 3.8. Methods and precautions concerning handling, storage, transport or fire
- 3.9. Procedures for destruction or decontamination
- 3.10. Emergency measures in case of an accident

SECTION 4. Analytical methods

Introduction

- 4.1. Methods used for the generation of pre-approval data
 - 4.1.1. Methods for the analysis of the active substance as manufactured
 - 4.1.2. Methods for risk assessment
- 4.2. Methods for post-approval control and monitoring purposes

SECTION 5. Toxicological and metabolism studies

Introduction

- 5.1. Studies on absorption, distribution, metabolism and excretion in mammals
 - 5.1.1. Absorption, distribution, metabolism and excretion after exposure by oral route
 - 5.1.2. Absorption, distribution, metabolism and excretion after exposure by other routes
- 5.2. Acute toxicity
 - 5.2.1. Oral
 - 5.2.2. Dermal
 - 5.2.3. Inhalation

- 5.2.4. Skin irritation
- 5.2.5. Eye irritation
- 5.2.6. Skin sensitisation
- 5.2.7. Phototoxicity
- 5.3. Short-term toxicity
 - 5.3.1. Oral 28-day study
 - 5.3.2. Oral 90-day study
 - 5.3.3. Other routes
- 5.4. Genotoxicity testing
 - 5.4.1. *In vitro* studies
 - 5.4.2. *In vivo* studies in somatic cells
 - 5.4.3. *In vivo* studies in germ cells
- 5.5. Long-term toxicity and carcinogenicity
- 5.6. Reproductive toxicity
 - 5.6.1. Generational studies
 - 5.6.2. Developmental toxicity studies
- 5.7. Neurotoxicity studies
 - 5.7.1. Neurotoxicity studies in rodents
 - 5.7.2. Delayed polyneuropathy studies
- 5.8. Other toxicological studies
 - 5.8.1. Toxicity studies of metabolites
 - 5.8.2. Supplementary studies on the active substance
 - 5.8.3. Endocrine disrupting properties
- 5.9. Medical data
 - 5.9.1. Medical surveillance on manufacturing plant personnel and monitoring studies
 - 5.9.2. Data collected on humans
 - 5.9.3. Direct observations
 - 5.9.4. Epidemiological studies
 - 5.9.5. Diagnosis of poisoning (determination of active substance, metabolites), specific signs of poisoning, clinical tests
 - 5.9.6. Proposed treatment: first aid measures, antidotes, medical treatment
 - 5.9.7. Expected effects of poisoning
- SECTION 6. **Residues in or on treated products, food and feed**
 - 6.1. Storage stability of residues
 - 6.2. Metabolism, distribution and expression of residues
 - 6.2.1. Plants
 - 6.2.2. Poultry
 - 6.2.3. Lactating ruminants

- 6.2.4. Pigs
 - 6.2.5. Fish
 - 6.3. Magnitude of residue trials in plants
 - 6.4. Feeding studies
 - 6.4.1. Poultry
 - 6.4.2. Ruminants
 - 6.4.3. Pigs
 - 6.4.4. Fish
 - 6.5. Effects of processing
 - 6.5.1. Nature of the residue
 - 6.5.2. Distribution of the residue in inedible peel and pulp
 - 6.5.3. Magnitude of residues in processed commodities
 - 6.6. Residues in rotational crops
 - 6.6.1. Metabolism in rotational crops
 - 6.6.2. Magnitude of residues in rotational crops
 - 6.7. Proposed residue definitions and maximum residue levels
 - 6.7.1. Proposed residue definitions
 - 6.7.2. Proposed maximum residue levels (MRLs) and justification of the acceptability of the levels proposed
 - 6.7.3. Proposed maximum residue levels (MRLs) and justification of the acceptability of the levels proposed for imported products (import tolerance)
 - 6.8. Proposed safety intervals
 - 6.9. Estimation of the potential and actual exposure through diet and other sources
 - 6.10. Other studies
 - 6.10.1. Residue level in pollen and bee products
- SECTION 7. *Fate and behaviour in the environment***
- 7.1. Fate and behaviour in soil
 - 7.1.1. Route of degradation in soil
 - 7.1.1.1. Aerobic degradation
 - 7.1.1.2. Anaerobic degradation
 - 7.1.1.3. Soil photolysis
 - 7.1.2. Rate of degradation in soil
 - 7.1.2.1. Laboratory studies
 - 7.1.2.1.1. Aerobic degradation of the active substance
 - 7.1.2.1.2. Aerobic degradation of metabolites, breakdown and reaction products
 - 7.1.2.1.3. Anaerobic degradation of the active substance
 - 7.1.2.1.4. Anaerobic degradation of metabolites, breakdown and reaction products
 - 7.1.2.2. Field studies
 - 7.1.2.2.1. Soil dissipation studies
 - 7.1.2.2.2. Soil accumulation studies

- 7.1.3. Adsorption and desorption in soil
 - 7.1.3.1. Adsorption and desorption
 - 7.1.3.1.1. Adsorption and desorption of the active substance
 - 7.1.3.1.2. Adsorption and desorption of metabolites, breakdown and reaction products
 - 7.1.3.2. Aged sorption
- 7.1.4. Mobility in soil
 - 7.1.4.1. Column leaching studies
 - 7.1.4.1.1. Column leaching of the active substance
 - 7.1.4.1.2. Column leaching of metabolites, breakdown and reaction products
 - 7.1.4.2. Lysimeter studies
 - 7.1.4.3. Field leaching studies
- 7.2. Fate and behaviour in water and sediment
 - 7.2.1. Route and rate of degradation in aquatic systems (chemical and photochemical degradation)
 - 7.2.1.1. Hydrolytic degradation
 - 7.2.1.2. Direct photochemical degradation
 - 7.2.1.3. Indirect photochemical degradation
 - 7.2.2. Route and rate of biological degradation in aquatic systems
 - 7.2.2.1. 'Ready biodegradability'
 - 7.2.2.2. Aerobic mineralisation in surface water
 - 7.2.2.3. Water/sediment study
 - 7.2.2.4. Irradiated water/sediment study
 - 7.2.3. Degradation in the saturated zone
- 7.3. Fate and behaviour in air
 - 7.3.1. Route and rate of degradation in air
 - 7.3.2. Transport via air
 - 7.3.3. Local and global effects
- 7.4. Definition of the residue
 - 7.4.1. Definition of the residue for risk assessment
 - 7.4.2. Definition of the residue for monitoring
- 7.5. Monitoring data

SECTION 8. *Ecotoxicological studies*

Introduction

- 8.1. Effects on birds and other terrestrial vertebrates
 - 8.1.1. Effects on birds
 - 8.1.1.1. Acute oral toxicity to birds
 - 8.1.1.2. Short-term dietary toxicity to birds
 - 8.1.1.3. Sub-chronic and reproductive toxicity to birds
 - 8.1.2. Effects on terrestrial vertebrates other than birds

- 8.1.2.1. Acute oral toxicity to mammals
- 8.1.2.2. Long-term and reproductive toxicity to mammals
- 8.1.3. Active substance bioconcentration in prey of birds and mammals
- 8.1.4. Effects on terrestrial vertebrate wildlife (birds, mammals, reptiles and amphibians)
- 8.1.5. Endocrine disrupting properties
- 8.2. Effects on aquatic organisms
 - 8.2.1. Acute toxicity to fish
 - 8.2.2. Long-term and chronic toxicity to fish
 - 8.2.2.1. Fish early life stage toxicity test
 - 8.2.2.2. Fish full life cycle test
 - 8.2.2.3. Bioconcentration in fish
 - 8.2.3. Endocrine disrupting properties
 - 8.2.4. Acute toxicity to aquatic invertebrates
 - 8.2.4.1. Acute toxicity to *Daphnia magna*
 - 8.2.4.2. Acute toxicity to an additional aquatic invertebrate species
 - 8.2.5. Long-term and chronic toxicity to aquatic invertebrates
 - 8.2.5.1. Reproductive and development toxicity to *Daphnia magna*
 - 8.2.5.2. Reproductive and development toxicity to an additional aquatic invertebrate species
 - 8.2.5.3. Development and emergence in *Chironomus riparius*
 - 8.2.5.4. Sediment dwelling organisms
 - 8.2.6. Effects on algal growth
 - 8.2.6.1. Effects on growth of green algae
 - 8.2.6.2. Effects on growth of an additional algal species
 - 8.2.7. Effects on aquatic macrophytes
 - 8.2.8. Further testing on aquatic organisms
- 8.3. Effect on arthropods
 - 8.3.1. Effects on bees
 - 8.3.1.1. Acute toxicity to bees
 - 8.3.1.1.1. Acute oral toxicity
 - 8.3.1.1.2. Acute contact toxicity
 - 8.3.1.2. Chronic toxicity to bees
 - 8.3.1.3. Effects on honeybee development and other honeybee life stages
 - 8.3.1.4. Sub-lethal effects
 - 8.3.2. Effects on non-target arthropods other than bees
 - 8.3.2.1. Effects on *Aphidius rhopalosiphi*
 - 8.3.2.2. Effects on *Typhlodromus pyri*
- 8.4. Effects on non-target soil meso- and macrofauna
 - 8.4.1. Earthworm — sub-lethal effects

- 8.4.2. Effects on non-target soil meso- and macrofauna (other than earthworms)
- 8.4.2.1. Species level testing
- 8.5. Effects on soil nitrogen transformation
- 8.6. Effects on terrestrial non-target higher plants
- 8.6.1. Summary of screening data
- 8.6.2. Testing on non-target plants
- 8.7. Effects on other terrestrial organisms (flora and fauna)
- 8.8. Effects on biological methods for sewage treatment
- 8.9. Monitoring data

SECTION 9. **Literature data**

SECTION 10. **Classification and labelling**

SECTION 1

Identity of the active substance

The information provided shall be sufficient to precisely identify each active substance and define it in terms of its specification and nature.

1.1. **Applicant**

The name and address of the applicant shall be provided, as well as the name, position, telephone, e-mail address and telefax number of a contact point.

1.2. **Producer**

The name and address of the producer of the active substance shall be provided, as well as the name and address of each manufacturing plant in which the active substance is manufactured. A contact point (name, telephone, e-mail address and telefax number) shall be provided. Where following approval of the active substances, there are changes in the location or number of producers, the information required shall again be notified to the Commission, the Authority and the Member States.

1.3. **Common name proposed or ISO-accepted, and synonyms**

The International Organization for Standardization (ISO) common name, or proposed ISO common name and where relevant, other proposed or accepted common names (synonyms), including the name (title) of the nomenclature authority concerned, shall be provided.

1.4. **Chemical name (IUPAC and CA nomenclature)**

The chemical name as given in Part III of Annex VI to Regulation (EC) No 1272/2008, or, if not included in that Regulation, in accordance with both the International Union of Pure and Applied Chemistry (IUPAC) and Chemical Abstracts (CA) nomenclature, shall be provided, where applicable.

1.5. **Producer's development code numbers**

Code numbers used to identify the active substance, and where available, formulations containing the active substance, during development work, shall be reported. For each code number reported, the material to which it relates, the period for which it was used, and the Member States or other countries in which it was used and is being used, shall be stated.

1.6. **CAS, EC and CIPAC numbers**

Chemical Abstracts Service (CAS), European Commission (EC) and Collaborative International Pesticides Analytical Council (CIPAC) numbers, where they exist, shall be reported.

1.7. **Molecular and structural formula, molar mass**

The molecular formula, molar mass and structural formula of the active substance, and where relevant, the structural formula of each isomer present in the active substance, shall be provided.

For plant extracts, a different approach may be taken if adequately justified.

1.8. Method of manufacture (synthesis pathway) of the active substance

The method of manufacture, in terms of the identity (name, CAS number, structural formula) and purity of the starting materials and whether they are commercially available, the chemical pathways involved, and the identity of impurities present in the final product, shall be provided, for each manufacturing plant. Detailed information shall be given as to the origin of those impurities. Each impurity shall be categorised as resulting from side reactions, impurities in the starting material, remaining reaction intermediates or starting materials. Their toxicological, ecotoxicological and environmental relevance shall be addressed. This information shall also include impurities that are not detected but that could theoretically be formed. Generally process engineering information is not required.

Where the required information is provided for a pilot plant production system, that information shall again be provided once industrial scale production methods and procedures have stabilised. Where available, industrial scale data shall be provided before approval under Regulation (EC) No 1107/2009. Where data on industrial scale production are not available, a justification shall be provided.

1.9. Specification of purity of the active substance in g/kg

The minimum content in g/kg of pure active substance in the manufactured material used for production of plant protection products, shall be reported. A justification shall be provided for the minimum content proposed in the specification; this shall include a statistical analysis of the data on at least five representative batches, as referred to in point 1.11. Additional supporting data may be provided to further justify the technical specification.

Where the required information is provided for a pilot plant production system, that information shall again be provided once industrial scale production methods and procedures have stabilised. Where available, industrial scale data shall be provided before approval under Regulation (EC) No 1107/2009. Where data on industrial scale production are not available, a justification shall be provided.

If the active substance is manufactured as technical concentrate (TK), the minimum and maximum content of the pure active substance shall be given, along with its content in the theoretical dry weight material.

If the active substance is a mixture of isomers, the ratio or the ratio range of the content of isomers shall be provided. The relative biological activity of each isomer, both in terms of efficacy and toxicity, shall be reported.

For plant extracts, a different approach may be taken if adequately justified.

1.10. Identity and content of additives (such as stabilisers) and impurities

The minimum and maximum content in g/kg of each additive shall be provided.

The maximum content in g/kg of each further component other than additives shall also be provided.

If the active substance is manufactured as technical concentrate (TK), the maximum content of each impurity shall be given, along with their content in the theoretical dry weight material.

Isomers that are not part of the ISO common name are considered as impurities.

Where the information provided does not fully identify a component (for example condensates), detailed information on the composition shall be provided for each such component.

Where the required information is provided for a pilot plant production system, that information shall again be provided once industrial scale production methods and procedures have stabilised. Where available, industrial scale data shall be provided before approval under Regulation (EC) No 1107/2009. Where data on industrial scale production are not available, a justification shall be provided.

For plant extracts, a different approach may be taken if adequately justified.

1.10.1. Additives

The trade name of components added to the active substance, prior to manufacture of the plant protection product, to preserve stability and facilitate ease of handling, hereinafter 'additives', shall also be provided. The following information shall, where relevant, be provided for such additives:

- (a) chemical name in accordance with IUPAC and CA nomenclature;
- (b) ISO common name or proposed common name if available;
- (c) CAS number, EC number;
- (d) molecular and structural formula;

- (e) molar mass;
- (f) minimum and maximum content in g/kg; and
- (g) function (for example stabiliser).

1.10.2. Significant impurities

Impurities present in quantities of 1 g/kg or more shall be considered as significant. For significant impurities the following information, where relevant, shall be provided:

- (a) chemical name in accordance with IUPAC and CA nomenclature;
- (b) ISO common name or proposed common name, if available;
- (c) CAS number, EC number;
- (d) molecular and structural formula;
- (e) molar mass; and
- (f) maximum content in g/kg.

Information on how the structural identity of the impurities was determined shall be given.

1.10.3. Relevant impurities

Impurities that are particularly undesirable because of their toxicological, ecotoxicological or environmental properties, shall be considered as relevant. For relevant impurities the following information, where relevant, shall be provided:

- (a) chemical name in accordance with IUPAC and CA nomenclature;
- (b) ISO common name or proposed common name if available;
- (c) CAS number, EC number;
- (d) molecular and structural formula;
- (e) molar mass; and
- (f) maximum content in g/kg.

Information on how the structural identity of the impurities was determined shall be reported.

1.11. Analytical profile of batches

At least five representative batches from recent and current industrial scale production of the active substance shall be analysed for content of pure active substance, impurities, additives and each further component other than additives, as appropriate. All of the representative batches shall be within the last five years of manufacture. Where data from the last five years of production are not available, a justification shall be provided. The analytical results reported shall include quantitative data, in terms of g/kg content, for all components present in quantities of 1 g/kg or more and typically should account for at least 980 g/kg of the material analysed. For plant extracts and semiochemicals (such as pheromones), justified exemptions can be made. The statistical basis for the content proposed in the technical specification shall be explained (for example: maximum level found in practice, average plus three standard deviations of levels found in practice, etc.). Supporting data may be provided to further justify the technical specification. The actual content of components which are particularly undesirable because of their toxicological, ecotoxicological or environmental properties shall be determined and reported even if present in quantities below 1 g/kg. Data reported shall include the results of the analysis of individual samples and a summary of that data, to show the minimum, maximum and mean content of each relevant component.

Where an active substance is produced in different plants the information set out in the first paragraph shall be provided for each of the plants separately.

In addition, where relevant, samples of the active substance produced at laboratory scale or in pilot production systems, shall be analysed, if such material was used in generating toxicological or ecotoxicological data. If this data is not available a justification shall be provided.

Where the information provided relates to a pilot plant production system, the information required shall again be provided once industrial scale production methods and procedures have stabilised. Where available, industrial scale data shall be provided before approval under Regulation (EC) No 1107/2009. Where data on industrial scale production are not available, a justification shall be provided.

SECTION 2

Physical and chemical properties of the active substance

2.1. **Melting point and boiling point**

The melting point or where appropriate the freezing or solidification point of purified active substance shall be determined and reported. Measurements shall be taken up to 360 °C.

The boiling point of purified active substance shall be determined and reported. Measurements shall be taken up to 360 °C.

Where melting point or boiling point cannot be determined because of decomposition or sublimation, the temperature at which decomposition or sublimation occurs shall be reported.

2.2. **Vapour pressure, volatility**

The vapour pressure of purified active substance at 20 °C or 25 °C shall be reported. Where vapour pressure is less than 10^{-5} Pa at 20 °C the vapour pressure at 20 °C or 25 °C shall be estimated by a vapour pressure curve with measurements at higher temperatures.

In the case of active substances which are solids or liquids, volatility (Henry's law constant) of purified active substance shall be determined or calculated from its water solubility and vapour pressure and be reported (in $\text{Pa} \times \text{m}^3 \times \text{mol}^{-1}$).

2.3. **Appearance (physical state, colour)**

A description of both the colour, if any, and the physical state of both the active substance as manufactured and purified active substance, shall be provided.

2.4. **Spectra (UV/VIS, IR, NMR, MS), molar extinction at relevant wavelengths, optical purity**

The following spectra, including a table of signal characteristics needed for interpretation, shall be determined and reported: ultraviolet/visible (UV/VIS), infrared (IR), nuclear magnetic resonance (NMR) and mass spectra (MS) of purified active substance.

Molar extinction at relevant wavelengths shall be determined and reported (ϵ in $\text{L} \times \text{mol}^{-1} \times \text{cm}^{-1}$). Relevant wavelengths include all maxima in the UV/visible absorption spectrum, as well as the wavelength range of 290-700 nm.

In the case of active substances which are resolved optical isomers, the optical purity shall be measured and reported.

Where necessary for the identification of the impurities considered to be of toxicological, ecotoxicological or environmental significance, the UV/visible absorption spectra, IR, NMR and MS spectra, shall be determined and reported.

2.5. **Solubility in water**

The water solubility of purified active substances under atmospheric pressure shall be determined and a value reported for 20 °C. These water solubility determinations shall be made in the neutral range (that is to say in distilled water in equilibrium with atmospheric carbon dioxide). If the pKa is between 2 and 12, water solubility shall also be determined in the acidic range (pH 4 to 5) and in the alkaline range (pH 9 to 10). Where the stability of the active substance in aqueous media is such that water solubility cannot be determined, a justification based on test data shall be provided.

2.6. **Solubility in organic solvents**

The solubility of the active substances as manufactured or purified active substance in the following organic solvents at 15 to 25 °C shall be determined and reported if less than 250 g/L; the temperature applied shall be specified. Results shall be reported as g/L.

- (a) Aliphatic hydrocarbon: preferably heptane
- (b) Aromatic hydrocarbon: preferably toluene
- (c) Halogenated hydrocarbon: preferably dichloromethane

(d) Alcohol: preferably methanol or isopropyl alcohol

(e) Ketone: preferably acetone

(f) Ester: preferably ethyl acetate.

If for a particular active substance, one or more of those solvents is unsuitable (for example reacts with test material), alternative solvents may be used instead. In such cases, choices of solvents shall be justified in terms of their structure and polarity.

2.7. Partition coefficient n-octanol/water

The n-octanol/water partition coefficient (K_{ow} or $\log P_{ow}$) of purified active substance and of all components of the residue definition for risk assessment shall be determined and reported for 20 °C or 25 °C. The effect of pH (4 to 10) shall be investigated when the active substance has a pK_a value between 2 and 12.

2.8. Dissociation in water

Where dissociation in water occurs, the dissociation constants (pK_a values) of the purified active substance shall be determined and reported for 20 °C. The identity of the dissociated species formed, based on theoretical considerations, shall be reported. If the active substance is a salt the pK_a value of the non-dissociated form of the active substance shall be given.

2.9. Flammability and self-heating

The flammability and self-heating of active substances as manufactured shall be determined and reported. A theoretical estimation based on structure shall be accepted if it meets the criteria set out in Appendix 6 of the United Nations' Recommendations on the Transport of Dangerous Goods Manual of Tests and Criteria⁽¹⁾. In justified cases, data for purified active substance may be used.

2.10. Flash point

The flash point of active substances as manufactured with a melting point below 40 °C shall be determined and reported. In justified cases, data for purified active substance may be used.

2.11. Explosive properties

The explosive properties of active substances as manufactured shall be determined and reported. A theoretical estimation based on structure shall be accepted if it meets the criteria set out in Appendix 6 of the United Nations 'Recommendations on the Transport of Dangerous Goods, Manual of Tests and Criteria'. In justified cases, data for purified active substance may be used.

2.12. Surface tension

The surface tension of purified active substance shall be determined and reported.

2.13. Oxidising properties

The oxidising properties of active substances as manufactured, shall be determined and reported. A theoretical estimation based on structure shall be accepted if it meets the criteria set out in Appendix 6 of the United Nations 'Recommendations on the Transport of Dangerous Goods Manual of Tests and Criteria'. In justified cases data for purified active substance may be used.

2.14. Other studies

Supplementary studies necessary for the classification of the active substance by hazard shall be carried out in accordance with Regulation (EC) No 1272/2008.

SECTION 3

Further information on the active substance

3.1. Use of the active substance

The information provided shall describe the intended purposes for which plant protection products containing the active substance are used, or are to be used and the dose and manner of their use or proposed use.

3.2. Function

The function shall be specified from among the following:

(a) acaricide;

(b) bactericide;

⁽¹⁾ United Nations New York and Geneva (2009) Publication ISBN 978-92-1-139135-0.

- (c) fungicide;
- (d) herbicide;
- (e) insecticide;
- (f) molluscicide;
- (g) nematicide;
- (h) plant growth regulator;
- (i) repellent;
- (j) rodenticide;
- (k) semio-chemical;
- (l) talpicide;
- (m) viricide;
- (n) other (shall be specified by the applicant).

3.3. **Effects on harmful organisms**

The nature of the effects on harmful organisms shall be stated:

- (a) contact action;
- (b) stomach action;
- (c) inhalation action;
- (d) fungitoxic action;
- (e) fungistatic action;
- (f) desiccant;
- (g) reproduction inhibitor;
- (h) other (shall be specified by the applicant).

It shall be stated whether or not the active substance is translocated in plants and where relevant whether such translocation is apoplastic, symplastic or both.

3.4. **Field of use envisaged**

The fields of use, existing and proposed, for plant protection products containing the active substance shall be specified from among the following:

- (a) field use, such as agriculture, horticulture, forestry and viticulture;
- (b) protected crops;
- (c) amenity;
- (d) weed control on non-cultivated areas;
- (e) home gardening;
- (f) house plants;
- (g) plant products storage practice;
- (h) other (shall be specified by applicant).

3.5. **Harmful organisms controlled and crops or products protected or treated**

Details of existing use and the intended use in terms of crops, groups of crops, plants, or plant products treated and where relevant protected shall be provided.

Where relevant, details of harmful organisms against which protection is afforded shall be provided.

Where relevant, effects achieved, such as sprout suppression, retardation of ripening, reduction in stem length, enhanced fertilisation shall be reported.

3.6. Mode of action

To the extent that it has been elucidated, a statement shall be provided as to the mode of action of the active substance in terms, where relevant, of the biochemical and physiological mechanisms and biochemical pathways involved. Where available, the results of relevant experimental studies shall be reported.

Where it is known that to exert its intended effect, the active substance has to be converted to a metabolite or breakdown product following application or use of plant protection products containing it, the following information shall be provided for active metabolite or breakdown products:

- (a) chemical name in accordance with IUPAC and CA nomenclature;
- (b) ISO common name or proposed common name;
- (c) CAS-number EC number;
- (d) molecular and structural formula; and
- (e) molar mass.

The information referred to in points (a) to (e) shall be cross referenced to and drawing on information provided under Sections 5 to 8, where relevant.

Available information relating to the formation of active metabolites and breakdown products shall be provided. Such information shall include:

- the processes, mechanisms and reactions involved,
- kinetic and other data concerning the rate of conversion and if known the rate limiting step,
- environmental and other factors effecting the rate and extent of conversion.

3.7. Information on the occurrence or possible occurrence of the development of resistance and appropriate management strategies

Where available, information on the occurrence or possible occurrence of the development of resistance or cross-resistance shall be provided.

Appropriate risk management strategies shall be addressed for national/regional areas.

3.8. Methods and precautions concerning handling, storage, transport or fire

A safety data sheet pursuant to Article 31 of Regulation (EC) No 1907/2006 of the European Parliament and of the Council ⁽¹⁾ shall be provided for all active substances.

The studies, data and information submitted, together with other relevant studies, data and information, shall both specify and justify the methods and precautions to be followed in the event of fire. The possible products of combustion in the event of fire shall be estimated, based on the chemical structure and the chemical and physical properties of the active substance.

3.9. Procedures for destruction or decontamination

In many cases the preferred or sole means to safely dispose of active substances, contaminated materials, or contaminated packaging is through controlled incineration in a licensed incinerator. Such incineration shall be carried out in accordance with the criteria set out in Council Directive 94/67/EC ⁽²⁾.

Other methods to dispose of the active substance, contaminated packaging and contaminated materials, where proposed, shall be fully described. Data shall be provided for such methods, to establish their effectiveness and safety.

3.10. Emergency measures in case of an accident

Procedures for the decontamination of water and soil in case of an accident shall be provided.

The studies, data and information submitted, together with other relevant studies, data and information, shall demonstrate the suitability of measures proposed for use in emergency situations.

⁽¹⁾ OJ L 396, 30.12.2006, p. 1.

⁽²⁾ OJ L 365, 31.12.1994, p. 34.

SECTION 4

Analytical methods**Introduction**

The provisions of this Section cover analytical methods used for the generation of pre-approval data and required for post-approval control and monitoring purposes.

Descriptions of methods shall be provided and include details of equipment, materials and conditions used.

On request, the following shall be provided:

- (a) analytical standards of the purified active substance;
- (b) samples of the active substance as manufactured;
- (c) analytical standards of relevant metabolites and all other components included in all monitoring residue definitions;
- (d) samples of reference substances for the relevant impurities.

Where possible, the standards referred to in points (a) and (c) shall be made commercially available and, on request, the distributing company shall be named.

4.1. Methods used for the generation of pre-approval data**4.1.1. Methods for the analysis of the active substance as manufactured**

Methods shall be provided, with a full description, for the determination of:

- (a) pure active substance in the active substance as manufactured and specified in the dossier submitted in support of approval under Regulation (EC) No 1107/2009;
- (b) significant and relevant impurities and additives (such as stabilisers) in the active substance as manufactured.

The applicability of existing CIPAC methods shall be assessed and reported. In case of use of a CIPAC method, further validation data shall not be required, but example chromatograms shall be submitted, where available.

The specificity of the methods shall be determined and reported. In addition, the extent of interference by other substances present in the active substance as manufactured (such as impurities or additives), shall be determined.

The linearity of methods shall be determined and reported. The calibration range shall extend (by at least 20 %) beyond the highest and lowest nominal content of the analyte in relevant analytical solutions. Either duplicate determinations at three or more concentrations or single determinations at five or more concentrations shall be made. The equation of the calibration line and the correlation coefficient shall be reported and a typical calibration plot shall be submitted. In cases where a non-linear response is used, this shall be justified by the applicant.

The precision (repeatability) of the methods shall be determined and reported. A minimum of five replicate sample determinations shall be made and the mean, the relative standard deviation and the number of determinations shall be reported.

For the determination of the active substance content, an assessment of accuracy of the method shall be made by an assessment of the interference and precision.

As regards additives and significant and relevant impurities:

- the accuracy of the methods shall be determined on at least two representative samples at levels appropriate to the batch data and material specification. The mean and the relative standard deviation of the recoveries shall be reported,
- the experimental determination of the limit of quantification (LOQ) shall not be required. However, it shall be demonstrated that the methods are sufficiently precise to analyse significant impurities at levels appropriate to the material specification and relevant impurities at a concentration equivalent to at least 20 % less than the specification limit.

4.1.2. *Methods for risk assessment*

Methods shall be submitted, with a full description, for the determination of non-isotope-labelled residues in all areas of the dossier, as set out in detail in the following points:

- (a) in soil, water, sediment, air and any additional matrices used in support of environmental fate studies;
- (b) in soil, water and any additional matrices used in support of efficacy studies;
- (c) in feed, body fluids and tissues, air and any additional matrices used in support of toxicology studies;
- (d) in body fluids, air and any additional matrices used in support of operator, worker, resident and bystander exposure studies;
- (e) in or on plants, plant products, processed food commodities, food of plant and animal origin, feed and any additional matrices used in support of residues studies;
- (f) in soil, water, sediment, feed and any additional matrices used in support of ecotoxicology studies;
- (g) in water, buffer solutions, organic solvents and any additional matrices used in the physical and chemical properties tests.

The specificity of the methods shall be determined and reported. Validated confirmatory methods shall be submitted if appropriate.

The linearity, recovery and precision (repeatability) of methods shall be determined and reported.

Data shall be generated at the LOQ and either the likely residue levels or ten times the LOQ. Where relevant, the LOQ shall be determined and reported for each analyte.

4.2. **Methods for post-approval control and monitoring purposes**

Methods, with a full description, shall be submitted for:

- (a) the determination of all components included in the monitoring residue definition as submitted in accordance with the provisions of point 6.7.1 in order to enable Member States to determine compliance with established maximum residue levels (MRLs); they shall cover residues in or on food and feed of plant and animal origin;
- (b) the determination of all components included for monitoring purposes in the residue definitions for soil and water as submitted in accordance with the provisions of point 7.4.2;
- (c) the analysis in air of the active substance and relevant breakdown products formed during or after application, unless the applicant shows that exposure of operators, workers, residents or bystanders is negligible;
- (d) the analysis in body fluids and tissues for active substances and relevant metabolites.

As far as practicable these methods shall employ the simplest approach, involve the minimum cost, and require commonly available equipment.

The specificity of the methods shall be determined and reported. It shall enable all components included in the monitoring residue definition to be determined. Validated confirmatory methods shall be submitted if appropriate.

The linearity, recovery and precision (repeatability) of methods shall be determined and reported.

Data shall be generated at the LOQ and either the likely residue levels or ten times the LOQ. The LOQ shall be determined and reported for each component included in the monitoring residue definition.

For residues in or on food and feed of plant and animal origin and residues in drinking water, the reproducibility of the method shall be determined by means of an independent laboratory validation (ILV) and reported.

SECTION 5

Toxicological and metabolism studies

Introduction

1. The relevance of generating toxicity data in animal models with dissimilar metabolic profiles to those found in humans shall be addressed, if such metabolic information is available, and taken into consideration for study design and risk assessment.
2. All potentially adverse effects found during toxicological investigations (including effects on organs/systems such as the immune system, the nervous system, or the endocrine system) shall be reported. Additional studies may be necessary to investigate the mechanisms underlying effects that could be critical to hazard identification or risk assessment.

All available biological data and information relevant to the assessment of the toxicological profile of the active substance tested, including modelling, shall be reported.

3. Where available, historical control data shall be provided routinely. The data submitted shall be for endpoints that could represent critical adverse effects, and shall be strain-specific and from the laboratory which carried out the index study. They shall cover a five-year period, centred as closely as possible on the date of the index study.
4. When preparing a study plan, available data on the test substance, such as its physico-chemical properties (such as volatility), purity, reactivity (such as rate of hydrolysis, electrophilicity) and structure-activity relationships of chemical analogues, shall be taken into account.
5. For all studies actual achieved dose in mg/kg body weight, as well as in other convenient units (such as mg/L inhalation, mg/cm² dermal), shall be reported.
6. The analytical methods to be used in toxicity studies shall be specific for the entity to be measured and shall be adequately validated. The LOQ shall be adequate for the measurement of the range of concentration anticipated to occur in the generation of the toxicokinetic data.
7. Where, as a result of metabolism or other processes in or on treated plants, in livestock, in soil, in ground water, open air, or as a result of processing of treated products, the terminal residue to which humans will be exposed contains a substance which is not the active substance itself and is not identified as a significant metabolite in mammals, toxicity studies shall, where technically possible, be carried out on that substance unless it can be demonstrated that human exposure to that substance does not constitute a relevant risk to health.

Toxicokinetic and metabolism studies relating to metabolites and breakdown products shall only be required if toxicity findings of the metabolite cannot be evaluated by the available results relating to the active substance.

8. The oral route shall always be used if it is practical. In cases where exposure of humans is mainly by the gas phase, it can be more appropriate to perform some of the studies via inhalation.
9. For dose selection, toxicokinetic data such as saturation of absorption measured by systemic availability of substance and/or metabolites shall be taken into consideration.

5.1. Studies on absorption, distribution, metabolism and excretion in mammals

Information on blood and tissues concentration of the active substance and relevant metabolites, for example around the time to reach the maximum plasma concentration (T_{max}), shall be generated in short and long-term studies on relevant species to enhance the value of the toxicological data generated in terms of understanding the toxicity studies.

The main objective of the toxicokinetic data is to describe the systemic exposure achieved in animals and its relationship to the dose levels and the time course of the toxicity studies.

Other objectives are:

- (a) to relate the achieved exposure in toxicity studies to toxicological findings and contribute to the assessment of the relevance of these findings to human health, with a particular regard to vulnerable groups;

- (b) to support the design of a toxicity study (choice of species, treatment regimen, selection of dose levels) with respect to kinetics and metabolism;
- (c) to provide information which, in relation to the findings of toxicity studies, contributes to the design of supplementary toxicity studies as outlined in point 5.8.2;
- (d) to compare the metabolism of rats with the metabolism in livestock as outlined in point 6.2.4.

5.1.1. *Absorption, distribution, metabolism and excretion after exposure by oral route*

Limited data restricted to one *in vivo* test species (normally rat) may be all that is required as regards absorption, distribution, metabolism and excretion after exposure by oral route. These data can provide information useful in the design and interpretation of subsequent toxicity tests. However, it shall be remembered that information on interspecies differences is crucial in extrapolation of animal data to humans and information on metabolism following administration via other routes may be useful in human risk assessments.

It is not possible to specify detailed data requirements in all areas, since the exact requirements will depend upon the results obtained for each particular test substance.

The studies shall provide sufficient information about the kinetics of the active substance and its metabolites in relevant species after being exposed to the following:

- (a) a single oral dose (low and high dose levels);
- (b) an intravenous dose preferably or, if available, a single oral dose with assessment of biliary excretion (low dose level); and
- (c) a repeated dose.

A key parameter is systemic bioavailability (F), obtained by comparison of the area under the curve (AUC) after oral and intravenous dosing.

When intravenous dosing is not feasible a justification shall be provided.

The design of the kinetic studies required shall include:

- (a) an evaluation of the rate and extent of oral absorption including maximum plasma concentration (C_{max}), AUC, T_{max} and other appropriate parameters, such as bioavailability;
- (b) the potential for bioaccumulation;
- (c) plasma half-lives;
- (d) the distribution in major organs and tissues;
- (e) information on the distribution in blood cells;
- (f) the chemical structure and the quantification of metabolites in biological fluids and tissues;
- (g) the different metabolic pathways;
- (h) the route and time course of excretion of active substance and metabolites;
- (i) investigations whether and to what extent enterohepatic circulation takes place.

Comparative *in vitro* metabolism studies shall be performed on animal species to be used in pivotal studies and on human material (microsomes or intact cell systems) in order to determine the relevance of the toxicological animal data and to guide in the interpretation of findings and in further definition of the testing strategy.

An explanation shall be given or further tests shall be carried out where a metabolite is detected *in vitro* in human material and not in the tested animal species.

5.1.2. *Absorption, distribution, metabolism and excretion after exposure by other routes*

Data on absorption, distribution, metabolism and excretion (ADME) following exposure by the dermal route shall be provided where toxicity following dermal exposure is of concern compared to that following oral exposure. Before investigating ADME *in vivo* following dermal exposure, an *in vitro* dermal penetration study shall be conducted to assess the likely magnitude and rate of dermal bioavailability.

Absorption, distribution, metabolism and excretion after exposure by the dermal route shall be considered on the basis of the above information, unless the active substance causes skin irritation that would compromise the outcome of the study.

Dermal absorption estimation from data generated in these studies on the active substance shall be critically assessed for relevance to humans. Dermal absorption measurement of the plant protection product is specifically considered under point 7.3 of Part A of the Annex to Regulation (EU) No 284/2013.

For volatile active substances (vapour pressure $> 10^{-2}$ Pascal) absorption, distribution, metabolism and excretion after exposure by inhalation may be useful in human risk assessments.

5.2. Acute toxicity

The studies, data and information to be provided and evaluated shall be sufficient to permit the identification of effects following a single exposure to the active substance, and in particular to establish, or indicate:

- (a) the toxicity of the active substance;
- (b) the time course and characteristics of the effects with full details of behavioural changes, clinical signs, where evident, and possible gross pathological findings at post-mortem;
- (c) the possible need to consider establishing acute reference doses (such as ARfD, aAOEL ⁽¹⁾);
- (d) where possible mode of toxic action;
- (e) the relative hazard associated with the different routes of exposure.

While the emphasis shall be on estimating the toxicity ranges involved, the information generated shall also permit the active substance to be classified in accordance with Regulation (EC) No 1272/2008. The information generated through acute toxicity testing is of particular value in assessing hazards likely to arise in accident situations.

5.2.1. Oral

Circumstances in which required

The acute oral toxicity of the active substance shall always be reported.

5.2.2. Dermal

Circumstances in which required

The acute dermal toxicity of the active substance shall be reported unless waiving is scientifically justified (for example where oral LD₅₀ ⁽²⁾ is greater than 2 000 mg/kg). Both local and systemic effects shall be investigated.

Findings of severe skin irritation (Grade 4 erythema or oedema) in the dermal study shall be used instead of performing a specific irritation study.

5.2.3. Inhalation

Circumstances in which required

The acute inhalation toxicity of the active substance shall be reported where any of the following apply:

- the active substance has a vapour pressure $> 1 \times 10^{-2}$ Pa at 20 °C;
- the active substance is a powder containing a significant proportion of particles of a diameter $< 50 \mu\text{m}$ ($> 1\%$ on weight basis);
- the active substance is included in products that are powders or are applied by spraying.

The head/nose only exposure shall be used, unless whole body exposure can be justified.

5.2.4. Skin irritation

The results of the study shall provide information on the potential for skin irritancy of the active substance including, where relevant, the potential reversibility of the effects observed.

⁽¹⁾ aAOEL, abbreviation for 'Acute AOEL'.

⁽²⁾ LD₅₀, abbreviation for 'Lethal Dose, 50%', that is to say the dose required to kill half the members of a tested population after a specified test duration.

Before undertaking *in vivo* studies for corrosion/irritation of the active substance, a weight-of-evidence analysis shall be performed on the existing relevant data. Where insufficient data are available, they can be developed through application of sequential testing.

The testing strategy shall follow a tiered approach:

- (1) the assessment of dermal corrosivity using a validated *in vitro* test method;
- (2) the assessment of dermal irritation using a validated *in vitro* test method (such as human reconstituted skin models);
- (3) an initial *in vivo* dermal irritation study using one animal, and where no adverse effects are noted;
- (4) confirmatory testing using one or two additional animals.

Circumstances in which required

The skin irritancy study of the active substance shall always be provided. Where available, a dermal toxicity study shown not to produce irritation of the skin at the limit test dose level of 2 000 mg/kg body weight shall be used to waive the need for any dermal irritation studies.

5.2.5. Eye irritation

The results of the study shall provide the potential of eye irritancy of the active substance including, where relevant, the potential reversibility of the effects observed.

Before undertaking *in vivo* studies for eye corrosion/irritation of the active substance, a weight-of-evidence analysis shall be performed on the existing relevant data. Where available data are considered insufficient, further data may be developed through application of sequential testing.

The testing strategy shall follow a tiered approach:

- (1) the use of an *in vitro* dermal irritation/corrosion test to predict eye irritation/corrosion;
- (2) the performance of a validated or accepted *in vitro* eye irritation study to identify severe eye irritants/corrosives (such as Bovine Corneal Opacity and Permeability (BCOP) assay, Isolated Chicken Eye (ICE) assay, Isolated Rabbit Eye (IRE) assay, Hen's Egg Test - Chorio-Allantoic Membrane assay (HET-CAM)), and where negative results are obtained, the assessment of eye irritation using an *in vitro* test method for identification of non-irritants or irritants, and where not available;
- (3) an initial *in vivo* eye irritation study using one animal, and where no adverse effects are noted;
- (4) confirmatory testing using one or two additional animals.

Circumstances in which required

The eye irritancy of the active substance shall always be tested, except where it is likely that severe effects on the eyes may be produced based on criteria listed in the test methods.

5.2.6. Skin sensitisation

The study shall provide sufficient information to assess the potential of the active substance to provoke skin sensitisation reactions.

Circumstances in which required

The study shall always be carried out, except where the active substance is a known sensitiser. The local lymph node assay (LLNA) shall be used, including where appropriate the reduced variant of the assay. In case the LLNA cannot be conducted, a justification shall be provided and the Guinea Pig Maximisation Test shall be performed. Where a guinea pig assay (Maximisation or Buehler), meeting OECD guidelines and providing a clear result, is available, further testing shall not be carried out for animal welfare reasons.

Since an active substance identified as a skin sensitiser can potentially induce hypersensitivity reaction, potential respiratory sensitisation should be taken into account when appropriate tests are available or when there are indications of respiratory sensitisation effects.

5.2.7. Phototoxicity

The study shall provide information on the potential of certain active substances to induce cytotoxicity in combination with light, for example active substances that are phototoxic *in vivo* after systemic exposure and distribution to the skin, as well as active substances that act as photoirritants after dermal application. A positive result shall be taken into account when considering potential human exposure.

Circumstances in which required

The *in vitro* study shall be required where the active substance absorbs electromagnetic radiation in the range 290-700 nm and is liable to reach the eyes or light-exposed areas of skin, either by direct contact or through systemic distribution.

If the Ultraviolet/visible molar extinction/absorption coefficient of the active substance is less than $10 \text{ L} \times \text{mol}^{-1} \times \text{cm}^{-1}$, no toxicity testing is required.

5.3. Short-term toxicity

Short-term toxicity studies shall be designed to provide information as to the amount of the active substance that can be tolerated without adverse effects under the conditions of the study and to elucidate health hazards occurring at higher dose levels. Such studies provide useful data on the risks for those handling and using plant protection products containing the active substance, among other possible exposed groups. In particular, short-term studies provide an essential insight into possible repeated actions of the active substance and the risks to humans who may be exposed. In addition short-term studies provide information useful in the design of chronic toxicity studies.

The studies, data and information to be provided and evaluated, shall be sufficient to permit the identification of effects following repeated exposure to the active substance, and in particular to further establish, or indicate:

- (a) the relationship between dose and adverse effects;
- (b) toxicity of the active substance including where possible the No Observed Adverse Effect Level (NOAEL);
- (c) target organs, where relevant (including immune, nervous and endocrine systems);
- (d) the time course and characteristics of adverse effects with full details of behavioural changes and possible pathological findings at post-mortem;
- (e) specific adverse effects and pathological changes produced;
- (f) where relevant the persistence and reversibility of certain adverse effects observed, following discontinuation of dosing;
- (g) where possible, the mode of toxic action;
- (h) the relative hazard associated with the different routes of exposure;
- (i) relevant critical endpoints at appropriate time points for setting reference values, where necessary.

Toxicokinetic data (that is to say blood concentration) shall be included in short term studies. In order to avoid increased animal use, the data may be derived in range finding studies.

If nervous system, immune system or endocrine system are specific targets in short term studies at dose levels not producing marked toxicity, supplementary studies, including functional testing, shall be carried out (see point 5.8.2).

5.3.1. Oral 28-day study

Circumstances in which required

Where available, 28-day studies shall be reported.

5.3.2. Oral 90-day study

Circumstances in which required

The short-term oral toxicity of the active substance to rodents (90-day), usually the rat, a different rodent species shall be justified, and non rodents (90-day toxicity study in dogs), shall always be reported.

In the 90-day study, potential neurotoxic and immunotoxic effects, genotoxicity by way of micronuclei formation and effects potentially related to changes in the hormonal system shall be carefully addressed.

5.3.3. Other routes

Circumstances in which required

For human risk assessment additional dermal studies shall be considered on a case by case basis, unless the active substance is a severe irritant.

For volatile active substances (vapour pressure $>10^{-2}$ Pascal) expert judgement (for example based on route-specific kinetic data) shall be required to decide whether the short term studies have to be performed by inhalation exposure.

5.4. Genotoxicity testing

The aim of genotoxicity testing shall be to:

- predict genotoxic potential,
- identify genotoxic carcinogens at an early stage,
- elucidate the mechanism of action of some carcinogens.

Appropriate dose levels, depending on the test requirements, shall be used in either *in vitro* or *in vivo* assays. A tiered approach shall be adopted, with selection of higher tier tests being dependent upon interpretation of results at each stage.

Special testing requirements in relation to photomutagenicity may be indicated by the structure of a molecule. If the Ultraviolet/visible molar extinction/absorption coefficient of the active substance and its major metabolites is less than $1\ 000\ \text{L} \times \text{mol}^{-1} \times \text{cm}^{-1}$, photomutagenicity testing is not required.

5.4.1. In vitro studies

Circumstances in which required

The following *in vitro* mutagenicity tests shall be performed: bacterial assay for gene mutation, combined test for structural and numerical chromosome aberrations in mammalian cells and test for gene mutation in mammalian cells.

However, if gene mutation and clastogenicity/aneuploidy are detected in a battery of tests consisting of Ames and *in vitro* micronucleus (IVM), no further *in vitro* testing needs to be conducted.

If there are indications of micronucleus formation in an *in vitro* micronucleus assay further testing with appropriate staining procedures shall be conducted to clarify if there is an aneugenic or clastogenic response. Further investigation of the aneugenic response may be considered to determine whether there is sufficient evidence for a threshold mechanism and threshold concentration for the aneugenic response (particularly for non-disjunction).

Active substances which display highly bacteriostatic properties as demonstrated in a range finding test shall be tested in two different *in vitro* mammalian cell tests for gene mutation. Non performance of the Ames test shall be justified.

For active substances bearing structural alerts that have given negative results in the standard test battery, additional testing may be required if the standard tests have not been optimised for these alerts. The choice of additional study or study plan modifications depends on the chemical nature, the known reactivity and the metabolism data on the structurally alerting active substance.

5.4.2. In vivo studies in somatic cells

Circumstances in which required

If all the results of the *in vitro* studies are negative, at least one *in vivo* study shall be done with demonstration of exposure to the test tissue (such as cell toxicity or toxicokinetic data), unless valid *in vivo* micronucleus data are generated within a repeat dose study and the *in vivo* micronucleus test is the appropriate test to be conducted to address this information requirement.

A negative result in the first *in vivo* test in somatic cells shall provide sufficient reassurance for active substances that are negative in the three *in vitro* tests.

For active substances for which an equivocal or a positive test result is obtained in any *in vitro* test, the nature of additional testing needed shall be considered on a case-by-case basis taking into account all relevant information using the same endpoint as in the *in vitro* test.

If the *in vitro* mammalian chromosome aberration test or the *in vitro* micronucleus test is positive for clastogenicity, an *in vivo* test for clastogenicity using somatic cells such as metaphase analysis in rodent bone marrow or micronucleus test in rodents shall be conducted.

If the *in vitro* micronucleus test for numerical chromosome aberrations on mammalian cells is positive or the *in vitro* mammalian chromosome test is positive for numerical chromosome changes, an *in vivo* micronucleus test shall be conducted. In case of positive result in the *in vivo* micronucleus assay, appropriate staining procedure such as fluorescence in-situ hybridisation (FISH) shall be used to identify an aneugenic and/or clastogenic response.

If either of the *in vitro* gene mutation tests is positive, an *in vivo* test to investigate the induction of gene mutation shall be conducted, such as the Transgenic Rodent Somatic and Germ Cell Gene Mutation Assay.

When conducting *in vivo* genotoxicity studies, only relevant exposure routes and methods (*such as* admixture to diet, drinking water, skin application, inhalation and gavage) shall be used. There shall be convincing evidence that the relevant tissue will be reached by the chosen exposure route and application method. Other exposure techniques (*such as* intraperitoneal or subcutaneous injection) that are likely to result in abnormal kinetics, distribution and metabolism shall be justified.

Consideration shall be given to conducting an *in vivo* test as part of one of the short-term toxicity studies described under point 5.3.

5.4.3. *In vivo* studies in germ cells

Circumstances in which required

The necessity for conducting these tests shall be considered on a case by case basis, taking into account information regarding toxicokinetics, use and anticipated exposure.

For most of the active substances recognised as *in vivo* somatic cell mutagens no further genotoxicity testing shall be necessary since they will be considered to be potential genotoxic carcinogens and potential germ cell mutagens.

However, in some specific cases germ cells studies may be undertaken to demonstrate whether a somatic cell mutagen is or is not a germ cell mutagen.

The type of mutation produced in earlier studies namely gene, numerical chromosome or structural chromosome changes, shall be considered when selecting the appropriate assay.

A study for the presence of DNA adducts in gonad cells may also be considered.

5.5. Long-term toxicity and carcinogenicity

The results of the long-term studies conducted and reported, taken together with other relevant data and information on the active substance, shall be sufficient to permit the identification of effects, following repeated exposure to the active substance, and in particular shall be sufficient to:

- identify adverse effects resulting from long-term exposure to the active substance,
- identify target organs, where relevant,
- establish the dose-response relationship,
- establish the NOAEL and, if necessary, other appropriate reference points.

Correspondingly, the results of the carcinogenicity studies taken together with other relevant data and information on the active substance, shall be sufficient to permit the evaluation of hazards for humans, following repeated exposure to the active substance, and in particular shall be sufficient:

- (a) to identify carcinogenic effects resulting from long-term exposure to the active substance;

- (b) to establish the species, sex, and organ specificity of tumours induced;
- (c) to establish the dose-response relationship;
- (d) where possible, to identify the maximum dose eliciting no carcinogenic effect;
- (e) where possible, to determine the mode of action and human relevance of any identified carcinogenic response.

Circumstances in which required

The long-term toxicity and carcinogenicity of all active substances shall be determined. If in exceptional circumstances it is claimed that such testing is unnecessary, that claim shall be fully justified.

Test conditions

A long-term oral toxicity study and a long-term carcinogenicity study (two years) of the active substance shall be conducted using rat as test species; where possible these studies shall be combined.

A second carcinogenicity study of the active substance shall be conducted using mouse as test species, unless it can be scientifically justified that this is not necessary. In such cases, scientifically validated alternative carcinogenicity models may be used instead of a second carcinogenicity study.

If comparative metabolism data indicate that either rat or mouse is an inappropriate model for human cancer risk assessment, an alternative species shall be considered.

Experimental data, including the elucidation of the possible mode of action involved and relevance to humans, shall be provided where the mode of action for carcinogenicity is considered to be non-genotoxic.

Where submitted, historical control data shall be from the same species and strain, maintained under similar conditions in the same laboratory and shall be from contemporaneous studies. Additional historical control data from other laboratories may be reported separately as supplementary information.

The information on historical control data provided shall include:

- (a) identification of species and strain, name of the supplier, and specific colony identification, if the supplier has more than one geographical location;
- (b) name of the laboratory and the dates when the study was performed;
- (c) description of the general conditions under which animals were maintained, including the type or brand of diet and, where possible, the amount consumed;
- (d) approximate age, in days, and weight of the control animals at the beginning of the study and at the time of killing or death;
- (e) description of the control group mortality pattern observed during or at the end of the study, and other pertinent observations (such as diseases, infections);
- (f) name of the laboratory and the examining scientists responsible for gathering and interpreting the pathological data from the study;
- (g) a statement of the nature of the tumours that may have been combined to produce any of the incidence data.

The historical control data shall be presented on a study by study basis giving absolute values plus percentage and relative or transformed values where these are helpful in the evaluation. If combined or summary data are submitted, these shall contain information on the range of values, the mean, median and, if applicable, standard deviation.

The doses tested, including the highest dose tested, shall be selected on the basis of the results of short-term testing and where available at the time of planning the studies concerned, on the basis of metabolism and toxicokinetic data. Dose selection should consider toxicokinetic data such as saturation of absorption measured by systemic availability of active substance and/or metabolites.

Doses, causing excessive toxicity shall not be considered relevant to evaluations to be made. Determination of blood concentration of the active substance (for example around T_{max}) shall be considered in long-term studies.

In the collection of data and compilation of reports, incidence of benign and malignant tumours shall not be combined. Dissimilar, un-associated tumours, whether benign or malignant, occurring in the same organ, shall not be combined for reporting purposes.

In the interests of avoiding confusion, conventional histopathological terminology commonly used when the study is conducted such as that published by the International Agency for Research on Cancer shall be used in the nomenclature and reporting of tumours. The system used shall be identified.

Biological material selected for histopathological examination shall include material selected to provide further information on lesions identified during gross pathological examination. Where relevant to the elucidation of mechanism of action and available, special histological (staining) techniques, histochemical techniques and electron microscopic examinations, might be of value, and when conducted, shall be reported.

5.6. Reproductive toxicity

Possible effects on reproductive physiology and the development of progeny shall be investigated and reported concerning the following aspects:

- Impairment of male and female reproductive functions or capacity, for example from effects on oestrus cycle, sexual behaviour, any aspect of spermatogenesis or oogenesis, or hormonal activity or physiological response which would interfere with the capacity to fertilise, fertilisation itself or development of the fertilised ovum up to and including implantation.
- Harmful effects on the progeny, for example any effect interfering with normal development, both before and after birth. This includes morphological malformations such as anogenital distance, nipple retention, and functional disturbances (such as reproductive and neurological effects).

Effects accentuated over generations shall be reported.

The active substance and its relevant metabolites shall be measured in milk as a second tier investigation where relevant effects are observed in the offspring or are expected (for example from a range-finding study).

Potential neurotoxic, immunotoxic effects and effects potentially related to changes in the hormonal system shall be carefully addressed and reported.

Investigations shall take account of all available and relevant data, including the results of general toxicity studies if relevant parameters (such as semen analysis, oestrous cyclicity, reproductive organ histopathology) are included, as well as knowledge concerning structural analogues to the active substance.

While the standard reference point for treatment responses shall be concurrent control data, historical control data may be helpful in the interpretation of particular reproductive studies. Where submitted, historical control data shall be from the same species and strain, maintained under similar conditions in the same laboratory and shall be from contemporaneous studies.

The information on historical control data provided shall include:

- (a) identification of species and strain, name of the supplier, and specific colony identification, if the supplier has more than one geographical location;
- (b) name of the laboratory and the dates when the study was performed;
- (c) description of the general conditions under which animals were maintained, including the type or brand of diet and, where possible, the amount consumed;
- (d) approximate age, in days, and weight of the control animals at the beginning of the study and at the time of killing or death;
- (e) description of the control group mortality pattern observed during or at the end of the study, and other pertinent observations (such as diseases, infections);

- (f) name of the laboratory and the examining scientists responsible for gathering and interpreting the pathological data from the study.

The historical control data shall be presented on a study by study basis giving absolute values plus percentage and relative or transformed values where these are helpful in the evaluation. If combined or summary data are submitted, these shall contain information on the range of values, the mean, median and, if applicable, standard deviation.

In order to provide useful information in the design and interpretation of developmental toxicity studies, information on blood concentration of the active substance in parents and foetus/offspring may be included in higher tier studies and reported.

5.6.1. *Generational studies*

The generational studies reported, taken together with other relevant data and information on the active substance, shall be sufficient to permit the identification of effects for reproduction, following repeated exposure to the active substance, and in particular shall be sufficient:

- (a) to identify direct and indirect effects on reproduction resulting from exposure to the active substance;
- (b) to identify any non-reproductive adverse effects occurring at lower doses than in short-term and chronic toxicity testing;
- (c) to establish the NOAELs for parental toxicity, reproductive outcome and pup development.

Circumstances in which required

A reproduction toxicity study in rats over at least two generations shall be reported.

The OECD extended one-generation reproductive toxicity study may be considered as an alternative approach to the multi-generation study.

Where necessary for a better interpretation of the effects on reproduction and as far as this information is not yet available, supplementary studies may be required to provide information on the affected gender and the possible mechanisms.

5.6.2. *Developmental toxicity studies*

The developmental toxicity studies reported, taken together with other relevant data and information on the active substance, shall be sufficient to permit the assessment of effects on embryonic and foetal development, following repeated exposure to the active substance, and in particular shall be sufficient:

- (a) to identify direct and indirect effects on embryonic and foetal development resulting from exposure to the active substance;
- (b) to identify any maternal toxicity;
- (c) to establish the relationship between observed responses and dose in both dam and offspring;
- (d) to establish NOAELs for maternal toxicity and pup development;
- (e) to provide additional information on adverse effects in pregnant as compared with non-pregnant females;
- (f) to provide additional information on any enhancement of general toxic effects of pregnant animals.

Circumstances in which required

Developmental toxicity studies shall always be carried out.

Test conditions

Developmental toxicity shall be determined for rat and rabbit by the oral route; the rat study shall not be conducted if developmental toxicity has been adequately assessed as part of an extended one-generation reproductive toxicity study.

Additional routes may be useful in human risk assessment. Malformations and variations shall be reported separately and combined in such a way that all relevant changes which are observed to occur in characteristic patterns in individual fetuses or those that can be considered to represent different grades of severity of the same type of change are reported in a concise manner.

Diagnostic criteria for malformations and variations shall be given in the report. The glossary of terminology under development by the International Federation of Teratology Societies shall be considered where possible.

When indicated by observations in other studies or the mode of action of the test substance, supplementary studies or information may be required to provide information on the postnatal manifestation of effects such as developmental neurotoxicity.

5.7. Neurotoxicity studies

5.7.1. Neurotoxicity studies in rodents

Neurotoxicity studies in rodents shall provide sufficient data to evaluate the potential neurotoxicity of the active substance (neurobehavioural and neuropathological effects) after single and repeated exposure.

Circumstances in which required

Such studies shall be performed for active substances with structures that are similar or related to those capable of inducing neurotoxicity, and for active substances which induce specific indications of potential neurotoxicity, neurological signs or neuropathological lesions in toxicity studies at dose levels not associated with marked general toxicity. Performance of such studies shall also be considered for substances with a neurotoxic mode of pesticidal action.

Consideration shall be given to including neurotoxicity investigations in routine toxicology studies.

5.7.2. Delayed polyneuropathy studies

Delayed polyneuropathy studies shall provide sufficient data to evaluate if the active substance may provoke delayed polyneuropathy after acute and repeated exposure. A repeated exposure study may be waived unless there are indications that the compound accumulates and significant inhibition of neuropathy target esterase or clinical/histopathological signs of delayed polyneuropathy occur at around the hen LD₅₀ as determined in the single dose test.

Circumstances in which required

These studies shall be performed for active substances of similar or related structures to those capable of inducing delayed polyneuropathy such as organophosphorus compounds.

5.8. Other toxicological studies

5.8.1. Toxicity studies of metabolites

Supplementary studies, where they relate to substances other than the active substance, are not a routine requirement. Decisions as to the need for supplementary studies shall be made on a case by case basis.

Where as a result of metabolism or other processes, metabolites from plants or in animal products, soil, groundwater, open air differ from those in animals used for the toxicology studies or are detected in low proportions in animals, further testing shall be carried out on a case by case basis, taking into account the amount of metabolite and the chemical structure of the metabolite compared to the parent.

5.8.2. Supplementary studies on the active substance

Supplementary studies shall be carried out where they are necessary to further clarify observed effects taking into account the results of the available toxicological and metabolism studies and the most important exposure routes. Such studies may include:

- (a) studies on absorption, distribution, excretion and metabolism, in a second species;
- (b) studies on the immunotoxicological potential;
- (c) a targeted single dose study to derive appropriate acute reference values (ARfD, aAOEL);
- (d) studies on other routes of administration;
- (e) studies on the carcinogenic potential;

(f) studies on mixture effects.

Studies required shall be designed on an individual basis, in the light of the particular parameters to be investigated and the objectives to be achieved.

5.8.3. *Endocrine disrupting properties*

If there is evidence that the active substance may have endocrine disrupting properties, additional information or specific studies shall be required:

- to elucidate the mode/mechanism of action,
- to provide sufficient evidence for relevant adverse effects.

Studies required shall be designed on an individual basis and taking into account Union or internationally agreed guidelines, in the light of the particular parameters to be investigated and the objectives to be achieved.

5.9. **Medical data**

Where available and without prejudice to Article 10 of Council Directive 98/24/EC ⁽¹⁾, practical data and information relevant to the recognition of the symptoms of poisoning and on the effectiveness of first aid and therapeutic measures shall be submitted. Such data and information shall include reports of any studies investigating antidote pharmacology or safety pharmacology. Where relevant, the effectiveness of potential antagonists to poisoning shall be investigated and reported.

Data and information relevant to the effects of human exposure, where available, shall be used to confirm the validity of extrapolations made and conclusions reached with respect to target organs, dose-response relationships, and the reversibility of adverse effects. Such data may be generated following accidental, occupational exposure or incidents of intentional self-poisoning, and shall be reported if available.

5.9.1. *Medical surveillance on manufacturing plant personnel and monitoring studies*

Reports of occupational health surveillance programs and of monitoring studies shall be submitted, supported with detailed information on the design of the programme, the number of exposed persons included in the programme, the nature of their exposure to the active substance, and their exposure to other potentially hazardous agents. Such reports shall, where feasible, include data relevant to the mechanism of action of the active substance. These reports shall, where available, include data from persons exposed in manufacturing plants, or during or after application of the active substance (for example from monitoring studies in operators, workers, residents, bystanders or victims of accidents). Available information on adverse health effects including allergenic responses in workers and others exposed to the active substance, shall be provided, and include where relevant details of any incident. The information provided shall, where available, include details of frequency, level and duration of exposure, symptoms observed and other relevant clinical information.

5.9.2. *Data collected on humans*

Where available, reports from studies with humans, such as tests on toxicokinetics and metabolism, or tests on skin irritation or skin sensitisation, shall be submitted.

In general, the reference values shall be based on animal studies, but if appropriate scientifically valid and ethically generated human data are available and show that humans are more sensitive and lead to lower regulatory limit values, these data shall take precedence over animal data.

5.9.3. *Direct observations*

Available reports from the open literature, relating to clinical cases and poisoning incidents, where they are from refereed journals or official reports, shall be submitted together with reports of any follow-up studies undertaken. Such reports shall, where available, contain complete descriptions of the nature, level and duration of exposure, as well as the clinical symptoms observed, first aid and therapeutic measures applied and measurements and observations made.

⁽¹⁾ OJ L 131, 5.5.1998, p. 11.

Where supported with the necessary level of detail, such documentation shall be used to confirm the validity of extrapolations from animal data to man and to identify unexpected adverse effects which are specific to humans.

5.9.4. *Epidemiological studies*

Relevant epidemiological studies shall be submitted, where available.

5.9.5. *Diagnosis of poisoning (determination of active substance, metabolites), specific signs of poisoning, clinical tests*

Where available, detailed description of the clinical signs and symptoms of poisoning, including the early signs and symptoms and full details of clinical tests useful for diagnostic purposes shall be provided including full details of the time courses involved relevant to the ingestion, dermal exposure or inhalation of varying amounts of the active substance.

5.9.6. *Proposed treatment: first aid measures, antidotes, medical treatment*

First aid measures to be used in the event of poisoning (actual and suspected) and in the event of contamination of eyes shall be provided. Therapeutic regimes for use in the event of poisoning or contamination of eyes, including where available the use of antidotes, shall be described in full. Information based on practical experience, where it exists and is available, in other cases on theoretical grounds, as to the effectiveness of alternative treatment regimes, where relevant, shall be provided. Contraindications associated with particular regimes, particularly those relating to 'general medical problems' and conditions, shall be described.

5.9.7. *Expected effects of poisoning*

Where known, the expected effects and the duration of these effects following poisoning shall be described. That description shall include the impact of:

- the type, level and duration of exposure, or ingestion, and
- varying time periods between exposure, or ingestion, and commencement of treatment.

SECTION 6

Residues in or on treated products, food and feed

6.1. **Storage stability of residues**

Studies concerning storage stability of residues shall investigate the stability of residues in plants, plant products and products of animal origin during storage prior to analysis.

Circumstances in which required

Provided that samples are frozen within 24 hours after sampling and unless a compound is otherwise known to be volatile or labile, stability data shall not be required for samples extracted and analysed within 30 days from sampling (six months in the case of radio-labelled material).

The stability of extracts shall be investigated if extracts are not analysed immediately.

Test conditions

Studies with non-radio-labelled active substances shall be carried out with representative substrates. They may be either performed on samples from treated crops or animals with incurred residues or by fortification experiments. In the latter case, aliquots of prepared control samples shall be spiked with a known amount of chemical before storage under normal storage conditions.

The studies shall address stability of individual components of the residue definition relevant to risk assessment, which may require spiking different samples with different analytes. In case of different analytical targets (for example targeting either single compounds or a common moiety) more than one set of storage stability data may be needed.

The duration of the stability studies shall be suitable to address the length over which the samples or extracts have been stored in the corresponding studies.

Detailed information with respect to the sample preparation and storage conditions (temperature and duration) of samples and extracts shall be submitted. Where the degradation during storage is significant (more than 30%) a change in the storage conditions or not storing the samples prior to analysis shall be considered. All studies where unsatisfactory storage conditions were used shall be repeated.

Storage stability data using sample extracts shall also be required unless samples are analysed within 24 hours of extraction.

Results shall be presented as absolute values in mg/kg and not adjusted by recovery, as well as percentage of nominal spike value.

6.2. **Metabolism, distribution and expression of residues**

Data on metabolism representative for existing or intended good agricultural practices (GAPs) shall be provided, together with a schematic diagram of the metabolic pathways in plants and animals with a brief explanation of the distribution and chemical reactions involved. These studies shall be conducted with one or more radio-labelled forms of the active substance and, where relevant, stereoisomer forms of the active substance and its metabolites. For plant extracts, a different approach may be taken if adequately justified.

For plants, the objectives of these studies shall be:

- (a) to provide an estimate of total terminal residues in the relevant portion of crops at harvest following treatment as proposed;
- (b) to identify the major components of the total terminal residue;
- (c) to indicate the distribution of residues between relevant crops parts;
- (d) to quantify the major components of the residue and to show the efficiency of extraction procedures for these components;
- (e) to characterise and quantify conjugated and bound residues;
- (f) to indicate the components to be analysed for in residue quantification studies (crop residue studies).

For food producing animals, the objectives of these studies shall be:

- (a) to provide an estimate of total terminal residues in edible animal products;
- (b) to identify the major components of the total terminal residue in edible animal products;
- (c) to indicate the distribution of residues between relevant edible animal products;
- (d) to provide evidence whether or not a residue should be classified as fat soluble;
- (e) to quantify the total residue in certain animal products (milk or eggs) and excreta;
- (f) to quantify the major components of the residue and to show the efficiency of extraction procedures for these components;
- (g) to characterise and quantify conjugated and bound residues;
- (h) to indicate the components to be analysed for in residue quantification studies (livestock feeding studies);
- (i) to generate data from which a decision on the need for feeding studies on food producing animals can be made.

The results of the metabolism study conducted with poultry, normally laying hens, shall be extrapolated to all food producing poultry whereas the results of the metabolism study conducted with ruminants, normally lactating goats and, where necessary, with pigs, shall be extrapolated to all food producing mammals.

Metabolites not found in the ADME studies or that cannot be explained as intermediates, but identified in metabolism/transformation studies (plant, food producing animals, processing and rotational crops) shall be considered relevant for the consumer risk assessment, unless it can be demonstrated by scientific evidence (such as structure-activity relationship, toxicological bridging studies) that, also in view of their concentration, they cause no potential risks to the consumer.

6.2.1. *Plants*

Circumstances in which required

Studies on plants shall be performed unless no part of the plants or plant products will be used as food or feed material or unless a 'zero' residue situation applies (such as bait applications).

Test conditions

The intended method of application (such as seed treatment, soil/foliar spraying, dipping, fogging) and the properties of the active substance (such as systemic properties or volatility) shall be taken into account when planning metabolism studies. Metabolism studies have to involve crops from different categories of crops in which plant protection products containing the active substance in question would be used. For this purpose crops shall be considered as falling into one of the following categories:

- (a) fruit (code F);
- (b) root crops (code R);
- (c) leafy crops (code L);
- (d) cereal/grass crops (code C/G);
- (e) pulses and oilseeds (code P/O);
- (f) miscellaneous.

The category 'miscellaneous' shall only be used on a case by case basis.

A metabolism study shall be submitted for each type of crop group for which use is proposed. In order to extrapolate results from metabolism studies with an active substance to all crop groups, metabolism studies on a minimum of three representative crops (from the different crop groups except 'miscellaneous') shall be conducted. If the results of these three studies indicate a comparable metabolic route (qualitatively and to a lesser extent quantitatively), then additional studies shall not be needed. If the results from the available studies from three of these categories indicate that the route of degradation is not similar in all three categories, studies from the remaining categories except 'miscellaneous' shall be provided.

If authorisation is sought for one crop group only, metabolism studies in one crop from that crop group shall be sufficient as long as the crop is truly representative of the crop group and the metabolic pathway is elucidated.

The studies shall reflect the intended use pattern of the active ingredient such as foliar, soil/seed or post-harvest treatments. If, for instance, three studies have been conducted using foliar application and at a later date soil application (such as seed treatment, granular or soil drench) is proposed, then at least one additional study reflecting soil application shall be conducted. The applicant shall discuss with the national competent authorities the possible replacement of a foliar study with a post-harvest study.

An evaluation of the results from different studies shall be submitted on:

- (a) the site of uptake (for example via leaves or roots);
- (b) the formation of metabolites and breakdown products;
- (c) the distribution of residues between relevant parts of the crop at harvest (with particular emphasis on food and feed);
- (d) the metabolic pathways.

If studies show that the active substance or relevant metabolites or breakdown products are not taken up by the crop, a rationale shall be given.

6.2.2. Poultry

Circumstances in which required

Metabolism studies on poultry shall be provided where the plant protection product is to be used in crops whose parts or products, also after processing, are fed to poultry and where the intake is expected to exceed 0,004 mg/kg bw/day⁽¹⁾.

Test conditions

Studies shall be carried out in laying hens.

Dose rates shall be at least equivalent to the likely maximum daily exposure resulting from all intended uses.

If the identification of metabolites cannot be carried out with dose rates of 10 mg/kg feed (dry matter), higher doses may be used.

If no feeding studies are carried out, plateau levels in eggs shall be demonstrated in the metabolism study taking into account that plateau levels usually occur no later than 14 days from the beginning of dosing in laying poultry.

6.2.3. Lactating ruminants

Circumstances in which required

Metabolism studies on lactating ruminants shall be provided where the plant protection product is to be used in crops whose parts or products, also after processing, are fed to ruminants and where the intake is expected to exceed 0,004 mg/kg bw/day.

Test conditions

Studies shall be carried out in lactating goats, where available, or in lactating cows as an alternative.

Dose rates shall at least be equivalent to the likely maximum daily exposure resulting from all intended uses.

If the identification of main metabolites cannot be carried out with dose rates of 10 mg/kg feed (dry matter), higher doses may be used.

If no feeding studies are carried out, plateau levels in milk shall be demonstrated in the metabolism study taking into account that plateau levels usually occur five to seven days after the beginning of dosing in lactating ruminants.

6.2.4. Pigs

Circumstances in which required

Metabolism studies on pigs shall be provided where the plant protection product is used in crops whose parts or products, also after processing, are fed to pigs and where it becomes apparent that metabolic pathways differ significantly in the rat as compared to ruminants and where the intake is expected to exceed 0,004 mg/kg bw/day.

Test conditions

Studies shall be carried out in pigs.

Dose rates shall at least be equivalent to the likely maximum daily exposure resulting from all intended uses.

If the identification of metabolites cannot be carried out with dose rates of 10 mg/kg feed (dry matter), higher doses may be used.

The duration of this study shall be the same as for lactating ruminants.

⁽¹⁾ mg/kg bw/day = mg active substance / kg body weight of the concerned species / day.

6.2.5. Fish

Circumstances in which required

Metabolism studies on fish may be required where the plant protection product is used in crops whose parts or products, also after processing, are fed to fish and where residues in feed may occur from the intended applications.

Results from studies provided for under point 8.2.2.3 may be used if it can be demonstrated with scientific evidence that the results of these studies may be assumed to be equivalent. Special consideration shall be given to the different routes of ingestion.

6.3. Magnitude of residue trials in plants

The objectives of magnitude of residue trials in plants shall be the following:

- to quantify the highest likely residue levels of all components of the different residue definitions in treated crops, at harvest or outloading from store, in accordance with the proposed GAP, and
- to determine, where appropriate, the decline rate of plant protection product residues in plants.

Circumstances in which required

These studies shall always be performed where the plant protection product is to be applied to plants or plant products that are used as food or feed or where residues from soil or other substrates can be taken up by such plants except where extrapolation from adequate data on another crop is possible.

When planning residue trials, it shall be borne in mind that information on the residues in ripe or unripe crops may be of interest with respect to the risk assessment in other areas like ecotoxicology or worker safety.

Test conditions

Supervised residue trials shall correspond to the proposed critical GAP. The test conditions (such as maximum number of proposed applications, shortest interval between applications, maximum application rate and concentration, most critical safety intervals ⁽¹⁾ with regard to exposure) shall be defined to identify the highest residues which may reasonably arise and shall be representative of the realistic conditions at the critical GAP in which the active substance is to be used.

When establishing a supervised residue trial programme, factors such as main growing areas and the range of conditions, likely to be encountered in the main growing areas concerned shall be considered.

Differences in agricultural production methods (for example outdoor versus indoor uses), seasons of production and types of formulations shall be taken into account.

For the evaluation of residue behaviour and the setting of maximum residue levels (MRLs) according to Regulation (EC) No 396/2005, the Union shall be divided into two zones, a Northern European and a Southern European zone. For the purpose of use in greenhouses, as post-harvest treatment and for treatment of empty storage rooms, one residue zone shall apply.

The number of trials necessary is difficult to determine before the evaluation of their results. Assuming all other variables having an impact on the residue levels are comparable, the minimum number of trials shall vary for each residue zone between a minimum of 4 trials for a minor crop and a minimum of 8 trials for a major crop.

However, if the GAP is the same in both residue zones, 6 trials equally distributed in the representative growing zones are normally sufficient for a minor crop.

The number of studies to be performed may be reduced if residue trials show that the residue levels in plants or plant products are lower than the LOQ. The number of trials shall not be below the minimum of three per zone for minor crops and four per zone for major crops.

⁽¹⁾ Safety intervals refer in this Section to pre-harvest intervals (PHIs), withholding periods or storage periods in the case of post-harvest treatments.

In cases where a 'zero' residue situation is predicted from representative plant metabolism studies, three trials shall be performed for commodities significant in diet. No trials shall be required for commodities insignificant in diet. A 'zero' residue situation shall be predicted where no detectable residues occur in studies with exaggerated application rates compared to the envisaged ones.

Provided that conditions are comparable and that trials are widely spread over different zones, it shall be sufficient to carry out trials over one growing season.

Part of the trials may be replaced by trials performed outside the Union, provided that they correspond to the critical GAP and that the production conditions (such as cultural practices, climatic conditions) are comparable.

Trials showing the residue behaviour in post-harvest treatments shall be carried out at different locations with different cultivars. A set of trials shall be carried out for each application method and storage condition, unless the worst case residue situation can be clearly identified.

Where a plant protection product has both a field use and an indoor use with the same GAP, a full data package shall be submitted for both situations, unless it is already accepted that one use is the critical GAP.

It shall be checked on a case-by-case basis, taking into account plant morphology and application conditions, whether extrapolation from the crop used for the metabolism study to other crops belonging to the same crop group is possible.

Where a significant part of the consumable commodity is present at the time of application, half of the supervised residue trials reported shall include data to show the effect of time on the level of residue present (residue decline studies), unless the consumable part is not exposed during application of the plant protection product under the proposed conditions of use. For crops harvested after blossom (such as fruits or fruiting vegetables) a significant part of the consumable crop is present from full blossom (BBCH 65) onwards. In case of most crops from which leafy parts are harvested (for example lettuce), this condition is satisfied if 6 true leaves, leaf pairs or whorls are unfolded (BBCH 16).

In case of an active substance for which an ARfD has been derived, the distribution of residues among single units may be investigated through variability studies. If a sufficient number of results is available, the default variability factor may be replaced by a specific factor derived from these studies.

6.4. Feeding studies

The objective of feeding studies shall be to determine residues in products of animal origin which result from residues in feed.

The results from a feeding study conducted with laying hens shall be extrapolated to all food producing poultry. The results from a feeding study with lactating cows and, where necessary, with pigs shall be extrapolated to all food producing mammals.

Circumstances in which required

Feeding studies shall be provided where metabolism studies indicate that residues at levels of above 0,01 mg/kg may occur in edible animal tissue, milk, eggs or fish, taking into account the residue levels in potential feeding stuffs, obtained at the $1 \times$ dose rate, calculated on the dry weight basis.

Feeding studies shall not be required where intake is below 0,004 mg/kg bw/day, except in cases where the residue, that is to say the active substance, its metabolites or breakdown products, as defined in the residue definition for risk assessment, tends to accumulate.

6.4.1. Poultry

Poultry feeding studies shall be carried out in laying hens. For each treatment regime chosen a minimum of nine chickens should be treated.

In general, the feed shall be administered in three dosages (first dose = expected residue level). The animals shall be dosed for a minimum of 28 days or until plateau level is reached in eggs.

6.4.2. Ruminants

Ruminant feeding studies shall be carried out in lactating cows. For each treatment regime chosen, a minimum of three dairy cows shall be treated.

In general, the feed shall be administered in three dosages (first dose = expected residue level). The animals shall be dosed for a minimum of 28 days or until plateau level is reached in milk.

6.4.3. Pigs

Where it appears from the metabolism studies that metabolic pathways differ significantly in pigs as compared to ruminants, a pig feeding study may be conducted. For each treatment regime chosen a minimum of three pigs shall be treated.

In general, the feed shall be administered in three dosages (first dose = expected residue level). The animals shall be dosed for at least the same time as ruminants.

6.4.4. Fish

A fish feeding study may be required where residues at levels above 0,01 mg/kg may be reasonably expected in edible tissues, based on the findings of the fish metabolism study and the estimated maximum residues which might occur in fish feed. Particular attention should be laid on lipophilic substances with an intrinsic tendency for accumulation.

6.5. Effects of processing

6.5.1. Nature of the residue

The objective of studies on the nature of the residue shall be to establish whether or not breakdown or reaction products arise from residues in the raw agricultural commodity during processing, which may require a separate risk assessment.

Circumstances in which required

Studies on the nature of residues in processing shall be provided where residues in products of plant or animal origin subject to processing may occur at a level of or higher than 0,01 mg/kg (based on the residue definition for risk assessment for the raw commodity). No studies shall, however, be required in the following cases:

- substances with a water solubility < 0,01 mg/L;
- only simple physical operations, not involving a change in temperature of the commodity are carried out, such as washing, trimming or pressing; or
- the distribution of residues between pulp and inedible peel is the only effect of processing.

Test conditions

Depending upon the expected level and chemical nature of the residue in the product of plant or animal origin, a set of representative hydrolysis situations simulating the relevant processing operations shall be investigated, where appropriate. Consideration shall also be given to the effects of processes other than hydrolysis and the potential for the formation of toxicologically significant breakdown products.

The studies shall be conducted with one or more radio-labelled forms of the relevant substance.

6.5.2. Distribution of the residue in inedible peel and pulp

The objectives of studies concerning distribution of the residue in inedible peel and pulp shall be:

- to determine the quantitative distribution of residues between inedible peel and pulp,
- to estimate peeling factors, and
- to allow a more realistic estimation of dietary intake of residues.

Circumstances in which required

These studies shall be provided for plant products where the peel is either inedible (such as melons, bananas) or is very rarely entirely eaten by consumers (such as citrus fruit).

Test conditions

These studies shall be performed as part of supervised residue trials, the number of results reported depending on the number of residue trials conducted. Special attention shall be paid to possible contamination of the pulp. Precautionary measures shall be taken in order to quantify a realistic highest residue level.

6.5.3. Magnitude of residues in processed commodities

The main objectives of studies concerning magnitude of residues in processed commodities shall be:

- to determine the quantitative distribution of residues in the various processed commodities used as food or feed,
- to estimate processing factors, and
- to allow a more realistic estimation of dietary intake of residues.

Circumstances in which required

The following points shall be taken into consideration when deciding whether it is necessary to carry out processing studies:

- (a) the dietary burden of a processed product in the human (such as apples) or animal diet (such as apple pomace);
- (b) the level of residue in the plant or plant product to be processed (normally $\geq 0,1$ mg/kg);
- (c) the physical and chemical properties of the active substance and its relevant metabolites (such as fat-solubility in case of oil seed processing); and
- (d) the possibility that breakdown products of toxicological significance may occur after processing of the plant or plant product.

If the level of residues is less than 0,1 mg/kg, processing studies shall be carried out if the contribution of the commodity under consideration to the theoretical maximum daily intake (TMDI) is ≥ 10 % of the ADI or if the estimated daily intake is ≥ 10 % of the ARfD for any European consumer group diet.

Processing studies shall not be required if plants or plant products are exclusively used raw (unprocessed) for food and feed purposes.

In some cases, a simple calculation shall be sufficient to determine the processing factor such as concentration from dehydration or dilution factors, as long as the process under consideration is not expected to have an influence on the nature of residues.

Industrial processing

If the properties of the active substance, the impurity or the metabolite, as appropriate, indicate that it might concentrate in a given processed fraction, then a processing study shall be necessary even in situations where the residue in the plant or plant product to be processed is lower than 0,1 mg/kg. In such cases, exaggerated application rates up to 5 × or shortened PHIs shall be applied where necessary to achieve a quantifiable residue in the plant or plant product to be processed. A processing study shall not be required if exaggerated application rates (up to 5 ×) fail to yield a quantifiable residue in the plant or plant product to be processed. Phytotoxicity shall be considered when contemplating exaggerated rate treatments.

Domestic processing

For domestic or home transformation processes and minor industrial ones, when no residues are found at or above 0,1 mg/kg in the raw agricultural commodity at recommended GAP from supervised field trials conducted at the maximum label rate and minimum PHI, no processing studies shall be required.

Test conditions

Processing studies shall represent domestic preparations (for example cooked vegetables) or commercial industrial processes (for example production of apple juice). Processing studies shall be carried out at least on a representative crop of a crop group, where use is envisaged. The choice of the crop and of the process shall be justified and explained.

The technology used in processing studies shall correspond as closely as possible to the actual conditions that are normally used. For each crop to be investigated two studies per process shall be carried out to determine concentration and dilution factors in processed commodities. If more than one processing method is in use, the one which is expected to give the highest residues in the processed product for human consumption shall be chosen. The results shall be extrapolated to all crops within a crop group undergoing the same process.

When the results (processing factor) of the two studies differ in the main processed products by more than 50 %, further studies shall be provided to derive a consistent processing factor.

Additional studies shall be carried out if, when using processing factors derived by extrapolation, the estimate of the dietary intake exceeds the ADI or ARfD. Those studies shall be carried out on major processes and commodities which contribute most to the ADI/ARfD exceedance.

6.6. Residues in rotational crops

Studies concerning residues in rotational crops shall be performed to allow the determination of the nature and extent of potential residue accumulation in rotational crops from soil uptake and of the magnitude of residues in rotational crops under realistic field conditions.

Rotational crop studies shall not be required for uses of plant protection products in permanent crops (such as citrus and pome fruits crop group), semi-permanent crops (such as asparagus, pineapples) or fungi, where rotations on the same substrate are not part of the normal agricultural practices.

6.6.1. Metabolism in rotational crops

The objectives of metabolism studies in rotational crops shall be:

- (a) to provide an estimate of the total terminal residues in the relevant portion of crops at harvest of rotational crops following treatment of the preceding crop as proposed;
- (b) to identify the major components of the total terminal residue;
- (c) to indicate the distribution of residues between relevant crop parts;
- (d) to quantify the major components of the residue;
- (e) to indicate additional components to be analysed for in residue quantification studies (field crop rotation studies);
- (f) to decide on restrictions in crop rotation; and
- (g) to decide on the necessity of field residue trials in rotational crops (limited field studies).

Circumstances in which required

Metabolism studies in rotational crops shall be provided if the parent compound or soil metabolites are persistent in soil or significant concentrations of metabolites in soil occur.

Rotational crop metabolism studies shall not be required if worst case conditions can be appropriately represented by other available studies in treated crops in accordance with point 6.2.1, where the plant protection product was applied directly to the soil (for example as a pre-planting or pre-emergence application).

Test conditions

Metabolism studies shall at least involve three crops from three different groups of crops: root and tuber vegetables, leafy vegetables and cereals. Data from further crop groups may be relevant for MRL setting. These crops shall be planted into soil treated at the recommended maximum total application rate for the preceding crops after an appropriate plant-back interval that mimics crop failure early in the vegetation of the crop, crop rotation in the same vegetation period or year and crop rotation in the next vegetation period or year.

6.6.2. *Magnitude of residues in rotational crops*

The objectives of studies on residues in rotational crops shall be:

- (a) to permit an evaluation of the magnitude of residues in rotational crops;
- (b) to decide on restrictions in crop rotation;
- (c) to provide information for assessing the overall significance of the residues for dietary risk assessment; and
- (d) to decide on the necessity of MRLs for rotational crops.

Circumstances in which required

If the metabolism studies indicate that residues of the active substance or of relevant metabolites or breakdown products either from plant or soil metabolism may occur ($> 0,01$ mg/kg), limited field studies and, if necessary, field trials shall be carried out.

Studies shall not be required in the following cases:

- no metabolism studies on rotational crops are to be performed, or
- metabolism studies on rotational crops show that no residues of concern are to be expected in rotational crops.

Test conditions

A tiered approach shall be adopted to fulfil the above mentioned objectives. In the first tier, limited field studies at two sites in major growing areas shall be conducted. The plant protection product for which authorisation is sought or a very similar formulation shall be used.

No further studies shall be required where, based on the result from the first tier studies, no detectable residues ($< 0,01$ mg/kg) in rotational crops are to be expected or if in metabolism studies no residues requiring risk assessment are observed.

For the second tier, additional data shall be submitted to enable appropriate evaluation of dietary risks and establishment of MRLs. These studies shall cover the common crop rotation practice. They shall be performed taking into account the requirements under point 6.3. Trials shall be conducted as closely as possible to agricultural practice on representative crops from major crop groups. At least four trials per crop shall be conducted across the Union in one year. These trials shall be performed in the main production areas across the Union at the highest application rate for the preceding crops. If annual applications of persistent active substances result in higher plateau concentrations in soil than a single application, the plateau concentration shall be taken into account. The necessary residue trials data shall be set up in consultation with the national competent authorities in the Member States.

6.7. **Proposed residue definitions and maximum residue levels**

6.7.1. *Proposed residue definitions*

The following elements shall be considered when judging which compounds are to be included in the residue definition:

- the toxicological significance of the compounds,
- the amounts likely to be present, and
- the analytical methods proposed for post-approval control and monitoring purposes.

Two different residue definitions may be needed: one for enforcement purposes, based on the marker concept, and one for risk assessment purposes, taking into account toxicologically relevant compounds.

Analytical work in residue trials and feeding studies shall cover all the components of the residue definition for risk assessment.

6.7.2. *Proposed maximum residue levels (MRLs) and justification of the acceptability of the levels proposed*

A maximum residue level shall be provided for all products of plant and animal origin covered by Regulation (EC) No 396/2005. In all other cases of products of plant and animal origin used as food or feed and in case of tobacco and medical herbs, a guideline level, that is to say a level derived on the same principles used for MRL setting, shall be provided.

For processed products processing factors shall be provided, unless no processing studies are required.

Furthermore, supervised trials median residue (STMR) and highest residue (HR) values shall be derived and, in cases where processing factors are proposed, STMR-P and HR-P values.

In exceptional cases, when the conditions laid down in Article 16(1) to Regulation (EC) No 396/2005 are met, MRLs may be proposed on the basis of monitoring data. In such cases the proposal shall cover the 95th percentile of the data population at the 95 % confidence level.

6.7.3. *Proposed maximum residue levels (MRLs) and justification of the acceptability of the levels proposed for imported products (import tolerance)*

Point 6.7.2 shall apply to MRLs proposed for imported products (import tolerances).

6.8. **Proposed safety intervals**

Safety intervals (that is to say pre-harvest intervals for envisaged uses, or withholding periods or storage periods, in the case of post-harvest uses) shall be set taking into account the pest to be controlled and the results from the residue trial data. These intervals shall last at least one day.

6.9. **Estimation of the potential and actual exposure through diet and other sources**

When estimating the exposure it shall be born in mind that the risk assessment has to take into account the residue definition established for risk assessment.

Where relevant, the possible presence of pesticide residues arising from sources other than current plant protection uses of active substances (for example use of active substances resulting in common metabolites, use as biocide or veterinary drug), and their aggregate exposure shall be taken into account. In addition, the cumulative exposure to more than one active substance shall, where relevant, be considered.

6.10. **Other studies**

6.10.1. *Residue level in pollen and bee products*

The objective of these studies shall be to determine the residue in pollen and bee products for human consumption resulting from residues taken up by honeybees from crops at blossom.

The type and conditions of the studies to be performed shall be discussed with the national competent authorities.

SECTION 7

Fate and behaviour in the environment

7.1. **Fate and behaviour in soil**

All relevant information on the type and the properties of the soil used in the studies, including pH, organic carbon content, particle size distribution and water holding capacity shall be reported.

The microbial biomass of soils used for laboratory degradation studies shall be determined immediately before the commencement and at the end of the study.

The soils used for degradation, adsorption and desorption or mobility studies shall be representative of the range of agricultural soils typical of the various regions of the Union where use exists or is anticipated.

The soils shall fulfil the following conditions:

- they shall cover a range of organic carbon content, particle size distribution and pH_(preferably CaCl₂) values, and
- where on the basis of other information, degradation or mobility are expected to be pH dependent, for example solubility and hydrolysis rate (see points 2.7 and 2.8), they shall cover approximately the following pH_(preferably CaCl₂) ranges: 5 to 6, 6 to 7 and 7 to 8.

Soils used shall, wherever possible, be freshly sampled. If use of stored soils is unavoidable, storage shall be carried out for a limited time (at the most three months) under defined and reported conditions, which are adequate to maintain soil microbial viability. Soils stored for longer periods of time may only be used for adsorption/desorption studies.

A soil having extreme characteristics with respect to parameters such as particle size distribution, organic carbon content and pH shall not be used.

Field studies shall be carried out in conditions as close to normal agricultural practice as possible on a range of soils and climatic conditions representative of the areas of use. Weather conditions shall be reported in cases where field studies are conducted.

7.1.1. *Route of degradation in soil*

The data and information provided, together with other relevant data and information, shall be sufficient to:

- (a) identify, if possible, the relative importance of the types of processes involved (balance between chemical and biological degradation);
- (b) identify the individual components present which at any time account for more than 10 % of the amount of active substance added, including, if possible, non-extractable residues;
- (c) identify, if possible, the individual components which in at least two sequential measurements, account for more than 5 % of the amount of active substance added;
- (d) identify, if possible, the individual components (> 5 %) for which at the end of the study the maximum of formation is not yet reached;
- (e) identify or characterise, if possible, other individual components present;
- (f) establish the relative proportions of the components present (mass balance); and
- (g) permit the soil residue of concern to which non-target species are or may be exposed, to be defined.

For the purposes of this Section non-extractable residues means chemical species originating from active substances contained in plant protection products used in accordance with good agricultural practice that cannot be extracted by methods which do not significantly change the chemical nature of these residues or the nature of the soil matrix. These non-extractable residues are not considered to include fragments through metabolic pathways leading to natural products.

7.1.1.1. *Aerobic degradation*

Circumstances in which required

The pathway or pathways of aerobic degradation shall be reported except where the nature and manner of use of plant protection products containing the active substance precludes soil contamination, such as indoor uses on stored products or brush applied wound healing treatments for trees.

Test conditions

Studies on the degradation pathway or pathways shall be reported for at least one soil. Oxygen levels shall be maintained at levels that do not restrict micro-organisms ability to metabolise aerobically. If there is reason to believe that the route of degradation is dependent on one or more properties of the soil, such as pH or clay content, the route of degradation shall be reported for at least one additional soil for which dependent properties are different.

Results obtained shall be presented in the form of schematic drawings showing the pathways involved, and in the form of balance sheets which show the distribution of radio-label as a function of time, as between:

- (a) active substance;
- (b) CO₂;

- (c) volatile compounds other than CO₂;
- (d) individual identified transformation products referred to in point 7.1.1;
- (e) extractable substances not identified; and
- (f) non-extractable residues in soil.

The investigation of degradation pathways shall include all possible steps to characterise and quantify non-extractable residues formed after 100 days when exceeding 70 % of the applied dose of the active substance. The techniques and methodologies applied shall be selected on a case-by-case basis. A justification shall be provided where the compounds involved are not characterised.

The duration of the study shall be at least 120 days, except where after a shorter period the levels of non-extractable residues and CO₂ are such that they can be extrapolated in a reliable way to 100 days. It shall be longer where this is necessary to establish the degradation pathway of the active substance and its metabolites, breakdown or reaction products.

7.1.1.2. Anaerobic degradation

Circumstances in which required

An anaerobic degradation study shall be submitted unless the applicant shows that exposure of the plant protection products containing the active substance to anaerobic conditions is unlikely to occur for the intended uses.

Test conditions

Point 7.1.1.1 shall apply as regards test conditions except oxygen levels which shall be minimised as to ensure that micro-organisms metabolise anaerobically.

7.1.1.3. Soil photolysis

Circumstances in which required

A soil photolysis study shall be submitted unless the applicant shows that deposition of the active substance on the soil surface is unlikely to occur or that photolysis is not expected to contribute significantly to the degradation of the active substance in soil for example due to low light absorbance of the active substance.

7.1.2. Rate of degradation in soil

7.1.2.1. Laboratory studies

Laboratory studies on soil degradation shall provide best possible estimates of the time required for degradation of 50 % and 90 % (DegT_{50,lab} and DegT_{90,lab}) of the active substance, its metabolites, breakdown and reaction products under laboratory conditions.

7.1.2.1.1. Aerobic degradation of the active substance

Circumstances in which required

The rate of degradation in soil shall be reported, except where the nature and manner of use of plant protection products containing the active substance preclude soil contamination such as indoor uses on stored products or brush applied wound healing treatments for trees.

Test conditions

Studies on the rate of aerobic degradation of the active substance shall be reported for three soils in addition to the one required under point 7.1.1.1. Reliable DegT₅₀ and 90 values shall be available for a minimum of four different soils.

The duration of the study shall be at least 120 days. It shall be longer where this is necessary to establish the kinetic formation fractions of the metabolites, breakdown or reaction products. If more than 90 % of the active substance is degraded before the period of 120 days expires, the test duration may be shorter.

In order to assess the influence of temperature on degradation, a calculation with an adequate Q₁₀ factor or an adequate number of additional studies at a range of temperatures shall be performed.

7.1.2.1.2. *Aerobic degradation of metabolites, breakdown and reaction products*

Circumstances in which required

Aerobic degradation (DegT50 and 90 values) from a minimum of three different soils shall be provided for metabolites, breakdown and reaction products which occur in soil if one of the following conditions is fulfilled:

- (a) they account for more than 10 % of the amount of active substance added at any time during the studies;
- (b) they account for more than 5 % of the amount of active substance added in at least two sequential measurements;
- (c) the maximum of formation is not reached at the end of the study but accounts for at least 5 % of the active substance at the final measurement;
- (d) all metabolites found in lysimeter studies at annual average concentrations exceed 0.1 µg/L in the leachate.

Studies shall not be required where three DegT50 and 90 values can be reliably determined from the results of the degradation studies where the active substance is applied as test substance.

Test conditions

Test conditions shall be those indicated in Section 7.1.2.1.1 except the test substance applied will be the metabolite, breakdown or reaction product. Studies on metabolites, breakdown and reaction products shall be provided where these are necessary to obtain reliable DegT50 and 90 values for at least three different soils.

7.1.2.1.3. *Anaerobic degradation of the active substance*

Circumstances in which required

The rate of anaerobic degradation of the active substance shall be reported where an anaerobic study has to be performed in accordance with point 7.1.1.2.

Test conditions

Anaerobic DegT50 and 90 values for the active substance are needed for the test conditions outlined in point 7.1.1.2.

7.1.2.1.4. *Anaerobic degradation of metabolites, breakdown and reaction products*

Circumstances in which required

Anaerobic degradation studies shall be provided for metabolites, breakdown and reaction products which occur in soil if they fulfil one of the following conditions:

- (a) at any time during the studies account for more than 10 % of the amount of active substance added;
- (b) in at least two sequential measurements account for more than 5 % of the amount of active substance added, if feasible;
- (c) at the end of the study the maximum of formation is not yet reached but accounts for at least 5 % of the active substance at the final measurement, if feasible.

The applicant may deviate from such requirement by showing that DegT50 values for metabolites, breakdown and reaction products can be reliably determined from the results of the anaerobic degradation studies with the active substance.

Test conditions

Studies on metabolites, breakdown and reaction products shall be provided for one soil for the test conditions outlined at point 7.1.1.2.

7.1.2.2. *Field studies*

7.1.2.2.1. *Soil dissipation studies*

The soil dissipation studies shall provide estimates of the time required for dissipation of 50 % and 90 % ($DisT50_{field}$ and $DisT90_{field}$) and, if possible, of the time required for degradation of 50 % and 90 % ($DegT50_{field}$ and $DegT90_{field}$), of the active substance under field conditions. Where relevant, information on metabolites, breakdown and reaction products shall be provided.

Circumstances in which required

Such studies shall be conducted for the active substance, its metabolites, breakdown and reaction products if one of the following conditions is fulfilled:

- (a) DegT50_{lab} for active substance, DegT50_{lab} or DisT50_{lab} for metabolites, breakdown and reaction products, in one or more soils determined at 20 °C and at a moisture content of the soil related to a pF value of 2 (suction pressure) is greater than 60 days; or
- (b) DegT90_{lab} for active substance, DegT90_{lab} or DisT90_{lab} for metabolites, breakdown and reaction products, in one or more soils determined at 20 °C and at a moisture content of the soil related to a pF value of 2 (suction pressure) is greater than 200 days.

However, where plant protection products containing the active substance are intended for use in cold climatic conditions, the studies shall be conducted if one of the following conditions is fulfilled:

- (a) DegT50_{lab} for active substance, DegT50_{lab} or DisT50_{lab} for metabolites, breakdown and reaction products, determined at 10 °C and at a moisture content of the soil related to a pF value of 2 (suction pressure) is greater than 90 days; or
- (b) DegT90_{lab} for active substance, DegT90_{lab} or DisT90_{lab} for metabolites, breakdown and reaction products, in one or more soils, determined at 10 °C and at a moisture content of the soil related to a pF value of 2 (suction pressure) is greater than 300 days.

If during field studies metabolites, breakdown and reaction products which are present in laboratory studies are below the lowest technically feasible LOQ, which shall not exceed an equivalent of 5 % (molar basis) of the nominal concentration of active ingredient applied, no additional information on the fate and behaviour of these compounds shall be provided. In those cases, a scientifically valid justification for any discrepancy between laboratory and field appearance of metabolites shall be provided.

Test conditions

Individual studies on a range of representative soils (normally at least four different types at different geographical locations) shall be continued until at least 90% of the amount applied has dissipated from the soil or been transformed to substances that are not the subject of the investigation.

7.1.2.2.2. Soil accumulation studies

Soil accumulation studies shall provide sufficient information to evaluate the possibility of accumulation of residues of the active substance and of metabolites, breakdown and reaction products. The soil accumulation studies shall provide estimates of the time required for dissipation of 50 % and 90 % (DisT50_{field} and DisT90_{field}) and, if possible, shall provide estimates of the time required for degradation of 50 % and 90 % (DegT50_{field} and DegT90_{field}), of the active substance under field conditions.

Circumstances in which required

Where on the basis of soil dissipation studies it is established that DisT90_{field}, in one or more soils, is greater than one year and where repeated application is envisaged, whether in the same growing season or in succeeding years, the possibility of accumulation of residues in soil and the level at which a plateau concentration is achieved shall be investigated except where reliable information can be provided by a model calculation or another appropriate assessment.

Test conditions

Long-term field studies shall be performed on at least two relevant soils at different geographical locations and involve multiple applications.

In absence of guidance being included in the list referred to under point 6 of the introduction, the type and conditions of the study to be performed shall be discussed with the national competent authorities.

7.1.3. Adsorption and desorption in soil

7.1.3.1. Adsorption and desorption

The information provided, together with other relevant data, shall be sufficient to establish the adsorption coefficient of the active substance and of its metabolites, breakdown and reaction products.

7.1.3.1.1. *Adsorption and desorption of the active substance*

Circumstances in which required

Studies on adsorption and desorption of the active substance shall be provided, except where the nature and manner of use of plant protection products containing the active substance preclude soil contamination such as indoor uses on stored products or brush applied wound healing treatments for trees.

Test conditions

Studies on the active substance shall be reported for at least four soils.

Where the batch equilibrium method cannot be applied due to fast degradation, methods such as studies with short equilibration times, QSPR (Quantitative Structure Property Relationship) or the HPLC (High-Performance Liquid Chromatography) method shall be considered as possible alternatives. Where the batch equilibrium method cannot be applied due to weak adsorption, column leaching studies (see point 7.1.4.1) shall be considered as an alternative.

7.1.3.1.2. *Adsorption and desorption of metabolites, breakdown and reaction products*

Circumstances in which required

Studies on adsorption and desorption shall be provided for all metabolites, breakdown and reaction products, for which in soil degradation studies one of the following conditions is fulfilled:

- (a) they account for more than 10 % of the amount of active substance added, at any time during the studies;
- (b) they account for more than 5 % of the amount of active substance added in at least two sequential measurements;
- (c) the maximum of formation is not reached at the end of the study but accounts for at least 5 % of the active substance at the final measurement;
- (d) all metabolites found in lysimeter studies at annual average concentrations exceeding 0,1 µg/L in the leachate.

Test conditions

Studies on metabolites, breakdown and reaction products shall be provided for at least three soils.

Where the batch equilibrium method cannot be applied due to fast degradation, methods such as studies with short equilibration times, QSPR or the HPLC method shall be considered as an alternative. Where the batch equilibrium method cannot be applied due to weak adsorption, column leaching studies (see point 7.1.4.1) shall be considered as an alternative.

7.1.3.2. *Aged sorption*

As a higher tier option, information on aged sorption may be provided.

Circumstances in which required

The need to carry out a study on aged sorption shall be discussed with the national competent authorities.

Test conditions

In absence of guidance being included in the list referred to under point 6 of the introduction, the type and conditions of the study to be performed shall be discussed with the national competent authorities. The influence on the rate of degradation shall also be considered. Aged sorption data shall be compatible with the model in which those values will be used.

7.1.4. *Mobility in soil*

7.1.4.1. *Column leaching studies*

7.1.4.1.1. *Column leaching of the active substance*

Column leaching studies shall provide sufficient data to evaluate the mobility and leaching potential of the active substance.

Circumstances in which required

Studies in at least four soils shall be carried out where in the adsorption and desorption studies provided for under point 7.1.2 it is not possible to obtain reliable adsorption coefficient values due to weak adsorption (such as $K_{oc} < 25$ L/Kg).

7.1.4.1.2. *Column leaching of metabolites, breakdown and reaction products*

The test shall provide sufficient data to evaluate the mobility and leaching potential of metabolites, breakdown and reaction products.

Circumstances in which required

Studies in at least three soils shall be carried out where in the adsorption and desorption studies provided for under point 7.1.2 it is not possible to obtain reliable adsorption coefficient values due to weak adsorption (such as $K_{oc} < 25$ L/Kg).

7.1.4.2. *Lysimeter studies*

Lysimeter studies shall be performed, where necessary, to provide information on:

- the mobility in soil,
- the potential for leaching to ground water,
- the potential distribution in soil.

Circumstances in which required

The decision whether lysimeter studies are to be carried out, as an experimental outdoor study in the framework of a tiered leaching assessment scheme shall take into account the results of degradation and other mobility studies and the predicted environmental concentrations in groundwater (PEC_{GW}), calculated in accordance with the provisions of Section 9 of Part A of the Annex to Regulation (EU) No 284/2013. The type and conditions of the study to be performed shall be discussed with the national competent authorities.

Test conditions

Studies shall cover the realistic worst case situation, and the duration necessary for observation of potential leaching, taking into account the soil type, climatic conditions, the application rate and the frequency and period of application.

Water percolating from soil columns shall be analysed at suitable intervals, while residues in plant material shall be determined at harvest. Residues in the soil profile in at least five layers shall be determined on termination of experimental work. Intermediate sampling shall be avoided, since removal of plants (except for harvesting in accordance with normal agricultural practice) and soil influence the leaching process.

Precipitation, soil and air temperatures shall be recorded at regular intervals, at least on a weekly base.

The depth of the lysimeters shall be at least 100 cm. The soil cores shall be undisturbed. Soil temperatures shall be similar to those pertaining in the field. Where necessary, supplementary irrigation shall be provided to ensure optimal plant growth and to ensure that the quantity of percolation water is similar to that in the regions for which authorisation is sought. When during the study the soil has to be disturbed for agricultural reasons it shall not be disturbed deeper than 25 cm.

7.1.4.3. *Field leaching studies*

Field leaching studies shall be performed, where necessary, to provide information on:

- the mobility in soil,
- the potential for leaching to ground water,
- the potential distribution in soil.

Circumstances in which required

The decision whether field leaching studies are to be carried out, as an experimental outdoor study in the framework of a tiered leaching assessment scheme shall take into account the results of degradation and

other mobility studies and the predicted environmental concentrations in groundwater (PEC_{GW}), calculated in accordance with the provisions of Section 9 of Part A of the Annex to Regulation (EU) No 284/2013. The type and conditions of the study to be performed shall be discussed with the national competent authorities.

Test conditions

Studies shall cover the realistic worst case situation, taking into account the soil type, climatic conditions, the application rate and the frequency and period of application.

Water shall be analysed at suitable intervals. Residues in the soil profile in at least five layers shall be determined on termination of experimental work. Intermediate sampling of plant and soil material shall be avoided (except for harvesting in accordance with normal agricultural practice), since removal of plants and soil influence the leaching process.

Precipitation, soil and air temperatures shall be recorded at regular intervals (at least on a weekly base).

Information on the groundwater table in the experimental fields shall be submitted. Depending on the experimental design, a detailed hydrological characterisation of the test field shall be carried out. If soil cracking is observed during the study this shall be fully described.

Attention shall be given to the number and the location of water collection devices. The placement of these devices in the soil shall not result in preferential flow paths.

7.2. **Fate and behaviour in water and sediment**

The information provided, taken together with that provided for one or more plant protection products containing the active substance, and other relevant information, shall be sufficient to establish or permit estimation of:

- (a) persistence in water systems (bottom sediment and water, including suspended particles);
- (b) the extent to which water and sediment organisms are at risk;
- (c) potential for contamination of surface water and groundwater.

7.2.1. *Route and rate of degradation in aquatic systems (chemical and photochemical degradation)*

The data and information provided, together with other relevant data and information, shall be sufficient to:

- (a) identify the relative importance of the types of processes involved (balance between chemical and biological degradation);
- (b) where possible, identify the individual components present;
- (c) establish the relative proportions of the components present and their distribution as between water, including suspended particles, and sediment; and
- (d) permit the residue of concern to which non-target species are or may be exposed, to be defined.

7.2.1.1. **Hydrolytic degradation**

Circumstances in which required

The hydrolysis rate of purified active substances shall be determined and reported at 20 °C or 25 °C. Studies on hydrolytic degradation shall also be performed for degradation and reaction products which account at any time for more than 10 % of the amount of active substance added in the hydrolysis study, unless sufficient information on their degradation is available from the test performed with the active substance. No additional hydrolysis information on degradates shall be required if they are considered to be stable in water.

Test conditions

The hydrolysis rate for pH 4, 7 and 9 under sterile conditions in the absence of light shall be determined and reported at 20 °C or 25 °C. For active substances that are stable or have a low rate of hydrolysis at 20-25 °C, the rate shall be determined at 50 °C, or another temperature above 50 °C. If degradation is observed at 50 °C or above, the degradation rate at at least three other temperatures shall be determined and an Arrhenius plot shall be constructed to permit an estimate to be made of hydrolysis rate at 20 °C and 25 °C. The identity of hydrolysis products formed and the rate constants observed, shall be reported. The estimated DegT50 values shall be reported for 20 °C or 25 °C.

7.2.1.2. Direct photochemical degradation

Circumstances in which required

For compounds with a molar (decadic) absorption coefficient (ϵ) $> 10 \text{ L} \times \text{mol}^{-1} \times \text{cm}^{-1}$ at a wavelength (λ) $\geq 295 \text{ nm}$ direct phototransformation of purified active substances shall be determined and reported unless the applicant shows that contamination of surface water will not occur.

Studies on direct photochemical degradation shall also be performed for metabolites, breakdown and reaction products which account at any time for more than 10 % of the amount of active substance added in the photolysis study, unless sufficient information on their degradation is available from the test performed with the active substance.

No additional photolysis information on degradates shall be required if they are considered to be stable under photolytic conditions.

Test conditions

The direct phototransformation in purified, (for example distilled) buffered water using artificial light under sterile conditions, if necessary using a solubiliser, shall be determined and reported. In the first theoretical step a maximum possible photolysis rate shall be estimated based on the molar extinction coefficient of the active substance. If photolysis is considered to be a potentially significant degradation pathway, photolysis experiments for range finding shall be carried out (tier 2). Determination of quantum yield and direct photolysis route/rate (tiers 3 and 4) shall be carried out for active substances where tier 2 indicates significant photolysis. The identity of breakdown products formed which exceed 10 % of the applied test substance at any time during the study, a mass balance to account for at least 90 % of the applied radioactivity, as well as photochemical half-life (DT50) shall be reported.

7.2.1.3. Indirect photochemical degradation

Circumstances in which required

Studies on indirect photochemical degradation may be submitted where there are indications from other available data that route and rate of degradation in the water phase can be significantly influenced by indirect photodegradation.

Test conditions

Studies shall be performed in an aqueous system containing organic (humic substances) and inorganic (salts) compounds in a composition that is typical for natural surface waters.

7.2.2. Route and rate of biological degradation in aquatic systems

7.2.2.1. 'Ready biodegradability'

Circumstances in which required

The 'ready biodegradability' test shall be performed. If no such test is provided, the active substance shall by default be considered not 'readily biodegradable'.

7.2.2.2. Aerobic mineralisation in surface water

The data and information provided, together with other relevant data and information, shall be sufficient to:

- (a) identify individual components present, which at any time account for more than 10 % of the amount of active substance added, including, where possible, non-extractable residues;
- (b) identify individual components present, which account for more than 5 % of the amount of active substance added in at least two sequential measurements, where possible;
- (c) identify individual components ($> 5 \%$) for which at the end of the study the maximum of formation is not yet reached, where possible;
- (d) identify or characterise, where possible, other individual components;
- (e) establish, where relevant, the relative proportions of the components (mass balance); and
- (f) permit, where relevant, the sediment residue of concern and to which non-target species are or may be exposed, to be defined.

Circumstances in which required

Studies on aerobic mineralisation in surface water shall be provided unless the applicant shows that contamination of open water (freshwater, estuarine and marine) will not occur.

Test conditions

The rate of degradation and the pathway or pathways shall be reported either for a 'pelagic' test system or for a 'suspended sediment' system. Where relevant, additional test systems, which differ with respect to organic carbon content, texture or pH shall be used.

Results obtained shall be presented in the form of schematic drawings showing the pathways involved, and in the form of balance sheets which show the distribution of radio-label in water and, where relevant, sediment as a function of time, as between:

- (a) active substance;
- (b) CO₂;
- (c) volatile compounds other than CO₂; and
- (d) individual identified transformation products.

The duration of the study shall not exceed 60 days unless the semi-continuous procedure with periodical renewal of the test suspension is applied. However, the period for the batch test may be extended to a maximum of 90 days, if the degradation of the test substance has started within the first 60 days.

7.2.2.3. Water/sediment study

The information provided, together with other relevant information, shall be sufficient to:

- (a) identify individual components present which at any time account for more than 10 % of the amount of active substance added, including, where possible, non-extractable residues;
- (b) identify individual components present which account for more than 5 % of the amount of active substance added in at least two sequential measurements, where possible;
- (c) identify individual components (> 5 %) for which at the end of the study the maximum of formation is not yet reached, where possible;
- (d) identify or characterise, where possible, also other individual components present;
- (e) establish the relative proportions of the components (mass balance); and
- (f) define the sediment residue of concern, to which non-target species are or may be exposed.

Where a reference is made to non-extractable residues these shall be defined as chemical species originating from active substances used in accordance with good agricultural practice that cannot be extracted by methods which do not significantly change the chemical nature of these residues or the nature of the sediment matrix. These non-extractable residues are not considered to include fragments through metabolic pathways leading to natural products.

Circumstances in which required

The water/sediment study shall be reported unless the applicant shows that contamination of surface water will not occur.

Test conditions

The degradation pathway or pathways shall be reported for two water/sediment systems. The two sediments selected shall differ with respect to organic carbon content and texture, and where relevant, with respect to pH.

Results obtained shall be presented in the form of schematic drawings showing the pathways involved, and in the form of balance sheets which show the distribution of radio-label in water and sediment as a function of time, as between:

- (a) active substance;
- (b) CO₂;
- (c) volatile compounds other than CO₂;
- (d) individual identified transformation products;
- (e) extractable substances not identified; and
- (f) non-extractable residues in sediment.

The duration of the study shall be at least 100 days. It shall be longer where this is necessary to establish the degradation pathway and water/sediment distribution pattern of the active substance and its metabolites, breakdown and reaction products. If more than 90 % of the active substance is degraded before the period of 100 days expires, the test duration may be shorter.

The degradation pattern of potentially relevant metabolites occurring within the water/sediment study shall be established either by extension of the study for the active substance, or by conducting a separate study for potentially relevant metabolites.

7.2.2.4. Irradiated water/sediment study

The same general provisions as provided under point 7.2.2.3 apply.

Circumstances in which required

If photochemical degradation is of importance a water/sediment study under influence of a light/dark regime may additionally be provided.

Test conditions

The type and conditions of the study to be performed shall be discussed with the national competent authorities.

7.2.3. Degradation in the saturated zone

The type and conditions of the study to be performed shall be discussed with the national competent authorities.

7.3. Fate and behaviour in air

7.3.1. Route and rate of degradation in air

The vapour pressure of purified active substance, as provided under point 2.2, shall be reported. An estimate of the half-life in the upper atmosphere of the active substance and any volatile metabolites, breakdown and reaction products, formed in soil or natural water systems, shall be calculated and reported.

Estimates of active substance upper atmospheric half-lives, based on monitoring data shall also be calculated, when monitoring data that enable this to be done, are available.

7.3.2. Transport via air

The type and conditions of the study to be performed shall be discussed with the national competent authorities.

Circumstances in which required

If the trigger for volatilisation, $V_p = 10^{-5}$ Pa (plant) or 10^{-4} Pa (soil) at a temperature of 20 °C, is exceeded and (drift) mitigation measures are required, data from confined experiments may be reported.

If needed, experiments to determine deposition following volatilisation may be provided.

The national competent authorities shall be consulted to decide whether this information is necessary.

7.3.3. Local and global effects

For substances that are applied in high amounts, the following effects shall be considered:

- global warming potential (GWP);
- ozone depleting potential (ODP);
- photochemical ozone creation potential (POCP);
- accumulation in the troposphere;
- acidification potential (AP);
- eutrophication potential (EP).

7.4. Definition of the residue

7.4.1. Definition of the residue for risk assessment

The residue definition relevant for risk assessment for each compartment shall be defined to include all components (active substance, metabolites, breakdown and reaction products) that were identified in accordance with the criteria referred to in this Section.

The chemical composition of residues occurring in soil, groundwater, surface water (freshwater, estuarine and marine), sediment and air, resulting from use, or proposed use, of a plant protection product containing the active substance, shall be taken into account.

7.4.2. *Definition of the residue for monitoring*

Considering the results of toxicological and ecotoxicological testing, the residue for monitoring shall be defined to include those components from the definition of the residue for risk assessment, which are considered relevant when assessing the results in those tests.

7.5. **Monitoring data**

Available monitoring data concerning fate and behaviour of the active substance and relevant metabolites, breakdown and reaction products in soil, groundwater, surface water, sediment and air shall be reported.

SECTION 8

Ecotoxicological studies

Introduction

1. All available biological data and information which is relevant to the assessment of the ecotoxicological profile of the active substance shall be reported. This shall include all potentially adverse effects found during routine ecotoxicological investigations. Where required by the national competent authorities, additional studies, necessary to investigate the probable mechanisms involved and to assess the significance of these effects, shall be carried out and reported on.
2. The ecotoxicological assessment shall be based on the risk that the proposed active substance used in a plant protection product poses to non-target organisms. In carrying out a risk assessment, toxicity shall be compared with exposure. The general term for the output from such a comparison is 'risk quotient' or RQ. It shall be noted that RQ can be expressed in several ways, for example, toxicity:exposure ratio (TER) and as a hazard quotient (HQ). The applicant shall take into account the information from Sections 2, 5, 6, 7 and 8.
3. It may be necessary to conduct separate studies for metabolites, breakdown or reaction products derived from the active substance where non-target organisms may be exposed and where their effects cannot be evaluated by the available results relating to the active substance. Before such studies are performed, the applicant shall take into account the information from Sections 5, 6 and 7.

Studies undertaken shall permit characterisation of metabolites, breakdown or reaction products as being significant or not, and reflect the nature and extent of the effects judged likely to arise.

4. In the case of certain study types, the use of a representative plant protection product instead of the active substance as manufactured may be more appropriate, for example testing of non-target arthropods, bees, earthworm reproduction, soil micro-flora and non-target terrestrial plants. In the case of certain plant protection product types (for example encapsulated suspension) testing with the plant protection product is more appropriate to testing with active substance when these organisms will be exposed to the plant protection product itself. For plant protection products where the active substance is always intended to be used together with a safener and/or synergist and/or in conjunction with other active substances, plant protection products containing these additional substances shall be used.
5. The potential impact of the active substance on biodiversity and the ecosystem, including potential indirect effects via alteration of the food web, shall be considered.
6. For those guidelines which allow for the study to be designed to determine an effective concentration (EC_x), the study shall be conducted to determine an EC_{10} , EC_{20} and EC_{50} , when required, along with corresponding 95 % confidence intervals. If an EC_x approach is used, a no observed effect concentration (NOEC) shall still be determined.

Existing acceptable studies that have been designed to generate a NOEC shall not be repeated. An assessment of the statistical power of the NOEC derived from those studies shall be carried out.

7. All of the aquatic toxicity data shall be used when developing a proposal for environmental quality standards (Annual Average EQS, AA-EQS; Maximum Acceptable Concentration EQS, MAC-EQS). The methodology for derivation of these endpoints is outlined in the 'Technical Guidance for Deriving Environmental Quality Standards ⁽¹⁾' for the Water Framework Directive 2000/60/EC of the European Parliament and of the Council ⁽²⁾.

⁽¹⁾ European Communities (2011) Publication ISBN: 978-92-79-16228-2.

⁽²⁾ OJ L 327, 22.12.2000, p. 1.

8. In order to facilitate the assessment of the significance of test results obtained, including the estimation of intrinsic toxicity and the factors affecting toxicity, the same strain (or recorded origin) of each relevant species shall, where possible, be used in the various toxicity tests specified.
9. Higher tier studies shall be designed and data analysed using suitable statistical methods. Full details of the statistical methods shall be reported. Where appropriate and necessary, higher tier studies shall be supported by chemical analysis to verify exposure has occurred at an appropriate level.
10. Pending the validation and adoption of new studies and of a new risk assessment scheme, existing protocols shall be used to address the acute and chronic risk to bees, including those on colony survival and development, and the identification and measurement of relevant sub-lethal effects in the risk assessment.

8.1. **Effects on birds and other terrestrial vertebrates**

For all avian and mammalian feeding studies, average achieved dose shall be reported, including where possible the dose in mg substance/kg body weight. Where dosing via the diet is utilised, the active substance shall be distributed uniformly in the diet.

8.1.1. *Effects on birds*

8.1.1.1. Acute oral toxicity to birds

The acute oral toxicity of the active substance to birds shall be determined.

Circumstances in which required

The effects of the active substance on birds shall be investigated except where the substance is included in plant protection products used, for example, in enclosed spaces and wound healing treatments where birds will experience neither direct nor secondary exposure.

Test conditions

A study shall be provided establishing the acute oral toxicity (LD₅₀) of the active substance. Where available, the study shall be performed with a quail species (Japanese quail (*Coturnix coturnix japonica*) or Bobwhite quail (*Colinus virginianus*)), since regurgitation is rare in these species. The study shall provide, where possible, LD₅₀ values. The lethal threshold dose, time courses of response and recovery, the LD₁₀ and LD₂₀ shall be reported together with the no observed effect level (NOEL) and gross pathological findings. Where LD₁₀ and LD₂₀ cannot be estimated, an explanation shall be provided. Study design shall be optimised for the achievement of an accurate LD₅₀.

The highest dose used in tests shall not exceed 2 000 mg substance/kg body weight, however, depending on the expected exposure levels in the field following the intended use of the compound, higher doses may be required.

8.1.1.2. Short-term dietary toxicity to birds

A study shall be provided establishing the short-term dietary toxicity. LC₅₀ values, lowest lethal concentration (LLC), where possible, NOEC values, time courses of response and recovery and pathological findings shall be reported in such study. LC₅₀ and NOEC values shall be converted to daily dietary dose (LD₅₀) expressed in mg substance/kg bw/day and NOEL expressed in mg substance/kg bw/day.

Circumstances in which required

A study on the dietary (five-day) toxicity of the active substance to birds shall only be required where the mode of action or results from mammalian studies indicate a potential for the dietary LD₅₀ measured by the short-term dietary toxicity study to be lower than the LD₅₀ based on an acute oral study. The short-term dietary toxicity test shall not be conducted for any other purpose than to determine intrinsic toxicity through dietary exposure, unless a justification of the need to do so is supplied.

Test conditions

The test species shall be the same as tested under point 8.1.1.1.

8.1.1.3. Sub-chronic and reproductive toxicity to birds

A study shall be provided establishing the sub-chronic and reproductive toxicity of the substance to birds. The EC₁₀ and EC₂₀ shall be reported. Where they cannot be estimated, an explanation shall be provided together with the NOEC expressed in mg substance/kg bw/day.

Circumstances in which required

The sub-chronic and reproductive toxicity of the active substance to birds shall be investigated, unless the applicant shows that exposure of adults, or exposure of nest sites during the breeding season is unlikely to occur. Such a justification shall be supported by information showing that no exposure or delayed effects will occur during the breeding season.

Test conditions

The study shall be conducted on the same species as tested under point 8.1.1.1.

8.1.2. *Effects on terrestrial vertebrates other than birds*

The following information shall be derived from the mammalian toxicological assessment based on the studies referred to in Section 5.

8.1.2.1. *Acute oral toxicity to mammals*

The acute oral toxicity of the active substance to mammals shall be determined and the LD₅₀ expressed mg substance/kg bw/day.

Circumstances in which required

The effects of the active substance on mammals shall be investigated except when the substance is included in plant protection products used, for example, in enclosed spaces and wound healing treatments where mammals will experience neither direct nor secondary exposure.

8.1.2.2. *Long-term and reproductive toxicity to mammals**Circumstances in which required*

The reproductive toxicity of the active substance to mammals shall be investigated, unless a justification is provided by the applicant showing that exposure of adults, during the breeding season is unlikely to occur. Such a justification shall be supported by information showing that no exposure or delayed effects will occur during the breeding season.

The most sensitive ecotoxicologically relevant mammalian long-term toxicological endpoint (NOAEL) expressed as mg substance/kg bw/day shall be reported. The EC₁₀ and EC₂₀ shall be reported together with the NOEC expressed in mg substance/kg bw/day. Where EC₁₀ and EC₂₀ cannot be estimated an explanation shall be provided.

8.1.3. *Active substance bioconcentration in prey of birds and mammals*

For active substances with a log Pow > 3, an assessment of the risk posed by bioconcentration of the substance in the prey of birds and mammals shall be provided.

8.1.4. *Effects on terrestrial vertebrate wildlife (birds, mammals, reptiles and amphibians)*

Available and relevant data, including data from the open literature for the active substance of concern, regarding the potential effects to birds, mammals, reptiles and amphibians (see point 8.2.3) shall be presented and taken into account in the risk assessment.

8.1.5. *Endocrine disrupting properties*

Consideration shall be given to whether the active substance is a potential endocrine disruptor according to Union or internationally agreed guidelines. This may be done in consulting the mammalian toxicology section (see Section 5). In addition, other available information on toxicity profile and mode of action shall be taken into account. If as a result of this assessment, the active substance is identified as a potential endocrine disruptor, the type and conditions of the study to be performed shall be discussed with the national competent authorities.

8.2. **Effects on aquatic organisms**

Reports of the tests referred to in points 8.2.1, 8.2.4 and 8.2.6 shall be submitted for every active substance and supported with analytical data on concentrations of the substance in the test media.

When aquatic toxicity studies are conducted with a poorly soluble substance, limit concentrations lower than 100 mg substance/L may be acceptable, however precipitation of the substance in the test medium shall be avoided and a solubiliser, auxiliary solvent or dispersing agent shall be used when appropriate. Testing using the plant protection product may be required by the national competent authorities if no biological effects occur at the solubility limit of the active substance.

Toxicity endpoints (such as LC₅₀, EC₁₀, EC₂₀, EC₅₀ and NOEC) shall be calculated on the basis of nominal or mean/initial measured concentrations.

8.2.1. *Acute toxicity to fish*

A study shall be provided on the acute toxicity to fish (LC₅₀) and details of observed effects.

Circumstances in which required

A test on rainbow trout (*Oncorhynchus mykiss*) shall be carried out.

Test conditions

The acute toxicity of the active substance to fish shall be determined. In order to minimise fish testing, a threshold approach to acute toxicity testing on fish shall be considered. An acute toxicity fish limit test shall be conducted at 100 mg substance/L or at an appropriate concentration selected from aquatic endpoints (points 8.2.4, 8.2.6 or 8.2.7) following consideration of the threshold exposure. When mortality is detected in the fish limit test an acute fish dose-response toxicity study shall be required to determine an LC₅₀ for use in the risk assessment conducted in accordance with the relevant risk quotient analysis (see point 2 of the introduction of this Section).

8.2.2. *Long-term and chronic toxicity to fish*

Circumstances in which required

A long-term or chronic toxicity study on fish shall be provided for all active substances where exposure of surface water is likely and the substance is deemed to be stable in water, that is to say there is less than 90 % loss of the original substance over 24 hours via hydrolysis (see point 7.2.1.1). A fish early life stage study shall be provided in these circumstances. However, if a fish full life cycle study is provided an early life stage study shall not be required.

8.2.2.1. *Fish early life stage toxicity test*

A fish early life stage toxicity test shall determine effects on development, growth and behaviour, and details of observed effects on fish early life stages. The EC₁₀ and EC₂₀ shall be reported together with the NOEC. Where EC₁₀ and EC₂₀ cannot be estimated, an explanation shall be provided.

8.2.2.2. *Fish full life cycle test*

A fish full life cycle test shall provide information on the effects on reproduction of the parental and the viability of the filial generation. The EC₁₀ and EC₂₀ shall be reported together with the NOEC.

For active substances that are not considered as potential endocrine disruptors, a fish full life cycle test may be required depending upon the persistence and bioaccumulative potential of the substance.

For active substances that fulfil the screening criteria on either of the fish screening assays, or for which there are other indications of endocrine disruption (see point 8.2.3), appropriate additional endpoints shall be included in the test and discussed with the national competent authorities.

Test conditions

Studies shall be designed to reflect concerns identified through lower tier testing, mammalian and bird toxicology studies and other information. The exposure regime shall be selected accordingly, taking account of the rates of application proposed.

8.2.2.3. *Bioconcentration in fish*

The test on bioconcentration in fish shall provide the steady-state bioconcentration factors, uptake rate constants and depuration rate constants, incomplete excretion, metabolites formed in fish and, if available, information on organ-specific accumulation.

All data shall be provided with confidence limits for each test substance. Bioconcentration factors shall be expressed as a function of both total wet weight and of the lipid content of the fish.

Data provided under point 6.2.5 shall be considered, where relevant, in addressing this point.

Circumstances in which required

The bioconcentration of the substance, shall be assessed where:

- the log Pow is greater than 3 (see point 2.7) or there are other indications of bioconcentration, and
- the substance is considered stable, that is to say there is less than 90 % loss of the original substance over 24 hours via hydrolysis (see point 7.2.1.1).

8.2.3. Endocrine disrupting properties

Consideration shall be given to whether the active substance is a potential endocrine disruptor in aquatic non-target organisms according to Union or internationally agreed guidelines. In addition, other available information on toxicity profile and mode of action shall be taken into account. If as a result of this assessment, the active substance is identified as a potential endocrine disruptor, the type and conditions of the studies to be performed shall be discussed with the national competent authorities.

8.2.4. Acute toxicity to aquatic invertebrates*Circumstances in which required*

The acute toxicity shall be determined for a *Daphnia* species (preferably *Daphnia magna*). For active substances with an insecticidal mode of action or which show insecticidal activity a second species shall be tested, for example Chironomid larvae or Mysid shrimps (*Americamysis bahia*).

8.2.4.1. Acute toxicity to *Daphnia magna*

A test shall be provided on the 24- and 48-hour acute toxicity of the active substance to *Daphnia magna*, expressed as the median effective concentration (EC₅₀) for immobilisation, and where possible, the highest concentration causing no immobilisation.

Test conditions

Concentrations up to 100 mg substance/L shall be tested. A limit test at 100 mg substance/L may be performed where the results of a range finding test indicate that no effects are to be expected.

8.2.4.2. Acute toxicity to an additional aquatic invertebrate species

A test shall be provided on the 24- and 48-hour acute toxicity of the active substance to an additional aquatic invertebrate species, expressed as the median effective concentration (EC₅₀) for immobilisation, and where possible, the highest concentration causing no immobilisation.

Test conditions

The conditions as set out in point 8.2.4.1 shall apply.

8.2.5. Long-term and chronic toxicity to aquatic invertebrates*Circumstances in which required*

A long-term or chronic toxicity study on aquatic invertebrates shall be provided for all active substances where exposure of surface water is likely and the substance is deemed to be stable in water, that is to say there is less than 90 % loss of the original substance over 24 hours via hydrolysis (see point 7.2.1.1).

A chronic toxicity study shall be submitted on one aquatic invertebrate species. If acute toxicity tests have been conducted on two aquatic invertebrate species the acute endpoints shall be taken into account (see point 8.2.4) in order to determine the appropriate species to be tested in the chronic toxicity study.

If the active substance is an insect growth regulator, an additional study on chronic toxicity shall be carried out using relevant non-crustacean species such as *Chironomus* spp.

8.2.5.1. Reproductive and development toxicity to *Daphnia magna*

The aim of the test on reproductive and development toxicity to *Daphnia magna* shall be to measure adverse effects such as immobilisation and loss of reproductive capacity and to provide details of observed effects. The EC₁₀ and EC₂₀ shall be reported together with the NOEC. Where EC₁₀ and EC₂₀ cannot be estimated, an explanation shall be provided.

8.2.5.2. Reproductive and development toxicity to an additional aquatic invertebrate species

The test on reproductive and development toxicity to an additional aquatic invertebrate species shall measure adverse effects such as immobilisation and loss of reproductive capacity and provide details of observed effects. The EC₁₀ and EC₂₀ shall be reported together with the NOEC. Where EC₁₀ and EC₂₀ cannot be estimated, an explanation shall be provided.

8.2.5.3. Development and emergence in *Chironomus riparius*

The active substance shall be applied to the water overlying sediment and effects on survival and development of *Chironomus riparius*, including effects on emergence of adults, shall be measured to provide endpoints for those substances considered to interfere with insect moulting hormones or that have other effects on insect growth and development. The EC₁₀ and EC₂₀ shall be reported together with the NOEC.

Test conditions

Concentrations of active substance in the overlying water and the sediment shall be measured to establish an EC₁₀, EC₂₀ and a NOEC. The active substance shall be measured often enough to allow the calculation of test endpoints based on nominal as well as time-weighted average concentrations.

8.2.5.4. Sediment dwelling organisms

When accumulation of an active substance in aquatic sediment is indicated or predicted by environmental fate studies, the impact on a sediment-dwelling organism shall be assessed. The chronic risk to *Chironomus riparius* or *Lumbriculus* spp. shall be determined. An appropriate alternative test species may be used where a recognised guideline is available. The active substance shall be applied to either the water or the sediment phase of a water/sediment system and the test shall take account of the major route of exposure. The key endpoint from the study shall be presented in terms of mg substance/kg dry sediment and mg substance/L water and the EC₁₀ and EC₂₀ shall be reported together with the NOEC.

Test conditions

Concentrations of active substance in the overlying water and the sediment shall be measured to establish an EC₁₀, EC₂₀ and a NOEC.

8.2.6. Effects on algal growth

Circumstances in which required

Testing shall be carried out on one green alga (such as *Pseudokirchneriella subcapitata*, synonym *Selenastrum capricornutum*).

For active substances that exhibit herbicidal activity a test on a second species from a different taxonomic group shall be performed such as a diatom, for example *Navicula pelliculosa*.

The EC₁₀, EC₂₀, EC₅₀ and corresponding NOEC values shall be provided.

8.2.6.1. Effects on growth of green algae

A test shall be provided establishing EC₁₀, EC₂₀, EC₅₀ for green algae and corresponding NOEC values for algal growth rate and yield, based on measurements of biomass or surrogate measurement variables.

Test conditions

Concentrations up to 100 mg substance/L shall be tested. A limit test at 100 mg substance/L may be performed when results of a range-finding test indicate that no effects are to be expected at lower concentrations.

8.2.6.2. Effects on growth of an additional algal species

A test shall be provided establishing EC₁₀, EC₂₀, EC₅₀ for an additional algal species and corresponding NOEC values for algal growth rate and yield, based on measurements of biomass (or surrogate measurement variables).

Test conditions

The test conditions as set out in point 8.2.6.1 shall apply.

8.2.7. *Effects on aquatic macrophytes*

A test shall be provided establishing EC₁₀, EC₂₀, EC₅₀ and corresponding NOEC values for *Lemna* species growth rate and yield, based on measurements of number of fronds and at least one additional measurement variable (dry weight, fresh weight or frond area).

For other species of aquatic macrophytes, a test shall provide sufficient information to evaluate impact on aquatic plants and provide EC₁₀, EC₂₀, EC₅₀ and corresponding NOEC values based on measurement of appropriate biomass parameters.

Circumstances in which required

A laboratory test with *Lemna* species shall be performed for herbicides and plant growth regulators and for substances where there is evidence from information submitted under point 8.6 of Part A of this Annex or point 10.6 of Part A of the Annex to Regulation (EU) No 284/2013 that the test substance has herbicidal activity. Additional testing may be required by the national competent authorities on other macrophyte species depending on the mode of action of the substance, or if clear indications of higher toxicity are apparent to dicotyledonous (for example auxin inhibitor, broad leaf herbicides) or other monocotyledonous (for example grass herbicides) plant species from efficacy or terrestrial non-target plants tests (see point 8.6 of Part A of this Annex and point 10.6 of Part A of the Annex to Regulation (EU) No 284/2013).

Additional aquatic macrophyte species tests may be undertaken on a dicotyledonous species, such as *Myriophyllum spicatum*, *Myriophyllum aquaticum* or a monocotyledonous species, such as aquatic grass *Glyceria maxima*, as appropriate. The need to perform such studies shall be discussed with the national competent authorities.

Test conditions

Concentrations up to 100 mg substance/L shall be tested. A limit test at 100 mg substance/L may be performed when results of a range-finding test indicate that no effects are to be expected.

8.2.8. *Further testing on aquatic organisms*

Further studies on aquatic organisms may be conducted to refine the identified risk and shall provide sufficient information and data to evaluate potential impact on aquatic organisms under field conditions.

Studies undertaken may take the form of additional species testing, modified exposure testing, microcosm or mesocosm studies.

Circumstances in which required

The need to perform such studies shall be discussed with the national competent authorities.

Test conditions

The type and conditions of the study to be performed shall be discussed with the national competent authorities.

8.3. **Effect on arthropods**

8.3.1. *Effects on bees*

Effects on bees shall be assessed and the risk evaluated, including the risk deriving from residues of the active substance or its metabolites in nectar, pollen and water, including guttation. Reports of the tests referred to in points 8.3.1.1, 8.3.1.2 and 8.3.1.3 shall be submitted, except where plant protection products containing the active substance are for exclusive use in situations where bees are not likely to be exposed such as:

- (a) food storage in enclosed spaces;
- (b) non-systemic preparations for application to soil, except granules;
- (c) non-systemic dipping treatments for transplanted crops and bulbs;
- (d) wound sealing and healing treatments;
- (e) non systemic rodenticidal baits;
- (f) use in greenhouses without bees as pollinators.

For seed treatments the risk from drift of dust during drilling of the treated seed shall be taken into account. As regards granules and slug pellets the risk from drift of dust during application shall be taken into account. If an active substance is systemic and to be used on seeds, bulbs, roots, applied directly to soil, irrigation water, or applied directly to or into the plant, for example by spraying or stem injection, the risk to bees foraging those plants shall be assessed, including the risk deriving from residues of the plant protection product in nectar, pollen and water, including guttation.

Where bees are likely to be exposed, testing by both acute (oral and contact) and chronic toxicity, including sub-lethal effects, shall be conducted.

Where exposure of bees to residues in nectar, pollen or water resulting from systemic properties of the active substance may occur and where the acute oral toxicity is $< 100 \mu\text{g}/\text{bee}$ or a considerable toxicity for larvae occurs, residues concentrations in these matrices shall be provided and the risk assessment shall be based on a comparison of the relevant endpoint with those residue concentrations. If this comparison indicates that an exposure to toxic levels cannot be excluded, effects shall be investigated with higher tier tests.

8.3.1.1. Acute toxicity to bees

Where bees are likely to be exposed, testing for acute oral and contact toxicity shall be performed.

8.3.1.1.1. *Acute oral toxicity*

A test for acute oral toxicity shall be provided establishing the acute LD_{50} values together with the NOEC. Sub-lethal effects, if observed, shall be reported.

Test conditions

The test shall be conducted with the active substance. Results shall be presented in terms of μg active substance/bee.

8.3.1.1.2. *Acute contact toxicity*

A test for acute contact toxicity shall be provided establishing the acute LD_{50} values together with the NOEC. Sub-lethal effects, if observed, shall be reported.

Test conditions

The test shall be conducted with the active substance. Results shall be presented in terms of μg active substance/bee.

8.3.1.2. Chronic toxicity to bees

A test for chronic toxicity to bees shall be provided establishing the chronic oral EC_{10} , EC_{20} , EC_{50} together with the NOEC. Where the chronic oral EC_{10} , EC_{20} , EC_{50} cannot be estimated, an explanation shall be provided. Sub-lethal effects, if observed, shall be reported.

Circumstances in which required

The test shall be carried out where bees are likely to be exposed.

Test conditions

The test shall be conducted with the active substance. Results shall be presented in terms of μg active substance/bee.

8.3.1.3. Effects on honeybee development and other honeybee life stages

A bee brood study shall be conducted to determine effects on honeybee development and brood activity. The bee brood study shall provide sufficient information to evaluate possible risks from the active substance on honeybee larvae.

The test shall provide the EC_{10} , EC_{20} and EC_{50} for adult bees, where possible, and larvae together with the NOEC. Where EC_{10} , EC_{20} , EC_{50} cannot be estimated, an explanation shall be provided. Sub-lethal effects, if observed, shall be reported.

Circumstances in which required

The test shall be carried out for active substances for which sub-lethal effects on growth or development cannot be excluded, unless the applicant shows that it is not possible that honeybee brood will be exposed to the active substance.

8.3.1.4. Sub-lethal effects

Tests investigating sub-lethal effects, such as behavioural and reproductive effects, on bees and, where applicable, on colonies may be required.

8.3.2. Effects on non-target arthropods other than bees

Circumstances in which required

Effects on non-target terrestrial arthropods shall be investigated for all active substances except where plant protection products containing the active substance are for exclusive use in situations where non-target arthropods are not exposed such as:

- food storage in enclosed spaces that preclude exposure,
- wound sealing and healing treatments,
- enclosed spaces with rodenticidal baits.

Two indicator species, the cereal aphid parasitoid *Aphidius rhopalosiphi* (Hymenoptera: Braconidae) and the predatory mite *Typhlodromus pyri* (Acari: Phytoseiidae) shall always be tested. Initial testing shall be performed using glass plates and mortality (and reproduction effects if assessed) shall be reported. Testing shall determine a rate-response relationship and LR₅₀⁽¹⁾, ER₅₀⁽²⁾ and NOEC endpoints shall be reported for assessment of the risk to these species in accordance with the relevant risk quotient analysis. If adverse effects can be clearly predicted from these studies then testing using higher tier studies may be required (see point 10.3 of Part A of the Annex to the Regulation (EU) No 284/2013 for further details).

With active substances suspected of having a special mode of action (such as insect growth regulators, insect feeding inhibitors) additional tests involving sensitive life stages, special routes of uptake or other modifications, may be required by the national competent authorities. The rationale for the choice of test species used shall be provided.

8.3.2.1. Effects on *Aphidius rhopalosiphi*

A test shall provide sufficient information to evaluate the toxicity in terms of LR₅₀ and NOEC of the active substance to *Aphidius rhopalosiphi*.

Test conditions

Initial testing shall be performed using glass plates.

8.3.2.2. Effects on *Typhlodromus pyri*

A test shall provide sufficient information to evaluate the toxicity in terms of LR₅₀ and NOEC of the active substance to *Typhlodromus pyri*.

Test conditions

Initial testing shall be performed using glass plates.

8.4. Effects on non-target soil meso- and macrofauna

8.4.1. Earthworm — sub-lethal effects

A test shall provide information on the effects on growth, reproduction and behaviour of the earthworm.

Circumstances in which required

Sub-lethal effects on earthworms shall be investigated where the active substance can contaminate soil.

⁽¹⁾ LR₅₀, abbreviation for 'Lethal Rate, 50 %', that is to say the application rate required to kill half the members of a tested population after a specified test duration.

⁽²⁾ ER₅₀, abbreviation for 'Effect Rate, 50 %', that is to say the application rate required to cause an effect on half the members of a tested population after a specified test duration.

Test conditions

Testing shall determine a dose-response relationship and the EC₁₀, EC₂₀ and NOEC shall enable the risk assessment to be conducted in accordance with the appropriate risk quotient analysis, taking into account likely exposure, the organic carbon content (f_{oc}) of the test medium and the lipophilic properties (K_{ow}) of the test substance. The test substance shall be incorporated into the soil to obtain a homogenous soil concentration. Testing with soil metabolites may be avoided if there is analytical evidence to indicate that the metabolite is present at an adequate concentration and duration in the study conducted with the parent active substance.

8.4.2. Effects on non-target soil meso- and macrofauna (other than earthworms)

Circumstances in which required

Effects on soil organisms, other than earthworms, shall be investigated for all test substances, except in situations where soil organisms are not exposed such as:

- (a) food storage in enclosed spaces that preclude exposure;
- (b) wound sealing and healing treatments;
- (c) enclosed spaces with rodenticidal baits.

For plant protection products applied as a foliar spray data on *Folsomia candida* and *Hypoaspis aculeifer* may be required by the national competent authorities. If data are available on both *Aphidius rhopalosiphii* and *Typhlodromus pyri* these may be used in an initial risk assessment. If concern is raised with either species tested under point 8.3.2, data on both *Folsomia candida* and *Hypoaspis aculeifer* shall be provided.

If data on *Aphidius rhopalosiphii* and *Typhlodromus pyri* are not available, then the data set out in point 8.4.2.1 shall be provided.

For plant protection products applied directly to soil as soil treatments either as a spray or as a solid formulation, testing shall be carried out on both on *Folsomia candida* and *Hypoaspis aculeifer* (see point 8.4.2.1).

8.4.2.1. Species level testing

A test shall provide sufficient information to perform an assessment of the toxicity of the active substance to the soil invertebrate indicator species *Folsomia candida* and *Hypoaspis aculeifer*.

Test conditions

Testing shall determine a dose-response relationship and the EC₁₀, EC₂₀ and NOEC shall enable the risk assessment to be conducted in accordance with the appropriate risk quotient analysis, taking into account likely exposure, the organic carbon content (f_{oc}) of the test medium and the lipophilic properties (K_{ow}) of the test substance. The test substance shall be incorporated into the soil to obtain a homogenous soil concentration. Testing with soil metabolites may be avoided if there is analytical evidence to indicate that the metabolite is present at an adequate concentration and duration in the study conducted with the parent active substance.

8.5. Effects on soil nitrogen transformation

A test shall provide sufficient data to evaluate the impact of active substances on soil microbial activity, in terms of nitrogen transformation.

Circumstances in which required

The test shall be carried out where plant protection products containing the active substance are applied to soil or can contaminate soil under practical conditions of use. In the case of active substances intended for use in plant protection products for soil sterilisation, the studies shall be designed to measure rates of recovery following treatment.

Test conditions

Soils used shall be freshly sampled agricultural soils. The sites from which soil is taken shall not have been treated during the previous two years with any substance that could substantially alter the diversity and levels of microbial populations present, other than in a transitory manner.

8.6. Effects on terrestrial non-target higher plants

8.6.1. Summary of screening data

The information provided shall be sufficient to permit the evaluation of effects of the active substance on non-target plants.

Circumstances in which required

Screening data shall establish whether test substances exhibit herbicidal or plant growth regulatory activity. The data shall include testing from at least six plant species from six different families including both mono- and dicotyledons. The tested concentrations and rates shall be equal or higher than the maximum recommended application rate and at a rate either to simulate use pattern under field conditions, with testing conducted after the final treatment, or at a rate applied directly that takes in to account the accumulation of residues following multiple applications of the plant protection product. If screening studies do not cover the specified range of species or the necessary concentrations and rates, tests as set out in point 8.6.2 shall be carried out.

For assessment of active substances with herbicidal or plant growth regulatory activity screening data shall not be used. Point 8.6.2 shall apply.

Test conditions

A summary of available data from tests used to assess biological activity and dose range finding studies, whether positive or negative, which may provide information with respect to possible impact on other non-target flora, shall be provided, together with an assessment as to the potential impact on non-target plant species.

These data shall be supplemented by further information, in summary form, on the observed effects on plants during the course of field testing, namely efficacy, residues, environmental fate and ecotoxicological field studies.

8.6.2. *Testing on non-target plants*

A test shall provide the ER₅₀ values of the active substance to non-target plants.

Circumstances in which required

For active substances that exhibit herbicidal or plant growth regulator activity, vegetative vigour and seedling emergence concentration/response tests shall be provided for at least six species representing families for which herbicidal/plant growth regulatory action has been found. Where, from the mode of action, it can be clearly established that either seedling emergence or vegetative vigour is effected, only the relevant study shall be conducted.

Data are not required, where exposure is negligible, for example in the case of rodenticides, active substances used for wound protection or seed treatment, or in the case of active substances used on stored products or in glasshouses where exposure is precluded.

Test conditions

Dose-response tests on a selection of 6 to 10 monocotyledon and dicotyledon plant species representing as many taxonomic groups as possible shall be provided.

8.7. **Effects on other terrestrial organisms (flora and fauna)**

Any available data on the effects of the product on other terrestrial organisms shall be submitted.

8.8. **Effects on biological methods for sewage treatment**

A test shall provide an indication as to the potential of the active substance on biological sewage treatment systems.

Circumstances in which required

Effects on biological methods for sewage treatment shall be reported where the use of plant protection products containing the active substance can give rise to adverse effects on sewage treatment plants.

8.9. **Monitoring data**

Available monitoring data concerning adverse effects of the active substance to non-target organisms shall be reported.

SECTION 9

Literature data

A summary of all relevant data from the scientific peer reviewed open literature on the active substance, metabolites and breakdown or reaction products and plant protection products containing the active substance shall be submitted.

SECTION 10

Classification and labelling

Proposals for the classification and labelling of the active substance in accordance with Regulation (EC) No 1272/2008 shall be submitted and justified, including:

- pictograms,
- signal words,
- hazard statements, and
- precautionary statements.

PART B

MICRO-ORGANISMS INCLUDING VIRUSES

TABLE OF CONTENTS

INTRODUCTION

1. IDENTITY OF THE MICRO-ORGANISM
 - 1.1. Applicant
 - 1.2. Producer
 - 1.3. Name and species description, strain characterisation
 - 1.4. Specification of the material used for manufacturing of formulated products
 - 1.4.1. Content of the micro-organism
 - 1.4.2. Identity and content of impurities, additives, contaminating micro-organisms
 - 1.4.3. Analytical profile of batches
2. BIOLOGICAL PROPERTIES OF THE MICRO-ORGANISM
 - 2.1. History of the micro-organism and its uses. Natural occurrence and geographical distribution
 - 2.1.1. Historical background
 - 2.1.2. Origin and natural occurrence
 - 2.2. Information on target organism(s)
 - 2.2.1. Description of the target organism(s)
 - 2.2.2. Mode of action
 - 2.3. Host specificity range and effects on species other than the target harmful organism
 - 2.4. Development stages/life cycle of the micro-organism
 - 2.5. Infectiveness, dispersal and colonisation ability
 - 2.6. Relationships to known plant or animal or human pathogens
 - 2.7. Genetic stability and factors affecting it
 - 2.8. Information on the production of metabolites (especially toxins)
 - 2.9. Antibiotics and other anti-microbial agents
3. FURTHER INFORMATION ON THE MICRO-ORGANISM
 - 3.1. Function

- 3.2. Field of use envisaged
- 3.3. Crops or products protected or treated
- 3.4. Method of production and quality control
- 3.5. Information on the occurrence or possible occurrence of the development of resistance of the target organism(s)
- 3.6. Methods to prevent loss of virulence of seed stock of the micro-organism
- 3.7. Recommended methods and precautions concerning handling, storage, transport or fire
- 3.8. Procedures for destruction or decontamination
- 3.9. Measures in case of an accident
4. ANALYTICAL METHODS
 - 4.1. Methods for the analysis of the micro-organism as manufactured
 - 4.2. Methods to determine and quantify residues (viable or non-viable)
5. EFFECTS ON HUMAN HEALTH
 - 5.1. Basic information
 - 5.1.1. Medical data
 - 5.1.2. Medical surveillance on manufacturing plant personnel
 - 5.1.3. Sensitisation/allergenicity observations, if appropriate
 - 5.1.4. Direct observation, e.g. clinical cases
 - 5.2. Basic studies
 - 5.2.1. Sensitisation
 - 5.2.2. Acute toxicity, pathogenicity and infectiveness
 - 5.2.2.1. Acute oral toxicity, pathogenicity and infectiveness
 - 5.2.2.2. Acute inhalation toxicity, pathogenicity and infectiveness
 - 5.2.2.3. Intraperitoneal/subcutaneous single dose
 - 5.2.3. Genotoxicity testing
 - 5.2.3.1. *In vitro* studies
 - 5.2.4. Cell culture study
 - 5.2.5. Information on short-term toxicity and pathogenicity
 - 5.2.5.1. Health effects after repeated inhalatory exposure
 - 5.2.6. Proposed treatment: first aid measures, medical treatment
 - 5.3. Specific toxicity, pathogenicity and infectiveness studies
 - 5.4. *In vivo* studies in somatic cells
 - 5.5. Genotoxicity — *In vivo* studies in germ cells
 - 5.6. Summary of mammalian toxicity, pathogenicity and infectiveness and overall evaluation
6. RESIDUES IN OR ON TREATED PRODUCTS, FOOD AND FEED
 - 6.1. Persistence and likelihood of multiplication in or on crops, feedingstuffs or foodstuffs
 - 6.2. Further information required
 - 6.2.1. Non-viable residues

- 6.2.2. Viable residues
- 6.3. Summary and evaluation of residue behaviour resulting from data submitted under points 6.1 and 6.2
- 7. FATE AND BEHAVIOUR IN THE ENVIRONMENT
 - 7.1. Persistence and multiplication
 - 7.1.1. Soil
 - 7.1.2. Water
 - 7.1.3. Air
 - 7.2. Mobility
- 8. EFFECTS ON NON-TARGET ORGANISMS
 - 8.1. Effects on birds
 - 8.2. Effects on aquatic organisms
 - 8.2.1. Effects on fish
 - 8.2.2. Effects on freshwater invertebrates
 - 8.2.3. Effects on algae growth
 - 8.2.4. Effects on plants other than algae
 - 8.3. Effects on bees
 - 8.4. Effects on arthropods other than bees
 - 8.5. Effects on earthworms
 - 8.6. Effects on non-target soil micro-organisms
 - 8.7. Additional studies
- 9. SUMMARY AND EVALUATION OF ENVIRONMENTAL IMPACT

Introduction

- (i) Active substances are defined in Article 2(2) of Regulation (EC) No 1107/2009 and include chemical substances and micro-organisms including viruses.

This Part provides data requirements for active substances consisting of micro-organisms, including viruses.

The term 'micro-organism' as defined in Article 3 of Regulation (EC) No 1107/2009 applies to, but is not limited to, bacteria, fungi, protozoa, viruses and viroids.

- (ii) For all micro-organisms that are subject to application all available relevant knowledge and information in literature should be provided.

The most important and informative information is obtained by the characterisation and identification of a micro-organism. Such information is found in Sections 1 to 3 (identity, biological properties and further information) which form the basis for an assessment of human health and environmental effects.

Newly generated data from conventional toxicological and/or pathological experiments on laboratory animals are normally required unless the applicant can justify, on the basis of the previous information, that the use of the micro-organism, under the proposed conditions of use, does not have any harmful effects on human and animal health or on groundwater or any unacceptable influence on the environment.

- (iii) Pending the acceptance of specific guidelines at international level, the information required shall be generated using available test guidelines accepted by the competent authority (e.g. USEPA

guideline ⁽¹⁾); where appropriate, test guidelines as described in Part A of this Annex should be adapted in such a way that they are appropriate for micro-organisms. Testing shall include viable and, if appropriate, non-viable micro-organisms, and a blank control.

- (iv) Where testing is done, a detailed description (specification) of the material used and its impurities, in accordance with point 1.4, must be provided. The material used shall be of that specification that will be used in the manufacture of preparations to be authorised.

Where studies are conducted using micro-organisms produced in the laboratory or in a pilot plant production system, the studies must be repeated using micro-organisms as manufactured, unless it can be demonstrated that the test material used is essentially the same for the purposes of the testing and assessment.

- (v) Where the micro-organism has been genetically modified, a copy of the evaluation of the data concerning the assessment of risk to the environment, as stated in Article 48 to Regulation (EC) No 1107/2009, has to be submitted.
- (vi) Where relevant, data shall be analysed using appropriate statistical methods. Full details of the statistical analysis shall be reported (e.g. all point estimates shall be given with confidence intervals, exact p-values should be given rather than stating significant/non significant).
- (vii) In the case of studies in which dosing extends over a period, dosing shall preferably be done using a single batch of the micro-organism, if stability permits.

If the studies are not performed using a single batch of the micro-organism, the similarity of the different batches has to be stated.

Whenever a study implies the use of different doses, the relationship between dose and adverse effect must be reported.

- (viii) If the plant protection action is known to be due to the residual effect of a toxin/metabolite or if significant residues of toxins/metabolites are to be expected not related to the effect of the active substance, a dossier for the toxin/metabolite has to be submitted in accordance with the requirements of Part A of this Annex.

1. IDENTITY OF THE MICRO-ORGANISM

The identification together with the characterisation of the micro-organism provides the most important information and is a key point for decision-making.

1.1. Applicant

The name and address of the applicant must be provided, as must the name, position, telephone and fax number of the appropriate person to contact.

Where, in addition, the applicant has an office, agent or representative in the Member State to which the application for approval is submitted, and if different, in the rapporteur Member State appointed by the Commission, the name and address of the local office, agent or representative must be provided, as must the name, position, telephone and fax number of the appropriate person to contact.

1.2. Producer

The name and address of the producer or producers of the micro-organism must be provided as must the name and address of each plant in which the micro-organism is produced. A contact point (preferably a central contact point, to include name, telephone and fax number) must be provided, with a view to providing updating information and responding to queries arising, regarding production technology, processes and the quality of product (including where relevant, individual batches). Where, following approval of the micro-organism, there are changes in the location or number of producers, the information required must again be notified to the Commission and the Member States.

1.3. Name and species description, strain characterisation

- (i) The micro-organism should be deposited at an internationally recognised culture collection and given an accession number and these details must be submitted.
- (ii) Each micro-organism that is subject to the application shall be identified and named at the species level. The scientific name and taxonomic grouping, i.e. family, genus, species, strain, serotype, pathovar or any other denomination relevant to the micro-organism, must be stated.

⁽¹⁾ USEPA Microbial Pesticide Test Guidelines, OPPTS Series 885, February 1996.

It must be indicated whether the micro-organism:

- is indigenous or non-indigenous at the species level to the intended area of application,
- is a wild type,
- is a spontaneous or induced mutant,
- has been modified, using techniques described in Part 2 of Annex IA and in Annex IB to Directive 2001/18/EC (*) of the European Parliament and of the Council.

In the latter two cases, all known differences between the modified micro-organism and the parent wild strain must be provided.

- (iii) Best available technology should be used to identify and characterise the micro-organism at the strain level. The appropriate test procedures and criteria used for identification (e.g. morphology, biochemistry, serology, molecular identification) must be provided.
- (iv) Common name or alternative and superseded names and code names used during the development, if any, must be provided.
- (v) Relationships to known pathogens shall be indicated.

1.4. **Specification of the material used for manufacturing of formulated products**

1.4.1. *Content of the micro-organism*

The minimum and maximum content of the micro-organism in the material used for manufacturing of formulated products, must be reported. The content shall be expressed in appropriate terms, such as number of active units per volume or weight or any other manner that is relevant to the micro-organism.

Where the information provided relates to a pilot plant production system, the information required must again be provided to the Commission and the Member States once industrial scale production methods and procedures have stabilised, if production changes result in a changed specification of purity.

1.4.2. *Identity and content of impurities, additives, contaminating micro-organisms*

It is desirable to have a plant protection product without contaminants (including contaminating micro-organisms), if possible. The level and nature of acceptable contaminants shall be judged from a risk assessment point of view, by the competent authority.

If possible and appropriate, the identity and maximum content of all contaminating micro-organisms, expressed in the appropriate unit, must be reported. The information on identity must be provided where possible as outlined in point 1.3 of Part B of this Annex.

Relevant metabolites (i.e. if expected to be of concern to human health and/or the environment) known to be formed by the micro-organism shall be identified and characterised at different states or growth stages of the micro-organism (see point (viii) of this introduction).

Where relevant detailed information on all components such as condensates, culture medium, etc. must be provided.

In the case of chemical impurities that are relevant for human health and/or the environment, the identity and maximum content, expressed in appropriate terms, must be provided.

In the case of additives, the identity and content in g/kg must be provided.

The information on identity of chemical substances such as additives must be provided as outlined in point 1.10 of Part A of this Annex.

1.4.3. *Analytical profile of batches*

Where relevant, the same data as outlined in point 1.11 of Part A of this Annex have to be reported, using the appropriate units.

2. BIOLOGICAL PROPERTIES OF THE MICRO-ORGANISM

2.1. **History of the micro-organism and its uses. Natural occurrence and geographical distribution**

Familiarity, interpreted as the availability of relevant knowledge of the micro-organism, shall be presented.

(*) OJ L 106, 17.4.2001, p. 1.

2.1.1. *Historical background*

The historical background of the micro-organism and its use (tests/research projects or commercial use) must be provided.

2.1.2. *Origin and natural occurrence*

The geographical region and the place in the ecosystem (e.g. host plant, host animal, or soil from which the micro-organism was isolated) must be stated. The method of isolation of the micro-organism shall be reported. The natural occurrence of the micro-organism in the relevant environment shall be given if possible at strain level.

In the case of a mutant, or a genetically modified micro-organism, detailed information should be provided on its production and isolation and on the means by which it can be clearly distinguished from the parent wild strain.

2.2. **Information on target organism(s)**

2.2.1. *Description of the target organism(s)*

Where relevant, details of harmful organisms against which protection is afforded, must be provided.

2.2.2. *Mode of action*

The principal mode of action shall be indicated. In connection with the mode of action it shall also be stated if the micro-organism produces a toxin with a residual effect on the target organism. In that case, the mode of action of this toxin shall be described.

If relevant, information on the site of infection and mode of entry into the target organism and its susceptible stages shall be given. The results of any experimental studies must be reported.

It shall be stated by which way an uptake of the micro-organism, or its metabolites (especially toxins) may occur (e.g. contact, stomach, inhalation). It must also be stated whether or not the micro-organism or its metabolites are translocated in plants and, where relevant, how this translocation takes place.

In case of pathogenic effect on the target organism, infective dose (the dose needed to cause infection with the intended effect on a target species) and transmissibility (possibility of spread of the micro-organism in the target population, but also from one target species to another (target) species) after application under the proposed condition of use shall be indicated.

2.3. **Host specificity range and effects on species other than the target harmful organism**

Any available information on the effects on non-target organisms within the area to which the micro-organism may spread shall be given. The occurrence of non-target organisms being either closely related to the target species or being especially exposed shall be indicated.

Any experience of the toxic effect of the active substance or its metabolic products on humans or animals, of whether the organism is capable of colonising or invading humans or animals (including immunosuppressed individuals) and whether it is pathogenic shall be stated. Any experience of whether the active substance or its products may irritate skin, eyes or respiratory organs of humans or animals and whether it is allergenic in contact with skin or when inhaled shall be stated.

2.4. **Development stages/life cycle of the micro-organism**

Information on the life cycle of the micro-organism, described symbiosis, parasitism, competitors, predators, etc., including host organisms, as well as vectors for viruses, must be presented.

The generation time and the type of reproduction of the micro-organism must be stated.

Information on the occurrence of resting stages and their survival time, their virulence and infection potential must be provided.

The potential of the micro-organism to produce metabolites, including toxins that are of concern for human health and/or the environment, in its different development stages after the release, must be indicated.

2.5. **Infectiveness, dispersal and colonisation ability**

The persistence of the micro-organism and information on its life cycle under the typical environmental conditions of use must be indicated. In addition, any particular sensitivity of the micro-organism to certain compartments of the environment (e.g. UV light, soil, water) must be stated.

The environmental requirements (temperature, pH, humidity, nutrition requirements, etc.) for survival, reproduction, colonisation, damage (including human tissues) and effectiveness of the micro-organism must be stated. The presence of specific virulence factors shall be indicated.

The temperature range at which the micro-organism grows must be determined, including minimum, maximum and optimum temperatures. This information is of particular value as a trigger for studies of effects on human health (Section 5).

The possible effect of factors such as temperature, UV light, pH, and the presence of certain substances on the stability of relevant toxins must also be stated.

Information on possible dispersal routes of the micro-organism (via air as dust particles or aerosols, with host organisms as vectors, etc.), under typical environmental conditions relevant to the use, must be provided.

2.6. **Relationships to known plant or animal or human pathogens**

The possible existence of one or more species of the genus of the active and/or, where relevant, contaminating micro-organisms known to be pathogenic to humans, animals, crops or other non-target species and the type of disease caused by them shall be indicated. It shall be stated whether it is possible, and if so, by which means to clearly distinguish the active micro-organism from the pathogenic species.

2.7. **Genetic stability and factors affecting it**

Where appropriate, information on genetic stability (e.g. mutation rate of traits related to the mode of action or uptake of exogenous genetic material) under the environmental conditions of proposed use must be provided.

Information must also be provided on the micro-organism's capacity to transfer genetic material to other organisms as well as its capacity to being pathogenic for plants, animals or man. If the micro-organism carries relevant additional genetic elements, the stability of the encoded traits shall be indicated.

2.8. **Information on the production of metabolites (especially toxins)**

If other strains belonging to the same microbial species as the strain subject to the application are known to produce metabolites (especially toxins) with unacceptable effects on human health and/or the environment during or after application, the nature and structure of this substance, its presence inside or outside the cell and its stability, its mode of action (including external and internal factors of the micro-organism necessary to action) as well as its effect on humans, animals or other non-target species shall be provided.

The conditions under which the micro-organism produces the metabolite(s) (especially toxin(s)) must be described.

Any available information on the mechanism by which the micro-organisms regulate the production of the(se) metabolite(s) shall be provided.

Any available information on the influence of the produced metabolites on the micro-organism's mode of action shall be provided.

2.9. **Antibiotics and other anti-microbial agents**

Many micro-organisms produce some antibiotic substances. Interference with the use of antibiotics in human or veterinary medicine must be avoided at any stage of the development of a microbial plant protection product.

Information on the micro-organism's resistance or sensitivity to antibiotics or other anti-microbial agents must be provided, in particular the stability of the genes coding for antibiotic resistance, unless it can be justified that the micro-organism has no harmful effects on human or animal health, or that it can not transfer its resistance to antibiotics or other anti-microbial agents.

3. FURTHER INFORMATION ON THE MICRO-ORGANISM

Introduction

- (i) The information provided must describe the intended purposes for which preparations containing the micro-organism are used, or are to be used and the dose and manner of their use or proposed use.

- (ii) The information provided must specify the normal methods and precautions to be followed in the handling, storage and transport of the micro-organism.
- (iii) The studies, data and information submitted, must demonstrate the suitability of measures proposed for use in emergency situations.
- (iv) The information and data referred to are required for each micro-organism, except where otherwise specified.

3.1. **Function**

The biological function must be specified from among the following:

- control of bacteria,
- control of fungi,
- control of insects,
- control of mites,
- control of molluscs,
- control of nematodes,
- control of weeds,
- other (must be specified).

3.2. **Field of use envisaged**

The field(s) of use, existing and proposed, for preparations containing the micro-organism must be specified from among the following:

- field use, such as agriculture, horticulture, forestry, and viticulture,
- protected crops (e.g. in greenhouses),
- amenity,
- weed control on non-cultivated areas,
- home gardening,
- house plants,
- stored products,
- other (specify).

3.3. **Crops or products protected or treated**

Details of existing and intended use in terms of crops, groups of crops, plants, or plant products protected, must be provided.

3.4. **Method of production and quality control**

Full information on how the micro-organism is produced in bulk must be provided.

Both production method/process and product must be subject to a continuous quality control by the applicant. In particular, the occurrence of spontaneous changing of major characteristics of the micro-organism and of the absence/presence of significant contaminants shall be monitored. The quality assurance criteria for the production shall be submitted.

The techniques used to ensure a uniform product, and the assay methods for its standardisation, maintenance and purity of the micro-organism must be described and specified (e.g. HACCP).

3.5. **Information on the occurrence or possible occurrence of the development of resistance of the target organism(s)**

Available information on the possible occurrence of the development of resistance or cross-resistance of the target organism(s) must be provided. Where possible, appropriate management strategies shall be described.

3.6. **Methods to prevent loss of virulence of seed stock of the micro-organism**

Methods to prevent loss of virulence of starting cultures shall be provided.

In addition, any method, if available, that could prevent the micro-organism from losing its effects on the target species must be described.

3.7. Recommended methods and precautions concerning handling, storage, transport or fire

A safety data sheet pursuant to Article 31 of Regulation (EC) No 1907/2006 must be provided for each micro-organism.

3.8. Procedures for destruction or decontamination

In many cases the preferred or sole means of safe disposal of micro-organisms, contaminated materials, or contaminated packaging, is through controlled incineration in a licensed incinerator.

Methods to dispose safely of the micro-organism or, where necessary, to kill it prior to disposal, and methods to dispose of contaminated packaging and contaminated materials, must be fully described. Data must be provided for such methods to establish their effectiveness and safety.

3.9. Measures in case of an accident

Information on procedures for rendering the micro-organism harmless in the environment (e.g. water or soil) in case of an accident must be provided.

4. ANALYTICAL METHODS

Introduction

The provisions of this Section only cover analytical methods required for post-registration control and monitoring purposes.

Post-approval monitoring might be considered for all areas of risk assessment. This is particularly the case when (strains of) micro-organisms that are non-indigenous to the intended area of application are considered for approval. For analytical methods used for generation of data as required in this Regulation or for other purposes the applicant has to provide a justification for the method used; where necessary separate guidance will be developed for such methods on the basis of the same requirements as defined for methods for post-registration control and monitoring purposes.

Descriptions of methods must be provided and include details of equipment, materials and conditions used. The applicability of any internationally recognised method must be reported.

As far as practicable these methods must employ the simplest approach, involve the minimum cost, and require commonly available equipment.

Data on specificity, linearity, accuracy and repeatability, as defined in points 4.1 and 4.2 of Part A of this Annex, are also required for methods used to analyse micro-organisms and their residues.

For this Section the following applies:

Impurities, relevant residues, metabolites, metabolites,	As defined in Regulation (EC) No 1107/2009
Relevant impurities	Impurities, as defined above, that are of concern for human or animal health and/or the environment

On request the following samples must be provided:

- (i) samples of the micro-organism as manufactured;
- (ii) analytical standards of relevant metabolites (especially toxins) and all other components included in the residue definition;
- (iii) if available, samples of reference substances for the relevant impurities.

4.1. Methods for the analysis of the micro-organism as manufactured

- Methods for the identification of the micro-organism.
- Methods for providing information on possible variability of seed stock/active micro-organism.

- Methods to differentiate a mutant of the micro-organism from the parent wild strain.
- Methods for the establishment of purity of seed stock from which batches are produced and methods to control that purity.
- Methods to determine the content of the micro-organism in the manufactured material used for the production of formulated products and methods to show that contaminating micro-organisms are controlled to an acceptable level.
- Methods for the determination of relevant impurities in the manufactured material.
- Methods to control the absence and to quantify (with appropriate limits of determination) the possible presence of any human and mammalian pathogens.
- Methods to determine storage stability, shelf-life of the micro-organism, if appropriate.

4.2. **Methods to determine and quantify residues (viable or non-viable)**

of:

- the active micro-organism(s),
- relevant metabolites (especially toxins),

on and/or in crop, in foodstuffs and feeding stuffs, in animal and human body tissues and fluids, in soil, in water (including drinking water, ground water and surface water) and in air where relevant.

Analytical methods for amount or activity of proteinaceous products shall also be included, e.g. by testing exponential cultures and culture supernatants in an animal cell bioassay.

5. EFFECTS ON HUMAN HEALTH

Introduction

- (i) Available information based on the properties of the micro-organism and corresponding organisms (Sections 1, 2 and 3), including health and medical reports may be sufficient for a decision whether the micro-organism would cause health effects (infectious/pathogenic/toxic) in humans or not.
- (ii) The information provided, taken together with that provided for one or more preparations containing the micro-organism, must be sufficient to permit an evaluation to be made as to the risks for man, directly and/or indirectly associated with the handling and use of plant protection products containing the micro-organism, and the risk for man handling treated products, and the risk for man arising from residual traces or contaminants remaining in food and water. In addition, the information provided must be sufficient to:
 - permit a decision to be made as to whether, or not, the micro-organism can be approved,
 - specify appropriate conditions or restrictions to be associated with any approval,
 - specify risk and safety phrases (once introduced) for the protection of man, animals and the environment to be included on packaging (containers),
 - identify relevant first aid measures as well as appropriate diagnostic and therapeutic measures to be followed in the event of infection or another adverse effect in man.
- (iii) All effects found during investigations shall be reported. Investigations which may be necessary in order to evaluate the probable mechanism involved, and to assess the significance of these effects, must also be performed.
- (iv) For all studies actual achieved dose in colony forming units per kg body weight (cfu/kg), as well as in other appropriate units, must be reported.
- (v) Evaluation of the micro-organism shall be carried out in a tier-wise manner.

The first tier (Tier I) includes available basic information and basic studies, which have to be performed for all micro-organisms. Expert judgment will be necessary to decide about the appropriate test programme on

a case-by-case basis. Newly generated data from conventional toxicological and/or pathological experiments on laboratory animals are normally required unless the applicant can justify, on the basis of the previous information, that the use of the micro-organism, under the proposed conditions of use, does not have any harmful effects on human and animal health. Pending the acceptance of specific guidelines at international level, the information required shall be generated using available test guidelines (e.g. USEPA OPPTS Guidelines).

Tier II studies must be conducted if tests under Tier I have shown adverse health effects. The type of study to be performed depends on the effects observed in the Tier I studies. Before performing such studies, the applicant shall seek agreement of the competent authorities on the type of study to be performed.

TIER I

5.1. Basic information

Basic information is required about the potential of the micro-organism to cause adverse effects such as ability to colonise, to cause damage and to produce toxins and other relevant metabolites.

5.1.1. Medical data

Where available, and without prejudice to the provisions of Article 10 of Directive 98/24/EC, practical data and information relevant to the recognition of the symptoms of infection or pathogenicity and on the effectiveness of first aid and therapeutic measures have to be submitted. Where relevant, the effectiveness of potential antagonists, shall be investigated and reported. Where relevant, methods to kill or render the micro-organism uninfected must be indicated (see point 3.8).

Data and information relevant to the effects of human exposure, where available and of the necessary quality, are of particular value, in confirming the validity of extrapolations made and conclusions reached with respect to target organs, virulence, and the reversibility of adverse effects. Such data can be generated following accidental or occupational exposure.

5.1.2. Medical surveillance on manufacturing plant personnel

Available reports of occupational health surveillance programmes, supported with detailed information on the design of the programme and on exposure to the micro-organism must be submitted. Such reports should, where feasible, include data relevant to the mechanism of action of the micro-organism. These reports shall, where available, include data from persons exposed in manufacturing plants or after application of the micro-organism (e.g. in efficacy trials).

Special attention shall be devoted to those whose susceptibility may be affected, e.g. pre-existing disease, medication, compromised immunity, pregnancy or breast feeding.

5.1.3. Sensitisation/allergenicity observations, if appropriate

Available information on the sensitisation and allergenic response of workers, including workers in manufacturing plants, agricultural and research workers and others exposed to the micro-organism must be provided, and include, where relevant, details of any incidences of hypersensitivity and chronic sensitisation. The information provided shall include details of frequency, level and duration of exposure, symptoms observed and other relevant clinical observation. Information shall be given about whether workers have been subjected to any allergy tests or interviewed about allergenic symptoms.

5.1.4. Direct observation, e.g. clinical cases

Available reports from the open literature on the micro-organism or closely related members of the taxonomic group (relating to clinical cases), where they are from reference journals or official reports, must be submitted together with reports of any follow-up studies undertaken. Such reports are of particular value and shall contain complete descriptions of the nature, level and duration of exposure, as well as the clinical symptoms observed, first aid and therapeutic measures applied and measurements and observations made. Summary and abstract information is of limited value.

If there are animal studies performed, reports relating to clinical cases can be of particular value in confirming the validity of interpretations from animal data to man and in identifying unexpected adverse effects which are specific to humans.

5.2. Basic studies

In order to make it possible to correctly interpret the obtained results, it is of greatest importance that the suggested test methods are relevant regarding species sensitivity, administration route, etc., and relevant from a biological and toxicological point of view. The way of administration of the test micro-organism depends on the main exposure routes to humans.

To evaluate medium- and long-term effects after acute, sub-acute or semi-chronic exposure to micro-organisms, it is necessary to use the options provided in the OECD guidelines, to extend the studies concerned with a recovery period (after which full macroscopic and microscopic pathology is to be performed, including an exploration for micro-organisms in the tissues and organs). This facilitates the interpretation of certain effects and provides the possibility to recognise infectiveness and/or pathogenicity, which in turn helps taking decisions on other issues such as the necessity to perform long-term studies (carcinogenicity etc., see point 5.3), and whether or not to perform residue studies (see point 6.2).

5.2.1. Sensitisation ⁽¹⁾

Aim of the test

The test will provide sufficient information to assess the potential of the micro-organism to provoke sensitisation reactions by inhalation as well as with dermal exposure. A maximised test has to be performed.

Circumstances in which required ⁽²⁾

Information on sensitisation must be reported.

5.2.2. Acute toxicity, pathogenicity and infectiveness

The studies, data and information to be provided and evaluated must be sufficient to permit the identification of effects following a single exposure to the micro-organism, and in particular to establish, or indicate:

- the toxicity, pathogenicity and infectiveness of the micro-organism,
- the time course and characteristics of the effects with full details of behavioural changes and possible gross pathological findings at post-mortem,
- where possible mode of toxic action,
- the relative hazards associated with the different routes of exposure, and
- blood analyses throughout the studies in order to evaluate the clearance of the micro-organism.

Acute toxic/pathogenic effects may be accompanied by infectiveness and/or more long-term effects which cannot be observed immediately. With a view to health evaluation, it is therefore necessary to carry out studies on the ability to infect in connection with oral intake, inhalation and intraperitoneal/subcutaneous injection by test mammals.

During the acute toxicity, pathogenicity and infectiveness studies, an estimation of the micro-organism and/or the active toxin clearance in the organs deemed to be relevant for microbial examination (e.g. liver, kidneys, spleen, lungs, brain, blood and site of administration) must be performed.

The observations to be made shall reflect expert scientific judgement and may include the micro-organism numeration in all the tissues likely to be affected (e.g. showing lesions) and in the main organs: kidneys, brain, liver, lungs, spleen, bladder, blood, lymphatic ganglia, gastrointestinal tract, thymus gland and lesions at the inoculation site in the dead or moribund animals and at interim and final sacrifice.

The information generated through acute toxicity, pathogenicity and infectiveness testing is of particular value in assessing hazards likely to arise in accident situations and consumer risks due to exposure to possible residues.

5.2.2.1. Acute oral toxicity, pathogenicity and infectiveness

Circumstances in which required

The acute oral toxicity, pathogenicity and infectiveness of the micro-organism must be reported.

⁽¹⁾ The available methods for testing dermal sensitisation are not suitable for testing micro-organisms. Sensitisation by inhalation is most probably a greater problem compared with dermal exposure to micro-organisms but so far, there are no validated test methods. Development of these kinds of methods is therefore of great importance. Until then, all micro-organisms should be regarded as potential sensitisers. This approach also takes into consideration immuno-compromised or other sensitive individuals in the population (e.g. pregnant women, new-born children or elderly).

⁽²⁾ As a consequence of the absence of proper test methods all micro-organisms will be labelled as potential sensitisers, unless the applicant wants to demonstrate the non-sensitising potential by submitting data. Therefore, this data requirement should be regarded as not obligatory but optional, on a provisional base.

5.2.2.2. Acute inhalation toxicity, pathogenicity and infectiveness

Circumstances in which required

The inhalation toxicity ⁽¹⁾, pathogenicity and infectiveness of the micro-organism must be reported.

5.2.2.3. Intraperitoneal/subcutaneous single dose

The intraperitoneal/subcutaneous test is considered a highly sensitive assay to elicit in particular infectiveness.

Circumstances in which required

The intraperitoneal injection is always required for all micro-organisms, however, expert judgement may be exercised to evaluate whether subcutaneous injection is preferred instead of intraperitoneal injection if the maximum temperature for growth and multiplication is lower than 37 °C.

5.2.3. Genotoxicity testing

Circumstances in which required

If the micro-organism produces exotoxins in accordance with point 2.8, then these toxins and any other relevant metabolites in the culture medium must also be tested for genotoxicity. Such tests on toxins and metabolites shall be performed using the purified chemical if possible.

If basic studies do not indicate that toxic metabolites are formed, studies on the micro-organism itself shall be considered depending on expert judgement on the relevance and validity of the basic data. In the case of a virus the risk of insertional mutagenesis in mammal cells or the risk of carcinogenicity has to be discussed.

Aim of the test

These studies are of value in:

- the prediction of genotoxic potential,
- the early identification of genotoxic carcinogens,
- the elucidation of the mechanism of action of some carcinogens.

It is important that a flexible approach is adopted, with selection of further tests being dependent upon interpretation of results at each stage.

Test conditions ⁽²⁾

Genotoxicity of cellular micro-organisms will be studied after breaking of the cells, wherever possible. Justification should be provided on the method of sample preparation used.

Genotoxicity of viruses shall be studied on infectious isolates.

5.2.3.1. *In vitro* studies

Circumstances in which required

Results of *in vitro* mutagenicity tests (bacterial assay for gene mutation, test for clastogenicity in mammalian cells and test for gene mutation in mammalian cells) must be provided.

5.2.4. Cell culture study

This information must be reported for intracellular replicating micro-organisms, such as viruses, viroids or specific bacteria and protozoa, unless the information from Sections 1, 2 and 3 clearly demonstrates that the micro-organism does not replicate in warm-blooded organisms. A cell culture study shall be performed in human cell or tissue cultures of different organs. Selection can be based on expected target organs after infection. If human cell or tissue cultures of specific organs are not available, other mammal cell and tissue cultures can be used. For viruses, the ability to interact with the human genome is a key consideration.

⁽¹⁾ An inhalation study may be replaced by an intratracheal study.

⁽²⁾ As the present test methods are designed to be performed on soluble chemicals, it is necessary that the methods are developed so as to become relevant for micro-organisms.

5.2.5. *Information on short-term toxicity and pathogenicity*

Aim of the test

Short-term toxicity studies must be designed to provide information as to the amount of the micro-organism that can be tolerated without toxic effects under the conditions of the study. Such studies provide useful data on the risks for those handling and using preparations containing the micro-organism. In particular, short-term studies provide an essential insight into possible cumulative actions of the micro-organism, and the risks to workers who may be intensively exposed. In addition short-term studies provide information useful in the design of chronic toxicity studies.

The studies, data and information to be provided and evaluated, must be sufficient to permit the identification of effects following repeated exposure to the micro-organism, and in particular to further establish, or indicate:

- the relationship between dose and adverse effects,
- toxicity of the micro-organism including where necessary the NOAEL for toxins,
- target organs, where relevant,
- the time course and characteristics of the effects with full details of behavioural changes and possible gross pathological findings at post-mortem,
- specific toxic effects and pathological changes produced,
- where relevant the persistence and reversibility of certain toxic effects observed, following discontinuation of dosing,
- where possible, the mode of toxic action, and
- the relative hazard associated with the different routes of exposure.

During the short-term toxicity study, an estimation of the micro-organism clearance in the main organs must be performed.

Investigations shall be included for pathogenicity and infectiveness end points.

Circumstances in which required

The short-term toxicity (minimum 28 days) of the micro-organism must be reported.

The choice of test species has to be justified. The choice of study length depends on acute toxicity and clearance data.

Expert judgement is required to decide what route of administration is preferable.

5.2.5.1. *Health effects after repeated inhalatory exposure*

Information on the health effects after repeated inhalatory exposure is considered necessary, particularly for the risk assessment of the occupational setting. Repeated exposure might influence the clearance capacity (e.g. resistance) of the host (human). Furthermore, for proper risk assessment the toxicity after repeated exposure to contaminants, growth medium, co-formulants and the micro-organism needs to be addressed. It should be kept in mind that the co-formulants in the plant protection product can influence the toxicity and infectiveness of a micro-organism.

Circumstances in which required

Information on the short-term infectiveness, pathogenicity and toxicity (respiratory route) of a micro-organism is required, unless the information already provided is sufficient to assess human health effects. This can be the case if it is demonstrated that the test material has no inhalable fraction and/or repeated exposure is not expected.

5.2.6. *Proposed treatment: first aid measures, medical treatment*

The first aid measures to be used in the event of infection and in the event of contamination of eyes must be provided.

Therapeutic regimes for use in the event of ingestion or contamination of eyes and skin must be described in full. Information based on practical experience, where it exists and is available, in other cases on theoretical grounds, as to the effectiveness of alternative treatment regimes, where relevant, must be provided.

Information on resistance to antibiotics must be provided.

(END OF TIER I)

TIER II

5.3. Specific toxicity, pathogenicity and infectiveness studies

In certain cases, it can be necessary to carry out supplementary studies to further clarify the adverse human effects.

In particular, if results from earlier studies indicate that the micro-organism may cause long-term health effects, studies on chronic toxicity, pathogenicity and infectiveness, carcinogenicity and reproductive toxicity must be carried out. Furthermore, where a toxin is produced, kinetic studies must be performed.

Studies required must be designed on an individual basis, in the light of the particular parameters to be investigated and the objectives to be achieved. Before performing such studies, the applicant shall seek agreement of the competent authorities on the type of study to be performed.

5.4. In vivo studies in somatic cells*Circumstances in which required*

If all the results of the *in vitro* studies are negative further testing must be done with consideration of other relevant information available. The test can be an *in vivo* study or an *in vitro* study using a different metabolising system from that/those previously used.

If the *in vitro* cytogenetic test is positive, an *in vivo* test using somatic cells (metaphase analysis in rodent bone marrow or micronucleus test in rodents) must be conducted.

If either of the *in vitro* gene mutation tests is positive, an *in vivo* test to investigate unscheduled DNA synthesis or a mouse spot test must be conducted.

5.5. Genotoxicity — In vivo studies in germ cells*Aim of the test and test conditions*

See point 5.4 of part A.

Circumstances in which required

When any result of an *in vivo* study in somatic cells is positive, *in vivo* testing for germ cell effects may be justified. The necessity for conducting these tests will have to be considered on a case-by-case basis, taking into account other relevant information available including use and expected exposure. Suitable tests would need to examine interaction with DNA (such as the dominant lethal assay), to look at the potential for inherited effects and possibly make a quantitative assessment of heritable effects. It is recognised that in view of their complexity, the use of quantitative studies would require strong justification.

(END OF TIER II)

5.6. Summary of mammalian toxicity, pathogenicity and infectiveness and overall evaluation

A summary of all data and information provided under points 5.1 through 5.5, must be submitted, and include a detailed and critical assessment of those data in the context of relevant evaluative and decision making criteria and guidelines, with particular reference to the risks for man and animals that may or do arise, and the extent, quality and reliability of the data base.

It must be explained whether exposure of animals or humans has any implications for vaccination or serological monitoring.

6. RESIDUES IN OR ON TREATED PRODUCTS, FOOD AND FEED**Introduction**

(i) The information provided, taken together with that for one or more preparations containing the micro-organism, must be sufficient to permit an evaluation to be made as to the risk for man and/or animals, arising from exposure to the micro-organism and its residual traces and metabolites (toxins) remaining in or on plants or plant products.

(ii) In addition, the information provided must be sufficient to:

- permit a decision to be made as to whether or not the micro-organism can be approved,
- specify appropriate conditions or restrictions to be associated with any approval

— where relevant, set maximum residue levels, preharvest intervals to protect consumers and waiting periods, to protect workers handling the treated crops and products.

- (iii) For the evaluation of risk arising from residues, experimental data on levels of exposure to the residue may not be required where it can be justified, that the micro-organism and its metabolites are not hazardous to humans in the concentrations that could occur as a result of authorised use. This justification can be based on open literature, on practical experience and on information submitted in Sections 1, 2 and 3 and Section 5.

6.1. Persistence and likelihood of multiplication in or on crops, feedingstuffs or foodstuffs

A substantiated estimation of persistence/competitiveness of the micro-organism and relevant secondary metabolites (especially toxins) in or on the crop under the environmental conditions prevailing at and after the intended use, taking into account in particular the information provided in Section 2, has to be delivered.

Moreover, the application shall state to which extent and on which basis it is considered that the micro-organism can (or cannot) multiply in or on the plant or plant product or during processing of raw products.

6.2. Further information required

Consumers may be exposed to micro-organisms for a considerable time as a result of the consumption of treated food commodities; potential effects on the consumers must, therefore, be derived from chronic or semi-chronic studies, so that a toxicological end point, such as the ADI, can be established for risk management.

6.2.1. Non-viable residues

A non viable micro-organism is a micro-organism that is not capable of replication or of transferring genetic material.

If relevant quantities of the micro-organism or of produced metabolites, especially toxins, have been found to be persistent in points 2.4 and 2.5, full experimental residue data as provided for in Section 6 of Part A of this Annex is required, if concentrations of the micro-organism and/or its toxins in or on the treated foodstuffs or feedingstuffs are expected to occur in concentrations higher than under natural conditions or in a different phenotypic state.

In accordance with Regulation (EC) No 1107/2009, the conclusion concerning the difference between natural concentrations and an elevated concentration due to treatment with the micro-organism, is to be based on experimentally obtained data, and not on extrapolations or calculations using models.

Before performing such studies, the applicant shall seek agreement of the competent authorities on the type of study to be performed.

6.2.2. Viable residues

If the information submitted in accordance with point 6.1 suggests persistence of relevant amounts of the micro-organism in or on treated products, food or feed, possible effects on humans and/or animals must be investigated, unless it can be justified from Section 5, that the micro-organism and its metabolites and/or degradation products are not hazardous to humans in the concentrations and of the nature that could occur as a result of authorised use.

In accordance with Regulation (EC) No 1107/2009, the conclusion concerning the difference between natural concentrations and an elevated concentration due to treatment with the micro-organism, is to be based on experimentally obtained data, and not on extrapolations or calculations using models.

The persistence of viable residues needs special attention if infectiveness or pathogenicity to mammals has been found in points 2.3 and 2.5 or in Section 5 and/or if any other information suggests a hazard to consumers and/or workers. In this case the competent authorities may require studies similar to those provided for in Part A.

Before performing such studies, the applicant shall seek agreement of the competent authorities on the type of study to be performed.

6.3. Summary and evaluation of residue behaviour resulting from data submitted under points 6.1 and 6.2**7. FATE AND BEHAVIOUR IN THE ENVIRONMENT****Introduction**

- (i) Information on the origin, the properties, and the survival of the micro-organism and its residual metabolites as well as its intended use form the basis for an assessment of environmental fate and behaviour.

Experimental data are normally required unless it can be justified that an assessment of its fate and behaviour in the environment can be performed with the information already available. This justification can be based on open literature, on practical experience and on information submitted in Sections 1 to 6. The function of the micro-organism in environmental processes is of particular interest.

- (ii) The information provided, taken together with other relevant information, and that for one or more preparations containing the micro-organism, must be sufficient to permit an assessment of its fate and behaviour as well as that of its residual traces and toxins, where they are of significance for human health and/or the environment.
- (iii) In particular, the information provided shall be sufficient to:
- decide whether, or not, the micro-organism can be approved,
 - specify appropriate conditions or restrictions to be associated with any approval,
 - specify the pictograms (once introduced), signal words, and relevant hazard and precautionary statements for the protection of the environment, which are to be included on packaging (containers),
 - predict the distribution, fate, and behaviour in the environment of the micro-organism and its metabolites as well as the time courses involved,
 - identify measures necessary to minimise contamination of the environment and impact on non-target species.
- (iv) Any relevant metabolites (i.e. of concern for human health and/or the environment) formed by the test organism under any relevant environmental conditions shall be characterised. If relevant metabolites are present in or produced by the micro-organism, data as outlined under Section 7 of Part A of this Annex may be required, if all of the following conditions are met:
- the relevant metabolite is stable outside the micro-organism, see point 2.8, and
 - a toxic effect of the relevant metabolite is independent of the presence of the micro-organism, and
 - the relevant metabolite is expected to occur in the environment in concentrations considerably higher than under natural conditions.
- (v) Available information on the relationship with naturally occurring wild type relatives shall be taken into account.
- (vi) Before performing studies as referred to below, the applicant shall seek agreement of the competent authorities on whether studies need to be performed and, if so, the type of study to be conducted. The information from the other Sections has, also, to be taken into account.

7.1. Persistence and multiplication

Where relevant, appropriate information on the persistence and multiplication of the micro-organism, in all environmental compartments has to be given, unless it can be justified that exposure of the particular environmental compartment to the micro-organism is unlikely to occur. Special attention shall be given to

- competitiveness under the environmental conditions prevailing at and after the intended use, and
- population dynamics in seasonally or regionally extreme climates (particularly hot summer, cold winter and rainfall) and to agricultural practices applied after intended use.

Estimated levels of the specified micro-organism in a time course after use of the product under the proposed conditions of use shall be given.

7.1.1. Soil

Information on viability/population dynamics shall be reported in several cultivated and uncultivated soils representative of soils typical of the various EU regions where use exists or is anticipated. The provisions on choice of soil and its collection and handling, as referred to in the introduction of point 7.1 of Part A, have to be followed. If the test organism is to be used in association with other media, e.g. rockwool, this must be included in the test range.

7.1.2. Water

Information should be reported on viability/population dynamics in natural sediment/water systems under both dark and illuminated conditions.

7.1.3. Air

In case of particular concerns for operator, worker or bystander exposure, information on the concentrations in air might be necessary.

7.2. Mobility

The possible spread of the micro-organism and its degradation products in relevant environmental compartments has to be evaluated, unless it can be justified that exposure of the particular environmental compartments to the micro-organism is unlikely to occur. In this context, the intended use (e.g. field or greenhouse, application to soil or to crops), life cycle stages, including occurrence of vectors, persistence and the ability of the organism to colonise adjacent habitats are of particular interest.

The spread, the persistence and probable transport ranges need special attention if toxicity, infectiveness or pathogenicity has been reported or if any other information suggests possible hazard to humans, animals or to the environment. In this case the competent authorities may require studies similar to those provided for in Part A. Before performing such studies, the applicant shall seek agreement of the competent authorities on the type of study to be performed.

8. EFFECTS ON NON-TARGET ORGANISMS

Introduction

- (i) The information on identity, biological properties and further information in Sections 1, 2, 3 and 7 is central to the assessment of impact on non-target species. Additional useful information may be found on fate and behaviour in the environment in Section 7 and on residue levels in plants in Section 6 which, together with information on the nature of the preparation and its manner of use, defines the nature and extent of potential exposure. The information submitted in accordance with Section 5 will provide essential information as to effects to mammals and the mechanisms involved.

Experimental data are normally required, unless it can be justified that an assessment of effects on non-target organisms can be performed with the information already available.

- (ii) The choice of the appropriate non-target organisms for testing of environmental effects shall be based on the identity of the micro-organism (including the host specificity, mode of action and ecology of the organism). From such knowledge it would be possible to choose the appropriate test-organisms, such as organisms closely related to the target organism.
- (iii) The information provided, taken together with that for one or more preparations containing the micro-organism, must be sufficient to permit an assessment of the impact on non-target species (flora and fauna), likely to be at risk from exposure to the micro-organism, where they are of environmental significance. Impact can result from single, prolonged or repeated exposure and can be reversible or irreversible.
- (iv) In particular, the information provided for the micro-organism, together with other relevant information, and that provided for one or more preparations containing it, shall be sufficient to:
 - decide whether, or not, the micro-organism can be approved,
 - specify appropriate conditions or restrictions to be associated with any approval,
 - permit an evaluation of short- and long-term risks for non-target species — populations, communities, and processes — as appropriate,

- classify the micro-organism as to biological hazard,
 - specify the precautions necessary for the protection of non-target species, and
 - specify the pictograms (once introduced), signal words, and relevant hazard and precautionary statements for the protection of the environment, to be mentioned on packaging (containers).
- (v) There is a need to report all potentially adverse effects found during routine investigations on environmental effects, to undertake and report, where required by the competent authorities, such additional studies which may be necessary to investigate the probable mechanisms involved and to assess the significance of these effects. All available biological data and information which are relevant to the assessment of the ecology profile of the micro-organism must be reported.
- (vi) For all studies, average achieved dose in cfu/kg body weight as well as in other appropriate units must be reported.
- (vii) It may be necessary to conduct separate studies for relevant metabolites (especially toxins), where these products can constitute a relevant risk to non-target organisms and where their effects cannot be evaluated by the available results relating to the micro-organism. Before such studies are performed, the applicant shall seek agreement of the competent authorities on whether such studies need to be performed and, if so, the type of study to be conducted. The information from Sections 5, 6 and 7 has to be taken into account.
- (viii) In order to facilitate the assessment of the significance of test results obtained, the same strain (or recorded origin) of each relevant species shall, where possible, be used in the various tests specified.
- (ix) Tests must be performed unless it can be justified that the non-target organism will not be exposed to the micro-organism. If it is justified that the micro-organism does not cause toxic effects or is not pathogenic or infective to vertebrates or plants, only reaction to appropriate non-target organisms must be investigated.

8.1. **Effects on birds**

Aim of the test

Information on toxicity, infectiveness and pathogenicity to birds must be reported.

8.2. **Effects on aquatic organisms**

Aim of the test

Information on toxicity, infectiveness and pathogenicity to aquatic organisms must be reported.

8.2.1. *Effects on fish*

Aim of the test

Information on toxicity, infectiveness and pathogenicity to fish must be reported.

8.2.2. *Effects on freshwater invertebrates*

Aim of the test

Information on toxicity, infectiveness and pathogenicity to freshwater invertebrates must be reported.

8.2.3. *Effects on algae growth*

Aim of the test

Information on effects on algal growth, growth rate and capacity to recover must be reported.

8.2.4. *Effects on plants other than algae*

Aim of the test

Information on effects on plants other than algae must be reported.

8.3. Effects on bees*Aim of the test*

Information on toxicity, infectiveness and pathogenicity to bees must be reported.

8.4. Effects on arthropods other than bees*Aim of the test*

Information on toxicity, infectiveness and pathogenicity to arthropods other than bees must be reported. The selection of the test species should be related to the potential use of the plant protection products (e.g. foliar or soil application). Special attention should be given to organisms used for biological control and organisms playing an important role in integrated pest management.

8.5. Effects on earthworms*Aim of the test*

Information on toxicity, infectiveness and pathogenicity to earthworms must be reported.

8.6. Effects on non-target soil micro-organisms

Impact on relevant non-target micro-organisms and on their predators (e.g. protozoa for bacterial inoculants) shall be reported. Expert judgement is required to decide whether additional studies are necessary. Such decision will take into consideration the available information in this Section and other Sections, in particular data on the specificity of the micro-organism, and the expected exposure. Useful information may also be available from the observations carried out in efficacy testing. Special attention shall be given to organisms used in integrated crop management (ICM).

8.7. Additional studies

The additional studies might include further acute studies on additional species or processes (such as sewage systems) or higher tier studies such as chronic, sub-lethal or reproductive studies on selected non-target organisms.

Before performing such studies, the applicant shall seek agreement of the competent authorities on the type of study to be performed.

9. SUMMARY AND EVALUATION OF ENVIRONMENTAL IMPACT

A summary and evaluation of all data relevant to the environmental impact, shall be carried out in accordance with the guidance given by the competent authorities of the Member States concerning the format of such summaries and evaluations. It shall include a detailed and critical assessment of those data in the context of relevant evaluative and decision making criteria and guidelines, with particular reference to the risks for the environment and non-target species that may or do arise, and the extent, quality and reliability of the data base. In particular the following issues shall be addressed:

- distribution and fate in the environment, and the time courses involved,
 - identification of non-target species and populations at risk, and the extent of their potential exposure,
 - identification of precautions necessary to avoid or minimise contamination of the environment, and for the protection of non-target species.
-

COMMISSION REGULATION (EU) No 284/2013

of 1 March 2013

setting out the data requirements for plant protection products, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market

(Text with EEA relevance)

THE EUROPEAN COMMISSION,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to 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 ⁽¹⁾, and in particular Article 78(1)(b) thereof,

Whereas:

- (1) In accordance with Article 8(4) of Regulation (EC) No 1107/2009, Commission Regulation (EU) No 545/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the data requirements for plant protection products ⁽²⁾ was adopted. It contains the data requirements for the authorisation of plant protection products, as set out in Annex III to Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant products on the market ⁽³⁾.
- (2) It is necessary to modify the data requirements concerning chemical preparations in order to take into account current scientific and technical knowledge.
- (3) More detailed information for the implementation of the data requirements is laid down in relevant guidance documents.
- (4) Regulation (EU) No 545/2011 should therefore be repealed.
- (5) A reasonable period should be allowed to elapse before the modified data requirements become applicable in order to permit applicants to prepare themselves to meet those requirements.
- (6) In order to permit Member States and the interested parties to prepare themselves to meet the new requirements, it is appropriate to lay down transitional measures concerning data submitted for applications for the approval, renewal of approval and amendment to the

conditions of approval of active substances and for applications for authorisation, renewal of authorisation and amendment to authorisation of plant protection products.

- (7) These transitional measures are without prejudice to Article 80 of Regulation (EC) No 1107/2009.
- (8) The measures provided for in this Regulation are in accordance with the opinion of the Standing Committee on the Food Chain and Animal Health and neither the European Parliament nor the Council has opposed them,

HAS ADOPTED THIS REGULATION:

*Article 1***Data requirements for plant protection products**

The data requirements for plant protection products provided for in Article 8(1)(c) of Regulation (EC) No 1107/2009 shall be as set out in the Annex to this Regulation.

*Article 2***Repeal**

Regulation (EU) No 545/2011 is repealed.

References to the repealed Regulation shall be construed as references to this Regulation.

*Article 3***Transitional measures as regards procedures concerning active substances**

With respect to active substances, Regulation (EU) No 545/2011 shall continue to apply as regards the following:

- (a) procedures concerning the approval of an active substance or an amendment to the approval of such a substance pursuant to Article 13 of Regulation (EC) No 1107/2009 for which the dossiers provided for in Article 8(1) and (2) thereof have been submitted by 31 December 2013;
- (b) procedures concerning the renewal of approval of an active substance pursuant to Article 20 of Regulation (EC) No 1107/2009 for which the supplementary dossiers referred to in Article 9 of Commission Regulation (EU) No 1141/2010 ⁽⁴⁾ have been submitted by 31 December 2013.

⁽¹⁾ OJ L 309, 24.11.2009, p. 1.

⁽²⁾ OJ L 155, 11.6.2011, p. 67.

⁽³⁾ OJ L 230, 19.8.1991, p. 1.

⁽⁴⁾ OJ L 322, 8.12.2010, p. 10.

*Article 4***Transitional measures as regards procedures concerning plant protection products**

1. Regulation (EU) No 545/2011 shall continue to apply as regards procedures concerning the authorisation of a plant protection product, as referred to in Article 28 of Regulation (EC) No 1107/2009, provided that the respective application has been submitted by 31 December 2015 and that the plant protection product contains at least one active substance for which the dossiers or supplementary dossiers have been submitted in compliance with Article 3.

2. By way of derogation from paragraph 1, from 1 January 2014 applicants may choose to apply the data requirements, as set out in the Annex to this Regulation. This choice shall be made in writing when submitting the application and shall be irrevocable.

*Article 5***Entry into force and date of application**

1. This Regulation shall enter into force on the twentieth day following that of its publication in the *Official Journal of the European Union*.

2. For procedures concerning the renewal of approval of active substances whose approval expires on 1 January 2016 or later, this Regulation shall apply as of entry into force.

As regards all other procedures, it shall apply from 1 January 2014.

This Regulation shall be binding in its entirety and directly applicable in all Member States.

Done at Brussels, 1 March 2013.

For the Commission
The President
José Manuel BARROSO

ANNEX

INTRODUCTION

Information to be submitted, its generation and its presentation

1. The information submitted shall meet the following requirements.
 - 1.1. The information shall be sufficient to evaluate efficacy and the foreseeable risks, whether immediate or delayed, which the plant protection product may entail for humans, including vulnerable groups, animals and the environment and contain at least the information and results of the studies referred to in this Annex.
 - 1.2. Any information on potentially harmful effects of the plant protection product on human and animal health or on groundwater shall be included as well as known and expected cumulative and synergistic effects.
 - 1.3. Any information on potentially unacceptable effects of the plant protection product on the environment, on plants and plant products shall be included as well as known and expected cumulative and synergistic effects.
 - 1.4. The information shall include all relevant data from the scientific peer reviewed open literature on the active substance, metabolites and breakdown or reaction products and plant protection products containing the active substance and dealing with side-effects on health, the environment and non-target species. A summary of this data shall be provided.
 - 1.5. The information shall include a full and unbiased report of the studies conducted as well as a full description of them. Such information shall not be required, where one of the following conditions is fulfilled:
 - (a) it is not necessary owing to the nature of the product or its proposed uses, or it is not scientifically necessary;
 - (b) it is technically not possible to supply.In such a case a justification shall be provided.
 - 1.6. Where relevant, the information shall be generated using test methods, which are included in the list referred to in point 6. In the absence of suitable internationally or nationally validated test guidelines, test guidelines accepted by the European competent authority shall be used. Any deviations shall be described and justified.
 - 1.7. The information shall include a full description of the test methods used.
 - 1.8. Where relevant, the information shall be generated in accordance with Directive 2010/63/EU of the European Parliament and of the Council ⁽¹⁾.
 - 1.9. The information shall include a list of endpoints for the plant protection product.
 - 1.10. The information shall include the proposed classification and labelling of the plant protection product in accordance with Regulation (EC) No 1272/2008 of the European Parliament and of the Council ⁽²⁾, where relevant.
 - 1.11. Information as provided for in Commission Regulation (EU) No 283/2013 ⁽³⁾ may be required by the competent authorities on co-formulants. Before requiring additional studies to be performed, the competent authorities shall assess all available information provided in accordance with other Union legislation.
 - 1.12. The information provided for the plant protection product and that provided for the active substance, shall be sufficient to:
 - (a) decide whether, or not, the plant protection product is to be authorised;
 - (b) specify conditions or restrictions to be associated with any authorisation;

⁽¹⁾ OL L 276, 20.10.2010, p. 33.

⁽²⁾ OJ L 353, 31.12.2008, p. 1.

⁽³⁾ See page 1 of this Official Journal.

- (c) permit an evaluation of short and long-term risks for non-target species, populations, communities and processes;
 - (d) identify relevant first aid measures as well as appropriate diagnostic and therapeutic measures to be followed in the event of poisoning in humans;
 - (e) permit a risk assessment of acute and chronic consumer exposure, including, where relevant, a cumulative risk assessment deriving from exposure to more than one active substance;
 - (f) permit an estimation of acute and chronic exposure to operators, workers, residents and bystanders including, where relevant, the cumulative exposure to more than one active substance;
 - (g) permit an evaluation to be made as to the nature and extent of the risks for humans, animals (species normally fed and kept by humans or food producing animals) and of the risks for other non-target vertebrate species;
 - (h) predict the distribution, fate, and behaviour in the environment, as well as the time courses involved;
 - (i) identify non-target species and populations for which hazards arise because of potential exposure;
 - (j) permit an assessment of the impact of the plant protection product on non target species;
 - (k) identify measures necessary to minimise contamination of the environment and impact on non-target species;
 - (l) classify the plant protection product as to hazard in accordance with Regulation (EC) No 1272/2008.
- 1.13. Where relevant, tests shall be designed and data analysed using appropriate statistical methods.
- 1.14. Exposure calculations shall refer to scientific methods accepted by the European Food Safety Authority (the Authority), when available. Additional methods, when used, shall be justified.
2. The requirements set out in this Regulation shall represent the minimum data to be submitted. Additional requirements at national level may be necessary in specific circumstances, that is to say specific scenarios, patterns of use other than those taken into account for approval. Careful attention shall be given to environmental, climatic and agronomic conditions when tests are set up and approved by the competent authorities.
3. **Good laboratory practice (GLP)**
- 3.1. Tests and analyses shall be conducted in accordance with the principles laid down in Directive 2004/10/EC of the European Parliament and of the Council ⁽¹⁾ where testing is done to obtain data on the properties or safety with respect to human or animal health or the environment.
- 3.2. By way of derogation from point 3.1, tests and analyses, required under the provisions of Sections 6 of Parts A and B, may be conducted by official or officially recognised testing facilities or organisations which satisfy at least the following requirements:
- (a) they have at their disposal sufficient scientific and technical staff having the necessary education, training, technical knowledge and experience for their assigned functions;
 - (b) they have at their disposal suitable equipment required for correct performance of the tests and measurements which they claim to be competent to carry out; that equipment is properly maintained and calibrated, where appropriate, before being put into service and thereafter according to an established programme;
 - (c) they have at their disposal appropriate experimental fields and, where necessary glasshouses, growth cabinets or storage rooms; the environment in which the tests are undertaken shall not invalidate their results or adversely effect the required accuracy of measurement;
 - (d) they make available to all relevant personnel operating procedures and protocols used for the trials;

⁽¹⁾ OJ L 50, 20.2.2004, p. 44.

- (e) they make available, where requested by the competent authority, prior to the commencement of a test, information on its location and on the tested plant protection products;
 - (f) they ensure that the quality of the work performed is appropriate to its type, range, volume and intended purpose;
 - (g) they maintain records of all observations, calculations and derived data and calibrations records and final test report as long as the product concerned is authorised in a Member State.
- 3.3. Officially recognised testing facilities and organisations, and, where requested by the competent authorities, official facilities and organisations shall:
- report to the relevant national authority all information necessary to demonstrate that they can satisfy the requirements provided for in point 3.2,
 - permit at any time the inspections, which each Member State shall regularly organise on its territory in order to verify the compliance with point 3.2.
- 3.4. By way of derogation from point 3.1:
- 3.4.1. For active substances consisting of micro-organisms or viruses, tests and analyses performed to obtain data on their properties and safety with respect to other aspects than human health, may be conducted by official or officially recognised testing facilities or organisations which satisfy at least the requirements specified at points 3.2 and 3.3.
- 3.4.2. Studies conducted before the application of this Regulation, although not fully compliant with GLP requirements or with current test methods, may be integrated into the assessment, when accepted by the competent authorities as scientifically valid, thereby removing the need for repeating animal tests, especially for carcinogenicity and reprotoxicity studies. This derogation applies to studies on all vertebrate species.
- 4. Test material**
- 4.1. Due to the influence that impurities and other components can have on toxicological and ecotoxicological behaviour, a detailed description (specification) of the material used shall be provided for each study submitted. Studies shall be conducted using the plant protection product to be authorised or bridging principles may be applied, for example use of a study on a product with a comparable/equivalent composition. A detailed description of the composition used shall be provided.
- 4.2. Where radio-labelled test material is used, radio-labels shall be positioned at sites (one or more as necessary), to facilitate elucidation of metabolic and transformation pathways and to facilitate investigation of the distribution of the active substance and of its metabolites, breakdown and reaction products.
- 5. Tests on vertebrate animals**
- 5.1. Tests on vertebrate animals shall be undertaken only where no other validated methods are available.
- Alternative methods to be considered shall include *in vitro* methods and *in silico* methods. Reduction and refinement methods for *in vivo* testing shall also be encouraged to keep the number of animals used in testing to a minimum.
- 5.2. The principles of replacement, reduction and refinement of the use of vertebrate animals shall be fully taken into account in the design of the test methods, in particular when appropriate validated methods become available to replace, reduce or refine animal testing.
- 5.3. Tests involving the deliberate administration of the active substance or the plant protection product to humans and non-human primates shall not be performed for the purpose of this Regulation.
- 5.4. For ethical reasons, study designs shall be carefully considered, taking into account the scope for reduction, refinement and replacement of animal tests. For example, by including one or more additional dose groups or time points for blood sampling in one study, it may be possible to avoid the need for another study.
6. For purposes of information and of harmonisation the list of test methods and guidance documents relevant to the implementation of this Regulation shall be published in the *Official Journal of the European Union*. This list shall be regularly updated.

PART A
CHEMICAL PLANT PROTECTION PRODUCTS

TABLE OF CONTENTS

SECTION 1 *Identity of the plant protection product*

- 1.1. Applicant
- 1.2. Producer of the plant protection product and the active substances
- 1.3. Trade name or proposed trade name and producer's development code number of the plant protection product if appropriate
- 1.4. Detailed quantitative and qualitative information on the composition of the plant protection product
 - 1.4.1. Composition of the plant protection product
 - 1.4.2. Information on the active substances
 - 1.4.3. Information on safeners, synergists and co-formulants
- 1.5. Type and code of the plant protection product
- 1.6. Function

SECTION 2 *Physical, chemical and technical properties of the plant protection product*

- 2.1. Appearance
- 2.2. Explosive and oxidising properties
- 2.3. Flammability and self-heating
- 2.4. Acidity/alkalinity and pH value
- 2.5. Viscosity and surface tension
- 2.6. Relative density and bulk density
- 2.7. Storage stability and shelf-life: effects of temperature on technical characteristics of the plant protection product
- 2.8. Technical characteristics of the plant protection product
 - 2.8.1. Wettability
 - 2.8.2. Persistent foaming
 - 2.8.3. Suspensibility, spontaneity of dispersion and dispersion stability
 - 2.8.4. Degree of dissolution and dilution stability
 - 2.8.5. Particle size distribution, dust content, attrition and mechanical stability
 - 2.8.5.1. Particle size distribution
 - 2.8.5.2. Dust content
 - 2.8.5.3. Attrition
 - 2.8.5.4. Hardness and integrity
 - 2.8.6. Emulsifiability, re-emulsifiability, emulsion stability
 - 2.8.7. Flowability, pourability and dustability
- 2.9. Physical and chemical compatibility with other products including plant protection products with which its use is to be authorised
- 2.10. Adherence and distribution to seeds
- 2.11. Other studies

SECTION 3 Data on application

- 3.1. Field of use envisaged
- 3.2. Effects on harmful organisms
- 3.3. Details of intended use
- 3.4. Application rate and concentration of the active substance
- 3.5. Method of application
- 3.6. Number and timing of applications and duration of protection
- 3.7. Necessary waiting periods or other precautions to avoid phytotoxic effects on succeeding crops
- 3.8. Proposed instructions for use

SECTION 4 Further information on the plant protection product

- 4.1. Safety intervals and other precautions to protect humans, animals and the environment
- 4.2. Recommended methods and precautions
- 4.3. Emergency measures in the case of an accident
- 4.4. Packaging, compatibility of the plant protection product with proposed packaging materials
- 4.5. Procedures for destruction or decontamination of the plant protection product and its packaging
 - 4.5.1. Neutralisation procedures
 - 4.5.2. Controlled incineration

SECTION 5 Analytical methods

Introduction

- 5.1. Methods used for the generation of pre-authorisation data
 - 5.1.1. Methods for the analysis of the plant protection product
 - 5.1.2. Methods for the determination of residues
- 5.2. Methods for post-authorisation control and monitoring purposes

SECTION 6 Efficacy data

Introduction

- 6.1. Preliminary tests
- 6.2. Testing effectiveness
- 6.3. Information on the occurrence or possible occurrence of the development of resistance
- 6.4. Adverse effects on treated crops
 - 6.4.1. Phytotoxicity to target plants (including different cultivars), or to target plant products
 - 6.4.2. Effects on the yield of treated plants or plant products
 - 6.4.3. Effects on the quality of plants or plant product
 - 6.4.4. Effects on transformation processes
 - 6.4.5. Impact on treated plants or plant products to be used for propagation
- 6.5. Observations on other undesirable or unintended side-effects
 - 6.5.1. Impact on succeeding crops
 - 6.5.2. Impact on other plants, including adjacent crops
 - 6.5.3. Effects on beneficial and other non-target organisms

SECTION 7 Toxicological studies

Introduction

- 7.1. Acute toxicity
 - 7.1.1. Oral toxicity
 - 7.1.2. Dermal toxicity
 - 7.1.3. Inhalation toxicity
 - 7.1.4. Skin irritation
 - 7.1.5. Eye irritation
 - 7.1.6. Skin sensitisation
 - 7.1.7. Supplementary studies on the plant protection product
 - 7.1.8. Supplementary studies for combinations of plant protection products
- 7.2. Data on exposure
 - 7.2.1. Operator exposure
 - 7.2.1.1. Estimation of operator exposure
 - 7.2.1.2. Measurement of operator exposure
 - 7.2.2. Bystander and resident exposure
 - 7.2.2.1. Estimation of bystander and resident exposure
 - 7.2.2.2. Measurement of bystander and resident exposure
 - 7.2.3. Worker exposure
 - 7.2.3.1. Estimation of worker exposure
 - 7.2.3.2. Measurement of worker exposure
- 7.3. Dermal absorption
- 7.4. Available toxicological data relating to co-formulants

SECTION 8 Residues in or on treated products, food and feed**SECTION 9 Fate and behaviour in the environment**

Introduction

- 9.1. Fate and behaviour in soil
 - 9.1.1. Rate of degradation in soil
 - 9.1.1.1. Laboratory studies
 - 9.1.1.2. Field studies
 - 9.1.1.2.1. Soil dissipation studies
 - 9.1.1.2.2. Soil accumulation studies
 - 9.1.2. Mobility in the soil
 - 9.1.2.1. Laboratory studies
 - 9.1.2.2. Lysimeter studies
 - 9.1.2.3. Field leaching studies
 - 9.1.3. Estimation of concentrations in soil
- 9.2. Fate and behaviour in water and sediment
 - 9.2.1. Aerobic mineralisation in surface water

- 9.2.2. Water/sediment study
- 9.2.3. Irradiated water/sediment study
- 9.2.4. Estimation of concentrations in groundwater
 - 9.2.4.1. Calculation of concentrations in groundwater
 - 9.2.4.2. Additional field tests
- 9.2.5. Estimation of concentrations in surface water and sediment
- 9.3. Fate and behaviour in air
 - 9.3.1. Route and rate of degradation in air and transport via air
- 9.4. Estimation of concentrations for other routes of exposure

SECTION 10 *Ecotoxicological studies*

Introduction

- 10.1. Effects on birds and other terrestrial vertebrates
 - 10.1.1. Effects on birds
 - 10.1.1.1. Acute oral toxicity to birds
 - 10.1.1.2. Higher tier data on birds
 - 10.1.2. Effects on terrestrial vertebrates other than birds
 - 10.1.2.1. Acute oral toxicity to mammals
 - 10.1.2.2. Higher tier data on mammals
 - 10.1.3. Effects on other terrestrial vertebrate wildlife (reptiles and amphibians)
- 10.2. Effects on aquatic organisms
 - 10.2.1. Acute toxicity to fish, aquatic invertebrates, or effects on aquatic algae and macrophytes
 - 10.2.2. Additional long-term and chronic toxicity studies on fish, aquatic invertebrates and sediment dwelling organisms
 - 10.2.3. Further testing on aquatic organisms
- 10.3. Effects on arthropods
 - 10.3.1. Effects on bees
 - 10.3.1.1. Acute toxicity to bees
 - 10.3.1.1.1. Acute oral toxicity
 - 10.3.1.1.2. Acute contact toxicity
 - 10.3.1.2. Chronic toxicity to bees
 - 10.3.1.3. Effects on honey bee development and other honey bee life stages
 - 10.3.1.4. Sub-lethal effects
 - 10.3.1.5. Cage and tunnel tests
 - 10.3.1.6. Field tests with honeybees
 - 10.3.2. Effects on non-target arthropods other than bees
 - 10.3.2.1. Standard laboratory testing for non-target arthropods

- 10.3.2.2. Extended laboratory testing, aged residue studies with non-target arthropods
- 10.3.2.3. Semi-field studies with non-target arthropods
- 10.3.2.4. Field studies with non-target arthropods
- 10.3.2.5. Other routes of exposure for non-target arthropods
- 10.4. Effects on non-target soil meso- and macrofauna
 - 10.4.1. Earthworms
 - 10.4.1.1. Earthworms — sub-lethal effects
 - 10.4.1.2. Earthworms — field studies
 - 10.4.2. Effects on non-target soil meso- and macrofauna (other than earthworms)
 - 10.4.2.1. Species level testing
 - 10.4.2.2. Higher tier testing
- 10.5. Effects on soil nitrogen transformation
- 10.6. Effects on terrestrial non-target higher plants
 - 10.6.1. Summary of screening data
 - 10.6.2. Testing on non-target plants
 - 10.6.3. Extended laboratory studies on non-target plants
 - 10.6.4. Semi-field and field tests on non-target plants
- 10.7. Effects on other terrestrial organisms (flora and fauna)
- 10.8. Monitoring data

SECTION 11 *Literature data*

SECTION 12 *Classification and labelling*

SECTION 1

Identity of the plant protection product

The information provided shall be sufficient to precisely identify the plant protection product and define it in terms of its specification and nature.

1.1. **Applicant**

The name and address of the applicant shall be provided, as well as the name, position, telephone, e-mail address and telefax number of a contact point.

1.2. **Producer of the plant protection product and of the active substances**

The name and address of the producer of the plant protection product and of each active substance in the plant protection product shall be provided, as well as the name and address of each manufacturing plant in which the plant protection product and active substance are manufactured. A contact point (name, telephone, e-mail address and telefax number) shall be provided.

If the active substance originates from a producer from which data in accordance with Regulation (EU) No 283/2013 have not been submitted previously, data to address those requirements shall be provided in order to establish equivalence of the active substance.

1.3. **Trade name or proposed trade name and producer's development code number of the plant protection product if appropriate**

All former and current trade names and proposed trade names and development code numbers of the plant protection product shall be provided. Where trade names and code numbers referred to, relate to similar but different plant protection products, full details of the differences shall be provided. The proposed trade name shall be such that it does not give rise to confusion with the trade name of already authorised plant protection products. Each code number shall be specific to a unique plant protection product.

1.4. Detailed quantitative and qualitative information on the composition of the plant protection product**1.4.1. Composition of the plant protection product**

For plant protection products the following information shall be reported:

- the content of the technical active substances (based on the specified minimum purity) and the declared content of pure active substances and, where relevant, the corresponding content of the variant (such as salts and esters) of the active substances,
- the content of safeners, synergists and co-formulants,
- the maximum content of relevant impurities, where appropriate.

In addition to the total active substance content, for slow or controlled release plant protection products (such as capsule suspension, CS) the free (non-encapsulated) and encapsulated active substance content and the release rate shall be given. Where possible, appropriate Collaborative International Pesticides Analytical Council (CIPAC) methods shall be used. If an alternative method is used this shall be justified by the applicant and a detailed description of the methodology used shall be given.

The concentration of each active substance shall be expressed as follows:

- for solids, aerosols, volatile liquids (maximum boiling point 50 °C) or viscous liquids (lower limit 1 Pa s at 20 °C), as % w/w and g/kg,
- for other liquids/gel formulations, as % w/w and g/l,
- for gases, as % v/v and % w/w.

1.4.2. Information on the active substances

For active substances their International Organisation for Standardisation (ISO) common names or proposed ISO common names, their CIPAC numbers, and, where available, the European Commission (EC) numbers shall be provided. Where relevant, it shall be stated which salt, ester, anion or cation is present.

1.4.3. Information on safeners, synergists and co-formulants

Safeners, synergists and co-formulants shall, where possible, be identified both by their chemical name as given in Part 3 of Annex VI to Regulation (EC) No 1272/2008 of the European Parliament and of the Council or, if not included in that Regulation, in accordance with both the International Union of Pure and Applied Chemistry (IUPAC) and Chemical Abstracts (CA) nomenclature. Their structural formula shall be provided. For each component of the safeners, synergists and co-formulants the relevant EC number and Chemical Abstracts Service (CAS) number, where they exist, shall be provided. For co-formulants which are mixtures, the composition shall be provided. Where the information provided does not fully identify the safener, synergist or co-formulant, an appropriate specification shall be provided. The trade name, where available, shall also be provided. Safety data sheets pursuant to Article 31 of Regulation (EC) No 1907/2006 (*) shall be provided. They shall be up to date and in accordance with other Union legislation.

For co-formulants the function shall be specified from among the following:

- (a) adhesive (sticker);
- (b) antifoaming agent;
- (c) antifreeze;
- (d) binder;
- (e) buffer;
- (f) carrier;
- (g) deodorant;
- (h) dispersing agent;
- (i) dye;

(*) OJ L 396, 30.12.2006, p. 1.

- (j) emetic;
- (k) emulsifier;
- (l) fertiliser;
- (m) preservative;
- (n) odourant;
- (o) perfume;
- (p) propellant;
- (q) repellent;
- (r) solvent;
- (s) stabiliser;
- (t) thickener;
- (u) wetting agent;
- (v) miscellaneous (shall be specified by the applicant).

A description of the formulation process shall be provided.

1.5. **Type and code of the plant protection product**

The type and code of plant protection product shall be designated according to the latest edition of the 'Manual on development and use of FAO and WHO specifications for pesticides' prepared by the FAO/WHO Joint Meeting on Pesticide Specifications (JMPS).

Where a plant protection product is not defined precisely in this publication, a full description of the physical nature and state of the plant protection product shall be provided, together with a proposal for a suitable description of the type of plant protection product and a proposal for its definition.

1.6. **Function**

The function shall be specified from among the following:

- (a) acaricide;
- (b) bactericide;
- (c) fungicide;
- (d) herbicide;
- (e) insecticide;
- (f) molluscicide;
- (g) nematocide;
- (h) plant growth regulator;
- (i) repellent;
- (j) rodenticide;
- (k) semio-chemicals;
- (l) talpicide;
- (m) viricide;
- (n) other (shall be specified by the applicant).

SECTION 2

Physical, chemical and technical properties of the plant protection product

The extent to which plant protection products for which authorisation is sought, comply with relevant FAO/WHO specifications, shall be stated. Divergences from these specifications shall be described in detail, and justified by the applicant.

2.1. Appearance

A description of the colour and of the physical state of the plant protection product shall be provided.

2.2. Explosive and oxidising properties

The explosive and oxidising properties of plant protection products shall be determined and reported. A theoretical estimation based on structure shall be accepted if it meets the criteria set out in Appendix 6 of the United Nations' Recommendations on the Transport of Dangerous Goods Manual of Tests and Criteria⁽¹⁾.

2.3. Flammability and self-heating

The flash point of liquids which contain flammable solvents shall be determined and reported. The flammability of solid plant protection products and gases shall be determined and reported. A theoretical estimation based on structure shall be accepted if it meets the criteria set out in Appendix 6 of the United Nations' Recommendations on the Transport of Dangerous Goods Manual of Tests and Criteria.

The self-heating shall be determined and reported.

2.4. Acidity/alkalinity and pH value

In the case of aqueous plant protection products, the pH value of the neat plant protection product shall be determined and reported.

In the case of solid and non-aqueous liquid plant protection products which are to be applied as aqueous dilutions the pH of a 1 % dilution of the plant protection product shall be determined and reported.

In the case of plant protection products which are acidic (pH < 4) or alkaline (pH > 10) the acidity or alkalinity shall be determined and reported.

2.5. Viscosity and surface tension

For liquid formulations the viscosity shall be determined at two shear rates and at 20°C and 40°C and reported together with the test conditions. The surface tension shall be determined at the highest concentration.

For liquid plant protection products containing ≥ 10 % hydrocarbons and for which the kinematic viscosity is less than 7×10^{-6} m²/sec at 40 °C the surface tension of the neat formulation shall be determined at 25 °C and reported.

2.6. Relative density and bulk density

The relative density of liquid plant protection products shall be determined and reported.

The bulk density (pour and tap) of plant protection products which are powders or granules shall be determined and reported.

2.7. Storage stability and shelf-life: effects of temperature on technical characteristics of the plant protection product

The stability of the plant protection product after accelerated storage for 14 days at 54 °C shall be determined and reported. Data generated from alternative time/temperature combinations (for example 8 weeks at 40 °C, 12 weeks at 35 °C or 18 weeks at 30 °C) may be submitted as alternative accelerated storage data. Consideration shall be given to performing this test in packaging made of the same material as the commercial packaging.

⁽¹⁾ United Nations New York and Geneva (2009) Publication ISBN 978-92-1-139135-0.

If the active substance content after the heat stability test has decreased by more than 5 % from the initial value, then information on the breakdown products shall be supplied.

For liquid plant protection products, the effect of low temperatures on stability shall be determined and reported.

The shelf life of the plant protection product at ambient temperature shall be determined and reported. Where shelf life is less than two years, the shelf life in months, with appropriate temperature specifications, shall be reported. The ambient temperature stability test shall be performed in packaging made of the same material as the commercial packaging. Where appropriate, data on the content of relevant impurities, before and after storage, shall be provided.

2.8. **Technical characteristics of the plant protection product**

The technical characteristics of the plant protection product shall be determined and reported at appropriate concentrations.

2.8.1. *Wettability*

The wettability of solid plant protection products, which are diluted for use shall be determined and reported.

2.8.2. *Persistent foaming*

The persistence of foaming of plant protection products to be diluted with water shall be determined and reported.

2.8.3. *Suspensibility, spontaneity of dispersion and dispersion stability*

The suspensibility and the spontaneity of dispersion of water dispersible products shall be determined and reported.

The dispersion stability of plant protection products such as aqueous suspo-emulsions (SE), oil-based suspension concentrates (OD) or emulsifiable granules (EG) shall be determined and reported.

2.8.4. *Degree of dissolution and dilution stability*

The degree of dissolution and the dilution stability of water soluble products shall be determined and reported.

2.8.5. *Particle size distribution, dust content, attrition and mechanical stability*

2.8.5.1. **Particle size distribution**

In the case of water dispersible products, a wet sieve test shall be conducted and reported.

The size distribution of particles in the case of powders and suspension concentrates shall be determined and reported.

The nominal size range of granules shall be determined and reported.

2.8.5.2. **Dust content**

The dust content of granular plant protection products shall be determined and reported.

If results show > 1 % w/w dust then the particle size of the dust generated shall be determined and reported.

2.8.5.3. **Attrition**

The attrition characteristics of granules and tablets which are loose packed shall be determined and reported.

2.8.5.4. **Hardness and integrity**

The hardness and integrity of tablets shall be determined and reported.

2.8.6. *Emulsifiability, re-emulsifiability, emulsion stability*

The emulsifiability, emulsion stability and re-emulsifiability of plant protection products, which exist as emulsions in the spray tank, shall be determined and reported.

- 2.8.7. *Flowability, pourability and dustability*
The following characteristics shall be determined and reported:
- the flowability of granular plant protection products,
 - the pourability of suspensions, and
 - the dustability of dustable powders following accelerated storage according to point 2.7.
- 2.9. **Physical and chemical compatibility with other products including plant protection products with which its use is to be authorised**
The physical and chemical compatibility of recommended tank mixes shall be determined and reported. Known non-compatibility shall be reported.
- 2.10. **Adherence and distribution to seeds**
In the case of plant protection products for seed treatment, both distribution and adhesion shall be determined and reported.
- 2.11. **Other studies**
Supplementary studies necessary for the classification of the plant protection product by hazard shall be carried out in accordance with Regulation (EC) 1272/2008.

SECTION 3

Data on application

Data on application shall be submitted and shall be consistent with good plant protection practice.

- 3.1. **Field of use envisaged**
The fields of use, existing and proposed, shall be specified from among the following:
- (a) field use, such as agriculture, horticulture, forestry and viticulture, protected crops, amenity, weed control on non-cultivated areas;
 - (b) home gardening;
 - (c) house plants;
 - (d) plant products storage practice;
 - (e) other (shall be specified by the applicant).
- 3.2. **Effects on harmful organisms**
The nature of the effects on harmful organisms shall be stated:
- (a) contact action;
 - (b) stomach action;
 - (c) inhalation action;
 - (d) fungitoxic action;
 - (e) fungistatic action;
 - (f) desiccant;
 - (g) reproduction inhibitors;
 - (h) other (shall be specified by the applicant).
- In addition, it shall be specified whether the plant protection product is systemic or not in plants.
- 3.3. **Details of intended use**
Details of the intended use shall be provided including, where relevant, the following information:
- effects achieved for example sprout suppression, retardation of ripening, reduction in stem length, enhanced fertilisation,

- types of harmful organisms controlled,
- plants or plant products to be protected.

3.4. **Application rate and concentration of the active substance**

For each method of application and each use, the rate of application per unit (ha, m², m³) treated, for plant protection product in g, kg, mL or L and active substance in g or kg shall be provided.

Application rates shall be expressed, as appropriate, in one of the following units:

- g, kg, mL or L per ha,
- kg or L per m³,
- g, kg, mL or L per tonne.

For protected crops and home gardening use rates shall be expressed in:

- g, kg, mL or L per 100 m², or
- g, kg, mL or L per m³.

The content of active substance shall be expressed, as appropriate, in:

- g or mL per L, or
- g or mL per kg.

3.5. **Method of application**

The method of application proposed shall be described fully, indicating the type of equipment to be used, if any, as well as the type and volume of diluent to be used per unit of area or volume.

3.6. **Number and timing of applications and duration of protection**

The maximum number of applications to be used and their timing shall be reported. Where relevant, the growth stages of the crop or plants to be protected and the development stages of the harmful organisms shall be indicated. Where possible, the interval between applications in days shall be stated.

The duration of protection afforded both by each application and by the maximum number of applications to be used, shall be indicated.

3.7. **Necessary waiting periods or other precautions to avoid phytotoxic effects on succeeding crops**

Where relevant, minimum waiting periods between last application and sowing or planting of succeeding crops, which are necessary to avoid phytotoxic effects on succeeding crops, shall be stated, and follow from the data provided in accordance with point 6.5.1.

Limitations on choice of succeeding crops, if any, shall be stated.

3.8. **Proposed instructions for use**

The proposed instructions for use of the plant protection product, to be printed on labels and leaflets, shall be provided.

SECTION 4

Further information on the plant protection product

4.1. **Safety intervals and other precautions to protect humans, animals and the environment**

The information provided shall follow from and be supported by the data provided for the active substances and that provided in accordance with Sections 7 and 8.

Where relevant, pre-harvest intervals, re-entry periods or withholding periods necessary to minimise the presence of residues in or on crops, plants and plant products, or in treated areas or spaces, with a view to protecting humans, animals and the environment, shall be specified, such as:

- (a) pre-harvest interval (in days) for each relevant crop;
- (b) re-entry period (in days) for livestock, to areas to be grazed;

- (c) re-entry period (in hours or days) for humans to crops, buildings or spaces treated;
- (d) withholding period (in days) for animal feeding stuffs and for post-harvest uses;
- (e) waiting period (in days), between application and handling treated products;
- (f) waiting period (in days), between last application and sowing or planting succeeding crops.

Where necessary in the light of the test results, information on any specific agricultural, plant health or environmental conditions under which the plant protection product may or may not be used shall be provided.

4.2. **Recommended methods and precautions**

The recommended methods and precautions concerning washing/cleaning of machinery and protective equipment, detailed handling procedures for the storage, at both warehouse and user level of plant protection products, for their transport and in the event of fire shall be provided by the applicant. The effectiveness of cleaning procedures shall be described in detail. Where available, information on combustion products shall be provided. The risks likely to arise and the methods and procedures to minimise the hazards arising, shall be specified. Procedures to preclude or minimise the generation of waste or leftovers shall be provided.

Where appropriate, the nature and characteristics of protective clothing and equipment proposed shall be provided. The data provided shall be sufficient to evaluate the suitability and effectiveness under realistic conditions of use (for example field or glasshouse circumstances).

4.3. **Emergency measures in the case of an accident**

Detailed procedures to be followed in the event of an emergency, whether arising during transport, storage or use, shall be provided and include:

- (a) containment of spillages;
- (b) decontamination of areas, vehicles and buildings;
- (c) disposal of damaged packaging, absorbents and other materials;
- (d) protection of emergency workers and residents, including bystanders;
- (e) first aid measures.

4.4. **Packaging, compatibility of the plant protection product with proposed packaging materials**

Packaging to be used shall be fully described and specified in terms of the materials used, manner of construction (for example extruded, welded), size and capacity, wall thickness, size of opening, type of closure and seals. Packaging shall be designed in order to limit as much as possible exposure of operators and of the environment.

All packaging used shall comply with the relevant Union legislation on transportation and safe handling.

4.5. **Procedures for destruction or decontamination of the plant protection product and its packaging**

Procedures for destruction and decontamination shall be developed for both small quantities (user level) and large quantities (warehouse level). The procedures shall be consistent with provisions in place relating to the disposal of waste and of toxic waste. The proposed means of disposal shall be without unacceptable influence on the environment and be the most cost effective and feasible.

4.5.1. *Neutralisation procedures*

Neutralisation procedures (such as by reaction with other substances to form less toxic compounds) for use in the event of accidental spillages shall be described, where such procedures can be applied. The products produced after neutralisation shall be practically or theoretically evaluated and reported.

4.5.2. *Controlled incineration*

Chemical active substances as well as plant protection products containing them, contaminated materials, or contaminated packaging shall be disposed of through controlled incineration in a licensed incinerator in accordance with the criteria laid down in Directive 94/67/EC of the Council ⁽¹⁾.

If controlled incineration is not the preferred method of disposal, full information on the alternative method of safe disposal used shall be provided. Data shall be provided for such methods, to establish their effectiveness and safety.

SECTION 5

Analytical methods

Introduction

The provisions of this Section cover analytical methods used for the generation of pre-authorisation data and required for post-authorisation control and monitoring purposes.

Descriptions of methods shall be provided and include details of equipment, materials and conditions used.

On request, the following shall be provided:

- (a) analytical standards of the purified active substance and of the plant protection product;
- (b) samples of the active substance as manufactured;
- (c) analytical standards of relevant metabolites and all other components included in all monitoring residue definitions;
- (d) samples of reference substances for the relevant impurities.

In addition, the standards referred to in points (a) and (c) shall, where possible, be made commercially available and, on request, the distributing company shall be named.

5.1. Methods used for the generation of pre-authorisation data

5.1.1. *Methods for the analysis of the plant protection product*

Methods shall be provided, with a full description, for the determination of:

- (a) active substance and/or variant in the plant protection product;
- (b) relevant impurities identified in the technical material or which may be formed during manufacture of the plant protection product or from degradation of the plant protection product during storage;
- (c) relevant co-formulants or components of co-formulants, where required by the national competent authorities.

In the case of a plant protection product containing more than one active substance and/or variant a method capable of determining each, in the presence of the other, shall be provided. If a combined method is not submitted, the technical reasons shall be stated.

The applicability of CIPAC methods shall be assessed and reported. In case of use of a CIPAC method, further validation data shall not be required, but example chromatograms shall be submitted, where available.

The specificity of the methods shall be determined and reported. In addition, the extent of interference by other substances present in the plant protection product (such as impurities or co-formulants), shall be determined.

⁽¹⁾ OJ L 365, 31.12.1994, p. 34.

The linearity of methods shall be determined and reported. The calibration range shall extend (by at least 20 %) beyond the highest and lowest nominal content of the analyte in relevant analytical solutions. Either duplicate determinations at three or more concentrations or single determinations at five or more concentrations shall be made. The equation of the calibration line and the correlation coefficient shall be reported and a typical calibration plot shall be submitted. In cases where a non-linear response is used, this shall be justified by the applicant.

The precision (repeatability) of the methods shall be determined and reported. A minimum of five replicate sample determinations shall be made, and the mean, the relative standard deviation and the number of determinations shall be reported. The accuracy of the methods shall be determined on at least two representative samples at levels appropriate to the material specification. The mean and the relative standard deviation of the recoveries shall be reported.

For relevant impurities and, where necessary, for relevant co-formulants the limit of quantification (LOQ) shall be determined and reported and shall be at a concentration of analyte, which is of toxicological or environmental significance, or at the concentration which is formed during storage of the product, where relevant.

5.1.2. *Methods for the determination of residues*

Methods shall be submitted, with a full description, for the determination of non-isotope-labelled residues in all areas of the dossier, as set out in detail in the following points:

- (a) in soil, water, sediment, air and any additional matrices used in support of environmental fate studies;
- (b) in soil, water and any additional matrices used in support of efficacy studies;
- (c) in feed, body fluids and tissues, air and any additional matrices used in support of toxicology studies;
- (d) in body fluids, air and any additional matrices used in support of operator, worker, resident and bystander exposure studies;
- (e) in or on plants, plant products, processed food commodities, food of plant and animal origin, feed and any additional matrices used in support of residues studies;
- (f) in soil, water, sediment, feed and any additional matrices used in support of ecotoxicology studies;
- (g) in water, buffer solutions, organic solvents and any additional matrices resulting from the physical and chemical properties tests.

The specificity of the methods shall be determined and reported. Validated confirmatory methods shall be submitted if appropriate.

The linearity, recovery and precision (repeatability) of methods shall be determined and reported.

Data shall be generated at the LOQ and either the likely residue levels or ten times the LOQ. The LOQ shall be determined and reported for each component in the residue definition.

5.2. **Methods for post-authorisation control and monitoring purposes**

As far as practicable these methods shall employ the simplest approach, involve the minimum cost, and require commonly available equipment.

Analytical methods for the determination of the active substance and relevant impurities in the plant protection product shall be submitted, unless the applicant shows that these methods already submitted in accordance with the requirements set out in point 5.1.1 can be applied.

The provisions set out in point 5.1.1 shall apply.

Methods, with a full description, shall be submitted for the determination of residues:

- in or on plants, plant products, processed food commodities, food and feed of plant and animal origin,
- in body fluids and tissues,
- in soil,
- in water,
- in air, unless the applicant shows that exposure of operators, workers, residents or bystanders is negligible.

The applicant may deviate from such requirement by showing that the methods submitted in accordance with the requirements set out in point 4.2 of Part A of the Annex to Regulation (EU) No 283/2013 can be applied.

The specificity of the methods shall enable all components included in the monitoring residue definition to be determined. Validated confirmatory methods shall be submitted if appropriate.

The linearity, recovery and precision (repeatability) of methods shall be determined and reported.

Data shall be generated at the LOQ and either the likely residue levels or ten times the LOQ. The LOQ shall be determined and reported for each component included in the monitoring residue definition.

For residues in or on food and feed of plant and animal origin and residues in drinking water, the reproducibility of the method shall be determined by means of an independent laboratory validation (ILV) and reported.

SECTION 6

Efficacy data

Introduction

1. The data supplied shall be sufficient to permit an evaluation of the plant protection product to be made. It shall be possible to evaluate the nature and extent of benefits that accrue following use of the plant protection product, in comparison to an untreated control and where they exist in comparison to suitable reference products and damage thresholds, and to define its conditions of use.
2. The number of trials to be conducted and reported shall reflect factors such as the extent to which the properties of the active substances it contains are known and on the range of conditions that arise, including variability in plant health conditions, climatic differences, the range of agricultural practices, the uniformity of the crops, the mode of application the type of harmful organism and the type of plant protection product.
3. Sufficient data shall be submitted to confirm that patterns of use of the plant protection product are representative of the regions and the range of conditions, likely to be encountered in the regions concerned, for which its use is intended. Where the applicant claims that tests in one or more of the proposed regions of use are unnecessary because conditions are comparable with those in other regions where tests have been carried out, the applicant shall substantiate the claim for comparability with documentary evidence.
4. In order to assess seasonal differences, if any, sufficient data shall be generated and submitted to confirm the performance of the plant protection product in each agronomically and climatically different region for each particular crop (or commodity)/harmful organism combination. Trials on effectiveness and phytotoxicity, where relevant, usually in at least two growing seasons shall be reported.
5. If the trials from the first season adequately confirm the validity of claims made on the basis of extrapolation of results from other crops, commodities or situations or from tests with closely similar plant protection products, the applicant shall provide a justification for not carrying out a second season's work. Where, because of climatic or plant health conditions or other reasons the data obtained in any particular season are of limited value for the assessment of performance, trials in one or more further seasons shall be conducted and reported.

6.1. Preliminary tests

Reports in summary form of preliminary tests, including glasshouse and field studies, used to assess the biological activity or dose range finding of the plant protection product and of the active substances it contains, shall be submitted as relevant when requested by the competent authority. These reports shall provide additional information for the competent authority in order to justify the recommended dose of the plant protection product and, where the plant protection product contains more than one active substance, the ratio of the active substances.

6.2. Testing effectiveness

The tests shall provide sufficient data to permit an evaluation of the level, duration and consistency of control or protection or other intended effects of the plant protection product in comparison to suitable reference products, where they exist.

Test conditions

A trial shall, where possible, consist of the following three components: test product, reference product and untreated control.

The performance of the plant protection product shall be investigated in relation to suitable reference products, where they exist. A plant protection product shall be considered a suitable reference product if it fulfils the following requirements: it is authorised and has proved a sufficient performance in practice under the conditions of the area of intended use (plant health, agricultural, horticultural, forestry, climatic, environmental, as appropriate). The working spectrum, time and method of application, mode of action shall be close to those of the tested plant protection product. If this is not possible, reference product and test product shall be applied according to their specified use.

Plant protection products shall be tested in circumstances where the target harmful organism has been shown to have been present at a level causing or known to cause adverse effects (yield, quality, operational benefit) on an unprotected crop or area or on plants or plant products which have not been treated or where the harmful organism is present at such a level that an evaluation of the plant protection product can be made.

On plant protection products for control of harmful organisms trials shall be performed which show the level of control of the species of harmful organisms concerned or of species representative of groups for which claims are made. Trials shall include the different stages of growth of life cycle of the harmful species, where this is relevant and the different strains or races, where these are likely to show different degrees of susceptibility. Where relevant, these considerations may be addressed in laboratory studies.

Trials to provide data on plant protection products which are plant growth regulators, shall show the level of effects on the species to be treated, and include investigation of differences in the response of a representative sample of the range of cultivars on which its use is proposed.

In order to clarify the dose response, dose rates lower than the recommended one shall be included in some trials in order to enable assessment of whether the recommended rate is the minimum necessary to achieve the desired effect.

The duration of the effects of treatment shall be investigated in relation to the control of the target organism or effect on the treated plants or plant products, as appropriate. When more than one application is recommended for the proposed use pattern of the product, trials shall be reported, which establish the duration of the effects of an application, the number of applications necessary and the desired intervals between them.

Evidence shall be submitted to show that the dose, timing and method of application recommended give adequate control, protection or have the intended effect in the range of circumstances likely to be encountered in practical use.

If there is clear evidence that the performance of the plant protection product is likely to be affected by environmental factors, such as temperature or rain, an investigation of the effects of such factors on performance shall be carried out and reported, particularly where it is known that the performance of chemically related products is so affected.

Where proposed label claims include recommendations for the use of the plant protection product with other plant protection products or adjuvants information on the performance of the mixture shall be provided.

Trials shall be designed to investigate specified issues, to minimise the effects of random variation between different parts of each site and to enable statistical analysis to be applied to results amenable to such analysis. The design, analysis, conduct and reporting of trials shall be in accordance with the specific standards of the European and Mediterranean Plant Protection Organisation (EPPO), where available. Deviations from available EPPO guidelines, may be acceptable provided the trials design meets the minimum requirements of the relevant EPPO standard, and is fully described and justified. The report shall include a detailed and critical assessment of the data.

A statistical analysis of results amenable to such analysis shall be carried out; where necessary the test guideline used shall be adapted to enable such analysis.

Where relevant, evidence of yield and quality may be required as a demonstration of effectiveness.

6.3. **Information on the occurrence or possible occurrence of the development of resistance**

Laboratory data and where it exists, field information relating to the occurrence and development of resistance or cross-resistance in populations of harmful organisms to the active substances, or to related active substances, shall be provided. Where such information is not directly relevant to the uses for which authorisation is sought or to be renewed (different species of harmful organism or different crops), it shall, if available, nevertheless be provided in summary form, as it may provide an indication of the likelihood of resistance developing in the target population.

Where there is evidence or information to suggest that, in commercial use, the development of resistance is likely, evidence shall be generated and submitted as to the sensitivity of the population of the harmful organism concerned to the plant protection product. In such cases a management strategy designed to minimise the likelihood of resistance developing in target species shall be provided. This management strategy shall have regard for and refer to any relevant existing strategies and restrictions already in place.

6.4. **Adverse effects on treated crops**

6.4.1. *Phytotoxicity to target plants (including different cultivars), or to target plant products*

The test shall provide sufficient data to permit an evaluation of the performance of the plant protection product and of the possible occurrence of phytotoxicity after treatment with the plant protection product.

Test conditions

For herbicides testing with a dose which is twice the recommended dose shall be required. For other plant protection products for which adverse effects, however transitory, are seen during the trials, performed in accordance with point 6.2, the margins of selectivity on target crops shall be established, using higher doses than the recommended rates of application. Where serious phytotoxic effects are seen, an intermediate application rate shall also be investigated.

Where adverse effects occur, but are claimed to be unimportant in comparison with the benefits of use or transient, evidence to support this claim is required. If necessary, yield measurement shall be submitted.

The safety of a plant protection product to the main cultivars of the main crops for which it is recommended shall be demonstrated, including effects of crop growth stage, vigour, and other factors which may influence susceptibility to damage or injury.

The extent of information necessary on other crops shall reflect their degree of similarity to the main crops already tested, the quantity and quality of data available on those main crops and how far the manner of use of the plant protection product, if relevant, is similar. It is sufficient to perform the test with the main plant protection product type to be authorised.

Where proposed label claims include recommendations for the use of the plant protection product with another plant protection product, this point shall apply to the mixture.

Observations concerning phytotoxicity shall be performed in the tests set out in point 6.2.

Where phytotoxic effects are seen, they shall be accurately assessed and recorded.

A statistical analysis of results amenable to such analysis should be carried out, where necessary the test guideline used shall be adapted to enable such analysis.

6.4.2. *Effects on the yield of treated plants or plant products*

The test shall provide sufficient data to permit an evaluation of the performance of the plant protection product and of possible occurrence of yield reduction or loss in storage of treated plants or plant products.

Circumstances in which required

The effects of plant protection products on the yield or yield components of treated plant products shall be determined where relevant. When treated plants or plant products are likely to be stored the effect on the yield after storage, including data on storage life, shall be determined where relevant.

6.4.3. *Effects on the quality of plants or plant product*

Appropriate observations of quality parameters may be required for individual crops (for example cereal grain quality, sugar content). Such information can be gathered from appropriate assessments in trials described under 6.2 and 6.4.1.

Where relevant, taint testing shall be conducted.

6.4.4. *Effects on transformation processes*

Where relevant, tests for effects on transformation processes shall be conducted.

6.4.5. *Impact on treated plants or plant products to be used for propagation*

Where relevant, sufficient data and observations shall be provided to permit an evaluation of possible adverse effects of a treatment with the plant protection product on plants or plant products to be used for propagation.

Circumstances in which required

Those data and observations shall be submitted, except where the proposed uses preclude use on crops intended for production of seeds, cuttings, runners, tubers or bulbs for planting, as appropriate.

6.5. **Observations on other undesirable or unintended side-effects**

6.5.1. *Impact on succeeding crops*

Sufficient data shall be provided to permit an evaluation of possible adverse effects of a treatment with the plant protection product on succeeding crops.

Circumstances in which required

Where data, generated in accordance with point 9.1, shows that significant residues of the active substance, its metabolites or breakdown products, which have or may have biological activity on succeeding crops, remain in soil or in plant materials, such as straw or organic material up to sowing or planting time of possible succeeding crops, observations shall be submitted on effects on the normal range of succeeding crops.

6.5.2. *Impact on other plants, including adjacent crops*

Sufficient data shall be reported to permit an evaluation of possible adverse effects of a treatment with the plant protection product on other plants, including adjacent crops.

Circumstances in which required

Observations shall be submitted on adverse effects on other plants, including the normal range of adjacent crops, when there are indications that the plant protection product could affect these plants via drift. Sufficient data shall be submitted to demonstrate that residues of the plant protection product do not remain in the application equipment after cleaning, and that there is no risk to subsequently treated crops.

6.5.3. *Effects on beneficial and other non-target organisms*

Any effects, positive or negative, on the incidence of other harmful organisms, observed in the tests performed in accordance with the requirements of this Section, shall be reported. Any observed environmental effects shall also be reported, such as effects on wildlife and non-target organisms, and especially effects on beneficial organisms in case of Integrated Pest Management (IPM).

SECTION 7

Toxicological studies

Introduction

1. For the evaluation of the toxicity of the plant protection product information shall be provided on acute toxicity, irritation and sensitisation of the active substance. The relevant calculation methods used for the classification of mixtures as laid down in Regulation (EC) No 1272/2008 shall, where appropriate, be applied in the hazard assessment of the plant protection product. Where available, information on mode of toxic action, toxicological profile and all other known toxicological aspects of the active substance and of substances of concern, shall be submitted.

2. Consideration shall be given to the possible effects of components on the toxic potential of the total mixture.

7.1. **Acute toxicity**

The studies, data and information to be provided and evaluated, shall be sufficient to permit the identification of effects following a single exposure to the plant protection product, to be assessed, and in particular to establish, or indicate:

- (a) the toxicity of the plant protection product;
- (b) toxicity of the plant protection product relative to the active substance;
- (c) the time course and characteristics of the effect with full details of behavioural changes and possible gross pathological findings at post-mortem;
- (d) where possible the mode of toxic action; and
- (e) the relative hazard associated with the different routes of exposure.

While the emphasis shall be on estimating the toxicity ranges involved, the information generated shall also permit the plant protection product to be classified in accordance with Regulation (EC) No 1272/2008, where applicable.

7.1.1. *Oral toxicity*

Circumstances in which required

A test for acute oral toxicity shall be carried out, unless the applicant can justify an alternative approach under Regulation (EC) No 1272/2008. In the latter case, acute oral toxicity of all components shall be provided or reliably predicted with a validated method. Consideration shall be given to the possible effects of components on the toxic potential of the total mixture.

7.1.2. *Dermal toxicity*

Circumstances in which required

A test for dermal toxicity shall be carried out on a case by case basis, unless the applicant can justify an alternative approach under Regulation (EC) No 1272/2008. In the latter case, acute dermal toxicity of all components shall be provided or reliably predicted with a validated method. Consideration shall be given to the possible effects of components on the toxic potential of the total mixture.

Findings of severe skin irritation or corrosion in the dermal study may be used instead of performing a specific irritation study.

7.1.3. *Inhalation toxicity*

The study shall provide the inhalation toxicity to rats of the plant protection product or of the smoke it generates.

Circumstances in which required

The study shall be carried out where the plant protection product:

- (a) is a gas or liquified gas;
- (b) is a smoke generating plant protection product or fumigant;
- (c) is used with fogging/misting equipment;
- (d) is a vapour releasing plant protection product;
- (e) is supplied in an aerosol dispenser;
- (f) is in a form of a powder or granules containing a significant proportion of particles of diameter $< 50 \mu\text{m}$ ($> 1 \%$ on a weight basis);
- (g) is to be applied from aircraft in cases where inhalation exposure is relevant;
- (h) contains an active substance with a vapour pressure $> 1 \times 10^{-2}$ Pa and is to be used in enclosed spaces such as warehouses or glasshouses;
- (i) is to be applied by spraying.

A study shall not be required if the applicant can justify an alternative approach under Regulation (EC) No 1272/2008, where applicable. For this purpose, acute inhalation toxicity of all components shall be provided or reliably predicted with a validated method. Consideration shall be given to the possible effects of components on the toxic potential of the total mixture.

The head/nose only exposure shall be used, unless whole body exposure can be justified.

7.1.4. *Skin irritation*

The results of the study shall provide the potential for skin irritancy of the plant protection product including the potential reversibility of the effects observed.

Before undertaking *in vivo* studies for corrosion/irritation of the plant protection product, a weight-of-evidence analysis shall be performed on the existing relevant data. Where insufficient data are available, they can be developed through application of sequential testing.

The testing strategy shall follow a tiered approach:

- (1) the assessment of dermal corrosivity using a validated *in vitro* test method;
- (2) the assessment of dermal irritation using a validated *in vitro* test method (such as human reconstituted skin models);
- (3) an initial *in vivo* dermal irritation study using one animal, and where no adverse effects are noted;
- (4) confirmatory testing using one or two additional animals.

Consideration shall be given to use the dermal toxicity study to provide irritancy information.

Findings of severe skin irritation or corrosion in the dermal study may be used instead of performing a specific irritation study.

Circumstances in which required

The skin irritancy of the plant protection product shall be reported based on the tiered approach, unless the applicant can justify an alternative approach under Regulation (EC) No 1272/2008. In the latter case, skin irritation properties of all components shall be provided or reliably predicted with a validated method. Consideration shall be given to the possible effects of components on the irritant potential of the total mixture.

7.1.5. *Eye irritation*

The results of the study shall provide the potential for eye irritation of the plant protection product, including the potential reversibility of the effects observed.

Before undertaking *in vivo* studies for eye corrosion/irritation of the plant protection product, a weight-of-evidence analysis shall be performed on the existing relevant data. Where available data are considered insufficient, further data may be developed through application of sequential testing.

The testing strategy shall follow a tiered approach:

- (1) the use of an *in vitro* dermal irritation/corrosion test to predict eye irritation/corrosion;
- (2) the performance of a validated or accepted *in vitro* eye irritation study to identify severe eye irritants/corrosives (such as BCOP, ICE, IRE, HET-CAM), and where negative results are obtained;
- (3) the assessment of eye irritation using an available, *in vitro* test method validated for plant protection products for identification of non-irritants or irritants, and when not available;
- (4) an initial *in vivo* eye irritation study using one animal, and where no adverse effects are noted;
- (5) confirmatory testing using one or two additional animals.

Circumstances in which required

Eye irritation tests shall be provided, unless it is likely that severe effects on the eyes may be produced or the applicant can justify an alternative approach under Regulation (EC) No 1272/2008. In the latter case, eye irritation properties of all components shall be provided or reliably predicted with a validated method. Consideration shall be given to the possible effects of components on the irritant potential of the total mixture.

7.1.6. *Skin sensitisation*

The study shall provide information to assess the potential of the plant protection product to provoke skin sensitisation reactions.

Circumstances in which required

The skin sensitisation test shall be carried out unless the active substances or co-formulants are known to have sensitising properties or the applicant can justify an alternative approach under Regulation (EC) No 1272/2008. In the latter case, skin sensitisation properties of all components shall be provided or reliably predicted with a validated method. Consideration shall be given to the possible effects of components on the sensitising potential of the total mixture.

The local lymph node assay (LLNA) shall be used, including where appropriate the reduced variant of the assay. In case the LLNA cannot be conducted, a justification shall be provided and the Guinea Pig Maximisation Test shall be performed. Where a guinea pig assay (Maximisation or Buehler), meeting OECD guidelines and providing a clear result, is available, further testing shall not be carried out for animal welfare reasons.

Since a skin sensitizer can potentially induce hypersensitivity reaction, potential respiratory sensitisation shall be taken into account when appropriate tests are available or when there are indications of respiratory sensitisation effects.

7.1.7. *Supplementary studies on the plant protection product*

The need to perform supplementary studies on the plant protection product shall be discussed with the national competent authorities on a case by case basis in the light of the particular parameters to be investigated and the objectives to be achieved (for example for plant protection products containing active substances or other components suspected to have synergistic or additive toxicological effects).

The type of the study shall be adapted to the endpoint of concern.

7.1.8. *Supplementary studies for combinations of plant protection products*

In cases where the product label includes requirements for use of the plant protection product with other plant protection products or with adjuvants as a tank mix, it may be necessary to carry out studies for a combination of plant protection products or for the plant protection product with adjuvant. The need to perform supplementary studies shall be discussed with the national competent authorities on a case by case basis, taking into account the results of the acute toxicity studies of the individual plant protection products and the toxicological properties of the active substances, the possibility for exposure to the combination of the products concerned, with particular regard to vulnerable groups, and available information or practical experience with the products concerned or similar products.

7.2. Data on exposure

For the purpose of this Regulation the following definitions apply:

- (a) operators are people who are involved in activities relating to the application of a plant protection product, such as mixing, loading, application, or relating to cleaning and maintenance of equipment containing a plant protection product; operators may be professionals or amateurs;
- (b) workers are people who, as part of their employment, enter an area that has previously been treated with a plant protection product or who handle a crop that has been treated with a plant protection product;
- (c) bystanders are people who casually are located within or directly adjacent to an area where application of a plant protection product is in process or has taken place, but not for the purpose of working on the treated area or with the treated commodity;
- (d) residents are people who live, work or attend any institution near to areas that are treated with plant protection products, but not for the purpose of working on the treated area or with the treated commodity.

In cases where the product label includes requirements for use of the plant protection product with other plant protection products or with adjuvants as a tank mix, the exposure assessment shall cover the combined exposure. Cumulative and synergistic effects shall be taken into account and reported in the dossier.

7.2.1. Operator exposure

Information shall be provided to permit an assessment of the extent of exposure to the active substances and toxicologically relevant compounds in the plant protection product likely to occur under the proposed conditions of use, taking into account cumulative and synergistic effects. It shall also provide a basis for the selection of the appropriate protective measures including personal protective equipment to be used by operators and to be specified on the label.

7.2.1.1. Estimation of operator exposure

An estimation shall be made, using where available a suitable calculation model, in order to permit an evaluation of the operator exposure likely to arise under the proposed conditions of use. Where relevant, this estimation shall take into account cumulative and synergistic effects resulting from the exposure to more than one active substance and toxicologically relevant compounds, including those in the product and tank mix.

Circumstances in which required

An estimation of operator exposure shall always be performed.

Estimation conditions

An estimation shall be made for each type of application method and application equipment proposed for use of the plant protection product taking account of the requirements resulting from Regulation (EC) No 1272/2008, where applicable, for handling the undiluted or diluted product.

The estimation shall address mixing/loading and application, and shall include clean-up activities and routine maintenance of the application equipment. Specific information on local use conditions (types and sizes of containers to be used, application equipment, typical work rates and application rates, spray concentration, field sizes, crop growing climatic conditions) shall be included.

At first an estimation shall be made with the assumption that the operator is not using any personal protective equipment.

Where appropriate, 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. Where protective measures are specified on the label, the estimation shall take these into account.

7.2.1.2. Measurement of operator exposure

The study shall provide data to permit an evaluation of the operator exposure likely to arise under the specific proposed conditions of use. The study shall be ethically sound.

Circumstances in which required

Exposure data for the relevant exposure routes shall be reported where there are no representative data in available calculation models or where the model-based risk assessment indicates that the relevant reference value is exceeded.

This will be the case, where the results of the estimation of operator exposure in accordance with point 7.2.1.1 indicate that one or both of the following conditions are fulfilled:

- (a) the AOEL established in the context of approval of the active substance may be exceeded;
- (b) the Limit Values established for the active substance and toxicologically relevant compounds of the plant protection product in accordance with Directive 98/24/EC and Directive 2004/37/EC may be exceeded.

The study shall be done under realistic exposure conditions taking into account the proposed conditions of use.

7.2.2. *Bystander and resident exposure*

Information shall be provided to permit an assessment of the extent of exposure to the active substances and toxicologically relevant compounds likely to occur under the proposed conditions of use, taking into account, where relevant, cumulative and synergistic effects. It shall also provide a basis for the selection of appropriate protective measures, including restricted entry intervals, exclusion of residents and bystanders from treatment areas and separation distances.

7.2.2.1 *Estimation of bystander and resident exposure*

An estimation shall be made, using where available a suitable calculation model in order to permit an evaluation of the bystander and resident exposure likely to arise under the proposed conditions of use. Where relevant, this estimation shall take into account cumulative and synergistic effects resulting from the exposure to more than one active substance and toxicologically relevant compounds, including those in the product and tank mix.

The applicant shall take into consideration that bystanders can be exposed during or after the application of plant protection products and residents may be exposed to plant protection products, mainly, but not only, by inhalation and dermal route and that infants and toddlers exposure may also occur by the oral route (through hand-mouth transfer).

Circumstances in which required

An estimation of bystander and resident exposure shall always be performed.

Estimation conditions

An estimation of bystander and resident exposure shall be made for each relevant type of application method. Specific information including maximum total dose and spray concentration shall be included. The estimation shall be made with the assumption that bystanders and residents do not use any personal protective equipment.

7.2.2.2 *Measurement of bystander and resident exposure*

The study shall provide data to permit an evaluation of the bystander and resident exposure likely to arise under the specific proposed conditions of use. The study shall be ethically sound.

Circumstances in which required

Exposure data for the relevant exposure routes shall be required where the model based risk assessment indicates that the relevant reference value is exceeded or where there are no representative data in available calculation models.

The study shall be done under realistic exposure conditions taking into account the proposed conditions of use.

7.2.3. *Worker exposure*

Information shall be provided to permit an assessment of the extent of exposure to the active substances and toxicologically relevant compounds in the plant protection product likely to occur under the proposed conditions of use and agricultural practices, taking into account cumulative and synergistic effects. It shall also provide a basis for the selection of appropriate protective measures, including waiting and re-entry periods.

7.2.3.1 *Estimation of worker exposure*

An estimation shall be made using, where available, a suitable calculation model, in order to permit an evaluation of the worker exposure likely to arise under the proposed conditions of use. Where relevant, this estimation shall take into account cumulative and synergistic effects resulting from the exposure to more than one active substance and toxicologically relevant compounds, including those in the product and tank mix.

Circumstances in which required

The estimation of worker exposure shall be completed when such exposure could arise under the proposed conditions of use.

Estimation conditions

An estimation of worker exposure shall be made for crops and tasks to be carried out. Specific information including description of post-applications activities, exposure duration, application rate, number of applications, minimum spray interval and growth stage, shall be provided. If data on the amount of dislodgeable residues under the proposed conditions of use are not available, default assumptions shall be used.

At first, the estimation shall be made using available data on the exposure to be expected with the assumption that the worker is not using any personal protective equipment. Where appropriate, a second estimation shall be made with the assumption that the worker is using effective and readily obtainable protective equipment which is feasible to be used and will be worn habitually by workers, for example because it was necessitated by other aspects of task being undertaken.

7.2.3.2. Measurement of worker exposure

The study shall provide data to permit an evaluation of the worker exposure likely to arise under the proposed conditions of use. The study shall be ethically sound.

Circumstances in which required

Exposure data for the relevant exposure routes shall be reported where the model based risk assessment indicates that the relevant reference value is exceeded or where there are no representative data in available calculation models.

This will be the case, where the results of the estimation of worker exposure in accordance with point 7.2.3.1 indicate that one or both of the following conditions are fulfilled:

- (a) the AOEL established in the context of approval of the active substance may be exceeded;
- (b) the Limit Values established for the active substance and toxicologically relevant compounds of the plant protection product in accordance with Directive 98/24/EC and Directive 2004/37/EC may be exceeded.

The study shall be done under realistic exposure conditions taking into account the proposed conditions of use.

7.3. Dermal absorption

The studies shall provide a measurement of the absorption through the skin of the active substances and toxicologically relevant compounds in the plant protection product to be authorised.

Circumstances in which required

The study shall be conducted when dermal exposure is a significant exposure route, and no acceptable risk is estimated using default absorption value.

Test conditions

Data from absorption studies, preferably using human skin *in vitro*, shall be reported.

Studies shall be performed on representative plant protection products at both in use dilution (when applicable) as well as the concentrated form.

In case studies do not correspond with the anticipated exposure situation (for example with regard to the type of co-formulant or the concentration), scientific argument shall be provided before such data can be used with confidence.

7.4. Available toxicological data relating to co-formulants

Where relevant, the applicant shall submit and assess the following information:

- (a) the registration number in accordance with Article 20(3) of Regulation (EC) No 1907/2006;
- (b) the study summaries included in the technical dossier submitted in accordance with Article 10(a)(vi) of Regulation (EC) No 1907/2006; and
- (c) the safety data sheet referred to in Article 31 of Regulation (EC) No 1907/2006.

The safety data sheet under point (c) shall also be submitted and assessed for the plant protection product.

Any other available information shall be submitted.

SECTION 8

Residues in or on treated products, food and feed

Data and information on residues in or on treated products, food and feed in accordance with Section 6 of Part A of the Annex to Regulation (EU) No 283/2013 shall be submitted, unless the applicant shows that the data and information already submitted for the active substance can be applied.

SECTION 9

Fate and behaviour in the environment

Introduction

1. Predicted environmental concentrations (PEC).
 - 1.1. A realistic worst-case estimation shall be made of the expected concentrations of the active substance and metabolites, breakdown and reaction products:
 - which account for more than 10 % of the amount of active substance added,
 - which account for more than 5 % of the amount of active substance added, in at least two sequential measurements,
 - for whose individual components (> 5 %) the maximum of formation is not yet reached at the end of the study, in soil, surface in soil, groundwater, surface water, sediment and air, following use as proposed or already occurring.
 - 1.2. For the purposes of the estimation of such concentrations the following definitions apply:
 - (a) Predicted environmental concentration in soil (PEC_S): the level of residues in the top layer of the soil and to which non-target soil organisms may be exposed (acute and chronic exposure).
 - (b) Predicted environmental concentration in surface water (PEC_{SW}): the level of residues, in surface water to which non-target organisms may be exposed (acute and chronic exposure).
 - (c) Predicted environmental concentration in sediment (PEC_{SED}): the level of residues, in sediment to which non-target benthic organisms may be exposed (acute and chronic exposure).
 - (d) Predicted environmental concentration in groundwater (PEC_{GW}): the level of residues in groundwater.
 - (e) Predicted environmental concentration in air (PEC_A): the level of residues in air, to which man, animals and other non-target organisms may be exposed (acute and chronic exposure).
 - 1.3. For the estimation of these concentrations all relevant information on the plant protection product and on the active substance shall be taken into account. Where relevant the parameters set out in Section 7 of Part A of the Annex to Regulation (EU) No 283/2013 shall be used.
 - 1.4. When models are used for estimation of predicted environmental concentrations they shall:
 - make a best-possible estimation of all relevant processes involved taking into account realistic parameters and assumptions,
 - where possible be reliably validated with measurements carried out under circumstances relevant for the use of the model,
 - be relevant to the conditions in the area of use.
 - 1.5. The information provided shall, where relevant, include that referred to in Section 7 of Part A of the Annex to Regulation (EU) No 283/2013.

2. For solid plant protection products, treated and coated seeds there shall be an assessment of the risk from dust drift on to non-target species during application or sowing. Until agreed dust dissipation rates are available, then likely exposure levels shall be determined using a range of application techniques, suitable dust measurement methodology and, where appropriate, mitigation measures.

9.1. **Fate and behaviour in soil**

9.1.1. *Rate of degradation in soil*

9.1.1.1. *Laboratory studies*

Laboratory studies on soil degradation shall provide best possible estimates of the time required for degradation of 50 % and 90 % ($\text{DegT50}_{\text{lab}}$ and $\text{DegT90}_{\text{lab}}$) of the active substance under laboratory conditions.

Circumstances in which required

The persistence and behaviour of plant protection products in soil shall be investigated unless it is possible to extrapolate from data obtained on the active substance and metabolites, breakdown and reaction products in accordance with the requirements set out in point 7.1.2.1 of Part A of the Annex to Regulation (EU) No 283/2013.

Where it is not possible to extrapolate from anaerobic incubation data obtained on the active substance and metabolites, breakdown and reaction products in accordance with the requirements set out in point 7.1.2.1 of Part A of the Annex to Regulation (EU) No 283/2013, an anaerobic degradation study shall be submitted unless the applicant shows that exposure of the plant protection product containing the active substance to anaerobic conditions is unlikely to occur for the intended uses.

Test conditions

Studies on the rate of aerobic degradation of the active substance shall be reported for at least four soils. Soil properties shall be comparable to those used for the aerobic studies performed in accordance with point 7.1.1 and 7.1.2.1 of Part A of the Annex to Regulation (EU) No 283/2013. Reliable DegT50 and 90 values shall be available for a minimum of four different soils.

Studies on the rate of anaerobic degradation of the active substance shall be carried out using the same procedure and comparable soil as for the anaerobic study performed in accordance with point 7.1.1.2 of Part A of the Annex to Regulation (EU) No 283/2013.

The kinetic formation fraction and degradation rates of potentially relevant metabolites shall be established, in the studies under both aerobic and anaerobic conditions by extension of the study for the active substance, where it is not possible to extrapolate from points 7.1.2.1.2 and 7.1.2.1.4 of Part A of the Annex to Regulation (EU) No 283/2013.

In order to assess the influence of temperature on degradation, a calculation with an adequate Q10 factor or an adequate number of additional studies at a range of temperatures shall be performed.

Reliable DegT50 and 90 values for metabolites, breakdown and reaction products shall be provided for at least three soils from the studies under aerobic conditions.

9.1.1.2. *Field studies*

9.1.1.2.1. *Soil dissipation studies*

The soil dissipation studies shall provide best-possible estimates of the time taken for dissipation of 50 % and 90 % ($\text{DisT50}_{\text{field}}$ and $\text{DisT90}_{\text{field}}$) and if possible the time taken for degradation of 50 % and 90 % ($\text{DegT50}_{\text{field}}$ and $\text{DegT90}_{\text{field}}$), of the active substance under field conditions. Where relevant, information on metabolites, breakdown and reaction products shall be reported.

Circumstances in which required

The dissipation and behaviour of plant protection products in soil shall be investigated unless it is possible to extrapolate from data obtained on the active substance and metabolites, breakdown and reaction products in accordance with the requirements set out in point 7.1.2.2.1 of Part A of the Annex to Regulation (EU) No 283/2013.

Test conditions

Individual studies on a range of representative soils (normally at least four different types at different geographical locations) shall be continued until at least 90% of the amount applied has dissipated from the soil or been transformed to substances that are not the subject of the investigation.

9.1.1.2.2. *Soil accumulation studies*

The tests shall provide sufficient data to evaluate the possibility of accumulation of residues of the active substance and of metabolites, breakdown and reaction products.

Circumstances in which required

Soil accumulation studies shall be reported unless it is possible to extrapolate from data obtained on the active substance and metabolites, breakdown and reaction products in accordance with the requirements set out in point 7.1.2.2.2 of Part A of the Annex to Regulation (EU) No 283/2013.

Test conditions

Long term field studies shall be performed on at least two relevant soils at different geographical locations and involve multiple applications.

In absence of guidance being included in the list referred to under point 6 of the introduction, the type and conditions of the study to be performed shall be discussed with the national competent authorities.

9.1.2. *Mobility in soil*

The information made available shall provide sufficient data to evaluate the mobility and leaching potential of the active substance and metabolites, breakdown and reaction products.

9.1.2.1. *Laboratory studies*

Circumstances in which required

The mobility of plant protection products in soil shall be investigated unless it is possible to extrapolate from data obtained in accordance with the requirements set out in points 7.1.2 and 7.1.3.1 of Part A of the Annex to Regulation (EU) No 283/2013.

Test conditions

The same provisions as provided under points 7.1.2 and 7.1.3.1 of Part A of the Annex to Regulation (EU) No 283/2013 apply.

9.1.2.2. *Lysimeter studies*

Lysimeter studies shall be performed, where necessary, to provide information on:

- the mobility in soil,
- the potential for leaching to ground water,
- the potential distribution in soil.

Circumstances in which required

The decision whether lysimeter studies are to be carried out, as an experimental outdoor study in the framework of a tiered leaching assessment scheme shall take into account the results of degradation and mobility studies and the calculated PEC_{GW}. The type of study to be conducted shall be discussed with the national competent authorities.

These studies shall be performed unless it is possible to extrapolate from data obtained on the active substance and metabolites, breakdown and reaction products in accordance with the requirements set out in point 7.1.4.2 of Part A of the Annex to Regulation (EU) No 283/2013.

Test conditions

Studies shall cover the realistic worst case situation, and the duration necessary for observation of potential leaching, taking into account the soil type, climatic conditions, the application rate and the frequency and period of application.

Water percolating from soil columns shall be analysed at suitable intervals, while residues in plant material shall be determined at harvest. Residues in the soil profile in at least five layers shall be determined on termination of experimental work. Intermediate sampling shall be avoided, since removal of plants (except for harvesting in accordance with normal agricultural practice) and soil influence the leaching process.

Precipitation, soil and air temperatures shall be recorded at regular intervals, at least on a weekly base.

The depth of the lysimeters shall be at least 100 cm. The soil cores shall be undisturbed. Soil temperatures shall be similar to those pertaining in the field. Where necessary, supplementary irrigation shall be provided to ensure optimal plant growth and to ensure that the quantity of percolation water is similar to that in the regions for which authorisation is sought. When during the study the soil has to be disturbed for agricultural reasons it shall not be disturbed deeper than 25 cm.

9.1.2.3. Field leaching studies

Field leaching studies shall be performed, where necessary, to provide information on:

- the mobility in soil,
- the potential for leaching to ground water,
- the potential distribution in soil.

Circumstances in which required

The decision whether field leaching studies are to be carried out, as an experimental outdoor study in the framework of a tiered leaching assessment scheme shall take into account the calculated PEC_{GW} and the results of degradation and mobility studies. The type of study to be conducted shall be discussed with the national competent authorities. These studies shall be performed unless it is possible to extrapolate from data obtained on the active substance and metabolites, breakdown and reaction products in accordance with the requirements set out in point 7.1.4.3 of Part A of the Annex to Regulation (EU) No 283/2013.

Test conditions

Studies shall cover the realistic worst case situation, taking into account the soil type, climatic conditions, the application rate and the frequency and period of application.

Water shall be analysed at suitable intervals. Residues in the soil profile in at least five layers shall be determined on termination of experimental work. Intermediate sampling of plant and soil material shall be avoided (except for harvesting in accordance with normal agricultural practice), since removal of plants and soil influence the leaching process.

Precipitation, soil and air temperatures shall be recorded at regular intervals (at least on a weekly base).

Information on the groundwater table in the experimental fields shall be submitted. Depending on the experimental design, a detailed hydrological characterisation of the test field shall be carried out. If soil cracking is observed during the study this shall be fully described.

Attention shall be given to the number and the location of water collection devices. The placement of these devices in the soil shall not result in preferential flow paths.

9.1.3. Estimation of concentrations in soil

PEC_S estimations shall relate both to a single application at the highest rate of application for which authorisation is sought, and to the maximum number at the shortest interval and highest rates of application for which authorisation is sought, and shall be expressed in terms of mg of active substance per kg of dry soil.

The factors which shall be considered in making PEC_S estimations relate to direct and indirect application to soil, drift, run off, and leaching and include processes such as volatilisation, adsorption, hydrolysis, photolysis,

aerobic and anaerobic degradation. Appropriate soil layer depths shall be used depending on the application method and soil cultivation. Where ground cover is present at time of application, the impact of crop interception in reducing soil exposure may be included in estimations.

Initial PEC_s, immediately after application, shall be provided for the active substance, metabolites, breakdown and reaction products. Appropriate short-term and long-term PEC_s calculations (time weighted averages) shall be provided for the active substance, metabolites, breakdown and reaction products with respect to data from ecotoxicological studies.

Calculation of plateau concentrations in soil shall be provided where on the basis of soil dissipation studies it is established that DisT90 > one year, and where repeated application is envisaged, whether in the same growing season or in succeeding years.

9.2. **Fate and behaviour in water and sediment**

9.2.1. *Aerobic mineralisation in surface water*

Circumstances in which required

The persistence and behaviour of plant protection products in open water (freshwater, estuarine and marine) shall be investigated unless it is possible to extrapolate from data obtained on the active substance and metabolites, breakdown and reaction products in accordance with the requirements set out in point 7.2.2.2 of Part A of the Annex to Regulation (EU) No 283/2013.

The test shall be reported unless the applicant shows that contamination of open water will not occur.

Test conditions

The rate of degradation and the pathway or pathways shall be reported either for a 'pelagic' test system or for a 'suspended sediment' system. Where relevant, additional test systems, which differ with respect to organic carbon content, texture or pH shall be used.

Results obtained shall be presented in the form of schematic drawings showing the pathways involved, and in the form of balance sheets which show the distribution of radio-label in water and, where relevant, sediment as a function of time, as between:

- (a) active substance;
- (b) CO₂;
- (c) volatile compounds other than CO₂;
- (d) individual identified transformation products;
- (e) extractable substances not identified; and
- (f) non-extractable residues in sediment.

The duration of the study shall not exceed 60 days unless the semi-continuous procedure with periodical renewal of the test suspension is applied. However, the period for the batch test may be extended to a maximum of 90 days, if the degradation of the test substance has started within the first 60 days.

9.2.2. *Water/sediment study*

Circumstances in which required

The persistence and behaviour of plant protection products in aquatic systems shall be investigated unless it is possible to extrapolate from data obtained on the active substance and metabolites, breakdown and reaction products in accordance with the requirements set out in point 7.2.2.3 of Part A of the Annex to Regulation (EU) No 283/2013.

The test shall be reported unless the applicant shows that contamination of surface water will not occur.

Test conditions

The degradation pathway or pathways shall be reported for two water/sediment systems. The two sediments selected shall differ with respect to organic carbon content and texture, and where relevant, with respect to pH.

Results obtained shall be presented in the form of schematic drawings showing the pathways involved, and in the form of balance sheets which show the distribution of radio-label in water and sediment as a function of time, as between:

- (a) active substance;
- (b) CO₂;
- (c) volatile compounds other than CO₂;
- (d) individual identified transformation products;
- (e) extractable substances not identified; and
- (f) non-extractable residues in sediment.

The duration of the study shall be at least 100 days. It shall be longer where this is necessary to establish the degradation pathway and water/sediment distribution pattern of the active substance and its metabolites, breakdown and reaction products. If more than 90% of the active substance is degraded before the period of 100 days expires, the test duration may be shorter.

The degradation pattern of potentially relevant metabolites occurring within the water/sediment study shall be established by extension of the study for the active substance, when it is not possible to extrapolate from point 7.2.2.3 of Part A of the Annex to Regulation (EU) No 283/2013.

9.2.3. *Irradiated water/sediment study*

If photochemical degradation is of importance, a water/sediment study under influence of a light/dark regime may additionally be reported.

Test conditions

The type and conditions of the study to be performed shall be discussed with the national competent authorities.

9.2.4. *Estimation of concentrations in groundwater*

The groundwater contamination routes shall be defined taking into account relevant agricultural, plant health, and environmental (including climatic) conditions.

9.2.4.1. Calculation of concentrations in groundwater

PEC_{GW} estimations shall relate to the maximum number and highest rates of application, at the shortest interval, and to the time of application for which authorisation is sought.

Relevant EU groundwater models shall be run. Where specific crops and circumstances are relevant, specific scenarios for typical use situations for the regions of use, for the respective crop or other situation of use shall be used. In case the behaviour in soil is dependent on soil parameters, respective parameters on degradation and adsorption in soil (DegT₅₀ and Koc values) reflecting this dependency shall be used. If identified metabolites, breakdown or reaction products are found to occur in concentrations above 0,1 µg/L in the leachate, an assessment of their relevance shall be required.

Suitable estimations (calculations) of predicted environmental concentration in groundwater PEC_{GW}, of active substance shall be submitted, unless it is clearly evident from the data on degradation or adsorption, taking worst case values, that leaching would be negligible under the intended areas of use.

For all metabolites, breakdown or reaction products identified as a part of the residue definition for risk assessment with respect to groundwater (see point 7.4.1 of Part A of the Annex to Regulation (EU) No 283/2013) a PEC_{GW} calculation shall be required for assessing their relevance.

Where identified metabolites, breakdown or reaction products are found to occur in concentrations above 0,1 µg/L in the leachate, an assessment of their relevance shall be required.

9.2.4.2. Additional field tests

The need to perform additional field tests and the type and conditions of the tests to be performed shall be discussed with the national competent authorities.

9.2.5. *Estimation of concentrations in surface water and sediment*

The surface water and sediment contamination routes shall be defined taking into account relevant agricultural, plant health, and environmental (including climatic) conditions. Suitable estimations (calculations) of predicted environmental concentration in surface water PEC_{SW} and sediment PEC_{SED} of active substance shall be submitted, unless the applicant shows that contamination will not occur. PEC_{SW} and PEC_{SED} estimations shall relate to the maximum number and highest rates of application, at the shortest interval, for which authorisation is sought, and be relevant to ditches, ponds, and streams.

Relevant EU surface water modelling tools shall be run. The factors which shall be considered in making PEC_{SW} and PEC_{SED} estimations relate to direct application to water, drift, run-off, discharge via drains and atmospheric deposition, and include processes such as volatilisation, adsorption, advection, hydrolysis, photolysis, biodegradation, sedimentation and re-suspension, and transfer between water and sediment. Initial maximum concentration following an application (global maximum), short-term and long-term PEC_{SW} calculations for relevant water bodies (time weighted averages) shall be provided. Corresponding initial maximum concentration following an application (global maximum), short-term and long-term PEC_{SED} calculations for relevant water bodies (time weighted averages) shall also be provided. These PEC values shall be provided for the active substance and all metabolites, breakdown and reaction products identified as a part of the residue definition for the risk assessment with respect to surface water and sediment. They shall be used to complete risk assessments, through a comparison with the endpoints derived from data from ecotoxicological studies.

Short-term and long-term PEC_{SW} and corresponding short-term and long-term PEC_{SED} calculations for relevant static water bodies (ponds; time weighted averages) and for relevant slow moving water bodies (ditches and streams; time weighted averages), shall be calculated with the aid of a moving time-window. Appropriate time windows with respect to data from ecotoxicological studies shall be applied.

The need to perform additional higher tier tests and the type and conditions of the tests to be performed shall be discussed with the national competent authorities.

9.3. **Fate and behaviour in air**

9.3.1. *Route and rate of degradation in air and transport via air*

If the trigger for volatilisation, $V_p = 10^{-5}$ Pa (for volatilisation from plant) or 10^{-4} Pa (for volatilisation from soil) at a temperature of 20 °C is exceeded and (drift) mitigation measures are required to reduce exposure to non-target organisms, model calculations of off-site deposition (PEC) originating from volatilisation shall be provided. The volatilisation term (PEC) shall be added into the relevant risk assessment procedures for PEC_S and PEC_{SW} . The calculation may be refined using data from confined experiments. Where relevant, laboratory, wind-tunnel or field experiments to determine PEC_S from deposition following volatilisation and mitigation measures shall be provided.

9.4. **Estimation of concentrations for other routes of exposure**

Suitable estimations (calculations) of predicted environmental concentration, of active substance and metabolites, breakdown and reaction products shall be submitted unless the applicant shows that contamination will not occur in case of exposure by other routes, such as:

- deposition of dust containing plant protection products by drift during sowing,
- indirect exposure of surface water via a sewage treatment plant (STP) after application of a plant protection product in storage rooms, and
- amenity use.

PEC estimations shall relate to the maximum number and highest rates of application, at the shortest interval, for which authorisation is sought, and be relevant to the relevant environmental compartments.

The type of information to be provided shall be discussed with the national competent authorities.

SECTION 10

Ecotoxicological studies**Introduction**

1. Testing of the plant protection product shall be necessary where its toxicity cannot be predicted on the basis of data on the active substance. Where testing is necessary, the aim shall be to demonstrate whether the plant protection product, taking account of content of active substance, is more toxic than the active substance. Thus bridging studies or a limit test may be sufficient. However, where a plant protection product is more toxic than the active substance (expressed in comparable units), definitive testing shall be required. Possible effects on organisms/ecosystems shall be investigated, unless the applicant shows that exposure of the organisms or ecosystems does not occur.

Tests and studies conducted using the plant protection product as test material necessary to assess the toxicity of the active substance shall be reported in the context of the relevant data requirement concerning the active substance.

2. All potentially adverse effects found during routine ecotoxicological investigations shall be reported and such additional studies, which may be necessary to investigate the mechanisms involved and assess the significance of these effects, shall be undertaken and reported.
3. Whenever a study implies the use of different doses, the relationship between dose and adverse effect shall be reported.
4. Where exposure data are necessary to decide whether a study has to be performed, the data obtained in accordance with Section 9 shall be used.

For the estimation of exposure of organisms, all information on the plant protection product and on the active substance shall be taken into account. A tiered approach shall start with default worst-case parameters for exposure and be followed by a parameter refinement based on the identification of representative organisms. Where relevant, the parameters set out in this Section shall be used. Where it appears from available data that the plant protection product is more toxic than the active substance, the toxicity data for the plant protection product shall be used for the calculation of appropriate risk quotients (see point 8 of this introduction).

5. The requirements laid down in this Section shall include certain study types that are set out in Section 8 of Part A of the Annex to Regulation (EU) No 283/2013 (such as standard laboratory tests with birds, aquatic organisms, bees, arthropods, earthworms, soil micro-organisms, soil meso-fauna and non-target plants). While each point shall be addressed, experimental data with a plant protection product shall be generated only if its toxicity cannot be predicted on the basis of data on the active substance. It may be sufficient to test the plant protection product with that species of a group that was most sensitive with the active substance.
6. A detailed description (specification) of the material used as provided for in accordance with point 1.4 shall be provided.
7. In order to facilitate the assessment of the significance of test results obtained, the same strain of each species shall, where possible, be used in the various toxicity tests specified.
8. The ecotoxicological assessment shall be based on the risk that the proposed plant protection product poses to non-target organisms. In carrying out a risk assessment, toxicity shall be compared with exposure. The general term for the output from such a comparison is 'risk quotient' (RQ). RQ may be expressed in several ways, for example, toxicity:exposure ratio (TER) and as a hazard quotient (HQ).
9. For those guidelines which allow for study to be designed to determine an effective concentration (EC_x), the study shall be conducted to determine an EC_{10} and EC_{20} along with corresponding 95 % confidence intervals. If an EC_x approach is used, a NOEC shall still be determined.

Existing acceptable studies that have been designed to generate a NOEC shall not be repeated. An assessment of the statistical power of the NOEC derived from those studies shall be carried out.

10. For solid formulations an assessment of the risk from dust drift on to non-target arthropods and plants shall be required. Details on the likely exposure levels shall be presented in accordance with Section 9 of this Annex. For aquatic life, the risk of movement of the whole particle as well as dust particles shall be considered. Until agreed dust dissipation rate assessments are available likely exposure levels shall be used in the risk assessment.
11. Higher tier studies using a plant protection product shall be designed and data analysed using suitable statistical methods. Full details of the statistical methods shall be reported. Where appropriate, higher tier studies shall be supported by chemical analysis to verify exposure has occurred at an appropriate level.
12. Pending the validation and adoption of new studies and of a new risk assessment scheme, existing protocols shall be used to address the acute and chronic risk to bees, including those on colony survival and development, and the identification and measurement of sub-lethal effects in the risk assessment.

10.1. **Effects on birds and other terrestrial vertebrates**

10.1.1. *Effects on birds*

Possible risks to birds shall be investigated if the toxicity of the plant protection product cannot be predicted on the basis of the data for the active substance, except, for example, where the plant protection product is used in enclosed spaces or for wound-healing treatments where birds will experience neither direct nor secondary exposure.

In the case of pellets, granules or treated seeds the amount of active substance in each pellet, granule or seed shall be reported as well as the size, weight and shape of pellets or granules. From that data, the number as well as the weight of pellets, granules or seeds required to achieve the LD₅₀⁽¹⁾ shall be calculated and reported as well.

In the case of baits the concentration of as in the bait (mg active substance/kg) shall be reported.

A risk assessment for birds shall be conducted in accordance with the relevant risk quotient analysis.

10.1.1.1. Acute oral toxicity to birds

Circumstances in which required

The acute oral toxicity of the plant protection product shall be investigated if toxicity cannot be predicted on the basis of the data for the active substance, or where results from mammalian testing give evidence of higher toxicity of the plant protection product compared to the active substance, unless the applicant shows that it is not likely that birds are exposed to the plant protection product itself.

Test conditions

The test shall provide, where possible, LD₅₀ values, the lethal threshold dose, time courses of response and recovery, the No Observed Effect Level (NOEL), and shall include gross pathological findings. Study design shall be optimised for the achievement of an accurate LD₅₀ rather than for any secondary endpoint.

The study shall be conducted on the species used in the study referred to in point 8.1.1 of Part A of the Annex to Regulation (EU) No 283/2013.

The highest dose used in tests shall not exceed 2 000 mg active substance/kg body weight, however, depending on the expected exposure levels in the field following the intended use of the compound, higher doses may be required.

10.1.1.2. Higher tier data on birds

Higher tier studies on birds shall be conducted where the first tiers of the risk assessment do not demonstrate that risk is acceptable.

10.1.2. *Effects on terrestrial vertebrates other than birds*

Possible risks to vertebrate species other than birds shall be investigated except when the test substance is included in plant protection products used, for example, in enclosed spaces and wound-healing treatments where vertebrate species other than birds will experience neither direct nor secondary exposure.

⁽¹⁾ LD₅₀, abbreviation for 'Lethal Dose, 50 %', that is to say the dose required to kill half the members of a tested population after a specified test duration.

Experimental testing of vertebrates shall only be carried out where the data required for risk assessment cannot be derived from the data generated in accordance with the requirements set out in Section 5 and 7 of Part A of the Annex to Regulation (EU) No 283/2013.

An acute and reproductive risk assessment for terrestrial vertebrates other than birds shall be conducted in accordance with the relevant risk quotient analysis.

10.1.2.1. Acute oral toxicity to mammals

Circumstances in which required

If exposure to the formulation is considered possible and the toxicity cannot be predicted on the basis of the data for the active substance, data on the acute oral toxicity of the plant protection product from the mammalian toxicological assessment shall also be considered (see point 5.8 of Part A of the Annex to Regulation (EU) No 283/2013).

10.1.2.2. Higher tier data on mammals

Higher tier studies on mammals shall be conducted where the first tiers of the risk assessment do not demonstrate that risk is acceptable.

10.1.3. *Effects on other terrestrial vertebrate wildlife (reptiles and amphibians)*

Where it cannot be predicted from the active substance data and, if relevant, the risk to amphibians and reptiles from plant protection products shall be addressed. The type and conditions of the studies to be provided shall be discussed with the national competent authorities.

10.2. **Effects on aquatic organisms**

Possible effects on aquatic species (fish, aquatic invertebrates, algae and in the case of herbicides and plant growth regulators, aquatic macrophytes) shall be investigated except where the possibility that aquatic species will be exposed can be ruled out.

A risk assessment for aquatic organisms shall be conducted in accordance with the relevant risk quotient analysis.

10.2.1. *Acute toxicity to fish, aquatic invertebrates, or effects on aquatic algae and macrophytes.*

Circumstances in which required

Testing shall be performed where:

- (a) the acute toxicity of the plant protection product cannot be predicted on the basis of the data for the active substance; or
- (b) the intended use includes direct application on water;
- (c) extrapolation on the basis of available data for a similar plant protection product is not possible.

Tests shall be carried out on one species from each of the three/four groups of aquatic organisms, that is to say fish, aquatic invertebrates, algae and, where relevant, macrophytes as referred to in point 8.2 of Part A of the Annex to Regulation (EU) No 283/2013, if the plant protection product itself may contaminate water.

However, where the available information permits to conclude that one of these groups is clearly more sensitive, tests on only the relevant group shall be performed.

If the plant protection product contains two or more active substances, and the most sensitive taxonomic groups for the individual active substances are not the same, testing on all three/four aquatic groups, that is to say fish, aquatic invertebrates, algae and, where relevant macrophytes, shall be required.

Test conditions

The relevant provisions as under points 8.2.1, 8.2.4, 8.2.6 and 8.2.7 of Part A of the Annex to Regulation (EU) No 283/2013 apply. In order to minimise fish testing a threshold approach shall be considered for testing acute toxicity in fish (see point 8.2.1 of Part A of the Annex to Regulation (EU) No 283/2013)

10.2.2. *Additional long-term and chronic toxicity studies on fish, aquatic invertebrates and sediment dwelling organisms*

The studies referred to in points 8.2.2 and 8.2.5 of Part A of the Annex to Regulation (EU) No 283/2013 shall be conducted for particular plant protection products, where it is not possible to extrapolate from data obtained in the corresponding studies on the active substance (for example the plant protection product is more acutely toxic than the active substance as manufactured by a factor of 10), unless it is demonstrated that exposure will not occur.

If chronic toxicity studies with the plant protection product are required, the type and conditions of the studies to be provided shall be discussed with the national competent authorities.

10.2.3. *Further testing on aquatic organisms*

The studies referred to in point 8.2.8 of Part A of the Annex to Regulation (EU) No 283/2013 may be required for particular plant protection products where it is not possible to extrapolate from data obtained in the corresponding studies for the active substance or another plant protection product.

10.3. **Effects on arthropods**

10.3.1. *Effects on bees*

The possible effects on bees shall be investigated except where the plant protection product is for exclusive use in situations where bees are not likely to be exposed such as:

- (a) food storage in enclosed spaces;
- (b) non-systemic plant protection products for application to soil, except granules;
- (c) non-systemic dipping treatments for transplanted crops and bulbs;
- (d) wound sealing and healing treatments;
- (e) non-systemic rodenticidal baits;
- (f) use in greenhouses without bees as pollinators.

Testing shall be required if:

- the plant protection product contains more than one active substance,
- the toxicity of a plant protection product cannot be reliably predicted to be either the same or lower than the active substance tested, in accordance with the requirements set out in points 8.3.1 and 8.3.2 of Part A of the Annex to Regulation (EU) No 283/2013.

For seed treatments the risk from drift of dust during drilling of the treated seed shall be taken into account. As regards granules and slug pellets the risk from drift of dust during application shall be taken into account. If the plant protection product is systemic and to be used on seeds, bulbs, roots, applied directly to soil, for example sprayed on to soil, granules/pellets applied to soil, irrigation water, or applied directly to or into the plant, for example by spraying or stem injection, then the risk to bees foraging those plants shall be assessed, including the risk deriving from residues of the plant protection product in nectar, pollen and water, including guttation.

Where bees are likely to be exposed, testing by both acute (oral and contact) and chronic toxicity, including sub-lethal effects, shall be conducted.

Where exposure of bees to residues in nectar, pollen or water resulting from systemic properties of the active substance may occur and where the acute oral toxicity is $< 100 \mu\text{g}/\text{bee}$ or a considerable toxicity for larvae occurs, residues concentrations in these matrices shall be provided and the risk assessment shall be based on a comparison of the relevant endpoint with those residue concentrations. If this comparison indicates that an exposure to toxic levels cannot be excluded, effects shall be investigated with higher tier tests.

10.3.1.1. Acute toxicity to bees

Where bee acute testing with the plant protection product is required, both acute oral and contact toxicity tests shall be conducted.

10.3.1.1.1. *Acute oral toxicity*

A test for acute oral toxicity shall be provided establishing the acute LD₅₀ values together with the NOEC. Sub-lethal effects, if observed, shall be reported.

Test conditions

Results shall be presented in terms of µg plant protection product/bee.

10.3.1.1.2. *Acute contact toxicity*

A test for acute contact toxicity shall be provided establishing the acute LD₅₀ values together with the NOEC. Sub-lethal effects, if observed, shall be reported.

Test conditions

Results shall be presented in terms of µg plant protection product/bee.

10.3.1.2. Chronic toxicity to bees

A test for chronic toxicity to bees shall be provided establishing the chronic oral EC₁₀, EC₂₀, EC₅₀ together with the NOEC. Where the chronic oral EC₁₀, EC₂₀, EC₅₀ cannot be estimated, an explanation shall be provided. Sub-lethal effects, if observed, shall be reported.

Circumstances in which required

The test shall be carried out where bees are likely to be exposed.

Test conditions

Results shall be presented in terms of µg plant protection product/bee.

10.3.1.3. Effects on honey bee development and other honey bee life stages

A bee brood study shall be conducted to determine effects on honey bee development and brood activity.

The bee brood test shall provide sufficient information to evaluate possible risks from the plant protection product on honey bee larvae.

The test shall provide the EC₁₀, EC₂₀ and EC₅₀ for adult bees/larvae (or an explanation if they cannot be estimated) together with the NOEC. Sub-lethal effects, if observed, shall be reported.

10.3.1.4. Sub-lethal effects

Tests investigating sub-lethal effects, such as behavioural and reproductive effects, on bees and, where applicable, on colonies may be required.

10.3.1.5. Cage and tunnel tests

The test shall provide sufficient information to evaluate:

- possible risks from the plant protection product for bee survival and behaviour, and
- impact on bees resulting from feeding on contaminated honey dew or flowers.

Sub-lethal effects shall be addressed, if necessary, by carrying out specific tests (for example foraging behaviour).

Circumstances in which required

When acute or chronic effects on colony survival and development cannot be ruled out, further testing shall be required especially if effects are observed in the honeybee brood feeding test (see point 8.3.1.3 of Part A of the Annex to Regulation (EU) No 283/2013) or if there are indications for indirect effects such as delayed action, effects on juvenile stages, or modification of bee behaviour; or other effects such as prolonged residual effects; in those cases cage/tunnel tests shall be carried out and reported.

Test conditions

The test shall be carried out using healthy queen-right honey bee colonies in which pathogens are low and regularly monitored.

10.3.1.6. *Field tests with honeybees*

The test shall have an adequate statistical power and shall provide sufficient information to evaluate possible risks from the plant protection product on bee behaviour, colony survival and development.

Sub-lethal effects shall be addressed, if necessary by carrying out specific tests (for example homing flight).

Circumstances in which required

When acute or chronic effects on colony survival and development cannot be ruled out, further testing shall be required if:

- effects are observed in the honeybee brood feeding test (see point 8.3.1.3 of Part A of the Annex to Regulation (EU) No 283/2013), or
- there are indications for indirect effects such as delayed action, effects on juvenile stages, or modification of bee behaviour or other effects such as prolonged residual effects.

In those cases field tests shall be carried out.

Test conditions

The test shall be carried out using healthy queen-right honey bee colonies in which pathogens are low and regularly monitored.

Test guideline

The design of higher tier studies to be used shall be discussed with the relevant competent authorities.

10.3.2. *Effects on non-target arthropods other than bees**Circumstances in which required*

Effects on non-target terrestrial arthropods shall be investigated for all plant protection products except where plant protection products containing the active substance are for exclusive use in situations where non-target arthropods are not exposed such as:

- (a) food storage in enclosed spaces that preclude exposure;
- (b) wound sealing and healing treatments;
- (c) enclosed spaces with rodenticidal baits.

Testing shall be required if:

- the plant protection product contains more than one active substance,
- the toxicity of a plant protection product cannot be reliably predicted to be either the same or lower than the active substance tested, in accordance with the requirements set out in point 8.3.2 of Part A of the Annex to Regulation (EU) No 283/2013.

For plant protection products, two indicator species, the cereal aphid parasitoid *Aphidius rhopalosiphii* (Hymenoptera: Braconidae) and the predatory mite *Typhlodromus pyri* (Acari: Phytoseiidae) shall be tested. Initial testing shall be performed using glass plates, and both mortality and effects on reproduction (if assessed) shall be reported. Testing shall determine a rate-response relationship and LR₅₀⁽¹⁾, ER₅₀⁽²⁾ and NOEC endpoints shall be reported for assessment of the risk to these species in accordance with the relevant risk quotient analysis.

⁽¹⁾ LR₅₀, abbreviation for 'Lethal Rate, 50 %', that is to say the application rate required to kill half the members of a tested population after a specified test duration.

⁽²⁾ ER₅₀, abbreviation for 'Effect Rate, 50 %', that is to say the application rate required to cause an effect on half the members of a tested population after a specified test duration.

For a plant protection product containing an active substance suspected of having a special mode of action (for example insect growth regulators, insect feeding inhibitors) additional tests involving sensitive life stages, special routes of uptake or other modifications, may be required. The rationale for the choice of test species used shall be provided.

Testing shall provide sufficient information to evaluate the toxicity (mortality) of the plant protection product to arthropods in the in-field as well as in the off-field area.

10.3.2.1. Standard laboratory testing for non-target arthropods

The test shall provide sufficient information to evaluate the toxicity of the plant protection product to the two indicator species (*Aphidius rhopalosiphi* (Hymenoptera: Braconidae) and *Typhlodromus pyri*) (Acari: Phytoseiidae) in accordance with the relevant risk quotient analysis.

Where adverse effects are indicated, testing using higher tier studies shall be required (see points 10.3.2.2 to 10.3.2.5) for further details. In higher tier assessment the risk quotient analysis used for standard laboratory non-target arthropod testing is not appropriate.

10.3.2.2. Extended laboratory testing, aged residue studies with non-target arthropods

The tests shall provide sufficient information to evaluate the risk of the plant protection product for arthropods using a more realistic test substrate or exposure regime.

Circumstances in which required

Further testing shall be required where effects are seen following laboratory testing in accordance with the requirements set out in point 10.3.2.1 and where the relevant risk quotient analysis indicates a risk to the standard indicator non-target arthropod species.

Firstly, the indicator species affected in standard Tier 1 laboratory testing (point 10.3.2.1) shall be tested. In addition, where an in-field risk is indicated to one or both standard indicator species, testing of one additional species shall be required. Where an off-field risk to the standard indicator species is indicated, testing of one further additional species shall be required.

An aged residue study shall be conducted with the most sensitive species to give information on the time scale needed for potential re-colonisation of treated in-field areas.

Test conditions

(a) Extended laboratory studies

Extended laboratory studies shall be carried out under controlled environmental conditions, by exposing laboratory-reared test organisms, or field collected specimens, to fresh and dried pesticide deposits applied to natural substrates, for example leaves, plants or natural soil under laboratory or field conditions.

(b) Aged residue studies

Aged residue studies shall assess the duration of effects on in-field non-target arthropods. They shall involve ageing of plant protection product deposits under field conditions (use of rain protection may be advisable), with exposure of the test organisms on treated leaves or plants either in the laboratory, under semi-field conditions or a combination of both (such as mortality assessment under semi-field conditions and reproduction assessment under laboratory conditions).

10.3.2.3. Semi-field studies with non-target arthropods

The tests shall provide sufficient information to evaluate the risk of the plant protection product for arthropods taking field conditions into account.

Circumstances in which required

Where effects are seen following laboratory testing in accordance with the requirements set out in point 8.3.2 of Part A of the Annex to Regulation (EU) No 283/2013 or point 10.3.2 of this Annex (for example relevant trigger values are breached), semi-field testing shall be required.

Test conditions

The tests shall be conducted under representative agricultural conditions and in accordance with the proposed recommendations for use, resulting in a realistic worst case study.

In semi-field testing the results from lower tier testing as well as the specific questions to be addressed shall be taken into account. In the selection of species for semi-field testing, the results from lower tier testing as well as the specific questions to be addressed shall be taken into account.

Testing shall include lethal and sub-lethal endpoints (for example integrated parameters in field studies), but such endpoints shall be interpreted with care since they are subject to high variability.

10.3.2.4. Field studies with non-target arthropods

The tests shall provide sufficient information to evaluate the risk of the plant protection product for arthropods taking field conditions into account.

Circumstances in which required

Where effects are seen following testing in accordance with the requirements set out in point 8.3.2 of Part A of the Annex to Regulation (EU) No 283/2013 or in accordance with points 10.3.2.2 or 10.3.2.3 of this Annex, and where the relevant risk quotient analysis indicates a risk to non-target arthropods, field testing shall be required.

Test conditions

The tests shall be conducted under representative agricultural conditions and in accordance with the proposed recommendations for use, resulting in a realistic worst case study.

Field trials shall allow the determination of short- and long-term effects on naturally occurring arthropod populations of a plant protection product following application in accordance with the proposed use pattern for the plant protection product under normal agricultural conditions.

10.3.2.5. Other routes of exposure for non-target arthropods

Where for particular arthropods (such as pollinators and herbivores) testing conducted in accordance with points 10.3.1 and 10.3.2.1 to 10.3.2.4 is not appropriate, additional specific testing shall be required, where there are indications that exposure by routes other than by contact occur (for example plant protection products containing active substances with systemic activity). Before undertaking such testing, the proposed design to be used shall be discussed with the relevant competent authorities.

10.4. Effects on non-target soil meso- and macrofauna**10.4.1. Earthworms**

The possible impact on earthworms shall be reported unless the applicant shows that it is not likely that earthworms are exposed, directly or indirectly.

A risk assessment for earthworm shall be conducted in accordance with the relevant risk quotient analysis.

10.4.1.1. Earthworms — sub-lethal effects

The test shall provide information on the effects on growth and reproduction of the earthworm.

Circumstances in which required

The sub-lethal toxicity of a plant protection product to earthworms shall be investigated if the relevant criteria as defined in point 8.4.1 of Part A of the Annex to Regulation (EU) No 283/2013 are met, and the toxicity of the plant protection product cannot be predicted on the basis of the data for the active substance, unless the applicant shows that no exposure occurs.

Test conditions

Testing shall determine a dose-response relationship and the EC₁₀, EC₂₀ and NOEC shall enable the risk assessment to be conducted in accordance with the appropriate risk quotient analysis, taking into account likely exposure, the organic carbon content (f_{oc}) of the test medium and the lipophilic properties (K_{ow}) of the

test substance. The test substance shall be incorporated into the soil to obtain a homogenous soil concentration. Testing with soil metabolites may be avoided if there is analytical evidence to indicate that the metabolite is present at an adequate concentration and duration in the study conducted with the parent active substance.

10.4.1.2. Earthworms — field studies

The test shall provide sufficient data to evaluate effects on earthworms under field conditions.

Circumstances in which required

Where the relevant risk quotient analysis indicates a chronic risk to earthworms a field study to determine effects under practical field conditions shall be conducted and reported as an option for refined risk assessment.

Test conditions

The study design shall reflect the proposed use of the plant protection product, the environmental conditions likely to arise and species that will be exposed.

If a study is to be used for risk assessment in relation to metabolites, their concentrations occurring shall be confirmed analytically.

10.4.2. Effects on non-target soil meso- and macrofauna (other than earthworms)

Circumstances in which required

Effects on soil organisms (other than earthworms) shall be investigated for all plant protection products, except in situations where soil organisms are not exposed such as:

- (a) food storage in enclosed spaces that preclude exposure;
- (b) wound sealing and healing treatments;
- (c) enclosed spaces with rodenticidal baits.

Testing shall be required if:

- the plant protection product contains more than one active substance,
- the toxicity of a plant protection product cannot be reliably predicted to be either the same or lower than the active substance tested in accordance with point 8.4.2 of Part A of the Annex to Regulation (EU) No 283/2013.

For plant protection products applied as a foliar spray, data on the relevant two non target arthropod species might be taken into account for a preliminary risk assessment. If effects do occur on either species, testing on *Folsomia candida* and *Hypoaspis aculeifer* shall be required (see point 10.4.2.1).

If data on *Aphidius rhopalosiphi* and *Typhlodromus pyri* are not available then the data outlined in point 10.4.2.1 shall be required.

For plant protection products applied as soil treatments directly to soil either as a spray or as a solid formulation, then testing shall be required on both *Folsomia candida* and *Hypoaspis aculeifer* (see point 10.4.2.1).

10.4.2.1. Species level testing

The test shall provide sufficient information to perform an assessment of the toxicity of the plant protection product to the soil invertebrate indicator species *Folsomia candida* and *Hypoaspis aculeifer*.

Test conditions

Testing shall determine a dose-response relationship and the EC₁₀, EC₂₀ and NOEC shall enable the risk assessment to be conducted in accordance with the appropriate risk quotient analysis, taking into account likely exposure, the organic carbon content (f_{oc}) of the test medium and the lipophilic properties (K_{ow}) of the active substance in the plant protection product. The plant protection product shall be incorporated into the soil to obtain a homogenous soil concentration.

10.4.2.2. Higher tier testing

The tests shall provide sufficient information to evaluate the risk of the plant protection product for soil organisms (other than earthworms) using a more realistic test substrate or exposure regime.

Circumstances in which required

Further testing shall be required where significant effects are seen following laboratory testing in accordance with the requirements set out in point 8.4.2.1 of Part A of the Annex to Regulation (EU) No 283/2013 or in accordance with point 10.4.2.1 of this Annex and where risk is indicated following the relevant risk quotient analysis.

The need to perform such studies and the type and conditions of the studies to be performed shall be discussed with the national competent authorities.

Test conditions

Higher-tier tests may take the form of community/population studies (for example, terrestrial model ecosystems, soil mesocosms) or field studies. Timing, levels and routes of exposure shall reflect those of the proposed use of the plant protection product. Key effect end-points include: changes in community and population structure of both micro and macro-organisms; species diversity; number and biomass of key species/groups.

10.5. **Effects on soil nitrogen transformation**

The test shall provide sufficient data to evaluate the impact of the plant protection products on soil microbial activity in terms of nitrogen transformation.

Circumstances in which required

The effects of plant protection products on soil microbial function shall be investigated if the toxicity of the plant protection product cannot be predicted on the basis of data for the active substance, unless the applicant shows that no exposure occurs.

10.6. **Effects on terrestrial non-target higher plants**

10.6.1. *Summary of screening data*

The effects of plant protection products on non-target plants shall be reported, if the toxicity of the plant protection product cannot be predicted on the basis of the data for the active substance, unless the applicant shows that no exposure occurs.

Circumstances in which required

Screening data shall be required for plant protection products other than those exhibiting herbicidal or plant growth regulator activity, and if the toxicity cannot be established from data on the active substance (point 8.6.1 of Part A of the Annex to Regulation (EU) No 283/2013). The data shall include testing from at least six plant species from six different families including both mono- and dicotyledons. The tested concentrations/rates shall be equal or higher than the maximum recommended application rate. If screening studies do not cover the specified range of species or the concentrations/rates necessary, then tests in accordance with point 10.6.2 shall be carried out.

Data are not required, where exposure is negligible, for example in the case of rodenticides, active substances used for wound protection or seed treatment, or in the case of active substances used on stored products or in glasshouses where exposure is precluded.

Test conditions

A summary of available data from tests used to assess biological activity and dose range finding studies, whether positive or negative, which may provide information with respect to possible impact on other non-target flora, shall be provided, together with an assessment as to the potential impact on non-target plant species.

These data shall be supplemented by further information, in summary form, on the observed effects on plants during the course of field testing, namely efficacy, residues, environmental fate and ecotoxicological field studies.

10.6.2. *Testing on non-target plants*

The test shall provide the ER₅₀ values of the plant protection product to non-target plants.

Circumstances in which required

Studies of effects on non-target plants shall be required for herbicide and plant growth regulator plant protection products and for other plant protection products, where risk cannot be predicted from screening data (see point 10.6.1) or when the risk cannot be reliably predicted on the basis of the active substance data generated in accordance with point 8.6.2 of Part A of the Annex to Regulation (EU) No 283/2013.

For all granules risk from drift of dust during time of application shall be considered.

Data shall not be required, where exposure is not likely (such as in the case of rodenticides, active substances used for wound protection or seed treatment, or in the case of active substances used on stored products or in glasshouses where exposure is precluded).

Test conditions

The test substance used shall be the plant protection product concerned or another relevant formulation, containing the active substance, and other relevant co-formulants.

For plant protection products that exhibit herbicidal or plant growth regulator activity, vegetative vigour and seedling emergence concentration/response tests shall be required for at least six species, representing families for which herbicidal/plant growth regulatory action has been found. Where, from the mode of action, it can be clearly established that either seedling emergence or vegetative vigour is only affected, only the relevant study shall be conducted.

Dose-response tests on a selection of 6 to 10 monocotyledon and dicotyledon plant species representing as many taxonomic groups as possible shall be required.

Where on the basis of screening data or other available information, a specific mode of action is evident, or significant differences in species sensitivities are identified, that information shall be used in the selection of the relevant test species.

10.6.3. *Extended laboratory studies on non-target plants*

If as a result of conducting studies in accordance with points 10.6.1 and 10.6.2 and carrying out a risk assessment, a high risk has been identified, an extended laboratory study on non-target plants addressing lower tier concerns may be required by the national competent authorities. The study shall provide information regarding the potential effects of the plant protection product on non-target plants following a more realistic exposure.

The type and conditions of the study to be performed shall be discussed with the national competent authorities.

10.6.4. *Semi-field and field tests on non-target plants*

Semi-field and field tests to study effects observed on non-target plants following realistic application may be submitted as a basis for a refined risk assessment. Testing shall address effects on plant abundance and biomass production at varying distances from the crop or at exposure levels representing varying distances from the crop.

The type and conditions of the study to be performed shall be discussed with the national competent authorities.

10.7. **Effects on other terrestrial organisms (flora and fauna)**

Any available data on the effects of the plant protection product on other terrestrial organisms shall be submitted.

10.8. **Monitoring data**

Available monitoring data concerning effects of the plant protection product to non-target organisms shall be reported.

SECTION 11

Literature data

A summary of all relevant data from the scientific peer reviewed open literature on the active substance, metabolites and breakdown or reaction products and plant protection products containing the active substance shall be submitted.

SECTION 12

Classification and labelling

Proposals for the classification and labelling of the plant protection product in accordance with Regulation (EC) No 1272/2008, where applicable, shall be submitted and justified, including:

- pictograms,
- signal words,
- hazard statements, and
- precautionary statements.

PART B

PREPARATIONS OF MICRO-ORGANISMS INCLUDING VIRUSES

TABLE OF CONTENTS

INTRODUCTION

1. IDENTITY OF THE PLANT PROTECTION PRODUCT
 - 1.1. Applicant
 - 1.2. Manufacturer of the preparation and the micro-organism(s)
 - 1.3. Trade name or proposed trade name, and manufacturer's development code number of the preparation if appropriate
 - 1.4. Detailed quantitative and qualitative information on the composition of the preparation
 - 1.5. Physical state and nature of the preparation
 - 1.6. Function
2. PHYSICAL, CHEMICAL AND TECHNICAL PROPERTIES OF THE PLANT PROTECTION PRODUCT
 - 2.1. Appearance (colour and odour)
 - 2.2. Storage stability and shelf-life
 - 2.2.1. Effects of light, temperature and humidity on technical characteristics of the plant protection product
 - 2.2.2. Other factors affecting stability
 - 2.3. Explosivity and oxidising properties
 - 2.4. Flash point and other indications of flammability or spontaneous ignition
 - 2.5. Acidity, alkalinity and if necessary pH value
 - 2.6. Viscosity and surface tension
 - 2.7. Technical characteristics of the plant protection product
 - 2.7.1. Wettability
 - 2.7.2. Persistent foaming
 - 2.7.3. Suspensibility and suspension stability
 - 2.7.4. Dry sieve test and wet sieve test
 - 2.7.5. Particle size distribution (dustable and wettable powders, granules), content of dust/fines (granules), attrition and friability (granules)
 - 2.7.6. Emulsifiability, re-emulsifiability, emulsion stability
 - 2.7.7. Flowability, pourability (rinsability) and dustability

- 2.8. Physical, chemical and biological compatibility with other products including plant protection products with which its use is to be authorised
 - 2.8.1. Physical compatibility
 - 2.8.2. Chemical compatibility
 - 2.8.3. Biological compatibility
- 2.9. Adherence and distribution to seeds
- 2.10. Summary and evaluation of data presented under points 2.1 to 2.9
3. DATA ON APPLICATION
 - 3.1. Field of use envisaged
 - 3.2. Mode of action
 - 3.3. Details of intended use
 - 3.4. Application rate
 - 3.5. Content of micro-organism in material used (e.g. in the diluted spray, baits or treated seed)
 - 3.6. Method of application
 - 3.7. Number and timing of applications and duration of protection
 - 3.8. Necessary waiting periods or other precautions to avoid phytopathogenic effects on succeeding crops
 - 3.9. Proposed instructions for use
4. FURTHER INFORMATION ON THE PLANT PROTECTION PRODUCT
 - 4.1. Packaging and compatibility of the preparation with proposed packaging materials
 - 4.2. Procedures for cleaning application equipment
 - 4.3. Re-entry periods, necessary waiting periods or other precautions to protect man, livestock and the environment
 - 4.4. Recommended methods and precautions concerning: handling, storage, transport or fire
 - 4.5. Measures in the case of an accident
 - 4.6. Procedures for destruction or decontamination of the plant protection product and its packaging
 - 4.6.1. Controlled incineration
 - 4.6.2. Others
5. ANALYTICAL METHODS
 - 5.1. Methods for the analysis of the preparation
 - 5.2. Methods to determine and quantify residues
6. EFFICACY DATA
 - 6.1. Preliminary tests
 - 6.2. Testing effectiveness
 - 6.3. Information on the occurrence or possible occurrence of the development of resistance

-
- 6.4. Effects on the yield of treated plants or plant products in terms of quantity and/or quality
 - 6.4.1. Effects on the quality of plants or plant products
 - 6.4.2. Effects on transformation processes
 - 6.4.3. Effects on the yield of treated plants or plant products
 - 6.5. Phytotoxicity to target plants (including different cultivars), or to target plant products
 - 6.6. Observations on undesirable or unintended side-effects, e. g. on beneficial and other non-target organisms, on succeeding crops, other plants or parts of treated plants used for propagating purposes (e. g. seeds, cuttings, runners)
 - 6.6.1. Impact on succeeding crops
 - 6.6.2. Impact on other plants, including adjacent crops
 - 6.6.3. Impact on treated plants or plant products to be used for propagation
 - 6.6.4. Effects on beneficial and other non-target organisms
 - 6.7. Summary and evaluation of data presented under 6.1 to 6.6
 - 7. EFFECTS ON HUMAN HEALTH
 - 7.1. Basic acute toxicity studies
 - 7.1.1. Acute oral toxicity
 - 7.1.2. Acute inhalation toxicity
 - 7.1.3. Acute percutaneous toxicity
 - 7.2. Additional acute toxicity studies
 - 7.2.1. Skin irritation
 - 7.2.2. Eye irritation
 - 7.2.3. Skin sensitisation
 - 7.3. Data on exposure
 - 7.4. Available toxicological data relating to non-active substances
 - 7.5. Supplementary studies for combinations of plant protection products
 - 7.6. Summary and evaluation of health effects
 - 8. RESIDUES IN OR ON TREATED PRODUCTS, FOOD AND FEED
 - 9. FATE AND BEHAVIOUR IN THE ENVIRONMENT
 - 10. EFFECTS ON NON-TARGET ORGANISMS
 - 10.1. Effects on birds
 - 10.2. Effects on aquatic organisms
 - 10.3. Effects on bees
 - 10.4. Effects on arthropods other than bees

10.5. Effects on earthworms

10.6. Effects on soil micro-organisms

10.7. Additional studies

11. SUMMARY AND EVALUATION OF ENVIRONMENTAL IMPACT

INTRODUCTION

- (i) This Part provides data requirements for the authorisation of a plant protection product based on preparations of micro-organisms including viruses.

The term 'micro-organism' as defined in the introduction of part B of the Annex to Regulation (EU) No 283/2013, also applies to the Part B of this Annex.

- (ii) Where relevant, data shall be analysed using appropriate statistical methods. Full details of the statistical analysis shall be reported (e.g. all point estimates shall be given with confidence intervals, exact p-values should be given rather than stating significant/non significant).
- (iii) Pending the acceptance of specific guidelines at international level, the information required shall be generated using test guidelines accepted by the competent authority (e.g. USEPA guideline⁽¹⁾); where appropriate test guidelines as described in Part A of the Annex to Regulation (EU) No 283/2013, shall be adapted in such a way that they are appropriate for micro-organisms. Testing shall include viable and, if appropriate, non-viable micro-organisms, and a blank control.
- (iv) Whenever a study implies the use of different doses, the relationship between dose and adverse effect must be reported.
- (v) Where testing is done, a detailed description (specification) of the material used and its impurities, in accordance with the provisions of point 1.4, must be provided.
- (vi) In cases where a new preparation is to be dealt with, extrapolation from Part B of the Annex to Regulation (EU) No 283/2013, could be acceptable, provided that all the possible effects of the co-formulants and other components, especially on pathogenicity and infectiveness, are also evaluated.

1. IDENTITY OF THE PLANT PROTECTION PRODUCT

The information provided, taken together with that provided for the micro-organism(s), must be sufficient to precisely identify and define preparations. The information and data referred to, unless otherwise specified, are required for all plant protection products. This is with the view to identify if any factor could alter the properties of the micro-organism as a plant protection product in comparison to the micro-organism as such, which is treated in Part B of the Annex to Regulation (EU) No 283/2013.

1.1. Applicant

The name and address of the applicant must be provided as must the name, position, telephone and fax number of the appropriate person to contact.

Where, in addition, the applicant has an office, agent or representative in the Member State in which the authorisation is being sought, the name and address of the local office, agent or representative shall be provided, as shall the name, position, telephone and fax number of the appropriate person to contact.

1.2. Manufacturer of the preparation and the micro-organism(s)

The name and address of the manufacturer of the preparation and of each micro-organism in the preparation must be provided as must the name and address of each manufacturing plant in which the preparation and micro-organism are manufactured.

A contact point (preferable a central contact point, to include name, telephone and fax numbers) must be provided for each manufacturer.

If the micro-organism originates from a producer from which data in accordance with Part B of the Annex to Regulation (EU) No 283/2013 had not been submitted previously, detailed information on the name and species description, as required in point 1.3 of Part B of the Annex to Regulation (EU) No 283/2013 and on impurities, as required in point 1.4 of Part B of the Annex to Regulation (EU) No 283/2013 have to be provided.

⁽¹⁾ USEPA Microbial Pesticide Test Guidelines, OPPTS Series 885, February 1996(<http://www.epa.gov/oppbppd1/biopesticides/guidelines/series885.htm>).

1.3. Trade name or proposed trade name, and manufacturer's development code number of the preparation if appropriate

All former and current trade names and proposed trade names and development code numbers of the preparation referred to in the dossier as well as the current names and numbers must be provided. Full detail of any differences must be provided. (The proposed trade name must not give rise to confusion with the trade name of already authorised plant protection products.)

1.4. Detailed quantitative and qualitative information on the composition of the preparation

(i) Each micro-organism that is subject to the application shall be identified and named at the species level. The micro-organism shall be deposited at a recognised culture collection and given an accession number. The scientific name must be stated, as well as the group assignment (bacteria, virus, etc.) and any other denomination relevant to the micro-organism (e.g. strain, serotype). In addition, the development phase of the micro-organism (e.g. spores, mycelium) in the marketed product shall be stated.

(ii) For preparations the following information must be reported:

- the content of the micro-organism(s) in the plant protection product and the content of the micro-organism in the material used for manufacturing of plant protection products. These must include the maximum, minimum and nominal content of the viable and non-viable material,
- the content of co-formulants,
- the content of other components (such as by-products, condensates, culture medium, etc.) and contaminating micro-organisms, derived from production process.

The contents shall be expressed in terms as provided for in Directive 1999/45/EC of the European Parliament and of the Council ⁽¹⁾ for chemicals and appropriate terms for micro-organisms (number of active units per volume or weight or any other manner that is relevant to the micro-organism).

(iii) Co-formulants must where possible, be identified either by their International Chemical Identification as given in Annex VI to Regulation (EC) No 1272/2008, or, if not included in that Regulation, in accordance with both IUPAC and CA nomenclature. Their structure or structural formula must be provided. For each component of the co-formulants the relevant EC (EINECS or ELINCS) number and CAS number where they exist, must be provided. Where the information provided does not fully identify a co-formulant, an appropriate specification must be provided. The trade name of co-formulants, where they exist, must also be provided.

(iv) For co-formulants the function must be given:

- adhesive (sticker),
- antifoaming agent,
- antifreeze,
- binder,
- buffer,
- carrier,
- deodorant,
- dispersing agent,
- dye,
- emetic,
- emulsifier,
- fertiliser,
- odorant,
- perfume,
- preservative,

⁽¹⁾ OJ L 200, 30.7.1999, p. 1.

- propellant,
- repellent,
- safener,
- solvent,
- stabiliser,
- synergist,
- thickener,
- wetting agent
- miscellaneous (specify).

(v) Identification of contaminating micro-organisms and other components derived from production process.

Contaminating micro-organisms must be identified as outlined in point 1.3 of Part B of the Annex to Regulation (EU) No 283/2013.

Chemicals (inert components, by-products, etc.) must be identified as outlined in point 1.10 of Part A of the Annex to Regulation (EU) No 283/2013.

Where the information provided does not fully identify a component, such as condensate, culture medium, etc., detailed information on the composition must be provided for each such component.

1.5. **Physical state and nature of the preparation**

The type and code of preparation must be designated in accordance with the 'Catalogue of pesticide formulation types and international coding system (GIFAP Technical Monograph No 2, 1989)'.

Where a particular preparation is not defined precisely in that catalogue, a full description of the physical nature and state of the preparation must be provided, together with a proposal for a suitable description of the type of preparation and a proposal for its definition.

1.6. **Function**

The biological function must be specified from among the following:

- control of bacteria,
- control of fungi,
- control of insects,
- control of mites,
- control of molluscs,
- control of nematodes,
- control of weeds,
- other (must be specified).

2. **PHYSICAL, CHEMICAL AND TECHNICAL PROPERTIES OF THE PLANT PROTECTION PRODUCT**

The extent to which plant protection products for which authorisation is sought comply with relevant FAO specifications, as agreed by the Group of Experts on Pesticide Specification of the FAO Panel of Experts on Pesticide Specifications, Registration Requirements and Application Standards, must be stated. Divergences from FAO specifications must be described in detail, and justified.

2.1. **Appearance (colour and odour)**

A description of both the colour and odour, if any, and the physical state of the preparation, must be provided.

2.2. Storage stability and shelf-life

2.2.1. *Effects of light, temperature and humidity on technical characteristics of the plant protection product*

- (i) The physical and biological stability of the preparation at the recommended storage temperature including information on the growth of contaminating micro-organisms must be determined and reported. The conditions under which the test has been performed must be justified.
- (ii) Additionally in the case of liquid preparations, the effect of low temperatures on physical stability, must be determined and reported in accordance with CIPAC Methods MT 39, MT 48, MT 51 or MT 54 as appropriate.
- (iii) The shelf life of the preparation at the recommended storage temperature must be reported. Where shelf life is less than two years, the shelf life in months, with appropriate temperature specifications, must be reported. Useful information is given in GIFAP Monograph No 17.

2.2.2. *Other factors affecting stability*

Effect of exposure to air, packaging, etc., on the product stability must be explored.

2.3. Explosivity and oxidising properties

Explosivity and oxidising properties will be determined as defined in point 2.2 of Part A of this Annex, unless it can be justified that it is technically or scientifically not necessary to perform such studies.

2.4. Flash point and other indications of flammability or spontaneous ignition

Flash point and flammability must be determined, as defined in point 2.3 of Part A of this Annex, unless it can be justified that it is technically or scientifically not necessary to perform such studies.

2.5. Acidity, alkalinity and if necessary pH value

Acidity, alkalinity and pH will be determined as defined in point 2.4 of Part A of this Annex, unless it can be justified that it is technically or scientifically not necessary to perform such studies.

2.6. Viscosity and surface tension

Viscosity and surface tension will be determined as defined in point 2.5 of Part A of this Annex, unless it can be justified that it is technically or scientifically not necessary to perform such studies.

2.7. Technical characteristics of the plant protection product

The technical characteristics of the preparation must be determined to permit a decision to be made as to its acceptability. If tests have to be performed, they must be done at temperatures compatible with survival of the micro-organism.

2.7.1. *Wettability*

The wettability of solid preparations which are diluted for use (e.g. wettable powders and water dispersible granules), must be determined and reported in accordance with CIPAC Method MT 53.3.

2.7.2. *Persistent foaming*

The persistence of foaming of preparations to be diluted with water, must be determined and reported in accordance with CIPAC Method MT 47.

2.7.3. *Suspensibility and suspension stability*

- The suspensibility of water dispersible products (e.g. wettable powders, water dispersible granules, suspension concentrates) must be determined and reported in accordance with CIPAC Method MT 15, MT 161 or MT 168 as appropriate.
- The spontaneity of dispersion of water dispersible products (e.g. suspension concentrates and water dispersible granules) must be determined and reported in accordance with CIPAC Methods MT 160 or MT 174 as appropriate.

2.7.4. *Dry sieve test and wet sieve test*

In order to ensure that dustable powders have a suitable particle size distribution for ease of application, a dry sieve test must be conducted and reported in accordance with CIPAC Method MT 59.1.

In the case of water dispersible products, a wet sieve test must be conducted and reported in accordance with CIPAC Method MT 59.3 or MT 167 as appropriate.

2.7.5. *Particle size distribution (dustable and wettable powders, granules), content of dust/fines (granules), attrition and friability (granules)*

- (i) The size distribution of particles in the case of powders, must be determined and reported in accordance with OECD Method 110.

The nominal size range of granules for direct application must be determined and reported in accordance with CIPAC MT 58.3, for water dispersible granules in accordance with CIPAC MT 170.

- (ii) The dust content of granular preparations, must be determined and reported in accordance with CIPAC Method MT 171. If relevant for operator exposure the particle size of dust must be determined and reported in accordance with OECD Method 110.
- (iii) The friability and attrition characteristics of granules, must be determined and reported once internationally agreed methods are available. Where already data are available they must be reported together with the method used.

2.7.6. *Emulsifiability, re-emulsifiability, emulsion stability*

- (i) The emulsifiability, emulsion stability and re-emulsifiability of preparations which form emulsions, must be determined and reported in accordance with CIPAC Method MT 36 or MT 173 as appropriate.
- (ii) The stability of dilute emulsions and of preparations which are emulsions, must be determined and reported in accordance with CIPAC Method MT 20 or MT 173.

2.7.7. *Flowability, pourability (rinsability) and dustability*

- (i) The flowability of granular preparations must be determined and reported in accordance with CIPAC Method MT 172.
- (ii) The pourability (including rinsed residue) of suspensions (e.g. suspension concentrates, suspo-emulsions), must be determined and reported in accordance with CIPAC Method MT 148.
- (iii) The dustability of dustable powders must be determined and reported in accordance with CIPAC Method MT 34 or another suitable method.

2.8. **Physical, chemical and biological compatibility with other products including plant protection products with which its use is to be authorised**

2.8.1. *Physical compatibility*

The physical compatibility of recommended tank mixes must be determined and reported.

2.8.2. *Chemical compatibility*

The chemical compatibility of recommended tank mixes must be determined and reported except where examination of the individual properties of the preparations would establish beyond reasonable doubt that there is no possibility of reaction taking place. In such cases it is sufficient to provide that information as justification for not practically determining the chemical compatibility.

2.8.3. *Biological compatibility*

The biological compatibility of tank mixes must be determined and reported. Effects (e.g. antagonism, fungicidal effects) on the activity of the micro-organism after mixing with other micro-organisms or chemicals must be described. The possible interaction of the plant protection product with other chemical products to be applied on the crops under the expected condition of use of the preparation shall be investigated, based on the efficacy data. Intervals between application of the biological pesticide and chemical pesticides shall be specified, if appropriate, in order to avoid loss of efficacy.

2.9. **Adherence and distribution to seeds**

In the case of preparations for seed treatment, both distribution and adhesion must be investigated and reported; in the case of distribution in accordance with CIPAC Method MT 175.

2.10. **Summary and evaluation of data presented under points 2.1 to 2.9**

3. DATA ON APPLICATION

3.1. Field of use envisaged

The field(s) of use, existing and proposed, for preparations containing the micro-organism must be specified from among the following:

- field use, such as agriculture, horticulture, forestry and viticulture,
- protected crops (e.g. in glasshouses),
- amenity,
- weed control on non-cultivated areas,
- home gardening,
- house plants,
- stored products,
- other (specify).

3.2. Mode of action

The way by which uptake of the product may occur (e.g. contact, stomach, inhalation) or the pest controlling action (fungitoxic, fungistatic action, nutrient competition, etc.) must be stated.

It must also be stated whether or not the product is translocated in plants and, where relevant, if such translocation is apoplastic, symplastic or both.

3.3. Details of intended use

Details of the intended use, e.g. types of harmful organisms controlled and/or plants or plant products to be protected, must be provided.

Intervals between the application of the plant protection product containing micro-organisms and chemical pesticides, or a list with active substances of chemical plant protection products not to be used together with the plant protection product containing micro-organisms on the same crop, shall also be provided.

3.4. Application rate

For each method of application and each use, the rate of application per unit (ha, m², m³) treated, in terms of g or kg or l for the preparation and in terms of appropriate units for the micro-organism, must be provided.

Application rates shall normally be expressed in g or kg/ha or in kg/m³ and where appropriate in g or kg/tonne; for protected crops and home gardening use rates shall be expressed in g or kg/100 m² or g or kg/m³.

3.5. Content of micro-organism in material used (e.g. in the diluted spray, baits or treated seed)

The content of micro-organism shall be reported, as appropriate, in number of active unit/ml or g or any other relevant unit.

3.6. Method of application

The method of application proposed must be described fully, indicating the type of equipment to be used, if any, as well as the type and volume of diluent to be used per unit of area or volume.

3.7. Number and timing of applications and duration of protection

The maximum number of applications to be used and their timing, must be reported. Where relevant the growth stages of the crop or plants to be protected and the development stages of the harmful organisms, must be indicated. Where possible and necessary the interval between applications, in days, must be stated.

The duration of protection afforded both by each application and by the maximum number of applications to be used, must be indicated.

3.8. Necessary waiting periods or other precautions to avoid phytopathogenic effects on succeeding crops

Where relevant, minimum waiting periods between last application and sowing or planting of succeeding crops, which are necessary to avoid phytopathogenic effects on succeeding crops, must be stated, and follow from the data provided under Section 6, point 6.6.

Limitations on choice of succeeding crops, if any, must be stated.

3.9. Proposed instructions for use

The proposed instructions for use of the preparation, to be printed on labels and leaflets, must be provided.

4. FURTHER INFORMATION ON THE PLANT PROTECTION PRODUCT**4.1. Packaging and compatibility of the preparation with proposed packaging materials**

(i) Packaging to be used must be fully described and specified in terms of the materials used, manner of construction (e.g. extruded, welded, etc.), size and capacity, size of opening, type of closure and seals. It must be designed in accordance with the criteria and guidelines specified in the FAO 'Guidelines for the Packaging of Pesticides'.

(ii) The suitability of the packaging, including closures, in terms of its strength, leakproofness and resistance to normal transport and handling, must be determined and reported in accordance with ADR methods 3552, 3553, 3560, 3554, 3555, 3556, 3558, or appropriate ADR Methods for intermediate bulk containers, and, where for the preparation child-resistant closures are required, in accordance with ISO standard 8317.

(iii) The resistance of the packaging material to its contents must be reported in accordance with GIFAP Monograph No 17.

4.2. Procedures for cleaning application equipment

Cleaning procedures for both application equipment and protective clothing must be described in detail. The effectiveness of the cleaning procedure must be determined, using e.g. biotests, and reported.

4.3. Re-entry periods, necessary waiting periods or other precautions to protect man, livestock and the environment

The information provided must follow from and be supported by the data provided for the micro-organism(s) and that provided under Sections 7 and 8.

(i) Where relevant pre-harvest intervals, re-entry periods or withholding periods necessary to minimise the presence of residues in or on crops, plants and plant products, or in treated areas or spaces, with a view to protecting man or livestock, must be specified e.g.:

— pre-harvest interval (in days) for each relevant crop,

— re-entry period (in days) for livestock, to areas to be grazed,

— re-entry period (in hours or days) for man to crops, buildings or spaces treated,

— withholding period (in days) for animal feedingstuffs,

— waiting period (in days), between application and handling treated products.

(ii) Where necessary, in the light of the test results, information on any specific agricultural, plant health or environmental conditions under which the preparation may or may not be used must be provided.

4.4. Recommended methods and precautions concerning: handling, storage, transport or fire

The recommended methods and precautions concerning handling procedures (detailed) for the storage, at both warehouse and user level of plant protection products, for their transport and in the event of fire must be

provided. Where relevant, information on combustion products must be provided. The risks likely to arise and the methods and procedures to minimise the hazards arising, must be specified. Procedures to preclude or minimise the generation of waste or leftovers must be provided.

Where relevant, assessment has to be done in accordance with ISO TR 9122.

The nature and characteristics of protective clothing and equipment proposed must be provided. The data provided must be sufficient to evaluate the suitability and effectiveness under realistic conditions of use (e.g. field or glasshouse circumstances).

4.5. Measures in the case of an accident

Whether arising during transport, storage or use, detailed procedures to be followed in the event of an accident, must be provided and include:

- containment of spillages,
- decontamination of areas, vehicles and buildings,
- disposal of damaged packaging, adsorbents and other materials,
- protection of emergency workers and bystanders,
- first aid measures.

4.6. Procedures for destruction or decontamination of the plant protection product and its packaging

Procedures for destruction and decontamination must be developed for both small quantities (user level) and large quantities (warehouse level). The procedures must be consistent with provisions in place relating to the disposal of waste and of toxic waste. The means of disposal proposed shall be without unacceptable influence on the environment and be the most cost effective and practical means of disposal feasible.

4.6.1. Controlled incineration

In many cases the preferred or sole means to safely dispose of plant protection products and in particular the co-formulants contained in it, contaminated materials, or contaminated packaging, is through controlled incineration in a licensed incinerator.

The applicant must provide detailed instructions for safe disposal.

4.6.2. Others

Other methods to dispose of plant protection products, packaging and contaminated materials, where proposed, must be fully described. Data must be provided for such methods, to establish their effectiveness and safety.

5. ANALYTICAL METHODS

Introduction

The provisions of this Section only cover analytical methods required for post-registration control and monitoring purposes.

It is desirable to have a plant protection product without contaminants, if possible. The level of acceptable contaminants shall be judged from a risk assessment point of view, by the competent authority.

Both production and product must be subject to a continuous quality control by the applicant. The quality criteria for the product shall be submitted.

For analytical methods used for generation of data as required in this Regulation or for other purposes the applicant has to provide a justification for the method used; where necessary separate guidance will be developed for such methods on the basis of the same requirements as defined for methods for post-registration control and monitoring purposes.

Descriptions of methods must be provided and include details of equipment, materials and conditions used. The applicability of existing CIPAC methods must be reported.

As far as practicable these methods must employ the simplest approach, involve the minimum cost, and require commonly available equipment.

For this Section the following applies:

Impurities, metabolites, relevant metabolites, residues	As defined in Article 3 of Regulation (EC) No 1107/2009
Relevant impurities	Impurities, as defined above, that are of concern for human or animal health and/or the environment

On request the following samples must be provided:

- (i) samples of the preparation;
- (ii) samples of the micro-organism as manufactured;
- (iii) analytical standards of the pure micro-organism;
- (iv) analytical standards of relevant metabolites and all other components included in the residue definition;
- (v) if available, samples of reference substances for the relevant impurities.

5.1. Methods for the analysis of the preparation

- Methods, which must be described in full, must be provided for the identification and the determination of the content of the micro-organism in the preparation. In the case of a preparation containing more than one micro-organism, methods capable of identifying and determining the content of each one should be provided.
- Methods to establish regular control of the final product (preparation) in order to show that it does not contain other organisms than the indicated ones and to establish its uniformity.
- Methods to identify any contaminating micro-organisms of the preparation.
- Methods used to determine the storage stability and shelf life of the preparation must be provided.

5.2. Methods to determine and quantify residues

Analytical methods for the determination of residues, as defined in point 4.2 of Part B of the Annex to Regulation (EU) No 283/2013 must be submitted unless it is justified that the information already submitted in accordance with the requirements of point 4.2 of Part B of the Annex to Regulation (EU) No 283/2013 is sufficient.

6. EFFICACY DATA

General

The data supplied must be sufficient to permit an evaluation of the plant protection product to be made. In particular it must be possible to evaluate the nature and extent of benefits that accrue following use of the preparation, where they exist in comparison to suitable reference products and damage thresholds, and to define its conditions of use.

The number of trials to be conducted and reported depends mainly on factors such as the extent to which the properties of the active substance(s) it contains are known and on the range of conditions that arise, including variability in plant health conditions, climatic differences, the range of agricultural practices, the uniformity of the crops, the mode of application, the type of harmful organism and the type of plant protection product.

Sufficient data must be generated and submitted to confirm that patterns determined hold for the regions and the range of conditions, likely to be encountered in the regions concerned, for which its use is to be recommended. Where an applicant claims that tests in one or more of the proposed regions of use are unnecessary because conditions are comparable with those in other regions where tests have been carried out, the applicant must substantiate the claim for comparability with documentary evidence.

In order to assess seasonal differences, if any, sufficient data must be generated and submitted to confirm the performance of the plant protection product in each agronomically and climatically different region for each particular crop (or commodity)/harmful organism combination. Normally trials on effectiveness or phytotoxicity, where relevant, in at least two growing seasons must be reported.

If to the opinion of the applicant the trials from the first season adequately confirm the validity of claims made on the basis of extrapolation of results from other crops, commodities or situations or from tests with closely similar preparations, a justification, which is acceptable to the competent authority for not carrying out a second season's work must be provided. Conversely, where, because of climatic or plant health conditions or other reasons the data obtained in any particular season are of limited value for the assessment of performance, trials in one or more further seasons must be conducted and reported.

6.1. Preliminary tests

Reports in summary form of preliminary tests, including glasshouse and field studies, used to assess the biological activity and dose range finding of the plant protection product and of the active substance(s) it contains, must be submitted when requested by the competent authority. These reports will provide additional information for the competent authority when it evaluates the plant protection product. Where this information is not submitted a justification which is acceptable to the competent authority must be provided.

6.2. Testing effectiveness

Aim of the tests

The tests shall provide sufficient data to permit an evaluation of the level, duration and consistency of control or protection or other intended effects of the plant protection product in comparison to suitable reference products, where they exist.

Test conditions

Normally a trial consists of three components: test product, reference product and untreated control.

The performance of the plant protection product must be investigated in relation to suitable reference products, where they exist. A suitable reference product is defined as an authorised plant protection product which has proved a sufficient performance in practice under the agricultural, plant health and environmental (including climatic) conditions in the area of proposed use. In general, formulation type, effects on the harmful organisms, working spectrum and method of application shall be close to those of the tested plant protection product.

Plant protection products must be tested in circumstances where the target harmful organism has been shown to have been present at a level causing or known to cause adverse effects (yield, quality, operational benefit) on an unprotected crop or area or on plants or plant products which have not been treated or where the harmful organism is present at such a level that an evaluation of the plant protection product can be made.

Trials to provide data on plant protection products for control of harmful organisms must show the level of control of the species of harmful organisms concerned or of species representative of groups for which claims are made. Trials must include the different stages of growth of life cycle of the harmful species, where this is relevant and the different strains or races, where these are likely to show different degrees of susceptibility.

Similarly, trials to provide data on plant protection products which are plant growth regulators, must show the level of effects on the species to be treated, and include investigation of differences in the response of a representative sample of the range of cultivars on which its use is proposed.

In order to clarify the dose response, dose rates lower than the recommended one must be included in some trials in order to enable to assess whether the recommended rate is the minimum necessary to achieve the desired effect.

The duration of the effects of treatment must be investigated in relation to the control of the target organism or effect on the treated plants or plant products, as appropriate. When more than one application is recommended, trials must be reported which establish the duration of the effects of an application, the number of applications necessary and the desired intervals between them.

Evidence must be submitted to show that the dose, timing and method of application recommended give adequate control, protection or have the intended effect in the range of circumstances likely to be encountered in practical use.

Unless there are clear indications that the performance of the plant protection product is unlikely to be affected to a significant degree by environmental factors, such as temperature or rain, an investigation of the effects of such factors on performance must be carried out and reported, particularly where it is known that the performance of chemically related products is so affected.

Where proposed label claims include recommendations for the use of the plant protection product with other plant protection product(s) or adjuvant(s) information on the performance of the mixture must be provided.

Test guideline

Trials must be designed to investigate specified issues, to minimise the effects of random variation between different parts of each site and to enable statistical analysis to be applied to results amenable to such analysis. The design, analysis and reporting of trials must be in accordance with European and Mediterranean Plant Protection Organisation (EPPO) guidelines 152 and 181. The report shall include a detailed and critical assessment of the data.

The trials must be carried out in accordance to specific EPPO guidelines, where available, or with guidelines satisfying at least the requirements of the corresponding EPPO guideline.

A statistical analysis of results amenable to such analysis must be carried out; where necessary the test guideline used must be adapted to enable such analysis.

6.3. Information on the occurrence or possible occurrence of the development of resistance

Laboratory data and where it exists, field information relating to the occurrence and development of resistance or cross-resistance in populations of harmful organisms to the active substance(s), or to related active substances, must be provided. Where such information is not directly relevant to the uses for which authorisation is sought or to be renewed (different species of harmful organism or different crops), it must, if available, nevertheless be provided, as it may provide an indication of the likelihood of resistance developing in the target population.

Where there is evidence or information to suggest that, in commercial use, the development of resistance is likely, evidence must be generated and submitted as to the sensitivity of the population of the harmful organism concerned to the plant protection product. In such cases a management strategy designed to minimise the likelihood of resistance or cross-resistance developing in target species must be provided.

6.4. Effects on the yield of treated plants or plant products in terms of quantity and/or quality

6.4.1. *Effects on the quality of plants or plant products*

Aim of the tests

The tests shall provide sufficient data to permit an evaluation of the possible occurrence of taint or odour or other quality aspects of plants or plant products after treatment with the plant protection product.

Circumstances in which required

The possibility of the occurrence of taint or odour in food crops must be investigated and be reported where:

- the nature of the products or its use is such that a risk of occurrence of taint or odour might be expected, or
- other products based on the same or a closely similar active ingredient have been shown to present a risk of occurrence of taint or odour.

The effects of plant protection products on other quality aspects of treated plants or plant products must be investigated and reported where:

- the nature of the plant protection product or its use could have an adverse influence on other quality aspects (for example in the case of use of plant growth regulators close to the harvest), or
- other products based on the same or a closely similar active ingredient have been shown to have an adverse influence on the quality.

Testing shall be conducted initially on the main crops on which the plant protection product is to be used, at twice the normal rates of application and using, where relevant, the main methods of processing. Where effects are observed it is necessary to perform testing at the normal rate of application.

The extent of investigation necessary on other crops will depend on their degree of similarity of the main crops already tested, the quantity and quality of data available on those main crops and how far the manner of use of the plant protection product and methods of processing the crops, are similar. It is generally sufficient to perform the test with the main formulation type to be authorised.

6.4.2. *Effects on transformation processes*

Aim of the tests

The tests shall provide sufficient data to permit an evaluation of the possible occurrence of adverse effects after treatment with the plant protection product on transformation processes or on the quality of their products.

Circumstances in which required

When the treated plants or plant products are normally intended for use in transformation process such as wine making, brewing or bread making and when at harvest significant residues are present, the possibility of the occurrence of adverse effects must be investigated and reported where:

- there are indications that the use of the plant protection product could have an influence on the processes involved (for example in the case of use of plant growth regulators or fungicides close to the harvest), or
- other products based on the same or a closely similar active ingredient have been shown to have an adverse influence on these processes or its products.

It is generally sufficient to perform the test with the main formulation type to be authorised.

6.4.3. *Effects on the yield of treated plants or plant products*

Aim of the tests

The test shall provide sufficient data to permit an evaluation of the performance of the plant protection product and of possible occurrence of yield reduction or loss in storage of treated plants or plant products.

Circumstances in which required

The effects of plant protection products on the yield or yield components of treated plant products must be determined where relevant. When treated plants or plant products are likely to be stored the effect on the yield after storage, including data on storage life must be determined where relevant.

This information will normally be available from the tests required under the provisions of point 6.2.

6.5. **Phytotoxicity to target plants (including different cultivars), or to target plant products**

Aim of the tests

The test shall provide sufficient data to permit an evaluation of the performance of the plant protection product and of the possible occurrence of phytotoxicity after treatment with the plant protection product.

Circumstances in which required

For herbicides and for other plant protection products for which adverse effects, however transitory, are seen during the trials, performed in accordance with point 6.2, the margins of selectivity on target crops must be established, using twice the recommended rate of application. Where serious phytotoxic effects are seen, an intermediate application rate must also be investigated.

Where adverse effects occur, but are claimed to be unimportant in comparison with the benefits of use or transient, evidence to support this claim is required. If necessary, yield measurement must be submitted.

The safety of a plant protection product to the main cultivars of the main crops for which it is recommended must be demonstrated, including effects of crop growth stage, vigour, and other factors which may influence susceptibility to damage or injury.

The extent of investigation necessary on other crops will depend on their degree of similarity to the main crops already tested, the quantity and quality of data available on those main crops and how far the manner of use of the plant protection product, if relevant, is similar. It is generally sufficient to perform the test with the main formulation type to be authorised.

Where proposed label claims include recommendations for the use of the plant protection product with other plant protection product(s), the previous paragraphs apply for the mixture.

Test guideline

Observations concerning phytotoxicity must be performed in the tests provided for in point 6.2.

Where phytotoxic effects are seen, they must be accurately assessed and recorded in accordance with EPPO guideline 135 or when a Member State requires so and when the test is carried out on the territory of this Member State, with guidelines satisfying at least the requirements of this EPPO guideline.

A statistical analysis of results amenable to such analysis must be carried out, where necessary the test guideline used must be adapted to enable such analysis.

6.6. Observations on undesirable or unintended side-effects, e. g. on beneficial and other non-target organisms, on succeeding crops, other plants or parts of treated plants used for propagating purposes (e. g. seeds, cuttings, runners)

6.6.1. Impact on succeeding crops

Aim of the information required

Sufficient data must be reported to permit an evaluation of possible adverse effects of a treatment with the plant protection product on succeeding crops.

Circumstances in which required

Where data, generated in accordance with point 9.1, shows that significant residues of the active substance, its metabolites or degradation products, which have or may have biological activity on succeeding crops, remain in soil or in plant materials, such as straw or organic material up to sowing or planting time of possible succeeding crops, observations must be submitted on effects on the normal range of succeeding crops.

6.6.2. Impact on other plants, including adjacent crops

Aim of the information required

Sufficient data must be reported to permit an evaluation of possible adverse effects of a treatment with the plant protection product on other plants, including adjacent crops.

Circumstances in which required

Observations must be submitted on adverse effects on other plants, including the normal range of adjacent crops, when there are indications that the plant protection product could affect these plants via vapour drift.

6.6.3. Impact on treated plants or plant products to be used for propagation

Aim of the information required

Sufficient data must be reported to permit an evaluation of possible adverse effects of a treatment with the plant protection product on plants or plant products to be used for propagation.

Circumstances in which required

Observations must be submitted on the impact of plant protection products on plant parts used for propagation except where the proposed uses preclude use on crops intended for production of seeds, cuttings, runners or tubers for planting, as appropriate.

(i) for seeds — viability, germination and vigour;

(ii) for cuttings — rooting and growth rates;

(iii) for runners — establishment and growth rates;

(iv) for tubers — sprouting and normal growth.

Test guideline

Seeds testing shall be done in accordance with ISTA Methods.

6.6.4. Effects on beneficial and other non-target organisms

Any effects, positive or negative, on the incidence of other harmful organisms, observed in the tests performed in accordance with the requirements of this Section, shall be reported. Any observed environmental effects must also be reported, especially effects on wildlife and/or beneficial organisms.

6.7. Summary and evaluation of data presented under 6.1 to 6.6

A summary of all data and information provided under points 6.1 to 6.6 must be provided, together with a detailed and a critical assessment of the data, with particular reference to the benefits that the plant protection product offers, adverse effects that do or may arise and measures necessary to avoid or minimise adverse effects.

7. EFFECTS ON HUMAN HEALTH

For proper evaluation of the toxicity including potential for pathogenicity and infectiveness of preparations sufficient information shall be available on acute toxicity, irritation and sensitisation of the micro-organism. If possible, additional information on mode of toxic action, toxicological profile and all other known toxicological aspects of the micro-organism shall be submitted. Special attention shall be given to co-formulants.

While performing toxicology studies, all signs of infection or pathogenicity shall be noted. Toxicology studies shall include clearance studies.

In the context of the influence that impurities and other components can have on toxicological behaviour, it is essential that for each study submitted, a detailed description (specification) of the material used, be provided. Tests must be conducted using the plant protection product to be authorised. In particular, it must be clear that the micro-organism used in the preparation, and the conditions of culturing it, are the same for which information and data are submitted in the context of Part B of the Annex to Regulation (EU) No 283/2013.

A tiered testing system will be applied to the study of the plant protection product.

7.1. Basic acute toxicity studies

The studies, data and information to be provided and evaluated, must be sufficient to permit the identification of effects following a single exposure to the plant protection product, and in particular to establish, or indicate:

- the toxicity of the plant protection product,
- toxicity of the plant protection product relative to the micro-organism,
- the time course and characteristics of the effect with full details of behavioural changes and possible gross pathological findings at post-mortem,
- where possible the mode of toxic action, and
- the relative hazard associated with the different routes of exposure.

While the emphasis must be on estimating the toxicity ranges involved, the information generated must also permit the plant protection product to be classified in accordance with Directive 1999/45/EC or Regulation (EC) No 1272/2008. The information generated through acute toxicity testing is of particular value in assessing hazards likely to arise in accident situations.

7.1.1. Acute oral toxicity

Circumstances in which required

An acute oral test shall always be carried only if the applicant cannot justify an alternative approach under Directive 1999/45/EC or Regulation (EC) No 1272/2008, where applicable.

Test method

The test must be carried out in accordance with Method B.1 bis or B.1 tris of Regulation (EC) No 440/2008.

7.1.2. *Acute inhalation toxicity*

Aim of the test

The test will provide the inhalation toxicity to rats of the plant protection product.

Circumstances in which required

The test must be carried out where the plant protection product:

- is used with fogging equipment,
- is an aerosol,
- is a powder containing a significant proportion of particles of diameter < 50 micrometre (> 1 % on a weight basis),
- is to be applied from aircraft in cases where inhalation exposure is relevant,
- is to be applied in a manner which generates a significant proportion of particles or droplets of diameter < 50 micrometre (> 1 % on a weight basis),
- contains a volatile component at greater than 10 %.

Test method

The test must be carried out in accordance with Method B.2 of Regulation (EC) No 440/2008.

7.1.3. *Acute percutaneous toxicity*

Circumstances in which required

An acute percutaneous test shall be conducted only if the applicant cannot justify an alternative approach under Directive 1999/45/EC or Regulation (EC) No 1272/2008, where applicable.

Test method

The test must be carried out in accordance with Method B.3 of Regulation (EC) No 440/2008.

7.2. **Additional acute toxicity studies**

7.2.1. *Skin irritation*

Aim of the test

The test will provide the potential of skin irritancy of the plant protection product including the potential reversibility of the effects observed.

Circumstances in which required

The skin irritancy of the plant protection product must always be determined, except where the co-formulants are not expected to be skin irritant or the micro-organism is shown not to be skin irritant or where it is likely, as indicated in the test guideline, that severe skin effects can be excluded.

Test method

The test must be carried out in accordance with Method B.4 of Regulation (EC) No 440/2008.

7.2.2. *Eye irritation*

Aim of the test

The test will provide the potential for eye irritation of the plant protection product, including the potential reversibility of the effects observed.

Circumstances in which required

The eye irritancy of the plant protection product must be determined, where the co-formulants are suspected to be eye irritant, except where the micro-organism is eye irritant or where it is likely, as indicated in the test guideline, that severe effects on the eyes may be produced.

Test method

The eye irritation must be determined in accordance with Method B.5 of Regulation (EC) No 440/2008.

7.2.3. Skin sensitisation

Aim of the test

The test will provide sufficient information to assess the potential of the plant protection product to provoke skin sensitisation reactions.

Circumstances in which required

The test must be carried out where the co-formulants are suspected to have skin sensitising properties, except where the micro-organism(s) or the co-formulants are known to have skin sensitising properties.

Test method

The tests have to be carried out in accordance with Method B.6 of Regulation (EC) No 440/2008.

7.3. Data on exposure

The risks for those in contact with plant protection products (operators, bystanders, workers), depend on the physical, chemical and toxicological properties of the plant protection product as well as the type of the product (undiluted/diluted), formulation type, and on the route, the degree and duration of exposure. Sufficient information and data must be generated and reported to permit an assessment of the extent of exposure to the plant protection product likely to occur under the proposed conditions of use.

In the cases where there is particular concern on the possibility of dermal absorption based on the information for the micro-organism available in Section 5 of Part B of the Annex to Regulation (EU) No 283/2013, or from the information provided for the preparation in this Section, further dermal absorption data can be necessary.

Results from exposure monitoring during production or use of the product must be submitted.

The abovementioned information and data must provide the basis for the selection of appropriate protective measures including personal protective equipment to be used by operators and workers and to be specified on the label.

7.4. Available toxicological data relating to non-active substances

Where relevant, the following information shall be submitted for each co-formulant:

- (a) the registration number as referred to in Article 20(3) of Regulation (EC) No 1907/2006 ⁽¹⁾,
- (b) the study summaries included in the technical dossier as referred to in Article 10(a)(vi) of Regulation (EC) No 1907/2006, and
- (c) the safety data sheet as referred to in Article 31 of Regulation (EC) No 1907/2006.

All other available information shall be submitted.

7.5. Supplementary studies for combinations of plant protection products

Aim of the test

In certain cases it may be necessary to carry out the studies as referred to under points 7.1 to 7.2.3 for a combination of plant protection products where the product label includes requirements for use of the plant protection product with other plant protection products and/or with adjuvants as a tank mix. Decisions as to the need for supplementary studies must be made on a case-by-case basis, taking into account the results of the acute toxicity studies of the individual plant protection products, the possibility for exposure to the combination of the products concerned and available information or practical experience with the products concerned or similar products.

7.6. Summary and evaluation of health effects

A summary of all data and information provided under paragraphs 7.1 through 7.5, must be submitted, and include a detailed and critical assessment of those data in the context of relevant evaluative and decision-making criteria and guidelines, with particular reference to the risks for man and animals that may or do arise, and the extent, quality and reliability of the database.

⁽¹⁾ OJ L 396, 30.12.2006, p. 1.

8. RESIDUES IN OR ON TREATED PRODUCTS, FOOD AND FEED

The same provisions as detailed in Section 6 of Part B of the Annex to Regulation (EU) No 283/2013, apply; the information required in accordance with this Section has to be provided unless it is possible to extrapolate the residue behaviour of the plant protection product on the basis of the data available for the micro-organism. Special attention shall be paid towards the influence of formulation substances on the residue behaviour of the micro-organism and its metabolites.

9. FATE AND BEHAVIOUR IN THE ENVIRONMENT

The same provisions as detailed in Section 7 of Part B of the Annex to Regulation (EU) No 283/2013 apply; the information required in accordance with this Section has to be provided unless it is possible to extrapolate the fate and behaviour of the plant protection product in the environment on the basis of the data available in Section 7 of Part B of the Annex to Regulation (EU) No 283/2013.

10. EFFECTS ON NON-TARGET ORGANISMS

Introduction

- (i) The information provided, taken together with that for the micro-organism(s), must be sufficient to permit an assessment of the impact on non-target species (flora and fauna), of the plant protection product, when used as proposed. Impact can result from single, prolonged or repeated exposure, and can be reversible, or irreversible.
- (ii) The choice of the appropriate non-target organisms for testing of environmental effects shall be based on the information on the micro-organism, as required in Part B of the Annex to Regulation (EU) No 283/2013, and on the information on the co-formulants and other components, as required by Sections 1 to 9 of this Annex. From such knowledge it would be possible to choose the appropriate test organisms, such as organisms closely related to the target organism.
- (iii) In particular, the information provided for the plant protection product, together with other relevant information, and that provided for the micro-organism, shall be sufficient to:
 - specify the hazard symbols, the indications of danger, and relevant risk and safety phrases or the pictograms, signal words, relevant hazard and precautionary statements, for the protection of the environment, to be mentioned on packaging (containers),
 - permit an evaluation of the short- and long-term risks for non-target species — populations, communities, and processes as appropriate,
 - permit an evaluation whether special precautions are necessary for the protection of non-target species.
- (iv) There is a need to report all potentially adverse effects found during routine investigations of environmental effects and to undertake and report such additional studies which may be necessary to investigate the mechanisms involved and assess the significance of these effects.
- (v) In general, much of the data relating to impact on non-target species, required for authorisation of plant protection products, will have been submitted and evaluated for the approval of the micro-organism(s).
- (vi) Where exposure data are necessary to decide whether a study has to be performed, the data obtained in accordance with Section 9 of Part B of this Annex, shall be used.

For the estimation of exposure of organisms all relevant information on the plant protection product and on the micro-organism must be taken into account. Where relevant the parameters provided for in this Section shall be used. Where it appears from available data that the plant protection product has a stronger effect than the micro-organism, the data on effects on non target organisms of the plant protection product have to be used for the calculation of relevant effect/exposure ratios.
- (vii) In order to facilitate the assessment of the significance of test results obtained, the same strain of each relevant species shall where possible be used in the various specified tests for effects on non target organisms.

10.1. Effects on birds

The same information as provided in point 8.1 of Part B of the Annex to Regulation (EU) No 283/2013 has to be reported where it is not possible to predict the effects of the plant protection product on the basis of the data available for the micro-organism, unless it can be justified that exposure of birds is unlikely to occur.

10.2. Effects on aquatic organisms

The same information as provided in point 8.2 of Part B of the Annex to Regulation (EU) No 283/2013 has to be reported where it is not possible to predict the effects of the plant protection product on the basis of the data available for the micro-organism, unless it can be justified that exposure of aquatic organisms is unlikely to occur.

10.3. Effects on bees

The same information as provided in point 8.3 of Part B of the Annex to Regulation (EU) No 283/2013 has to be reported where it is not possible to predict the effects of the plant protection product on the basis of the data available for the micro-organism, unless it can be justified that exposure of bees is unlikely to occur.

10.4. Effects on arthropods other than bees

The same information as provided in point 8.4 of Part B of the Annex to Regulation (EU) No 283/2013 has to be reported where it is not possible to predict the effects of the plant protection product on the basis of the data available for the micro-organism, unless it can be justified that exposure of arthropods other than bees is unlikely to occur.

10.5. Effects on earthworms

The same information as provided in point 8.5 of Part B of the Annex to Regulation (EU) No 283/2013 has to be reported where it is not possible to predict the effects of the plant protection product on the basis of the data available for the micro-organism, unless it can be justified that exposure of earthworms is unlikely to occur.

10.6. Effects on soil micro-organisms

The same information as provided in point 8.6 Part B of the Annex to Regulation (EU) No 283/2013 has to be reported where it is not possible to predict the effects of the plant protection product on the basis of the data available for the micro-organism, unless it can be justified that exposure of non target soil micro-organisms is unlikely to occur.

10.7. Additional studies

Expert judgement is required to decide whether additional studies are necessary. Such decision will take into consideration the available information in this and other Sections, in particular data on the specificity of the micro-organism, and the expected exposure. Useful information may also be available from the observations carried out in efficacy testing.

Special attention shall be given to possible effects on naturally occurring and deliberately released organisms of importance in IPM. In particular the compatibility of the product with IPM shall be taken into consideration.

Additional studies might include further studies on additional species or higher tier studies such as studies on selected non-target organisms.

Before performing such studies, the applicant shall seek agreement of the competent authorities on the type of study to be performed.

11. SUMMARY AND EVALUATION OF ENVIRONMENTAL IMPACT

A summary and evaluation of all data relevant to the environmental impact shall be carried out in accordance with the guidance given by the competent authorities of the Member States concerning the format of such summaries and evaluations. It shall include a detailed and critical assessment of those data in the context of relevant evaluative and decision making criteria and guidelines, with particular reference to the risks for the environment and non-target species that may or do arise, and the extent, quality and reliability of the database. In particular the following issues shall be addressed:

- prediction of distribution and fate in the environment, and the time courses involved,
 - identification of non-target species and populations at risk, and prediction of the extent of potential exposure,
 - identification of precautions necessary to avoid or minimise contamination of the environment, and for the protection of non-target species.
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